United States Department of State

Washington, D.C. 20520

April 29, 2016

Case No. F-2015-06322
Segment: IPS-02, IPS-04, IPS-05

Mr. William F. Marshall
425 Third Street SW, Suite 800
Washington, DC 20024

Dear Mr. Marshall:

I refer to our letter dated March 31, 2016, regarding the release of certain Department of State material under the Freedom of Information Act (the "FOIA"), 5 U.S.C. §552.

Our review is ongoing and we have determined that 20 additional documents may be released in full and 84 may be released with excisions. All released material is enclosed.

An enclosure explains the FOIA exemptions and other grounds for withholding material. Where we have made excisions, the applicable exemptions are marked on each document. All non-exempt material that is reasonably segregable from the exempt material has been released.

We will keep you informed as your case progresses. If you have any questions, your attorney may contact Trial Attorney, Caroline Anderson, at (202) 305-8645 or Caroline.J.Anderson@usdoj.gov. Please refer to the case number shown above in all correspondence about this case.

Sincerely,

Susan C. Weetman for

Eric F. Stein, Acting Co-Director
Office of Information Programs and Services

Enclosures: As stated.

The Freedom of Information Act (5 USC 552)

FOIA Exemptions

(b)(1) Withholding specifically authorized under an Executive Order in the interest of national defense or foreign policy, and properly classified. E.O. 12958, as amended, includes the following classification categories:

- 1.4(a) Military plans, systems, or operations
- 1.4(b) Foreign government information
- 1.4(c) Intelligence activities, sources or methods, or cryptology
- 1.4(d) Foreign relations or foreign activities of the US, including confidential sources
- 1.4(e) Scientific, technological, or economic matters relating to national security, including defense against transnational terrorism
- 1.4(f) U.S. Government programs for safeguarding nuclear materials or facilities
- 1.4(g) Vulnerabilities or capabilities of systems, installations, infrastructures, projects, plans, or protection services relating to US national security, including defense against transnational terrorism
- 1.4(h) Information on weapons of mass destruction

(b)(2) Related solely to the internal personnel rules and practices of an agency

(b)(3) Specifically exempted from disclosure by statute (other than 5 USC 552), for example:

ARMEX	Arms Export Control Act, 22 USC 2778(e)
CIA	Central Intelligence Agency Act of 1949, 50 USC 403(g)
EXPORT	Export Administration Act of 1979, 50 App. USC 2411(c)(1)
FSA	Foreign Service Act of 1980, 22 USC 4003 & 4004
INA	Immigration and Nationality Act, 8 USC 1202(f)
IRAN	Iran Claims Settlement Act, Sec 505, 50 USC 1701, note

(b)(4) Privileged/confidential trade secrets, commercial or financial information from a person

(b)(5) Interagency or intra-agency communications forming part of the deliberative process, attorney-client privilege, or attorney work product

(b)(6) Information that would constitute a clearly unwarranted invasion of personal privacy

(b)(7) Information compiled for law enforcement purposes that would:

- (A) interfere with enforcement proceedings
- (B) deprive a person of a fair trial
- (C) constitute an unwarranted invasion of personal privacy
- (D) disclose confidential sources
- (E) disclose investigation techniques
- (F) endanger life or physical safety of an individual

(b)(8) Prepared by or for a government agency regulating or supervising financial institutions

(b)(9) Geological and geophysical information and data, including maps, concerning wells

Other Grounds for Withholding

NR Material not responsive to a FOIA request, excised with the agreement of the requester

From: hr15@att.blackberry.net
Sent: Thursday, January 22, 2009 9:20 PM
To: Miguel Rodriguez <miguel_rodriguez@clinton.senate.gov>
Subject: Re: Ledbetter

RELEASE IN FULL

Yeah! Well, that's only right
------Original Message------
From: Miguel Rodriguez
To: Hillary Clinton
Sent: Jan 22, 2009 6:58 PM
Subject: Ledbetter

I know you have a new portfolio, but I thought you'd be interested to know that the Ledbetter bill just passed the Senate by a vote of 61-37 The House will pass the bill next week, likely permitting the President sign it into law shortly thereafter.

Congratulations on a great first day

From: H <hdr22@clintonemail.com> **RELEASE IN FULL**
Sent: Friday, January 30, 2009 5:06 AM
To: Huma Abedin <HAbedin@hillaryclinton com>
Subject: Fw: Washington Post article on Administration's Iran policy

Pls print.

From: "Mills, Cheryl D"
Date: Fri, 30 Jan 2009 04:38:14 -0500
To: <hdr22@clintonemail com>
Subject. Fw: Washington Post article on Administration's Iran policy

Fyi

From: LaVine, Christopher M
To: NEWS-Mahogany
Cc: NEWS-NEA; SES-O; Knopf, Payton L; Hale, David M; NEWS-Iran
Sent: Thu Jan 29 22:50:25 2009
Subject: Washington Post article on Administration's Iran policy

Colleagues,

Ops thought you might be interested in this WPost article on the Administration's Iran policy. Thank you,

Regards,

Chris LaVine

Operations Center

Writings Offer Look at Administration Debate on Iran

By Glenn Kessler

Washington Post Staff Writer

Friday, January 30, 2009; A12

President Obama and Secretary of State Hillary Rodham Clinton in the past week have sent repeated signals to Iran that the door is now wide open for direct talks between the two countries three decades after the Iranian revolution, but U.S. officials say the method, the pace and the tenor of that diplomacy still remain to be settled.

But while officials say a plan will not be in place for several months, key players in the discussions have outlined their views in papers they wrote before joining the administration, giving a unique window into the administration's debate.

Obama, during a private discussion with Jewish leaders a year ago, also provided a road map to his thinking.

HA 09/01/2015

"The time, I believe, has come to talk directly to the Iranians and to lay out our clear terms: their end of pursuit of nuclear weapons, an end of their support of terrorism and an end of their threat to Israel and other countries in the region," Obama said, according to a transcript. Bigger "carrots," he said, will give the United States more leverage to win support for sanctions if Iran rebuffs the approach.

One complicating factor is that Iran will hold a presidential election in June. American officials want to avoid taking steps that might bolster the stature of the current president, Mahmoud Ahmadinejad, whose anti-Semitic rants and hostile attitude toward the West make him a potentially difficult interlocutor for diplomatic outreach.

Another complicating factor is that the United States and five other powers have demanded that Iran suspend its uranium enrichment program before substantive talks can begin on its nuclear program. Any sudden change in that approach may alarm allies.

Finally, the government in Iran is so opaque that officials want to be sure they are communicating with the right power centers. "It is unclear who exactly that dialogue would be with in Iran," White House spokesman Robert Gibbs said yesterday.

Dennis Ross, the former Middle East envoy who will be Clinton's senior adviser on Iran, has recommended that the initial approach to Iran take place through a "direct, secret back channel," which would be one way to avoid empowering Ahmadinejad or publicly undercutting the ongoing nuclear negotiations.

"Keeping it completely private would protect each side from premature exposure and would not require either side to publicly explain such a move before it was ready," Ross wrote in a lengthy paper, titled "Diplomatic Strategies for Dealing With Iran," published by the Center for a New American Security in September. "It would strike the Iranians as more significant and dramatic than either working through the Europeans or non-officials -- something that is quite familiar."

Ross said the United States should ask the Iranian representative during the private talks to explain how his government sees U.S. goals toward Iran and how Iran thinks the United States perceives Iranian goals. The purpose of this dialogue, he wrote, is to "find a way to show the Iranians that we are prepared to listen and to try to understand Iranian concerns and respond to them, but ultimately no progress can be made if our concerns cannot also be understood and addressed."

Ross conceded that it may be difficult "to set up such a direct channel that is also authoritative," because in the Iranian system, the president has much less power than the supreme leader, Ayatollah Ali Khamenei.

Another top Obama adviser, Gary Samore of the Council on Foreign Relations, argued for a more public approach, without requiring Iran to suspend its enrichment activities: direct bilateral talks, preferably with a representative of the supreme leader, that would cover a range of issues, including the nuclear program, U.S.-Iranian relations, Iraq and the Israeli-Palestinian peace process. Samore, who will be the top nonproliferation official at the White House National Security Council, co-authored with Bruce Riedel of the Brookings Institution a paper published last month that outlined this concept.

The Bush administration had some secret contacts with Iranian officials before the Iraq war and held ambassador-to-ambassador meetings in Iraq and Afghanistan. But it never attempted a broad dialogue, despite an apparent effort by some Iranian officials to reach out after Iraqi leader Saddam Hussein was toppled in 2003. Samore recommended that the administration proceed "cautiously" and develop its negotiating strategy through "high-level bilateral and multilateral consultations" with the governments

seeking to negotiate with Iran -- Britain, France, Germany, Russia and China -- and with Middle Eastern allies.

It was important, Samore said, that the United States not be seen as abandoning the larger framework for nuclear talks; in fact, "opening a bilateral channel with Iran may help invigorate the multilateral process."

A top State Department official, Undersecretary William J. Burns, will begin such consultations when he meets with representatives to the Iran negotiating group in Europe next week. A senior European diplomat said yesterday that European leaders would welcome a U.S-Iranian dialogue but that it must be handled carefully. "The possibility of a dialogue with the U.S. is a very important card in our game" with Iran, he said. "We don't have many cards left."

A more provocative approach was advocated by John Brennan, Obama's White House director for counterterrorism, in a paper published in July. Brennan pressed for toning down rhetorical jabs at Iran and ignoring anti-American comments from Iranian officials, and also stressed the need for a presidential envoy to handle negotiations with Iran. In order to smooth the path for dialogue, he also argued for the "political courage" to admit that Iran has significantly scaled back its use of terrorism in the past decade. "It would not be foolhardy" to encourage greater assimilation of Hezbollah -- the armed political movement backed by Syria and Iran -- in the Lebanese political system, even though Washington officially considers Hezbollah a terrorist organization, Brennan wrote.

Another important policymaker, Defense Secretary Robert M. Gates, pressed for a carefully focused dialogue when he co-led a Council on Foreign Relations task force on Iran in 2004. "A 'grand bargain' that would settle comprehensively the outstanding conflicts between Iran and the United States is not realistic," the task force concluded. Instead, the United States should selectively engage Iran on issues where the U.S. and Iranian interests converge and build on incremental progress.

Gates, a holdover from the Bush administration, felt it was important such discussions begin before the nuclear concerns were resolved -- a position that puts him firmly in sync with Obama's approach.

From: Prameela Bartholomeusz [redacted] B6
Sent: Thursday, January 22, 2009 3:33 AM
To: hr15@att.blackberry.net
Cc: prameelarb [redacted] B6
Subject: Congratulations, Madam Secretary!

RELEASE IN PART B6

Madam Secretary,

Congratulations and thank you! Many of us are truly grateful and relieved to know you will be such an integral part of American foreign policy going forward, And having read your books, volunteered in six states for your campaign and watched the confirmation hearings as well as your farewell speech, I know we can count on so much more.

I wanted to reach out to you for a few other reasons:

1) Please thank Chelsea for me, whom I met for the first time in person in Austin, TX at the after debate party (where I also met you for the first time). She listened to some ideas and requested I contact her chief of staff, Barie Lurie, so they could follow through and Chelsea followed through! With this contact, I was referred to Maggie Williams, Amee Patel and Capricia Marshall and was able to really make a positive impact in Austin & Houston (where I was for three weeks as a volunteer for the campaign). Chelsea, thank you for hearing me. I believe this is one of the reasons I was selected to be on hte Platform Committee. You are amazing and I think you should run for a House or Senate seat some day (soon).

2) Just following the below email is an article referring to a Commission for Change, President Obama indicated last August he would support. It was the response to the controversies raised once again at the Platform Committee. I was the committee member that asked on the call with you the night before the meeting, whether I could raise the caucus issue I did that as well as submitted the amendment regarding the primary calendar. As I know you agree, voter rights are sacred. I spoke with Jeff Berman regarding being a member of the commission. He suggested I contact my state party (CA). Chris Jennings, Ann O'Leary (met in Pittsburgh at Platform Committee) and Craig Smith (met at Rules Committee meeting in Denver) are all aware of my fight for amendments affecting voter rights. Anything you can do to verify my sincerity with Chris & Craig and recommend me to Sen Feinstein and Sen Boxer for this commission would be tremendous. You have my word that I will not look back with regard to these voter rights issues, but will look forward. (Lady Lynn de Rothschild knows me as well and I am sorry to say that I supported the McCain/Palin ticket in the final weeks-I truly believed Sen McCain was more likely to include you in his cabinet).

3) I joined The New Agenda as a founding member, a non-partisan group advocating women's rights http://thenewagenda.net/ . There is much work to be done! I will remain devoted to this cause through this organization as long as it remains non-partisan and maintains the level of professionalism that such an organization warrants. Would like to see more women in government and would like to address domestic violence [redacted] We hope you will on occasion share your wisdom with us and make us aware of what more we can be doing. B6

I hope you will respond to me through Capricia like you had done once before regarding the Commission for Change. Or maybe through Chris or Craig.

BTW, I would like to be on your campaign staff for the 2016 election!

God's speed and a tight hug,
Prameela Bartholomeusz
DNC Platform Committee Member
[redacted] B6

---------- Forwarded message ----------
From: **Prameela Bartholomeusz** [redacted] B6
Date: Sun, Nov 16, 2008 at 10:46 PM
Subject: Please accept SOS!
To: "hr15@att.blackberry.net" <hr15@att.blackberry.net>

Dear Senator Clinton,

We pray you accept! The success of the Obama Administration is dependent on the team it is comprised of at the highest levels. You are an important part of the better future for America (sorry to place so much on your shoulders). We know how passionate you are about healthcare reform, addressing the economic crisis, education, women's rights and related legislation. As SOS, you will have the stage you need to be successful. You can do it all...you're Hillary Clinton! And I mean that with respect, confidence and sincerity. Our thoughts and prayers are with you.

Best,
Prameela Bartholomeusz
DNC Platform Committee Member for HRC
(with pride)

Obama responds with proposal for 2012 reform commission

Barak Obama has called for rule changes to be worked out for the 2012 primary/caucus season and to push back the start date. The timing of the announcement, coming just one week before the GOP convention takes up its own reform proposal, is clearly meant to encourage the Republicans to take action and for new bi-partisan cooperation on this most complex issue.

The Washington Post:

Obama Team Seeks Changes in Primaries

By Dan Balz
Washington Post Staff Writer
Thursday, August 21, 2008; A03

Sen. Barack Obama's presidential campaign will call next week for the creation of a commission to revise the rules for selecting a presidential nominee in 2012, with a goal of reducing the power of superdelegates, whose role became a major point of contention during the long battle for the Democratic nomination between Obama and Sen. Hillary Rodham Clinton.

The commission also will be urged to redraw the nominating calendar for 2012 to avoid starting the primaries and caucuses so early, and also to look specifically at ensuring more uniform rules and standards for those caucuses.

Obama campaign manager David Plouffe said the campaign will ask delegates at the national convention in Denver to approve a resolution approving the establishment of a 35-member Democratic Change Commission. The charter would authorize the Democratic National Committee chairman to appoint the commission soon after the election and ask it to report back by January 2010.

The proposed changes grew out of discussions between Obama's campaign, officials at the Democratic National Committee and representatives from Clinton's campaign, Plouffe said.

The most important change involves superdelegates -- the elected officials and party leaders who have automatic seats at national conventions and are free to vote for any candidate of their choice.

Their role became hugely controversial during the long battle between Obama and Clinton. Obama supporters feared that the superdelegates could override the results of the primaries and caucuses and hand Clinton the nomination.

"The number of superdelegates has gotten too large in relation to overall delegates," Plouffe said. "We want to give more control back to the voters. . . . Everyone thinks there ought to be more weight given to the results of the elections."

The commission will be encouraged to consider either reducing the number of superdelegates eligible to attend the national conventions or increasing the number of pledged delegates -- those elected on the basis of caucus and primary results.

The other significant change is the call to redraw the primary and caucus calendar. The 2008 calendar received significant criticism both for the early starting dates for the Iowa caucuses and New Hampshire primary and also because so many states were crowded into the first month of what turned out to be a five-month battle.

Under the system envisioned by the Obama and Clinton campaigns, most contests could not be held before March, except for those in a handful of states authorized to go earlier -- presumably in February rather than January

Plouffe also said the commission will be urged to look for ways to avoid the bunching of states on particular days. Almost two dozen states held Democratic contests on Super Tuesday, Feb. 5, and party officials hope to avoid a repeat in 2012.

The other major area the commission will be asked to examine is the operation of caucuses in states that choose that process rather than a primary. The caucuses drew criticism, particularly from the Clinton campaign, which said that they restricted participation and that in some states they lacked the necessary infrastructure to ensure fairness.

"We agree that we ought to make sure they're funded properly, staffed properly and run smoothly, and even see if people ought to be eligible to vote absentee," Plouffe said.

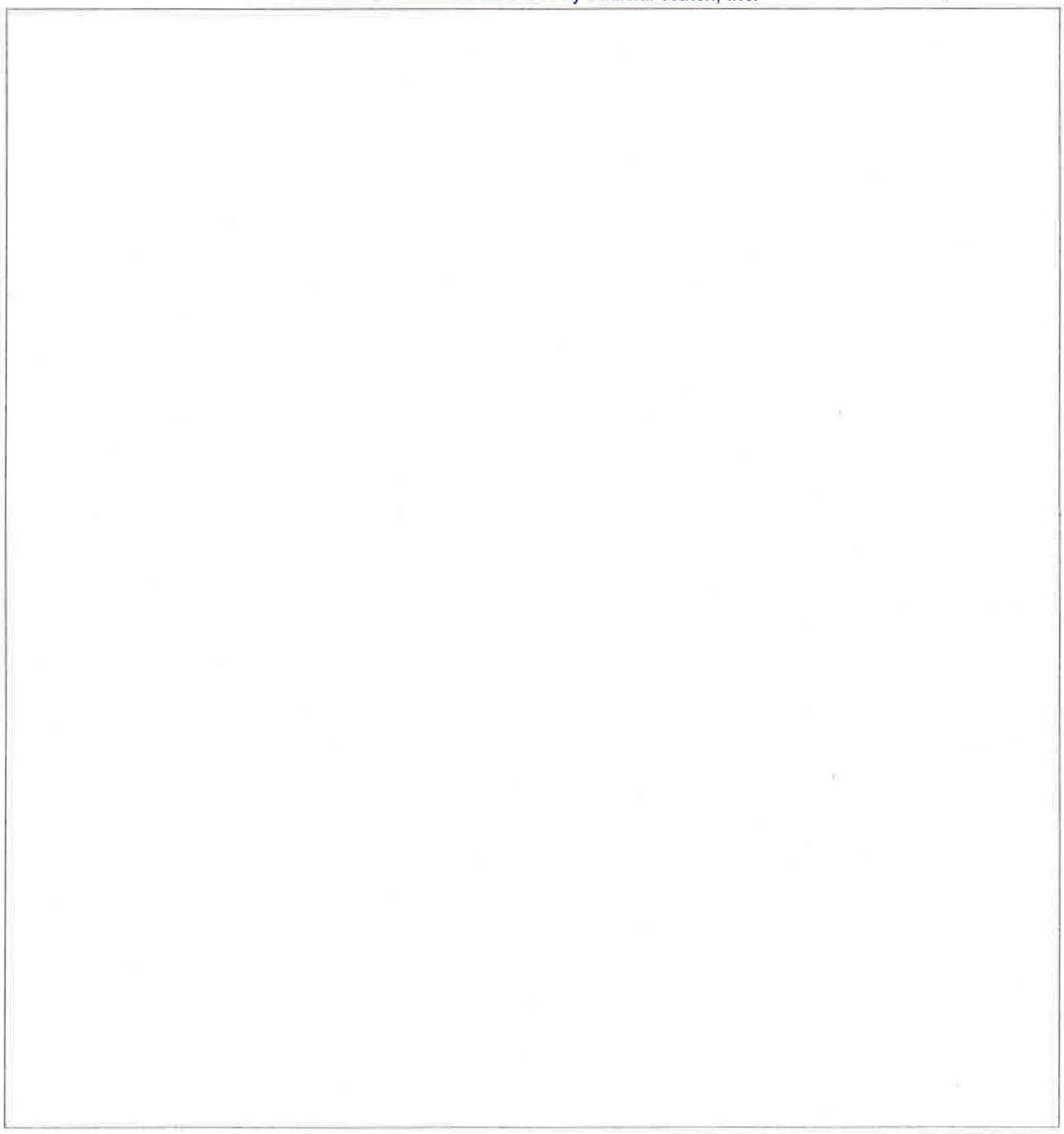
Link to article.

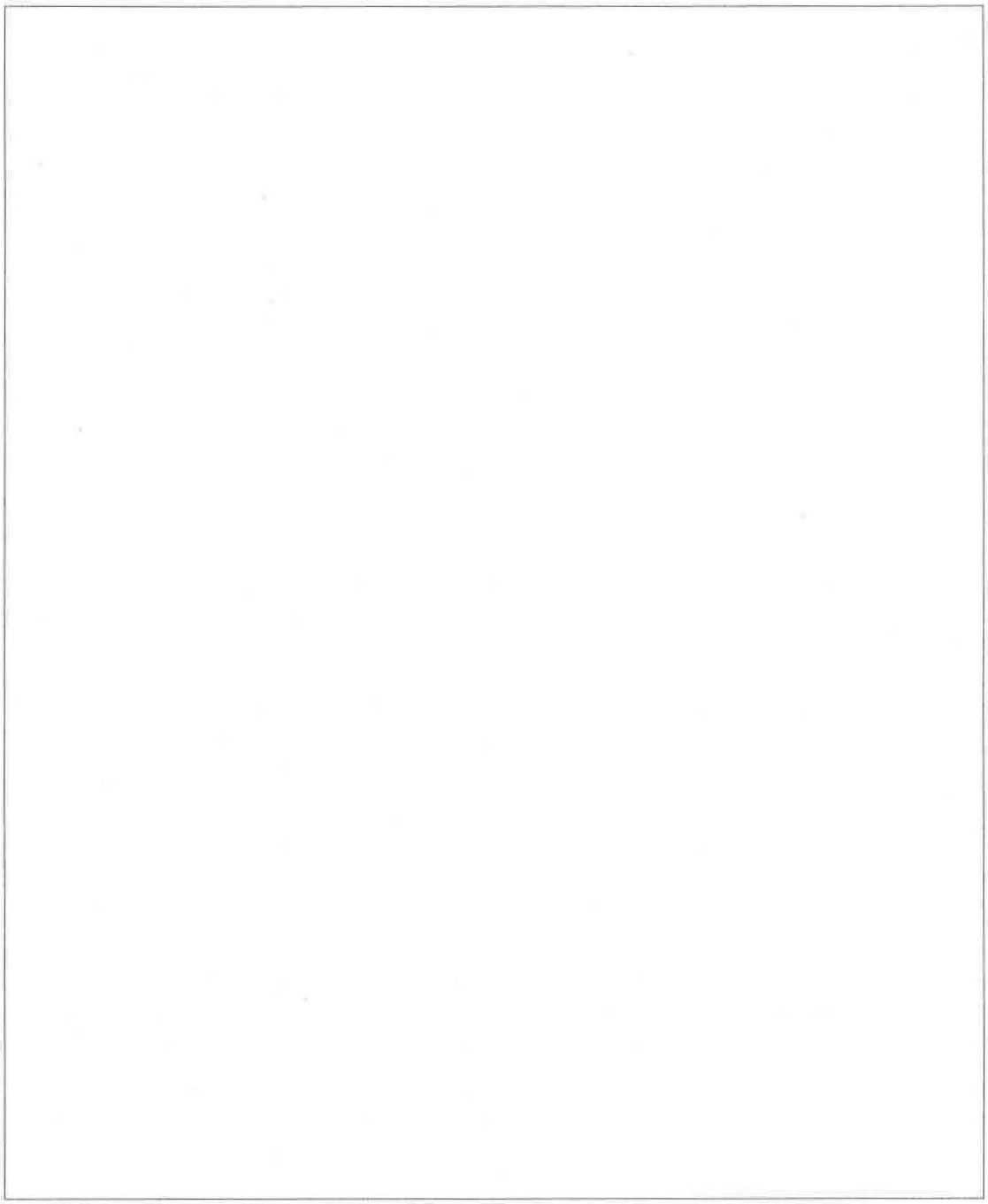
Submitted on August 21, 2008 - 8:24pm.

RELEASE IN PART B5

Statement by Senator George J. Mitchell
Washington, DC
January 22, 2009

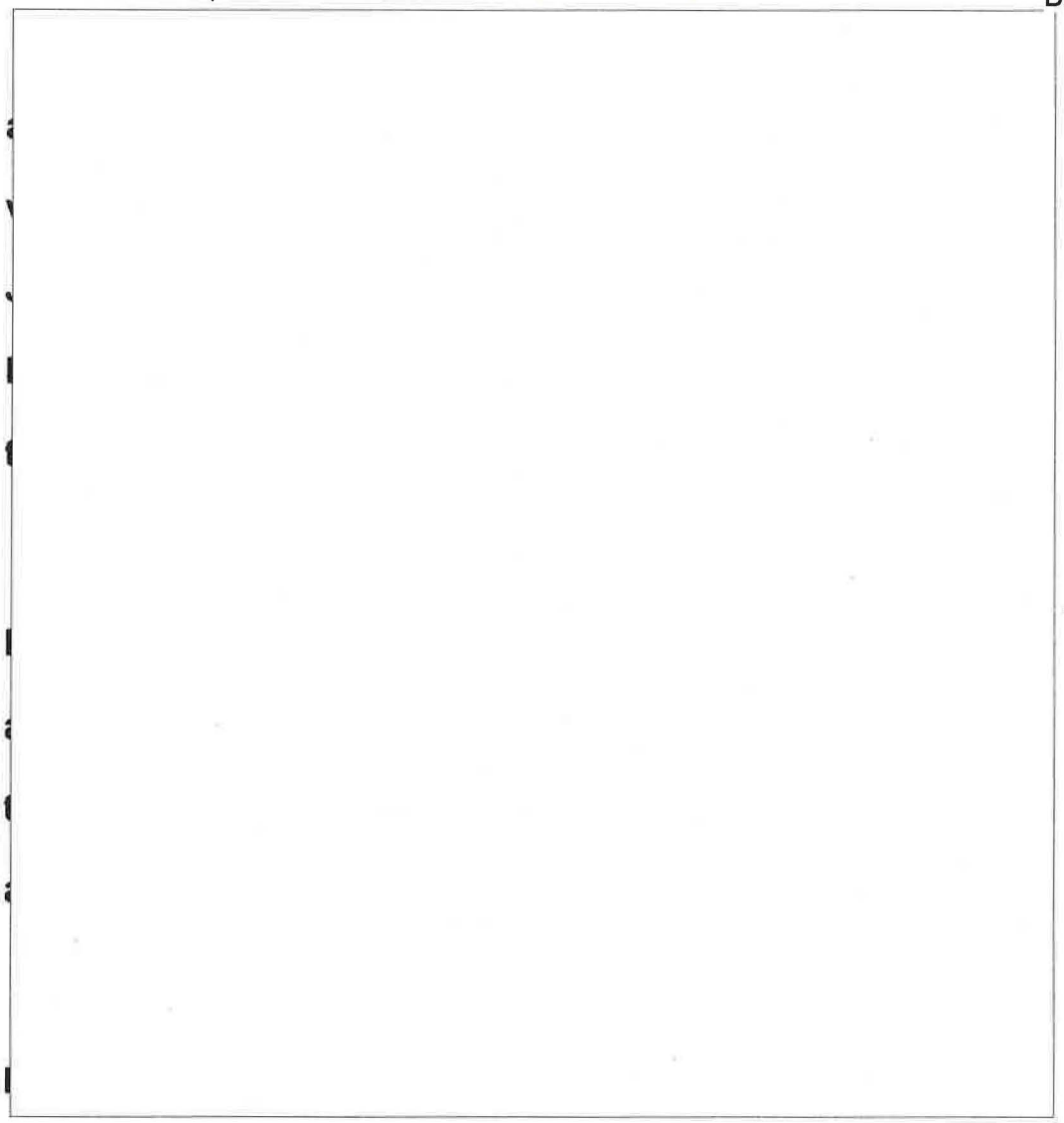
B5





B5

B5



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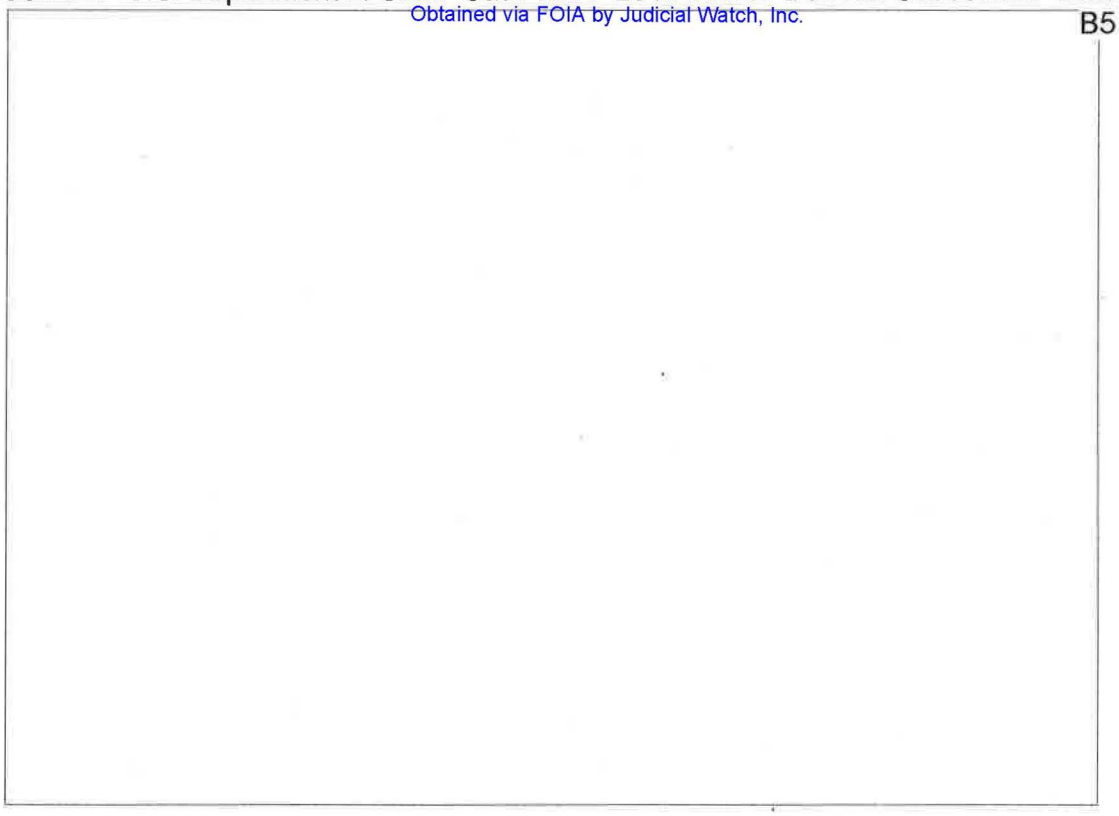


From: Huma Abedin [redacted]
Sent: Thursday, January 22, 2009 8:39 AM
To: humamabedin [redacted]
Subject: PrintFw: Envoy announcement 8am version
Attach: Envoys Announcement 1 22.09 LM 8 am.doc

B6

RELEASE IN PART B6

-----Original Message-----
From: Baer Daniel [redacted]
To: Huma Abedin
CC: Lissa Muscatine [redacted]
Sent: Thu Jan 22 08:08:52 2009
Subject: Envoy announcement 8am version

<<Envoys Announcement 1 22.09 LM 8 am.doc>>.

Draft
8 am

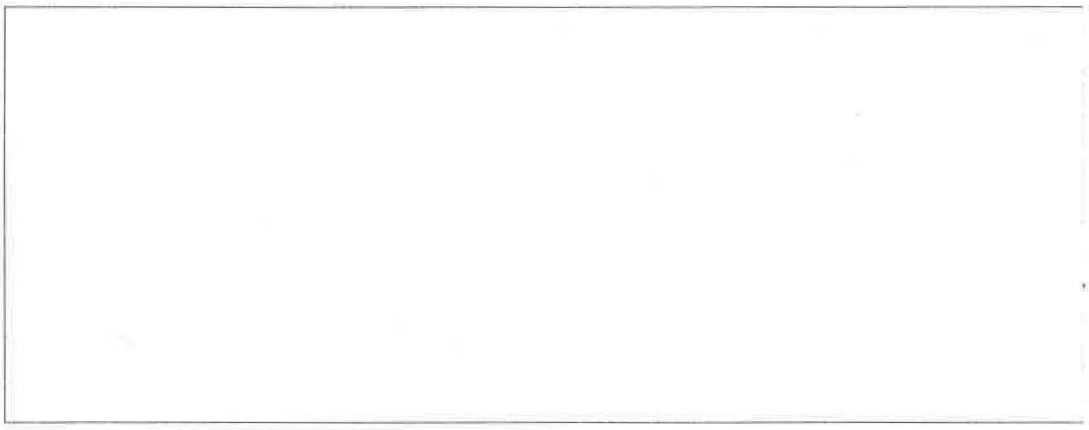
RELEASE IN PART B5

SECRETARY OF STATE HILLARY RODHAM CLINTON
ANNOUNCEMENT OF SPECIAL ENVOYS
THE DEPARTMENT OF STATE
WASHINGTON, DC
JANUARY 22, 2009

B5

[redacted]

HA 09/01/2015



From: hr15@att.blackberry.net
Sent: Thursday, January 22, 2009 9:18 PM
To: Roy Spence
Subject: Re: Madame-Well done today-It seems they are so jazzed you are there! So is America and the world!

RELEASE IN PART
B6

B6

Well, so far so good, Bro. Now what do I do for an encore?

From: Roy Spence
Date: Thu, 22 Jan 2009 18:17:38 -0600
To: hr15@att.blackberry.net<hr15@att.blackberry.net>
Subject: Madame-Well done today-It seems they are so jazzed you are there! So is America and the world!

"Secretary of State Hillary Clinton received a rousing welcome this morning when she arrived at Foggy Bottom for the first time, as cheering foreign service and civil service employees packed every inch of the C Street lobby, including the balcony overlooking the flags of foreign nations."...

From: hrl5@att.blackberry net
Sent: Thursday, January 22, 2009 9:19 PM
To: Jake Sullivan [redacted] B6
Subject: Re So much for being careful about China and currency!

RELEASE IN PART
B6

Say what??? I just hope they keep buying our debt!! Thanks for all your help in getting us off to a good start

From: Jake Sullivan
Date Thu, 22 Jan 2009 19 12.05 -0500
To. hrl5@att.blackberry net<hrl5@att.blackberry.net>
Subject: So much for being careful about China and currency!

Geithner Says China Is Manipulating Its Currency

By JACKIE CALMES and DAVID STOUT
Published January 22, 2009

From: Cheryl Mills [redacted] B6
Sent: Thursday, January 22, 2009 9:22 PM
To: Kiki McLean [redacted] Philippe Reines1 [redacted] Caroline Adler <cadler [redacted]; Lona Valmoro <lona_valmoro@clinton senate.gov>; Robert Wood <WoodRA@state.gov>
Cc: Huma Abedin [redacted]
Subject: RE: Couple of things

RELEASE IN PART B6

agree – next week but early – Monday or Tuesday on press folks

From: Kiki McLean [mailto: [redacted]
Sent: Thursday, January 22, 2009 7:57 PM
To: Philippe Reines1; Caroline Adler; Lona Valmoro; Cheryl Mills; Robert Wood
Cc: Huma Abedin
Subject: Re: Couple of things

Ageee

From: "Philippe"
Date: Thu, 22 Jan 2009 23:57:38 +0000
To: Caroline Adler [redacted]; Lona Valmoro<lona_valmoro@clinton.senate.gov>; Cheryl Mills [redacted]; Robert Wood<WoodRA@state.gov>
Subject: Re: Couple of things
I'd let USAID event and images do the talking tomorrow, she can stop by the briefing room next week - armed with some specific newsmaking announcement, rather than just taking questions (if she goes to the room, she has to take Qs)

If HRC agrees to next week, Robert could tell them tomorrow so they feel touched

From: "Caroline Adler"
Date: Thu, 22 Jan 2009 18:39:14 -0500
To: <Lona_Valmoro@clinton.senate.gov>; Cheryl Mills [redacted]
Subject: Couple of things

Hi all -

There are a couple of things that just came up in a conversation with Robert and I wanted to quickly ask you about them:

--Robert thinks it would be good for HRC to stop by the press briefing tomorrow, and if not tomorrow sometime next week. He said the press covered today's events, but it would go very far for hrc to spend even 10 minutes just with them. She could deliver remarks (3-5min) and then take 1-2 questions. The press will normally be briefed at 11am, but Robert says this can be at any time HRC is free.

--The other seems less time sensitve. Apparently the podium in the briefing room is very high tech and the technicians can create a podium/lighting scheme specific to HRC. Robert was wondering if - when HRC has 15 minutes in the next few weeks - she could go to the briefing room and have the settings configured for her.

Thanks!
Caroline

From: hr15@att.blackberry.net
Sent: Thursday, January 22, 2009 9:23 PM
To: Cheryl Mills
Subject: Re: susan rice was confirmed tonight so should likely send her note or call for congrats

B6

RELEASE IN PART B6

What about Jack and Jim?
------Original Message------
From: Cheryl Mills
To: Huma Abedin
Cc: Hillary Clinton
Sent: Jan 22, 2009 9:14 PM
Subject: susan rice was confirmed tonight so should likely send her note or call for congrats

From: hr15@att.blackberry net
Sent: Thursday, January 22, 2009 9:24 PM
To: Lona Valmoro <lona_valmoro@clinton.senate gov>, Huma Abedin <Huma_Abedin@clinton.senate.gov>
Subject: Schedule

RELEASE IN PART B5,B6

Since we couldn't do the scheduling today, I wanted to send you the following info for your followup:

B6

In no particular order-

[redacted] His # is [redacted] Pls call to explore whether that's possible

B5

Pls keep track of Congressional recesses so we know when they occur for purposes of planning.

For the potential to-do list:

[redacted]

B5

[redacted]

B5

More to come when we meet

HA 09/01/2015

From: Abedin, Huma <AbedinH@state gov>
Sent: Friday, January 30, 2009 6:53 AM
To: humamabedin[redacted]
Subject: Fw: Morning Press Briefing and Clips
Attach: 013009 Press Briefing doc; 013009 Press Clips doc

RELEASE IN PART B6

B6

From: Bishop, Christopher W
To: Abedin, Huma
Cc: Macmanus, Joseph E; S_SpecialAssistants; Sullivan, Jacob J
Sent: Fri Jan 30 06:45:28 2009
Subject: Morning Press Briefing and Clips

Good Morning Huma—please let us know if you need anything else.

Christopher

Christopher W. Bishop
Special Assistant to the Secretary of State
202-647-9573

From: Burns Strider [redacted] B6 RELEASE IN PART B6
Sent: Wednesday, February 4, 2009 9:54 PM
To: Clinton Hillary <hdr22@clintonemail.com>
Subject: this is just horrible:

One of your Veterans, Colonel Hal Donahue, wrote this for Huffington... he documents it with news clips and DoD links:

A Military Family Treated Shabbily -- a Demand for Accountability

Our fallen warriors' families should NEVER need a United States senator to find out how their loved one died. Yet, one did. Thank you, Senator Bob Casey for stepping in when no one else would to help an anguished mother and her family learn how her son died. Another thank you for exposing the weakness and decay developing in the military.

On January 2, 2008, Sgt. Ryan Maseth, a highly decorated Army ranger and a valuable national resource, stepped into the community shower of his Iraq building Perhaps looking forward to a relaxing shower, young Maseth reached out to turn on the water and died, a victim of electrocution.

According to a CNN Special Investigations Unit story by Abbie Boudreau and Scott Bronstein from attorney statements, when fellow soldiers kicked down the door, they smelled burning hair, and they rushed over, saw Sgt. Maseth lying there unconscious, and one of the rescuers himself was shocked electrically and sustained a fairly good jolt because the water and the pipes were still electrified. The next day, Cheryl Harris, a mother with three sons serving in Iraq, was informed of his death.. She had feared such news might come one day. An article shortly after his death demonstrates clearly both the anguish of Sergant Maseth's family and a bit about the man.

"I did ask exactly, 'How did Ryan die? What happened to him?' And he had told me that Ryan was electrocuted," Ms Harris said. That was not the full story and after misleading statements, a US Senator, Robert Casey, D PA, was needed to uncover the complete answer to that question. What developed was a story of military officers betraying their troops; DOD civilians protecting private contractors rather than soldiers and very likely negligent homicide.

Now, I know the public has visions of soldiers dying "taking the hill" or "sweeping the skies in sleek fighters" but reality can be so horribly different, mundane even. Roads, of necessity, swept too quickly and soldiers die. A soldier on routine patrol takes off their helmet to wipe the sweat from brow and a sniper takes that moment to put a round through the soldier's skull. A soldier uses a latrine at a "safe" base and a stray round takes the soldier's life. These things happen. The US military was the leader in controlling these types of loses. Because, emotional and family feelings aside, the loss of Sgt Maseth hurt US military capability and reduced our ability to fight the Iraq war. This is the real bottom-line. This is one of the major reasons why we have Red Flag and Top Gun etc; so we can learn to prevent these losses in the confusion of actual war. Things appear to have changed.

According to a *Pittsburgh Tribune-Review* story; "Report: U.S. troops exposed to 231 shock incidents" by Robin Acton,January 29, 2009;

....The 45-page document -- a high-level request for corrective action generated last fall -- found that Texas-based military contractor KBR Inc. failed to properly ground and bond its electrical systems, which contributed to soldiers "receiving shocks in KBR-maintained facilities on average once every three days since data was available in Sept. 2006."

HA 09/01/2015

... The report adds that government search results of a KBR-maintained database revealed that 231 electrical-shock incidents occurred in the period from September 2006 through July 31, 2008 -- indicating that the activity continued long after the death of Sgt. Ryan Maseth, 24, who suffered cardiac arrest after stepping into his Baghdad shower on Jan. 2, 2008.

A January 30, 2009, *Pittsburgh Post-Gazette* editorial, "Death by shower: Punish those who betrayed the troops in Iraq" acknowledges what came next.

.. Subsequently, his parents filed a wrongful death suit in Allegheny County, against Houston-based KBR Inc., alleging that KBR allowed U.S. troops to continue to use electrical systems that it knew to be dangerous. The soldier's mother, Cheryl Harris, also testified to Congress

For his part, Pennsylvania Sen. Bob Casey has been zealous in keeping this issue alive by demanding explanations from the Defense Department. The combined pressure seems to have paid off: The Associated Press reported last week that an Army investigation now deems the soldier's death a "negligent homicide" instead of an accident...

U.S. Senator Robert Casey (D-PA) kept the pressure on The Department of Defense (DoD) to determine that there were at least 18 deaths by electrocution in Iraq and he is working to eliminate the causes and to demand accountability from all involved. For the problem is not just employing unqualified, non government contractors but the integrity of officers and civilians throughout the Army and DoD. U. S. Senator Byron Dorgan (D-SD) said:

I believe DOD has been less than truthful to the families of soldiers who were electrocuted at military bases in Iraq because of shoddy contract work. It's time for some straight talk about accountability.

Last year Senator Dorgan chaired a Senate Democrat Policy Committee hearing into the electrocutions of soldiers in Iraq. Following that hearing, Senators Dorgan and Casey requested that the pentagon conduct a theatre-wide investigation into KBR's electrical work in Iraq. Astonishingly, the Army agreed, then used KBR to do much of the review. The result was continued work for KBR with a request for improved performance.

Now times are changing The same January 30, 2009, *Pittsburgh Post-Gazette* editorial said it better than I ever could:

"Sen. Casey is still pressing for answers -- and anyone who supports the troops should stand with him. He and Democratic Sen. Byron Dorgan of North Dakota, who has held hearings on contracting abuses, are demanding accountability for the death of Sgt. Maseth and others. It is overdue. Praise the heroes and punish those who hurt them."

Not just for just for our fallen but for the safety of our nation. If the military is unable to rely upon the honesty and integrity of its officers and NCO's, then the effectiveness of our military and the safety of our nation are in jeopardy

Burns Strider
Founding Partner
The Eleison Group

www.eleisongroup.com

HA 09/01/2015

From: H <hdr22@clintonemail com>
Sent: Wednesday, February 4, 2009 10:19 PM
To: Cheryl Mills [redacted] B6
Subject: Re: just called you - got vox mail - got about 15 min in me

RELEASE IN PART B6

I'm calling your cell.

From: "Cheryl Mills"
Date: Wed, 4 Feb 2009 22:17:58 -0500
To: <hdr22@clintonemail.com>
Subject: just called you - got vox mail - got about 15 min in me

From: H <hdr22@clintonemail.com>
Sent: Wednesday, February 4, 2009 10:21 PM
To: Cheryl Mills [redacted] B6
Subject: Re: just called you - got vox mail - got about 15 min in me

RELEASE IN PART B6

Your mailbox. Is full--pls call me again.

From: "Cheryl Mills"
Date: Wed, 4 Feb 2009 22:17:58 -0500
To: <hdr22@clintonemail.com>
Subject: just called you - got vox mail - got about 15 min in me

RELEASE IN PART B6

B6

From: Burns Strider
Sent: Thursday, February 5, 2009 4:15 AM
To: Clinton Hillary <hdr22@clintonemail.com>
Subject: Shovel Ready Jobs Needed in Washington

Posted at

Progressive Revival: http://blog.beliefnet.com/progressiverevival/2009/02/shovel-ready-jobs-needed-in-wa.html

And

Faithful Democrats: www.faithfuldemocrats.com

Shovel Ready Jobs Needed in Washington

By: Burns Strider
Thursday February 5, 2009

Cross Posted at www.faithfuldemocrats.com

Pungent piles of Republican nay-saying to the American jobs and stimulus package are getting so deep in Washington that shovel-ready jobs are needed to shovel it all to the dump. Could this be the Republican job creation package?

The rigid ideological orthodoxy leading Republicans to oppose the jobs bill ignores the pain of middle and working Americans. We have seen this approach already and we have suffered its outcome too deeply.

Their answer to the imploding economic situation is much like the answer they had to Katrina - unleash the awesome power of under-funding, inexperience and an unwilling, pervading philosophy that sees no possibility and allows for no creativity.

Consider some of the things they call waste:

- Resources to design and construct a boat for the Coast Guard. How in the world could we allow such? This would create jobs in places like the coasts of Virginia and Mississippi while adding to the ability of the Coast Guard to do their jobs

- Funding for housing the Department of Homeland Security. We can not allow construction jobs be created in order to create space for the agency charged with out safety.

- Money for screening and preventing STD's. What are the Democrats thinking? Health care jobs created while making Americans healthy? What?

- More support for the National Endowment for the Arts Yes, I can see how creating jobs by putting more teachers in the schools to educated and teach our children is a nasty, horrible big government plot.

- Resources for putting computers in community colleges. Well, we certainly can not allow computers to

go to the community college students. People may have to be hired to make those computers and for who? Community college students?

- Funding for flood reduction on the Mississippi River and canal inspection in urban areas. That is a bad idea, folks. Jobs to protect rural Americans along the River and make sure canals are safe running along places such as the Lower 9th Ward in New Orleans is just a bad idea.

Their list of "wasteful spending" is long. I could continue. And, yes, I have a problem with it. They have an agenda and it does not match up with the urgency for action in which our nation finds itself.

I do not have a problem with Republicans speaking their minds and assertively putting their markers down, and concerns on the table. Heck, it's their job. They are part of the process and their input is needed. But, they are doing themselves a disservice and the American people additional pain when they readily and without thought revert to the same old tone death and ideological-based attacks they have been using over the past 25 years

In their attempt to "im-Palin" the Democrats with the divide and conquer approach, ripping off constituency after constituency by trying to find the various hot buttons that add up to sizeable opposition and disengagement they are really further impaling the American people through inaction.

Creating jobs can and should have multiple positive results such as jobs that teach our children, jobs that build boats and jobs that make Americans healthier. Our families and communities deserve no less. Enough of narrow agenda-driven approaches that have proven results - failure.

Sometimes rigid ideological orthodoxy gets so caught up in its own hubris, its own rules and beliefs that no one notices, anymore, the baby in the manger.

American families and communities need help. Shovel ready jobs should be about more than shoveling away the failed agendas of the past.

Burns Strider
Founding Partner
The Eleison Group

www.eleisongroup.com

From: Abedin, Huma <AbedinH@state.gov>
Sent: Thursday, February 5, 2009 6:28 AM
To: humamabedin [redacted] B6
Subject: Marina print
Attach: 020509 State Clips doc, 020509 State Briefing.doc

RELEASE IN PART
B6

From: Davis, Jennifer L (S Staff)
To: Abedin, Huma
Cc: S_SpecialAssistants
Sent: Thu Feb 05 06:24:05 2009
Subject: Press Items, 020509

Good morning, Huma!

From: Abedin, Huma <AbedinH@state.gov>
Sent: Thursday, February 5, 2009 8:38 AM
To: humamabedin [redacted] B6
Subject: PrintFw: Huma --

RELEASE IN PART B6

From: Andrew Tobias
To: Abedin, Huma
Sent: Sun Feb 01 17:52:46 2009
Subject: Huma --

Hey, so I asked if I could send you two ideas and you immediately said yes –

. . . but then it was literally the Inauguration and then the confirmation and then and first week's madness and now the Super Bowl . . .

So on the theory that you NEVER have a slow time, here is my first idea:

==========

The US should lead the world in adopting a global minimum wage treaty, requiring each signatory to establish a minimum wage – however low – and requiring "best efforts" to raise that wage each year until it reaches the median minimum wage for all the signatories.

All voluntary, but a matter of national pride and -- when quantified this way -- something to shoot for.

The idea is for us, as the once and future moral leader of the world, and economic engine, to acknowledge the dignity of work and attempt to kick off a virtuous cycle.

E.g., Bangladesh might set its wage at 2 cents a day – but take pride in growing it faster than anyone else in the world, up 50% (reaching 3 cents) within just 5 years.

Morocco might have a slower ***percentage*** improvement, but be able to say that in absolute terms, its wage grew faster in a particular period than any other African country.

There can be lots of ways to show progress. The point is to get everyone trying to show it.

- Mathematically, you can't actually have all countries reach the median – as the median would keep rising as they approached it. But what a great problem to have!
- Zero cost to the U.S. treasury.
- Shows respect to U.S. Labor movement – attempt to break the "race to the bottom."
- Gives people at the bottom a fairer shake, but also helps employers who WANT to give that fairer shake, yet can't now because doing so unilaterally would put them at a competitive disadvantage.
- If all the competitors in an industry must raise wages, no one competitor is disadvantaged. The price of a burger might go up a nickel; the cost of a hotel room, a dollar . . . but people will not abandon fast food for home cooking over a nickel or sleep in their car over a dollar.
- If it's not overdone, raising the minimum wage should have far more positive effects than negative. It enhances the value of work and personal dignity. It creates more spending power, which ultimately enriches the entire national economy, including the wealthy few.

==========

So that's it. I had a chance to mention this to President Clinton this fall and he liked it, but I wasn't sure how to follow up.

With appropriate spadework, perhaps The Secretary of State -- standing with President Obama and the Secretary of Labor, John Sweeney and the rest -- could unveil the text of this Treaty ("Whereas, the dignity of human labor . . .") in time for Labor Day Weekend?

Or even sooner, given the need to change global psychology and give people hope for the future?

Idea #2 follows in next email.

Hug,

Andy

From: Abedin, Huma <AbedinH@state.gov>
Sent: Thursday, February 5, 2009 8:41 AM
To: humamabedin[redacted] B6
Subject: PrintFw: Huma - idea #2

RELEASE IN PART B6

From: Andrew Tobias
To: Abedin, Huma
Sent: Sun Feb 01 17:56:46 2009
Subject: Huma - idea #2

Here is my second idea, equally tied to our relations with the rest of the world.

I'm sure you know the endless horror stories of how we treat foreign visitors to our country.

It's really cut down on potential tourism (and business travel and students wanting to study here).

Even with the US was "on sale," with a plummeting dollar, our tourism numbers weren't nearly as good as, say, the UK.

So the idea is to spend $1 billion a year to generate an extra $30 billion a year in revenue – at the same time generating substantial international good will.

Imagine the speech:

"Over the past eight years," the President and Secretary of State and Secretary of Transportation could say on a world stage, "it became distressingly cumbersome and sometimes even unpleasant for visitors to enter our country.

"Yes, we need to protect our citizens by careful screening at customs – and will. But no longer will we do this at the expense of hospitality.

"The following steps will be taken to improve the welcome of visitors to ours shores:

- First, the number of customs agents will be increased as needed to cut the standard wait time at our major ports of entry to 20 minutes or less.
- Second, while our visitors ARE standing in line, they will be offered complimentary hot chocolate and tea in the winter; complimentary lemonade and iced tea in the summer. Folding or rolling chairs will be provided to those desiring them. Multilingual volunteers – a Greeter Corps, proud to show our hospitality – will be available to answer visitor questions while in line.

"We anticipate the added cost per incoming visitor to be less than $25 – a small price to pay to create a favorable first impression on people who, on average, spend $2,000 while they are our guests.

"We will do this, first, because we are a warm and welcoming people. Second, as a small but real signal to the world that 'we're back' – we are rejoining the community of nations. And third, because we want the word to spread that America is once again, and as it has always been, a great place to vacation, a great place to study, a great place to do business."

#

So that's it. I just pulled the $2,000 figure out of the air, but it has to be something vaguely like that. I think it has to be a good investment.

A huge hug to you and your boss. Please let me know your thoughts (I'm a big boy; I can take straight talk).

Your fan,

Andy

From: Abedin, Huma <AbedinH@state.gov>
Sent: Thursday, February 5, 2009 8:51 AM
To: humamabedin[redacted] B6
Subject: Jin printFw: Memo for HRC

RELEASE IN PART B6

From: Jin Chon
To: Abedin, Huma
Sent: Tue Feb 03 17:52:01 2009
Subject: Fw: Memo for HRC

Hi Huma - I sent this to your FOH account but it bounced back. It was great to see you last night. I mentioned the memo below to HRC last night and she asked me to get it to her.

Let me know if you have any downtime coming up soon. Would be great to get lunch and catch up.

Cheers!

Jin

Draft Memo

To: Secretary of State-Designate Hillary Clinton Transition Team

From: Jin Chon

Date: January 18, 2009

Re: Specialty Media in the Age of Secretary Clinton

Specialty media played a major role in this year's presidential election during both the primary and general campaigns by providing information on key issues to niche audiences. The public hunger for news and information about the candidates and their positions ensured that the campaign got regular coverage from media sources as diverse as daytime talk shows like *The View* to Country Music Television to ethnic outlets like *La Opinion, India Abroad* and the *Jewish Telegraphic Agency (JTA)* The heightened interest from specialty media is unlikely to abate as the Obama administration takes over the reins of government and begins to address the multitude of challenges facing the nation at home and abroad.

As Secretary of State, Hillary Clinton should tap into this heightened media interest and the enormous well of goodwill she has developed with many of these specialty media outlets through her time in the Senate and especially from her presidential campaign. Unlike the elite, Inside-the-Beltway reporters who are constantly on the hunt for controversy and internal friction within the administration, specialty media outlets are more focused on substantive policy issues and want to find ways to connect these complex issues to a human face. Further, the thirst for access from these outlets puts the State Department in a position of strength in negotiating amount of coverage and topics to be discussed. Many will agree to do a written Q&A or restrict questioning to previously approved topics. These outlets can create vital support for official policy or pending legislation among key domestic constituency groups but also create momentum for policy abroad As the media environment continues to become more and more globally interconnected, it will be critical for the leadership of the State Department to leverage all

of these media opportunities to amplify and deliver messages that advance policymaking.

For the most part, specialty media outlets have been vastly underutilized by the leadership of the State Department, instead relying heavily on the Sunday shows and network and cable news to communicate the administration's foreign policy agenda. For example, of the over 550 media interviews Secretary Rice conducted during her tenure (does not include media availabilities or press conferences) only a handful of those can be considered to be with specialty media In fact, she only did five interviews with outlets that reach the African-American community (2 with *Ebony*, 1 each with *Essence, American Urban Radio, and Tavis Smiley*) and even though many ethnic specialty media outlets have operations in the U.S., she rarely did interviews with them stateside and instead, would do brief interviews during a trip to that region. Most of the specialty media that Secretary Rice did was in the world of sports, demonstrating her devotion to sports like football and golf.

Unlike previous Secretaries of State, Hillary Clinton will come to the State Department with a national constituency who can be grassroots voices to their Members of Congress and the White House She will have unparalleled star power and abilities to use her brand to turn good policy ideas into concrete programs. Specialty media can be an important tool in achieving this vision. This memo provides an analysis of the specialty media interviews conducted by Secretary Rice and outlines opportunities for the incoming leadership of the State Department to fully leverage the unique opportunities presented by specialty media outlets.

Women

Even though Secretary Rice is only the second woman to be appointed Secretary of State, she had relatively little interaction with media that reaches women. And while she spoke about various women's issues throughout her tenure, Secretary Rice did little to engage the public at large to advance important policy issues like microfinance and human trafficking. In fact, she only did three interviews that specifically reach women: *PEOPLE Magazine* in December 2008, *Girl Scout Magazine* in September 2008, and iVillage.com in May 2007.

Hillary Clinton has made it clear that she will be a strong advocate for women's rights and economic and educational opportunity But in order to increase funding for these types of programs, she will need the help of supporters from around the country to secure Congressional approval. Here are a few ways that Hillary Clinton can use specialty media to build support for her agenda:

- Daytime Talk Shows – Politics and public policy have become staple topics of daytime talk shows like no other time in history. The line between daytime talk shows and hard news becomes more and more blurred as headlines in one realm make headlines in the other

    - Oprah – In the world of daytime talk, Oprah continues to dominate and in the past few years, she has tackled many important foreign policy issues that are often ignored by mainstream press. For example, she has recently done shows dedicated to genocide in Darfur, the violence in the Democratic Republic of Congo, and the Lord's Resistance Army in Uganda. These shows are often led by special correspondents Lisa Ling and CNN's Anderson Cooper. Oprah's influence goes beyond the 8 million in the U.S. who watch her show daily but extends to the millions who watch her in 139 countries. In the past year, she has worked to incorporate her international audience by using Skype technology to have real viewers from around the world ask questions to her guests.

    - Ellen – While Ellen does not spend many shows dealing with serious foreign policy issues, she does use her show to support important causes and raise money for them. Further, her show is syndicated internationally to ten countries, including Canada, Australia, and India. She is a big supporter of Hillary Clinton and is willing to use her platform to help promote the agenda of the new Secretary of State.

- The View – What The View lacks in international distribution, it makes up for it by creating a media echo chamber based on the intense discussions that take place every weekday during the Hot Topics segments. While, foreign affairs have only been an occasional topic on the show, now with Hillary Clinton as Secretary of State, that level is expected to spike dramatically. The influence of the show on Americans' understanding of foreign policy is already evident. For example, when President Ahmadinejad spoke at Columbia University, Whoopi Goldberg provided the audience with tips on how to pronounce his name [say I'M A DINNER JACKET] and in a recent show discussing Hillary Clinton's appointment to Secretary of State, Whoopi mentioned how she would like to be the Ambassador to Hungary. Later that day, the former Hungarian ambassador to the U.S. posted a YouTube video singing a song and inviting Whoopi to Hungary as his special guest and then The View showed the video during Hot Topics the next day.

- Entertainment News Shows – Coverage of politics exploded on all the entertainment news shows this year and they continue to cover the new administration regularly Hillary Clinton did numerous interviews with Entertainment Tonight/The Insider, Access Hollywood, EXTRA, and Inside Edition during the campaign. Together these shows reach an audience of 25 million viewers everyday. Working with these outlets can help shape Americans' opinion of foreign policy and provide a human face to the issues that the State Department is promoting.

- National Radio – National radio shows are an easy and effective way to reach an enormous audience. Two shows in particular should be a target for the leadership of the State Department:

  - Delilah – The Delilah show broadcasts for four hours every weekday and reaches 10 million people in over 200 media markets. Delilah herself is a major advocate for adoption and foster care. She also has her own foundation called Point Hope which provides resources for Liberian refugees based in Ghana
  - Ryan Seacrest Morning Show – As host of American Idol, E News, and his own nationally-syndicated morning show, an interview with Ryan Seacrest gets amplified many times over He has also been active on important global issues, championing the annual Idol Gives Back show, which provides fund for charities, including Malaria No More, The Global Fund for HIV/AIDS, and Save the Children.

- Magazines – Many American women's magazines have international editions that share brand identity and monthly content. One idea would be to have Secretary Clinton author a monthly column in one of these magazines like *Glamour*, which has editions in the UK, Italy, Germany, France, Spain, Russia, Mexico, Greece, South Africa, Hungary, The Netherlands, Sweden, and Romania. Also, placing human interest stories that reflect specific policies in publications like *PEOPLE* and *US Weekly* will be important ways to reach American women

Ethnic Media

While ethnic media played an important role in the campaign, the influence of these outlets among domestic constituency groups and in turn, audiences abroad cannot be understated as Hillary Clinton becomes the next Secretary of State and addresses the crises affecting their homelands. There are many opportunities to engage these publications beyond one-on-one interviews. These publications would be extremely happy to accept written Q&A interviews, op-eds, etc

- Arab Media: In her four years as head of the State Department, Secretary Rice did 33 interviews with Arab television network, more than any other non-US network or cable station She regularly did interviews with Al Arabiya, Al-Hurra, and BBC Arabic Television. She did not do any interviews with Al-Jazeera. However, as much as she provided access to Arab media overseas, she did not do any interviews with domestic Arab American media, which could have helpful in building support for the administration's policies for a very complicated region And while most Arab

American media is local, there is a station call Middle Eastern Broadcasting Network (MBN) based in the Detroit-area that gets wider reach (distribution in MI, VA, and by satellite) and has much stronger penetration among this key constituency. Cultivating US-based Arab American media can be an important way to change the impression that Americans are largely anti-Arab/Muslim by demonstrating that there is a vibrant and thriving community here at home.

- Jewish/Israeli Press: Secretary Rice conducted eight interviews with Jewish or Israeli press – most of the interviews took place in Israel. But, it's important to note that domestic outlets like JTA and *The Forward* as well as Israeli newspapers like *Haaretz* and *Jerusalem Post* have a strong Washington presence.

- Korean Press: Even with the intense negotiations around the North Korean nuclear program, Secretary Rice only did four interviews with Korean television media and it all took place during her trips to Asia. She did not do any interviews with the Korean newspapers, *Korea Daily* or *Korea Times* even though they have wide circulation in several major American markets (New York, Los Angeles, Chicago, Washington, DC, etc.). Engaging the Korean American reporters in the U.S. on a regular basis can help shape the views of not only the Korean American community here but also impact public opinion on the peninsula.

- Chinese Press: Based on the transcripts on the State Department Web site, it does not appear that Secretary Rice did any interviews with Chinese or Chinese-American media outlets. That's unfortunate considering that newspapers like *Sing Tao Daily* and *World Journal* have reporters in Washington and regularly cover American foreign policy. *Sing Tao Daily* is Hong Kong's second largest newspaper and has 16 international editions. Sing Tao Daily has several U.S. bureaus, including Washington, DC, New York, Los Angeles, and San Francisco, just to name a few. *World Journal* is owned by UDN Group, one of the largest media companies in Taiwan, and has the highest readership of any Chinese newspaper in the U.S. with circulation in almost every major American city.

- Indian/Pakistani Press: In four years, Secretary Rice conducted only four interviews with Indian or Pakistani media. She did three interviews in March 2005 (Pakistani Television, India Toady, and NDTV) and another one with Zee News in March 2006. Yet with the many challenges in the reason, it will be important for the leadership of the State Department to engage the media in this region. The most important reporter to reach out to is Aziz Haniffa, Managing Editor for India Abroad, which is owned by the Indian Internet news site, rediff.com. Aziz has very good contacts within the Indian-American political community. The only high-level person that Aziz has interviewed at the State Department during the Bush administration was Nicholas Burns in January 2006. Aziz has already reported that Rahul Verma will be appointed to Assistant Secretary for State for Legislative Affairs.

- Hispanic Press: Secretary Rice did 15 interviews with Hispanic media, most of it with the international networks like Univision, Telemundo, Televisa, and CNN en Espagnol However, she largely avoided Hispanic print media and never sat down with a reporter from EFE, the fourth largest newswire in the world. In addition to the standard news shows for the major Spanish-language television networks, Hillary Clinton should also look at sitting down with prominent media figures like Don Francisco and Cristina Saralegui. In order to ensure that the Latino community in the U.S. knows all the work being done on the Latin American front, radio personalities like Piolin should be engaged and given access to the Secretary.

- African American Press: As mentioned earlier, Secretary Rice did few interviews with the Black press but as the new administration comes to power, it is clear that there will be heightened coverage of the all its activities For example, Ebony/JET and Essence have both announced that they will be hiring full-time White House correspondents, joining April Ryan of American Urban Radio Networks. In addition, it will be important to communicate with media from organizations like The Trotter Group and NNPA. Lastly, reaching out to radio hosts like Tom Joyner and Steve Harvey

will be important ways to ensure that the State Department is getting its message out to the African-American community.

Other Important Specialty Media

- Late Night Talk Shows – Shows like Late Night with David Letterman, The Tonight Show, and The Daily Show will be keeping close tabs on Secretary Clinton's activities and no doubt, find whatever they can for comedic value. With Conan O'Brien shifting to The Tonight Show slot in May 2009 and Jay Leno getting his own weekday prime time spot at 10 pm, there will even more opportunity to work with these shows to bring a of mix light and more serious topics to the American public.

- MTV – In February 2002, Secretary Colin Powell participated in a forum with young people around the world. That would be the last contact that MTV had with the Bush administration until Secretary Rice sat down with Gideon Yago in September 2006. Communicating with young people around the world should be a priority for Secretary Clinton and the State Department should consider working with MTV to host an annual global forum, like the one Secretary Powell did in 2002.

From: Abedin, Huma <AbedinH@state.gov>
Sent: Thursday, February 5, 2009 8:52 AM
To: humamabedin [redacted] B6
Subject: PrintFw: Bono
Attach: Foward Thinking Profile.doc

RELEASE IN PART B6

From: Lucy Matthew
To: Abedin, Huma
Sent: Wed Feb 04 11:30:57 2009
Subject: Bono

Huma, hi! How are you in the new digs... Please find below an email from Bono for the Secretary with attachment... Thanks, and hope you are well, Lucy

Secretary Hillary,

How is the new job.... hope you are settling in ok... Chelsea keeps an eye on our Jordan in Colombia, what a delight she is.

This is very short notice and probably impossible, and I'd like to emphasize this is not my subject at all – but I found these people, Forward Thinking, who work on the Middle East, to be very inspiring. One of them is an Irish priest (of course)... They really do seem to have a relationship with the Israeli hard right as well as Hamas which is apparently unique for a western organization. I'm sure Gordon Brown knows of them through the UK Ambassador to the UN Jeremy Greenstock who is advising and and working with them.

It turns out that Sir Jeremy is in the capitol this Friday – Forward Thinking has asked if I would recommend him and them to you for a meeting. Its impossibly short notice, and I'm sure you must be inundated with people wanting to give you their take. You may know him anyway. If you as I suspect have zero time, or they do not check out, please ignore this request. I'm only writing at their request because they certainly seemed like the real deal to me, and what they said made a lot of sense.

I'm sending along some info and contact details and will leave with you do to as you please.

Next time I write it will be about our shared passion, justice for the poorest of the poor... or an invitation to a U2 gig...I promise.

Love,
Bono

PS hi to your hubby.

FORWARD THINKING PROFILE

RELEASE IN PART
B6

Oliver McTernan, Director
Email: [redacted] B6
Office: +442077342303

Forward Thinking was founded in 2004 as an independent non-denominational UK registered charity. We are a demand-driven, facilitative organisation that works:

- To promote a more inclusive peace process in the Middle East.
- To facilitate a global dialogue between the religious and secular political worlds.
- To promote in the UK greater understanding and confidence between the diverse grassroots Muslim communities and the wider society including the Media and the British establishment.

Our Middle East Initiative is based on the belief that a durable peace agreement to end the Israeli-Palestinian conflict can only be achieved through the active participation of those who are regarded as political or religious hardliners. Whatever its achievements, a main shortcoming of the Oslo agreements was a steadfast failure to recognise the necessity of including religious and ideological conservatives on both sides in the process This legacy has resulted in a situation in which significant players on both sides were not included in and definitely do not identify with the principles upon which these previous negotiations were based. Forward Thinking believes as long as the voices of non-convinced constituencies are not included in the dialogue, no long-term and sustainable solution can be reached .Our prime focus is to promote a more inclusive peace process through dialogue with key Israeli and Palestinian stakeholders and political/religious leaders who previously had been unengaged.

Over the past four years we have formed credible working relationships and trust with a number of key political players on both sides of the conflict. In the Israeli Knesset we have established a cross party group of members who represent mainly right wing constituencies that have not previously being part of the peace dialogue: these include Likud, SHAS, Kadima, Labour and Yisrael Beiteinu parties. On the Palestinian side we are in dialogue with the reform minded members of the Fatah movement as well as with the leaders of Hamas and Islamic Jihad We have regular unilateral meetings, working on the principle of total transparency, each side knowing who our other partners are. Our experience suggests that behind the rhetoric of rejection currently voiced by both Palestinian and Israeli hard-liners, both recognise the need to deal with the other.

Our goal is to prepare both sides for direct engagement when the timing is appropriate. We hold regular meetings with policy makers from the international community to discuss the situation in the region. Our main achievement in the past year was to establish with the financial support of the Swiss Government The Palestinian Institute for the Study of Conflict Resolution and Governance in Gaza. The centre provides a neutral space for members of the various political factions to meet as well as training in conflict resolution theory and practice.

HA 09/01/2015

Our Global Dialogue Initiative is based on the belief that the resolution of some political conflicts that fuel Islamic-Western polarization may be impossible without a greater involvement of religious, social and political movements by more secular political leaders and policy-makers. We seek to foster deeper understanding, respect, and relationships of trust – which may subsequently form the basis for cooperative action - amongst leaders and activists from four sectors:

- European political leaders and policy-makers;
- American political leaders and policy-makers;
- Influential Muslim faith-based and faith-motivated social and political activists;
- Influential Christian faith-based and faith-motivated social and political activists (esp. American Evangelicals).

In partnership with the UN Alliance of Civilizations, the King Faisal Center for Research and Islamic Studies, the Turkish Institue SETA and the Swiss Ministry of Foreign Affairs, Forward Thinking took the lead in convening meetings in Nyon and Lisbon aimed at helping to bridge both secular-religious divides as well as perceived Muslim-Western divides. The Lisbon meeting was hosted by the Portuguese Government. The Spanish and Turkish governments have agreed to host future meetings.

FT UK Programme aims to help grassroots Muslim communities to engage with the Establishment and the wider British society without fearing the loss of their faith identity We work in partnership with a large number of culturally and religiously diverse Muslim communities and groups across the UK. We do not claim to represent any particular group or community. We recognize the importance of Muslims retaining a strong faith identity whilst being engaged fully with the rest of British society. To achieve these goals we provide capacity building support to a number of Muslim charitable organizations working at a local and national level. As we enjoy unique access to many isolated communities we have been engaged by the Home Office to organize regular two day educational visits for senior government staff and policy decision makers to diverse grassroots communities. We hold regular meetings for young people and community leaders. We work in partnership with Muslim organizations in addressing issues of concern. We organize meetings for journalists and broadcasters to help create greater understanding of faith issues and community concerns.

Organizational Structure

To remain an effective demand driven organization Forward Thinking's goal is to remain lean and flexible. We operate from a rent free shared office space in central London with a small staff of six, two of whom are part time. We have a board of three trustees to whom the staff is accountable. We have a larger group of distinguished international advisors who are available to provide diplomatic, political, and theological guidance to the staff and the board of trustees as required.

OJ McTernan
Director
December 2008

From: williamsbarrett[redacted]
Sent: Thursday, February 5, 2009 10:52 AM
To: hdr22@clintonemail.com
Subject: Re: State Department Paperwork

B6

RELEASE IN PART B6

In ameeting all day but robby and I have discussed please include hin in discussions.

Sent from my Verizon Wireless BlackBerry

From: "H"
Date: Thu, 5 Feb 2009 14:28:16 +0000
To: Mills, Cheryl D<MillsCD@state.gov>; Maggie Williams<williamsbarrett[redacted]>; <hdr22@clintonemail.com>
Subject: Re: State Department Paperwork

Let's discuss as soon as I get in.

From: "Mills, Cheryl D"
Date: Thu, 5 Feb 2009 08:26:34 -0500
To: <williamsbarrett[redacted]>; <hdr22@clintonemail.com>
Subject: FW: State Department Paperwork

HRC/Maggie:

FYI in case Tamera raises any issues or concerns.

I asked Heather to send her an email regarding staff who were getting paperwork because they were slated to come in the building.

There is a larger management issue I want to discuss with you.

cdm

From: Samuelson, Heather F
Sent: Wednesday, February 04, 2009 8:31 PM
To: 'Luzzatto[redacted]
Cc: Mills, Cheryl D; robbymook[redacted]
Subject: State Department Paperwork

Tamera,

I wanted to let you know that I plan to send the State Department's hiring paperwork to the following Senate staffers.

While we do not have start dates for them yet, nor do we know which office/ bureau they will be assigned to, we wanted to get them started on the hiring paperwork.

Please let me if you have any questions or concerns.

Many thanks,

Heather
[redacted] cell
(202) 647-0646 office

B6

HA 09/01/2015

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B6

From: Cheryl Mills [redacted] B6 RELEASE IN PART B6
Sent: Friday, February 6, 2009 6:39 AM
To: hdr22@clintonemail.com
Subject: FW: Quote of the Day

FYI (if they only knew . . . we're winging it too!)

From: DelPiano, Matt
Sent: Thursday, February 05, 2009 5:12 PM
To: Kives, Michael; O'Connor, David
Subject: Quote of the Day

"Obama is winging it. He has one hundred and forty people in the White House and none of them know what they are doing. The only person that is being smart, thoughtful and measured is....Hillary Rodham Clinton"

- ***Karl Rove to Matt DelPiano***

February 5th, 2009

HA 09/01/2015

From: Abedin, Huma <AbedinH@state.gov>
Sent: Friday, February 6, 2009 7:05 AM
To: humamabedin [redacted] B6
Subject: Marina print
Attach: 020609 State Clips.doc; 020609 State Briefing.doc

RELEASE IN PART
B6

From: Davis, Jennifer L (S Staff)
To: Abedin, Huma
Cc: S_SpecialAssistants
Sent: Fri Feb 06 06:12:10 2009
Subject: Press Items 020609

Morning, Huma.

HA 09/01/2015

From: H <hdr22@clintonemail.com>
Sent: Friday, February 6, 2009 9:00 PM
To: Tamera Luzzatto <tamera_luzzatto@clinton.senate.gov>
Subject: Re: Update

RELEASE IN PART
B6

Congratulations [redacted] B6

Hope you're well--H
------Original Message------
From: Tamera Luzzatto
To: 'hdr22@clintonemail.com'
Sent: Feb 5, 2009 3:43 PM
Subject: Update

Sorry for any repetition but my report from Senate Land is:

Good progress it seems for Gillibrand. [redacted] practically lives there, and not an easy process for everyone. Some of our staff like mail room are volunteering.

[redacted] will give them post March time [redacted]

[redacted] are now happy Gillibrand staff in DC.

[redacted] seems to making great progress in finalizing NYC and regional hires, roles, and salaries. KG's CoS is fine abt potential of some NYC pple going to State -- would rather get their help right away to get systems in place.

And related to State, [redacted] is a pleasure. Feels like virtually all staff are getting signals they need, hired by KG, hearing of good chance to be at State, or hearing something else.

[redacted]

Love, T

From: Luzzatto, Tamera (Clinton) <Tamera_Luzzatto@clinton.senate.gov>
Sent: Friday, February 6, 2009 9:40 PM
To: 'hdr22@clintonemail.com'; 'AbedinH@state.gov'
Subject: Fw: Confidential

RELEASE IN PART B6

I doubt this was sent to just me, so checking if you got too

B6

----- Original Message -----
From Bill White
Sent: Fri Feb 06 20:59:08 2009
Subject: Confidential

B6

From: Mills, Cheryl D <MillsCD@state.gov>
Sent: Saturday, February 7, 2009 6:41 AM
To: Sullivan, Jacob J <SullivanJJ@state.gov>; Slaughter, Anne-Marie <SlaughterA@state.gov>, Chollet, Derek H <CholletDH@state.gov>; Slaughter, Anne-Marie <SlaughterA@state.gov>; Muscatine, Lissa <MuscatineL@state.gov>
Cc: Lew, Jacob J <LewJJ@state.gov>
Subject: FW: Forget State vs. Treasury -NY TIMES OP-ED
Attach: nytlogo153x23.gif; Op-Ed Contributors - Transitions - Forget State vs Treasury - NYTimes com htm

RELEASE IN PART B6

FYI - See note and op ed below

B6

From: Hormats, Robert
Sent: Friday, February 06, 2009 6:27 PM
To: Mills, Cheryl D
Subject: Forget State vs. Treasury -NY TIMES OP-ED

<<Op-Ed Contributors - Transitions - Forget State vs. Treasury - NYTimes.com.htm>> **Hello Cheryl,**

It was great to see you last night. I very much enjoyed our conversation.

One point that I wanted to follow up on was the discussion of countries looking inward to resolve their financial/economic problems. I think we need to be very careful on that issue. Doing that, especially if it involves even a little protection, invites others to do the same. And exports necessary for us to get out of our downward spiral.

The attached piece, which I mentioned in our discussion, focuses on this topic. I think that the history here is highly relevant to Hillary's trip and the crisis we face today.

I hope you and she find it of interest.

Have a great weekend.

Best regards,
Bob Hormats

The New York Times

Opinion

Forget State vs. Treasury

By ROBERT HORMATS and DAVID M. KENNEDY
Published: November 29, 2008

AMONG the parallels between our present financial turmoil and the Great Depression of the 1930s, few are more important to understand than the implications of economic upheaval for national security. One lesson from the Depression bears repeating loudly: Economic policy and foreign policy are not two distinct domains. They constitute a strategic nexus whose interconnections we ignore at our peril.

The perception that the United States was too enfeebled by its domestic travails to defend its interests emboldened Japan to invade Manchuria in 1931. The spectacle of Depression-era America continued to feed Japanese aggression, leading eventually to the brazen gamble that a single blow at Pearl Harbor might so demoralize the economically enervated Americans that they would throw in the towel and leave Asia to Japan.

In the 1930s, as now, in the face of severe economic affliction the temptation was strong to turn inward, to "put our own house in order" and tend to the international neighborhood later. That was Franklin Roosevelt's policy in 1933. "Our international trade relations, though vastly important, are in point of time and necessity secondary to the establishment of a sound national economy," he said in his first inaugural address.

Accordingly, Roosevelt left unchallenged the Smoot-Hawley Tariff passed during the Hoover administration, and he added some nationalist measures of his own. Perhaps his worst decision was to scuttle London's World Economic Conference in 1933, convened to discuss international debt rescheduling, exchange-rate stabilization and the restoration of the gold standard. The conference afforded the last, desperate chance to deliver a concerted international counterpunch to the worldwide depression. Yet Roosevelt effectively withdrew the American delegation in July by declaring

that the United States would have no further truck with the "old fetishes of so-called international bankers."

Among those who drew malign conclusions was Hitler. Watching events from his Berlin chancellery, he calculated that the economic weakness of his adversaries opened vistas of opportunity for conquest. The inability of the democracies to cooperate economically portended their inability to cooperate militarily or diplomatically And the ailing economy that was driving the United States inward removed America from Hitler's geopolitical calculus altogether

On Nov. 5, 1937, having re-armed Germany in violation of its Versailles Treaty obligations, Hitler presented his senior political and military officials with an exhaustive blueprint for aggression Over four hours, he analyzed in detail the probable reactions of other powers, including Britain, France, Russia, Italy, Japan, Belgium and Czechoslovakia. He did not even mention the United States, which he deemed incapable of offering serious resistance By going AWOL in London in 1933, Roosevelt emboldened the man whose armed forces he would have to confront on the beaches of Normandy a decade later.

Depression and war were harsh teachers, but the lesson was learned. Surveying the economic chaos that had helped precipitate the war, Harry Dexter White, a Treasury Department official who was the principal architect of the International Monetary Fund and the World Bank, warned in 1942 that "the absence of a high degree of economic collaboration among the leading nations will, during the coming decade, inevitably result in economic warfare that will be but the prelude and instigator of military warfare on an even vaster scale."

At war's end, American leaders started initiatives that replaced the discredited policies of economic nationalism with new rules and institutions to avert protectionism and exchange-rate turmoil, and to foster expanded international trade and investment. For more than two generations, the I M F., the World Bank and the General Agreement on Tariffs and Trade (later the World Trade Organization) did much to underwrite global political stability as well as America's and the world's prosperity.

To govern is to choose, but economic versus foreign policy is a false choice. The national security stakes are too high to allow aggressors or terrorists to conclude that America is too economically distracted to defend its interests. And global peace and prosperity, including economic growth in foreign markets and the flow of capital on which the United States is dependent, remain highly improbable without continued — indeed, renewed — American leadership, political as well as economic

A crucial test of governing awaits the Obama administration. It must pursue economic recovery at home and around the globe and the reinvigoration of multilateral coordination abroad. Failure to revive the sagging domestic economy will make broader security and foreign policy goals more difficult to accomplish, as Americans seek refuge in economic nationalism and foreigners lose confidence in Washington's leadership. The political and economic cooperation needed to resolve the current crisis is as essential to America's domestic well-being as it is to the successful pursuit of our worldwide strategic interests.

The Depression and World War II were not two distinct events Depression incubated war. The war, in turn, gave birth to the array of multilateral institutions that long served to avert another global economic crisis. Keeping that relationship in mind now can help this country to resist, and encourage others to resist, pressures for inward-looking trade and investment policies and withdrawal from international engagement..

It took a depression and a war to transform an older order. If we act swiftly and smartly, ours may be a happier fate. We have what may well be a once-in-a-lifetime opportunity to build an international economic architecture for a new century and in the process bolster our security. If we don't seize it, we may be doomed to repeat some pretty nasty history

Robert Hormats, a managing director of Goldman Sachs, is the author of "The Price of Liberty Paying for America's Wars From the Revolution to the War on Terror " David M Kennedy is a professor of history at Stanford and the author of "Freedom From Fear. The American People in Depression and War, 1929-1945."

More Articles in Opinion » A version of this article appeared in print on November 30, 2008, on page WK9 of the New York edition.

From: H <hdr22@clintonemail.com> B6
Sent: Saturday, February 7, 2009 10:08 AM
To: Huma Abedin [redacted]
Subject: Re:

RELEASE IN PART B6

I'm talking to him now.

From: "Huma Abedin"
Date: Sat, 7 Feb 2009 09:58:00 -0500
To: <hdr22@clintonemail.com>
Subject: Re:

Trying to track him down

-----Original Message-----
From. H <hdr22@clintonemail.com>
To. Huma Abedin
Sent: Sat Feb 07 09:47:28 2009
Subject: Re

I tried but no answer. Can you track him down and connect to the house
------Original Message------
From. Huma Abedin
To: hdr22@clintonemail.com
Sent: Feb 7, 2009 8.41 AM
Subject:

Richard Holbrooke asking to speak.
He's on cell [redacted]

B6

From: Cheryl Mills [redacted] B6

Sent: Sunday, February 8, 2009 7 23 AM

To: hdr22@clintonemail.com

Subject: RE: Follow up

RELEASE IN PART B6

I will call you now

-----Original Message-----
From: H [mailto:hdr22@clintonemail.com]
Sent: Sunday, February 08, 2009 5:48 AM
To: Cheryl Mills
Subject: Follow up

When can you talk this am?

From: H <hdr22@clintonemail.com>
Sent: Sunday, February 8, 2009 9:48 AM
To: Huma Abedin [redacted] B6
Subject: Re Reminder

RELEASE IN PART B6

I did but I was never given a time and it was not on the schedule so I thought it couldn't be arranged

---

From: "Huma Abedin"
Date Sun, 8 Feb 2009 09:28:43 -0500
To. <hdr22@clintonemail.com>
Subject. Re Reminder

Claire and lauren had arranged. My understanding is you agreed to do it today.

-----Original Message-----
From: H <hdr22@clintonemail.com>
To. Huma Abedin
Sent. Sun Feb 08 09:23 48 2009
Subject: Re: Reminder

I did not know so thx for the headsup. Who should have told me? It's not on the schedule Lona sent me. The only thing on that is the shuttle
------Original Message------
From. Huma Abedin
To: hdr22@clintonemail com
Cc Oscar Flores
Sent: Feb 8, 2009 9:01 AM
Subject: Reminder

Just a reminder, you have your 11:30am call with ambassador ryan crocker today. Ops will connect call to house

From: Jake Sullivan [redacted] B6
Sent: Sunday, February 8, 2009 5:54 PM
To: hdr22@clintonemail.com
Subject: NYT story on Japanese layoffs

RELEASE IN PART B6

In case you hadn't seen:

http://www.nytimes.com/2009/02/08/world/asia/08japan.html?_r=1&ref=world

February 8, 2009

In Japan, New Jobless May Lack Safety Net

By MARTIN FACKLER

OITA, Japan — Koji Hirano said his "mind went blank" with disbelief when he and other workers at a Canon digital camera factory in this southern city were suddenly called into a cafeteria in late October and told they were being laid off.

The shock turned to fear when they were also ordered to vacate their employer-provided apartments, a common job benefit here. With no savings from his monthly take-home pay of as little as $700, he said, he faced certain homelessness

"They were going to kick us out into the winter cold to die," said Mr. Hirano, 47.

The current economic crisis has spread joblessness and distress across the world, and Japan has been no exception — with output plunging at historic rates, the unemployment rate leapt to 4.4 percent in December from 3.9 percent the month before. But what has proved more shocking has been the fact that so many of those laid off have been so vulnerable, with hundreds and perhaps thousands finding themselves cast into the streets.

Mr. Hirano and the others laid off by Canon are part of a new subclass of Japanese workers created during a decade of American-style deregulation. As short-term employees they have none of the rights of so-called salarymen or even the factory workers for Japan's legions of small manufacturers.

To make matters worse, they can expect little in the way of unemployment or welfare benefits. In Japan, a country with little experience of widespread unemployment until recently, there is an inadequate safety net for laid-off workers.

According to the Labor Ministry, about 131,000 layoffs have been announced since October Of those, only about 6,000 were culled from the majority of Japanese workers who hold traditional full-time jobs, which are still often held for life. The overwhelming majority — some 125,000, the ministry says — are so-called nonregular workers, who are sent by staffing agencies or hired on short-term contracts with lower pay, fewer benefits and none of the legal protections against layoffs of regular full-time employees.

Mr. Hirano and other former temporary workers at Canon were allowed to stay in their apartments for a few extra months after a public outcry reached all the way to the prime minister. But others have not been so lucky. Over the New Year holiday some 500 disgruntled former temporary workers made homeless by layoffs built an impromptu tent city in a Tokyo park adjacent to the Labor Ministry.

As never before, the global downturn has driven home how a decade of economic transformation has eroded Japan's gentler version of capitalism, in which companies once laid off employees only as a last resort.

"This recession has opened the nation's eyes to its growing social inequalities," said Masahiro Abe, a professor at Dokkyo University who specializes in labor relations. "There is a whole population of workers who are outside the traditional support net."

Until a decade ago, nonregular workers accounted for less than a quarter of Japan's total work force, and included subcontractors and others outside the lifetime employment system as well as students or homemakers working part-time jobs at restaurants or convenience stores.

But the number of nonregular workers took off after an easing of labor laws in 1999 and again in 2004 allowed temporary workers to work on factory lines and in other jobs once largely restricted to full-time workers During Japan's economic recovery in this decade, companies added millions of less expensive temporary employees while continuing to reduce overall numbers of full-time staff.

Today, 34.5 percent of Japan's 55.3 million workers are nonregular employees, including many primary breadwinners for households, according to the Internal Affairs Ministry.

Under the nation's traditional company-centered social welfare system, created after World War II, companies were expected to look after employees until retirement and beyond, serving as the main conduit for pensions and other benefits, and keeping jobless rosters empty by not laying off workers.

Even the limited government job-loss benefits were devised with lifetime employees in mind. To receive unemployment insurance, for instance, workers must have held the same job for at least a year, effectively excluding most temporary workers, whose contracts can be as short as two months. This has left at least half of Japan's 17.8 million nonregular workers ineligible for unemployment aid, say labor experts and Labor Ministry officials.

According to the Organization for Economic Cooperation and Development, Japan spends about 0.3 percent of its gross domestic product on unemployment benefits, far below Western European countries and about the same as the United States, which tolerates far more social dislocation and poverty than Japan.

According to labor experts and Labor Ministry officials, Japan needs to revamp the system to fit a more dynamic labor market in which not all jobs are held for life, and to prevent layoffs from being so financially devastating.

"Japan's social safety net has failed to keep up with changes in the labor market," said Yusuke Inoue, a section chief in the Labor Ministry's bureau of stable employment. "We must build a safety net that suits this more deregulated working environment."

After a public outcry, Tokyo has promised to expand unemployment benefits to those who have worked six months or more. The government has also tried to shore up the traditional system by pressuring companies to elevate more nonregular workers to full-time status, with Prime Minister Taro Aso telling companies in December that "regular employment is best "

Some of the first layoffs to gain national attention were at two Canon factories in Oita, where some 1,100 temporary workers were let go, including Mr. Hirano.

As a temporary worker, Mr. Hirano was technically the employee of a staffing agency, and not of the factory where he worked. As a result, Canon executives even refused at first to accept a letter written by him and other laid-off temporary workers asking for their jobs back, Mr. Hirano said. After 30 minutes of discussion in front of the factory's gate, the executives finally took the letter, he said. He said he never got a response.

In a written response to questions from The New York Times, Canon said it had underestimated the difficulties faced by the laid-off temporary workers in the current economic downturn and would offer them more aid, including help in staying longer in their apartments.

Mr. Hirano and other laid-off temporary workers said their annual pay was about $22,000 a year, below what many labor experts call Japan's poverty line of $25,000 a year.

To make ends meet, even when employed, Mr. Hirano said he usually cooked a small stew of cabbages and carrots every night in the tiny kitchen in the corner of his one-room apartment. He added chicken to the stew only on days it was on sale at the supermarket, he said.

Mr. Hirano and others said they had applied for a dozen jobs each, with no luck in the current market. With their meager savings running out, they said, they had applied for welfare a half dozen times in two months, only to be rejected by officials who said they were not trying hard enough to find new employment. The officials said the former workers were ineligible for unemployment support because they had worked at Canon less than a year

Just in case he gets kicked out of the apartment suddenly, Mr. Hirano has packed most of his belongings in a half dozen cardboard boxes that sit in a corner of his room, next to an unmade futon and a table covered in résumés.

Mr. Hirano and his co-workers said they felt betrayed. They said that they had believed that if they worked hard, Canon would reward them with an offer of direct employment, at higher pay.

"We did our best, so Canon should have taken care of us," said one 32-year-old laid-off worker who was so ashamed of his situation that he asked that only his family name, Murakami, be used. "That is the Japanese way. But this isn't Japan anymore."

From: H <hdr22@clintonemail.com>
Sent: Saturday, February 14, 2009 10:43 PM
To: Huma Abedin <HAbedin@hillaryclinton.com>
Subject: Stationery

RELEASE IN FULL

Is someone bringing any of my stationery? Can you ask Claire to have a supply available, including the long narrow cards I've been using.

From: H <hdr22@clintonemail com>
Sent: Friday, February 20, 2009 6:57 AM
To: Cheryl Mills <CMills@hillaryclinton.com>
Subject: Just landed

RELEASE IN FULL

In China. Will be at hotel soon. Any news to report?

From: Jiloty, Lauren C <JilotyLC@state.gov>
Sent: Friday, February 20, 2009 5 41 PM
To: hdr22@clintonemail.com
Cc: Abedin, Huma <AbedinH@state.gov>
Subject: No new voice messages

RELEASE IN FULL

###

Lauren Jiloty
Special Assistant to
Secretary Hillary Rodham Clinton

From: H <hdr22@clintonemail.com>
Sent: Sunday, February 22, 2009 10:32 PM
To: Hillary Clinton <hr15@att.blackberry.net>
Subject: Fw: Hope all is well in your first global trip as SOS for "humanpotential"

RELEASE IN FULL

From Roy Spence
Date: Sat, 14 Feb 2009 20:51:56 -0600
To: hdr22@clintonemail.com<hdr22@clintonemail.com>
Subject: Hope all is well in your first global trip as SOS for "human potential"

From: Jiloty, Lauren C <JilotyLC@state.gov>
Sent: Monday, February 23, 2009 7 36 AM
To: hdr22@clintonemail com
Cc: Abedin, Huma <AbedinH@state gov>
Subject: no new voice messages, 7 36 AM EST

RELEASE IN FULL

###

Lauren Jiloty
Special Assistant to
Secretary Hillary Rodham Clinton

HA 09/01/2015

From: H <hdr22@clintonemail.com>
Sent: Monday, February 23, 2009 9:47 PM
To: Cheryl Mills <CMills@hillaryclinton.com>
Subject: Can you talk?

RELEASE IN FULL

Call my house Thx.

From: Jiloty, Lauren C <JilotyLC@state.gov>
Sent: Tuesday, February 24, 2009 10:42 AM
To: hdr22@clintonemail.com
Cc: Abedin, Huma <AbedinH@state.gov>
Subject: no new voice mails

RELEASE IN FULL

###

From: Jiloty, Lauren C <JilotyLC@state.gov>
Sent: Wednesday, February 25, 2009 10:24 AM
To: hdr22@clintonemail.com
Subject: RE: no new voice messages

RELEASE IN FULL

Im not sure. I just checked again and there is nothing there. I'll take a look at it when you are back. It's possible that they are text messages. I will figure it out.

From: H [mailto:hdr22@clintonemail.com]
Sent: Wednesday, February 25, 2009 10:18 AM
To: Jiloty, Lauren C
Subject: Re: no new voice messages

Why does my phone say it has two messages?

From: "Jiloty, Lauren C"
Date: Wed, 25 Feb 2009 09:27:45 -0500
To: <hdr22@clintonemail.com>
Subject: no new voice messages
###

Lauren Jiloty
Special Assistant to
Secretary Hillary Rodham Clinton

HA 09/01/2015

Subcommittee Chairmen and Ranking Members

- Subcommittee on Africa and Global Health
  Chairman Donald M. Payne
  Ranking Member Christopher H. Smith

- Subcommittee on Asia, the Pacific, and the Global Environment
  Chairman Eni F. H. Faleomavaega
  Ranking Member Donald A. Manzullo

- Subcommittee on Europe
  Chairman Robert Wexler
  Ranking Member Elton Gallegly

- Subcommittee on Terrorism, Nonproliferation, and Trade
  Chairman Brad Sherman
  Ranking Member Edward R. Royce

- Subcommittee on International Organizations, Human Rights, and Oversight
  Chairman Bill Delahunt
  Ranking Member Dana Rohrabacher

- Subcommittee on the Middle East and South Asia
  Chairman Gary L. Ackerman
  Ranking Member Dan Burton

- Subcommittee on the Western Hemisphere
  Chairman Eliot L. Engel
  Ranking Member Connie Mack

From: Luzzatto, Tamera (Clinton) <Tamera_Luzzatto@clinton.senate.gov>
Sent: Thursday, February 26, 2009 11:54 AM
To: 'hdr22@clintonemail.com'
Subject: Fw Visit

RELEASE IN FULL

Small FYI. Of all people, Idaho's new Sen's chief asked to visit with me He noted they went on Foreign Relations and he's ranking on the middle east subcomm.

From: Sandy, John (Risch)
To: Luzzatto, Tamera (Clinton)
Sent: Thu Feb 26 11:12:15 2009
Subject: Visit

Tamera,
Thank you for giving me a bit of your time.
What a wonderful opportunity you have had during your service with Senator Clinton.
Please pass along to the Secretary that we from Idaho extend wishes to her for her upmost success.
I wish you the very best in the next phase of your life.
I fully realize that we have only know each other for a few minutes but I am very sincere in saying that if there is ever anything I can do for you please do hesitate to ask.
John

From: H <hdr22@clintonemail.com>
Sent: Thursday, February 26, 2009 5:42 PM
To: Lauren Jiloty <JilotyLC@state.gov>
Subject: Fw: Aspirational Diplomacy

RELEASE IN FULL

Pls print.

From: Doug Hattaway
Date: Thu, 26 Feb 2009 12:06:41 -0500
To: <hdr22@clintonemail.com>
Subject: RE: Aspirational Diplomacy

Hi. Your first trip seems to have been successful from a communications point of view. The images of you from abroad were very positive. You looked friendly and firm with foreign leaders, and engaging with the people. It sure seemed like you were having fun!

The US media coverage was pretty good overall. The positive analysis focused on your "straightforward" style, campaign-like events, and the enthusiastic reception you received. The overall theme was a new approach to the world, which was exactly what the world needed to see.

As you know, there was some negative reaction to the perception that you put human rights on a back burner with China. The analysis of it was mixed (not uniformly negative) from the human rights commentators I saw quoted.

If it would be helpful, I'd be glad to have my team work up a content analysis of the coverage and commentary about your trip and that issue. You may recall we produced media content charts on our campaign events, to show us what messages were breaking through. The quantitative data helps to evaluate the coverage objectively, and may suggest ideas for message moving forward.

I'm sure your team has discussed it, but for what it's worth I think it would be helpful to remain visibly proactive on the human rights front. As you know, it's a central component of how many people define America's "moral leadership."

A speech to amplify the Administration's approach and commitment to the issue would be useful to some extent. It would likely be seen as a reaction to criticism, which is okay if the content generates positive commentary.

The main thing is to have a consistent stream of substantive words and deeds that advance human rights over time, which is more important than lecturing foreign diplomats and will win over the human rights advocates.

Per our previous exchange, if you'd like to get together to discuss the democracy area, of course I'd be glad to do that.

All the best, Doug

From: H [mailto:hdr22@clintonemail.com]
Sent: Saturday, February 14, 2009 8:57 PM
To: Doug Hattaway
Subject: Re: Aspirational Diplomacy

Doug,

This is very helpful and along the lines of what I've been thinking. I hope we can get together when I'm back to

talk about this whole area. All the best.

From: Doug Hattaway
Date: Thu, 12 Feb 2009 09:43:57 -0500
To: <hdr22@clintonemail.com>
Subject: RE: Aspirational Diplomacy

Hi! Hope you're doing well. Things look to be going very well at State.

I wanted to pass along another thought, this time about our message and approach to supporting democracy around the world. This is based on my work with NDI in the Middle East and North Africa.

As you may recall, I worked with the government of Lebanon, political parties and NGOs in a number of countries. We kept running into problems with the way democracy assistance was viewed in the U.S. and abroad.

Because of Bush's belligerence and the way the Republicans talk about advancing democracy as "promoting American values" and "winning the ideological war," the word "democracy" itself was tainted.

People who should support democracy and democratic governance were suspicious or hostile. Democratic reformers in many countries were put on the defensive, and even put in danger.

The Republican approach was more about selling democracy. Karen Hughes went around delivering lectures. They ran advertising campaigns, which were not well received overseas. (That's not surprising, since polls show commercial marketing and Hollywood exports contribute to negative perceptions of America.)

This is not to belittle good work done in public diplomacy, but the general orientation toward selling democracy as a concept (particularly in the context of invading Iraq) was ineffective at best and counter-productive at worst.

In response, we developed a new way to talk about this work that would distinguish our (Democratic) approach from the Republicans.

We talked about it as "helping people build democratic institutions." This frames the U.S. as helping people on the ground, rather than lecturing them about abstract principles. "Democratic institutions" are fair elections, representative political parties, independent citizens' groups and government that is open and accountable.

We focused on the benefits to foreign publics: "Democratic institutions and processes can help people in any society resolve conflicts peacefully and improve their lives."

And to the American public: "Helping people build more democratic societies will contribute to greater peace and stability throughout the world."

This isn't to retreat from proactively advancing democracy, which Democrats have long embraced. It's framing the work in more concrete terms and focusing on the benefits to people's lives.

I hope that's useful food for thought. There's more to this, and I'm happy to chat about it if you're interested. We can also talk about the aspirational messaging, if you'd like to follow up on our previous exchange on that.

Keep up the great work, Doug

From: H [mailto:hdr22@clintonemail.com]
Sent: Wednesday, January 28, 2009 9:46 PM
To: Doug Hattaway
Subject: Re: Aspirational Diplomacy

Doug,

So good to hear from you and this was very useful. I'd love to talk about it further. I'll contact you about setting up a time to get together. Thanks so much. All the best, H

From: H <hdr22@clintonemail.com>
Sent: Thursday, February 26, 2009 9:29 PM
To: Cheryl Mills <CMills@hillaryclinton.com>
Subject: I'm home

RELEASE IN FULL

If you want to call before 11. Thx

From: Valmoro, Lona J <ValmoroLJ@state.gov>
Sent: Saturday, February 14, 2009 9:13 PM
To: hdr22@clintonemail.com
Subject: Re: Domestic Violence Forum in NYC - April 18th

RELEASE IN PART
B6

Pls respond to this invite.

Will do.

From: H
To: Valmoro, Lona J
Sent: Sat Feb 14 21:00:15 2009
Subject: Fw: Domestic Violence Forum in NYC - April 18th

From: Prameela Bartholomeusz
Date: Sat, 14 Feb 2009 12:38:52 -0800
To: hr15@att.blackberry.net<hr15@att.blackberry.net>
Subject: Domestic Violence Forum in NYC - April 18th

Madam Secretary,

It would be an honor and privilege to have you present at a Domestic Violence Forum that the bipartisan women's group, the New Agenda, is sponsoring in NYC on April 18, 2009. Since the election, I have been seeking a home and a voice to fulfill my personal goals of giving back and investing my energies towards women's causes. I have joined The New Agenda as a founding member with the goal of supporting women in government and being an advocate for women's rights/issues. We were one of the first women's groups to speak out in support of Kirsten Gillebrand's appointment, which we believe was a win for America.

Domestic Violence in America is an issue long ignored and the statistics are staggering:
- $1.8 Billion of wages and productivity are lost to DV each year.
- 8 million workdays are lost by DV victims each year (it is equivalent to 32,000 full time jobs).
- $4.1 billion is spent annually on medical and mental health care as a direct result of DV.
- DV is the # cause of homelessness in 44% of the cities surveyed.

These are the statistics provided by a women's group that will be represented on our panel at the DV Forum.
We would like to invite you and will invite Kirsten Gillebrand to join us in recognizing this tragedy for what it is for women and draw attention to the need to address this issue as the economic downturn drives these statistics even higher. Next steps would be to call for President Obama to declare a month as Domestic Violence Awareness month as a part of the larger agenda of seeing a new Commission for Women's Issues formed in 2009 by the Obama Administration.

Please support these efforts by being our guest at the Domestic Violence Forum in NYC on April 18th. The exact timing will be coordinated based on your schedule and availability.

You will also be receiving this letter from a source closer to you to ensure receipt. I fear this will go to your spam inbox. I have received a response from Capricia Marshall on your behalf in the past but I no longer have her contact information.

Kind regards,
Prameela Bartholomeusz
The New Agenda

[redacted]

B6

From: Huma Abedin [redacted] B6
Sent: Saturday, February 14, 2009 10:19 PM
To: humamabedin [redacted] B6
Subject: PrintFw. From Vartan Gregorian

RELEASE IN PART B6

-----Original Message-----
From. H <hdr22@clintonemail.com>
To: Huma Abedin
Sent: Sat Feb 14 20:53.54 2009
Subject: Fw· From Vartan Gregorian

Pls print.

B6

From· williamsbarrett[redacted]
Date· Fri, 13 Feb 2009 16·58:34 -0500
To: <hdr22@clintonemail com>
Subject: From Vartan Gregorian

FYI
Vartan wanted you to see -- this is like to be published somewhere -- thought it was pretty interesting

An Opportunity Missed, But Not Lost: What President Bush Should Have Written to Iranian President Mahmoud Ahmadinejad

This February marks the 30th anniversary of the Iranian revolution In what may yet prove to be an historical milestone of another kind, on February 10. President Mahmoud Ahmadinejad of Iran <http://topics nytimes.com/top/news/international/countriesandterritories/iran/index html?inline=nyt-geo> appeared to reach out to the Obama administration, saying that Tehran was ready for "talks based on mutual respect and in a fair atmosphere " This possible overture in what has otherwise seemed to be an unbreachable divide between the United States and Iran during the administration of President George W Bush reminded me that the possibility of rapproche ment between our two nations arose just a few years ago, but was ignored. I am referring to the fact that in May 2006, President Ahmadinejad wrote a far-ranging, 18-page letter to President George Bush discussing religious values, history and international relations. The letter went unanswered. During Ahmadinejad's visit to the UN later that year, he expressed his deep disappointment that President Bush had not responded to his missive.

As a student of the region and of United States-Iran relations, I believed then, and I believe now, that this was a missed opportunity—one of many. Ahmadinejad's letter provided President Bush with an opportunity to address the Iranian people directly to highlight America's longstanding relationship with Iran and clarify the Bush administration's views on the U.S.-Iran relationship.

At the time, thinking about these issues, I drafted a letter that might have served as a response by President Bush to the Iranian people I offer it here.

=0 A
Vartan Gregorian

Dear President Ahmadinejad,

Your letter and recent public utterances have prompted me to review Iran's many contributions to the world, its relationship with the United States and the outstanding issues that now confront our two countries.

Mr President, let me begin by stating that Americans are deeply mindful and respectful of the renowned achievements and rich cultural legacy of Iranian civilization, which reflect a virtually unparalleled degree of historical continuity We are especially cognizant of the role that religion has played in your country's development. Some 2,500 years ago, Iranians gave the world Zoroastrianism, which among its core tenets, affirmed man's absolute free will to choose between evil and a Divine Creator, and our common destiny to face a final Day of Judgment. Although manifested in many different forms, these ancient tenets have been shared by the world's great religions. They underscore the basic truth that human beings not only can decide for themselves what is right and wrong, but also are accountable for their actions.

In the sixth century20BC, Iranians gave us the Achaemenid Empire, and its enlightened leaders, Cyrus and Darius It was Cyrus the Great who decreed that "all should be free to worship their gods without impediments or persecution"—a proclamation unique, not only for its time, but for centuries to come. Ending the Babylonian captivity of the Jews, Cyrus allowed their return to Palestine, and supported their right to live by Biblical law. His respect for cultural diversity and rights for the empire's "many people of many tongues" was emulated by his successors, making the Achaemenid Empire one of the most tolerant and pluralistic in history. This far-flung empire also served as a bridge between East and West, as Iranian art and architecture adorned the great cities of the empire from Babylon to Persepolis The Achaemonids` unique administrative system became a model for other empires, while its emphasis on the teaching of science and philosophy, further advanced by its successor, the Sassanid empire, greatly influenced the eventual development of universities throughout the region and beyond.

Iran has endured many trials and tribulations over the ensuing centuries Although conquered by the Arabs in the seventh century and converted to Islam, Iranians, drawing on their own early beliefs, helped to develop and then adhered to Shi'a Islam. At the dawn of the 16th century, the Safavids, with the glorious city of Isfaha n

as their capital, unified Iran and adopted Shi'a Islam as their empire's official religion. In the process, Iran was not only able to retain its cultural distinctiveness but also to infuse Islam with its great humanistic traditions Reviving Iran's ancient devotion to religious tolerance, the Safavid king, Shah Abbas, treated Iran's Christians and Jews benevolently, and welcomed those fleeing persecution from other lands. It was this reputation that prompted Europe's Christian powers to seek his collaboration

In that connection, it is important to keep in mind that throughout history, Iran's greatest strength has not derived from its arms or material wealth alone, but from its rich and resilient culture. For centuries, Iran conquered and in turn was conquered by many invading armies, including Macedonians, Arabs, Turks and Mongols Yet the invaders were ultimately won over by Iranian culture, which, in effect, made them its converts and brought about the continual rejuvenation of the Iranian state. In the pursuit of knowledge, Iranians actively sought contact with scientists and philosophers from different regions Even during periods of foreign domination, Iran's artistic and scientific spirit flourished and its poets, mystics and philosophers produced one of the greatest bodies of literature in the Muslim world and created a remarkable cultural and scientific heritage that still re sonates today

Having noted Iran's great cultural and historical legacy, and its ability to both enrich and be enriched through its interaction with other civilizations, let me now turn to the issue of United States-Iran relations. It is my contention that, with a few notable exceptions, especially during the last three decades, Iranians and Americans have, on the whole, enjoyed remarkably positive relations. This strong legacy of mutual amity and respect provides reason for optimism that both our countries will be able to put aside our current differences and reestablish the goodwill that once served us both so well.

To begin with, we are proud that during the 19th and the first half of the 20th centuries, our missionaries worked throughout Iran Although they converted few Muslims to Christianity, they did establish the first modern hospitals and the first modern educational institutions in Iran. In 1856, the United States granted Iran most favored nation trade status and welcomed Iranian students to its universities When Iranians launched their constitutional revolution in 1906, Americans welcomed the establishment of a constitutional monarchy. The young American schoolteacher, Howard Baskerville, who joined the constitutionalists and was martyred in Tabriz in 1909, is still regarded as one of the heroes of the revolution It was also an American, W. Morgan Schuster, who came to the aid of Iran and organized its customs to serve as a revenue source designed not to be controlled by either Great Britain or Russia, and wrote a classic, anti-colonial book, The Strangling of Persia.

When, despite its neutrality during World War I, Iran was invaded by Russian and Ottoman troops, the United States defended its territorial integrity Americans later welcomed an Iranian delegation to Versailles, where President Woodrow Wilson was the lone world leader to support Iran's claim for compensation from Britain and Russia for the effects of their wartime occupation. During World War II, following the Allied occupation of Iran and the exile of Reza Shah Pahlavi, the United States and its allies retained the institution of the monarchy as a symbol of unity and continuity of Iranian statehood During that period, Iran played a crucial role as a conduit for American assistance to the Soviet war effort At the end of the war it was, once again, the United States that resolutely protected the territorial integrity of Iran and forced the Soviets to leave the northern part of the country without allowing a Soviet monopoly over its energy resources.

After the outbreak of the Cold War, the United States recognized the vital importance of Iran as a regional power We helped build Iran's armed forces by providing training as well as over a billion dollars of modern armaments, and supported Iran's leadership of the Baghdad Pact and Central Treaty Organization. Between 1953 and 1978, we provided Iran with the most advanced weapons systems on a par with those available to our NATO allies We were eager to help Iran become a modern economic and political superpower in the region and thus provided Iran with a broad range of economic assistance, as well, including support for the diversification of its energy resources

American acceptance of Iran's decision to nationalize its oil industry in 1951, coupled with its successful resistance to Great Britain's plans to seize Iranian oil fields by force, was followed by U.S assistance to modernize these operations This assistance enabled Iran to raise its oil production and prices, which, in turn, gave the country the necessary revenues to modernize its economy, armed forces, and physical and social infrastructure.

During the height of the Cold War, the United States and its allies, as well as the Soviet Union and its Warsaw Pact partners, made various miscalculations and errors Both camps were20so obsessed with one another's seemingly monolithic doctrines and zero-sum policies that they misjudged the nature of such potent historic and cultural forces as religion and nationalism. After the departure of Soviet troops from Iran, the United States remained deeply concerned about possible Communist infiltration, especially during the premiership of Dr. Mohammed Mossadegh. Although Dr. Mossadegh was hosted at the White House by President Harry Truman, who compared him to American patriots Thomas Jefferson and Thomas Paine, and was hailed by Time Magazine as its "Man of the Year" in 1951, by the time a new American presidential administration took office in 1952, Cold War imperatives and mistrust were ascendant

In 1953, the United States, assisted by local elements opposed to the Mossadegh government, including religious leaders such as Ayatollah Abolqasem Kashani, military officers, monarchists and others, precipitated its demise. We did not recognize that a nationalist, secular and democratic Iran would have been a great counterforce against Communism. Neither did we appreciate the sagacity of the Iranian national leadership and the power of nationalism We were wrong On the other hand, we were right in assisting with the modernization of the Iranian armed forces, which became one of the major factors that made Iran a great regional power and helped it defend itse lf against well-armed Iraqi aggression in 1979 It is a fact that the United States was a long-time supporter of Mohammad Reza Shah Pahlavi, who succeeded his father as Iran's ruler. As a pro-Western, secular nationalist, America viewed the Shah as an important bulwark against Communism. The United States supported the Shah's ambitions to make Iran a regional superpower and also considered it, as we do today, a key to regional stability America welcomed Iran's efforts to promote economic ties among Iran, Afghanistan, Pakistan and other powers in an effort to avert conflict, which would only impede Iran's and the region's prospects.

Contrary to Iran's official propaganda, the United States did not break diplomatic relations in response to the Iranian Revolution, which we accepted and with which we endeavored to establish a working relationship. We broke our diplomatic ties only in 1979 when, in violation of international law, Iranian elements occupied the U.S Embassy in Tehran, seized fifty-six American diplomats and held them hostages for 444 days.

Mr President, no country, certainly no country in possession of the vast power of the United States, would have failed to act under such circumstances But we restrained our response, because the powerful have the option not to exercise their power. The United States chose this option, not out of weakness, but out of a sense of responsibility. It distinguished between the Iranian government, and its people and their basic common sense and decency. With hopes that reason would eventually prevail, the U S reluctantly tolerated the situation because of the importance we placed on the long-term relationship between our countries. Given the history of this painful period, it is continually surprising that, when abroad, Iranian officials never mention the hostage crisis that triggered the breakup of our diplomatic relations

Let me now turn to a more recent and vexing problem that has proven to be a major obstacle to the reestablishment of normal diplomatic relations and the resumption of our historically positive interaction. Notwithstanding your recent reaffirmation of Iran's adherence to the Nuclear Non-Proliferation Treaty (NPT), which your country ratified in 1970, and your pledge that "all [your] nuclear activities are transparent, peaceful and under the watchful eye of International Atomic Energy Agency [IAEA]," we continue to have grave concerns—not about Iran's official pledges but rather, about its actions and intentions

Why, you ask, do we challenge what you view as your legally recognized rights under the NPT? To be clear, we have never been opposed to Ir an's being able to enjoy

"the peaceful benefits of nuclear energy." However, as you well know, this is a qualified right, mandating that all signatories to the NPT meet certain requirements. In our opinion—and those of other countries and the IAEA, itself—you have given insufficient attention to such requirements Let me remind you that the United States was the driving force behind the development of Iran's nuclear research capacity through the Atoms for Peace program and reached agreement with Iran as long ago as 1957 for cooperation on civil uses of atomic power A decade later, it was the United States that supplied technical assistance and fuel for a nuclear reactor. America supported the establishment of the Atomic Energy Organization of Iran in 1974 and, in the following year, concluded a fifteen-year pact calling for the construction of eight nuclear reactors in Iran while encouraging the Massachusetts Institute of Technology to provide training for Iranian nuclear engineers In 1978, just a year before the Iranian revolution, the United States signed yet another agreement with Iran to facilitate further cooperation in the field of nuclear energy. It was, in fact, Iran's revolutionary government that decided in 1979 to suspend the country's nuclear program, only to later seek its revival with external assistance from both state and non-state actors.

Although we welcomed Iran's supreme religious leader, Ayatollah Ali Khamenei's fatwa against Iran's "stockpiling, production or use of nuclear weapons," given the disturbing revelations about your 18-year-long, mostly clandestine nuclear program, your unwillingness to respond satisfactorily to certain questions about your past nuclear activities and determined efforts to produce fissile material despite IAEA and UN Security Council demands to desist, it is not surprising that doubts remain about your ultimate intentions. Your own assertion that Islam, by its very nature, is incompatible with nuclear weapons is, unfortunately, not reassuring in view of the fact that we have witnessed the apparent alacrity with which Pakistan, an Islamic state, developed its own nuclear weapons Perhaps the Shi'a Islam that guides Iran compels the country to hew more closely to the spirit of Islam, and under no circumstances would Iran consider following Pakistan's example. But, as you know, the international community, as expressed through various UN Security Council resolutions, is not prepared to take such a calculated risk. The issue, then, is not Iran's rights under the NPT; the issue is one of trust—whether certain elements in the Iranian government might be tempted to take the next step and develop a nuclear weapons program. The aim of America and its allies is to dissuade you from embarking on such a course

Hence, the challenge is to balance Iran's exercise of its NPT-mandated rights with the need to ensure its compliance with legally binding treaty obligations. Let me reiterate that we have always welcomed consideration of a wide range of creative options for addressing Iranian concerns and those of the international community, including proposals for guaranteed supplies of nuclear fuel from specific countries such as Russia, or from the IAEA. The United States has expressed its readiness to end its decades-long policy not to have direct talks with Iran and is prepared to sit down with you and discuss all the issues that separate us, including Iran's current nuclear enrichment program and Iran's links with groups inimical to peace in the region. In the spirit of mutual respect, we also are ready to discuss your legitimate aspirations as a major regional power and to cease all talk of "regime change" in Iran as well as to provide your country with the security assurances it seeks to protect its sovereignty and independence. All of this is possible only if we find an internationally acceptable resolution to the problem posed by Iran's enrichment of uranium.

The primary obstacle to direct, bilateral dialogue—a goal that you yourself have affirmed in interviews with Western media—is your determination to continue with this enrichment in violation of UN Security Council resolutions. If your nuclear energy program leads to a nuclear weapons program, it will have a destabilizing effect on future developments in the Gulf Region by threatening to spur a nuclear race among other states with the knowledge and capacity- -as well as the financial resources, which is the case with such countries as Saudi Arabia—to develop not only nuclear energy, but nuclear weapons in order to maintain parity and achieve a "nuclear balance of power." In addition, the actual development of a weapon is not necessary in order to have the world acknowledge the sophistication and ability of Iranian scientists; their knowledge has already brought Iran into the select group of forty states with nuclear capacity. Our hope is that Iran, even if it has the resources to develop a nuclear weapon, also will have the resolve and wisdom to refrain from doing so. In exchange for verifiable forbearance and compliance with international norms and legal obligations, Iran will not only be in a position to enjoy mutually beneficial relations with the United States, but also with the European Union, other regional and world powers and, potentially, with the broad membership of the World Trade O rganization.

It is important to underscore that the United States is not against Iran or the Iranian people If that were the case, the U.S would not have helped defeat two of Iran's major, long-term adversaries, Saddam Hussein and the Taliban, whose demise has helped Iran reassert its regional power and influence. Regrettably, both the United States and Iran, suspicious of one another's aims, have missed several opportunities in recent years to normalize diplomatic relations. Following the tragic events of September 11, 2001, we were greatly impressed that two Iranian leaders, Ayatollah Ali Khamenei and President Muhammad Khatami, were among the first world figures to condemn the dastardly assault on America and the killing of innocent civilians. As President Khatami said, "the horrific attacks. were perpetrated by [a] cult of fanatics who had self-mutilated their ears and tongues, and could only communicate with perceived opponents through carnage and destruction." Indeed, President Khatami described 9/11 as "one of the greatest calamities" of our time. Americans were also deeply moved by the spontaneous candlelight vigil held in Tehran to honor the victims of these attacks. Iran's assistance was welcomed during the struggle to dislodge the Taliban in Afghanistan as was the development assistance Iran provided to the Afghan government and people. Although this empathe tic and collaborative spirit was not capitalized upon to establish a more lasting, positive relationship, such missteps do not have to determine our future path.

As we both know, Iran and the United States have many common interests in the region. In Iraq, both support the success of the duly elected government of Prime Minister Nouri al-Maliki, the country's unity and territorial integrity, and the avoidance of sectarian strife that might incite a larger regional Shi'a-Sunni conflict. A strong, vibrant Iraq will also provide Iran with a reliable trading partner and assist in the broader economic development of the region, to the benefit of all concerned Similarly, both countries support the unity, stability and development of Afghanistan, the repatriation of Afghan refugees now on Iranian soil, the defeat of a resurgent and militant Taliban, and the eradication of the country's opium crop, which has contributed to Iran's growing problems with heroin addiction and the spread of HIV/AIDS.

In our view, the potential for establishing a mutually beneficial, cooperative relationship between Iran and the United States has been diminished by persistent official Iranian hostility Dismayingly, ever since the Iranians seized the U.S Embassy in 1979, there have been periodic, well-orchestrated, officially inspired demonstrations throughout Iran against the United States, at which the dominant chant for some thirty years has been "Death to America " Iranian leaders also nev er seem to tire of calling America the very incarnation of the "Great Satan," without specifying whether they are impugning America's policies, its government, its people, or all of the above. When Americans take offense at these ritualistic, "spontaneous" denunciations, they are told by Iranians not to take such anti-American utterances seriously. But when the United States, after three decades of such provocations, describes Iran as part of an "Axis of Evil" for its support of anti-U S . anti-Western, anti-Arab allies of the U S. and Europe, and anti-Israeli activities—including those of militarist and terrorist groups—Iranian officials are offended because, unlike their own utterances, which they claim are only rhetorical, they paradoxically assert that only statements made by Americans must be taken at face value.

Other pronouncements by Iranian leaders and by you, personally, Mr. President, are equally troubling Since Iran was one of the original signatories of the UN Charter, which affirmed the territorial integrity and sovereignty of all states, a right that you reaffirmed in your address to the United Nations on September 19, 2006, your call for the elimination of the state of Israel, questioning of its validity and mockery of the Holocaust are an affront to both logic and human decency. After all, Iran was one of the first countries to sign the Genocide Convention and—directly to that point —in 1942, was refuge for an estimated 115,000 Jewish refugees, mostly Polish, fleeing Nazi persecution In the poignant words of one Polish Jewish émigré, Helena Woloch, "Exhausted by hard labor, disease and starvation.. we disembarked at the port of Pahlevi [where] .we knelt down together in our thousands along the sandy shoreline to kiss the soil of Persia. We were free at last and had reached our long-for promised land " Iran has, in fact, one of the world's oldest Jewish communities. There is a mausoleum for the biblical figures Esther and Mordechai in Hamadan, and for David in Susa. One can disagree with Israeli policies and defend Palestinian rights without belittling the historical tragedy that befell the Jewish people.

In that connection, and in light of the current impasse in the region, the United States, together with leading Arab states, supports a two-state solution to the Palestinian-Israeli dispute. Ultimately, it is up to the Palestinians to negotiate an agreement that they believe is just and that will allow them to realize their long-sought aspiration

for statehood Once they do, the United States, the Arab League, Turkey and other powers, including Iran, have an obligation to help ensure that such an agreement is long-lasting and provides the region with much needed peace and an opportunity to fulfill its great economic and social potential

The time has come to acknowledge that mature countries living in an increasingly interdependent world can no longer afford to communicate through slogans, recriminations and tendentious rhetoric. Investing the precious financial and human resources of Iran in posturing and in demonizing the United States and its allies is conducive neither to mutual understanding nor peace Statesmen should eschew these affectations in favor of problem solving. The resolution of the endemic problems that divide the U.S. and Iran requires an honest, realistic and mutually respectful approach that lowers the temperature and volume of public oratory, and opens channels of quiet and discreet dialogue and diplomacy.

Despite Iran's roots in antiquity, it is, demographically, a young country, with more than two-thirds of the population under the age of thirty Improved, normal relations with the United States and its allies will help Iran achieve its tremendous potential and fulfill the specific responsibilities spelled out in your 1979 Constitution, which states that its ultimate objectives are:

"...achieving the economic independence of the society, uprooting poverty and deprivation, and fulfilling human needs in the process of development while preserving=2 0human liberty. ...[including] ensuring conditions and opportunities of employment for everyone, with a view to attaining full employment, ..and [allowing for] all citizens of the country, both men and women, to equally enjoy the protection of the law and enjoy all human, political, economic, social and cultural rights."

These are rights that resonate deeply with Americans. The United States takes pride in the fact that, prior to, and even after the severance of diplomatic relations with Iran, American universities provided opportunities for higher education and training for over 100,000 Iranian students, including doctors, engineers, architects and scholars in the humanities and social sciences. Americans also are gratified that there are an estimated one million Iranian-Americans living in the United States and fully integrated into American society Having taken full advantage of the opportunities that a free society offers to all our citizens, they have made significant contributions in many areas and have achieved impressive academic, professional and financial success while retaining their cultural heritage.

The United States welcomes a new chapter in the history of both Iran and the U.S. that builds on the vibrant record of cooperation and goodwill that has long marked Iranian-America relations, and offers even greater opportunities for the people of both countries to prosper and live in peace. In the wise and timeless words of guidance from the great Hazrat Ali ibn Abi Talib, the fourth Caliph and son-in-law of the Prophet Mohammed, to the newly appointed governor of Egypt, ".. Peace will bring rest and comfort to your armies, will relieve you of anxieties and worries, and will bring prosperity and affluence to your people "

I close this letter with another quote from Caliph Ali, who is revered in Iran His words speak even more profoundly to the specific challenges and opportunities facing a great state, such as Iran, which seeks to follow the path of righteousness laid out by its founding spiritual leader, and recognizes the inherent fallibility, as well as redemptive potential, that marks the human condition.

"...There are two kinds of people, those who have the same religion as you [and] are brothers to you, and those who have religions other than yours, [who] are human beings like you. Men of either category suffer from the same weaknesses and disabilities that human beings are inclined to, they commit sins, indulge in vices either intentionally or foolishly and unintentional ly without realizing the enormity of their deeds Let your mercy and compassion come to their rescue and help in the same way and to the same extent that you expect Allah to show mercy and forgiveness to you."

Sincerely,

George W. Bush

B6

From: Huma Abedin [redacted]
Sent: Saturday, February 14, 2009 10:19 PM
To: humamabedin [redacted]
Subject: PrintFw: State/Treas

RELEASE IN PART B5,B6

-----Original Message-----
From. H <hdr22@clintonemail.com>
To Huma Abedin
Sent: Sat Feb 14 20:54:34 2009
Subject: Fw: State/Treas

Pls print.

From: Jake Sullivan
Date: Sat, 14 Feb 2009 20:09:37 -0500
To. <hdr22@clintonemail.com>
Subject: Re: State/Treas

B5

Again apologies -- not sure why these emails just arrived.

[redacted]

A paper laying out the basic structure we have proposed is in the binder you received tonight Happy to discuss further tomorrow.

On Sat, Feb 14, 2009 at 2:26 PM, H <hdr22@clintonemail.com> wrote: B5

[redacted]

From: H <hdr22@clintonemail com>
Sent: Saturday, February 14, 2009 11 21 PM
To: Bill Owens
Cc: Huma Abedin <HAbedin@hillaryclinton.com>
Subject: Following up

B6

RELEASE IN PART B6

Dear Bill--

I enjoyed talking w you about my upcoming trip to China and appreciate, as always, your insights and advice.

I hope I will be able to see you in Beijing, and, by copy of this email, I am asking my Deputy COS, Huma Abedin, to advise you of my schedule so we can try to connect in person while I'm there.

In any event, I will follow up on the points you made in my meetings. All the best, Hillary

From: Capricia Penavic Marshall [redacted] B6
Sent: Saturday, February 14, 2009 11 25 PM
To: hdr22@clintonemail com
Subject:

RELEASE IN PART
B6

Please let me know if you still need to speak

From: Abedin, Huma <AbedinH@state.gov>
Sent: Sunday, February 15, 2009 6:51 AM
To: humamabedin[redacted] B6
Subject: Marina print
Attach: StateBriefing090215[1].doc; StateClips090215[1].doc

RELEASE IN PART B6

From: Diekman, Lauren M
To: Abedin, Huma
Cc: S_SpecialAssistants; SES-O_OS; SES-O_SWO-Only
Sent: Sun Feb 15 06:00:51 2009
Subject: Daily Press Clips and News Briefing

Ms. Abedin,

Please see the attached Press Clips and News Briefing as requested.

Thank you,

Lauren Diekman
Operations Specialist
State Department Operations, S/ES-O

HA 09/01/2015

From: Valmoro, Lona J <ValmoroLJ@state.gov>
Sent: Sunday, February 15, 2009 9:58 AM
To: Abedin, Huma <AbedinH@state.gov>; humamabedi[redacted]
Subject: final schedule for monday -- attached
Attach: February.16.09.final.doc

B6

RELEASE IN PART
B6

SCHEDULE FOR SECRETARY HILLARY RODHAM CLINTON
MONDAY, FEBRUARY 16, 2009

RELEASE IN PART B6

FINAL

TOKYO, JAPAN

SPECIAL ASSISTANT:	**LONA VALMORO**	
	OFFICE (202) 647-9071	B6
	CELL	
STAFF ASSISTANT:	**LINDA DEWAN**	
	OFFICE (202) 647-5733	
	CELL	
TOKYO:	**JASON MACK**	
	CELL	
JAKARTA:	**EUGENE BAE**	
	CELL	
SEOUL:	**JR LITTLEJOHN**	
	CELL	
BEIJING:	**KATIE STANA**	
	CELL	

PREV RON En route Tokyo

7:30 pm (5:30 am EST) **ARRIVE** Haneda Airport,Tokyo

Greeters: James Zumwalt, Charge d'Affaires
Ms. Ann Kambara, Tokyo American Center Director
Shintaro Ito, State Secretary For Foreign Affairs
Ambassador Ichiro Fujisaki, Japanese Ambassador to the U.S.
Mr. Kazuyoshi Umemoto, MFA DG First North American Bureau
Mr Yoshinori Furkawa, Haneda Airport Administration

7:40 pm
8:00 pm **ARRIVAL CEREMONY IN TOKYO**
VIP Imperial Room, Haneda Airport
OPEN PRESS

- HRC enters the room with Charge Zumwalt, Ms. Kambara, A/S Hill and GOJ Officials.

- State Secretary for Foreign Affairs Shintaro Ito makes welcoming remarks.

SCHEDULE FOR SECRETARY HILLARY RODHAM CLINTON
MONDAY, FEBRUARY 16, 2009

- HRC makes brief remarks, takes group photos with the Special Olympians and astronauts, and departs.

8:05 pm **DEPART** Haneda Airport
En route Hotel Okura
[drive time. 25 minutes]

Main: HRC, Huma
Spare Limo: Sullivan
Charge Limo: Zumwalt and Kambara
Staff Van 1: Bader, Selva, Stern, and Wood
Staff Van 2: Alston, Lumpkin, Macmanus, Muscatine, and Wohlers
Staff Van 3: Beale, Coleman, and Crosby
Press Van: Kiki McLean, Simon and Traveling Press

8:30 pm **ARRIVE** Hotel Okura
(6:30 am EST)

Greeter: Mr. Noriyoshi Ogawa, President and General Manager, Hotel Okura

HRC RON Hotel Okura
WJC RON [redacted] B6

Weather:
Tokyo, Japan: Partly cloudy, high 54, low 37.

RON: Hotel Okura Tokyo
2-10-4 Toranomon
Minato-ku, Tokyo 105-001 Japan
Phone: + 81 (3) 3582-0111
Fax: +81 (3) 3582-3707

From: Abedin, Huma <AbedinH@state.gov>
Sent: Sunday, February 15, 2009 11:08 AM
To: humamabedin [redacted] B6
Subject: Fw: Last Asia trip pre-departure schedule
Attach: Secy Clinton Asia trip schedule 2-09 doc.docx

RELEASE IN PART B7(C),B6

From: Wohlers, Paul
To: Bennett, Virginia L; Sullivan, Jacob J; Abedin, Huma; McLean, Lori A; Slaughter, Anne-Marie; Burns, Deborah M; Valmoro, Lona J; Shapiro, Andrew J; Miotke, Jeffrey A (OES); 'Lissa Muscatine' ; Lukens, Lewis A; D Duty Officer; Sim Jessica L (PACE); Coleman, Claire L; Macmanus, Joseph E; Wood, Robert A (PACE); Cook, Brian K; [redacted] B6 B7(C) (DS/P/SD); [redacted] Col JCS SJS ACJCS' ; 'jbader [redacted]; Stern, Todd D
Cc: Beale, Courtney A Kramer; Crosby, John R; Ruggles, Taylor V; Smith, Daniel B; Merten, Kenneth H; Zeya, Uzra S; Thompson, Dean R; Sullivan, Stephanie S; SES-O_SWO-Only; Davis, Jennifer L (S Staff); Bishop, Christopher W; Russell, Daniel A; Crocker, Bathsheba N; Dewan, Linda L; Adler, Caroline E; Davies, Glyn T; Arvizu, Alex A; Marciel, Scot A; Scandola, JoAnn E; Norris, John J
Sent: Sat Feb 14 21:24:42 2009 B6
Subject: Last Asia trip pre-departure schedule

I also will be bringing copies to the plane tomorrow. From then on, final daily schedules will be coming from the advance officers.

Paul D. Wohlers
Deputy Executive Secretary, S/ES
202-647-5302

From: H <hdr22@clintonemail.com>
Sent: Sunday, February 15, 2009 9:42 PM
To: Cheryl Mills [redacted] B6
Subject: Re. Any word from Kim?

RELEASE IN PART B6

Let me know I'm taking off. Bye.
------Original Message------
From: Cheryl Mills
To. hdr22@clintonemail com
Sent: Feb 15, 2009 9.40 PM
Subject: RE. Any word from Kim?

yes- tomorrow.

but we only have a cell that he indicates that he does not take messages from

-----Original Message-----
From. H [mailto:hdr22@clintonemail.com]
Sent. Sunday, February 15, 2009 9:40 PM
To· Cheryl Mills
Subject· Re: Any word from Kim?

Should I call him?
------Original Message------
From· Cheryl Mills
To: hdr22@clintonemail com
Sent· Feb 15, 2009 9:37 PM
Subject: RE: Any word from Kim?

not yet - he may take weekend to mean through Monday given it's a holiday

-----Original Message-----
From H [mailto:hdr22@clintonemail.com]
Sent. Sunday, February 15, 2009 9·37 PM
To Cheryl Mills
Subject: Any word from Kim?

From: Abedin, Huma <AbedinH@state.gov>
Sent: Thursday, February 19, 2009 11:05 AM
To: humamabedin [redacted] B6
Subject: PrintFw: U.S. Commission on International Religious Freedom - 22 USC 6431

RELEASE IN PART B6

From: Mills, Cheryl D
To: Abedin, Huma
Cc: 'hdr22@clintonemail.com'
Sent: Thu Feb 19 09:36:49 2009
Subject: FW: U.S. Commission on International Religious Freedom - 22 USC 6431

FYI - can't recall if she got this but shared the substance with her.

From: Kennedy, Patrick F
To: Mills, Cheryl D
Sent: Tue Feb 17 19:08:41 2009
Subject: U.S. Commission on International Religious Freedom - 22 USC 6431
Cheryl

Per discussion today

9 member body ? three appointed by POTUS, three by House, and three by Senate

Amb. at Large is ex-officio, non-voting member

Regards

pat

§ 6431. Establishment and composition

How Current is This?

(a) In general

There is established the United States Commission on International Religious Freedom.

(b) Membership

(1) Appointment

The Commission shall be composed of?

(A) the Ambassador at Large, who shall serve ex officio as a nonvoting member of the Commission; and

(B) Nine [1] other members, who shall be United States citizens who are not being paid as officers or employees of the United States, and who shall be appointed as follows:

(i) Three members of the Commission shall be appointed by the President.

(ii) Three members of the Commission shall be appointed by the President pro tempore of the Senate, of which two of the members shall be appointed upon the recommendation of the leader in the Senate of the political party that is not the political party of the President, and of which one of the members shall be appointed upon the recommendation of the leader in the Senate of the other political party.

(iii) Three members of the Commission shall be appointed by the Speaker of the House of Representatives, of which two of the members shall be appointed upon the recommendation of the leader in the House of the political party that is not the political party of the President, and of which one of the members shall be appointed upon the recommendation of the leader in the House of the other political party.

(2) Selection

(A) In general

Members of the Commission shall be selected among distinguished individuals noted for their knowledge and experience in fields relevant to the issue of international religious freedom, including foreign affairs, direct experience abroad, human rights, and international law.

(B) Security clearances

Each member of the Commission shall be required to obtain a security clearance.

(3) Time of appointment

The appointments required by paragraph (1) shall be made not later than 120 days after October 27, 1998.

(c) Terms

(1) In general

The term of office of each member of the Commission shall be 2 years. The term of each member of the Commission appointed to the first two-year term of the Commission shall be considered to have begun on May 15, 1999, and shall end on May 14, 2001, regardless of the date of appointment to the Commission. The term of each member of the Commission appointed to the second two-year term of the Commission shall begin on May 15, 2001, and shall end on May 14, 2003, regardless of the date of appointment to the Commission. In the case in which a vacancy in the membership of the Commission is filled during a two-year term of the Commission, such membership on the Commission shall terminate at the end of that two-year term of the Commission. Members of the Commission shall be eligible for reappointment to a second term.

(2) Establishment of staggered terms

(A) In general

Notwithstanding paragraph (1), members of the Commission appointed to serve on the Commission during the period May 15, 2003, through May 14, 2005, shall be appointed to terms in accordance with the provisions of this paragraph.

(B) Presidential appointments

Of the three members of the Commission appointed by the President under subsection (b)(1)(B)(i) of this section, two shall be appointed to a 1-year term and one shall be appointed to a 2-year term.

(C) Appointments by the President pro tempore of the Senate

Of the three members of the Commission appointed by the President pro tempore of the Senate under subsection (b)(1)(B)(ii) of this section, one of the appointments made upon the recommendation of the leader in the Senate of the political party that is not the political party of the President shall be appointed to a 1-year term, and the other two appointments under such clause shall be 2-year terms.

(D) Appointments by the Speaker of the House of Representatives

Of the three members of the Commission appointed by the Speaker of the House of Representatives under subsection (b)(1)(B)(iii) of this section, one of the appointments made upon the recommendation of the leader in the House of the political party that is not the political party of the President shall be to a 1-year term, and the other two appointments under such clause shall be 2-year terms.

(E) Appointments to 1-year terms

The term of each member of the Commission appointed to a 1-year term shall be considered to have begun on May 15, 2003, and shall end on May 14, 2004, regardless of the date of the appointment to the Commission. Each vacancy which occurs upon the expiration of the term of a member appointed to a 1-year term shall be filled by the appointment of a successor to a 2-year term.

(F) Appointments to 2-year terms

Each appointment of a member to a two-year term shall identify the member succeeded thereby, and each such term shall end on May 14 of the year that is at least two years after the expiration of the previous term, regardless of the date of the appointment to the Commission.

(d) Election of Chair

At the first meeting of the Commission after May 30 of each year, a majority of the members of the Commission present and voting shall elect the Chair of the Commission.

(e) Quorum

Six voting members of the Commission shall constitute a quorum for purposes of transacting business.

(f) Meetings

Each year, within 15 days, or as soon as practicable, after the issuance of the Country Report on Human Rights Practices, the Commission shall convene. The Commission shall otherwise meet at the call of the Chair or, if no Chair has been elected for that calendar year, at the call of six voting members of the Commission.

(g) Vacancies

Any vacancy of the Commission shall not affect its powers, but shall be filled in the manner in which the original appointment was made. A member may serve after the expiration of that member?s term until a

successor has taken office. Any member appointed to fill a vacancy occurring before the expiration of the term for which the member?s predecessor was appointed shall be appointed only for the remainder of that term.

(h) Administrative support

The Administrator of General Services shall provide to the Commission on a reimbursable basis (or, in the discretion of the Administrator, on a nonreimbursable basis) such administrative support services as the Commission may request to carry out the provisions of this subchapter.

(i) Funding

Members of the Commission shall be allowed travel expenses, including per diem in lieu of subsistence at rates authorized for employees of agencies under subchapter I of chapter 57 of title 5 while away from their homes or regular places of business in the performance of services for the Commission.

From: Abedin, Huma <AbedinH@state.gov>
Sent: Thursday, February 19, 2009 11:05 AM
To: humamabedin [redacted] B6
Subject: PrintFw: NOTE to HRC from J Prince (you can print attached if easier)
Attach: 2009-02-18 Memo for S from JPrince - draft.docx; ATT61682.txt

RELEASE IN PART
B5,B6

----- Original Message -----
From: Mills, Cheryl D
To: Abedin, Huma
Cc: Mills, Cheryl D; 'hdr22@clintonemail.com' <hdr22@clintonemail.com>
Sent: Thu Feb 19 09:30:37 2009
Subject: FW: NOTE to HRC from J Prince (you can print attached if easier)

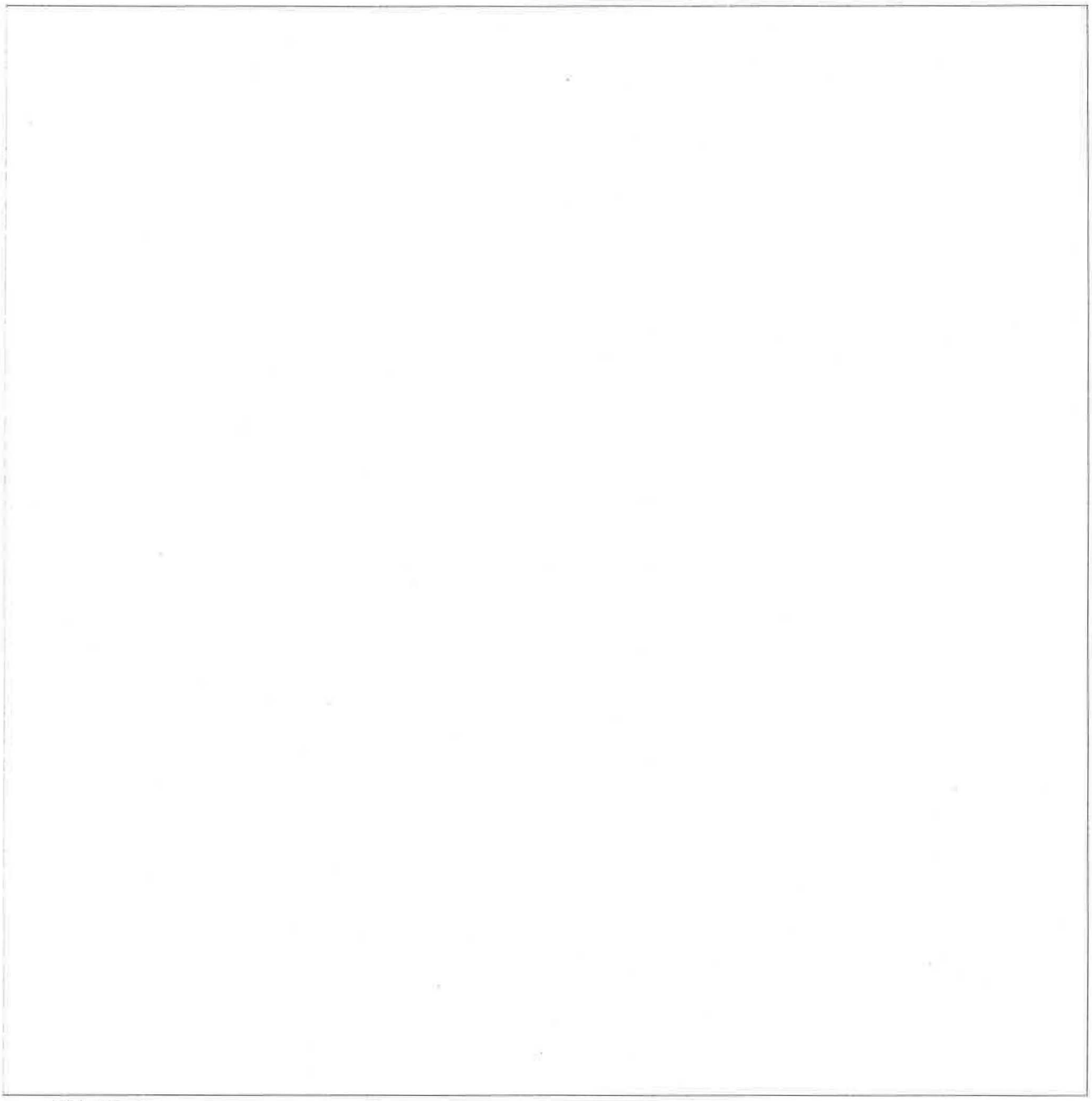
NOTE FOR THE SECRETARY
February 18, 2009

B5

FROM: Jonathan Prince
SUBJECT: Putting the diplomacy back in public diplomacy

[redacted]

B5



-----Original Message-----
From: Jonathan Prince [redacted] B6
Sent: Wednesday, February 18, 2009 3:28 PM
To: Mills, Cheryl D
Subject: note

Here you go, I bolded a few sentences too, the ones that were essentially recs, and [redacted] B5

From: Burns Strider
Sent: Thursday, February 19, 2009 5.50 PM
To: hdr22@clintonemail.com
Subject: RE: YOU GO!!!

B6

RELEASE IN PART
B6

You would have to travel to all my old "20-something" stomping grounds for your first trip... it totally exacerbates my envy! The Baptist Mission offices for Japan are in the area of Tokyo that houses many of the foreign embassies and legations... the Mission has marvelous quarters for guests...

I always found the silence around the legislative building in Tokyo (isn't it called the Diet or something like that?) pretty analogous to how little is really known of how things are moved to reality and fruition in their governmental processes... Japan is more of an enigma to me than China... there's something basic, core-like about China (not always good) that I felt and understood...

Beijing is a remarkable city... one of my favorites on the globe... there's a hill on the backside of the Forbidden City... the hill is called Jingshahn... its man-made with a massive open pagoda at the top... it was made to keep the evil spirits from the north out of the Forbidden City...

BTW: the news coming out of your trip is refreshing... it's a very American trip you are carrying out... how long has it been since Americans have been able to open the paper and see their voice to the world lecturing at a foreign university... talking about Democratic ideals and the human experience as seen through the American dream... its really cool what you are doing...

Hang in there...

Burns Strider
Founding Partner
The Eleison Group

www.eleisongroup.com

From: H [mailto:hdr22@clintonemail.com]
Sent: Wednesday, February 18, 2009 11:56 AM
To: Burns Strider
Subject: Re: YOU GO!!!

Thanks for keeping up w me! This is sent all the way from Jakarta.

HA 09/01/2015

From: "Burns Strider"
Date: Tue, 17 Feb 2009 13:17:32 -0500
To: Clinton Hillary<hdr22@clintonemail.com>
Subject: YOU GO!!!

"Clinton's remarks came in response to a question about the "prejudice" in the United States against Muslims because of terrorism, a term she rejected forcefully, pointing to the history of Christians. 'I am a Christian,' she said. 'Through the centuries we have had many people who have done terrible things in the name of Christianity. They have perverted the religion.'"

This is one of your strongest areas when discussing faith, if I may say so, boss .. Not knocking your brand but honestly assessing the perversions wrought by human dictate vs the authentic, pure and lofty ideals taught and exemplified by God... You do it naturally when talking about your own denomination and when talking about faith writ large...

There's an intrinsic value found in the world's holy teachings that is found nowhere else. The Golden Rule abounds across the spectrum, for example... Beyond the shadows of human failure there's a common purpose and good that inspires all the nations...

Burns Strider
Founding Partner
The Eleison Group

www.eleisongroup.com

From: Huma Abedin [redacted] B6
Sent: Friday, February 20, 2009 10 27 AM
To: hdr22@clintonemail com
Subject:

RELEASE IN PART B6

Steinbergs office thinks you are trying to reach him Ops can connect you if you do
I tried to knock on your door to check [redacted]
Will wake you at 7am

From: H <hdr22@clintonemail.com>
Sent: Saturday, February 21, 2009 11:48 PM
To: Huma Abedin <HAbedin@hillaryclinton.com>
Subject: Fw: Fwd: A case of great minds perhaps????Capitalizing on Connectivity

RELEASE IN PART
B6

Pls print.

B6

B6

From: williamsbarrett
Date: Sat, 21 Feb 2009 18:32:03 -0500
To: <hdr22@clintonemail.com>; <cmills
Subject: Fwd: A case of great minds perhaps????Capitalizing on Connectivity

Note from Judith after having read this article - (thanks for this Cheryl - was Anne-Marie preparing a more formal memo on public diplomacy

I swear I did not read this before I wrote the memo I just sent!!! However, it does support the proposition I described. Nice to know many of us are on the same page. Now all we have to do its make it happen, and fast!

JM

How to Succeed in the Networked Century

By Bradley W. Bloch, Huffington Post
Posted February 20, 2009 | 10:12 AM (EST)

A large part of the reason Barack20Obama defeated Hillary Clinton in last year's Democratic primary can be reduced to the fact that he mobilized his bottom-up network better than she mobilized her top-down one. So it was notable that even before formally taking over the State Department, Clinton named Anne-Marie Slaughter, Dean of Princeton's Woodrow Wilson School, to lead the department's internal think tank, the Policy Planning Staff. Slaughter has been a vocal advocate of viewing the world through a network lens. Most recently, her article in the current issue of Foreign Affairs, "America's Edge: Power in the Networked Century," argues that America's best future lies in positioning itself as the world's most networked nation, the hub of information, ideas, and resources flowing though the global economy

I couldn't agree more, having argued here that the White House, rather than focusing on illusory conflicts of interest involving the Clinton Foundation, should be encouraging the State Department to steal what they can from the Clinton Global Initiative and similar groups -- organizations that facilitate innovation by acting as the network broker between innovators, governments, and private enterprise. Slaughter's article extends this argument to important policy arenas, but in the process raises an important issue that will need to be addressed if networks are to play a substantial role in securing America's place in the world.

As Slaughter points=2 0out, the ability to innovate, seize opportunity, and marshal resources to advance an agenda boils down to managing and orchestrating networks Slaughter cites a number of examples of what can be achieved through what is sometimes called "network entrepreneurship": multinational collaboration regarding the financial crisis; the success of a coalition of NGOs in working to ban the use of land mines; and an improved response to public health threats through a network established by the Centers for Disease Control.

Unfortunately, these success stories are more the exception than the rule. The fact is that even in the upper echelons of decision-making, we are notoriously poor at managing and orchestrating networks. Indeed,

immeasurable opportunities are lost and efforts needlessly duplicated in areas ranging from global health to business development because our network skills are rooted in a less complex, more hierarchical, top-down past. For the United States to position itself as the most powerful player in "the networked century," those capabilities will have to evolve significantly. That will require two broad developments:

First, we need to take a more holistic, dynamic view of the people within our -- and everyone else's -- networks. We tend to think of people in terms of three attributes: their job title, where they have worked, and where they were educated. In an earlier time, this may have been sufficient to understand a person's place in a network and to fairly well guess their skills, who they0Amight be connected to, and what their priorities might be. In today's more fluid world, however, people cross borders, change careers, and recast alliances much more readily, each stage in their trajectory potentially expanding and reshaping their network -- and certainly reshaping who they are and what they have to offer.

This is the basis of Slaughter's contention that we need to view immigrant communities and the emerging generation of "First Globals" (18- to 29-year-old Americans who are inclined to live and study abroad in greater numbers than their predecessors) as potential links to new markets and opportunities around the globe But in order to do this, you need to know the various facets of a person's life -- where they've lived, what they're interested in personally and professionally, who their mentors have been and so on. In a networked world powered more on personal initiative, skill sets and relationships than hierarchical position, a person's job title and other résumé details no longer are as reliable indicators of a person's potential to effect change in the global network and the resources he or she commands.

Second, we need to become more methodical and data driven in our approach to networks. Professional sports like baseball and basketball have been in the midst of a data revolution that is reshaping how players are evaluated. Instead of relying merely on received wisdom and personal experience, coaches and scouts are using reams of data that are questioning=2 0old assumptions about what makes for a star player, and using that insight to build teams. (So it was that Nate Silver, whose political web site has set new standards for election forecasting, actually began as a baseball analyst.) There needs to be a similar data revolution in networks Rather than manage them in an ad hoc fashion with instinct and imperfect memories as we do now, we need to develop and use analytical tools that will allow us to track more complex networks, see patterns over time, and identify key players who act as the gateway to different clusters of ideas, resources, and support. Many components of these analytical tools exist, but they need to be further developed and brought into the mainstream.

Anne-Marie Slaughter is correct to see network entrepreneurship as the critical capability for the twenty-first century, in the same way that trade (itself a specialized example of network entrepreneurship) was in the mercantile period But maintaining oneself as a trading power required more than just ships and goods. It also required better navigation tools, most notably the discovery of a reliable means of measuring the longitude of ships at sea. The old method of dead reckoning -- and the risks it brought of inefficient routing if not catastrophic shipwreck -- was no longer acceptable. Solving the problem was considered so critical to the national interest that Britain established the Longitude Prize to spur on a solution.

=0 A

We don't need a similar "Network Prize"; many of the tools we need to understand networks already exist. Instead, we need public and private-sector decision makers to see that competitive advantage in the networked century goes to those who develop the most sophistication in using those tools and the networks they illuminate

America's Edge: Power in the Networked Century

By Anne-Marie Slaughter

From *Foreign Affairs* , January/February 2009

Summary: The United States' unique ability to capitalize on connectivity will make the twenty-first century an American century.

ANNE-MARIE SLAUGHTER is Dean of the Woodrow Wilson School of Public and International Affairs and Bert G. Kerstetter '66 University Professor of Politics and International Affairs at Princeton University.

We live in a networked world. War is networked: the power of terrorists and the militaries that would defeat them depend on small, mobile groups of warriors connected to one another and to intelligence, communications,

and support networks. Diplomacy is networked: managing international crises -- from SARS to climate change -- requires mobilizing international networks of public and private actors. Business is networked· every CEO advice manual published in the past decade has focused on the shift from the vertical world of hierarchy to the horizontal world of networks. Media are networked: online blogs and other forms of participatory media depend on contributions from readers to create a vast, networked conversation. Society is networked· the world of MySpace is creating a global world of "OurSpace," linking hundreds of millions of individuals across continents. Even religion is networked· as the pastor Rick Warren has argued, "The only thing big enough to solve the problems of spiritual emptiness, selfish leadership, poverty, disease, and ignorance is the network of millions of churches all around the world."

In this world, the measure of power is connectedness. Almost 30 years ago, the psychologist Carol Gilligan wrote about differences between the genders in their modes of thinking. She observed that men tend to see the world as made up of hierarchies of power and seek to get to the top, whereas women tend to see the world as containing webs of relationships and seek to move to the center. Gilligan's observations may be a function of nurture rather than nature; regardless, the two lenses she identified capture the differences between the twentieth-century and the twenty-first-century worlds.

The twentieth-century world was, at least in terms of geopolitics, a billiard-ball world, described by the political scientist Arnold Wolfers as a system of self-contained states colliding with one another. The results of these collisions were determined b y military and economic power. This world still exists today. Russia invades Georgia, Iran seeks nuclear weapons, the United States strengthens its ties with India as a hedge against a rising China. This is what Fareed Zakaria, the editor of Newsweek International, has dubbed "the post-American world," in which the rise of new global powers inevitably means the relative decline of U.S influence

The emerging networked world of the twenty-first century, however, exists above the state, below the state, and through the state. In this world, the state with the most connections will be the central player, able to set the global agenda and unlock innovation and sustainable growth. Here, the United States has a clear and sustainable edge.

THE HORIZON OF HOPE

The United States' advantage is rooted in demography, geography, and culture. The United States has a relatively small population, only 20-30 percent of the size of China's or India's. Having fewer people will make it much easier for the United States to develop and profit from new energy technologies. At the same time, the heterogeneity of the U.S. population will allow Washington to extend its global reach. To this end, the United States should see its immigrants as living links back to their home countries and encourage a two-way flow of people, products, and ideas.

The United States is the anchor of the Atlantic hemisphere, a broadly defined area that includes Africa, the Americas, and Europe. The leading countries in the Atlantic hemisphere are more peaceful, stable, and economically diversified than those in the Asian hemisphere. At the same time, however, the United States is a pivotal power, able to profit simultaneously from its position in the Atlantic hemisphere and from its deep ties to the Asian hemisphere The Atlantic and Pacific Oceans have long protected the United States from invasion and political interference. Soon, they will shield it from conflicts brought about by climate change, just as they are already reducing the amount of pollutants that head its way. The United States has a relatively horizontal social structure -- albeit one that has become more hierarchical with the growth of income inequality -- as well as a culture of entrepreneurship and innovation. These traits are great advantages in a global economy increasingly driven by networked clusters of the world's most creative people.

On January 20, 2009, Barack Obama will set about restoring the moral authority of the United States. The networked world provides a hopeful horizon. In this world, with the right policies, immigrants can be a source of jobs rather than a drain on resources, able to link their new home with markets and suppliers in their old homes. Businesses in the United States can orchestrate global networks of producers and suppliers. Consumers can buy locally, from revived local agricultural and customized small-business economies, and at the same time globally, from anywhere that can advertise online. The United States has the potential to be the most innovative and dynamic society anywhere in the world.

LIFE IN A NETWORKED WORLD

In 2000, Procter and Gamble made a decision that reinvented how the company would do business in the twenty-first century. Instead of closely guarding its secret recipes for everything from soaps to potato chips, Procter and Gamble chose to open up its patent portfolio, making virtually all its formulas available to anyone willing to pay a licensing fee. At the same time, it asked its top managers to bring in half of their ideas for new

products and services from outside the company. They now look to far-flung groups of inventors around the world and online, where innovators gather at sites such as InnoCentive, an auction Web site for ideas. Don Tapscott and Anthony Williams, the authors of Wikinomics· How Mass Collaboration Changes Everything, call businesses like InnoCentive "ideagoras," modern-day public squares that join people looking to sell their ideas with businesses seeking to buy them. In 2006, Samuel Palmisano, the head of IBM, predicted in these pages that corporations would move from being multinational, with small, self-replicated versions of themselves in every market, to being what he calls "globally integrated enterprises." Today, IBM funnels tasks to wherever they will be done best.

Consider the experience of Li and Fung, the world's largest and most successful export sourcing company. Its clients are retailers of virtually every kind of pr oduct known to man, or at least made by man. The job of Li and Fung is to identify suppliers from over 40 countries around the world and connect them in order to fill specific orders. The resulting networks must be fast, flexible, and able to work to a common high standard. According to William and Victor Fung, two of the current owners of the family business, the secret of sourcing is "orchestrating networks." It is the managerial equivalent of creating a system in which one can select a destination on a Paris metro map and see a possible route light up with a connecting web of differently colored lines -- except, of course, that riders at each station might have their own ideas about how best to travel.

At first, these global webs may seem to be just the next generation of outsourcing. But something much deeper is going on. Outsourcing requires a central command that specifies precisely what and how much should be produced and then, through an established hierarchy, communicates those decisions to producers in multiple nations. In contrast, under a system of peer production, supply chains become "value webs," in which suppliers become partners and, instead of just supplying products, actually collaborate on their design. Boeing is a particularly striking example, given how it could be seen as the heart of old-style manufacturing. It has shifted from being simply an airplane manufacturer to being a "systems integrator," relying on a horizontal network of partners collaborating in real time. The y share both risk and knowledge in order to achieve a higher level of performance It is not simply a change in form but a change in culture Hierarchy and control lose out to community, collaboration, and self-organization. At its core, a company can be quite small, often no more than a central node of leaders and manager-integrators. But with the right networks, it can reach anywhere innovators, factories, and service providers can be found. In this world, as Tapscott and Williams write, "only the connected will survive."

Nongovernmental organizations (NGOs), too, have realized the power of connections. An early example was the International Campaign to Ban Landmines, which began in 1991 as a coalition of six NGOs from North America and Europe. It eventually grew to include over 1,100 groups in some 60 countries, and with this breadth came clout. After it won the Nobel Peace Prize in 1997, the network successfully pushed for a global treaty banning the use of land mines (although China, Russia, and the United States, among others, have refused to sign it). NGOs pursuing other causes have followed suit. In 1995, a small group of human rights organizations began calling for the creation of an international criminal court to try war criminals. They succeeded in convincing governments to establish a permanent court in 1998. Today, the Coalition for the International Criminal Court includes over 2,000 organizations from every corner of the world, which are now working to expand the court's jurisdiction. More recently, a global alliance of NGOs has been instrumental in pushing for action to stop the ongoing violence in Darfur.

In each of these cases, NGOs gained leverage over otherwise reluctant states. They formed transnational networks that multiplied their lobbying power and put their message on the agendas of international institutions. As Francis Sejersted, then chair of the Nobel Committee, noted when he recognized the land-mine campaign, "The mobilisation and focusing of broad popular involvement which we have witnessed bears promise that goes beyond the present issue. It appears to have established a pattern for how to realise political aims at the global level."

Governments have been slower to understand twenty-first-century challenges and to reform themselves accordingly, but they, too, are gradually moving toward a more networked structure. A report entitled The Embassy of the Future, issued by the Center for Strategic and International Studies in 2007, calls for U.S. diplomats to be "decentralized, flexible, and mobile," as well as "connected, responsive, and informed." U.S. embassy staff would have a more "distributed presence," both virtually and physically, if they worked at multiple locations and with a wide range of different groups in their host countries.

Similarly, Julie Gerberding, director of the Centers for Disease Control, realized after the anthrax scare in 2001 and the SARS crisis in 2002 that the CDC needed to create a network of public and private actors from arou nd

the world. Managing this network would, in turn, require a much more flexible and horizontal organization at the CDC's headquarters, in Atlanta. Gerberding was expected to get results but lacked the authority necessary to produce them. For Gerberding, the solution was to find partners around the world and to connect them in ways that would allow for the creation and sharing of knowledge during a crisis. Many judges and government regulators have had a similar insight. Bankruptcy judges, for example, now communicate with one another around the world, signing agreements to manage together the bankruptcies of multinational corporations. The current financial crisis could have been even worse if the world's central bankers had not already been connected and able to coordinate their actions.

Power can also flow from connections across different sectors. In his book Superclass: The Global Power Elite and the World They Are Making, David Rothkopf explains how leaders connect across different power structures, from the worlds of business and finance to those of politics and the arts. "In fact," he writes, "such linkages are as distinguishing a characteristic of the superclass as wealth or individual position." In other words, it is connectivity, more than money or stature, that determines individual power. This dynamic can even extend to terrorist groups such as al Qaeda. John Robb, a former air force colonel and military strategist, has observed that Mohamed Atta was the leader of the 9/11 hijackers because, although no20formal hierarchy existed in the group, "Atta had twenty-two connections to other people in the network, much more than any other, which gave him control of the operation."

The power that flows from this type of connectivity is not the power to impose outcomes. Networks are not directed and controlled as much as they are managed and orchestrated. Multiple players are integrated into a whole that is greater than the sum of its parts -- an orchestra that plays differently according to the vision of its conductor and the talent of individual musicians Obama's team-based campaign, with its relatively flat structure and emphasis on individual organizers, is a model of the twenty-first century's management style.

Most important, networked power flows from the ability to make the maximum number of valuable connections. The next requirement is to have the knowledge and skills to harness that power to achieve a common purpose. The United States is already following this model in a few specific ways. In combating terrorism, it has been able to stop planned attacks thanks to a dense global network of law enforcement officers, counterterrorism officials, and intelligence agencies. The U.S. government dramatically improved its standing in the Muslim world due to its swift and effective relief effort in Asia following the December 2004 tsunami. It coordinated an emergency-response strategy among government agencies and aid workers in Australia, India, Japan, and the United States itself. More recently, when the20global financial crisis hit this past fall, the United States first reached out to central banks around the world to coordinate a monetary response and then reached out to central banks in key emerging markets to make sure their foreign currency needs were being met.

From this vantage point, predictions of an Asian century -- such as those made by Kishore Mahbubani, a foreign policy scholar and dean of the Lee Kwan Yew School of Public Policy, in Singapore -- seem premature. Even Zakaria's argument about "the rise of the rest" takes on a different significance. If, in a networked world, the issue is no longer relative power but centrality in an increasingly dense global web, then the explosion of innovation and entrepreneurship occurring today will provide that many more points of possible connection. The twenty-first century looks increasingly like another American century -- although it will likely be a century of the Americas rather than of just America

MORE PEOPLE, MORE PROBLEMS

Demography is often cited as the chief factor behind the relative decline of the West China and India make up over a third of the world's population, while Europe and Japan are actually shrinking and the United States is suddenly a relatively small nation of 300 million. This argument, however, rests largely on assumptions formed in the nineteenth and twentieth centuries. Throughout most of human history, territory and population translated into military and economic power. Military power de pended on the number of soldiers a state could put into the field, the amount of territory an enemy had to cross to conquer it, and the economy's ability to supply the state's army. Population size mattered for economic power because without trade a state needed a domestic market large enough for manufacturers and merchants to thrive. With trade, however, small mercantile nations such as the Netherlands and Portugal were able to punch far above their weight In the nineteenth century, to increase their power, small countries expanded their territory through colonization. But by the twentieth century, as political unrest in the colonial world grew, the advantages of trading rather than ruling became increasingly clear. Although the United States and the Soviet Union, two great continental powers, dominated the second half of the twentieth century, the countries that grew the richest were often the smallest. In 2007, the ten countries with the highest per capita GDPs all had populations smaller than that of New York City, with one

notable exception: the United States.

In the twenty-first century, less is more. Domestic markets must be big enough to allow national firms to obtain a foothold so as to withstand international competition (although such markets can be obtained through free-trade areas and economic unions). But beyond this minimum, if trade barriers are low and transportation and communication are cheap, then size will be more of a burden than a benefit. When both markets and production are global, t hen productive members of every society will generate income across multiple societies. Business managers in one country can generate value by orchestrating a global and disparate network of researchers, designers, manufacturers, marketers, and distributors. It will remain the responsibility of government, however, to provide for the less productive members of society, namely, the elderly, the young, the disabled, and the unemployed -- think of them as national overhead costs. From this perspective, the 300 million citizens in the United States look much more manageable than the more than a billion in China or India

A shrinking population can actually act as a catalyst for innovation. In China, the answer to many problems is simply to throw people at them -- both because people are the most available commodity and because the Chinese government needs to provide as many jobs as possible. In Japan, by contrast, the answer is to innovate. Nintendo, the Kyoto-based gaming giant, is bringing much of its manufacturing back to Japan from China and other parts of Asia. How can it possibly compete using high-cost Japanese labor? It will not have to -- its new factories are almost entirely automated, with only a handful of highly skilled employees needed to run them. This approach uses less energy, costs less, and guarantees a higher standard of living for the Japanese population As the priority shifts from economic growth to sustainable growth, the formula of fewer people plus better and greener technology will look=2 0increasingly attractive.

Finally, size carries its own set of political challenges. Over the past four centuries, the arrow of history has pointed in the direction of national self-determination. Empires and multiethnic countries have steadily divided and subdivided into smaller units so that nations, or dominant ethnic groups, could govern themselves. Ninety years after Woodrow Wilson laid out his vision of self-determination for the Balkan states, the process continues in Kosovo In many ways, the breakup of the Soviet Union was another round of the decolonization and self-determination movement that began in the 1940s. It continues today with the conflicts over Abkhazia and South Ossetia, as well as with the potential for conflict on the Crimean Peninsula and in eastern Ukraine. Much of China's 5,000-year history has been a saga of the country's splitting apart and being welded back together. The Chinese government, like the Indian government, legitimately fears that current pockets of instability could quickly translate into multiple secessionist movements.

The United States faces no threats to its essential unity, which has been forged by a political and cultural ideology of unity amid diversity. The principal alternative to this ideology is the solution employed by the European Union and the Association of Southeast Asian Nations (ASEAN), in which individual states come together as larger economic and, gradually, quasi-political units. The most promising dimension of recent Chinese politics has been its adopt ion of a version of this solution with regard to Hong Kong and Macao -- and one day Beijing may apply this model to Taiwan.

The United States benefits not only from its limited population but also from who makes up that population. It has long attracted the world's most entrepreneurial, creative, and determined individuals. A vast mixing of cultures has created an atmosphere for a fruitful cross-fertilization and innovation. These arguments still hold. In San Francisco, for instance, a new municipal telephone help line advertises that it can talk with callers in over 150 languages. This diversity, and the creativity that it produces, is visible everywhere: in Hollywood movies, in American music, and at U.S. universities. At Princeton University this past fall, five of the six student award winners for the highest grade point averages had come from abroad: from China, Germany, Moldova, Slovenia, and Turkey.

In the nineteenth- and twentieth-century era of nation-states, the United States absorbed its immigrants and molded them into Americans, thereby creating the national cohesion necessary to build military and economic strength. Today, diversity in the United States means something more. Immigrant communities flourish not only in large cities but also in smaller towns and rural areas. A mosaic has replaced the melting pot, and, more than ever, immigrants connect their new communities to their countries of origin. Along the southern border of the United States, for instance, immigration experts talk abo ut "transnational communities," about clusters of families in the United States linked with the villages of Mexico and Central America. Now, where you are from means where you can, and do, go back to -- and whom you know and trust enough to network with.

Consider, for example, how valuable the overseas Chinese community has been to China. Alan Wang, a former student of mine, was born in China, moved to Australia with his family at the age of 12, and went to college and

law school there. He later came to the United States to pursue a graduate degree at Harvard For a while, he practiced law with a large British firm in London, and then moved to its Shanghai office. When I asked him how he identified himself, he replied, "overseas Chinese." Millions of people similar to Wang have spread out from China throughout Southeast Asia, Australia, the United States, and Canada, creating trading and networking opportunities for people in all those places. Similarly, the United States must learn to think of its ethnic communities as the source of future generations of "overseas Americans." Already, young Chinese Americans and Indian Americans are heading back to their parents' homelands to seek opportunity and make their fortunes. Soon, the children of U.S. immigrants from Africa, Asia, Latin America, and the Middle East will follow a similar path and return to their ethnic homelands, at least for a time. The key to succeeding in a networked economy is being able to harvest the best ideas and innovatio ns from the widest array of sources. In this regard, the United States is plugged into all corners of the global brain.

Beyond its immigrant communities, the United States can also depend on a new generation to forge connections around the world. John Zogby, the influential pollster, calls Americans between the ages of 18 and 29 "the First Globals," a group he describes as "more networked and globally engaged than members of any similar age cohort in American history." More than half of the respondents aged 18 to 29 in a poll conducted in the United States in June 2007 by Zogby International said that they had friends or family living outside the United States, vastly more than any other U.S. age group. Other Zogby polls have shown that this generation holds passports in roughly the same proportion as other age groups but uses them far more frequently. A quarter of this group, according to Zogby's data, believes that they will "end up living for some significant period in a country other than America."

These young people spreading out around the world will be a huge asset to the United States. Children born abroad who acquire U.S. citizenship as a result of their parents' heritage or life decisions will add to this number. A college classmate of mine was born to Hungarian immigrants in Canada and later acquired U.S. citizenship. After graduation, he moved to China and then Japan, where he gained a Japanese residency permit while also applying for Hungarian citizenship He20now lives with his Chinese wife in Beijing, where his daughter was born. Not long after her birth, he took her to Tokyo so that she could register as a U.S. citizen and reenter China on a U.S. passport. These stories are legion in any large global city -- couples from two different countries who are raising their children in a third or fourth or even fifth country. For many people who orbit in this floating cloud of nationalities, a U S. passport, particularly now that the United States has relaxed its rules on dual citizenship, has become a new kind of reserve currency. With one, even the most venturesome and peripatetic have the guarantee of the political and cultural stability of the West. The United States must devise the incentives and conditions that will allow it to both encourage this phenomenon and profit from it.

THE WORLD IS ROUND AGAIN

For most of modern history, the Eurocentric view of the world has placed North and South America in a hemisphere of their own -- the Western Hemisphere. Today, the world is mapped in the round, with Asia in the East and Africa, the Americas, and Europe in the West. That, at least, is how some Asians increasingly think of themselves. In his recently published book, The New Asian Hemisphere: The Irresistible Shift of Global Power to the East, Mahbubani argues that the era of "Western domination of world history is over" and that the world is witnessing an "Asian march to modernity."

But if half of t he world is now "the East," defined as the Asian hemisphere, then the other half is the Atlantic hemisphere, made up of Africa, the Americas, and Europe. It is quite a promising neighborhood, home to a wealth of human, economic, material, and natural resources. Politically, Europe and North America constitute a spreading community of liberal democracies that accounts for one-sixth of the world's population, almost 60 percent of global GDP, and the two primary global reserve currencies. More trade and direct investment pass over the Atlantic Ocean than any other part of the world -- over $2 trillion in cumulative foreign direct investment alone. The potential for further integration of the hemisphere is enormous.

Even more important is the potential for deeper economic integration within the Americas On energy questions, Canadian oil sands and Brazilian sugar cane are more promising than depending on Russian pipelines or Sudanese oil. Markets for renewable energy -- such as from biomass, wind, geothermal technology, and other sources -- are growing in Latin America. Miami is already a financial center for Latin America, and the steady growth of the Latino population in the United States will only deepen intra-American investment. The rise of Brazil and, to a somewhat lesser extent, Mexico will create an emerging counterbalance to the United States south of its border. But any initiative for strengthening economic ties must come from the United States itself. It first must address its immigration policy and then, si milar to the economic and political assistance it provided

From: Huma Abedin <habedin [redacted] B6
Sent: Sunday, February 22, 2009 12:15 AM
To: humamabedin [redacted]
Subject: PrintFw: Fwd: Memo for the Secretary of State
Attach: Memo to the Secretary of State 02.18.09:doc

RELEASE IN PART
B6

-----Original Message-----
From. H <hdr22@clintonemail.com>
To. Huma Abedin
Sent: Sat Feb 21 23:47.51 2009
Subject Fw: Fwd Memo for the Secretary of State

P <<Memo to the Secretary of State 02 18.09.doc>> ls print.

From williamsbarrett [redacted]
Date: Sat, 21 Feb 2009 18:26.59 -0500
To. <hdr22@clintonemail.com>
Subject: Fwd: Memo for the Secretary of State

This is the memo we discussed

B6

From: Huma Abedin [redacted]
Sent: Sunday, February 22, 2009 12:16 AM
To: humamabedin [redacted]
Subject: PrFw:

RELEASE IN PART B6

-----Original Message-----
From: H <hdr22@clintonemail com>
To. Huma Abedin
Sent. Sat Feb 21 23:48:07 2009
Subject: Fw:

Pls print.
------Original Message------
From Bill Owens
To: 'hdr22@clintonemail.com'
Sent: Feb 21, 2009 6:38 PM
Subject:

Dear Hillary,

I think your "listening tour" has been inspiring to all of us who have cared about our relationships with Asia. I had dinner last night in Beijing with about a dozen very well placed senior generals and politicians You would have liked their comments about your visit. I'm proud of what you're doing and always here to help when I can It was very nice to see you at the Embassy. After such an arduous trip, I thought you were great with the staff/Marines/Peace Corps (and the kids!).

I hope you'll have a chance to think about the "complementary engagement" one pager on mil/econ/political friendships (which I'm afraid I too quickly passed to you). I think the effort is helpful to what you're doing on a more formal level

Warm best wishes, I'm cheering for you, Bill Owens

B6

From: Huma Abedin [redacted]
Sent: Sunday, February 22, 2009 12:16 AM
To: humamabedin [redacted]
Subject: PrFw: Fwd: a second memo
Attach: McHale Memo II to SecState 02.19.09.doc

RELEASE IN PART B6

-----Original Message-----
From. H <hdr22@clintonemail com>
To: Huma Abedin
Sent: Sat Feb 21 23 48.38 2009
Subject: Fw Fwd: a second memo

P <<McHale Memo II to SecState 02.19.09.doc>> ls print.

From: williamsbarret [redacted]
Date Sat, 21 Feb 2009 18:28:16 -0500
To: <hdr22@clintonemail.com>, <cmills [redacted]
Subject Fwd a second memo

This is second memo prepared by Judith - follow up to the first. m

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From: Roy Spence [redacted] B6
Sent: Sunday, February 22, 2009 4:45 PM
To: hdr22@clintonemail.com
Cc: Hillary Clinton <hr15@att.blackberry net>
Subject: Madame Sis-Your trip was incredible. Of course I was not there...

RELEASE IN PART
B6

But the look and feel and the out pouring of "love and respect for you" and your core purpose of standing for the ideal that everyone should have the opportunity to live up his or her god-given potential-may not spoken-but from the visuals and the blogs ---was deeply displayed...especially with the women and young women. I simply do not know quite how you keep doing all the good you do...but I thank God for you [redacted]

[redacted] Maggie/Cheryl and team is moving the Gallup world poll stuff forward-Judy and I met with them 2 times. The data is stunning.
Like you...

Love you-your devoted Bro!!!

RS
Ride at Dawn

From: H <hdr22@clintonemail.com>
Sent: Sunday, February 22, 2009 6:39 PM
To: Maggie Williams [redacted]
Subject: Re: Fwd. a second memo

B6

RELEASE IN PART
B6

I just landed and will have these printed I'd like to set up a time to meet w you and Judith soon Hope all is well

From: williamsbarrett[redacted]
Date: Sat, 21 Feb 2009 18:28 16 -0500
To. <hdr22@clintonemail.com>; <cmill[redacted]
Subject. Fwd a second memo

This is second memo prepared by Judith - follow up to the first. m

HA 09/01/2015

From: Strobe Talbott [redacted]
Sent: Sunday, February 22, 2009 7:51 PM
To: HRC <hr15@att.blackberry.net>
Subject: an early rave review is already in...

B6

RELEASE IN PART B6

Andrea Mitchell came by our house straight from Andrews (to pick up Alan who was here for a book party), and she was exceedingly positive about how the trip played within the press corps in the back of the plane. And she's not a pushover on such things. So by that standard, as well as others, feel good. And welcome home. S.

==========

Strobe Talbott
President, The Brookings Institution
1775 Massachusetts Avenue NW
Washington, DC 20036
[redacted]

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B6

RELEASE IN PART
B6

From: H <hdr22@clintonemail.com>
Sent: Sunday, February 22, 2009 9:31 PM
To: Cheryl Mills [redacted]
Subject: Re: Can we talk tonight?

Great. Are you calling secure?
------Original Message------
From: Cheryl Mills
To: hdr22@clintonemail.com
Sent Feb 22, 2009 8:58 PM
Subject: Re: Can we talk tonight?

I can do now

-----Original Message----
From. H <hdr22@clintonemail.com>
To: Cheryl Mills
Sent: Sun Feb 22 18:37:51 2009
Subject Can we talk tonight?

I just landed and will be home shortly We can try a secure call at your convenience. [redacted] Let me know what time works.

From: H <hdr22@clintonemail com> B6
Sent: Sunday, February 22, 2009 9:54 PM
To: Cheryl Mills
Subject: Re: Can we talk tonight?

RELEASE IN PART
B6

I'm holding on a secure line. Are you also trying to get on?
------Original Message------
From: Cheryl Mills
To: hdr22@clintonemail.com
Sent: Feb 22, 2009 9 39 PM
Subject: RE. Can we talk tonight?

they were supposed to connect us - I called some time ago to do a secure call with you -- call them and ask them to try the connection

-----Original Message-----
From. H [mailto:hdr22@clintonemail com]
Sent: Sunday, February 22, 2009 9 39 PM
To: Cheryl Mills
Subject: Re Can we talk tonight?

Are you calling me? What #? I called ops and they gave me your "secure" cell which I just tried but only got a long high pitched whining sound
------Original Message------
From: Cheryl Mills
To: hdr22@clintonemail.com
Sent: Feb 22, 2009 8.58 PM
Subject: Re Can we talk tonight?

I can do now

-----Original Message-----
From. H <hdr22@clintonemail com>
To: Cheryl Mills
Sent: Sun Feb 22 18:37:51 2009
Subject Can we talk tonight?

I just landed and will be home shortly. We can try a secure call at your convenience. Let me know what time works.

From: Cheryl Mills [redacted] B6
Sent: Sunday, February 22, 2009 10:02 PM
To: hdr22@clintonemail.com
Subject: Re: Can we talk tonight?

RELEASE IN PART B6

I just spoke to ops and called you reg line - we have to wait until we see each other b/c thje technology is not working

-----Original Message-----
From. H <hdr22@clintonemail.com>
To: Cheryl Mills
Sent: Sun Feb 22 21:38:46 2009
Subject. Re: Can we talk tonight?

Are you calling me? What #? I called ops and they gave me your "secure" cell which I just tried but only got a long high pitched whining sound.
------Original Message------
From: Cheryl Mills
To: hdr22@clintonemail com
Sent Feb 22, 2009 8.58 PM
Subject: Re Can we talk tonight?

I can do now

-----Original Message----
From. H <hdr22@clintonemail.com>
To· Cheryl Mills
Sent: Sun Feb 22 18:37:51 2009
Subject: Can we talk tonight?

I just landed and will be home shortly We can try a secure call at your convenience [redacted] Let me know what time works.

From: H <hdr22@clintonemail.com> B6
Sent: Sunday, February 22, 2009 10:08 PM
To: Cheryl Mills [redacted]
Subject: Re: Can we talk tonight?

RELEASE IN PART
B6

Pls try again- [redacted]

From: "Cheryl Mills"
Date: Sun, 22 Feb 2009 22:02:23 -0500
To: <hdr22@clintonemail.com>
Subject: Re: Can we talk tonight?

Just did - no answer

-----Original Message-----
From: H <hdr22@clintonemail.com>
To: Cheryl Mills
Sent: Sun Feb 22 22:01:52 2009
Subject: Re Can we talk tonight?

I give up Call me on my home #.
------Original Message------
From: Cheryl Mills
To: hdr22@clintonemail.com
Sent: Feb 22, 2009 9:39 PM
Subject: RE: Can we talk tonight?

they were supposed to connect us - I called some time ago to do a secure call with you -- call them and ask them to try the connection

-----Original Message-----
From: H [mailto:hdr22@clintonemail.com]
Sent: Sunday, February 22, 2009 9:39 PM
To: Cheryl Mills
Subject: Re Can we talk tonight?

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------Original Message------
From: Cheryl Mills
To: hdr22@clintonemail.com
Sent: Feb 22, 2009 8:58 PM
Subject: Re Can we talk tonight?

I can do now

-----Original Message-----
From: H <hdr22@clintonemail.com>
To: Cheryl Mills
Sent: Sun Feb 22 18:37:51 2009
Subject: Can we talk tonight?

I just landed and will be home shortly We can try a secure call at your convenience. [redacted] Let me know what time works.

HA 09/01/2015

From: Huma Abedin
Sent: Sunday, February 22, 2009 10:56 PM
To: humamabedin
Subject: PrintFw: Hearing and Gaza

B6

RELEASE IN PART B6

-----Original Message-----
From: H <hdr22@clintonemail.com>
To: Huma Abedin
Sent: Sun Feb 22 22:24:00 2009
Subject: Fw: Hearing and Gaza

Pls print

From: "Mark Hyman, MD"
Date: Mon, 16 Feb 2009 10:43:24 -0500
To: Hillary Clinton<hr15@att.blackberry.net>, Hillary Clinton<hdr22@clintonemail.com>
Subject: Hearing and Gaza

Dear Hillary,

Thinking of you a lot these days in gratitude for opening the door to the Senate and allowing the perspective of Functional medicine to be heard – the hearing is set for February 26th If you want to connect while I am in DC from the 24th to the 28th for the IOM meeting and the hearing– let me know

When I finish writing my testimony I will send it to you – if you have a few minutes (which I realize is unlikely) I would welcome any input or advice.

The main reason I wanted to touch base was to forward this email from James Gordon about his work in Gaza.. Considering what is ahead of you I thought his perspective from the ground might be helpful.

His contact info is below if you want to contact him

Fondly,

Mark

------ Forwarded Message
From: James Gordon
Date: Mon, 16 Feb 2009 10:21:47 -0500
To: Mark Hyman
Subject: Re: Updated Plan

I'd like to talk with Hillary about the situation in Gaza and the very real prospects for peace that I believe are there, possibilities that we have for a variety of reasons ignored or dismissed or allowed to be "taken off the table " It's time for a fresh perspective and a deep, informed commitment to peace and I believe she can bring these, and I can be of help to her.

I've made over a dozen visits to Gaza in the last 7 years, know quite a bit about the populations's state of mind: We've worked intensively with 20,000 traumatized children and adults and have interacted with some of the major families (tribes) as well as the government, UN and NGO bureaucracies I've also met with political leadership from Hamas and Fatah (in both Gaza and the West Bank) as well as independent intellectuals I have too a pretty good understanding of the various Israeli perspectives and state of mind and have worked with every segment of Israeli society from UltraOrthodox to militantly secular, from the settlers removed from Gaza to the soldiers and government officials who removed them Finally, our major funder for this work (Tom Harkin had helped us obtain some seed money from the CDC) is Chuck Feeney who helped with the Irish peace process and is potentially interested in economic development in Gaza as well as in our humanitarian and mental health work.

I feel I can help Hillary seize this moment of crisis and turn it into an extraordinary opportunity There is, underneath the understandable fear and anger and the posturing so much yearning for peace, and perhaps I can help her find ways to use it creatively and effectively.

Thanks so much for being willing to contact her

Jim

James S. Gordon, M.D.
www.jamesgordonmd.com <http://www.jamesgordonmd.com>

Founder and Director
The Center for Mind-Body Medicine
5225 Connecticut Avenue, NW, Suite 414
Washington, DC 20015

www.cmbm.org <http://www.cmbm.org>

------ End of Forwarded Message

HA 09/01/2015

From: Abedin, Huma <AbedinH@state.gov>
Sent: Monday, February 23, 2009 7:02 AM
To: humamabedin[redacted] B6
Subject: Marina print
Attach: 022309 Press Briefing.doc; 022309 Press Clips.doc

RELEASE IN PART B6

From: Bishop, Christopher W
To: Abedin, Huma
Cc: S_SpecialAssistants; Macmanus, Joseph E; Sullivan, Jacob J
Sent: Mon Feb 23 07:01:36 2009
Subject: Morning Press

Good Morning Huma,

Let us know if you need anything else.

Christopher

Christopher W. Bishop
Special Assistant to the Secretary of State
202-647-9573

HA 09/01/2015

From: Rattner, Steven [redacted]
Sent: Monday, February 23, 2009 1:48 PM
To: hr15@att.blackberry.net
Subject: My news

B6

RELEASE IN PART B6

Hillary:

Just to let you know that it's now official For whatever it's worth, here is the official description of my responsibilities:

Steven Rattner is joining the Treasury Department as Counselor to the Secretary. In that capacity, he will advise Secretary Timothy Geithner regarding a variety of economic and financial matters and will lead the team advising Secretary Geithner and National Economic Council Director Lawrence Summers on the automobile sector.

Thanks for all your support and offers of help while I was working through this.

Steve

Steven Rattner
Managing Principal

Quadrangle Group LLC
375 Park Avenue
New York NY 10152
[redacted]
www.quadranglegroup.com

From: Eric Bederman [redacted] B6
Sent: Monday, February 23, 2009 5:21 PM
To: Lauren Jiloty <jilotylc@state.gov>; Huma Abedin [redacted]
Subject: RE: Mort Zuckerman

RELEASE IN PART B6

TY Will do.

Subject: RE: Mort Zuckerman
Date: Mon, 23 Feb 2009 17:17:35 -0500
From: JilotyLC@state.gov
To: eric[redacted]; humamabedin[redacted]

Mine is fine.
Thanks eric.

From: Eric Bederman[redacted]
Sent: Monday, February 23, 2009 5:17 PM
To: Jiloty, Lauren C; Huma Abedin
Subject: Mort Zuckerman

Got a message from Amy at Mort Zuckerman's office asking what the best email address would be for Mort to send a message to HRC? Assume it should go to one of you gals?

- Eric B.

HA 09/01/2015

From: Huma Abedin
Sent: Monday, February 23, 2009 7:30 PM
To: humamabedin
Subject: PrintFw: One of your people at State. Fw: Global Partnership Center Website

B6

RELEASE IN PART B6

-----Original Message-----
From: H <hdr22@clintonemail.com>
To: Huma Abedin
Sent: Mon Feb 23 17:14:39 2009
Subject: Fw. One of your people at State. Fw: Global Partnership Center Website

Pls print.
-----Original Message-----
From: "Burns Strider"

Date: Mon, 23 Feb 2009 17 02:59
To: <hdr22@clintonemail.com>
Subject. One of your people at State. Fw Global Partnership Center Website

See comments below from Robert . He's been an active volunteer, doing online faith blogging for me for a couple of years. and is in your Global Partnership office Incredible young man. .

-----Original Message-----
From: Lalka, Robert T <LalkaRT@state.gov>
To. bstrider
Sent: Mon Feb 23 16:42:26 2009
Subject: FW: Global Partnership Center Website

Burns,

I just realized that tonight's when the Delta State reception is happening and I'm hoping to make it. Just in case, I wanted to write to let you know that I had the chance to meet the Secretary for the first time today. She was visiting the East Asia and Pacific Affairs Office to thank them for their work on her first trip abroad; and, man, the folks here just seem to love her...

I also haven't sent you a link to the Global Partnership Center's website as promised, so I have enclosed the link with the quotes we are using in the "read more" boxes you'll see on the right side of the page.

Hope to see you again tonight,

Best,
Rob

http://www.state.gov/s/d/rm/partnerships/
"Diplomacy is primarily a government mission. But there are lots of ways that nongovernment actors, like corporations, like religious organizations, like charities and foundations, are actually building relationships with foreign governments and foreign people all the time, which, if done in the right way, are really value added to who we are as a nation and what we can achieve " -Secretary of State Hillary Clinton
"I think it's a real opportunity for us if we can figure how best to better coordinate and facilitate the private sector and the not-for-profit and religious community of the United States on behalf of humanitarian and commercial efforts."
- Secretary of State Hillary Clinton
"The State Department will be firing on all cylinders to provide forward-thinking, sustained diplomacy in every part of the world, applying pressure wherever it may be needed, but also looking for

opportunities, exerting leverage, cooperating with our military and other agencies of government, partnering with nongovernmental organizations, the private sector, and international organizations, using modern technologies for public outreach, empowering negotiators who can protect our interests while understanding those of our negotiating partners. Diplomacy is hard work. But when we work hard, diplomacy can work, not just to defuse tensions, but to achieve results that advance our security interests and values "
- Secretary of State Hillary Clinton
"I want more partnerships . .I don't think there's any substitute for having seasoned, experienced professionals and experts leading our efforts on diplomacy and development and working, where possible, in partnership and coordination with the private sector and the not-for profit sector."
-Secretary of State Hillary Clinton
"You know, right now in Rwanda, a number of foundations, a number of churches, a number of private sector actors are all working to try to build that country back up. So I would hope that when we look at the State Department, we think of the role of foreign policy, diplomacy, and development as involving not just those who are the Foreign Service officers and the Civil Service professionals and the development experts, but really it's all hands on deck We have a lot of work to, in my view, kind of repair damage and get out there and present America as we know we are "
-Secretary of State Hillary Clinton

Also, I remember mentioning this study to you:
http://www.brookings.edu/reports/2008/~/media/Files/rc/reports/2008/07_national_security_brainard/07_national_security_brainard.pdf Check out the sections on development and human rights (pages 17 and 18), and if it's something you'd like to read more on, there are a number of good reads, including one I just finished called Security By Other Means, which I would be happy to lend to you.

Robert Tice Lalka
Work: 202.647.3408 | Fax: 202.647.3311

Public-Private Partnerships Liaison
at the Global Partnership Center

http://www.state.gov/s/d/rm/partnerships

US Department of State
2201 C Street NW Suite 3800
Washington, DC 20520
United States of America

From: Cheryl Mills [redacted] B6
Sent: Tuesday, February 24, 2009 4:58 AM
To: hdr22@clintonemail com
Subject: FW: From my father-in-law who is in Japan on business...

RELEASE IN PART
B6

FYI below

New York University
70 Washington Square South
New York, NY 10012

From: Maya Seiden [redacted]
Sent: Monday, February 23, 2009 10:21 AM
To: Sean Maloney
Cc: Cheryl Mills
Subject: Re: From my father-in-law who is in Japan on buisness...

The colliquial translation is 'Isn't Hillary awesome?'

Quite a statement from men in a culture that is not exactly known for its advancement of women.

On Feb 23, 2009, at 10:01 AM, "Sean Maloney" [redacted] wrote:

> P.S. Maya will have to translate the Japanese for you.
> *Also, in case Cheryl wants to know, everyone in Japan loves Hirari-san. Her trip was extraordinarily successful. Everyone has been talking about her with great fondness and admiration. Every taxi driver (nearly) has said something like "Hirari-san wa segoii desu ne!"*
> Sean Maloney, New York University
> [redacted]

From: Abedin, Huma <AbedinH@state.gov>
Sent: Tuesday, February 24, 2009 6:40 AM
To: humamabedin [redacted] B6
Subject: Marina print
Attach: 022409 State Clips.doc; 022409 State Briefing.doc

RELEASE IN PART B6

From: Davis, Jennifer L (S Staff)
To: Abedin, Huma
Cc: S_SpecialAssistants
Sent: Tue Feb 24 06:35:45 2009
Subject: Morning Press, 2/24/09

Good morning, Huma.

From: Berger, Samuel R. [redacted] B6
Sent: Tuesday, February 24, 2009 1:29 PM
To: hdr22@clintonemail.com
Subject:

RELEASE IN PART B6

HRC: The Chinese see a new era of cooperation. By throwing away the old talking points, you have changed the landscape. Sensational trip Sandy

From: Burns Strider [redacted] B6
Sent: Tuesday, February 24, 2009 6:34 PM
To: hr15@att.blackberry.net
Subject: What the Bible Says about Federal Budgets..
Attach: Scripture on the Budget- Part 1.doc

RELEASE IN PART B6

Three of eight posts are up at www.faithfuldemocrats.com from the updated *Primer on Scripture and the Budget for 2009.*

The second posting is also attached: *The Responsibility of the Nation and Its Government to "the Least of These"*

Over the next week at Faithfuldemocrats.com, we are going to publish each section of the updated *Primer on Scripture and the Budget for 2009*, which is organized by theme Our hope is that you will use this resource, share it with friends, and discuss it in the comment section...and that together we can make a positive contribution to the upcoming budget debates that will shape our country's priorities and demonstrate where its heart truly lies.

The sections and future posts are titled:

The Responsibility of the Nation and Its Government to "the Least of These"
The Policy Implications of Praying, "Thy Kingdom Come..."
On Corruption and the Exploitation of Workers
The Sin of Helping the Rich at the Expense of the Poor
The Blessedness of the Poor and Our Christian Responsibility to Them
Wealth, Materialism, and the Bible's View of an "Ownership Society"
Countering the Right's Pharisaical Approach to Moral Legalism
Concluding Thoughts: Applying Scripture in a Pluralistic Society

Back in 2006, the budget debate followed immediately on the heels of Congressional consideration of the Marriage Amendment. As a result, there was a desire by a number of Democratic leaders for a reference guide that would more easily allow Democrats to authentically speak out against the extreme and selective use of scripture by the Republicans and their allies on the Right. The first "Guide to Scripture and the Budget" that included scriptural references and simple talking points to help equip Christian Democrats in their response to Republican budget arguments was distributed shortly before the 2006 budget debate.

My underlying assumption in writing and continuing to update this document is that Democrats should not cede the prophetic language of scripture and its ability to inspire and frame issues in a moral context to the other side. Many traditional Democratic positions are rooted in the teachings of scripture, and it is time Democrats stopped losing on the Bible.

The language of scripture is a language that calls people to turn their attention away from selfish desire and personal gain and to focus instead on serving God and their neighbors. Furthermore, it is a language that speaks with moral clarity and purpose. Therefore it speaks with authority to the policy debates currently underway in our country. In short, it is a language Democrats cannot afford to ignore.

One aspect of the Democratic response to the upcoming Republican budget attacks must be a willingness by "faithful Democrats" to discuss budget and tax policies from a moral perspective and to challenge Republicans to apply the same moral codes to kitchen table issues that they so eagerly embrace on bedroom issues...because we all know that ***as soon as we start talking about budget and taxes, the Republicans will put away their Bibles and turn to Darwinian social and economic theories to support their policy positions.***

The first chapter of the Book of Isaiah begins with the prophet cataloguing the decline of the city of Jerusalem into injustice, where its former greatness is besmirched by its obsession with materialism and wealth. It is important to remember that the prophets are speaking against the government "rulers" and the nation as a whole. The prophets in scripture are not calling for individual piety and charity but for systemic societal/governmental reform. And they specifically challenge government leaders to remember that the nation's leaders are called to help the powerless and those in greatest need, not those with the most power and money.

Isaiah clearly states what God expects of leaders: "Wash yourselves; make yourselves clean; remove the evil of your doings from before my eyes; cease to do evil, learn to do good, seek justice, rescue the oppressed, defend the orphan, plead for the widow" (Isaiah 1:16-17). [note: he does not say, "cut federal funding for state child services"]

Here is what a true "Justice Sunday" should focus on from Jeremiah's exhortation of the king about his responsibility as head of government: "Did not your father eat and drink and do justice and righteousness? Then it was well with him. 16He defended the cause of the poor and needy, and so all went well. Is that not what it means to know me?" declares the Lord. 17"But your eyes and your heart are set only on dishonest gain, on shedding innocent blood and on oppression and extortion" (Jeremiah 22:15-17).

Taken together with Micah 6:8, this forms the core of the prophetic message: To know God as a nation means to take care of the poor and ensure that justice is done on behalf of the needy: "He has showed you, O man, what is good. And what does the Lord require of you? To act justly, to love mercy, and to walk humbly with your God" (Micah 6:8).

There are obvious parallels between ancient Jerusalem and the role that big donors and lobbyist played in setting government priorities in Washington that contributed to the ouster of the GOP from Congress and the White House in the 2006 & 2008 elections respectively· "Everyone loves a bribe and runs after gifts. They do not defend the cause of the fatherless. The widow's cause does not come before them."(Isaiah 1:23)

"The Lord takes his place in court and rises to judge his people. He enters into judgment against the elders and leaders of his people saying, "It is you who have ruined my vineyard; the plunder from the poor is in your houses" (Isaiah 3:14).

"You seem eager for God to come near you. Yet on the day of your fasting, you do as you please and exploit all your workers. Yet is not this the kind of fasting I, your Lord, have chosen. to loose the chains of injustice...to share your food with the hungry and to provide the poor wanderer with shelter—when you see the naked, to clothe them?" (Isaiah 58: 2-7).

"He who oppresses the poor shows contempt for their Maker, but whoever is kind to the needy honors God" (Proverbs 14:31).

"If you do away with the yoke of oppression, with the pointing finger and malicious talk, 10and if you spend yourselves in behalf of the hungry and satisfy the needs of the oppressed, then your light will rise in the darkness, and your night will become like the noonday. 11 The Lord will

guide you always; he will satisfy your needs" (Isaiah 58: 9-11).

Nehemiah (who rebuilt Jerusalem after the Babylonian exile) enforces social justice through the power of the state and addresses an insidious problem that sadly still plagues us to this day (predatory lending): "Still others were saying, "We have had to borrow money to pay the king's tax on our fields and vineyards. 5 Although we are of the same flesh and blood as our countrymen and though our sons are as good as theirs, yet we have to subject our sons and daughters to slavery…we are powerless, because our fields and our vineyards belong to others." 6 When I heard their outcry and these charges, I was very angry. 7 I told the [nobles and government officials], "You are exacting usury from your own countrymen!" So I called together a large meeting to deal with them 8 and said… "What you are doing is not right…let the exacting of usury stop! 11 Give back to them immediately their fields, vineyards, olive groves and houses, and also the usury you are charging them—the hundredth part of the money, grain, new wine and oil." 12 "We will … do as you say," they replied. Then I summoned the priests and made the nobles and officials take an oath to do what they had promised." (Nehemiah 5:1-13)

From the New Testament: "Mercy triumphs over judgment! What good is it, my brothers, if a man claims to have faith but has no deeds? Can such faith save him? 15Suppose a brother or sister is without clothes and daily food. 16If one of you says to him, "Go, I wish you well; keep warm and well fed," but does nothing about his physical needs, what good is it? 17In the same way, faith by itself, if it is not accompanied by action, is dead"(James 2: 14-17).

Scripture sets a very high bar for public morality as well as for private behavior. Although we can easily rationalize why alternatives to the commands of Scripture might be more "sensible" and "realistic," if people are going to insist on applying scripture to the bedroom, they must be willing to apply it to the boardroom as well. The Bible leaves no room for trickle-down economics. Jesus and the Prophets do not say, "Help the widow and orphan by supporting businesses in an effort to prop up the stagnant economy"! On the contrary, when a rich young man asks Jesus what he must do to inherit the Kingdom of God ("go to heaven" in today's terminology), "Jesus answered, "If you want to be perfect, go, sell your possessions and give to the poor, and you will have treasure in heaven. Then come, follow me" (Matthew 19:21—note Jesus says this is what the man must do before he can follow Christ). The Bible's call repeated throughout the Old and New Testament is for direct action by government leaders on behalf of the least of these…nothing less.

From: Cheryl Mills [redacted]
Sent: Tuesday, February 24, 2009 10:05 PM
To: hr15@att.blackberry.net; hdr22@clintonemail.com
Subject: just called your house twice - but keep getting hang up - was calling to check in - I'm on [redacted]

B6

RELEASE IN PART
B6

From: Mark J. Penn [redacted] B6
Sent: Tuesday, February 24, 2009 10:16 PM
To: hr15@att.blackberry.net
Subject: pretty good speech

RELEASE IN PART
B6

Basically a copy of all the techniques we used – well done and certainly what he needed. Serious, patriotic and always appearing to bring people together. Very much the kind of stuff that works.

You have been getting good reviews on your tours – I always liked having a leadership track and a human track and you have been doing both, but I would be careful about seeming too silly as it could make you look irrelevant. Obama has serious, direct, and powerful leadership style.

My biggest worry would be that the policies may not work.

From: H <hdr22@clintonemail.com>
Sent: Wednesday, February 25, 2009 8:23 AM
To: Tamera Luzzatto [redacted] B6
Subject: How are you?

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B6

I tried calling you at all your numbers Let me know when we can talk and what # to call?

From: jkcanc [redacted] B6
Sent: Wednesday, February 25, 2009 9:04 AM
To: Hillary Clinton <hdr22@clintonemail.com>
Subject: Welcome Back

RELEASE IN PART
B6

Hillary,
Sent you a message to your old address by mistake Lauren will provide you a hard cy. Welcome back, all the best, Jack
Sent via BlackBerry by AT&T

From: Huma Abedin [redacted] B6
Sent: Thursday, February 26, 2009 6:26 AM
To: hdr22@clintonemail.com
Subject: Re. Calls

RELEASE IN PART
B6

China call confirmed for 7 30
Lavrov will be later this morning.

-----Original Message-----
From: H <hdr22@clintonemail.com>
To: Huma Abedin
Sent: Wed Feb 25 23:52:18 2009
Subject. Re Calls

Ok
------Original Message------
From: Huma Abedin
To: hdr22@clintonemail com
Sent Feb 25, 2009 11:50 PM
Subject: Calls

Call with foreign minister yang has been confirmed for tomorrow morning at 7:30am while u r with isabelle. Lavrov will be right after probably.

HA 09/01/2015

From: Gary Gensler [redacted] B6
Sent: Thursday, February 26, 2009 8:37 AM
To: hr15@att.blackberry.net
Subject: Harkin plans to suppport

RELEASE IN PART B6

Hillary,

My Senate confirmation hearing today went well. Senator Harkin said afterward that he planned to poll the committee shortly but saw no opposition at this time and would try to schedule a committee vote next week. The newswire story below suggest his support now.

Senators Mikulski & Cardin along with former Senator Sarbanes introduced me today.

Off the Committee, both Senators Feinstein and Senator Levin have signaled their support as well.

Your call to Senator Harkin and following your specific advice on how to address my past in the Clinton Administration was of the greatest help.

Thank you once again for all of your support.

Gary

Sen. Harkin Plans To Support CFTC Nominee *Gensler*

DOWJONES Newswires factiva

Source. Dow Jones News Service
Date: 02/25/2009
By Sarah N. Lynch
Of DOW JONES NEWSWIRES

WASHINGTON (Dow Jones)--Senate Agriculture Chairman Tom Harkin signaled Wednesday that he intends to support the nomination of Gary ***Gensler*** to chair the U S. Commodity Futures Trading Commission despite some lingering concerns

Harkin's support came after ***Gensler***, at a hearing Wednesday, sought to reassure the Iowa Democrat and other senators on the panel that his views on swaps regulation have evolved since his tenure at the Treasury Department during the Clinton administration.

"I think that Mr. ***Gensler*** was very forthright in saying his views have changed over the years," Harkin said. "I will be polling the committee, but I don't expect any opposition. I assume that we will be moving his name forward." If the committee approves ***Gensler***'s nomination, ***Gensler*** will face a confirmation vote from

the full Senate.

Harkin had previously raised concerns about ***Gensler***'s involvement in talks over the Commodity Futures Modernization Act, passed in 2000, which deregulated swaps. At the time, ***Gensler*** was a senior Treasury official.

Harkin hit ***Gensler*** with a tough first question at ***Gensler***'s confirmation hearing Wednesday, recalling testimony ***Gensler*** gave in 1999. Quoting ***Gensler*** as saying he "positively, unambiguously" agreed with former Treasury Secretary Lawrence Summers in opposing additional regulations for over-the-counter derivatives, Harkin pressed ***Gensler*** on whether or not his beliefs have changed.

Gensler responded: "Looking back now, it is clear to me that all of us that were involved at the time, and certainly myself, should have done more to protect the American public through aggressive regulation."

"We should have fought harder for some of the things we raised with Congress at the time," he added.

Since President Barack Obama first nominated ***Gensler*** to the CFTC late last year, ***Gensler*** has worked hard behind the scenes to convince Harkin and other lawmakers that he would be a tough regulator if confirmed as the agency's chairman. ***Gensler*** has said he didn't participate in discussions on the Commodity Futures Modernization Act at certain times in 1998, when he was recused, but he did get involved after that recusal period expired.

His efforts have paid off in winning over key lawmakers like Sen. Dianne Feinstein, D-Calif., who has been critical of the CFTC's oversight in the past. Feinstein indicated late Tuesday that she plans to support the nomination.

Sens. Benjamin Cardin and Barbara Mikulski, both Democrats from ***Gensler***'s home state of Maryland, also urged the Senate Agriculture Committee to support ***Gensler*** on Wednesday.

Responding to questions from the committee, ***Gensler*** said that he wished he had fought harder for uniform regulation for all physical commodities when he served at Treasury. At the time, he said, those in favor of uniform regulations were unable to get it into the legislation. If confirmed, ***Gensler*** pledged to take the issue up again.

He also said he would support a regulatory regime for derivatives dealers. As an example of why such reforms are needed, he cited the unit at American International Group (AIG) which issued credit-default swaps without having the collateral to back the provisions in those contracts.

Sen. Kent Conrad, D-N.D., a member of the committee, said Wednesday he deeply regrets supporting the deregulation of swaps in 2000, adding that ***Gensler*** also shares some of the blame for it.

"At least for some of that, you gave us bum advice," Conrad said.

Gensler said he believes it's clear the regulatory system failed, and he pledged to push for tough new reforms If confirmed, he said, he will support mandating clearing for standardized over-the-counter products as well as putting some of those derivatives on regulated exchanges For customized products that don't lend themselves to clearing, ***Gensler*** said he would push to enact strict reporting and record-keeping requirements.

He also reiterated Wednesday he believes speculation and index investing did contribute in part to the run-up in agricultural and energy commodities last summer and he would do more to prevent excessive speculation if confirmed That would entail re-examining the rules governing hedge exemptions, which allow traders to get around position limits if they are hedging a business risk

"I am a proud believer in financial reform, tough regulation and enforcement," ***Gensler*** said.

-By Sarah N Lynch, Dow Jones Newswires; 202-862-6634; sarah.lynch@dowjones com [02-25-09 1743ET]

HA 09/01/2015

From: Abedin, Huma <AbedinH@state.gov>
Sent: Friday, February 27, 2009 7:03 AM
To: humamabedin[redacted] B6
Subject: Marina print
Attach: 022709 State Briefing docx, 022709 State Clips docx

RELEASE IN PART B6

From: Bishop, Christopher W
To: Abedin, Huma
Cc: S_SpecialAssistants; Macmanus, Joseph E; Sullivan, Jacob J
Sent: Fri Feb 27 07:02:18 2009
Subject: Morning News Clips

Good Morning Huma,

Please let us know if you need anything else.

C

Christopher W. Bishop
Special Assistant to the Secretary of State
202-647-9573

Testimony of Mark Hyman, M.D.

Founder and Medical Director

The UltraWellness Center

Vice-Chairman, Institute for Functional Medicine

SENATE HEALTH REFORM TESTIMONY
INTEGRATIVE CARE: A PATHWAY TO A HEALTHIER NATION

Senate Committee on Health, Education, Labor and Pensions

Chairman: Senator Edward M. Kennedy

Ranking Member: Senator Michael B. Enzi

Senator Tom Harkin & Senator Barbara Mikulski

United States Senate

Senate Dirksen Building

Washington, DC

February 26, 2009

Reforming the United States Health Care System:
Mastering the Challenge of Chronic Disease

Executive Summary: Testimony of Mark Hyman, MD

Effective Health Care Reform: Addressing the Drivers of Costs and Chronic Disease

- The current medical and scientific paradigm of acute care medicine has been unable to effectively address the epidemic of chronic disease and its associated costs.
- There is a new paradigm which addresses the fundamental underlying causes of chronic disease, and can form the basis for a more effective model of medical education, practice, and research that over time will generate dramatic cost savings.
- There are specific initiatives and strategies based on this new paradigm that can help transform our sick care system into a health care system.

The Right Solution for the Problem of Chronic Disease

- This new paradigm is personalized, preventive, participatory, predictive, and patient centered. It is proactive rather than reactive. It is based on addressing the causes of disease and optimizing biologic function in the body's core physiologic systems, not only treating the symptoms.
- It based on systems biology or medicine That model exists today, and is called ***Functional Medicine.***
- Functional medicine is a system of personalized care, a **new "operating system"** that directly addresses **how environment and lifestyle influence our genes to create imbalances in our core biologic systems that, over time, manifest as disease.** It is this kind of medicine that is needed to create real successes in 21st century medicine.
- Even if we get everything else right in health care reform, it won't matter unless we address the underlying causes of illness that drive both costs and the development of chronic disease.

Clinical Examples: Systems Medicine in the Clinic

- Case examples of Functional medicine in chronic disease in autoimmune, digestive, behavioral, and hormonal disorders illustrating the power and implications for transforming the quality of our health care and reducing the economic burden of chronic disease.
- Report on pilot program for children using functional medicine showing a 16-fold reduction in costs from dramatically better health outcomes with integrated health care teams based on Functional medicine.

Key Avenues for Change: Recommendations

1. Re-tooling medical education and research to match the science of systems medicine. This would involve funding the development of training programs in medical schools and residencies, and supporting initiatives for certification and training in functional medicine for existing practitioners through establishing a fully funded university affiliated Institute for Lifestyle and Systems Medicine
2. Creation of Functional medicine demonstration projects in federally funded community health centers, with integrated health care teams focusing on treating chronic disease and providing

education about lifestyle and wellness. These would form the foundation for the development of clinical practice networks of Functional medicine for education and research.

Reforming the United States Health Care System:
Mastering the Challenge of Chronic Disease

Testimony of Mark Hyman, MD
Before the Senate Committee on Health, Education, Labor and Pensions
February 26, 2009

Chairman Kennedy, Ranking Member Enzi and distinguished members of the Committee: Thank you for this opportunity to share the dramatic changes in medical thinking and practice that must be the central focus of health care reform. My name is Dr. Mark Hyman. I am a practicing physician and vice chair of the Board of Directors of the Institute for Functional Medicine. As a practicing functional medicine physician, I am on the front lines of a scientific medical revolution.

Effective Health Care Reform: Addressing the Drivers of Costs and Chronic Disease

My testimony will show that:

- The current medical and scientific paradigm of acute care medicine has been unable to effectively address the epidemic of chronic disease and its associated costs.
- There is a new paradigm which addresses the fundamental underlying causes of chronic disease, and can form the basis for a more effective model of medical education, practice, and research that over time will generate dramatic cost savings and improved health outcomes.
- There are specific initiatives and strategies based on this new paradigm that can help quickly transform our sick care system into a health care system.

Even if we get everything else right in health care reform, it won't matter unless we address the underlying causes of illness that drive both costs and the development of chronic disease. This innovative approach to chronic disease cannot only prevent but also more effectively TREATS chronic disease.

We must change not only the WAY we do medicine, but also the medicine we DO. We must improve not only financing and delivery of health care, but also our fundamental scientific approach to chronic disease—an epidemic that now affects 133 million Americans and accounts for 78% of health care costs.

This way of doing medicine, or Functional medicine, is a system of personalized, patient centered care based on **how our environment and lifestyle choices act on our genes to create imbalances in our core biologic systems. Those imbalances show up as the signs and symptoms we call disease.**

It is best solution for our health care crisis. The solution is not our current acute care model, which though extremely effective for acute disease, leads to worse outcomes and higher costs when applied to chronic disease because it doesn't address WHY people are sick.

This new paradigm is personalized, preventive, participatory, predictive, prospective, and patient centered It is proactive rather than reactive. It is based on addressing the causes of disease and optimizing biologic function in the body's core physiologic systems, not only treating the symptoms. It based on systems biology or medicine. That model exists today, and is called ***Functional Medicine.***

The Right Solution for the Problem of Chronic Disease

Our current model of medicine is unsustainable because it cannot stem the rising tide of chronic disease. Relying only on reforms in access, financing, electronic records, malpractice, reduction in medical errors, coordination of care, and research on new drug therapies – while retaining the acute-care model – will be untenable. These reforms are necessary but not sufficient to avoid the collapse of our health care system that may soon mirror our current financial crisis. These reforms do not alter the fundamental approach to prevention and treatment. If we focus on improving the way we practice the medicine of the past, we will still have the medicine of the past. If we improve the wrong type of care, then we will simply be doing the wrong things better.

Acute-care medicine is designed for acute illness, trauma, and end-stage disease for which it is the best in the world. It is disease-, drug- and procedure-based. Our current medical education focuses on sickness rather than health; journals publish about disease management not causality. Disease based acute care medicine is the WRONG model to address chronic illness, because it doesn't address WHY people are sick, or the underlying mechanisms and biologic causes. That is why we spend more than any other industrialized nation and are near the bottom of the list for all major health outcomes, and are witnessing a decline in life expectancy for the first time in history.

Functional medicine is not a new treatment, test, or procedure but a new **"operating system"** or method for problem solving and processing complex clinical information. It is a fundamentally different WAY OF THINKING about the origins and mechanisms of illness. It encompasses all the TOOLS of healing and medicine, both conventional and integrative. And it provides a common language, a map or GPS system for navigating through the puzzle of chronic illness. A growing coalition of practitioners, educators, and scientists is dedicated to advancing this model. We have introduced 20,000 physicians and health care providers to functional medicine since 1991, and we wrote the *Textbook of Functional Medicine* in 2005 to describe both the underlying science and the practical clinical strategies and tools that comprise this new model.

We have begun a certification program in functional medicine and are building key educational programs for residencies throughout the country. We are partnering with Harvard

in strategic research to document the extent and scope of practice as well as the efficacy of this model as a better roadmap for chronic disease.

Through a scholarship program funded by one of my patients, we have trained over 50 academic faculty and fellows from major institutions who are part of the Consortium of Academic Health Centers for Integrative Medicine (funded by the Bravewell Collaborative) including Harvard, Yale, Duke, Johns Hopkins, USCF, and the University of Arizona. We are also collaborating with the American Academy of Family Practice and the American Dietetic Association. We collaborate and advance the foundational work of James Gordon, MD at the Center for Mind Body Medicine and Dean Ornish, MD at the Preventive Medicine Research Institute

Clinical Examples: Systems/Functional Medicine in the Clinic

Let me illustrate how this works with real people.

A Pilot Program For Functional Medicine: Reducing Costs 16 Fold in Sick Children

At the University of Minnesota, Dr. Anne Kelly developed a model of care based on Functional medicine called the *U Special Kids* program It was for the 5% of the sickest children who generated 60% of the total costs, mostly from unplanned hospitalizations. In one year, the costs incurred by that population dropped from $4 million to $250,000, or more than $50,000 per enrollee, or a 16-fold decrease in costs. Yet the program was cancelled in November 2008 after one year because less than 10% of the high science, low tech, and high touch approach was reimbursable.

We cannot control costs by reducing access to effective programs. We must increase access to integrated health care teams that include a variety of health professionals, all of whom are trained in the appropriate chronic disease model. Both the science and methodology exist to utilize functional medicine for such teams on a wide scale.

Reform must also encompass re-structuring financing and financial incentives to prioritize health care, not just sick care. We cannot afford incremental change. The health our nation, our future generations, and the health of our economy depend on addressing the explosion of chronic disease and associated health care costs.

A Woman with Treatment Resistant Autoimmune Disease

Cris Scoufos, a 40-year-old woman came to see me after 5 years of uncontrolled ulcerative colitis with bloody diarrhea, joint pain and cystic acne, which started after 4 rounds of antibiotics for respiratory infections. She was treated unsuccessfully at the Mayo Clinic with the most advanced, dangerous and expensive immunosuppressive therapies. Just before returning to Mayo to start a new investigational drug, she saw me. We simply eliminated common food sensitivities, treated yeast infections, and normalized the function of her digestive tract with probiotics, digestive enzymes, fish oil, and vitamin D. After just 6 weeks of treatment she went back to Mayo and was found to have a completely normal bowel, and

her joint pain, fatigue, and cystic acne resolved by treating the upstream triggers instead of the downstream symptoms. We cannot get to the solution for chronic disease with our current methods of diagnosis and treatment.

Here is her email to me shortly after her visit to Mayo Clinic. Her before and after photos are attached.

Dear Dr. Hyman,

I am so thankful for all that you are helping me with. I prayed for God to guide me to someone who could show me how to properly care for my body so that I could heal and that the honor and glory would belong to Him. Instead of asking for God to just heal me, like I had for four and a half years, I asked for guidance on what I needed to do.

After failing all conventional drug treatments I was told I would have to go into an investigational drug study next. My trip to Mayo Clinic had been planned and I was nervous about the choices I was going to have to make. My colonoscopy in April 2008 showed 45cm of ulceration.

The trip to see you the last week of August was planned in one week and everything fell together so easily. It seems like it was meant to be. I started following your recommendations right away, even though I haven't incorporated all of the supplements in yet, the change has been amazing.

My colonoscopy at the Mayo Clinic in Rochester, Minnesota was last Monday, October 13th. My physician Dr. Sandborn, who is highly regarded in the gastroenterology field as one of the best in the country, told me that there is no ulceration left in my large intestine and there was only some scarring. I have completely healed! It is amazing! I was still bleeding just two months ago and now I am completely healed. It has been a very long five years and I thought you would want to know just how much your help has made in my life. Thank you very much. You have been the instrument that God has sent into my life for healing.

Unending blessings to you and your loved ones,

Cris Scoufos

A Doctor with Autoimmune Arthritis

A 57-year-old vascular surgeon was seen with debilitating autoimmune psoriatic arthritis that had been unsuccessfully treated with Humira, methotrexate, and NSAIDs; he also had migraines, reflux, constipation, and fatigue. He was symptom free and off all medications only 6 weeks after changing his diet, fixing nutritional deficiencies, and addressing imbalances in his digestive system, which is home to more than 70% of the immune system.

A Woman with Multiple Chronic Diseases

A 46-year-old woman, having seen a dozen doctors over a dozen years, came to me with 29 different diagnoses, including depression, hypertension, obesity, polycystic ovarian syndrome, migraines, heavy uterine bleeding, asthma, sinusitis, irritable bowel syndrome, fibromyalgia, osteoarthritis and psoriasis. Each disease was treated with the best available conventional treatment. But she was still sick, despite 9 medications

Of course, she didn't have 29 separate diseases. She had imbalances in a few core networks of physiologic function – digestive, immunologic, and hormonal – that gave rise to all her symptoms. The underlying cause of all her "diseases" was an autoimmune response to gluten, leading to autoimmune thyroid disease and severe vitamin D deficiency because of malabsorption. Six weeks after eliminating gluten, improving her diet, replacing thyroid hormone and vitamin D, her 29 diseases were completely gone, along with 21 pounds.

A Boy with Attention Deficit Disorder and Asthma and Allergies

Clayton Lampert was a 12-year-old boy with severe attention deficit hyperactivity disorder, behavior problems, and poor school performance on Ritalin for years. He also had illegible handwriting or dysgraphia. He also had apparently "unrelated" problems of asthma, allergies, hives, stomachaches, headaches, insomnia, muscle cramps, and anxiety. He had a history frequent infections and antibiotics. He had seen 5 specialists (lung, GI, allergist, psychiatrist and neurologist) and was on 7 medications for allergies, asthma, pain, and ADHD. No one asked how everything was connected, or how his diet of junk food and sugar made him sick.

His immune system was activated, his digestion not working and he was nutritionally deficient in zinc, omega 3 fats, magnesium and vitamin B6. We simply normalized his function by removing impediments to health (junk food diet, food sensitivities, overgrowth of yeast, and lead) and providing the ingredients necessary for optimal biologic function - whole foods diet, additional nutrients including B6, magnesium, zinc, omega 3 fats and probiotics. In two months he returned without any physical or psychiatric symptoms and was off all his medication. How many children suffer needlessly when we have the solutions to these problems? Here is his mother's email to me about his progress. And below is his handwriting sample before and two months after treatment.

Dear Dr. Hyman,

We had a 504 meeting at Clayton's school this morning (where the teachers, school counselor, parents, and principal all get together to review "the plan" for kids with special educational needs—in Clayton's case prompted by the ADHD diagnosis). This was the first time in his entire schooling history that everything seems to be going well. The input from his teachers was that he is "a different kid" than they saw in the first half of the year and that they're amazed by the difference. The school nurse hasn't seen him since March (and he used to be in her office several times a week). The school psychologist said his social skills are very good, age appropriate, and that she sees no problems at all. She also noted that Clayton seems very proud of himself and his new health and that he's taking good ownership of all the

changes in his diet. He even seems to be shrugging it off when the other kids at school tell him he's an "alien" because he doesn't drink soda.

This was just such a fantastic meeting and I wanted to pass along the good news and say Thank You!

Recovery from Dementia

The power of this approach is that it can be often applied without the intervention of a trained professional. Below is the story of a woman's whose husband recovered from dementia by following the principles of Functional medicine. This recovery was likely due to a reversible nutritional cause. Other causes of dementia, which is not a homogenous disease, may respond differently, however the social and economic impact of this method can no longer be ignored.

Eight years ago, at the age of 42, I met and married the love of my life, Robert Foster. We both have felt that "we" were absolutely "meant to be together". Two years ago I began worrying whether or not the "moments" of forgetfulness meant the beginning of dreaded Alzheimer's disease. I began to educate myself obsessively, and came to the conclusion that the traditional route of pharmaceutical drugs was the wrong approach to combat this beast. I would not accept that the "only" outcome was a horrible death sentence. My beloved husband's cognitive function took a sudden and alarming spiral downward this past fall. The formal diagnosis of "Alzheimer's" was no less heartbreaking, but I felt lucky to have had those two years to do the precious research and reading, where I was given the extraordinary gift of awareness and respect for Functional Medicine.

Knowing instinctively that this was the only answer to the war we needed to fight – it was here that I sought help. I was made aware of Dr. Hyman by another Functional Medicine doctor a couple of years ago, and have followed his work and have read several of his books. Having a program to follow, was the answer to a prayer.....literally. The actual "turnaround" has been so dramatic that I have been hesitant to share the results, not wanting to offer unwarranted "hope" to others, as it sounds "too good to be true". I do not want this to sound like "hype" – or as the "magic pill" that cured Alzheimer's, but I do think it would be irresponsible not to share our astounding results.

The bottom line--five days after starting the program, my husband had gone from not being able to hold a thought, constantly misplacing any number of objects, repeating questions and thoughts, and not being able to drive (as he would get lost), to the normal functioning man I married. The "comeback" is NOT 100%-- it IS over 90%. He is able to hold his concentration on a project for hours at a time. He is able to get into the car and run errands flawlessly. He carries out a conversation and relates to it hours or days later. He is able to recall telephone numbers and addresses. I have my husband back. I have no doubt the change in diet, addition of specific supplements, the detox program, and the addition of regular exercise, are responsible for these results. I pray that the miraculous results are multiplied a million times over, and others feel the joy and relief that I have had. Dr. Hyman – our eternal thanks and gratitude.

Key Avenues for Change: Recommendations

While there are many questions still to be answered, and research to be done, it is time to act. Based on the aforementioned considerations, I submit that public and private sector investment must be made in the following areas:

1. Re-tooling medical education and research to match the science of systems medicine. I recommend the establishment a sustainably funded university affiliated ***Institute for Lifestyle and Systems Medicine/Functional Medicine***. This would be the national center and prototype for the development of training programs in medical schools, residencies, and postgraduate certification and training in Functional medicine for existing practitioners and ancillary health professionals. Sixty seven percent of the 250,000 primary care doctors are currently dissatisfied with medicine and 80% are seeking new ways to practice based on this emerging model of medicine. The goal should be 20,000 fully trained practitioners in five years.

2. Creation of Functional medicine ***demonstration projects in federally funded community health centers***, with integrated health care teams focusing on treating chronic disease and providing education about lifestyle and wellness. These would form the foundation for the development of clinical practice networks of Functional medicine for education and research.

3. The establishment of a ***White House and/or Congressional Office for Health and Wellness*** to coordinate all efforts in this area as detailed in the WIN proposal submitted by Dr. Wayne Jonas.

Conclusion

Most chronic disease today is not necessary. While conventional medicine has been great for acute disease, Functional medicine is the model for easing the heavy burden of chronic disease from which our society—indeed, the whole world—suffers today.

Thank you.

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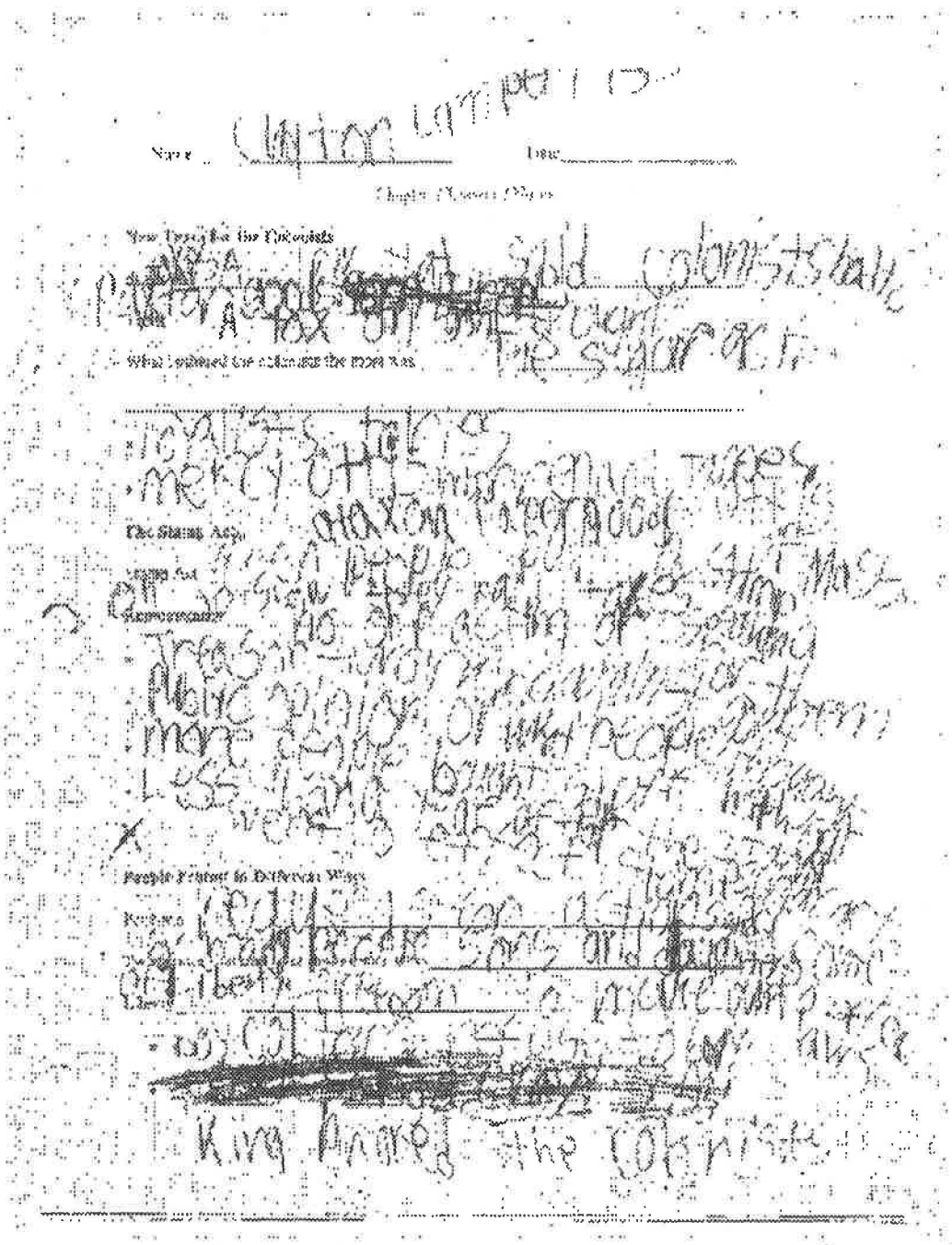
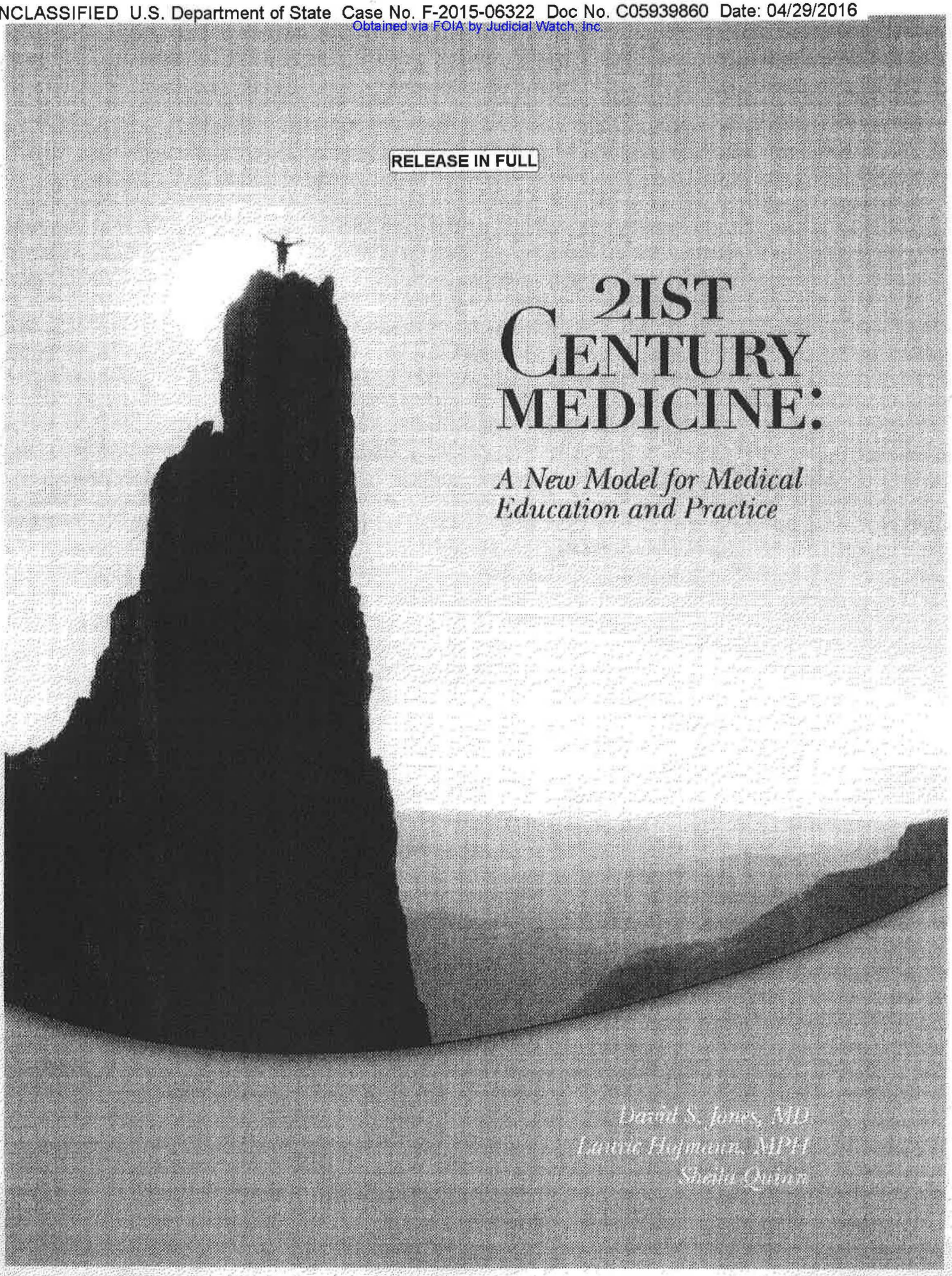


CLAYTON LAMPERT

Clayton Lampert 136

1. I wrote this sentence.
2. I have several radios.
3. Since when do you have an x box?
4. I am thinking of something.
5. I am better at math than my sister.
6. Though the cat was old, it was still very playful.
7. We're all in this together.
8. The water was calm until the alligator attacked.
9. Usually it is quiet in my room.
10. I am very happy most of the time.
11. While you were at school, I went skiing.
12. You ate the whole cake!!!
13. I went on a cruise on the English canal.
14. I am good at mathmatics.
15. I listen to music alot.
16. My Dad took a physical.
17. I have an education.
18. The old man was not very



21ST CENTURY MEDICINE:

A New Model for Medical Education and Practice

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21ST CENTURY MEDICINE:

A New Model for Medical Education and Practice

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Preface

Beginning a Journey of Discovery

The document you are about to read emerged from a systematic process of inquiry and intentionality about some of the most critical issues in health care today. While there are many vital structural factors to be addressed elsewhere (reimbursement practices, insurance coverage, electronic medical records, and the medical home concept), our attention and expertise are here focused on the content and process of care. The path we followed to conceive of, research, and write this white paper on 21st century medicine can be traced back to 2006, when the Fountainhead Foundation approved a grant to The Institute for Functional Medicine (IFM) to establish and manage a scholarship program for medical schools and residency programs to send selected faculty, students, and residents to learn about functional medicine. Over a two-year period, 43 scholarships were awarded, representing 15 medical schools and six residency programs. The impact and opportunities that have grown out of this seed funding have been significant, immediate, and wide-ranging across academic medicine, clinical programs, fellowships, and residency programs.

Our interviews, meetings, and follow-up discussions with scholarship recipients and their colleagues underscored the fact that IFM needed to provide a rationale and methodology for facilitating a more systematic and widespread introduction of functional medicine into these diverse institutions and programs. It is very arduous to modify both the process and content of medical education. There must be a compelling reason and a clear path toward the goal. Our journey, therefore, involved documenting the urgent need for a major shift in medical education, and then describing a model of care that can be adapted to the teaching needs of medical (and other health professions) schools and residency programs. In so doing, we provide both the justification for, and a description of, the change that must occur to equip clinicians to adapt successfully to the healthcare demands of the 21st century.

We looked first at relevant major themes in health care today (Chapters 2 and 3): the epidemic of chronic disease; the evolution of evidence-based medicine; the poor performance of the acute-care model in a chronic-care environment; the emergence of new paradigms such as systems biology, integrative medicine, and personalized care; and the lack of consensus on how to address these issues in a systematic way. This journey took us deep into the literature of costs vs. performance, science vs. art, research vs. clinical practice, and the many ideas about how to consolidate the gains of the 20th century without losing flexibility or constraining the promise of new information and new models of care for the future.

With this background in place, we began to explore how all of this looks and feels to the individual clinician who is immersed in the daily demands of clinical practice (Chapters 4 and 5). This, of course, is where the rubber meets the road. We found that not only have we failed to materially assist most primary care practitioners in understanding how to make better use of evidence, and in translating new tools and ideas into their clinical practice, but we have left clinical medicine poorly equipped to address two critical elements: (1) managing the uncertainty that is inherent in

clinical practice, and (2) creating a healing partnership with patients. We found that clinicians are no longer taught how to integrate the science and the art of medicine—indeed, the art of medicine has all but disappeared as a subject of teaching. From the evidence-based medicine (EBM) perspective, all you really need to do is gather data, focus the data toward securing the diagnosis, and then research the evidence about the best molecule (Rx) or procedure to treat that diagnosis. Doctors in the EBM, acute-care model have almost become technicians. Converging pressures have reinforced this model by forcing doctors to focus their office visits more and more narrowly, and to deliver care in less and less time (often for less and less money).

If that model worked, we wouldn't have had grounds for writing this paper. Unfortunately, the model has failed spectacularly to help stem the rising tide of chronic disease (Chapter 2). Fortunately, however, there is plenty of evidence that this is not the only way forward. Physicians and other practitioners can be taught to shift into a personalized, systems-medicine approach that is much better adapted to the complex demands of chronic disease. They can learn to gather and analyze patient data differently. They can twist the kaleidoscope and apply critical thinking to the use of evidence. And they can create healing partnerships that allow both patients and practitioners to achieve insight and then to evaluate that insight in the light of knowledge and experience.

The Institute for Functional Medicine has developed a model of comprehensive care and primary prevention for complex, chronic illness that is grounded in both the science (the Functional Medicine Matrix Model™) and the art (the healing partnership in the therapeutic encounter) of clinical medicine. We call this model functional medicine, and we have taught it for many years. It is not a separate discipline or specialty—it is an approach to clinical care that is comprehensive and patient-centered, personalized and grounded in science. It can be taught to and practiced by any health practitioner who has a background in the basic medical sciences and clinical practice, and it can adapt quickly and easily to emerging evidence. It can also provide a common language, shared principles and organizing tools, and a consistent analytic process to support and facilitate integrated health care.

Reintegrating the Science and Art of Medicine

There are always two deeply powered processes at work in any life-changing endeavor. Human beings require both denotative and connotative information for mastery—that is, we need both data and intuition, science and art. Brain scientists have made great progress in illuminating the deep creative processes by which our "minds" make use of the "matter" of our brains.[1,2,3,4,5,6] Clinicians, particularly, need to bring to the therapeutic encounter the unique qualities of both right- and left-brain function that have been emerging from brain science research. In the last decade, wider use of functional imaging technology has delivered a much clearer picture of coordinated brain function—why and how it occurs.

Jill Bolte Taylor, PhD was a neuroanatomist at Harvard Medical School when she sustained an aneurismal stroke in the primary speech areas of the left brain. In her video presentation to the TED (Technology, Entertainment, Design) group,[7] she describes the integrated functionality of the two sides of the brain in a way that can inform our understanding about a comprehensive patient-care model that respects and integrates both the science and the art of medicine. Her articulation of her "stroke of insight"[8] vividly illustrates important aspects of the new pattern that we must weave together:

...when you look at the brain, it's obvious that the two cerebral cortices are completely separate from one another. For those of you who understand computers, our right hemisphere functions like a parallel processor. While our left hemisphere functions like a serial processor. The two hemispheres do communicate with one another through the corpus collosum, which is made up of some 300 million axonal fibers. But other than that, the two hemispheres are completely separate. Because they process information differently, each hemisphere thinks about different things, they care about different things, and dare I say, they have very different personalities.

Our right hemisphere is all about this present moment. It's all about right here right now. Our right hemisphere thinks in pictures and it learns kinesthetically through the movement of our bodies. Information in the form of energy streams in simultaneously through all of our sensory systems. And then it explodes into this enormous collage of what this present moment looks like. What this present moment smells like and tastes like, what it feels like and what it sounds like. I am an energy being connected to the energy all around me through the consciousness of my right hemisphere. We are energy beings connected to one another through the consciousness of our right hemispheres as one human family.

My left hemisphere is a very different place. Our left hemisphere thinks linearly and methodically. Our left hemisphere is all about the past, and it's all about the future. Our left hemisphere is designed to take that enormous collage of the present moment. And start picking details and more details and more details about those details. It then categorizes and organizes all that information. Associates it with everything in the past we've ever learned and projects into the future all of our possibilities. And our left hemisphere thinks in language. It's that ongoing brain chatter that connects me and my internal world to my external world. But perhaps most important, it's that little voice that says to me, "I am. I am." And as soon as my left hemisphere says to me "I am," I become separate. I become a single solid individual separate from the energy flow around me and separate from you.

Continuing the Journey

We find ourselves at the beginning of the 21st century faced with a healthcare system in disarray on many levels. We must reassemble the disparate pieces of this baffling puzzle into a new and more coherent pattern. The intention of this document is to establish the need for a new model of care, and to make conscious, transparent, and usable the functional medicine model. We will show how this integrated model can better meet the needs of a population afflicted with steadily increasing rates of chronic disease. We believe that these changes will also help physicians establish a more satisfying basis for clinical practice.

The diligent work and thinking of 20th century clinicians and scientists have brought us to this moment with many tools and key concepts, including:

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- the art and science of clinical medicine
- systems biology and personalized, systems medicine
- prospective health care
- patient-centered health care
- the chronic-care model and the chronic-care team
- integrative medicine
- nutrigenomics, pharmacogenomics, proteomics, metabolomics
- evidence-based medicine (EBM)
- right and left brain functionality and the healing partnership
- the science and practice of creating insight as part of the therapeutic encounter
- the process of managing the uncertainty inherent in the clinical encounter

Ultimately, we will transform medical education and clinical care for chronic disease only if we can elucidate both the urgency of and the pathway toward a new model. We will succeed as 21st century physicians only if we attack the underlying drivers of chronic disease and rising costs—the complex, lifelong interactions of lifestyle, environment, and genetics. We will create an integrated healthcare system only if we provide a common set of principles, concepts, and practices that can be taught to and used by all members of the healthcare team. To these ends, we have used our time, expertise, and commitment to synthesize a model of health care for the 21st century that cogently integrates the best components of both established and emerging knowledge and practices. We describe in these pages a healing partnership that can readily adapt to new approaches and new evidence, that engages all parts of the brain, and that strengthens the bodies, minds, and spirits of both physicians and patients as they share the path toward improved health.

Our heartfelt thanks to the Bitzer Family
and the Fountainhead Foundation
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that has made this project possible.

David S. Jones, MD
President, The Institute for Functional Medicine

Laurie Hofmann, MPH
Executive Director, The Institute for Functional Medicine

Sheila Quinn
Consulting Author and Editor

Chapter 1

INTRODUCTION

Opportunity

If done right, the development of a health care system that focuses on personalized health planning will be every bit as transformational as the coupling of science to medicine was in the early 20th century.

—RALPH SNYDERMAN, MD, AND R. SANDERS WILLIAMS, MD[9]

Throughout the medical system, the heartbeat of impending change has been heard with increasing intensity since the turn of the century. Concepts such as prospective health care, personalized medicine, systems biology, nutritional genomics, integrative medicine, the chronic-care model, and others represent diverse aspects of the impetus to devise a substantively different way of approaching health care in the 21st century. The shift in prevalence from acute to chronic disease[10,11], and a growing recognition of the inherent limitations and consequences of shaping medicine primarily around an acute-care model[12] are among the most powerful forces that are driving change. The context of uncertainty that pervades the realm of clinical care[13] demands a comprehensive and flexible model that can integrate evidence relevant to the individual without forcing physicians and other practitioners to manage complex, chronic disease using an acute-care model that is ill-suited to the task. Transformation is imminent—the opportunity is now.

The "next next transformation" will change the paradigm to focus on health—positively defined and measured as something other than the "absence of disease"; conceived as an integrated function of biology, environment, and behavior; and measured as a product of physical, mental, social, and spiritual variables.

—MICHAEL JOHNS, MD, AND KENNETH BRIGHAM, MD[14]

As we come to the close of the first decade of the 21st century, the opportunity to influence the strategic decisions that will redirect medical education and practice for the foreseeable future will encounter many challenges. Philosophies of health and disease, exciting new models of delivery and management of care, practitioner diversity and interrelationships, emerging perspectives on science and evidence, and the teaching of analytical thinking and clinical reasoning are all under pressure to evolve. Resistance to change and eagerness for it exist simultaneously within all established systems; both perspectives represent important issues that must be addressed successfully to ensure that changes are purposeful, practical, and effective. Educational programs and leaders will be called upon to set the pace of change, identify the best models, integrate those models into existing curriculums, and advocate for widespread adoption.

We can facilitate this process by taking into account the substantial common ground that already exists among many of the leading innovative paradigms, even when they are not directly comparable in intent or in practical applications. Congruent elements can be identified, extracted, and synthesized to inform a comprehensive new model that will be compatible with both established and emerging approaches to health education and practice. In addition, there are important principles and practices that can provide a solid foundation for synthesizing these congruent elements into a workable new model.

Visualizing and implementing a fresh approach to health and disease will require collaborative efforts and systems that work to the benefit of patients and practitioners alike. In this paper, we will describe how certain key forces and concepts are critical components of a dedicated effort to achieve productive and lasting improvements in our healthcare system. We will demonstrate how the common themes in these overlapping paradigms represent fertile terrain for synthesizing a comprehensive new model. We will identify elements that must be added to the common themes to create an effective model for teaching and practice. And we will describe that new model and advance suggestions about how to strengthen and implement it. The ideas are (metaphorically) bursting out of the literature, essential tools are being developed, and the pivotal technologies are rapidly advancing—the moment is ripe with promise.

Purpose

Our overarching purpose in writing this paper is to illuminate a path toward health and vitality for patients—not an easy or straightforward task in a world of increasing complexity and epidemic levels of chronic disease (Chapter 2). ***The intention of this document is to establish the need for a new model of care and to make conscious, transparent, and usable the functional medicine model.*** We offer to academic medicine leaders, practicing physicians, and other health professionals a model that we believe will substantially improve management of disease risk and assessment—as well as treatment for the millions of patients who already suffer from complex, chronic disease—using personalized, systems-oriented, cost-effective approaches. Blending the foundational principles and practices of functional medicine with the substantial common ground that already exists in emerging models clarifies a more comprehensive and effective model of teaching and practice for medical schools, residency programs, and eventually other health profession schools. Such an ambitious goal will succeed only if the plans rest upon a solid foundation that resonates strongly with leaders and early adopters in medical education and the health professions. Strategic objectives and effective tools to guide action steps appropriately will be required. The need for change and the matching of solutions to problems must be clear and persuasive. This paper will analyze emerging trends and needs and address the power of this synthesized model to shape those trends and meet critical needs in order to help improve the education and effectiveness of healthcare practitioners and offer their patients a better path toward lifelong health.

Emerging Models

From among the creative and fascinating new paradigms, we will address six that have emerged as leaders and already claim many adherents. They share a great deal of common ground that is critical to a synthesized, comprehensive model for 21st century medicine. Each of these new models, while incomplete in itself, contains elements that help to ensure compatibility and integration

into an overarching approach. These will be discussed in much greater detail in Chapter 3, but here we introduce the key concepts of each model. (There are other models of note, of course, including the Future of Family Medicine project and the Medical Home project; information on both of these is provided in the Appendix. In the body of this paper, however, we have narrowed our discussion to the models that appear to have the greatest potential impact on the actual content of care, rather than the structure of care.)

A graphic representation of some of the common themes and key concepts in these six models can be seen in Figure 1.

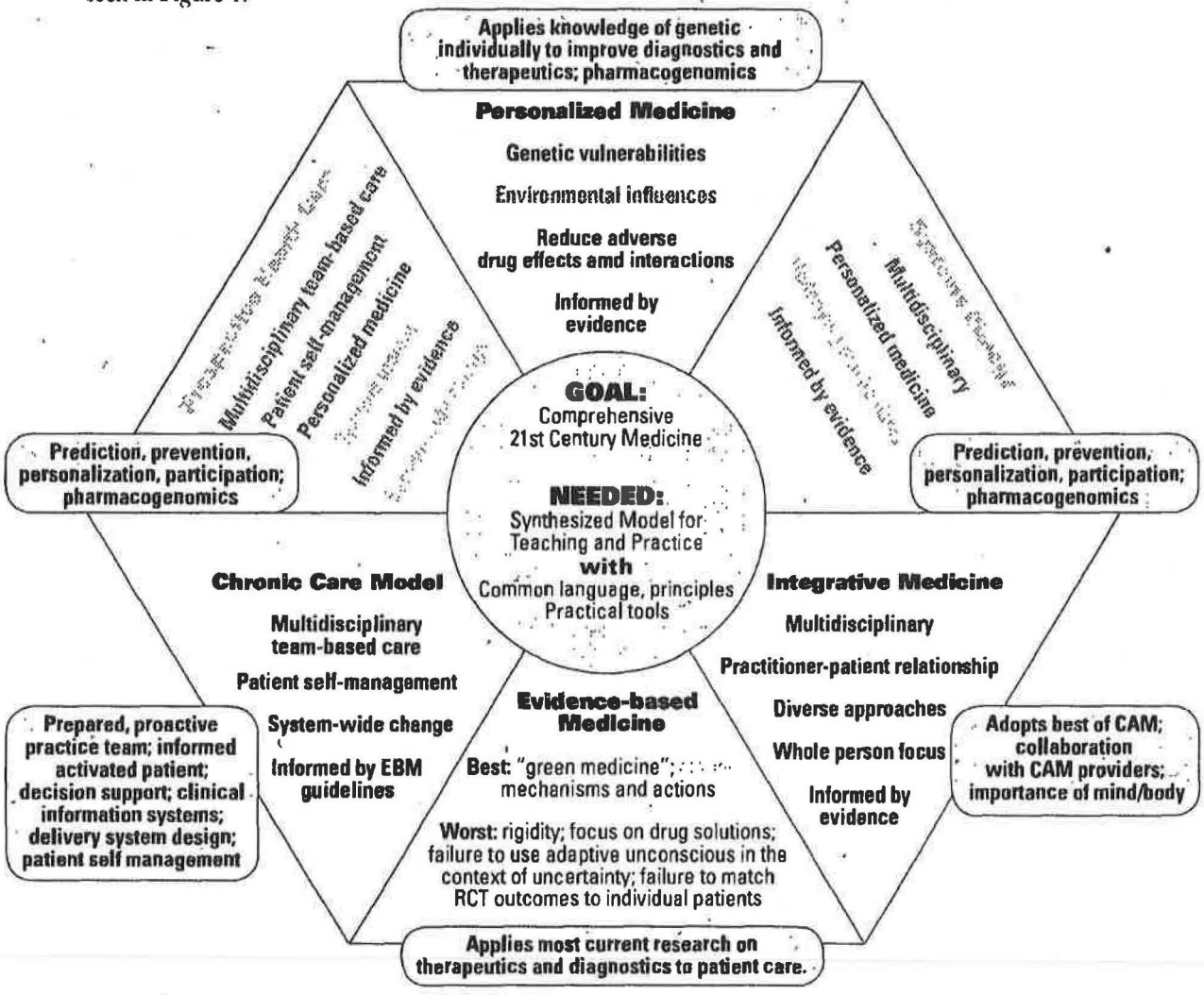


Figure 1: Common Themes and Key Concepts Among Emerging Models in Medical Education and Clinical Practice

1. Personalized medicine

Personalized medicine is often rather narrowly defined to comprise primarily the development of genetic tests to identify risk factors for adverse or unpredictable drug effects and to identify individuals who are most appropriate for certain kinds of drug therapies or diagnostic procedures.[15, 16] This kind of assessment should certainly help to improve the matching of drugs and diagnostics to individual patients and, as a result, may also help to reduce death, disability, and costs associated with individual differences in the biotransformation of drugs and other substances.[17] However, under the rubric of personalized medicine lie many other complex issues relevant to biochemical, physiological, genetic, and environmental individuality that must also be attended to if we hope to reverse the modern epidemic of chronic disease and assist patients toward healthier lives. This broader model of personalized care has already become an explicit component of systems biology and prospective health care, and it is implicit in the chronic-care model and integrative medicine as well. Personalized medicine is critical to the future of health care.

2. Prospective health care

A bold new model for 21st century medicine called prospective health care was proposed in 2003 by Snyderman and Williams.[18] Pilot projects have been initiated and are being tested now at Duke University. In a 2006 article,[19] Snyderman and Langheier described their rationale in terms completely consistent with the focus of functional medicine for the past two decades:

> Chronic diseases develop as a consequence of an individual's baseline susceptibility coupled with their exposure to environmental factors. These may trigger initiating events, leading to the accumulation of pathological changes and the onset and progression of chronic disease. Today, most health-care expenditure is focused on the later stages of this process, long after the development of many underlying pathological changes. Until recently, it could be argued that the focus on treating disease was justified because the ability to predict, track, and prevent its onset was not technically feasible. This is no longer the case, and the emerging sciences of genomics, proteomics, metabolomics, medical technologies and informatics are revolutionizing the capability to predict events and enable intervention before damage occurs. Personalized risk prediction and strategic health-care planning will facilitate a new form of care, which we have called "prospective health care."

Including the same four elements as systems biology (prediction, prevention, personalization, and participation), prospective health care offers a much broader perspective, describing structural and procedural transformations that must also occur in reimbursement, research, risk management assessment, record keeping, and the delivery of care.[20] The thrust of these changes is "toward managing disease risk and providing personalized care for chronic and acute disease."[21]

3. Chronic-care model

The full chronic-care model (CCM), first conceived in 1998, was formally presented in a 2001 publication by Wagner et al.[22] Since that time, it has undergone serious study, implementation, and revision to accommodate experiences in clinical settings and findings from research. Emerging evidence has shown fairly conclusively that patient outcomes in a variety of chronic conditions can be improved whenever substantive progress is made on integrating the elements of this model into clinical practice. Core elements include:

- Productive interactions between informed, activated patients and prepared practice teams
- Effective patient self-management strategies
- Delivery system redesign (team approach; multidisciplinary, planned interventions instead of acute, reactive interventions; use of case managers; regular follow-up)
- Decision support (integration of evidence-based guidelines into the flow of clinical practice so that information to support clinical decision making is readily available)
- Clinical information system (the use of a database and other resources that bring timely, relevant information to both physicians and patients)
- Community resources and policies

CCM has in common with prospective health care a strong emphasis on redesigning the systems that support and shape clinical practice. Both have explicit emphases on a team approach to chronic care, the necessity of patient self-management, and the urgent need to involve community resources and attract the attention of policymakers.

4. Evidence-based medicine

Evidence-based medicine (EBM) is "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients." The practice of EBM means integrating individual clinical expertise with the best available external clinical evidence from systematic research."[i]

We include EBM in the analysis of emerging models because of its growing influence on clinical practice and medical education. Although it is not, in and of itself, a type of medical education or clinical practice, at its best it can provide practitioners and healthcare delivery organizations with more current and focused decision support through the integration of relevant research findings into clinical decision making. Although EBM is intended to reduce uncertainty and improve the consistent use of best practices in patient care, experimental designs have not yet caught up with the complexity of chronic disease, the multiple needs and diverse presentations of patients in the clinical setting, and the multifactorial interventions that are required to address such diversity and

[i] Used with permission of the Centre for Evidence-based Medicine.
A more expanded definition of Evidence-based medicine is included in the Appendix.

complexity.[23] EBM cannot replace analytical thinking, clinical reasoning, and clinical experience,[24] although sometimes it is presented as doing just that. Improperly applied, EBM can place patients in serious jeopardy.[25] Ideally, it can be used to increase practitioner effectiveness if its strengths are appropriately utilized and its limitations are clear: "The methods of EBM do not supply 'correct' answers but rather information that can improve clinical judgment."[26] Ultimately the appropriate use of EBM relies on a more precise definition of what constitutes relevance and best evidence for each individual patient encounter.

5. Systems biology

The Institute for Systems Biology in Seattle, Washington, identifies four factors that comprise its field: prediction, prevention, personalization, and participation. Although elsewhere systems biology is not defined quite so broadly, it is useful to consider it through this wide-angle lens, for it makes readily apparent the interconnections with integrative medicine, prospective health care, and personalized medicine that open the door to a synthesized model. Systems biology as currently pursued focuses primarily, as does personalized medicine, on genetic mechanisms in drug responses, but given a broad vision—and the will and funding to execute on that vision—it could become the scientific engine driving clinical medicine toward the model we are proposing. A more detailed description from the Institute for Systems Biology's Web site is provided in the Appendix.

6. Integrative medicine

In the years since 1990, when eight academic medical institutions first met to discuss the emerging field of integrative medicine, active participation among academic medical centers has grown dramatically. Now more than 40 institutions[a] are members of the Consortium of Academic Health Centers for Integrative Medicine (CAHCIM), comprising many of the finest medical schools in the country, with several having endowed centers or foundations to support expanded development in the field. Their collective mission is:

> ...to help transform medicine and health care through rigorous scientific studies, new models of clinical care, and innovative educational programs that integrate biomedicine, the complexity of human beings, the intrinsic nature of healing and the rich diversity of therapeutic systems. [27]

Their definition of integrative medicine is:

> ...the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals and disciplines to achieve optimal health and healing.

[a] See list of CAHCIM members in the Appendix.

Several elements of integrative medicine are highly relevant to the model proposed in this paper:

- The openness to new diagnostic and therapeutic strategies (e.g., nutrients, botanicals, mind-body interventions, acupuncture) and to cooperation with health professionals from other disciplines signals an important readiness to develop a fully integrated healthcare model—one in which the patient is the central focus and all practitioners have in common certain critical elements of language, philosophy, and clinical practice.
- The commitment to adopt innovative approaches in education is essential to the transformation of medicine.
- The emphasis on the value of practitioner-patient relationships and the focus on the whole person will play a significant role in the medicine of the future. These values—formerly so intrinsic a part of medicine that they went almost unnoticed—are receiving renewed attention now that their disappearance from much of medical care has become apparent. They are absolutely vital components of a transformed approach to health care.

Summary

In this white paper, we will establish the need for a new model of education and care; we will address forces that may represent obstacles to change; and we will explore the key concepts and elements already present in science and medicine that are ripe for synthesis into a new, more comprehensive model. Our goal is to make improvement in medical education programs and clinical practice *feasible* – not in an abstract or ideal sense, but in the real world with all its resistance to change and discomfort with emerging concepts. To that end, funding has already been secured for the development of a pilot project for adapting the model to medical education. Before being finalized, each phase of the project will be reviewed by a small group of leaders within academic medicine who are interested in achieving a major shift in medical education, so that we tailor our recommendations to the audience with as close a fit as possible. Our aim is nothing short of inspiring system-wide change—the transformation of medicine is imminent, it is urgently needed, and it is entirely possible.

Chapter 2

THE CHANGING MEDICAL ENVIRONMENT

Background

There are, literally, innumerable facts and statistics available with which to describe and analyze health and health care. Any discussion must of necessity be based on a selected subset of the data and, thus, subject to the bias of the authors. We have, for example, omitted such critical issues as the reimbursement structure, governmental regulatory influences, health disparities, environmental degradation, and the uses of technology—all topics on which reams of important material have been written. Our goal here is not to cover everything that is either problematic or of value within the medical environment, but to concentrate our thinking on well-established data that help to illuminate an overarching problem—that we are losing the battle against chronic disease and that fundamental change will be required to improve our performance.

Global and economic issues

The healthcare system is influenced by increasingly complex and varied issues. Although many of these are beyond the scope of this paper, we would be remiss if we did not at least acknowledge their importance:

- The growing ethnic diversity of the U.S. population poses challenges of communication, varied beliefs and preferences about treatment, and the adverse impact of the standard American diet (SAD) on genetically vulnerable populations. [An excellent overview of emerging global health issues that are brought to the U.S. by immigrant populations can be found in the July/August 2008 issue of *Health Affairs*, which focuses on India and China. These articles demonstrate unequivocally that health issues in the developing countries parallel those of the developed world, as affluence, sedentary lives, and fragmentation of communities increase while food quality and diversity decrease.]
- The transmissibility of new diseases (e.g., avian flu) between species and across the world's continents poses a special challenge to both acute and chronic care.[28]

- Economic shifts that are strongly affected by global markets could have profound effects on the U.S. model of healthcare financing, an issue that has been under considerable scrutiny for many years already. Increasingly, the evidence identifies our patchwork approach to reimbursement as a considerable barrier to equitable and effective care.[29]
- Importation and transportation of foods, prescription drugs, botanicals, and nutraceuticals among countries with widely differing quality control and environmental standards will affect virtually every citizen over time.

While we focus in this paper on models for clinical practice and medical education, we should keep the above issues in mind, because they will continue to influence both the healthcare system and individual health

The pharmaceutical and acute-care models

The acute-care model is characterized by rapid differential diagnosis aimed at prescribing a drug (or procedure) that will ameliorate the patient's presenting symptoms and avert the immediate threat.[30] It minimizes the involvement of the patient, who functions as a mostly passive recipient of the procedure or prescription.[31] It is not a model that reimburses the practitioner for looking into why the patient became ill, or whether she/he will be back many times for manifestations of the same underlying problem.[32] Instead, it prioritizes quick solutions to the most pressing problems. It is, of course, absolutely essential in emergency and hospital-based care, but difficulties arise when this model is applied to ongoing, community-based care, a process that accelerated under the managed-care movement (which turned out to be far more about managing costs than managing care) and the direct-to-patient advertising of drugs. With hindsight, it seems as though everything has been pushing the system toward this narrowed focus, regardless of it (Figure 2).

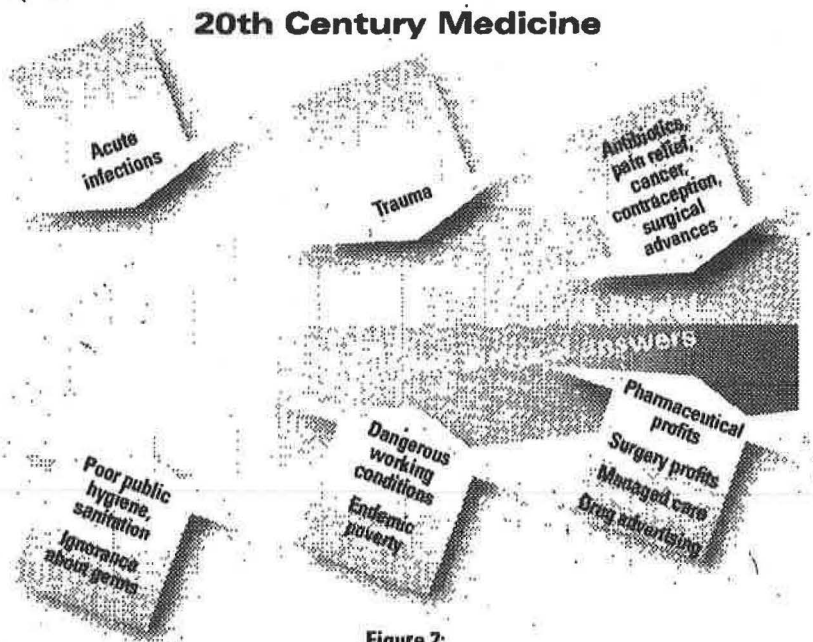


Figure 2:
Forces Narrowing the Focus of 20th Century Medicine

The advances achieved by drugs in curing acute infections and managing some of the most threatening diseases mankind has faced were dramatic in the last century. The extended romance with pharmaceutical medicine, which first blossomed in the early 1930s when penicillin began to cure previously intractable infectious diseases, has now dominated medicine and medical education for more than seven decades. From depression to diabetes, from heart disease to asthma, the search for therapeutic compounds that can be patented as drugs continues unabated. The accompanying financial incentives have attracted (and perhaps distracted, see **Sidebar**) some of the best minds and most influential leaders in research and medical education, including those engaged in the development of systems biology and personalized medicine, both of which are primarily focused on pharmacogenomics at this time (see Chapter 3 and the Appendix for more information on these models).

Costs and Performance in the Battle for Health

It is discouraging to note that among the vast array of peer-reviewed medical research reports published every year, there is so little that addresses whether the overall health of the population shows an adequate positive response to current medical treatment. Thousands upon thousands of studies compare one drug to another without ever acknowledging that Americans are far less healthy—at far greater cost—than their counterparts in the rest of the industrialized world. The reduction in deaths from, for example, heart disease is emphasized,[39] while the fact that we have failed to prevent CVD—even while reducing, through drugs, the prevalence of CVD risk factors such as hypertension and high cholesterol[40] —is too often ignored. In fact, we must turn primarily to philanthropic or governmental agencies for data and analyses that reveal the scope of the failure. "The Milken Institute recently estimated that the most common chronic diseases cost the economy more than $1 trillion annually, mostly from lost worker productivity, which could balloon to nearly $6 trillion by the middle of the century."[41] If nothing else, that estimate alone should galvanize us to action!

Research Bias: The Pharmaceutical Hegemony in Funding and Focus

Opportunities lost are perhaps the greatest concern in the dominance of the pharmaceutical research model. Too often, the search for drugs that will pay off for investors and executives of pharmaceutical companies determines the research agenda.[33] Rather than being driven by patient needs, public health priorities, or scientific curiosity about mechanisms and pathways, the profit motive is the driver of the research agenda, and the gains to science and health are collateral outcomes, not central purposes. Lest we think this is trivial, consider that 70% of the money for clinical drug trials in the U.S. comes from the pharmaceutical industry.[34]

"Scientifically, a neutral or negative trial is as valuable as a positive one," although commercially this is clearly not the case."[35] Unless all results are available to the scientific community, the evidence record about those drugs that are investigated can be significantly skewed by the absence of negative or neutral findings. The value to academic researchers (and their institutions) of bringing in large clinical trials with drug company funding may be very significant; promotions, recognition, and supplemental income provide a triple-threat incentive that is virtually impossible to ignore when considering research priorities.[36, 37]

Many studies have shown a bias toward positive results when the research was funded by the drugs' manufacturers.[38]

The broad education in science and clinical arts that physicians experience today is expressed in clinical practice through a constricting and linear process that is primarily aimed at naming a drug of choice for the patient at hand.[42] Unfortunately, 50 years of such practices have failed to stem the rising tide of chronic diseases among both young and old,[43] while related problems have emerged to cause great concern:

- The **cost of care** is unmanageably high and rising,[44] driven by the high costs of hospitalization[45] and drugs,[46, 47] but also fueled by increasing prevalence of complex, chronic disease at all ages of the population.[48, 49] It is estimated, for example, that more than half of all Americans suffer from one or more chronic diseases,[50] and that the 8 million Medicare beneficiaries who have five or more chronic conditions accounted for over two-thirds of the program's $302 billion in spending in 2004.[51]

> The Milken Institute report, *An Unhealthy America* (October 2007), provides the following food for thought:
>
> "To quantify the potential savings from healthier lifestyles and plausible but modest advances in treatment, we compared a "business-as-usual" baseline scenario with an optimistic scenario that assumes reasonable improvements in health-related behavior and treatment. The major changes contemplated here are weight control combined with improved nutrition, exercise, further reductions in smoking, more aggressive early disease detection, slightly faster adoption of improved therapies, and less-invasive treatments....
>
> "Across the seven diseases, the optimistic scenario would cut treatment (direct) costs in 2023 by $217 billion.... And the cumulative avoidable treatment costs from now through 2023 would total a whopping $1.6 trillion. Note that this would be a gift that keeps on giving, saving hundreds of billions annually in the years beyond 2023.
>
> **"All told, our analysis implies that modest reductions in avoidable factors—unhealthy behavior, environmental risks, and the failure to make modest gains in early detection and innovative treatment—will lead to 40 million fewer cases of illness and a gain of over $1 trillion annually in labor supply and efficiency by 2023.** Compared to the costs we project under the business-as-usual scenario, this represents a 27 percent reduction in total economic impact."

- Table 1 displays the **bookends of health: rankings on infant mortality and life expectancy.** The U.S. makes a very poor showing on both, particularly for a country whose citizens have been taught to believe they have the best health care in the world. The U.S. spends twice the median per-capita costs calculated by the Organization for Economic Cooperation and Development (OECD),[52] has extraordinarily poor outcomes for such a massive investment,[53] and does not even provide coverage for all its citizens (an estimated 47 million currently uninsured[54]; 75 million under- and uninsured combined[55]).

Table 1. Infant Mortality and Life Expectancy Rankings of the United States

Ranking	Country	Infant Mortality[1]	Country	Life Expectancy[2]	Ranking
1	Sweden	2.8	Japan	81.4	1
2	Japan	3.2	Switzerland	80.6	2
3	Finland	3.5	Sweden	80.6	3/4
4	Norway	3.6	Australia	80.6	3/4
5	Czech Republic	3.9	Canada	80.3	5
6	Germany	4.1	Italy	79.9	6/7
7	France	4.2	France	79.9	6/7
8	Spain	4.3	Spain	79.8	8
9	Switzerland	4.3	Norway	79.7	9
10	Austria	4.5	Israel	79.6	10
11	Denmark	4.5	Greece	79.4	11
12	Australia	4.6	Austria	79.2	12
13	Canada	4.6	New Zealand	79.0	13/14
14	Portugal	4.9	Germany	79.0	13/14
15	United Kingdom	5.0	United Kingdom	78.7	15
16	Ireland	5.2	Finland	78.7	16
17	Greece	5.3	United States	78.0	17/18/19
18	Italy	5.7	Denmark	78.0	17/18/19
19	New Zealand	5.7	Cyprus	78.0	17/18/19
20	Korea, South	6.1			
21	United States	6.4			

1. Infant deaths per 1,000 live births.
2. Life expectancy at birth, in years, both sexes.
Source: U.S. Census Bureau, International Database
From http://www.infoplease.com/ipa/A0004393.html

- The **"quick fix" mentality** that drug dependence has fostered in patients creates an unhealthy cycle that drives further drug dependence. Sensible and distinguished voices calling for major long-term investments in helping people establish healthy behaviors and in ensuring a healthy planet have heretofore been mostly ignored in the struggle for attention and funding. And yet, with only a few exceptions, the development of chronic disease is predominantly influenced by multiple interactions between genes and environment experienced over many years; neither factor alone is enough—the genes must be plunged into an adverse environment to express disease and they must be rescued from such environments to restore health (not just suppress symptoms).

- **Walter Willett:** "For most diseases contributing importantly to mortality in Western populations, epidemiologists have long known that nongenetic factors have high attributable risks, often at least 50 or 90%, even when the specific etiologic factors are not clear."[56]
- **Kenneth Thorpe:** "Health behavior such as overconsumption of food, lack of exercise, smoking, and stress accounts for 40% to 50% of morbidity and mortality."[57]
- **Robert Heaney:** "Discerning the full role of nutrition in long-latency, multifactorial disorders is probably the principal challenge facing nutritional science today. The first component of this challenge is to recognize that inadequate intakes of specific nutrients may produce more than one disease, may produce diseases by more than one mechanism, and may require several years for the consequent morbidity to be sufficiently evident to be clinically recognizable as 'disease.'"[58]

- Drug-resistance phenomena,[59] **adverse drug reactions**,[60] and adverse interactions between drugs and foods,[61] drugs and botanicals,[62] and drugs and other drugs[63] now affect millions of lives each year and are a cause of death in unprecedented numbers.[64] Rates of visits to provide care for adverse drug reactions increased by one-third between 2001 and 2004.[65]

On a deeper level, the drug paradigm—and the most rigid part of the evidence-based movement that supports it—may adversely affect clinical judgment. To minimize time spent with patients, physicians are forced to focus on prescribing the "right" drug. Very often, however, the evidence about the "right" drug rests on studies that do not reflect a real patient population as seen in clinical practice[66]; multiple comorbidities, for example, are usually excluded from RCTs.[67, 68] Until very recently, nearly all clinical trials failed to account for variations in individual biochemistry and physiology, as well.[69, 70]

This shift toward rapid prescribing results in a de-emphasis on establishing therapeutic relationships and exploring the patient's story. Time pressures applied by reimbursement entities make it very difficult to do the analytical thinking that develops broad pattern-recognition abilities. Immensely valuable clinical skills for managing complex, chronic disease and multiple comorbidities are thus being sidelined; as that happens, fears about innovation and creativity surface, a retreat to dogma and linearity becomes apparent, and the idea that the job of medicine is to find the right drug(s) for the most parsimonious diagnosis preoccupies mainstream thought. Such forces separate the physician from many analytical and inferential skills that are likely to be extremely useful in the search for common underlying pathways of chronic disease and for new approaches designed to intervene where such disease actually originates—in the patient's unique mix of biochemistry, genetics, and environment.

The focus on drugs could be considered both cause and effect of the dominance of the acute-care model that has come to characterize medicine today. As the challenges of infectious disease and trauma gave ground to advances in drugs and surgery, startling successes strengthened the belief that modern medicine would eventually conquer most diseases with those tools. A perspective that only intensified as the profits to be made from drugs and surgery became a magnet for both individuals and institutions. Few scientists or physicians in the 1950s and 60s foresaw a moment when the challenge of chronic disease would swamp the healthcare system and prove resistant to the miracles of 20th century medicine.

Now, however, in the 21st century, we are fully aware that **complex, lifelong interactions between our genes and environmental degradation,[71] unhealthy diets[72] (fueled by changes in both eating habits and food supply[73]), stress,[74, 75, 76] sedentary lives,[77] and social fragmentation of families and communities[78] have surged to the forefront as interwoven causes of chronic disease that are not amenable to treatment with an acute-care model.** (Figure 3 depicts the pressures that are forcing a broader process of clinical thinking and care.) With an aging population, these effects are present through many more years of life and thus become impressive cost drivers (see, for example, the Medicare data in Figure 4). The system must expand to address these interconnected trends. Broad-based pattern-recognition and communications skills will be needed to prevent, treat, and reverse the declining function associated with these pervasive influences. We must transform our system of health care through new models for medical education, acute and chronic disease management, research, health insurance, and fiscal responsibility.

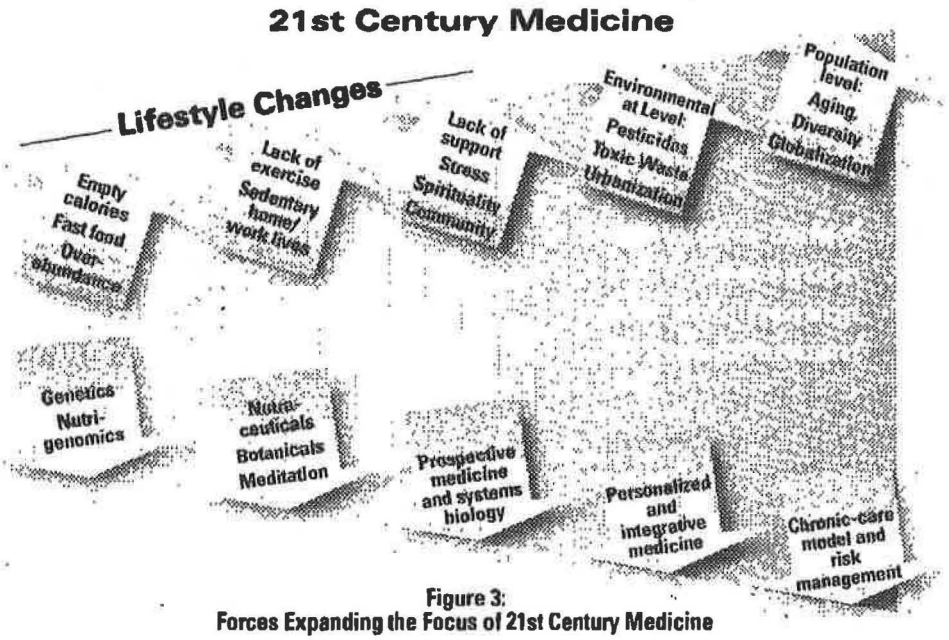


Figure 3:
Forces Expanding the Focus of 21st Century Medicine

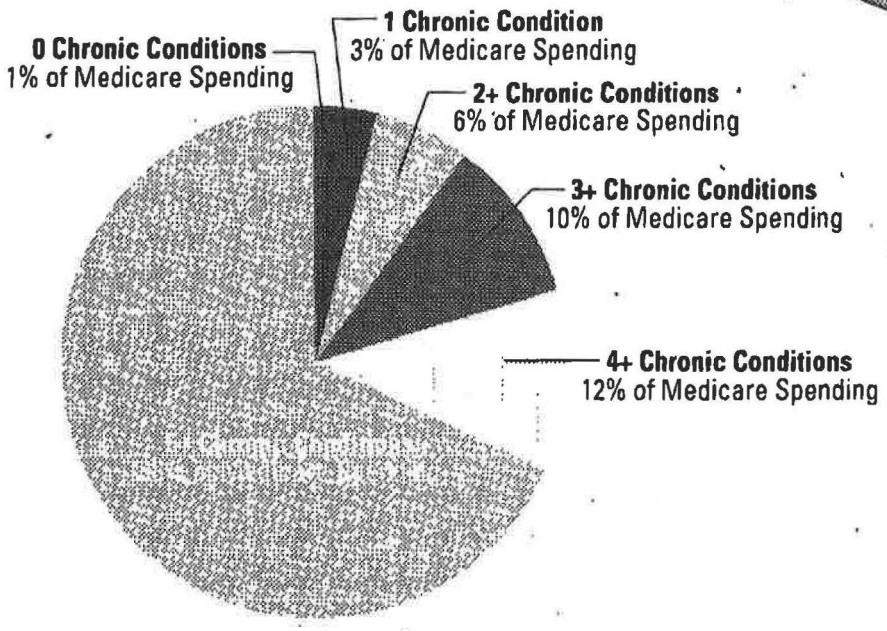


Figure 4:
Medicare Spending as a Function of Number of Chronic Conditions

Data from Chronic Conditions: Making the Case for Ongoing Care Johns Hopkins University and The Wobert Wood Johnson Foundation: Partnership for Solutions, September 2004.

The seemingly intractable poor performance of American medicine on a wide range of health measures[79, 80] forces us to pose some critical questions:

- Does the investment in a paradigm that identifies drugs as the treatment of choice across a broad array of diagnoses still produce the same returns on investment that were achieved in earlier decades?
- Is a system that seeks to reduce doctor-patient face time to the fewest possible minutes, and that measures effectiveness by how little time and money are spent, going to enable us to address population-wide health needs in the century ahead?
- Does the acute-care model respond appropriately to the needs of patients already suffering from complex, chronic disease and multiple comorbidities, as well as to the exigency of preventing those diseases for currently healthy people and future generations?

We suggest that not only is the evidence persuasive that the answer to those questions is "no," but that the continued almost exclusive reliance on pharmaceutical answers to an epidemic of complex, chronic disease may constitute an unintended rejection of some practices critical to improving our response to today's urgent problems.

Changing Patterns: From Acute to Chronic Disease

The changes in mortality and morbidity in the United States over the last century have been described as a shift from an age of "pestilence and famine" to an age of "degenerative and man-made diseases."[81] In other words, infections and undernutrition as relatively straightforward causes of illness and (often early) death have been overwhelmingly superseded by chronic, degenerative conditions caused by multiple, complex influences. In addition to the discovery and development of antibiotics, the great achievements of the public health system[82]—vaccinations; safety in municipal water and sewage systems, foods, medicine, workplace, highways and motor vehicles; prenatal and pediatric care; reduction in smoking—were among the most critical factors in making this shift, particularly in the first half of the 20th century.

Medicine's focus on the development of a sophisticated and multifaceted pharmaceutical war chest to cope with infectious disease achieved many notable successes. Unfortunately, infectious disease still has an uncomfortable persistence—a way of breaking out in a different guise just when it was thought to be under control—witness the emergence of AIDS, the ability of bacteria and viruses to become resistant to drug treatments, and the ever-evolving influenza virus, to name a few examples. There is no question, however, that pneumonia, influenza, tuberculosis, and diarrhea/enteritis (the leading causes of death in the United States in the early 1900s) have been replaced by heart disease, cancer, and cerebrovascular disease at the top of the mortality list.[83]

The tremendous advantage of this shift is that we can live much longer with chronic than acute diseases.[iii] Cardiovascular disease (CVD), for example, is the biggest killer,[iv] even though three of its four primary risk factors (hypertension, hypercholesterolemia, smoking) have been significantly reduced.[84] Unfortunately, the fourth, diabetes, has increased.[85] Pharmaceutical and surgical interventions have evolved to address both secondary prevention and symptom management. The upshot of this massive, long-term effort is that people with CVD are living longer and the incidence of death from this disease has substantially decreased.[86]

We could stop there and declare victory, but that would be tragically shortsighted. Although we have reduced the mortality associated with many serious chronic diseases, the prevalence of, for example, cancer, diabetes, asthma, and heart disease—and the conditions that precede and perpetuate them—has grown, rather than diminished. Rising disease prevalence is complex, of course, composed of at least three primary factors: "...a rise in the population prevalence of disease, changes in clinical thresholds (and awareness) for treating and diagnosing disease, and new technologies that allow physicians to treat additional patients with a particular medical condition. A rise in total disease prevalence (both diagnosed and undiagnosed) is associated with changing population risk factors such as obesity. For instance, among adults ages 20–74, obesity prevalence increased from 14.5% (1976–1980) to 30.4% 20 years later (1999–2000). During the same period, total diabetes prevalence, which is clinically linked to obesity, increased 53%, and diagnosed (treated) diabetes prevalence increased 43%."[87]

[iii] In the last century, overall life expectancy has risen from 51 to 79.4 years for women and from 48 to 73.9 years for men. Source: Chapter on Human Health, EPA Report on the Environment, 2003. Available at http://www.epa.gov/roe/roe/html/roeHealthSt.htm.

[iv] "According to the NCHS, if all forms of major CVD were eliminated, life expectancy would rise by almost seven years. If all forms of cancer were eliminated, the gain would be three years." Heart Disease and Stroke Statistics—2008 Update, American Heart Association. Cited source: U.S. Decennial Life Tables for 1989-91, Volume 1, No. 4. Eliminating Certain Causes of Death, 1989-91. NCHS, September 1999.

The current (and growing) dominance of chronic and degenerative diseases in the population is accompanied by many grave problems in addition to shortened life expectancy for today's children: increasing disability over time, lowered quality of life, and far greater costs—both for direct treatment and as a result of important factors such as lowered productivity, reduced income due to early disability, and the cost of supporting disabled people in society for many years. As discussed above, the cost of simply treating—with all the tools and expertise at our command—the current epidemic of chronic disease threatens to either bankrupt us or to displace resources needed for other urgent priorities such as education, infrastructure, social security, defense, research, and countless other vital activities.

We also know with greater certainty that longer life without vitality and health imposes a considerable burden in addition to the costs of treatment:

- Depression is strongly associated with chronic disease; it has become one of the world's most common conditions and results in severely decreased quality of life and increased direct and indirect costs.[99]
- Overall health-related quality of life (HRQOL) has gone down as chronic disease rates have risen. The Mortality and Morbidity Weekly Report Surveillance Summaries reported that "during 1993-2001, the mean number of physically unhealthy days, mentally unhealthy days, overall unhealthy days, and activity limitation days was higher after 1997 than before 1997. ...Adults increasingly rated their health as fair or poor and decreasingly rated it as excellent or very good."[100]
- Prolonged stress is exerted on families that provide care for disabled elders. "An estimated 16 million Americans—more people than live in all of New England—find themselves 'sandwiched' between two generations, struggling to raise their kids while caring for an aging loved one. That number is about to explode: In 25 years, there will be 60 million Americans between the ages of 66 and 84, many of them needing full- or part-time care."[101]

The Role of Obesity in Chronic Disease

Focusing on the role of obesity in chronic disease could pay untold dividends. "[O]ne of the most heritable of human traits,"[88] obesity is also profoundly influenced by lifestyle and environment.[89] It fuels (and can be exacerbated by) chronic diseases with high morbidity as well as mortality—cancer, diabetes (now projected to touch 30-40% of all Americans during their lifetimes), heart disease, and depression. As an outcome of the rise in diabetes and other obesity-driven diseases, Olshansky et al. made the shocking projection in 2005 that "... the steady rise in life expectancy during the past two centuries may soon come to an end."[90] In other words, if current trends continue unchecked, future generations will have shorter and less healthy lives than the adults of today.

The urgency of this situation is underscored in many compelling—and poignant—scientific papers that highlight some of the profound effects of the obesity epidemic on all age groups:

- **Elderly:** "Obese seventy-year-olds will live about as long as those of normal weight but will spend more than $39,000 more on health care. Moreover, they will enjoy fewer disability-free life years and experience higher rates of diabetes, hypertension, and heart disease."[91]
- **Adults:** "Two-thirds of adults in the United States today are obese or overweight."[92] "...the prevalence of diagnosed type 2 diabetes mellitus continued to increase concurrently

- Creativity and innovation are lost to underemployment or unemployment and the shrinking work force must support an increasingly disabled aging population for many more years.

We can and should feel grateful that the threat of acute disease decreased so substantially over the last century and, concomitantly, that our life expectancy increased dramatically. We must also recognize, however, the urgent need to redirect some of our healthcare dollars, energy, expertise, and time toward stopping and ultimately reversing the spread of chronic disease. While it is certainly true that we all must die of something, and conquering acute disease made space for chronic diseases to rise to the top of the mortality charts, we cannot allow our much longer lives to be increasingly haunted by unprecedented rates of chronic disease and its accompanying disability, depression, and sharply rising costs. Instead of spending all our resources on managing symptoms and secondary prevention, we must turn our attention to causal factors. We know with steadily increasing confidence and knowledge that the primary driver of chronic disease is the interaction among genes, activities of daily living (lifestyle), and the environment. Describing a model that folds that very general awareness into actual clinical practice, enabling physicians to acquire effective skills and tools for addressing the unique pattern of each individual patient's life and health, is the ultimate goal of this paper.

Improving the Response to Chronic Disease

Chronic disease is now the principal cause of disability and use of health services and consumes 78% of health expenditures. (p. 1057 in the publication cited) [D]eveloping a different way to practice medicine for chronic disease is at the heart of any solution to the problem.
(p. 2975, a reply to letters generated by the cited publication)

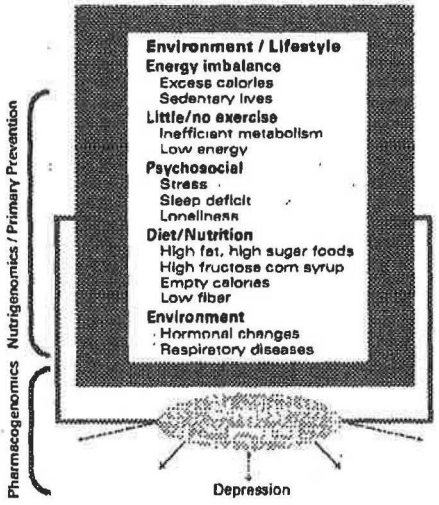
—Halstead Holman, MD, JAMA, 2004[107]

The burden of harm conveyed by the collective impact of all of our health care quality problems is staggering. It requires the urgent attention of all the stakeholders: the health care professions, health care policymakers, consumer advocates and purchasers of care. The challenge is to bring the full potential

with increases in obesity."[94]

- **Adolescents:** "...extrapolation from current data suggests that adolescent overweight will increase rates of CHD among future young and middle-aged adults, resulting in substantial morbidity and mortality ... more than 100,000 excess cases of CHD attributable to the increased obesity."[94]
- **Children:** Type 2 diabetes, previously almost unheard of in children, "...has become common among the pediatric age population, accounting for ~40% of all diabetes diagnosed."[95]

A (highly simplified) model of the multiple, complex influences that create obesity and associated chronic diseases:



If we concentrate our resources at the bottom of the diagram, on pharmacogenomics, we have already lost the battle; chronic disease is already entrenched and the costs of treating it will only rise.

benefit of effective health care to all Americans while avoiding unneeded and harmful interventions and eliminating preventable complications of care. Meeting this challenge demands a readiness to think in radically new ways about how to deliver health care services and how to assess and improve their quality. Our present efforts resemble a team of engineers trying to break the sound barrier by tinkering with a Model T Ford. We need a new vehicle or perhaps, many new vehicles. The only unacceptable alternative is not to change.

—Mark Chassin, MD, MPH; IOM National Roundtable on Health Care Quality, JAMA, 1998[103]

The three arenas in which fundamental change is required in order to improve both prevention and treatment of chronic disease are medical education, clinical care (which is conditioned by medical education), and consumer/patient behavior. This paper focuses primarily on clinical care.

Medical education

The Institute of Medicine report, *Crossing the Quality Chasm*, in the chapter on "Preparing the Workforce" (p. 213) observes: "Despite changes that have been made, the fundamental approach to medical education has not changed since 1910."[104] The report also addresses some of the factors that make changing medical education very difficult. However, it does not directly address the imperative to integrate creative and innovative approaches to chronic disease into the process. Medical education must teach physicians to quickly and skillfully differentiate situations requiring an acute-care intervention from those presenting the very different challenge of complex, chronic disease. Once that differentiation is achieved, then physicians must be given new tools, information, and skills with which to address the common comorbidities and complexities of chronic disease. Key concepts that underlie and will facilitate these fundamental changes are presented in Chapters 4 and 5 of this paper.

Clinical care

Changes in the roles of both patients and clinicians are critical to transforming our healthcare system. Chapter 4 addresses "The Clinician's Dilemma": how to practice in such a way that both the continuing advances of science

It is important to note, however, that there is no precise, predictive formula. One person's obesity is not identical in cause, signs and symptoms, or secondary outcomes to another's, and thus both treatment and prevention must be individualized to accommodate the genetics, lifestyle, and environment of each patient. Any model for managing chronic disease that does not address all of these components will fall short in comprehensiveness and effectiveness. In a 2008 publication in *Circulation*,[96] the American Heart Association described a comprehensive population-based approach to preventing obesity, including the following key strategies (among others):

- Prevention at the population level, with emphasis on key risk subgroups
- Differentiating environmental and policy approaches from clinically-based interventions
- Use of an ecological model that "includes multiple layers of influences on eating and physical activity across multiple societal sectors"

Often in medicine the marshaling of substantial and focused resources to fight a public health problem ware upon the research agenda. While there are many questions yet to be answered about how and why obesity develops and how and why it is such a risk factor for other serious diseases, it is a long and expensive process to test and verify strategies for prevention and treatment.[97] We cannot afford that delay; there are far too many lives at stake. Dr. Richard Horton, editor-in-chief of *The Lancet*,

and the essential art of medicine are integrated seamlessly into clinical practice, neither overshadowing the other. Clinicians must improve their capacity to incorporate important emerging evidence into a personalized, systems-oriented model of care, within the context of a strong healing partnership with patients. Chapter 5 presents the functional medicine model and methods that facilitate this evolution as well as an approach to establishing and strengthening the healing relationship. Two cases that exemplify the process are presented.

Consumer (Patient) needs and preferences

The growth and sustained energy of consumer interest in alternative and complementary medicine over the last quarter century is one indicator of the desire patients have for a different kind of healthcare system. Although not addressed directly in this paper, healthcare consumers must be assisted to take a lifelong interest in the forces that push each of us toward health or disease. As difficult as it is for physicians and other health practitioners to alter their mode of practice, that's how difficult it is for patients to alter their mode of living to maximize the prospects of health and minimize the risks of disease. These changes represent a major undertaking and we will not be successful unless both consumers and providers of health care commit to a long-term, sustained effort.

addressed this issue in an editorial titled, "The Precautionary Principle":

We must act on facts, and on the most accurate interpretation of them, using the best scientific information. That does not mean we must sit back until we have 100% evidence about everything. Where the state of the health of the people is at stake, the risks can be so high and the cost of corrective action so great, that prevention is better than cure. We must analyze the possible benefits and cost of action and inaction. Where there are significant risks of damage to the public health, we should be prepared to take action to diminish those risks even when the scientific knowledge is not conclusive, if the balance of likely costs and benefits justifies it.[90]

We must act in concert with emerging research, being willing and able to adapt as new information becomes available. That is why we need a model of care that is comprehensive, yet flexible; science-based but not rigidly bound to an imperfect and incomplete evidence base; personalized and holistic. That model will be presented and discussed in Chapters 4 and 5.

Chapter 3

PERSONALIZED MEDICINE

If it were not for the great variability among individuals, medicine might as well be a science, not an art.

—SIR WILLIAM OSLER, 1892

What is it?

Personalized medicine can be described as the effort to define and strengthen the art of individualizing health care by integrating the interpretation of patient data (medical history, family history, signs, and symptoms) with emerging "-omic" technologies—nutritional genomics[v], pharmacogenomics[vi], proteomics[vii], and metabolomics[viii].[105] Developing these strategies is critical to enabling physicians to match individual patients to the best diet, environment, nutraceuticals, and pharmaceuticals for their genetic make-up—a process that will eventually revolutionize medicine. Such a comprehensive individual fingerprint is still many years away from being feasible in research or clinical practice. It is not too early, however, to begin learning about it and applying key concepts and early data to patient care in incremental steps as the evidence base advances.

To date, the research underlying personalized medicine has concentrated mostly on pharmacogenomics. The knowledge that "a relatively large number of patients treated for cancer, infectious disease, psychiatric

[v] **Nutritional genomics or, as commonly used, nutrigenomics:** The study of how different foods may interact with specific genes to increase the risk of common chronic diseases such as type 2 diabetes, obesity, heart disease, stroke, and certain cancers. Nutrigenomics also seeks to provide a molecular understanding of how common chemicals in the diet affect health by altering the expression of genes and the structure of an individual's genome. The premise underlying nutrigenomics is that the influence of diet on health depends on an individual's genetic make-up. (From MedicineNet.com)

[vi] "...**pharmacogenomics** includes identifying candidate genes and polymorphisms, correlation of polymorphisms with therapies, prediction of drug response and clinical outcomes, reduction in adverse events, and selection and dosing of drugs based on genotype." (Issa, 2007)

[vii] **Proteomics:** The study of the proteome, the complete set of proteins produced by a species, using the technologies of large scale protein separation and identification. The term proteomics was coined in 1994 by Marc Wilkins who defined it as "the study of proteins, how they're modified, when and where they're expressed, how they're involved in metabolic pathways and how they interact with one another." (From MedicineNet.com)

[viii] **Metabolomics/Metabonomics:** The study of metabolic responses to drugs, environmental changes and diseases. Metabonomics is an extension of genomics (concerned with DNA) and proteomics (concerned with proteins). Following on the heels of genomics and proteomics, metabonomics may lead to more efficient drug discovery and individualized patient treatment with drugs, among other things. (From MedicineNet.com)

illnesses, respiratory diseases and cardiovascular conditions are not responding to the drugs they are given"[106] has been one of the key drivers of the field. The process of developing new drugs specifically designed for personalized applications involves many phases: identification and screening of candidate genes; detection and description of various polymorphisms that affect drug response (e.g., slow or rapid metabolizers); the correlation of each polymorphism with possible therapeutic targets; and the evaluation of clinical outcomes with large enough study sizes to create confidence in the efficacy of the new strategy. All of these steps must occur before selection of a drug and specification of therapeutic dosage can be based on genotype.[107] Once the drug development process is complete, the transformation of research-based data into a new tool for clinical practice must await a cost-effective screening test for patients (a process that involves many challenging and time-consuming phases—see **Sidebar**), delineation of which patients should be screened and at what stage in their care, and long-term follow-up to check for possible adverse effects of therapy. The identification of drugs already in the pharmacopeia that have inter-individual variability in dosing, efficacy and/or side effects that would make them amenable to a pharmacogenomics approach will also be a lengthy and expensive process, as there are thousands of drugs that could be tested for such personalized applications. Screening tests to detect various polymorphisms must also be developed and they must be cost effective if they are to be utilized routinely in clinical care. Pharmacodiagnostic tests that enable clinicians to quickly and cost effectively identify patients who are at risk for adverse drug responses "must possess high sensitivity and specificity with regards to their predictive performance."[108]

A couple of examples will indicate the incalculable potential—and the complexity and costliness—of pharmacogenomics as a clinical strategy:

- **New drug development:** Herceptin® (trastuzumab) is a monoclonal antibody developed to treat breast cancer that over-expresses HER2 (human epidermal growth factor receptor 2). This characteristic "is associated with an aggressive phenotype, high recurrence rate and reduced survival"[110] and it affects approximately 25-30% of breast cancer patients.[111] Before a drug could even be conceptualized, the HER2 protein

Integrating Pharmacogenomic Testing in Clinical Practice

McKinnon et al.[109] describe a general process for developing pharmacogenomics tests that can be used in clinical practice. Each of these steps represents a point at which poor outcomes may completely stall the development of an affordable and effective clinical test:

1. Identify circumstances in which knowledge of inter-individual variation in drug response is likely to improve clinical (or financial) outcomes)
2. Find a significant genotype-phenotype association
3. Determine reproducibility across ethnic populations
4. Propose model of how genotyping would guide clinical practice
5. Collect data on cost effectiveness of new pharmacogenomic profile vs. current practice
6. Educate stakeholders on appropriate use
7. Implement testing in a staged manner

had to be detected and reliably identified, and many breast cancers had to be analyzed to discover the proportion with overexpressed HER2. Then, the search for a drug targeted to this trait could begin. Ultimately, trastuzumab was developed, tested, and validated in research trials as an effective treatment for breast cancers that over-express HER2; its ability to work with other chemotherapeutic agents was also assessed. Two cost-effective screening tests were developed and are now available—immunohistochemistry (IHC—appropriate as a general screening tool for all breast cancer) and fluorescence in situ hybridization (FISH—used as further screening for patients with 2+ and 3+ IHC scores).[112] And "...five recent adjuvant breast cancer trials have demonstrated an astonishing and highly reproducible benefit in halving the recurrence rate and reducing mortality in patients with this phenotype."[113]

- **Existing drug specifications:** Warfarin, an effective anticoagulant in use for many decades, has "a narrow therapeutic range because of both genetic and environmental factors,"[114] and has been under-prescribed because of "historically high rates of drug-associated adverse events."[115] Understanding these factors sufficiently well to alter dosing appropriately would enable this cost-effective drug to be used more widely. Studies assessing the role of patient demographics and known variants in CYP2C9 alleles and VKORC1 genotypes have been performed, and therapeutic response to warfarin is now known to vary among Jewish (both Ashkenazi and Sephardic origins), African American, and Asian patients.[116, 117, 118] In 2005, "the U.S. FDA Clinical Pharmacology Sub-Committee (CPSC) of the Advisory Committee for Pharmaceutical Science voted to re-label the dosing of warfarin to take into consideration the new information."[119] It is not known how many patients already on warfarin have undergone testing to re-evaluate their dosage since the prescribing recommendations were changed. However, at least one study has determined that "prospective application of a multivariate CYP2C9 gene-based warfarin dosing model is feasible,"[120] and another reported that "a quantitative dosing algorithm incorporating genotypes for 2C9 and VKORC1 could substantially improve initial warfarin dose-selection and reduce related complications."[121]

The incorporation of nutrigenomics (the effect of diet on gene expression), nutrigenetics (effect of genetics on response to diet, foods, or nutrients), proteomics, and metabolomics into the personalized medicine model has moved much more slowly,[122, 123] perhaps simply as a reflection of the marked dominance of drug treatments that characterizes our healthcare system and shapes the funding priorities (see Sidebar in Chapter 2). However, much that is learned in pharmacogenomics will drive the knowledge base in these related fields as well because the underlying principle is common to all: individual genetic variations affect our physiological and biochemical response to virtually everything we are exposed to. This represents a fundamental alteration in our understanding of health and disease. The knowledge of how to identify and manage these individual differences is acutely needed for lifelong prevention of chronic disease. It won't be enough to say "Eat more vegetables and less fat and sugar." We will need to be able to individualize healthy diets, add targeted nutraceuticals, prescribe specific exercise programs, advise stress reduction efforts, plan to avoid certain pollutants, all based on individual genetic variations. Ultimately, personalized medicine will not be fully realized until all the influences, effects, and interactions are researched

and described in such a way that practitioners are able to bring them to bear on an individual patient's health and on lifelong prevention of chronic disease.

Strengths and weaknesses

The ultimate promise of personalized medicine is its potential to uncover "the causes of the causes" of disease.[124] From the unlocking of the human genome to the development of proteomics (wherein we begin to understand how the proteins made by genes behave[125]), scientists can now demonstrate how individualized both health and disease really are. It's a powerful and exciting model that is already beginning to affect both research and clinical practice. Its strength is the rapidly developing science (all the –omics) that opens new vistas and new possibilities for dramatically increasing the effectiveness of individualized prevention and treatment strategies.

On the other hand, the many challenges of transferring this model to clinical practice are daunting; they include:

- The "clinical complexity of genomic-based diagnostics and treatment."[126] A recent NIH report phrases the complexity question clearly: "An enormous scientific challenge now presents itself: What are the best ways to understand, prevent, and treat common, chronic diseases like heart disease, cancer, addiction, and mental illness when it is apparent that they are the result of interactions between individuals—in all their biological complexity—and their ever-changing physical, behavioral, and societal environments?"[127]
- Excessive cost[128]
- Regulatory issues[129, 130]
- Ethical concerns[131]
- The need for new information technology[132]

At the level of patient care, additional complex challenges arise that may take decades to resolve:

- Devising accurate and cost-effective genomic and/or proteomic screening tools
- Identifying biomarkers that will indicate whether/when an active adverse process is in play for specific conditions in a given patient
- Testing and validating diagnostic tools across many populations
- Selecting appropriate patients for screening and demonstrating the usefulness of screening in improving patient outcomes through long-term clinical trials
- Convincing third-party payers to reimburse for screening tests (likely to happen only when the results from long-term trials demonstrate cost-effectiveness)
- Interpreting individual patient screening reports appropriately
- Devising and validating effective interventions based on individual screening results

Common ground with other emerging models

As shown in Figure 1 (Chapter 1), personalized medicine shares many features with other emerging models: the emphasis on discovering individual patients' genetic vulnerabilities, the vision of individualized diagnoses and treatment, and the reliance on a powerful (and still emerging) scientific evidence base. It also shares with other models the absence of a clear and practical method of integrating emerging information into medical education and practice. Nor does it address structural and multidisciplinary issues in clinical practice that are part of the chronic-care model and integrative medicine.

Role in a synthesized, comprehensive model of 21st century medicine

Despite the rapidly evolving research base, therefore, personalized medicine does not (yet) have a robust, consistent architecture for clinical applications, nor does it describe a clear pathway toward achieving that goal. Research designs are still in development, and research findings do not specify how personalized medicine may (or may not) contribute to a new model of care for chronic disease. Even when a gene mutation, or SNP, can be identified, we may still be "six degrees of separation removed from the functional aspects of the disease,"[133] because gene analysis does not tell us which protein and protein pathways are affected and what the aberrant protein is doing. "Proteins are actually the drug targets; analysis of genes and gene expression just gives an indication of whether or not the proteins may be present."[134] The same can be said of the effects of diet, environmental toxins, psychosocial influences, and many other lifestyle and environmental factors on gene expression and protein function. For these reasons, it is difficult to plan for the integration of this model into medical education in a systematic way in the near future.

It will be necessary, therefore, to ensure that whatever transformative model is used, it will allow clinicians to integrate new and useful information from personalized medicine as and when it becomes available, and will also empower them to respond effectively now to the urgent need for improved prevention and management of complex, chronic disease. Perhaps the single most valuable portion of the personalized medicine model at the moment is the transparency it brings to the concept of patient individuality. The evidence clearly reveals that each patient is a unique individual—one whose gene expression patterns are constantly in flux and whose complex and ever-changing response to treatment, environment, and lifestyle will challenge physicians to listen differently, see differently, and respond differently than taught by the linear model of acute care.

Prospective Medicine

"The ability to identify those individuals most at risk for developing chronic diseases and to provide a customized means to prevent or slow that progression are emerging competencies and provide the foundation for prospective care."

—Ralph Snyderman, MD and R. Sanders Williams, MD [135]

What is it?

A relatively new concept introduced in 2003, prospective medicine is a descriptive rather than a prescriptive term, encompassing "personalized, predictive, preventive, and participatory medicine."[136] Snyderman argues persuasively that a comprehensive system of care would address not only new technologies (e.g., identification of biomarkers, use of electronic and personalized health records), but also delivery systems, reimbursement mechanisms, and the needs of a variety of stakeholders (government, consumers, employers, insurers, and academic medicine). Prospective medicine does not claim to stake out new scientific or clinical territory; instead, it focuses on creating an innovative synthesis of technologies and models—particularly personalized medicine (the "-omics") and systems biology—in order to "determine the risk for individuals to develop specific diseases, detect the disease's earliest onset, and prevent or intervene early enough to provide maximum benefit. Each individual would have a personalized health plan to accomplish this."[137]

Strengths and weaknesses

A very compelling element of prospective medicine is the call for fundamental change in clinical practice—from treating people only when they are sick enough to visit the doctor's office to prospectively examining individual risks and developing comprehensive preventive strategies based on the best available evidence at the time. This would, indeed, revolutionize medicine; not only would it shift the focus of primary care, but it would establish a serious partnership between patient and clinician aimed at lifelong health. Snyderman emphasizes the need for clinical medicine and the emerging genomic models to integrate their respective knowledge and skills to create the best outcomes for patients. He discusses some diagnostic and risk-assessment tools that are already available, such as the following examples:

- Know Your Number®, a program that "uses … synthesis modeling to quantify an individual's risk of developing chronic, preventable, obesity-related diseases such as diabetes, chronic obstructive pulmonary disease, and heart disease. In addition, KYN calculates what modifiable factors are contributing to that risk so that individuals can take steps to improve their overall risk profile."[138] Although Know Your Number is not available directly to consumers, other similar programs are. One example is Navigenics Health Compass,[139] offering "A scan of your whole genome, carried out by a government-certified laboratory that captures data on 1.8 million of your genetic risk markers." For $2500, individuals can obtain an analysis of their "genetic predisposition for a variety of common health conditions, and the information, support and guidance to know what steps you can take to prevent, detect or diagnose them early." For $250 per year, they will have a subscription that entitles them to regular updates.
- Biomarkers can be assessed through an analysis of 250 serum proteins ($3400). According to the company's Web site: "Biophysical250 … measures 250 different biomarkers that may indicate the presence of diseases and conditions often before symptoms appear. Unlike standard physicals that measure only up to 40 biomarkers, Biophysical250 simultaneously assesses hundreds of biomarkers used by 12 different medical specialties."[140]
- Two gene-expression assays that predict recurrence of breast cancer in patients with stage I or II node-negative breast cancer. These tests can be used to individualize follow-up treatment by helping to determine "the need for systemic adjuvant therapy in such patients."[141]

Also compelling is the call to involve a broad range of stakeholders to "work together to develop innovative applications of new technologies and appropriate delivery models."[142] It is certainly true that reimbursement strategies and academic training practices will have to evolve to encompass such a broad-based new model of care, and retraining existing practitioners must become a high priority.

What's missing? Like the other emerging models we are discussing, prospective medicine does not provide a clear road map for integrating these new technologies into clinical practice. Precisely how, one wonders, will the 500,000+ MDs and DOs already in practice be retrained? How will academic medicine evolve? How many patients can spend $2500-$3500 on laboratory tests to assess risk biomarkers? How much new and expensive testing is actually necessary compared to how much risk is already clear when a comprehensive history is taken and a thorough examination including (mostly) standard laboratory tests is performed? And what, exactly, will change in clinical practice once expanded information is in hand from these new technologies? Will doctors still be in the same position they are in today—suggesting better diet, losing weight, and reducing stress without knowing how to help their patients make all of that happen?

The big missing piece in prospective medicine (at least as described thus far in the literature) lies in the absence of a clear, practical, and systematic method for altering clinical practice. Recognizing that the interactions between doctor and patient and between patients and their lifestyle-environment exposures and choices are where real change happens, Johns and Brigham,[143] offer this commentary on a post-prospective medicine world:

> *This "next next transformation" will identify "healthy" biologic processes (i.e., homeostatic) and provide tools for measuring early deviations from health ("unhealth") that are not necessarily disease specific but that predict dire outcomes and warrant health-focused interventions. For example, many chronic diseases (diabetes, atherosclerosis, autoimmune diseases) share inflammation as a common mechanism. Characterizing an individual inflammatory phenotype may be a potent health predictor. And inflammatory responses to stress can be modified by behavior. Such health-focused treatment is the logical step beyond the "next transformation" that Snyderman and Yoediono advocate.*

Common ground with other emerging models

Prospective medicine urges the integration of the developing sciences of personalized medicine and systems biology with the skills and knowledge of clinicians, and describes recommendations for revisions in reimbursement mechanisms and medical education that will be required in order to implement a comprehensive new system of care. It clearly relies on the emerging evidence base, but not to the exclusion of other important information. It does not specifically address the chronic-care model, nor issues of integrated care or integrative medicine; neither diagnostic approaches nor treatment strategies appear to include a multidisciplinary model of care.

Role in a synthesized, comprehensive model of 21st century medicine

Because prospective medicine relies on personalized medicine and systems biology for the science of risk-assessment, many of its strengths and its limitations are found in those two models. It is, however, more comprehensive in sweep than either of them, incorporating not only technologies such as electronic health records but also acknowledging the need for simultaneous reform of the reimbursement structure and the training of future physicians. Thus, it is an important step forward, but it still lacks a robust, consistent architecture for clinical applications.

Chronic-Care Model

What is it?

The chronic-care model (CCM) is briefly outlined in Chapter 1 and fairly thoroughly described in the Appendix, where extensive material from the Improving Chronic Care Web site is included. The primary focus of this model is to include "...the essential elements of a healthcare system that encourage high-quality chronic disease care.... the community, the health system, self-management support, delivery system design, decision support and clinical information systems. Evidence-based change concepts under each element, in combination, foster productive interactions between informed patients who take an active part in their care and providers with resources and expertise."[144] The CCM is a response to powerful evidence that patients with chronic conditions often do not obtain the care they need, and that the healthcare system is not currently structured to facilitate such care (see **Sidebar**).

Strengths and weaknesses

The chronic-care model has the advantage of having been around for more than a decade; it has undergone considerable testing and revision. Implementation trials have indicated that, when enough of the model can be implemented, compliance with current algorithms and guidelines can be improved for conditions such as diabetes,[146, 147] depression,[148] and tobacco cessation.[149] The CCM is a structure-of-care (or process-of-care) more than a content-of-care model; it describes a multidisciplinary, multi-stakeholder approach to delivering care that will improve both patient and practitioner compliance with current evidence-based best practices. For this reason, integrating new technologies, such as those emerging from personalized medicine, are not explicitly addressed; one might assume that as those tools make their way into clinical guidelines and algorithms, they will become part of the CCM as well. However important improving the structure of care may be—and we certainly agree that it is important—the care thus provided will still be limited to the current medical model, which does not address individualizing care, lifelong primary prevention, or reversal of chronic disease, and which is primarily pharmaceutical in nature. We could

The Institute of Medicine's report, *Crossing the Quality Chasm,*[145] comments extensively on the unmet needs of those with chronic conditions:

- **Page 4:** "... there remains a dearth of clinical programs with the infrastructure required to provide the full complement of services needed by people with heart disease, diabetes, asthma, and other common chronic conditions (Wagner et al., 1996). The fact that more than 40% of people with chronic conditions have more than one such condition argues strongly for more sophisticated mechanisms to communicate and coordinate care (The Robert Wood Johnson Foundation, 1996)."
- **Page 9:** "Care for the chronically ill needs to be a collaborative, multidisciplinary process."
- **Page 28:** "In a population increasingly afflicted by chronic conditions, the health care delivery system is poorly organized to provide care to those with such conditions."
- **Page 29:** "Thus the American health care system does not have well-organized programs to provide the full complement of services needed by people with such chronic conditions as heart disease, cancer, diabetes, and asthma."
- **Page 89:** "Common chronic conditions should serve as a starting point for the restructuring of health care delivery because, as noted in Chapter 1, chronic conditions are now the leading cause of illness, disability, and death in the United States, affecting almost half

imagine implementing, for example, personalized medicine using the chronic-care model, but no mechanism for achieving that is described. In fact, just implementing the full CCM itself is a very difficult proposition that encounters many barriers (e.g., no consensus on the value of the changes, limited change management skills within organizations, too many competing priorities, and failure to engage the commitment of physicians).[150] The Academic Chronic Care Collaborative, representing 22 academic medical centers, has reported some initial promising outcomes from their experiences with implementing aspects of the CCM.[151] It is worth noting that these institutions were committed to providing effective leadership and resources for the change process. The Agency for Healthcare Research and Quality provides an extensive *Toolkit for Implementing the Chronic Care Model in an Academic Environment.*[152]

Common ground with other emerging models

The CCM shares with integrative medicine an emphasis on a multidisciplinary care model, the use of evidence-based best practices, and engagement of the patient in self-care. It does not address biochemical and physiological individuality, any of the emerging genomic technologies, or the influence of underlying mechanisms of disease. It shares with prospective health care a focus on structural, system-wide change, although the two models emphasize different aspects of structural change.

Role in a synthesized, comprehensive model of 21st century medicine

The CCM advances our knowledge of how to improve the structure or process of care for chronic disease using standard approaches, but it does not advance our ability to select more effective strategies for actually improving both treatment and prevention. Still lacking is a robust, consistent architecture for selecting the most effective clinical applications for each unique patient.

of the population and accounting for the majority of health care resources used (Hoffman et al., 1996)."

- **Page 94:** "Four chronic conditions (cardiovascular disease, cancer, chronic obstructive pulmonary disease, and diabetes) account for almost three-quarters of all deaths in the United States (Centers for Disease Control and Prevention, 1999)."
- **Page 211:** "The ability to plan care and practice effectively using multidisciplinary teams takes on increasing importance as the proportion of the population with chronic conditions grows, requiring the provision of a mix of services over time and across settings.... A changing relationship between clinicians and their patients also calls for new skills in communication and support for patient self-management, especially for patients with chronic conditions. Collaborative management requires collaboration between clinicians and patients in defining problems, setting goals, and planning care; training and support in self-management; and continuous follow-up (Von Korff et al., 1997). Patients with chronic conditions who are provided with knowledge and skills for self-management have been shown to experience improvements in health status and reduced hospitalizations (Lorig et al., 1999). Clinicians need to have skills to train patients in techniques of good self-management."

Evidence-based Medicine (EBM)

What is it?

EBM is a tool for improving clinical practice. Its stated goal is to ensure that clinical decision making is grounded in the best available evidence. Despite its many limitations, it wields a great deal of power over medical training, clinical practice, and—increasingly—reimbursement decisions and legal determinations.[153, 154] We include it in our discussion of emerging models because of its multifaceted influences on patient care. Although it is beyond the scope of this paper to explore EBM in depth, it is critical to the future of health care to understand its strengths and weaknesses. To that end, we provide a brief description of this evolving paradigm.

Since the late 1970s, various efforts have been made to systematize the use of research findings in clinical decision making.[155] Rather than expecting each practitioner to establish and maintain a constant surveillance over a rapidly expanding evidence base, and to know which studies should generate the highest level of confidence, specific guidelines have been proposed concerning the interpretation of evidence that influences clinical decision making. There have been many definitions and ratings of what constitutes poor, good, and best evidence, but in the early 1990s, the term evidence-based medicine appeared for the first time,[156, 157] reflecting an increasing consensus that a more standardized approach to the use of medical evidence was on the way. Early efforts sought explicitly to reduce "...the emphasis on unsystematic clinical experience and pathophysiological rationale" while promoting "the examination of evidence from clinical research."[158]

A hierarchy of evidence reliability was proposed, with meta-analyses and systematic reviews at the top and personal communications at the bottom (see Figure 5). Over the years, this hierarchy has been revised and adapted many times for a number of reasons:

- It did not identify a mechanism for decreasing or increasing an assessment of value based upon, for example, study size, adequacy of blinding, bias, directness of the evidence, and other factors.[159]

» **Page 237:**
"Patients with chronic conditions, for which certain routine examinations and tests are crucial in order to prevent complications, do not all get the care they need."

Note: Citations included in the above quotations are available in the Institute of Medicine report, but are not provided here.

- It failed to accommodate many important criteria for translating evidence into clinical practice—for example, the degree to which outcomes being tested were important to patients, whether results were consistent with past studies, and whether confidence intervals were overly broad.[160]
- It inappropriately identified systematic reviews and meta-analyses as evidence (they are, rather, interpretations of the evidence and should be produced, at least in part, based on EBM principles).[161, 162]
- It did not differentiate between quality of evidence and strength of recommendations. "High quality evidence doesn't necessarily imply strong recommendations, and strong recommendations can arise from low quality evidence."[163]

One example of a subsequent adaptation is provided in Figure 6, where we can see that other useful criteria were added to the model, altering the earlier and more simplistic assessment of evidence usefulness.[164]

The basic concepts have continued to evolve. "In 2000, the Evidence-Based Medicine Working Group presented the second fundamental principle of EBM: the hierarchy of evidence being the first. Whatever the evidence, value and preference judgments are implicit in every clinical decision. A key implication of this second principle is that clinical decisions, recommendations, and practice guidelines must not only attend to the best available evidence, but also to the values and preferences of the informed patient."[165]

A major advance over the use of any hierarchy, however complex, has been the development of the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system. Figure 7 shows a partial representation of this system; in practice, it has other important elements as well. The GRADE system describes a very sophisticated, multi-level evaluation of evidence; its purpose is to strengthen recommendations for clinical practice and to increase confidence in those recommendations. Because of its complexity, however, it is not intended for use by individual clinicians, who generally have neither the time nor the expertise to implement it. It is aimed primarily at researchers and clinical guideline developers, who have not heretofore used a consistent and uniform methodology that is transparent to all potential users.[166] GRADE software is now available for free at the GRADE Working Group's Web site,[167] making it even more likely that its use will continue to expand.

1. A Systematic reviews; meta - analyses
   B RCTs
   C Experimental designs
2. A Cohort control studies
   B Case control studies
3. A Consensus conference
   B Expert opinion
   C Observational study
   D Other types of study (e.g., interview -based)
   E Quasi-experimental, qualitative design
4. Personal communication

Figure 5:
Heirarchy of evidence (Sackett)

	Effectiveness	Appropriateness	Feasibility
Excellent	Systematic reviews Multi-center studies	Systematic reviews Multi-center studies	Systematic reviews Multi-center studies
Good	RCTs Observational studies	RCTs Observational studies Interpretive studies	RCTs Observational studies Interpretive studies
Fair	Uncontrolled trials; dramatic results Before and after studies Non-randomized CTs	Descriptive studies Focus groups	Descriptive studies Action research Before and after studies Focus groups
Poor	Descriptive studies Case studies Expert opinion Studies with poor methodology	Expert opinion Case studies Studies with poor methodology	Expert opinion Case studies Studies with poor methodology

Figure 6:
Heirarchy of evidence (Evans)

HA 09/01/2015

A. Criteria for Assigning Level of Evidence

Type of Evidence	
Randomized trial	High
Observational study	Low
Any other type of research evidence	Very Low
Increase level if:	
Strong association	(+1)
Very strong association	(+2)
Evidence of a dose-response gradient	(+1)
Plausible confounders reduce observed effect	(+1)
Decrease level if:	
Serious or very serious limitations in quality	(-1) or (-2)
Important inconsistency	(-1)
Some or major uncertainty about directness	(-1) or (-2)
Imprecise or sparse data*	(-1)
High probability or reporting bias	(-1)

B. Definitions for levels of evidence

High Further research is not likely to change our confidence in the effect estimate

Moderate Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very Low Any estimate of effect is uncertain

*Few outcome events or observations or wide confident limits around an effect estimate

Figure 7:
Overview of the GRADE system for evaluating evidence (Bagshaw)

Over the years, a number of studies have verified that teaching EBM will, in fact, significantly increase the degree to which practitioners apply it.[160] Training is more successful if it is both experiential and didactic.[169, 170, 171] Unfortunately, there are very few studies available as yet that tell us whether EBM improves overall patient health over a period of years.

Strengths and weaknesses

There can be little doubt that a thoughtful evaluation of evidence is an indispensable factor in delivering high-quality health care. The emergence of formal assessment processes reflects a desire to establish greater clarity and confidence about the reliability of evidence. Even a

casual user of Medline or PubMed quickly becomes aware of the overwhelming quantity of published research available today; it is a daunting prospect to identify the best or most relevant papers among hundreds or thousands that may be available on a particular topic. For example, a PubMed search for the phrase *evidence-based medicine* in titles and abstracts returns nearly 5000 entries encompassing dozens of journals! There are, of course, tools for narrowing a search term or process, but it is still inordinately time consuming to obtain, read, evaluate, and then compare even a few individual research papers on a specific subject. Such a process, even if an EBM hierarchy is used, is also subject to a great deal of individual bias. Thus, any tool that provides significant and reliable assistance in such an endeavor is welcome, and that is one of the primary rationales for the development of clinical guidelines.[fn]

As the use of EBM has become increasingly widespread, its limitations and weaknesses have also become more apparent. Paramount among the problems is that EBM reflects an acute-care model: it most often assumes that the goal of care is a single diagnosis followed by a hierarchy of (primarily) single-agent treatments. Although GRADE has made an admirable attempt to compensate for many EBM weaknesses, these fundamental goals remain the gold standard. Therefore, EBM fails at the same point where the research itself fails—in its inability to account for unique patient geno/phenotypes, multiple comorbidities, and personalized approaches to care that include multiple interventions for complex, chronic disease. Such multifaceted interventions may include dietary, nutraceutical, pharmaceutical and/or surgical recommendations, as well as many options from the natural medicine world (e.g., botanical medicine, acupuncture and oriental medicine, body/mind practices).

EBM and any guidelines derived from applying an EBM model to the evidence are, of course, only as good as the underlying research, which presents several problems:

- Not only is the research agenda disproportionately driven by the pharmaceutical industry, but it is tainted by the failure to publish negative or neutral results and by industry bias (see Chapter 2).
- Much of generally accepted medical practice has not been systematically evaluated. For example: "Of around 2500 treatments covered [in *BMJ Clinical Evidence*] 13% are rated as beneficial, 23% likely to be beneficial, 8% as trade off between benefits and harms, 6% unlikely to be beneficial, 4% likely to be ineffective or harmful, ***and 46%, the largest proportion, as unknown effectiveness*** [italics added]."[172]
- Individuals studied in RCTs do not reflect the patient population seen most often in primary care; confidence in the transferability of the data is thereby reduced.[173]
- "Randomized trials, especially if evaluating complex interventions or with strict inclusion/exclusion criteria, often only provide data in a clinical context that does not exist outside the trial itself and have limited power to detect harm.... Systematic reviews require vigilant interpretation and should not necessarily be considered as high level evidence due to issues related to ... incomplete reporting and the inclusion of evidence from trials of poor quality.... Meta-analyses are not primary evidence; they are statistically assisted interpretations of

[fn] "Clinical guidelines are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" —Institute of Medicine, 1990. They define the role of specific diagnostic and treatment modalities in the diagnosis and management of patients. The statements contain recommendations that are based on evidence from a rigorous systematic review and synthesis of the published medical literature"—http://www.nhlbi.nih.gov/guidelines/about.htm.

primary evidence. They have been shown to contradict confirmatory trials, especially when such meta-analyses are based upon small, low quality studies."[171]

- "Even the most promising findings of basic research take a long time to translate into clinical experimentation, and adoption in clinical practice is rare."[175] Evidence-based guidelines of genomic applications are even more rare, and thus are unavailable to practitioners who rely on EBM processes to update their clinical practices.[176]

Common ground with other emerging models

EBM is, to differing degrees, part of all the other models described in this paper. Since EBM focuses primarily on mechanisms for translating research findings into clinical applications, it is less useful for those aspects of personalized medicine and systems biology that concentrate on the basic research itself. Also, as noted above, integrating personalized assessment and treatment with EBM models is not yet feasible on a systematic basis. It will be extremely interesting to see whether this can be done.

Role in a synthesized, comprehensive model of 21st century medicine

In our opinion, the role of EBM is strongest in acute-care situations, where the physician or healthcare team must focus on short-term and fairly narrowly defined issues. When we consider its role in outpatient primary care for complex, chronic disease, however, it is more difficult to make an overall determination of usefulness. Certainly there are situations where EBM and the clinical guidelines that flow out of it are extremely useful. In general, however, it seems easier to see the problems (described above) than it is to detect the benefits. Nonetheless, there is great benefit to researchers, practitioners, and patients in improving our ability to objectively and systematically evaluate data and determine clinical usefulness. Overall, this is perhaps the most important role that EBM will play over time.

Systems Biology

What is it?

Although there is not yet a universally recognized definition of systems biology, the National Institute of General Medical Services (NIGMS) at NIH provides the following explanation: "A field that seeks to study the relationships and interactions between various parts of a biological system (metabolic pathways, organelles, cells, and organisms) and to integrate this information to understand how biological systems function."[177] The *Molecular Systems Biology Blog on Systems & Synthetic Biology* poses—and provides some possible answers to—the question of why it appears to be difficult to come up with a concise and generally applicable definition: "One of the reasons might be that every definition has to respect a delicate balance between 'the yin and the yang' of the discipline: the integration of experimental and computational approaches; the balance between genome-wide systematical approaches and smaller-scale quantitative studies; top-down versus bottom-up strategies to solve systems architecture and functional properties." The blog hypothesizes that, "despite the diversity in opinions and views, there might be two main aspects that are conserved across these definitions: a) a system-level approach attempts to consider *all*

the components of a system; b) the properties and interactions of the components are linked with functions performed by the intact system via a *computational model*."[178]

We would add to the NIGMS definition that it is also vital to understand how the human system interacts with the environment, as well as how all the components act and interact. We see systems biology as a broad term for the basic science underlying the personalized medicine revolution (described above). While the fields of personalized, prospective, and integrative medicine all recognize (to varying degrees) the importance of nutritional genomics, pharmacogenomics, metabolomics, and proteomics to the future of health care, most of the scientific research has been generated by systems biologists (whether or not they identify with that term or any of the many definitions proposed). Thus far, although systems biology *claims* virtually the same broad territory as personalized medicine, it actually *focuses* almost exclusively on pharmacogenomics—in the Willie Sutton idiom, "That's where the money is." Attention to the applicability of those findings to patient care (i.e., the gene-environment interaction that creates the phenotype) is what connects systems biology to personalized medicine.

Strengths and weaknesses

Identifying the nature and effects of the myriad interactions that occur where human biology is exposed to the environment is almost unimaginably complex. Yet that effort is critical to a better understanding of the multifactorial nature of disease development. We know that "the causes of most chronic diseases will require an understanding of both the genetic and environmental contribution to their etiology.... The most critical issue is how to relate exposure-disease association studies to pathways and mechanisms.... Scientists will need tools with the capacity to monitor the global expression of thousands of genes, proteins and metabolites simultaneously.... Even when all the highly relevant genes and their interactions with specific environmental components have been identified, it will still be difficult to relate the influence of an individual's genotype to their disease phenotype due to the added complexity of gene-gene interactions, post-translational processing, and protein-protein interactions."[179]

Because of the magnitude and complexity of the challenge, "Systems biology research should create an interactive inter-disciplinary scientific culture. For progress to occur experts in engineering, physics, mathematics, and computer science must join biochemists, cell biologists, and physiologists in the effort to figure out how to obtain the required data and develop the sophisticated computational approaches that will be needed to make viable predictions."[180] This is a long-term prospect, of course, although early studies have shown some highly beneficial outcomes of genomic medicine[181] (a plausible term for applying the findings of systems biology to patient care).

Many of the same obstacles discussed earlier in this chapter vis-à-vis personalized medicine and pharmacogenomics are inherently shared by systems biology. In addition to barriers of cost, complexity, equipment, ethics, and education, "the evidence and importance of most pharmacogenomics associations are not sufficient to overcome the barriers to clinical implementation.... It is likely that complementary technologies, such as metabonomics, will be able to compensate for some limitations of genotype-phenotype association."[183]

Common ground with other emerging models

Systems biology seeks to elucidate the biological underpinnings of disease risk and apply that knowledge within a personalized, predictive, prospective, and participatory model of patient care. The science of systems biology clearly underlines the congruent goals of personalized medicine, prospective medicine, and—to a lesser extent—integrative medicine. It is not entirely congruent with evidence-based medicine, because it has not yet generated a large number of clinical trials. In fact, systems biology somewhat reverses the direction of EBM described above, in that it takes us back to a more "pathophysiological rationale" of disease and treatment. Eventually, research models will be devised to test the effectiveness and reliability of patient care based on diagnostic tests and therapeutic recommendations derived from systems biology.

Role in a synthesized, comprehensive model of 21st century medicine

Systems biology illuminates the science that will support a new model of health care—one that is based on an intimate understanding of complex human systems interacting with complex environments and unique genetic inheritances. In order to achieve its greatest potential, it must broaden its scope far beyond pharmacogenomics, which represents a very small portion of what we need to know about preventing and treating complex, chronic disease.

Integrative Medicine

What is it?

"Integrative medicine can be defined as an approach to the practice of medicine that makes use of the best available evidence taking into account the whole person (body, mind, and spirit), including all aspects of lifestyle. It emphasizes the therapeutic relationship and makes use of both conventional and complementary/alternative approaches."[105] The field is now nearly 10 years old and it is the only one of the emerging models discussed in this paper to explicitly encompass the integration of therapeutics that, until recently, were the sole purview of complementary and alternative medicine* (CAM). A number of forces are responsible for the emergence of this new discipline:

- The initial driver was undoubtedly the burgeoning interest in and demand for CAM displayed by consumers over many years. As reported in the *Annals of Internal Medicine* in 2001, "Use of CAM therapies by a large proportion of the study sample is the result of a secular trend that began at least a half century ago. This trend suggests a continuing demand for CAM therapies that will affect health care delivery for the foreseeable future."[106]
- The establishment of the NIH National Center for Complementary and Alternative Medicine (NCCAM) provided research funding to investigate CAM therapies. As research into CAM therapies revealed many effective natural (nonpharmaceutical, nonsurgical) approaches to

*A widely used definition of CAM therapies from the Osler Institute at Harvard: "clinical services not routinely used within conventional care, such as chiropractic, acupuncture, massage therapy, homeopathy, meditation, music therapy, therapeutic touch, yoga, Reiki, and advice involving herbal products and other dietary supplements."

a wide variety of diseases and conditions, it was thought desirable for physicians to understand CAM in much greater depth[187] and to devise a pathway for validated approaches to be brought into the standard "medicine chest."[188]

- The philanthropic funding of centers and departments of integrative medicine within the academic medicine community (e.g., University of Arizona, Harvard, Vanderbilt, Duke; also see list in the Appendix of members of the Consortium of Academic Health Centers for Integrative Medicine) brought high-level attention to the educational element: "Integration of CAM with conventional health care requires educational venues that prepare conventionally trained caregivers with a sufficient knowledge base for assessing beneficial and detrimental interactions between CAM and conventional care approaches; development of criteria for making informed referrals to CAM practitioners; and enhanced research capacity."[189]
- Integrative medicine might also be characterized as a response to the increasing depersonalization of health care that came with the rise of HMOs, greater use of technology, decreasing time spent in the outpatient visit, and the insertion of third-party payers into the doctor-patient relationship.[190]

Integrative medicine curriculums now commonly describe a fairly comprehensive set of core competencies that include dietary interventions, nutraceuticals, botanical medicines, body-mind practices (see, for example, **Sidebar** on meditation), energy medicine (e.g., acupuncture), and manual medicine (e.g., massage, chiropractic).[191,192] The balance of didactic knowledge (for the purpose of providing better-informed advice and referrals to patients) vs. practical skills (for actually integrating clinical applications) varies from program to program.

Strengths and weaknesses

Integrative medicine is an important step toward a functionally integrated healthcare system that includes all appropriately credentialed practitioners. Not only does it provide an avenue for validated CAM therapies

Meditation and Brain Science

Meditation may be one of the best studied body-mind modalities. The effects of meditation on the brain have been studied using sophisticated functional MRI (fMRI) and electroencephalographic (EEG) techniques. Not only have researchers detected significant differences in brain activity between experienced meditators and nonmeditators (or inexperienced meditators), but there also may be detectable differences resulting from the particular type of meditation studied.[193] Although more substantial differences can be found with long-term meditators, even a short training period of eight weeks "produces demonstrable effects on brain and immune function."[194] Some findings suggest that "the resting state of the brain may be altered by long-term meditative practice," and that "attention and affective processes…are flexible skills that can be trained."[195] The practical implications of such findings, if replicated on a large scale, could be considerable. One report concluded that "it is plausible from our results that meditation may strengthen the ability to inhibit cognitive and emotional mental processes such as rumination that can lead to or exacerbate stress, anxiety, or depression."[196] A subsequent study to test this hypothesis returned startling results[197]:

> MBCT [mindfulness-based cognitive therapy] was more effective than m-ADM [maintenance antidepressant medication] in reducing residual depressive symptoms and psychiatric comorbidity and in

to be more widely used, but it supports the interdisciplinary team concept in both educational and clinical settings. It allows patients greater freedom of choice in both therapies and providers, and it encourages dialogue among all health practitioners.

There is a danger that integrative medicine physicians will extend their practices beyond the scope of their education. Completing a program in integrative medicine does not turn an MD or a DO into a trained chiropractor, acupuncturist, naturopathic physician, or other such practitioner. It is important that those who wish to fully practice an alternative discipline seek comprehensive training from accredited institutions, just as those who wish to practice as medical doctors must do.

improving quality of life in the physical and psychological domains. There was no difference in average annual cost between the two groups. Rates of ADM usage in the MBCT group was [illegible] reduced, and 46 patients (75%) completely discontinued their ADM. For patients treated with ADM, MBCT may provide an alternative approach for relapse prevention.

Common ground with other emerging models

Integrated medicine uses evidence-based medicine to select the practices to integrate. It is multidisciplinary and oriented toward whole-person health care. It is the only one of the models to explicitly integrate alternative practitioners and approaches, to emphasize the importance of the practitioner-patient relationship, and to bring body-mind issues to the fore. Other than EBM, it is the only one that already has a significant foothold within academic medicine.

Role in a synthesized, comprehensive model of 21st century medicine

Integrative medicine provides great leadership in demonstrating the importance of a more integrated healthcare system and in creating academic models to educate practitioners in this new approach. It could benefit from a greater emphasis on genomic medicine, perhaps by incorporating some of the principles or recommendations of personalized or prospective medicine.

Chapter 4

THE CLINICIAN'S DILEMMA

[W]hat we observe is not nature itself, but nature exposed to our method of questioning.
Natural science, does not simply describe and explain nature;
it is part of the interplay between nature and ourselves.

—WERNER HEISENBERG, PHYSICS AND PHILOSOPHY, 1958

We have spent, to this point, a great deal of time and effort exploring both the challenge of 21st century medicine—to first halt and then reverse the epidemic of chronic disease—and some of the most prominent among many proposed solutions. We hope we have achieved a shared recognition that our current tools and approaches are not sufficient to the task, and that changes in the practice of medicine are necessary and imminent. At the same time, we cannot ignore the challenge of making these conclusions relevant to the individual practice of medicine. For, ultimately, most health care is delivered one patient and one practitioner at a time. In this chapter, we explore the clinician's dilemma: how to practice in such a way that both the continuing advances of science and the essential art of medicine are integrated seamlessly into clinical practice, neither overshadowing the other. It won't matter how intelligent and persuasive the arguments for change may be if we cannot convert them into practical approaches that can be taught to and adopted by individual clinicians.

This paper is not intended as an exploration of the actual clinical interventions that comprise functional medicine nor of the extensive science that underlies them. For that purpose, we refer the reader to the books, monographs, and courses available through The Institute for Functional Medicine (IFM).[n] In these final two chapters, we address clinical practice at a different level, presenting the foundational concepts and principles that we believe should shape the coming changes in health care.

The Central Hub of 21st Century Medicine

The primary principle around which 21st century medicine—functional medicine—*will revolve is personalized, systems medicine.* Grouping people into categories based on organ system diseases, and then

[n] A complete list of IFM publications and courses can be found at www.functionalmedicine.org.

prescribing as though all people with a given diagnosis were inherently alike, is beginning to give way to a model that recognizes each patient's genetic and environmental uniqueness. Clinicians must develop the knowledge and skills to deliver individually tailored care. They must be able (and willing) to incorporate the science of systems biology, the emerging discipline of personalized care, and a much broader array of assessment, therapeutic, and preventive strategies into a new therapeutic relationship.

Each human emerges from a mold that has but one model.[xiii] Uniqueness continues to develop throughout life as a result of myriad influences. Family, school, work, community, diet, exercise, stress, and environmental toxicity all communicate information from outside the organism to the epigenetic translational structures that are married to nuclear DNA and that create powerful downstream effects on the genome, proteome, and metabolome. This phenomenon of biochemical uniqueness was recognized, researched, and documented in the 20th century, and is the foundation from which many key constructs have evolved, including systems biology and systems medicine, prospective health care, patient-centered health care, nutrigenomics, pharmacogenomics, proteomics, and metabolomics/metabonomics (see Chapter 3).

Decision Making in the Face of Uncertainty

From this chaotic, nonlinear interplay of complex factors, involving the integration of both genetics and context of living, emerges the haunting reality that all care is provided in a context of uncertainty. This is the shadow side of modern clinical medicine and it poses a daunting conundrum—how do you structure and systematize the assessment and treatment of patients when each is the product of a multitude of unique genetic and environmental influences and interactions? Kathryn Montgomery in her scholarly book, *How Doctors Think*, directly addresses this challenging issue:

> Complexity and uncertainty are built into the physician's effort to understand the particular in light of general rules.... The obstacle they encounter is the radical uncertainty of clinical practice: not just the incompleteness of medical knowledge but, more important, the imprecision of the application of even the most solid-seeming fact to a particular patient.[xiv]

What elevates the importance (and the stress) of clinical care over the work of, for instance, engineers, lawyers, accountants, and other nonclinical professionals is its continuous involvement in matters of life and death. The cost of failure is so high—death, when life might have been possible; illness, when health might have been attainable. The daily unconscious concern of every clinician is the weight of this cumulative decision making—inherently uncertain and lacking full (or sometimes even adequate) information to inform the clinical picture. Dr. Jerome Groopman in his provocative book with the same title, *How Doctors Think*, addressed this issue from his clinical perspective:

> Uncertainty creeps into medical practice through every pore. Whether a physician is defining a disease, making a diagnosis, selecting a procedure, observing outcomes, assessing probabilities, assigning preferences, or putting it all together, he is walking on very slippery terrain. It is difficult for non-physicians, and for many physicians, to appreciate how complex these tasks

[xiii] The potential for human cloning might be considered the exception to this rule. However, exact replication from a clone donor cannot duplicate the pre and post epigenetic imprinting that skews the exactness of a clone

are, how poorly we understand them, and how easy it is for honest people to come to different conclusions.[99]

Personalized, systems medicine serves to inform us about the enormity of the uncertainty. The message is clear: there is no one-size-fits-all solution to resolve any specific diagnosis. The limitations of clinical algorithms and evidence-based medicine can now be more clearly discerned. We can no longer allow them to skew our understanding of the larger picture, however difficult it may be to look at unflinchingly. We are at a crossroads where only honesty about the limitations of strategies that seek to avoid or ignore uncertainty will suffice.

> For the great enemy of truth is very often not the lie — deliberate, contrived, and dishonest — but the myth — persistent, persuasive, and unrealistic. Too often we hold fast to the clichés of our forbears. We subject all facts to a prefabricated set of interpretations. We enjoy the comfort of opinion without the discomfort of thought.
>
> —John F. Kennedy, Yale Commencement, 1962

Medicine has attempted historically, through a number of shifts in perspective, to provide greater certainty to both practicing clinicians and patients, a patently valuable goal. Setting aside traditional methods of instilling confidence—oracles or shamans, for example—science has been a very important tool for reducing uncertainty.

Twentieth century medicine completed a great philosophical and practical transformation into the *organ system* model of disease and diagnosis. This provided an evolving and reassuring sense of control and certainty as a result of ever-increasing specialization (often described as knowing more and more about less and less) as well as unreal fascinating scientific breakthroughs in understanding the nature of life, health, and disease. From early x-rays through the sophisticated imaging processes in use today, through ever more complex and detailed biochemical pathways, we have explored the silos of mammalian organ systems taxonomy. Objective facts accreted in uncountable numbers during the 1900s, describing human anatomy, physiology, and mechanisms of dysfunction from the cellular level to the specific organs themselves. The medical specialties (e.g., cardiology, neurology, nephrology) emerged and grew strong from these historic breakthroughs.

Near the end of the 20th century, however, the reality of the web-like, chaotic, nonlinear and complex nature of life (and health)—exposed by advances in the systems-oriented life sciences—began to erode this reassuring sense of certainty. Twenty-first century medicine has now come face-to-face with the practical implications of uncertainty—a problem that flummoxed many mid-20th century physicists (including the great Albert Einstein, who ultimately rejected what is now an accepted principle) when they first confronted Heisenberg's articulation of the principle of uncertainty in physics. Fortunately, once the seriousness of this issue is consciously acknowledged, management strategies can be developed. First, however, we have to stop denying the presence and power of uncertainty in medicine. Research by brain scientists using advanced imaging and electronic technologies and analytic techniques equips the clinician with important knowledge for facing squarely the daunting task of assessing and treating each patient as a unique individual, shaped by innumerable complex interactions between genetics and the cumulative influences of daily life.

The rest of this chapter will discuss these findings and will describe why the context of uncertainty in medicine requires a change in our view of evidence and the therapeutic relationship, and a considerable expansion in the clinical tool kit of the practitioner. The increasingly technical (and increasingly brief) clinical encounter that has characterized the last few decades in medicine can be transformed into a *healing partnership* through the appropriate integration of relevant evidence from clinical trials, the knowledge gained from breakthroughs in brain science and systems biology, and an expanded clinical armamentarium. Within this complex relational system can be found effective strategies for individualized assessment and treatment, taking into account the uncertainty generated by the complex genetic and environmental uniqueness of each patient—we can, in fact, begin the practice of *personalized, systems medicine* today.[200, 201]

Evidence-based Medicine in the Clinical Setting: Uses and Limitations

The scientific method disciplines the creative process of human inquiry. In the applied biological sciences (e.g., clinical medicine) prior to World War II, evaluation of emerging therapeutics was mainly the purview of recognized leaders in the medical profession, based primarily on their clinical experience and reputations, and without the rigor of systematic controls or external standards.[202] To improve the quality of evidence and render a more accurate judgment with less personal bias, postwar researchers developed the randomized controlled trial (RCT) protocol. The major characteristics of this method include blinded assessment (of subjects, investigators, or both), often in the presence of a placebo control; random assignment to comparable groups; and inferential statistics as a surrogate for establishing causation.[203]

The reliance on the expert gave way to reliance on results from RCTs. Clinicians could no longer reduce uncertainty by following the lead of a confident expert, but they increasingly appreciated the power of the double-blind, randomized, placebo-controlled clinical trial—a step up in certitude.[204, 205] Putting aside, for the moment, the many problems inherent in the RCT model, not the least of which is the bias introduced by the influence of big Pharma,[206, 207, 208, 209] let's briefly explore EBM—the offspring of the RCT model—as understood and used by clinicians to reduce uncertainty.

Proponents of the RCT as the gold standard for unbiased research results have fostered its preeminence in the applied medical fields, both in primary and specialty care. They have argued for and developed algorithms for grading recommendations based on a research quality scale that ranks methodologies in descending order of accepted best evidence:[210, 211]

- Systematic reviews and meta-analyses of RCT studies
- RCTs
- Nonrandomized intervention studies
- Nonexperimental studies
- Expert opinion

Amid the early excitement generated by this new schema, certain assumptions were posited as foundational:

> A new paradigm for medical practice is emerging. *Evidence-based medicine de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making* and stresses the examination of evidence from clinical research. Evidence-based medicine requires new skills of the physician, including efficient literature searching and the application of formal rules of evidence evaluating the clinical literature.[212] [Italics added.]
>
> —Evidence-based Medicine Working Group, JAMA, 1992

The application of EBM in the clinical setting is described as following this general scenario:[213, 214]

- Select specific clinical questions from the patient's problem(s)
- Search the literature or databases for relevant clinical information
- Appraise the evidence for:
  - validity against the hierarchy of evidence as described above, and
  - usefulness to the patient and practice
- Implement useful findings in everyday practice

Arguments in favor of EBM infusion into both medical education and clinical practice are based on the following facts and inferences:[215, 216]

- Available new evidence can and should lead to major changes in patient care
- Practicing physicians often fail to obtain available newer relevant evidence
- Medical knowledge and clinical performance deteriorate over time without the leavening of newer evidence influencing clinical decisions
- Traditional continuing medical education (CME) alone is inefficient and generally does not improve clinical performance without significant follow-up and evaluation measures
- The discipline of using evidence-based medicine can keep clinicians up-to-date

In a cogent paper in *The Lancet* in 1999, van Weel and Knottnerus responded to the proddings of many eminent medical thought leaders to move ahead quickly and comprehensively with the integration of EBM into the clinical setting by pointing out the many difficulties of using this schema to manage the care of individual patients with complex, chronic illness:[217]

- EBM tends to concentrate on research methodology and reduces clinical practice to the technical implementation of research findings. In a more colloquial view, it is the tail wagging the dog. Rather than using clinical judgment to guide the choice of relevant evidence, EBM is structured with a hierarchy of evidence as the driver of clinical judgment.

- The structure of RCT methodology assumes the consequences of individual variability in response to treatment will "wash out" if the subject pool is large enough and the statistical analyses sophisticated enough. *While this may be true for populations, it seriously limits the applicability of the research in primary care, where therapy is delivered one unique patient at a time.*
- Co-morbid conditions are the usual justified reason for the exclusion of many patients from RCTs, *so the very patients most in need of usable evidence (e.g., those with complex, chronic conditions) are often not in the cohorts of patients being studied,* making the findings from the research trials very limited in their applicability.
- In primary care, treatment usually involves several interventions, sometimes delivered concurrently and sometimes sequentially. Unfortunately, combinations of evidence-based interventions do not sum to a treatment plan that is evidence-based. Interactions between single interventions may increase or decrease their efficacy (even under ideal trial conditions), when blended into a comprehensive plan. Adverse interactions among treatments may, and often do, occur.
- Clinical research does not focus on the overall outcome of composite interventions because of the complexity of such studies and the absence of well-developed tools for studying such whole systems approaches.
- Drug interventions have been studied more extensively than nonpharmacological interventions, in part due to the technical and methodological difficulties in the design of RCTs for nondrug interventions (and, in part, because of the nonpatentable nature of most lifestyle interventions). This situation creates a significant problem in primary care, where the use of educational, dietary, and lifestyle interventions is attractive because of their resonance with the principle of "maximum effect using minimum resources."

In marked contrast to the assertions of the EBM Working Group cited earlier, van Weel and Knottnerus suggest that the driving force behind EBM should be a coherent system of fundamental research in *pathophysiology and the humanities,* combined with careful clinical observations, on which systematic (RCT-based) evidence of effectiveness is superimposed. Existing clinical practice should be supported or, if erroneous, corrected on the basis of this coherent system. They go on to propose that "two complementary approaches are needed to strengthen the evidence base of nonpharmacological interventions and complex multifaceted strategies. First, the generic characteristics of complex interventions must be acknowledged as essential for its evaluation. Second, a methodology to allow the assessment of complex effects should be further developed."

Dr. David Mant in his seminal 1999 paper, "Can randomized trials inform clinical decisions about individual patients?" takes a slightly different tack in exploring the irony that the RCT combines strength of concept for the population being studied with weakness of specific application to the individual patient:[21a]

> The paradox of the clinical trial is that it is the best way to assess whether an intervention works, but is arguably the worst way to assess who will benefit from it... However, the nub of the argument for me is that randomized controlled trials are primarily about medical interventions and not patients. In clinical trials, patients are randomized to allow a comparison of intervention efficacy unbiased by the individuality of patient. This methodological approach provides society with powerful protection against witch-doctoring, and helps us eliminate the inefficiencies in the provision of medical care described by Cochrane. *But the methodological minimization of information on effectiveness in relation to the individual patient leaves an evidence gap for clinicians.* [Italics added.]

Dr. Alan Feinstein, from the Department of Medicine at Yale University, echoes similar reservations in his article, "Problems in the evidence of evidence-based medicine."[219] Larry Culpepper and Thomas Gilbert, in their Lancet commentary, "Evidence and ethics," focus on this same difficulty in the primary care arena.[220] Although the debate has continued over the past decade, these reasoned arguments have been heard less frequently as the push toward EBM has gained momentum. However, the problems described above have not been solved. Rather, with the advent of personalized medicine and systems biology, it is even more clear that the reductionist simplicity of the RCT frequently does not work to address the significant questions now facing 21st century practitioners in their struggle to cope with the epidemic of complex, chronic disease.[221,222,223,224,225]

We can now begin to understand why the effect of research findings on clinical practice has been weaker than the early proponents of EBM postulated. The first problem that has impeded the successful application of EBM to patient care is the complex nature of the translation of research studies to the individual patient's unique clinical problem(s)—what Larry Weed called knowledge coupling.[226, 227] John Hampton, Professor of Cardiology, University Hospital, Nottingham, England, in a review titled "Evidence-based medicine, opinion-based medicine, and real-world medicine," reasons: *"Clinical trials will tell us what treatments are effective, but not necessarily which patients should receive them... Treatment must always be tailored to the individual patient."*[220] (We would add to that statement that RCTs can only tell us what treatments are effective *from among those studied*. The decision about what to investigate introduces so much bias into the evidence base that it would be difficult to overstate its impact.)

Added to this methodological conundrum are the real-world exigencies of daily clinical practice that make it virtually impossible to acquire, collate, and filter all relevant evidence prior to direct application to the unique needs of the patient. Imagine a clinic where, after each therapeutic encounter—involving both appropriate history taking and physical examination procedures—a problem list is developed and then carefully subjected to a medical literature search and analysis. The pace of clinical practice will not tolerate the inertia of such a process, even to improve the care of patients who may be in desperate need of new interventions based on emerging evidence.

A second major issue is even more complex. If medical care were as simple as making a diagnosis and then prescribing an appropriate pharmacologic agent (or agents), then the EBM system, as presently configured and applied, might work—but only if appropriate *Problem Oriented Evidence that Matters* (POEMs)[xiii, 230] were available for each medical problem (and disregarding, for the moment, that most

[xiii] To assist the practicing physician's effective inclusion of new evidence into daily practice, both government-sponsored and commercially affiliated organizations have moved EBM forward with a collation of filtered studies called: *Problem Oriented Evidence that Matters* (POEMs). Most POEMs and most studies in the Cochrane Collection are research trials of pharmacologic therapeutic interventions. It is now possible to search these specific databases or self-developed relevant databases that review groups of studies that directly link research findings with specific clinical problems.

chronic disease is complicated by multiple comorbidities that are rarely addressed by POEMs). Unfortunately, the "better living through chemistry" dream that fueled half a century of research has not, in fact, created a healthier population (see Chapter 2).[231] Although many acute medical problems do appear to respond consistently as envisioned by the EBM model, more than 70% of health problems presenting to clinicians today are both chronic and complex[232] (Chapter 2), and they require a different approach. "Treating only known biological components of disease minimizes the ability of the practitioner to tailor therapeutic interventions to individual patients."[233]

Despite these sobering facts, physician education, training, and reimbursement, as well as research designs for clinical studies that physicians depend upon for effective decision making, continue to be focused primarily on an acute-care model that emphasizes pharmacologic solutions for complex, chronic problems, leaving the discerning clinician without the evidence and tools needed for addressing their patients' complex needs.

It's not enough, of course, for us to understand what's wrong. We must also seek better solutions for these urgent problems, regardless of the difficulty of the task and the elusiveness of the answers. The RCT tool was developed during a specific period in our medical history and worked well to differentiate the traditionalists, who claimed that clinical experience trumped bench science, from the scientists, who perceived the value in systematic inquiry. Major strides in treatment have occurred in the intervening 50 to 60 years as a result of the shift toward the use of RCT methodology. But we are now at another nodal decision point, unique to our cultural and medical evolution. We need more sophisticated tools to shed light on the nature of the web-like interweaving of mechanisms at work in complex, chronic illness.[234, 235, 236] While alternate study designs and statistical methodologies are being developed for analyzing complex data sets,[237, 238, 239] we must return the practice of EBM to its original mission of using evidence to inform clinical experience and to expand the understanding of basic mechanisms of health and disease.[240, 241] This will help to reverse the decade-long plunge toward "... reducing clinical practice to the technical implementation of research findings."[242, 243]

In sum, we are now facing another major transition in how we perceive and utilize evidence in clinical medicine. Thomas Kuhn offers this insightful analysis:

> When defects in an existing paradigm accumulate to the extent that the paradigm is no longer tenable, the paradigm is challenged and replaced by a new way of looking at the world. Medical practice is changing, and the change, which involves using the medical literature more effectively in guiding medical practice, is profound enough that it can appropriately be called a paradigm shift.

A Science-Using Profession

Given the serious limitations of applying the EBM model in clinical practice, we must ask two questions central to the future of medicine:

- How do we develop an effective therapeutic relationship based upon (1) efficacious, reproducible, and personalized clinical applications that are solidly anchored in science, (2) emerging knowledge about the multifactorial causes of chronic disease, and (3) an expanded awareness of the nature of clinical/critical thinking?

- How do we transition from an EBM-based, guideline-driven, prescriptive clinical practice to an individualized, patient-centered approach that captures both the science and the art of medicine?

First, we must recognize that most clinicians, by professional training and inclination, are not scientists. ***Clinical medicine is a science-using profession.*** It is true that diagnosis and treatment have become intensely science-using activities, but these activities have a distinctly different process and endpoint than those of the professional scientist.[245] "Physicians start from the demands of the patient's condition and not from the demand for generalizable knowledge, and their goal is just as particular: to treat the patient's illness, not to test the therapy."[246] The evidence needs of clinical medicine are also distinctly different. The focus on application and usefulness centers on how the evidence informs the assessment and treatment process for each individual patient, given that patient's unique genetic propensities and unique environmental influences.

At a number of points in this paper, we have documented how most clinical evidence based on RCTs informs about cohorts of patients with similar signs and symptoms (the basis of diagnosis and diagnostic groups), but not does not necessarily provide decision support for an individual patient. The primary responsibility of the attending clinician is to ferret out meaningful evidence for each patient, knowing that unique genomic specificities may predispose that patient to unanticipated results. From this perspective, evidence often serves to qualify *insight*, but when applied in a simplistic or statistically linear way, can create unintended mischief.[247] From this perspective, every maneuver, either further assessment or therapeutic intervention, becomes a clinical probe that must be assessed in partnership with the client as the shared journey of investigation and healing proceeds.

Dr. Sackett, founder and advocate for EBM, was quite clear about this in the early development of EBM: "Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.... *Good doctors use both individual clinical expertise and the best available external evidence and neither alone is enough.*"[248] [Italics added.]

The combining of these elements can be viewed as a Venn diagram, where the best outcomes occur when all three elements are represented (Figure 8).

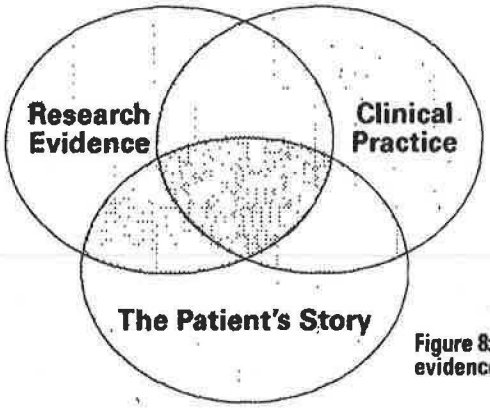


Figure 8: Optimal Outcomes: Applying evidence-based medicine to the real world

David Deutsch, in *The Fabric of Reality*, describes the need for a next step in using the science of underlying pathophysiological mechanisms of disease in the clinical setting of medicine:

> The science of medicine is perhaps the most frequently cited case of increasing specialization seeming to follow inevitably from increasing knowledge, as new cures and better treatments for more diseases are discovered. But as medical and biochemical research comes up with deeper explanations of disease processes (and healthy processes) in the body, understanding is also on the increase. More general concepts are replacing more specific ones as common, underlying molecular mechanisms are found for dissimilar diseases in different parts of the body. Once a disease can be understood as fitting into a general framework, the role of the specialist diminishes.... Physicians... can look up such facts as are known. But [more importantly] they may be able to apply a general theory to work out the required treatment, and expect it to be effective even if it has never been used before.[246]

The real question now facing every discerning, informed clinician[247] is how to bring relevant, graded, emerging scientific evidence to the complex list of problems made unique by the patient's genetic susceptibilities and potentialities that, in turn, communicate constantly with the ever-changing environment within which the patient lives. No RCT can inform, *in a specific way*, the appropriate clinical roadmap for assessment and planning for therapeutic interventions in this complex environment.[248] Clinicians must use science; it is a powerful tool. But they should be in charge of how and when to use it, not dominated and intimidated by it.

The Heuristics that Guide Doctors' Thinking

We believe it is fair to say that the fear of uncertainty has led us to narrow our field of vision far too soon. "Science has not one method, but many. These include observation in the natural world, experimentation in the laboratory, mathematical proof, computer simulation with real data, analysis of surveys and demographical statistics, and thought experiments for the great geniuses, such as Galileo and Einstein.

Another Perspective on the Biomedical Model

The complexity of the developing explanatory models has been serially addressed in the *Annals of Family Medicine*, a peer-reviewed medical journal "dedicated to advancing knowledge essential to understanding and improving health and primary care," including the development of methodology and theory for addressing this conundrum. In the article, "The biopsychosocial model 25 years later: Principles, practice, and scientific inquiry,"[249] the authors critique the limitations of the conventional biomedical model and the research methodologies that evolve from this model and preview the evolving model of complexity and causality and the nested model of structural causality":

> Few morbid conditions could be interpreted as being of the nature "one microbe, one illness"; rather, there are usually multiple interacting causes and contributing factors. Thus, obesity leads to both diabetes and arthritis; both obesity and arthritis limit exercise capacity, adversely affecting blood pressure and cholesterol levels; and all of the above, except perhaps arthritis, contribute to both stroke and coronary artery disease. Some effects (depression after a heart attack or stroke) can then become causal (greater likelihood of a second similar event).... These observations set the stage for models of circular causality that describe how a series of feedback loops sustain a specific pattern of behavior over time.[250, 251, 252] Complexity science is an attempt to understand these complex recursive and emergent properties of systems[253, 254] and to find interrelated proximal causes that might be changed with the right set of interventions.[255]

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The Heuristics that Guide Doctors' Thinking

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Has broad-based and open-minded scientific inquiry been skewed by EBM and its hierarchy of evidence codification and ranking?[260, 261, 262, 263, 264, 265] Is the hegemony of EBM in contemporary medicine, as exemplified by Drs. Montori and Guyatt,[266] closing the door on the reintegration of the science and art of medicine?[m] We need to ask what we have surrendered by de-emphasizing "unsystematic clinical experience and pathophysiologic rationale." What is the irreplaceable loss in patient outcomes with the dismissing of experience, intuition, and wisdom? What must we do to develop skills and methodologies appropriate to clinical decision making in a context of uncertainty?

[m] In their 2008 review of the progress in EBM, VM Montori and GH Guyatt reiterate a basic principle of EBM cited earlier in this chapter: "Evidence-based medicine *de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale* (italics added) as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research. Ignoring the significant push back from the international scientific and clinical community regarding the hobbling effects of EBM on both research and translational medicine

There is a robust literature that explores the actual methodologies used by clinicians who must make decisions when time and information are limited and the outcome is uncertain. It is clear from brain research that there is an important difference between the human brain and other features of the universe. The brain is a complicated, nonlinear, living system capable of self-organization. The brain does not respond to incoming stimuli in a direct, reflex-like action but continuously changes, constructing its own neural activity patterns in order to adapt to and synchronize with external stimuli. Genetic makeup and continuous stimuli from the environment are the only factors that create individual differences; the twin magnets of chaos and self-organization shape the constant interplay of those factors. The human mind is highly capable of dual processing; in fact, the continuous and virtually seamless integration of reason to test intuition and of intuition to generate the creative thinking that fuels rational inquiry is what advances insight and knowledge.

We usually represent problems in a linear fashion despite the convincing evidence that this type of modeling is not appropriate or adequate for studying the nervous system or human behavior.[267, 268] This naturally leads to some interesting conclusions about the interrelationship of brain and mind when faced with decision making in a sea of uncertainty.[269, 270, 271, 272, 273] The mind is an adaptive toolbox with genetically, culturally, and individually created and transmitted rules of thumb. These rules of thumb are called heuristics and are foundational to daily function, intuition, or inspiration.[274] *The study of judgment under uncertainty is the study of heuristics.* The human species' response to uncertainty is to rely upon experience, coupled with knowledge, data, and applied wisdom through processes such as heuristics and insight.

Heuristics and "rules of thumb" are synonyms terms. It is important to distinguish between heuristic and analytic thinking. For instance, heuristic thinking is indispensable for discovering a mathematical proof, whereas analytic thinking is necessary for checking the steps of the proof.[275] A limited number of simplifying heuristics rather than more formal and extensive algorithmic processing is the rule.[276] The classic example of a heuristic that most people have experienced is the "rule of thumb" (gaze heuristic) used for catching a ball, as illustrated in Figure 9.

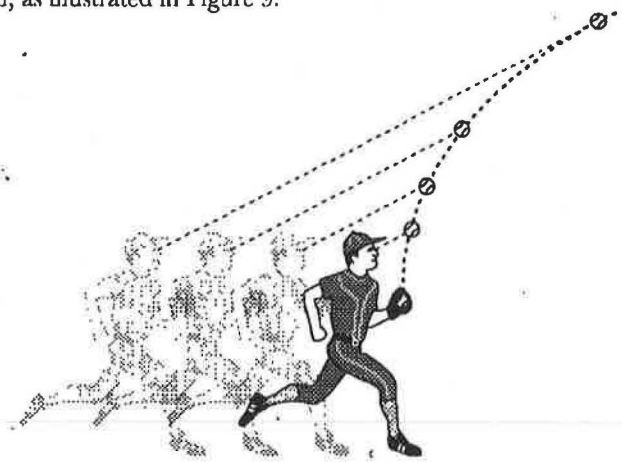

Figure 9:
How to catch a fly ball Players rely on unconscious rules of thumb. When a ball comes in high, a player fixates his gaze on the ball, starts running, and adjusts his speed so that the angle of the gaze remains constant.

The angle of gaze is the angle between the eye and the ball, relative to the ground. For years, brain scientists assumed that a complex process of computations was required for tasks like catching a ball. The artificial intelligence (AI) groups attempted to duplicate these tasks with robotic technologies. However, research by the 'heuristics' groups showed a very different process at work.[277] It turns out that a player who uses the *gaze* rule does not need to measure wind, air resistance, spin, or the other complex, causal variables. "All the relevant facts are contained in one variable: the angle of gaze. Note that a player using the *gaze heuristic* is not able to compute the point at which the ball will land. Yet the heuristic leads the player to the landing point....most fielders are blissfully unaware of the gaze heuristic, despite it simplicity. Once the rationale underlying an intuitive feeling is made conscious, however, it can be taught."[278]

Elwyn et al., in their well reasoned paper, "Decision analysis in patient care,"[279] demonstrate the efficacy and comprehensiveness of this methodology. Naylor summarizes in his editorial comments on their paper (published in the *Lancet*):

> The process of individualized decision analysis might best be viewed as a way of enhancing communication with patients, rather than as a "black box" from which directives emerge. But if that is the ultimate aim, it seems more useful to develop simple decision aids aimed at helping patients and doctors share information and work through tough choices in the clinical setting. To that end, Elwyn and colleagues call on clinicians and patients to communicate better while embracing fast and frugal rules of thumb [heuristics]. In so doing they have arguably drawn their readers full circle *from clinical art to bedside science and back again*. It is ironic, moreover, that the best lessons in *fast and frugal rules of thumb* may well come from understanding the cognitive processes of those master clinicians who consistently make superb decisions without obvious recourse to the canon of evidence-based medicine.[280] [Italics added.]

If we are to develop both a clinical methodology and a curriculum that will approximate the best characteristics of successful clinicians, we must compare what is usually done with what could be done. A very pertinent example of how we might transform medical care affects the primary heuristic of contemporary medicine—the patient history and physical exam reporting structure (the H&P heuristic)—that dominates all communication among healthcare practitioners today. We will then compare it to the new heuristic developed by IFM to achieve a more comprehensive communication tool.

Every healthcare provider recognizes this formal construct for medical information and communication. It both describes and dictates the process of the patient visit. The story that emerges from a clinical encounter is typically organized around the following elements:

From Patient Encounter to the Diagnosis:
The Conventional Medical Heuristic

- **Chief Complaint (CC)***
- **History of Present Illness (HPI)***
- **Past Medical History (PMH)***
- **Review of Organ Systems (ROS)***
- **Medication and Supplement History***
- **Dietary History***
- **Social, Lifestyle, Exercise History****
- **Physical Examination (PE)***
- **Laboratory and Imaging Evaluations***
- **Assessment and Diagnosis***
- **Treatment Interventions *usually pharmaceutical and/or procedure-based)***

*** = STANDARD PRACTICE**
**** = EXPANDED MODEL**

It is not always recognized that this construct facilitates the "fast and frugal processing" needed to efficiently collect, collate, and use patient information. The conventional H&P heuristic propels all information headlong toward the diagnosis, with the intention of identifying and prescribing the pharmaceutical or procedural therapy associated with that diagnosis. Each individual diagnosis is viewed as a distinct entity unto itself—often investigated during separate office calls and/or by different practitioners. There is no place in the conventional H&P heuristic to tie together multiple diagnoses into a consistent and coherent patient narrative. There is no identification of the antecedent conditions that may predispose the patient to the triggering of dysfunctional adaptive responses, nor of the mediators that may perpetuate the dysfunction. Thus, patients filtered through this conventional heuristic never have a chance to be fully heard and understood in the context of their whole life experience. Instead, their stories are reduced to a series of diagnoses, treated by different specialists, often in isolation from one another.

The H&P heuristic was shaped by, and thus reinforces, the organ-system model of disease, with its distinct and separate information silos, rather than a systems-medicine perspective that encourages the search for common underlying mechanisms of, and pathways to, disease.

IFM's functional medicine heuristic (FM heuristic) expands upon the same basic structure we are all familiar with, but organizes the information to integrate the patient's genetic and developmental susceptibilities (*antecedents*), historical *triggers*, and ongoing *mediators* of disease. Thus, the patient's story emerges with greater detail, a broader context, and a different focus and ultimate goal:

HA 09/01/2015

The Functional Medicine Heuristic

- **Chief Complaint (CC)**
- **History of Present Illness (HPI)**
- **Past Medical History (PMH)**
  —Explore antecedents, triggers, and mediators of CC, HPI, and PMH
- **Review of Organ Systems (ROS)**
  —Genetic predispositions?
- **Medication and Supplement History**
- **Dietary History**
- **Social, Lifestyle, Exercise History**
- **Physical Examination (PE)**
- **Laboratory and Imaging Evaluations:**
  —Immune/inflammatory imbalance
  —Energy imbalance/mitochondrial dysfunction
  —Digestive/absorptive and microbiological imbalance
  —Detoxification/biotransformation/excretory imbalance
  —Imbalance in structural, boundary, and membrane integrity
  —Hormonal and neurostransmitter imbalances
  —Imbalance in mind - body - spirit integration
- **Initial Assessment:**
  —Enter data on Matrix form; look for common themes
  —Review underlying mechanisms of disease
  —Recapitulate patient's story
  —Organ system-based diagnosis
  —Functional medicine assessment: underlying mechanisms of disease; genetic and environmental influences
- **Treatment Plan:**
  —Individualized
  —Dietary, lifestyle, environmental
  —Nutritional, botanical, psychosocial, energetic, spiritual
  —May include pharmaceuticals and/or procedures

As can be seen in the FM heuristic, the diagnosis is one factor among many that help the clinician and patient explore why and how a condition was triggered and why and how the dysfunction is being mediated. From a disciplined filtering of the patient information through the Functional Medicine Matrix Model™, patterns emerge that illuminate both the underlying causes of dysfunction as well as plausible (and multiple) points of leverage where individualized treatment can create improved function. The potential interventions reflect a broader array of health vectors than just pharmaceutical and procedural interventions because the FM heuristic elicits a pattern that helps the clinician and patient identify where lifestyle and environmental interventions can be applied.

Because clinical reasoning is very often grounded in heuristics (simplified models that guide evaluation and treatment at an unconscious level of awareness), we argue that to change the outcome, we must change the model. The ability to utilize heuristics when time and information are limited and outcomes are uncertain is a very special cognitive trait—an evolutionary breakthrough in adaptive cognition. To understand and refine clinical reasoning and clinical practice—to ultimately improve outcome—a deeper understanding of these adaptive skills must be understood and consciously applied.

Insight

If we are to develop an effective model for the healing partnership, we must also explore the research that illuminates the emergence of insight as a reproducible phenomenon.[x] Brain research has illuminated very different functions of the left and right brain that explicate the objective neural correlates of a brain that produces insight. Among the most important features of this emerging view of brain function are the following:

- Solving computational questions is primarily a left-brain function. Asking a computational question triggers left-brain activity at the expense of right-brain function. (This has tremendous relevance to the interactions between doctor and patient. When a patient is interrupted with a computational question in the midst of an attempt to describe a pattern of dysfunction, the patient's own opportunity for insight may be lost.)
- If the left hemisphere excels at denotation—storing the primary meaning of a word—the right hemisphere deals with connotation, everything that gets left out of a dictionary definition, such as the emotional charge in a sentence or a metaphor. Language is so complex that the brain has to process it in two different ways at the same time. As humans, we need to see both the forest and the trees. The right hemisphere is what helps you see the forest.[201, 202]
- Much of the research into the adaptive unconscious (aka unconscious cognition) suggests that pattern recognition capacity resides in the right brain, but is not specifically localized.[203, 204] Solving questions requiring insight generates activity that starts in the prefrontal cortex and eventually extends throughout the cortex and deeper structures, searching for possible experiential information that contributes to the emergence of a pattern. It is the appearance of that pattern that sparks the "aha" or "Eureka!" experience in the connotative language centers of the right brain.

In brief, left-brain function helps us with the denotative, computational, linear functions of life and thought, whereas the right brain provides the connotative shadings that give depth and character and color to meaning. Right-brain function is the source of pattern recognition and moments of insight.

The researchers in this field have produced a robust and credible body of research about pattern recognition from experiments that delineate and substantiate the functions of unconscious cognition (the

[x] "What is insight? The term 'insight' is used to designate the clear and sudden understanding of how to solve a problem. Insight is thought to arise when a solver breaks free of unwarranted assumptions, or forms novel, task-related connections between existing concepts or skills." (Bowden EM. New approaches to demystifying insight. TRENDS in Cognitive Sciences. 2005;9(7):322-28.)

adaptive unconscious) that shape moments and expressions of insight.[205, 206, 207] Reproducible patterns of brain activity correlate with the experience of insight.[208] The prefrontal cortex does not simply function as an aggregator of information. Instead, like the conductor of an orchestra, brain wave activity and energy expenditure are coordinated as if instructed by the prefrontal cortex maestro, waving its baton and directing the players.

This is known as top-down processing, since the prefrontal cortex (the top of the brain) is directly modulating the activity of other areas. Studies show that cells in the right hemisphere are more broadly tuned than cells in the left hemisphere, with longer branches and more dendritic spines. As a consequence, neurons in the right hemisphere are collecting information from a larger area of cortical space. They are less precise but better connected. When the brain is searching for an insight, these are the cells that are most likely to produce it. A small fold of tissue on the surface of the right hemisphere, the anterior superior temporal gyrus (aSTG), becomes unusually active in the second before the insight. The activation is described as sudden and intense, a surge of electricity leading to a rush of blood.[209, 210]

One of the unusual aspects of insight is not the revelation itself but what happens afterward. The adult brain is an infinite library of associations, a cacophony of competing ideas, and yet, as soon as the right association appears, we *know*. The new thought, which is represented by that rush of gamma waves in the right hemisphere, immediately grabs our attention. As soon as the insight happens, it seems so obvious. People can't believe they didn't see it before.[291, 292, 293]

Insight researches call the "aha" experience the *moment of categorical insight*. This moment of epiphany registers as a new pattern of neural activity in the prefrontal cortex. The brain cells have been altered by the breakthrough. An insight is a restructuring of information—it's seeing the same old thing in a completely new way. Once that restructuring occurs, you never go back.[294]

Insight and the Healing Partnership

"While it's commonly assumed that the best way to solve a difficult problem is to focus, minimize distractions, and pay attention only to the relevant details, this clenched state of mind may inhibit the sort of creative connections that lead to sudden breakthroughs. We suppress the very type of brain activity that we should be encouraging. Jonathan Schooler has recently demonstrated that making people focus on the details of a visual scene, as opposed to the big picture, can significantly disrupt the insight process. 'It doesn't take much to shift the brain into left-hemisphere mode, he said.'"[295] We can extrapolate that, as clinicians, although we don't ignore evidence, when we want insight about a patient's condition, we are clearly better off not turning to left-brain analysis of the most recent RCTs. And, when we want the patient's insight, we must learn to elicit the patient's story (pattern) and really listen to it.

Research focused on the typical, clinical therapeutic encounter has noted that clinicians interrupt the patient's flow of conversation within the first 12 to 18 seconds (or less) of the patient's response to a question.[296, 297] This reproducible phenomenon in the conventional clinical setting makes sense if you compare the heuristic for contemporary medicine to the functional medicine heuristic. The heuristic of conventional medicine (rule of thumb) achieves the stated goal in an expeditious manner: clinicians use it to identify the primary organ system domain of the presenting problem and then focus on the differential diagnosis within that domain, marching resolutely to the final diagnosis. This is

a computational process, without need for a partnership that can produce insight into the underlying causes and mechanisms of the medical problem.

The functional medicine heuristic, on the other hand, requires a carefully nurtured and protected partnership between the clinician and the patient to illuminate the underlying mechanisms of the patient's illness(es). The FM heuristic requires an iterative, cooperative process that yields a more complete narrative story. From a thorough investigation of the antecedents, triggers and mediators of the patient's condition, emerge information and insights that can help to shape a deeper and more comprehensive therapeutic response.

Summary

We have devoted this chapter to achieving a better understanding of an urgent problem facing clinicians today: how to combine both science and art, evidence and insight, into an individualized, patient-centered approach to complex, chronic disease. We do not claim to have *the* (sole or definitive) answer. But we do offer a new focus for both education and practice that can be described and substantiated, taught and practiced. We have presented findings that suggest that the management of uncertainty—the inherent context of clinical medicine—requires a change in the therapeutic relationship on the part of both clinician and patient and a change in how we view and use evidence. The technical therapeutic encounter that has characterized a great deal of patient care for last few decades must be transformed into a healing partnership through appropriate applications of scientific understanding, evidence from clinical trials, and a new understanding of brain function.

The Institute for Functional Medicine's model of comprehensive care and primary prevention for complex, chronic illnesses (described further in Chapter 5) is grounded in both science (the Functional Medicine Matrix Model; evidence about common underlying mechanisms and pathways of disease; evidence about effective approaches to the environmental and lifestyle sources of disease) and art (the healing partnership and the search for insight in the therapeutic encounter). These two cornerstones of clinical medicine must be integrated into our teaching and practice in order to achieve what we owe to our patients and ourselves—a more effective response to the epidemic of chronic disease. We assert that this can be done.

Chapter 5

FUNCTIONAL MEDICINE: A 21ST CENTURY MODEL OF PATIENT CARE AND MEDICAL EDUCATION

It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has. The good physician treats the disease; the great physician treats the patient who has the disease.

—WILLIAM OSLER

Treat the patient, not the diagnosis.

—THE INSTITUTE FOR FUNCTIONAL MEDICINE

In this chapter, we will review the basic principles, constructs, and methodology of functional medicine. It is not the purpose of this paper to recapitulate the range and depth and science of functional medicine; books and monographs covering that material in great detail are already available for the interested clinician and for use in health professions schools. Our purpose in the first part of this chapter is to describe how functional medicine is organized to deliver personalized, systems medicine and, as such, is equipped to respond to the challenge of treating complex, chronic disease more effectively. In the second part of the chapter, we will discuss how clinicians can be helped to re-integrate the art and science of medicine to create a healing partnership.

Part I: What is Functional Medicine?

Functional medicine conceptualizes health and illness as part of a continuum in which all components of the human biological system interact dynamically with the environment. These interactions produce patterns that change over time in individuals. To manage the complexity inherent in this approach, functional medicine has adopted practical models for obtaining and evaluating clinical information that leads to individualized, patient-centered therapies.

Functional medicine encompasses a dynamic approach to assessing, preventing, and treating complex, chronic disease. It helps clinicians identify and ameliorate dysfunctions in the physiology and biochemistry of the human body as a primary method of improving patient health. In this model of practice, we emphasize that chronic disease is almost always preceded by a period of declining function in one or more of the body's systems. Returning patients to health requires reversing (or substantially improving) the specific dysfunctions that have contributed to the disease state.

Those dysfunctions are, for each of us, the result of lifelong interactions among our environment, our lifestyle, and our genetic predispositions. Each patient, therefore, represents a unique, complex, and interwoven set of influences on intrinsic functionality that have set the stage for the development of disease or the maintenance of health.

Historically, the word "functional" has been used somewhat pejoratively in medicine. It has implied a disability associated with either a geriatric or psychiatric problem. We suggest, however, that this is a very limited definition of an extremely useful word. Medicine has not really produced an efficient method for identifying and assessing changes in basic physiological processes that produce symptoms of increasing duration, intensity, and frequency, even though we know that such alterations in function often represent the first signs of conditions that, at a later stage, become pathophysiologically definable diseases. If we broaden the use of functional to encompass this view, *functional medicine* becomes the science and art of detecting and reversing alterations in function that clearly move a patient toward chronic disease over the course of a lifetime. Thus, with functional medicine, we begin to define a model of patient care that seeks to identify underlying chronic dysfunctions associated with altered physiological processes and to maximize functionality at all levels of body, mind, and spirit.

One way to conceptualize where functional medicine falls in the continuum of health and health care is to examine the functional medicine "tree." In its approach to complex, chronic disease, functional medicine encompasses the whole domain represented by the graphic shown in Figure 10, but *first* addresses the patient's core clinical imbalances, fundamental physiological processes, environmental inputs, and genetic predispositions. Diagnosis, of course, is part of the functional medicine model, but the emphasis is on understanding and improving the functional core of the human being as the starting point for intervention.

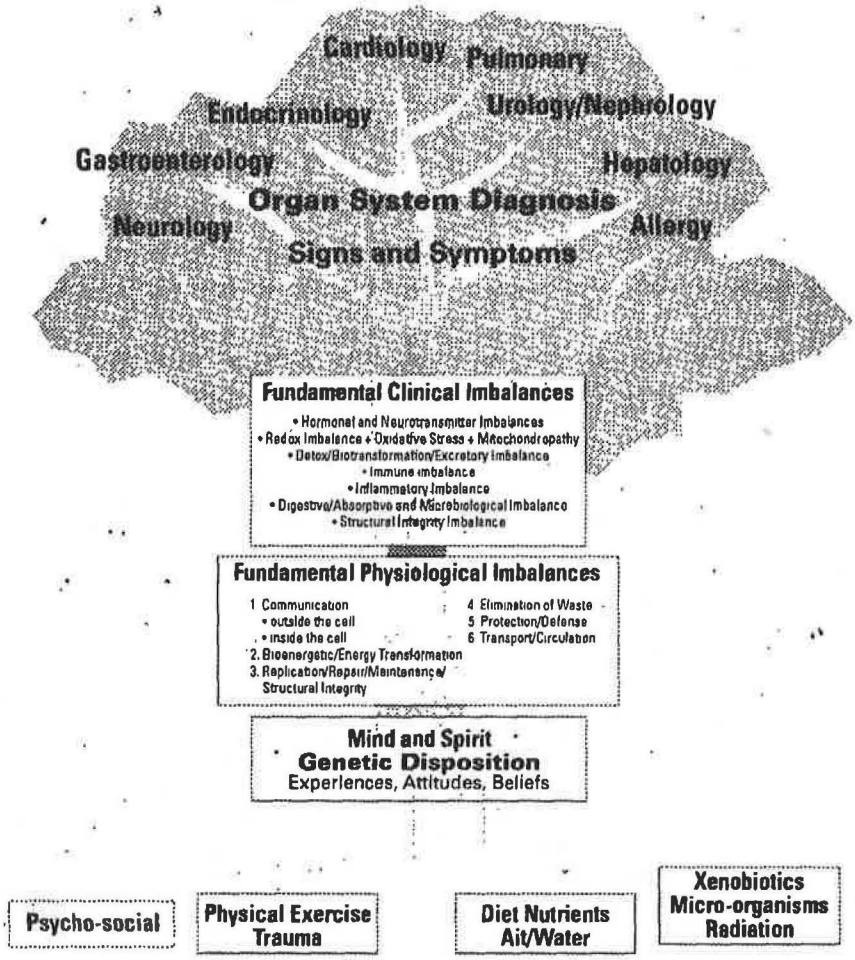

Figure 10:
The Continuum of Health and Health Care

Functional medicine clinicians focus on restoring balance to the dysfunctional systems by strengthening the fundamental physiological processes that underlie them, and by adjusting the environmental and lifestyle inputs that nurture or impair them. This approach leads to therapies that focus on restoring health and function, rather than simply controlling signs and symptoms.

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Principles

Seven basic principles characterize the functional medicine paradigm:

- Acknowledging the **biochemical individuality** of each human being, based on the concepts of genetic and environmental uniqueness
- Incorporating a **patient-centered** rather than a disease-centered approach to treatment
- Seeking a dynamic balance among the internal and external factors in a patient's body, mind, and spirit
- Addressing the **web-like interconnections** of internal physiological factors
- Identifying **health as a positive vitality**—not merely the absence of disease—and emphasizing those factors that encourage a vigorous physiology
- **Promoting organ reserve** as a means of enhancing the health span, not just the life span, of each patient
- Functional medicine is a **science-using profession**

Environmental Inputs

At the base of the medicine tree graphic are found the building blocks of life, as well as the primary influences on them. When we talk about influencing gene expression, we are interested in the interaction between environment in the broadest sense and any genetic predispositions with which a person may have been born—including the epi genome[m]. Many environmental factors that affect genetic expression are (or appear to be) a matter of choice (such as diet and exercise); others are very difficult for the individual patient to alter or escape (air and water quality, toxic exposures); and still others may be the result of unavoidable accidents (trauma, exposure to harmful microorganisms in the food supply). Some factors that may appear modifiable are heavily influenced by the patient's economic status—if you are poor, for example, it may be impossible to choose more healthful food, decrease stress in the workplace and at home, or take the time to exercise and rest properly. Existing health status is also a powerful influence on the patient's ability to alter environmental input. If you have chronic pain, exercise may be extremely difficult; if you are depressed, self-activation is a huge challenge.

[m]Epigenetics—the study of how environmental factors can affect gene expression without altering the actual DNA sequence, and how these changes can be inherited through generations.

HA 09/01/2015

The influence of these inputs on the human organism is indisputable and they are often powerful agents in the battle for health. Ignoring them in favor of the quick fix of writing a prescription means the cause of the underlying dysfunction may be obscured, but is usually not eliminated. In general terms, the environmental inputs listed below should be considered when working to reverse dysfunction or disease and restore health:

- Diet (type and quantity of food, food preparation, calories, fats, proteins, carbohydrates)
- Nutrients (both dietary and supplemental)
- Air
- Water
- Microorganisms (and the general condition of the soil in which food is grown)
- Physical exercise
- Trauma
- Psychosocial and spiritual factors (including family, work, community, economic status, stress, and belief systems)
- Xenobiotics
- Radiation

Fundamental Physiological Processes

There are certain physiological processes that are necessary to life. These are the "upstream" processes that can go awry and create "downstream" dysfunctions that eventually become disease entities. Functional medicine requires that clinicians consider these in evaluating patients, so that intervention can occur at the most fundamental level possible. They are:

1. Communication
   - outside the cell
   - inside the cell
2. Bioenergetics/Energy Transformation
3. Replication/Repair/Maintenance/Structural Integrity
4. Elimination of Waste
5. Protection/Defense
6. Transport/Circulation

Although these fundamental physiological processes are usually taught in the first two years of medical training, where they are appropriately presented as the foundation of modern, scientific patient care, subsequent training in the clinical sciences often fails to fully integrate knowledge of the functional mechanisms of disease with therapeutics and prevention, emphasizing instead teaching/

learning based on organ system diagnosis.[299] Focusing predominantly on organ system diagnosis without examining the underlying physiology that produced the patient's signs, symptoms, and disease often leads to managing patient care by matching diagnosis to pharmacology. The job of the healthcare provider then becomes a technical exercise in finding the drug or procedure that best hits the diagnosis (not necessarily the patient), leading to a significant curtailment of critical thinking pathways: "Medicine, it seems, has little regard for a complete description of how a myriad of pathways result in any clinical state."[299]

Even more important, pharmacologic treatments are often prescribed without careful consideration of their physiological effects across all organ systems and physiological processes (and genetic variations).[300] Pharmaceutical companies have exploited this weakness. Did you ever see a drug ad that urged the practitioner to carefully consider the impact of all other drugs being taken by the patient before prescribing a new one? The marketing of drugs to specific specialty niches, and the use of sound bite sales pitches that suggest discrete effects, skews healthcare thinking toward this narrow, linear logic, as notably exemplified by the COX-2 inhibitor drugs that were so wildly successful on their introduction, only to be subsequently withdrawn or substantially narrowed in use due to collateral damage.[301, 302]

Core Clinical Imbalances

The functional medicine approach to assessment, both before and after diagnosis, charts a course using different navigational assumptions. Every health condition instigates a quest for information centered on understanding when and how the specific biological system(s) under examination spun out of control to begin manifesting dysfunction and/or disease. Analyzing all the elements of the patient's story, the signs and symptoms, and the laboratory assessment through a matrix focused on functionality requires analytic thinking and a willingness on the part of the clinician to reflect deeply on underlying biochemistry and physiology. The foundational principles of how the human organism functions—and how its systems communicate and interact—are essential to the process of linking ideas about multifactorial causation with the perceptible effects we call disease or dysfunction.

To assist clinicians in this process, functional medicine has adapted and organized a set of *core clinical imbalances* that function as the intellectual bridge between the rich basic science literature concerning physiological mechanisms of disease (first two years of medical training) and the clinical studies, clinical experience, and clinical diagnoses of the second two years of medical training. The core clinical imbalances serve to marry the mechanisms of disease with the manifestations and diagnoses of disease. Many common underlying pathways of disease are reflected in a few basic clinical imbalances:

- Immune/inflammatory imbalance
- Energy imbalance/mitochondrial dysfunction
- Digestive/absorptive and microbiological imbalance
- Detoxification/biotransformation/excretory imbalance
- Imbalance in structural, boundary, and membrane integrity

- Hormonal and neurotransmitter imbalances
- Imbalance in mind-body-spirit integration

Using this construct, it becomes much clearer that one disease/condition may have multiple causes (i.e., multiple clinical imbalances), just as one fundamental imbalance may be at the root of many seemingly disparate conditions (see Figure 11).

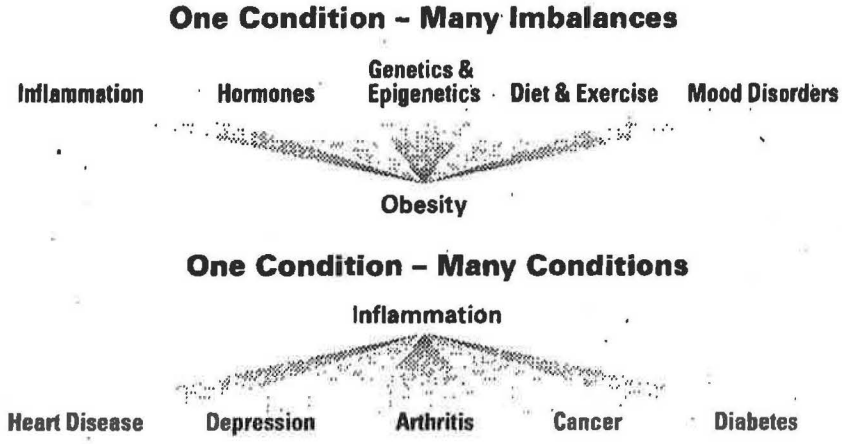


Figure 11:
Core Clinical Imbalances—Multiple Influences

The most important precept to remember about functional medicine is that restoring balance—in the patient's environmental inputs and in the body's fundamental physiological processes—is the key to restoring health.

Constructing the Model

Combining the principles, environmental inputs, fundamental physiological processes, and core clinical imbalances creates a new information-gathering-and-sorting architecture for clinical practice. This new model includes an explicit emphasis on principles and mechanisms that weld meaning and mechanistic explanations to the diagnosis and deepen the clinician's understanding of the often overlapping ways things go wrong. Any methodology for constructing a coherent story and an effective therapeutic plan in the context of complex, chronic illness must be flexible and adaptive. Like an accordion file that can compress and expand upon demand, the amount and kind of data needed will necessarily change in accordance with the patient's situation and the clinician's time and ability to piece together the underlying threads of dysfunction. There are many pathways to illness; therefore, the accordion file must expand to incorporate a much larger database of relevant information. For example, the Chief Complaint, History of Present Illness, and Past Medical History sections must expand to include a thorough investigation of antecedents, triggers, and mediators. Personalized medical care without this expanded investigation will fall short.

Distilling the data from the expanded history, physical exam, and laboratory into a narrative story line that includes antecedents, triggers, and mediators can be challenging. Key to developing a thorough narrative is organizing the story according to the seven common underlying mechanisms that influence health (the core clinical imbalances), as shown on the Functional Medicine Matrix Model™ form (see Figure 12).

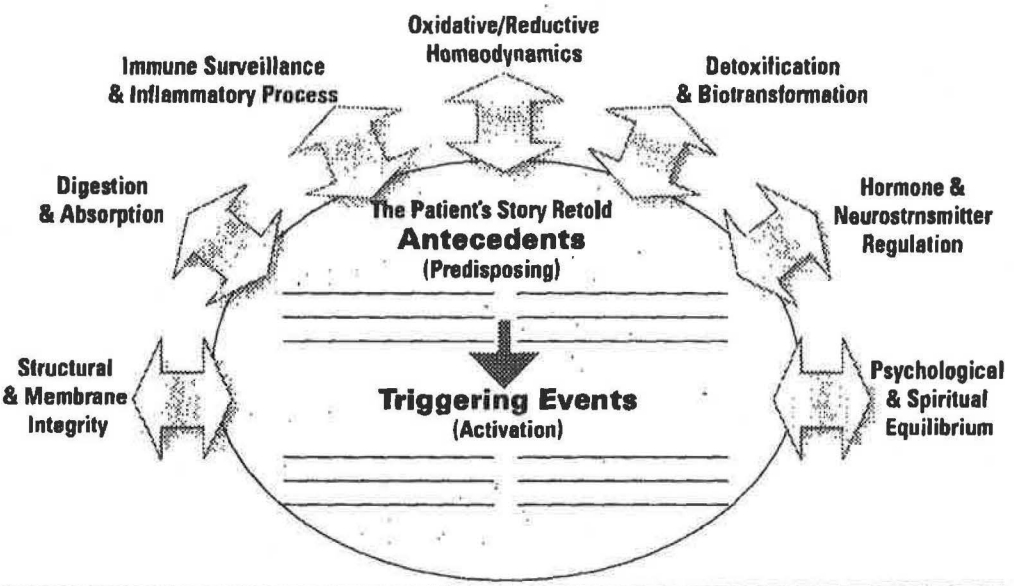


Figure 12:
The Functional Medicine Matrix Model™ form

The Matrix form helps organize and prioritize information, and also clarifies the level of present understanding, thus illuminating where further investigation is needed. For example, indicators of inflammation on the matrix might lead the clinician to request tests for specific inflammatory markers (such as hsCRP, interleukin levels, and/or homocysteine). Essential fatty acid levels, methylation pathway abnormalities, and organic acid metabolites help determine adequacy of dietary and nutrient intakes. Markers of detoxification (glucuronidation and sulfation, cytochrome P450 enzyme heterogeneity) can determine functional capacity for molecular biotransformation. Neurotransmitters and their metabolites (vanilmandelate, homo vanillate, 5-hydroxyindoleacetate, quinolinate) and hormone cascades (gonadal and adrenal) have obvious utility in exploring messenger molecule balance. CT scans, MRIs, or plain x-rays extend our view of the patient's structural dysfunctions. The use of

bone scans, DEXA scans, or bone resorption markers[303, 304] can be useful in further exploring the web-like interactions of the matrix. Newer, useful technologies such as functional MRIs, SPECT or PET scans offer more comprehensive assessment of metabolic function within organ systems. It is the process of completing a comprehensive history and physical and then charting these findings on the matrix that best directs the choice of laboratory work and successful treatment.

A completed Matrix form facilitates the review of common pathways, mechanisms, and mediators of disease, and helps clinicians select points of leverage for treatment strategies. However, even with the matrix as an aid to synthesizing and prioritizing information, it can be very useful to consider the impact of each variable at five different levels:

1. Whole body (the "macro" level)
2. Organ system
3. Metabolic or cellular
4. Subcellular/mitochondrial
5. Subcellular/gene expression

Therapies should be chosen for their potential impact on the most central imbalances of the particular patient. Evaluating interventions that are available at each of the five levels can help to identify a reasonably comprehensive set of options from which to choose. The following lists incorporate only a few examples of various types of interventions within these five different levels.

1. **Whole body interventions:** Because the human organism is a complex adaptive system, with countless points of access, interventions at one level will affect points of activity in other areas as well. For example, improving the patient's sleep will beneficially influence the immune response, melatonin levels, T cell lymphocyte levels, and will help to decrease oxidative stress. Exercise reduces stress, improves insulin sensitivity, and improves detoxification. Reducing stress (and/or improving stress management) can reduce cortisol levels, improve sleep, improve emotional well being, and reduce the risk of heart disease. Changing the diet can have myriad effects on health, from reducing inflammation to reversing coronary artery disease.
2. **Organ system interventions:** These interventions are used more frequently in the acute presentation of illness. Examples include splinting; draining lesions; repairing lacerations; reducing fractures, pneumothoraxes, hernias or obstructions; or removing a stone to re-establish whole organ function. There are many interventions that improve organ function. For example, bronchodilators improve air exchange, thereby decreasing hypoxia, reducing oxidative stress, and improving metabolic function and oxygenation in a patient with reactive airway disease.

3. **Metabolic or cellular interventions:** Cellular health can be addressed by insuring the adequacy of macronutrients, essential amino acids, vitamins, and cofactor minerals in the diet (or, if necessary, from supplementation). An individual's metabolic enzyme polymorphisms can profoundly affect his or her nutrient requirements. For example, adding conjugated linoleic acid (CLA) to the diet can alter the PPAR system, affect body weight, and modulate the inflammatory response.[305, 306, 307] However, in a person who is diabetic or insulin resistant, adding CLA may induce hyperproinsulinemia, which is detrimental.[308, 309] Altering the types and proportions of carbohydrates in the diet may increase insulin sensitivity, reduce insulin secretion, and fundamentally alter metabolism in the insulin-resistant patient. Supporting liver detoxification pathways with supplemental glycine and N-acetylcysteine improves the endogenous production of adequate glutathione, an essential antioxidant in the central nervous system and GI tract.

4. **Subcellular/mitochondrial interventions:** There are many examples of mitochondrial nutrient support interventions.[310, 311] Inadequate iron intake causes oxidants to leak from mitochondria, damaging mitochondrial function and mitochondrial DNA. Making sure there is sufficient iron helps alleviate this problem. Inadequate zinc intake (found in >10% of the U.S. population) causes oxidation and DNA damage in human cells.[312] Insuring the adequacy of antioxidants and cofactors for the at-risk individual must be considered in each part of the matrix. Carnitine, for example, is required as a carrier for the transport of fatty acids from the cytosol into the mitochondria, improving the efficiency of beta oxidation of fatty acids and resultant ATP production. In patients who have had significant weight-carnitine undernutrition can result in fatty acids undergoing omega oxidation, a far less efficient form of metabolism.[313] Patients with low carnitine may also respond to riboflavin supplementation.[314]

5. **Subcellular/gene expression interventions:** Many compounds interact at the gene level to alter cellular response, thereby affecting health and healing. Any intervention that alters NFκB entering the nucleus, binding to DNA, and activating genes that encode inflammatory modulators such as IL-6 (and thus CRP), cyclooxygenase 2, IL-1, lipoxygenase, inducible nitric oxide synthase, TNF-α, or a number of adhesion molecules will impact many disease conditions.[315, 316] There are many ways to alter the environmental triggers for NFκB, including lowering oxidative stress, altering emotional stress, and consuming adequate phytonutrients, antioxidants, alpha-lipoic acid, EPA, DHA, and GLA.[317] Adequate vitamin A allows the appropriate interaction of vitamin A-retinoic acid with over 370 genes.[318] Vitamin D in its most active form intercalates with a retinol protein and the DNA exon and modulates many aspects of metabolism including cell division in both healthy and cancerous breast, colon, prostate, and skin tissue.[319] Vitamin D has key roles in controlling inflammation, calcium homeostasis, bone metabolism, cardiovascular and endocrine physiology, and healing.[320]

Experience using this model, along with improved pattern-recognition skills, will often lessen the need for extensive laboratory assessments. There will always be, however, certain clinical conundrums that simply cannot be assessed without objective data and, for most patients, there may be an irreducible minimum of laboratory assessments required to accumulate information. For example, in the clinical workup of attention spectrum disorders in children, heavy metal exposure and toxicity may play an important role. Heavy metal body burden cannot be sensibly assessed without

laboratory studies. Another example is in the context of the progressive, ongoing workup. When clinical acumen and educated steps in both assessments and therapeutic trials do not yield expected improvement, lab testing often provides rewarding information when focused on the unexpected outcomes in the progressive workup. This is frequently the context for focused genomic testing. In most initial workups, lab and imaging technologies can be reserved for those complex cases where the initial interventions prove insufficient to the task of functional explication.

Even using the functional medicine model that has been reviewed here, no single practitioner—and no single discipline—can cover all the viable therapeutic options. Interventions will differ by training, licensure, specialty focus, and even by beliefs and ethnic heritage. However, all healthcare disciplines (and all medical specialties) can—to the degree allowed by their training and licensure—use a functional medicine approach, including integrating the matrix as a basic template for organizing and coupling knowledge and data. So, functional medicine can provide a common language and a unified model to facilitate integrated care. Regardless of what discipline the primary care provider has been trained in, developing a network of capable, collaborative clinicians with whom to co-manage challenging patients and to whom referrals can be made for therapies outside the primary clinician's own expertise will enrich patient care and strengthen the clinician-patient relationship.

Part II: The Healing Partnership— A Synthesis of the Art and Science of Medical Practice

We form partnerships to achieve an objective. For example, a business partnership forms to engage in commercial transactions for financial gain; a marriage partnership forms to build a caring, supportive home-centered environment. A *healing partnership* forms to heal the patient through the integrated application of both the art of medicine (insight driven) and the science of medicine (evidence driven). An effective partnership requires that trust and rapport be established. Patients must feel comfortable telling their stories and revealing intimate information and significant events.

The characteristics of a *therapeutic encounter* are fundamentally different from a *healing partnership*, and each emerges from specific emphases in training. In the therapeutic encounter, the relationship forms to assess and treat a medical problem using (usually) an organ system structure, a differential diagnosis process, and a treatment toolbox focused on pharmacology and medical procedures. The therapeutic encounter pares down the information flow between physician and patient to the minimum needed to identify the organ system domain of most probable dysfunction, followed by a sorting system search (the *differential diagnosis heuristic*). The purpose of this relationship is to arrive at the most probable diagnosis as quickly as possible and select an intervention based on probable efficacy. The relationship is a left brain-guided conversation controlled by the clinician, steeped in Bayesian statistics (EBM), and characterized by algorithmic processing and statistical thinking.[321, 322]

The functional medicine *healing partnership* forms with a related but broader purpose: to help the patient heal by identifying the underlying mechanisms and influences that initiated and continue to mediate the patient's illness(es). This type of relationship emphasizes a shared responsibility for both identifying the causes of the patient's condition and achieving insight about enduring solutions. The healing partnership is critical to the delivery of *personalized, systems medicine*, and to manage the uncertainty (choices

under risk inherent in clinical practice. Here, in the healing partnership, we find the appropriate utilization and integration of left-brain and right-brain functions.

Germane to this discussion, Dr. Jerome Groopman—quoted previously in Chapter 4—states:

> So a thinking doctor returns to language: "Tell me the story again as if I'd never heard it—what you felt, how it happened, when it happened."[323]

In language, we have the fullest expression of the integration of left- and right-brain function. Language is so complex that the brain has to process it in different ways simultaneously—both denotatively and connotatively. For complexity and nuance to emerge in language, we need the left brain to see the trees, the right brain to help us see and understand the forest.[324, 325]

To grasp the profound importance of the *healing partnership* to the creation of a system of medicine adequate to the demands of the 21st century, we need to briefly address the nature of healing and its role in the therapeutic relationship. We have noted an emerging body of research in this area.[326, 327, 328] As Louise Acheson, MD, MS, Associate Editor for the *Annals of Family Practice*, articulated recently in that journal :

> It is challenging to research this ineffable process called healing.... Hsu and colleagues asked focus groups of nurses, physicians, medical assistants, and randomly selected patients to define healing and describe what facilitates or impedes it.[330] The groups arrived at surprisingly convergent definitions: "Healing is a dynamic process of recovering from a trauma or illness by working toward realistic goals, restoring function, and regaining a personal sense of balance and peace." They heard from diverse participants that "healing is a journey" and "relationships are essential to healing."

In the 20th century, contemporary medicine, traditionally considered a healing profession, evolved away from the role of *healer of the sick* to that of *curing disease through modern science.* Research into this transition reveals that healing was/is associated with themes of wholeness, narrative, and spirituality. Professionals and patients alike report healing as an intensely personal, subjective experience involving a reconciliation of meaning for an individual and a perception of wholeness. The biomedical model as currently configured no longer encompasses these traditional characteristics for practitioners. Healing in a holistic sense has faded from medical attention and is rarely discussed in biomedical research reports. Contemporary medicine considers the wholeness of healing to be beyond its orthodoxy—the domain of the nonscientific and nonmedical.[331]

Research into the role of healing in the medical environment has recently generated some thoughtful and robust investigations. John Scott and his co-investigators' research into the healing relationship found very similar descriptions to those of Hsu's group, mentioned above. The participants in the study[332] articulated aspects of the healing partnership as:

1. Valuing and creating a nonjudgmental emotional bond
2. Appreciating power and consciously managing clinician power in ways that would most benefit the patient
3. Abiding and displaying a commitment to caring for patients over time

Three relational outcomes result from these processes: trust, hope, and a sense of being known. Clinician competencies that facilitate these processes are self-confidence, emotional self-management, mindfulness, and knowledge.[333] In this rich soil, the healing partnership flourishes.

The starting point for creating a healing partnership is the patient's experience: *People, not diseases, can heal.* The integration of brain science research discussed in Chapter 4—to frame and apply right- and left-brain functions to create a *mindful, insightful* context—enhances the healing partnership during the therapeutic encounter. Mindful integration of brain function is at the heart of a healing partnership. Some of the basic steps for establishing a healing partnership include:

1. Allow patients to express, without interruption,[xxi] their story about why they have come to see you. (This is an elaboration of the Chief Complaint and Present Illness.) The manner in which the patient frames the initial complaints often presages later insight into the root causes. Any interruption in this early stage of narrative moves the patient back into left-brain processing and away from insight.[334]
2. After focusing on the main complaint, encourage the patient's narrative regarding their present illness(es). Clarifications can be elicited by further open-ended questioning (e.g., "tell me more about that"; "what else do you think might be going on?"). During this portion of the interview, there is a switching back and forth between right- and left-brain functions.
   - During this conversation, signs and symptoms of the present illness are distributed by the practitioner into the Functional Medicine Matrix Model form, according to the functional medicine heuristic sorting system described in Chapter 4.
   - The parsing is determined by an assessment of probable underlying causes—based on the robust research evidence base about common underlying mechanisms of disease—and ongoing mediators of the disease.
3. Next, convey to the patient in the simplest terms possible that to achieve lasting solutions to the problem(s) for which he/she has come seeking help, a few fundamental questions must be asked and answered in order to understand the problem in the context of the patient's personal life. This framing of the interview process moves the endeavor from a left-brain compilation to a narrative that encourages insight—based on complex pattern recognition—about the root causes of the problem.
4. Explaining the structure of the next step helps the patient participate in a journey of exploration about their illness—and their search for health. At this stage, partial control is handed over to the patient with the statement: *"Without your help, we cannot understand your medical problem in the depth and breadth you deserve."* Leo Galland, MD originally articulated the structure for the patient's part of the investigation in his antecedents/triggers/mediators schema (ATM model).[335] (An excerpt from his outstanding chapter on this topic in the *Textbook of Functional Medicine* is included in the Appendix.)

[xxi] Research focused on the therapeutic encounter has repeatedly found that clinicians interrupt the patient's flow of conversation within the first 18 seconds or less, often denying the patient an opportunity to finish. (Beckman DB, et al. The effect of physician behavior on the collection of data. Ann Intern Med. 1984;101:692-96.)

a) For determining **antecedent conditions**, the following questions are very useful:

- When was the present problem not a problem? When were you free of this problem?
- What were the circumstances surrounding the appearance of the problem?
- Have similar problems appeared in family members?

b) For **triggers**, the following question is critical:

- What conditions, activities, or events seemed to initiate the problem? (Microbes and stressful personal events are examples, but illustrate quite different categories of triggers. Triggers by themselves are usually insufficient for disease formation, so triggers must be viewed within the context of the antecedent conditions.)

c) **Mediators** of the problem are influences that help perpetuate it.

- There can be specific mediators of disease in the patient's activities, lifestyle, and environment. Many diverse factors can affect the host's response to stressors.
- Any of the core clinical imbalances, discussed above and shown on the Functional Medicine Matrix Model, can transform what might have been a temporary change in homeostasis into a chronic allostatic condition.

It helps at this juncture to emphasize again that the following issues are elemental in forming a healing partnership:

- Only the patient can inform the partnership about the conditions that provided the soil from which the problem(s) under examination emerge(s). The patient literally owns the keys to the joint deliberation that can provide insight about the process of achieving a healing outcome.
- The professional brings experience, wisdom, tools, and techniques that can be applied to the journey of healing. The professional also works to create the context for a healing insight to emerge.
- The patient's information, input, mindful pursuit of insight, and engagement become "the horse before the cart." The cart carries the clinician—the person who guides the journey using evidence, experience, and judgment, and who contributes the potential for expert insight.

The crux of the healing partnership is an equal investment of focus by both clinician and patient. They work together to identify the right places to apply leverage for change. Patients must commit to engage both their left-brain skills and their right-brain function to inform and guide the exploration to the next steps in assessment, therapy, understanding, and insight. Clinicians must also engage both the left-brain computational skills and the right-brain pattern-recognition functions that, when used together, can generate insight about the patient's story.

Two patient case studies (presented below) provide a glimpse into a functional medicine practice and the healing partnership that is necessary for success. The Appendix contains a form developed by IFM faculty for enhancing the pattern-recognition process in ulcerative colitis.

Patient #1: Kikuchi syndrome in an 18 year old female—insight from the healing partnership

Lila was an 18-year-old female transitioning from high school to college, who during the intervening summer experienced rapid onset of unexplained fever, profound fatigue, and lymphadenitis, especially pronounced in the cervical region. Her extended family included physicians, one who lived locally and led the initial investigation. The differential included lymphoma; because of the seriousness of this possible diagnosis, a biopsy of the enlarged cervical lymph nodes was completed expeditiously. Fortunately, the biopsy was more consistent with Kikuchi syndrome than lymphoma. The pathology of Kikuchi is a histocytic necrotizing lymphadenitis. Her ANA was positive at 1:320, speckled. Kikuchi syndrome is presumed to be an immune response of T cells and histiocytes to an infectious agent, probably viral. At this point, I was asked to consult with the patient and her parents.

The patient was articulate, intelligent (she had been accepted to Harvard), and appeared recovered from the acute phase of her illness. Her father and mother were both present during the consultation. Lila was asked to narrate her story. During the telling of her story, I sorted her symptoms and signs using the FM Heuristic (Chapter 4) and the Functional Medicine Matrix Model (discussed above). At the end of recounting of her story, I explained to her and her parents the functional medicine sorting system, postulating that what we now knew from the history, lab results, and the biopsy was that Lila's immune system had probably been activated by a triggering agent (e.g., microbe, toxicant). I explained that our job now required forming a partnership, using Lila's and her parents' experiences through this episode of illness and my experience with immune-mediated illnesses to build a hypothetical story together.

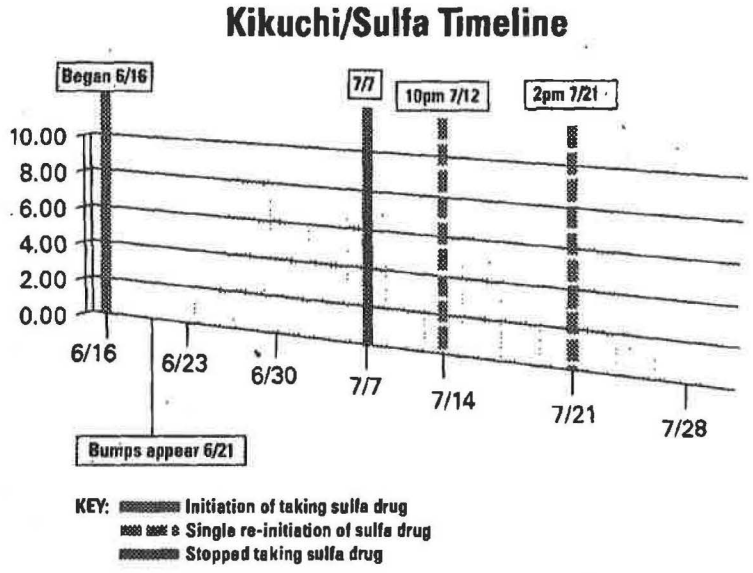
I further explained that we would need to consider the conditions in Lila's family and "habits of living" history that could be antecedent to her illness. I explained that we would then move to the possible triggers in her recent past that might be causal or correlative in the acute expression of her illness. I explained that once an acceptable model emerged from our joint inquiry into the antecedents and triggers of her present illness, we would evaluate the possible probes that might elicit further information or generate treatment plans. They agreed to work together with me using this partnering model.

They were not aware of any exceptional family history of autoimmune or other immune dys-regulatory illnesses. The family's lifestyle, including eating and exercise habits, was laudable. We next addressed the issues of triggers. We knew from reading research sources on Kikuchi syndrome that the most common cause of the lymphadenitis associated with the syndrome was a microbe trigger. The parents were hopeful that we could perform lab analyses for a host of potential viral agents. Lila interrupted her parents at this point to advocate for quite a different possible cause.

Lila recounted that she had been seen in the regional dermatologic referral center for her worsening *acne vulgaris*. The treatment recommended by the consulting dermatologist was a sulfa-containing antibiotic. Before coming for consultation in my clinic, Lila had posited to her dermatologist and her primary care physician that her lymphadenitis was an adverse drug reaction. She and her parents had been told that the severity of her illness, if caused by a drug reaction, would necessarily be accompanied by a rash; she, however, was absent a rash. She had been advised to continue her antibiotic. Her parents retreated from this inquiry in the face of the authoritative disclaimer by both the specialist and the family doctor.

However, Lila did not retreat from her insight. We discussed her intuition (insight) and her reasoning. On the basis of her hypothesis, we jointly finalized a plan that included abstinence from her antibiotic. I advised against a planned back-packing trip to Mexico because of possible toxicant exposures in that environment that might confound her clinical story. We chose to call this a therapeutic probe with my added advice regarding follow-up. (We planned a low allergy diet and detoxification program IF the simple step of removing the triggering agent proved to be an insufficient intervention.)

That evening, I received an email from Lila with the following graph of her illness:



Outcome: Lila has been asymptomatic following continued abstinence from the sulfa-containing antibiotic. She has started her first semester at Harvard. The student health center physician became very interested in her story and has provided regular follow up, including lab. Her ANA titer has slowly returned to normal. No further interventions have been required. She has sought non-pharmacologic treatment interventions for her acne.

Patient #2: Ulcerative Colitis in a 45 year old female—providing a context for insight

The next case illustrates the use of this same model: the pursuit of an antecedent and/or initial trigger for illness (these categories often overlap considerably)—that is, we looked for causes underneath the surface explanations for her condition. This 45-year-old female presented at my office for IBS and diverticulitis with a recent history of hemicolectomy for infectious colitis. The patient's primary residual postsurgical complaints were diffuse abdominal pain and loose stooling alternating with constipation. The review of her present illness revealed a history since her mid-twenties of "gut problems" (her words), including intermittent loose stools with alternating constipation. She had also over the years become intolerant of a plethora of foods. As a result, she had received thorough work-ups for food allergies and intolerances and was trying to follow a rather patchwork diet plan in response to these previous lab evaluations. She had received imaging and endoscopic procedures. However, she had not had follow-up colonoscopy since her surgery. We discussed the need to do follow-up endoscopy to evaluate her present symptoms (to rule out possible post-surgical adhesions complicating stool passage).

The conversation soon shifted into the ATM (antecedents, triggers, and mediators) portion of the investigation. After describing the joint responsibilities for a deeper understanding (insight) regarding her GI maladies, we moved to the questions regarding antecedents for her condition. She denied any family history of similar GI illnesses in her siblings. I then asked the question: *"When was the present problem not a problem? That is, when were you free of the problem and what were the circumstances of the problem's first appearance?"*

At this point, our conversation stopped. She looked a bit flummoxed and asked to consider the question further and more fully answer it when she next returned. At her next appointment, she returned to the question, stating that she wanted to share an experience that preceded her first episode of GI irritability. She said that she had not shared this story with any physician before in the context of the clinical workups for her GI problems. She then told the following story:

> I left home at an early age to escape my father. He sexually abused me and my sisters. There did not seem to be any way to stop him; my mother seemed powerless, even when she walked into an abusive episode. In desperation, I left my sisters and my family, married and moved away.
>
> My mother called me one afternoon, years after my leaving home. By that time I was a mother myself, having married and started my own family. My mother was quite upset and related that one of my sisters had arrived at her door, confronting her with the accusation of my father's sexual abuse of her in childhood and the lack of protection by our mother. My mother was adamant in her denial of knowledge of such wrongdoing by my father (my father had died in the intervening years since my leaving home).
>
> I was silent for a moment on the phone with my mother. I then made a choice to placate my mother; I responded to her distress with a lie: "Mother, you know how my sister is; she is so hysterical."

> My response seemed to settle my mother down. However, now that you have asked, this was the beginning of my gut problems. I stuffed that lie about our childhood with our father deep down into my gut and my gut has not been normal since.

Outcome: My patient's therapy for her GI problems has been guided by both this insight regarding the origins of her illness as well as by my professional expertise in the area of both mind-body connections and GI physiology. Her therapeutic interventions focused on the 4R functional medicine approach to GI dysfunctions[336] and EMDR psychotherapeutic modalities developed for PTSD[337] (an approach that has emerged from work with returning GIs from the Gulf War and the Afghanistan and Iran conflicts). She now reports no further problems referable to her GI tract.

Our healing partnership helped elicit the insights that focused our attention on a fundamental issue that was critical to her healing. Without the supportive, mindful context that encouraged her insight to emerge, we would not have had the comprehensive patient story that was necessary for resolution of her problems. In this journey together, both left-brain computation (clinical and scientific evidence about the importance of the 4R GI dysfunction program and EMDR therapy in the context of PTSD) and right-brain functionality (a context for insight) were necessary.

As described in Chapter 4, insight researchers call this "aha" experience the *moment of categorical insight.* The epiphany registers as a new pattern of neural activity in the prefrontal cortex. The brain cells have been altered by the breakthrough. An insight is a restructuring of information—it's seeing something in a completely new way. Once that restructuring occurs, you never go back.[338]

Summary

At The Institute for Functional Medicine (IFM) we believe that functional medicine exemplifies a systems-oriented, personalized medicine that recognizes the common underlying mechanisms of complex and chronic diseases that cut across multiple organ systems to shape a patient's trajectory toward health or disease. IFM's model of comprehensive care and primary prevention for complex, chronic illnesses is grounded in both science (the Functional Medicine Matrix Model™; evidence about common underlying mechanisms and pathways of disease; evidence about effective approaches to the environmental and lifestyle sources of disease) and art (the *healing partnership* and the search for insight in the therapeutic encounter). We have shown how this approach offers both a conceptual model and pragmatic tools that help to integrate the best of emerging models in both conventional and integrative medicine. When practiced with an explicit emphasis on the importance of pattern-recognition and heuristic competencies inherent to right-brain function, a healing partnership can flourish, insight can be achieved, and a broad array of assessment and therapeutic tools can be utilized. We can produce a *mindful* medical practice paradigm shift that can encompass the uniqueness of each person, deriving probabilities that are clinically meaningful.

As articulated in Gerd Gigerenzer's thoughtful book, *Rationality for Mortals: How People Cope with Uncertainty,* heuristic processing (right brain) and statistical thinking (left brain) are "complementary mental tools, not mutually exclusive strategies; our minds need both."[19] Through this uniting of competencies, we can incorporate the strengths of both science and art to craft an effective, personalized, and integrative approach to patient care. Without both elements steadily at work, we will find it exceptionally difficult to address successfully the epidemic of chronic disease that is the challenge of 21st century medicine.

References

[1] Walter Freeman How Brains Make Up Their Minds. 2000. Columbia University Press

[2] Peter Dayan, L. F. Abbott. Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems. The MIT Press, 2005.

[3] Roland Baddeley (Editor), Peter Hancock (Editor), Peter Foldiák (Editor). Information Theory and the Brain. Cambridge University Press. 2008.

[4] Eric R Kandel In Search of Memory: The Emergence of a New Science of Mind, W. W Norton; 2007.

[5] Roberto Cabeza (Editor), Alan Kingstone (Editor). Handbook of Functional Neuroimaging of Cognition The MIT Press, 2 edition, 2006.

[6] Henry P. Stapp. Mindful Universe: Quantum Mechanics and the Participating Observer (The Frontiers Collection) Springer, 1 edition 2007

[7] http://www.ted.com/index.php/talks/jill_bolte_taylor_s_powerful_stroke_of_insight.html (1/1/09)

[8] Jill Bolte Taylor. My Stroke of Insight. Viking. Penguin Group. New York. 2006

[9] Snyderman R, Williams RS. Prospective medicine. The next health care transformation. Acad Med. 2003;78:1079-84.

[10] Partnership for Solutions. Chronic Conditions: Making the Case for Ongoing Care. A Project of Johns Hopkins University and The Robert Wood Johnson Foundation. September 2004. Available at http://www.partnershipforsolutions.org/DMS/files/chronicbook2004.pdf.

[11] American College of Physicians. The impending collapse of primary care medicine and its implications for the state of the nation's health care. A report from the American College of Physicians, January 30, 2006. Available at http://www.acponline.org/advocacy/events/state_of_healthcare/statehc06_1.pdf.

[12] Thorpe KE. The rise in health care spending and what to do about it. Health Aff. 2005;24(6):1436-45

[13] Groopman J. How Doctors Think. Houghton Mifflin: New York, 2007-2008. Pp. 151-155.

[14] Johns MME, Brigham KL. Transforming health care through prospective medicine: The first step. Acad Med. 2008;83(8):706.

[15] McKinnon RA, Ward MB, Sorich MJ. A critical analysis of barriers to the clinical implementation of pharmacogenomics. Ther Clin Risk Manag. 2007;3(5):751-9.

[16] Issa AM. Personalized medicine and the practice of medicine in the 21st century. McGill J Med. 2007 10(1):53-57

[17] Swen JJ, Huizinga TW, Gelderblom H, et al. Translating pharmacogenomics: challenges on the road to the clinic. PLoS Medicine. August 2007 | Volume 4 | Issue 8 | e209

[18] Snyderman R, Williams RS. Prospective medicine: The next health care transformation. Acad Med. 2003;78:1079-84.

[19] Snyderman R, Langheier J. Prospective health care: the second transformation of medicine. Genome Biol. 2006,7(2):104.1-104.8.

[20] Syderman R, Yoediono Z. Prospective health care and the role of academic medicine: Lead, follow, or get out of the way. Acad Med. 2008;83(8):707-714.

[21] Johns MME, Brigham KL. Transforming health care through prospective medicine: The first step. Acad Med. 2008;83(8):706.

[22] Wagner EH, Austin BT, Davis C, et al. Improving chronic illness care: translating evidence into action. Health Affairs. 2001;20(6):64-78.

[23] Mutch DM, Wahli W, Williamson G. Nutrigenomics and nutrigenetics: the emerging faces of nutrition. FASEB J. 2005;19:1602-16

[24] Montgomery K. How Doctors Think: Clinical Judgment and the Practice of Medicine. Oxford University Press. New York, NY. 2006 Ch 2.

[25] Groopman J. How Doctors Think. Houghton Mifflin: New York, 2007-2008. Pp. 236-239

[26] Montgomery K. How Doctors Think: Clinical Judgment and the Practice of Medicine. Oxford University Press. New York, NY, 2006. P. 90.

[27] http://www.imconsortium.org/

[28] Racaniello VR. Emerging infectious disease. J Clin Investigation, 2004,113(6).796-8.

[29] Johns MME, Brigham KL. Transforming health care through prospective medicine: The first step. Acad Med. 2008;83(8):706.

[30] Ely JW, Osheroff JA, Gorman PN, et al. A taxonomy of generic clinical questions: classification study. BMJ. 2000;321:429-32.

[31] Holman H. Chronic disease—The need for a new clinical education JAMA. 2004;292(9).1057-1059.

[32] American College of Physicians. The Impending Collapse of Primary Care Medicine and its Implications for the State of the Nation's Health Care: A Report from the American College of Physicians. January 30. 2006

[33] Overholt A. Health and the profit motive. FastCompany.com. Accessed at http://www.fastcompany.com/node/46025/print

[34] Bodenheimer T. Uneasy alliance: Clinical investigators and the pharmaceutical industry. N Engl J Med. 2000,342(20):1539-44.

[35] Fiscella K, Stocker D. The commercialization of clinical research: who pays the piper, calls the tune? Fam Pract. 2004;21:335-6.

[36] Angell M. Is academic medicine for sale? N Engl J Med 2000;342(20):1516-18

[37] Ross LF, Norton JW, Young SA, et al. Is academic medicine for sale? Letters responding to Angell's editorial of that title. N Engl J Med 2000;343(7).508-10.

[38] Bodenheimer T. Uneasy alliance: Clinical investigators and the pharmaceutical industry. N Engl J Med. 2000;342(20).1539-44

[39] Kramarow E, Lubitz J, Lentzner H, Gorina Y. Trends in the health of older Americans, 1970-2005. Health Affairs. 2007;25(5).1417-25.

[40] Gregg EW, Cheng YJ, Cadwell BL, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005;293(15).1868-74Gregg EW, Cheng YJ, Cadwell BL, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005,293(15):1868-74.

[41] _____The high cost of health care (editorial). The New York Times, November 25, 2007. Accessed at http://www.nytimes.com/2007/11/25/opinion/25sun1.html

[42] Ely JW, Osheroff JA, Gorman PN, et al. A taxonomy of generic clinical questions: classification study. BMJ. 2000;321:429-32.

[43] Thorpe KE, Florence CS, Howard H, Joski P. The rising prevalence of treated disease: effects on private health insurance spending. Health Affairs, Web exclusive, June 27, 2005.

[44] _____The high cost of health care (editorial). The New York Times, November 25, 2007. Accessed at http://www.nytimes.com/2007/11/25/opinion/25sun1.html.

[45] Strunk BC, Ginsburg PB, Gabel JR. Tracking health care costs: hospital care surpasses drugs as they key cost driver. Health Affairs. Web exclusive, September 26, 2001.

[46] Lichtenberg FR. Are the benefits of newer drugs worth their cost? Evidence from the 1996 MEPS. Health Affairs. 2001;20(5):241-51.

[47] Appleby J. Prices for some drugs skyrocket. USA Today, August 7, 2008. Accessed at http://www.usatoday.com/money/industries/health/drugs/2008-08-07-costlydrugs_N.htm

[48] Thorpe KE, Florence CS, Joski P. Which medical conditions account for the rise in health care spending? Health Affairs, Web exclusive, August 25, 2004

[49] Thorpe KE, Florence CS, Howard H, Joski P. The rising prevalence of treated disease: effects on private health insurance spending. Health Affairs, Web exclusive, June 27, 2005.

[50] DeVol R, Bedroussian A. An Unhealthy America: The Economic Burden of Chronic Disease. The Milken Institute, October 2007.

[51] Dr. Gerard Anderson, Partnership for Solutions, "Medicare and Medicaid Are Programs for People with Chronic Illness ... But Do Not Know It," presentation to General Accounting Office, February 5, 2004; Partnership for Solutions, *Chronic Conditions: Making the Case for Ongoing Care*, December 2002; Medicare spending data from U.S. Department of Health and Human Services

[52] Bureau of Labor Education, University of Maine. The U.S. Health Care System: Best in the world, or just the most expensive? Summer, 2001.

[53] The Commonwealth Fund Commission on a High Performance Health System. Why Not the Best? Results from the national scorecard on U.S. health system performance, July 2008.

[54] Morrissey S, Curfman GD, Drazen JM. Health of the nation—coverage for all Americans. N Engl J Med. 2008;359(8),855-6.

[55] The Commonwealth Fund Commission on a High Performance Health System. Why Not the Best? Results from the national scorecard on U.S. health system performance, July 2008.

[56] Willett WC. Balancing life-style and genomics research for disease prevention. Science 2002; 296:695-97

[57] Thorpe KE, Florence CS, Howard H, Joski P. The rising prevalence of treated disease: effects on private health insurance spending. Health Affairs, Web exclusive, June 27, 2005.

[58] Heaney RP. Long-latency deficiency disease: insights from calcium and vitamin D. Am J Clin Nutr 2003;78:912-9.

[59] Racaniello VR. Emerging infectious disease. J Clin Investigation, 2004;113(6):796-8

[60] Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998;279:1200-5.

[61] Sorensen JM. Herb-drug, food-drug, nutrient-drug, and drug-drug interactions: mechanisms involved and their medical implications. J Altern Complement Med. 2002 Jun,8(3):293-308.

[62] Huang CF, Lin SS, Liao PH, et al. The immunopharmaceutical effects and mechanisms of herb medicine. Cell Mol Immunol. 2008;5(1):23-31.

[63] Sorensen JM. Herb-drug, food-drug, nutrient-drug, and drug-drug interactions: mechanisms involved and their medical implications. J Altern Complement Med. 2002 Jun,8(3):293-308.

[64] Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998;279:1200-5.

[65] The Commonwealth Fund Commission on a High Performance Health System. Why Not the Best? Results from the national scorecard on U.S. health system performance, July 2008.

[66] Zetin M, Hoepner CT, Bjornson L. Rational antidepressant selection: Applying evidence-based medicine to complex real-world patients. Psychopharmacol Bull. 2006,39.38-104.

[67] Hordijk-Trion M, Lenzen M, Wijns W, Peter de Jaegere P, et al. Patients enrolled in coronary intervention trials are not representative of patients in clinical practice: results from the Euro Heart Survey on Coronary Revascularization. Eur Heart J. 2006;27.671-8.

[68] Mengis C, Aebi S, Tobler A, Dahler W, Fey MF. Assessment of differences in patient populations selected for or excluded from participation in phase III acute myelogenous leukemia trials. J Clin Oncology. 2003;21(21):3933-9

[69] Hedaya R, Quinn S. Depression: Advancing the Treatment Paradigm. The Institute for Functional Medicine; Gig Harbor, WA: 2008.

[70] Jones DS. Changing the evidence model. Chapter 5 in Textbook of Functional Medicine (DS Jones, ed) The Institute for Functional Medicine, Gig Harbor, WA: 2005

[71] Ramos RG, Olden K. Gene-environment interactions in the development of complex disease phenotypes. Int J Environ Res Public Health. 2008,5(1):4-11

[72] Lakdawalla DN, Goldman DP, Shang B. The health and cost consequences of obesity among the future elderly. Health Affairs, September 26, 2005 (Web exclusive)

[73] Kumanyika SK, Obarzanek E, Stettler N, Bell R, et al. Population-based prevention of obesity: The need for comprehensive promotion of healthful eating, physical activity, and energy balance. Circulation. 2008;118 428-64

[74] Kivimaki M, Virtanen M, Elovainio M, Kouvonen A, Vaananen A, Vahtera J. Work stress in the etiology of coronary heart disease--a meta-analysis. Scand J Work Environ Health. 2006 Dec;32(6).431-42

[75] Gareau MG, Silva MA, Perdue MH. Pathophysiological mechanisms of stress-induced intestinal damage. Curr Mol Med. 2008 Jun;8(4):274-81

[76] Logan JG, Barksdale DJ. Allostasis and allostatic load: expanding the discourse on stress and cardiovascular disease. J Clin Nurs. 2008 Apr;17(7B).201-8

[77] Lakdawalla DN, Goldman DP, Shang B. The health and cost consequences of obesity among the future elderly. Health Affairs, September 26, 2005 (Web exclusive).

[78] Hedaya RJ. Stress, spirituality, poverty and community—effects on health. Chapter 33 in Jones DS (Ed), Textbook of Functional Medicine. The Institute for Functional Medicine, Gig Harbor, WA: 2005

[79] The Commonwealth Fund Commission on a High Performance Health System. Why Not the Best? Results from the national scorecard on U.S. health system performance, July 2008.

[80] Bureau of Labor Education, University of Maine. The U.S. Health Care System. Best in the world, or just the most expensive? Summer, 2001.

[81] Armstrong GL, Conn LA, Pinner RW. Trends in infectious disease mortality in the United States during the 20th century. JAMA 1999,281(1):61-6

[82] Ten great public health achievements—United States, 1900-1999. Morbidity and Mortality Weekly Report, April 2, 1999,48(12).

[83] Centers for Disease Control. Leading causes of death, 1900-1998. Accessed at http://www.cdc.gov/nchs/data/dvs/lead1900_98.pdf.

[84] Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005;293(15):1868-74.

[85] Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005;293(15):1868-74

[86] Kramarow E, Lubitz J, Lentzner H, Gorina Y. Trends in the health of older Americans, 1970-2005. Health Affairs. 2007,26(5):1417-25.

[87] Thorpe KE, Florence CS, Howard H, Joski P. The rising prevalence of treated disease: effects on private health insurance spending. Health Affairs, Web exclusive, June 27, 2005.

[88] Froguel P, Blakemore AI. The power of the extreme in elucidating obesity. N Engl J Med. 2008;359(9):891-3.

[89] Lakdawalla DN, Goldman DP, Shang B. The health and cost consequences of obesity among the future elderly. Health Affairs, September 26, 2005 (Web exclusive).

[90] Olshansky SJ, Passaro DJ, Hershow RC, Layden J, et al. A potential decline in life expectancy in the United States in the 21st century. NEJM. 2005,352(11):1138-45.

[91] Lakdawalla DN, Goldman DP, Shang B. The health and cost consequences of obesity among the future elderly. Health Affairs, September 26, 2005 (Web exclusive).

[92] Olshansky SJ, Passaro DJ, Hershow RC, Layden J, et al. A potential decline in life expectancy in the United States in the 21st century. NEJM. 2005;352(11):1138-45

[93] Kumanyika SK, Obarzanek E, Stettler N, Bell R, et al. Population-based prevention of obesity. The need for comprehensive promotion of healthful eating, physical activity, and energy balance. Circulation. 2008;118:428-64.

[94] Bibbins-Domingo K, Coxson P, Pletcher MJ, et al. Adolescent overweight and future adult coronary heart disease. N Engl J Med 2007;357(23):2371-9.

[95] Caballero B, Wang Y Commentary: Obesity and mortality—light at the end but still a long tunnel. Int J Epidemiol. 2006;35 21-22.

[96] Kumanyika SK, Obarzanek E, Stettler N, Bell R, et al. Population-based prevention of obesity. The need for comprehensive promotion of healthful eating, physical activity, and energy balance. Circulation 2008,118:428-64.

[97] Prentice RL, Willett WC, Greenwald P, et al Nutrition and physical activity and chronic disease prevention: research strategies and recommendations. J Natl Canc Inst. 2004;96(17).1276-87.

[98] Horton R. Commentary: The new new public health of risk and radical engagement Lancet. 1998;352(9124):251-52.

[99] Hedaya R, Quinn S. Depression: Advancing the Treatment Paradigm. A Functional Medicine Monograph The Institute for Functional Medicine: Gig Harbor, WA, 2008

[100] Zahran HS, Kobau R, Moriarty DG, Zack MM, et al. Health-Related Quality of Life Surveillance—United States, 1993-2002. MMWR Surveillance Summaries. October 28, 2005;54(SS04);1-35. Accessed at http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5404a1.htm.

[101] CBS Evening News. The Sandwich Generation May 8, 2006.

[102] Holman H. Chronic disease—The need for a new clinical education. JAMA. 2004;292(9):1057-1059.

[103] Chassin MR, Galvin RW. The urgent need to improve health care quality. Institute of Medicine National Roundtable on Health Care Quality JAMA. 1998;280(11),1000-05

[104] Institute of Medicine Committee on Quality of Health Care in America. Crossing the Quality Chasm: A New Health System for the 21st Century. National Academy Press. Washington, DC, 2001

[105] Issa AM. Personalized medicine and the practice of medicine in the 21st century. McGill J Med. 2007 10(1):53-57.

[106] Jorgensen JT. From blockbuster medicine to personalized medicine. Personalized Med 2008;5(1):55-63.

[107] Issa AM. Personalized medicine and the practice of medicine in the 21st century. McGill J Med. 2007 10(1):53-57.

[108] Jorgensen JT. From blockbuster medicine to personalized medicine. Personalized Med. 2008,5(1):55-63.

[109] Dinh P, de Azambuja E, Cardoso F, Piccart-Gebhart MJ. Facts and controversies in the use of trastuzumab in the adjuvant setting Nat Clin Pract Oncol 2008 Sep 9. [Epub ahead of print]

[110] Issa AM. Personalized medicine and the practice of medicine in the 21st century. McGill J Med. 2007 10(1):53-57.

[111] Dendukuri N, Khetani K, McIsaac M, Brophy J. Testing for HER2-positive breast cancer: a systematic review and cost-effectiveness analysis. CMAJ. 2007,176(10):1429-34.

[112] Dinh P, de Azambuja E, Cardoso F, Piccart-Gebhart MJ Facts and controversies in the use of trastuzumab in the adjuvant setting. Nat Clin Pract Oncol. 2008 Sep 9. [Epub ahead of print]

[113] Scott SA, Edelmann L, Kornreich R, Desnick RJ. Warfarin pharmacogenetics: CYP2C9 and VKORC1 genotypes predict different sensitivity and resistance frequencies in the Ashkenazi and Sephardi Jewish populations. Am J Hum Genet. 2008 Feb;82(2) 495-500 Epub 2008 Jan 17.

[114] Caldwell MD, Awad T, Johnson JA, Gage BF, et al CYP4F2 genetic variant alters required warfarin dose. Blood. 2008 Apr 15;111(8):4106-12. Epub 2008 Feb 4.

[115] Momary KM, Shapiro NL, Viana MA, Nutescu EA, Helgason CM, Cavallari LH Factors influencing warfarin dose requirements in African-Americans.

[116] Pharmacogenomics. 2007 Nov;8(11):1535-44

[117] Tham LS, Goh BC, Nafziger A, Guo JY, Wang LZ, Soong R, Lee SC A warfarin-dosing model in Asians that uses single-nucleotide polymorphisms in vitamin K epoxide reductase complex and cytochrome P450 2C9. Clin Pharmacol Ther. 2006 Oct;80(4):346-55.

[118] Scott SA, Edelmann L, Kornreich R, Desnick RJ Warfarin pharmacogenetics: CYP2C9 and VKORC1 genotypes predict different sensitivity and resistance frequencies in the Ashkenazi and Sephardi Jewish populations. Am J Hum Genet. 2008 Feb;82(2):495-500 Epub 2008 Jan 17

[119] Issa AM. Personalized medicine and the practice of medicine in the 21st century McGill J Med. 2007 10(1):53-57 McKinnon RA, Ward MB, Sorich MJ. A critical analysis of barriers to the clinical implementation of pharmacogenomics Ther Clin Risk Manag 2007;3(5):751-9.

[120] Hillman MA, Wilke RA, Yale SH, et al. A prospective randomized pilot trial of model-based warfarin dose initiation using CYP2C9 genotype and clinical data. Clin Med Res. 2005;3(3);137-45.

[121] Carlquist JF, Horne BD, Muhlestein JB, Lappe DL, et al. Genotypes of the cytochrome p450 isoform, CYP2C9, and the vitamin K epoxide reductase complex subunit 1 conjointly determine stable warfarin dose: a prospective study. J Thromb Thrombolysis. 2006;22(3).191-7.

[122] Ghosh D, Skinner MA, Laing WA. Pharmacogenomics and nutrigenomics: synergies and differences Eur J Clin Nutr. 2007,61:567-74

[123] Subbiah MT Nutrigenomes and nutraceuticals: the next wave riding on personalized medicine Trans Res. 2007;149:55-61.

[124] Mabry PL, Olster DH, Morgan GD, Abrams DB. Interdisciplinarity and systems science to improve population health A view from the NIH Office of Behavioral and Social Sciences Research. Am J Prev Med 2008;35(2S).

[125] Culliton BJ Nanomedicine—The power of proteins: A conversation with Lance Liotta and Emanual Petricoin Health Aff 2008;27(4) w310-w314 Published online June 17, 2008.

[126] Phillips KA, Liang SY, Van Bebber S; Canpers Research Group. Challenges to the translation of genomic information into clinical practice and health policy. Utilization, preferences and economic value. Curr Opin Mol Ther 2008;10(3):260-6

[127] Mabry PL, Olster DH, Morgan GD, Abrams DB. Interdisciplinarity and systems science to improve population health. A view from the NIH Office of Behavioral and Social Sciences Research. Am J Prev Med. 2008;35(2S).

[128] Benner SA, Hoshika S, Sukeda M, et al. Synthetic biology for improved personalized medicine Nucleic Acids Symp. 2008. Series No. 52;243-4

[129] Richmond TD. The current status and future potential of personalized diagnostics: Streamlining a customized process Biotechnol Annu Rev 2008;14:411-22.

[130] de Leon J Pharmacogenomics. The promise of personalized medicine for CNS disorders. Neuropsychopharmacology. 2008;Sep 17 [Epub ahead of print]

[131] McKinnon RA, Ward MB, Sorich MJ. A critical analysis of barriers to the clinical implementation of pharmacogenomics. Ther Clin Risk Manag 2007,3(5):751-9.

[132] Issa AM. Personalized medicine and the practice of medicine in the 21st century McGill J Med 2007 10(1):53-57

[133] Culliton BJ. Nanomedicine—The power of proteins A conversation with Lance Liotta and Emanual Petricoin. Health Aff. 2008;27(4):w310-w314 Published online June 17, 2008

[134] Culliton BJ. Nanomedicine—The power of proteins. A conversation with Lance Liotta and Emanual Petricoin Health Aff. 2008,27(4):w310-w314 Published online June 17, 2008

[135] Snyderman R, Williams RS. Prospective medicine: The next health care transformation. Acad Med. 2003;78:1079-84.

HA 09/01/2015

[116] Snyderman R, Yoediono Z. Prospective health care and the role of academic medicine: lead, follow, or get out of the way. Acad Med. 2008;83(8):707-14.

[117] Snyderman R, Williams RS. Prospective medicine: The next health care transformation. Acad Med. 2003;78:1079-84

[118] Predictive model focuses on morbidity. New program quantifies risk in terms that get attention. Disease Management Advisor. 2007;13(8): August. Accessed October 22, 2008 at http://www.knowyournumber.com/pdf/DMA_2099.pdf.

[119] Information accessed October 22, 2008 at: http://www.navigenics.com/healthcompass/Overview/;jsessionid=0AC087B7DEFA99327D03E99696D603DD.129781-prodappl.

[120] Information accessed October 22, 2008 at: http://www.biophysicalcorp.com/assessments/know-more.aspx.

[121] Dobbe E, Gurney K, Kickow S, et al. Gene-expression assays: new tools to individualized treatment of early stage breast cancer. Am J Health Syst Pharm. 2008;65:23-8.

[122] Snyderman R, Williams RS. Prospective medicine: The next health care transformation. Acad Med. 2003;78:1079-84.

[123] Johns MM, Brigham KL. Transforming health care through prospective medicine. The first step. Acad Med. 2008;83(8):706.

[124] Information accessed October 23, 2008 at. http://www.improvingchroniccare.org/index.php?p=Model_Elements&s=18

[125] Institute of Medicine Committee on Quality of Health Care in America. Crossing the Quality Chasm. A New Health System for the 21st Century. National Academy Press: Washington, DC, 2001.

[126] Nutting PA, Dickinson WP, Dickinson LM, et al. use of chronic-care model elements is associated with higher-quality care for diabetes. Ann Fam Med. 2007;5:14-20

[127] Dipiero A, Dorr DA, Kelso C, Bowen JL. Integrating systematic chronic care for diabetes into an academic general internal medicine resident-faculty practice. J Gen Intern Med. 2008; August 28. [Epub ahead of print]

[128] Henke RM, Chou AF, Chanin JC, et al. Physician attitude toward depression care interventions: Implication for implementation of quality improvement initiatives. Implementation Science. 2008;3:40-9

[129] Hung DY, Shelley DR. Multilevel analysis of the chronic-care model and 5A services for treating tobacco use in urban primary care clinics. Health Serv Res. 2008; September 8 [Epub ahead of print]

[130] Hroscikoski MC, Solberg LI, Sperl-Hillen JM, et al. Challenges of change: A qualitative study of chronic-care model implementation. Ann Fam Med. 2006,4:317-26.

[131] Baxley EG, Stanek M. The AAMC Academic Chronic Care Collaborative: Family medicine's participation and lessons learned. Ann Fam Med. 2007,5(2).183-4.

[132] www.ahrq.gov/populations/chroniccaremodel/chronicintro.htm

[133] Beltran DJ and Lubow HW and Driedger AA. Letters and response to "Why is evidence-based medicine the legal standard of practice?" Medscape J Med. 2008;10(1 and 3).

[134] Hurwitz B. How does evidence based guidance influence determinations of medical negligence? BMJ. 2004;329:1024-8.

[135] GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004; 328(7454):1490-7.

[136] Evidence-based Medicine Working Group. Evidence-based medicine: A new approach to teaching the practice of medicine. JAMA 1992,68:2420-5.

[137] Sackett DL, Rosenberg WM. The need for evidence-based medicine. J Royal Soc Med. 1995,88:620-4.

[138] Guyatt G, Cook D, Haines B. Evidence based medicine has come a long way. BMJ. 2004;329.990-1.

[139] Guyatt GH, Oxman AD, Vist GE, et al. GRADE: What is "quality of evidence" and why is it important to clinicians? BMJ. 2008, 336(7651):995-8.

[140] Guyatt GH, Oxman AD, Vist GE, et al. GRADE: What is "quality of evidence" and why is it important to clinicians? BMJ. 2008, 336(7651):995-8.

[141] Guyatt GH, Oxman AD, Vist GE, et al. GRADE. What is "quality of evidence" and why is it important to clinicians? BMJ. 2008; 336(7651):995-8

[142] Bagshaw SM, Bellomo R. The need to reform our assessment of evidence from clinical trials: A commentary. Philos Ethics Humanit Med. 2008;3:23-33.

[143] Guyatt GH, Oxman AD, Vist GE. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336:

[144] Evans D. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. J Clin Nurs. 2003; 12. 77–84

[145] Montori VM, Guyatt GH. Progress in evidence-based medicine. JAMA. 2008;300(15):1814-6.

[146] Schunemann AH, Oxman AD, Brozek J. GRADE: grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ. 2008;336.1106-10

[147] http://www.gradeworkinggroup.org/toolbox/index.htm

[148] Del Mar C, Glasziou P, Mayer D. Teaching evidence based medicine. BMJ. 2004,329:989-90

[149] Straus S, Jones G. What has evidence based medicine done for us? BMJ. 2004;329 987-988.

[150] Lockwood DN, Armstrong M, Grant AD. Integrating evidence based medicine into routine clinical practice: seven years' experience at the Hospital for Tropical Diseases, London. BMJ. 2004,329:1020-3

[151] Coomarasamy A, Khan KS. What is the evidence that postgraduate teaching in evidence based medicine changes anything? A systematic review. BMJ. 2004,329:1017-21.

[152] http://clinicalevidence.bmj.com/ceweb/about/knowledge.jsp

[153] Cleophas TJ, Zwinderman AH. Clinical trials are often false positive: a review of simple methods to control the problem. Curr Clin Pharmacol. 2006,1(1):1-4.

[154] Bagshaw SM, Bellomo R. The need to reform our assessment of evidence from clinical trials: A commentary. Philos Ethics Humanit Med. 2008,3:23-33.

[155] Contopoulos-Ioannidis DG, Ntzani E, Ioannidis JP. Translation of highly promising basic science research into clinical applications. Am J Med. 2003;114(6) 477-84

[156] Khoury MJ, Gwinn M, Yoon PW, et al. The continuum of translation research in genomic medicine: how can we accelerate the appropriate integration of human genome discoveries into health care and disease prevention? Genet Med. 2007;9(10):665-74.

[157] http://publications.nigms.nih.gov/thenewgenetics/glossary.html#S Accessed October 27, 2008.

[158] http://blog-msb.embo.org/blog/2007/07/what_is_systems_biology_3.html. Accessed October 27, 2008

[159] Ramos RG, Olden K. Gene-environment interactions in the development of complex disease phenotypes. Int J Environ Res Public Health. 2008,5(1):4-11.

[160] http://www.systemsbiology.org/Systems_Biology_in_Depth/Premise_of_Systems_Biology. Accessed October 27, 2008.

[161] Scheuner MT, Sieverding P, Shekelle PG. Delivery of genomic medicine for common chronic adult diseases. A systematic review. JAMA. 2008;299(11):1320-34

[162] Swen JJ, Huizinga TW, Gelderblom H, et al. Translating pharmacogenomics: challenges on the road to the clinic. PLoS Medicine. 2007;4(8).e209-e210

[163] McKinnon RA, Ward MB, Sorich MJ. A critical analysis of barriers to the clinical implementation of pharmacogenomics. Ther Clin Risk Manage. 2007,3(5):751-9.

[164] Auffray C, Chen Z, Hood L. Review: Systems medicine: the future of medical genomics and healthcare. Genome Medicine. 2009, 1:2:1-11.

HA 09/01/2015

[105] Kligler B, Maizes V, Schachter S, et al. Core competencies in integrative medicine for medical school curricula: A proposal. Acad Med. 2004;79:521-31.

[106] Kessler RC, Davis RB, Foster DF, et al. Long-term trends in the use of complementary and alternative medical therapies in the United States. Ann Int Med. 2001;135:262-8

[107] Koneful J. The challenge of educating physicians about complementary and alternative medicine. Acad Med 2002;77:847-50.

[108] Kligler B, Maizes V, Schachter S, et al. Core competencies in integrative medicine for medical school curricula: A proposal Acad Med 2004;79 521-31

[109] Gaylord SA, Mann JD Rationales for CAM education in health professions training programs. Acad Med. 2007;82(10).927-33.

[110] Kligler B, Maizes V, Schachter S, et al. Core competencies in integrative medicine for medical school curricula: A proposal. Acad Med. 2004;79.521-31

[111] University of Texas Medical Branch at Galveston, Family Medicine Residency Program, Complementary and Integrative Medicine Curriculum, 2003-04.

[112] Driskо J. University of Kansas Medical Center Program in Integrative Medicine Fellowship Curriculum August 2008-July 2009

[113] Lutz A, Slagter HA, Dunne JD, Davidson RJ. Attention regulation and monitoring in meditation. Trends Cogn Sci. 2008,12(4):163-9

[114] Davidson RJ, Kabat-Zinn J, Schumacher J, et al. Alterations in brain and immune function produced by mindfulness meditation. Psychosom Med. 2003;65.564-70.

[115] Lutz A Long-term meditators self-induce high-amplitude gamma synchrony during mental practice. PNAS. 2004;101(46):16369-73.

[116] Brefczynski-Lewis JA, Lutz A, Schaefer HS, Levinson DB, Davidson RJ. Neural correlates of attentional expertise in long-term meditation practitioners. PNAS. 2007;104(27).11483-88

[117] Kuyken W, Byford S, Taylor RS, et al. Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. J Consulting Clin Psych 2008;Vol 76(6):966-978.

[118] Kathryn Montgomery. How Doctors Think. Oxford Univ Press. 2006.

[119] Jerome Groopman. How Doctors Think, pgs 51-52.

[120] Sieberts SK. Schadt EE. Moving toward a system genetics view of disease. Mamm Genome 2007; 18:389-401..

[121] Holman H Chronic disease—The need for a new clinical education. JAMA. 2004;292(9):1037-1039.

[122] Marks HM. The progress of experiment: science and therapeutic reform in the United States, 1900-1990 Cambridge: Cambridge University Press, 1995

[123] Kaptchuk TJ. Intentional ignorance: a history of blind assessment in medicine Bull Hist Med. 1998;72(3):389-433.

[124] Genuis, SK, Genuis SJ Exploring the continuum: medical information to effective clinical practice. Paper I: the translation of knowledge into clinical practice. Journal of Evaluation in Clinical Practice. 2006. 12 (1): 49–62.

[125] Bagshaw, SM & Bellomo, R. The need to reform our assessment of evidence from clinical trials: A commentary. Philosophy, Ethics, and Humanities in Medicine 2008, 3.23.

[126] Genuis, SJ, Genuis SK Exploring the conunuum. medical information to effective clinical practice Paper II. Towards aetiology-centred clinical practice. Journal of Evaluation in Clinical Practice. 12 (1):63–75

[127] Gardiner Harris. Research Center Tied to Drug Company New York Times. November 25, 2008.

[128] DeAngelis CD. The Influence of Money on Medical Science. JAMA, Published online August 7, 2006

[129] Nieto A, et al. Adverse Effects of Inhaled Corticosteroids in Funded and Nonfunded Studies. Arch Intern Med. 2007;167(19):2047-2053.

[210] Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ 2001;323:334-36.

[211] Guyatt GH, Sinclair J, Cook. DJ, Glasziou P. Users' guides to the medical literature: XVI. How to use a treatment recommendation. JAMA. 1999,281(19):1836-43.

[212] Evidence-based medicine. A new approach to teaching the practice of medicine. Evidence-Based Medicine Working Group JAMA 1992;268(17).2420-25

[213] Geyman JP. Evidence-based medicine in primary care: an overview. J Am Board Fam Pract. 1998,11:46-56

[214] Rosenberg W, Donald A Evidence based medicine: an approach to clinical problem-solving. BMJ. 1995;310 1122-26

[215] Sackett DL Evidence-based medicine: how to practice and teach EBM. New York: Churchill Livingston, 1997.2-16.

[216] Davidoff F, et al. Evidence based medicine BMJ 1995; 310:1085-86.

[217] Weel CV, Knottnerus JA. Evidence-based interventions and comprehensive treatment Lancet. 1999;353.916-18.

[218] Mant D. Can randomized trials inform clinical decisions about individual patients? Lancet. 1999;353.743-46.

[219] Feinstein AR, Horwitz RI. Problems in the "evidence" of "evidence-based medicine." Am J Med. 1997,103:529-35.

[220] Culpepper L, Gilbert TT. Evidence and ethics Lancet. 1999;353 829-31

[221] Auffray C, Chen Z, Hood L. Review: Systems medicine: the future of medical genomics and healthcare. Genome Medicine 2009; 1.2:1-11.

[222] Ramos RG, Olden K Gene-Environment Interactions in the Development of Complex Disease Phenotypes. Int J Environ Res Public Health 2008;5(1):4-11.

[223] Bell IR, Koithan M. Models for the study of whole systems. Integ Cancer Ther. 2006 5(4):293-307.

[224] Bagshaw, SM & Bellomo, R The need to reform our assessment of evidence from clinical trials: A commentary Philosophy, Ethics, and Humanities in Medicine 2008, 3:23.

[225] Katerndahl,, Crabtree,.B Creating Innovative Research Designs: The 10-Year Methodological Think Tank Case Study. Annals of Family Medicine 2006, 4 (5):443

[226] Weed LL. Zimny NJ The problem-oriented system, problem-knowledge coupling, and clinical decision making. Phys Ther. 1989;69(7):565-8.

[227] Weed LL. Medical Records, Medical Education, and Patient Care The Problem-Oriented Record as a Basic Tool. Chicago: Year Book Medical Publisher, Inc.: 1970.

[228] Hampton JR. Evidence-based medicine, opinion-based medicine, and real-world medicine. Perspect Biol Med. 2002;45(4):549-68.

[229] Grahame-Smith D. Evidence based medicine: Socratic dissent. BMJ. 1995,310:1126-27.

[230] Definition of POEMs published in tips from other journals. Am Fam Physician. 2005,71(1):153.

[231] A DuPont advertising slogan 1939 http://heritage.dupont.com/touchpoints/tp_1939/depth.shtml

[232] http://www.cdc.gov/ped/issues/2004/apr/04_0006.htm

[233] Starfield B. Threads and Yarns: Weaving the Tapestry of Comorbidity. Ann Fam Med 2006;4:101.

[234] Cerutti A, Sinorini MG Non-linear algorithms for processing biological signals. Comput Methods Programs Biomed. 1996; 51:51-73.

[235] Smart A, Martin P, Parker M. Tailored medicine: whom will it fit? Bioethics. 2004; 18:322-42.

[236] Bell IR, Koithan M Models for the study of whole systems. Integ Cancer Ther. 2006 5(4).293-307

[237] Bland, J. Alternative therapies—a moving target. Altern Ther Health Med. 2005;11(2):2-4.

[240] Bagshaw; SM & Bellomo, R. The need to reform our assessment of evidence from clinical trials. A commentary. Philosophy, Ethics, and Humanities in Medicine 2008, 3:23.

[241] Auffray C, Chen Z, Hood L. Review. Systems medicine: the future of medical genomics and healthcare. Genome Medicine. 2009; 1:2:1-11.

[242] Evidence-based medicine. A new approach to teaching the practice of medicine. Evidence-Based Medicine Working Group. JAMA. 1992;268(17):2420-25.

[243] Sackett, DL. Evidence based medicine: what it is and what it isn't BMJ. 1996;312:71-72

[244] Weel CV, Knottnerus JA. Evidence-based interventions and comprehensive treatment. Lancet. 1999;353:916-18

[245] Greenhalgh T, et. al. Learning in Practice. BMJ. 2003;326:142-45

[246] Kuhn TS. The Structure of Scientific Revolutions. Chicago, Ill: University of Chicago Press; 1970.

[247] Dornhurst AC. Information Overload. Why Medical Education Needs a Shake-up. Lancet 1981. 2:513-14.

[248] Montgomery K. How Doctors Think: Clinical Judgment and the Practice of Medicine. Oxford University Press: New York, NY, 2006. P. 31-33.

[249] Jerome Groopman. How Doctors Think. Houghton Mifflin. NY. NY 2007, Chapter 10.

[250] Sackett, DL. BMJ 1996; 312:71-72.

[251] Borrell-Carrio F, et al. The biopsychosocial model 25 years later: Principles, practice, and scientific inquiry. Ann Fam Med. 2004; 2(6):.576-82.

[252] Mackie JL. Causes and conditions. Amer Philosoph Q. 1965,2:245-64

[253] Mackie JL. The Cement of the Universe. A Study of Causation Oxford UK: Oxford University Press; 1974.

[254] Bateson G. Steps to an Ecology of Mind: A Revolutionary Approach to Man's Understanding of Himself. New York, NY: Ballantine Books; 1972.

[255] Fraser SW, Greenhalgh T. Coping with complexity: educating for capability. BMJ. 2001,323:799-803.

[256] Miller WL, Crabtree BF, McDaniel R, Stange KC. Understanding change in primary care practice using complexity theory J Fam Pract. 1998, 46:369-76

[257] Borrell-Carrio F, et al. The biopsychosocial model 25 years later: Principles, practice, and scientific inquiry. Ann Fam Med. 2004; 2(6):576-82

[258] David Deutsch. The Fabric of Reality. New York, NY: Penguin Press, 1997:16.

[259] Little P, et al. Preferences of patients for patient centred approach to consultation in primary care: observational study. BMJ 2001;322:1-7.

[260] Mant D. Can randomized trials inform clinical decisions about individual patients? Lancet 1999;353.743-46.

[261] Gigerenzer G. *Rationality for Mortals: How People Cope with Uncertainty* Oxford University Press, 2008. pg.vi.

[262] Bagshaw; SM & Bellomo, R. The need to reform our assessment of evidence from clinical trials: A commentary. Philosophy, Ethics, and Humanities in Medicine 2008, 3:23.

[263] Grossman J, Mackenzie FJ. The Randomized Controlled Trial: gold standard, or merely standard? Perspectives in Biology and Medicine, 2005. 48 (4):516–34.

[264] Paul Glasziou, Jan Vandenbroucke, Iain Chalmers Assessing the quality of research BMJ 2004. 328, (3).39-41

[265] Mercer S, et al. Study Designs for Effectiveness and Translation Research: Identifying Trade-offs. Am J Prev Med 2007;33(2):139-154.

[266] Genuis J. Diagnosis: contemporary medical hubris; Rx: a tincture of humility. Journal of Evaluation in Clinical Practice. 2005.12; (1): 24–30.

[267] Miles A., Grey J.E., Polychronis A., Price N & Melchiorri C. Developments in the evidence-based health care debate. Journal of Evaluation in Clinical Practice. 2004. 10:129–142

[268] Montori VM, Guyatt GH. Progress in Evidence Based Medicine JAMA. 2008,300:1814-16

[269] Walter Freeman How Brains Make Up Their Minds. 2000. Columbia University Press

[270] Yun Kuzyk's review of Walter Freeman's book: How Brains Make Up Their Minds, on Amazon.com.

[271] Peter Dayan, L. F. Abbott. Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems. The MIT Press; 2005.

[272] Roland Baddeley (Editor), Peter Hancock (Editor). Peter Foldiák (Editor). Information Theory and the Brain. Cambridge University Press. 2008

[273] Eric R. Kandel In Search of Memory. The Emergence of a New Science of Mind. W. W. Norton, 2007,

[274] Roberto Cabeza (Editor). Alan Kingstone (Editor).Handbook of Functional Neuroimaging of Cognition The MIT Press; 2 edition, 2006

[275] Henry P Stapp. Mindful Universe: Quantum Mechanics and the Participating Observer (The Frontiers Collection) Springer; 1 edition 2007

[276] Gerd Gigerenzer. Gut Feelings. Penguin Books London, 2007

[277] Gerd Gigerenzer Rationality for Mortals. Oxford U Press. Oxford, 2008.

[278] Thomas Gilovich, et al. Heuristics & Biases. Cambridge University Press. 2002.

[279] See previous three endnotes.

[280] Gerd Gigerenzer Gut Feelings Penguin Books London, 2007, pg 10-11.

[281] Elwyn G. et al. Decision analysis in patient care. Review. Lancet. 2001; 358: 571–74

[282] Naylor, C. Clinical decisions: From art to science and back again. The Lancet. 2001. 358:523-24

[283] Fiore S. and Schooler, J. Right hemisphere contributions to creative problem solving: Converging evidence for divergent thinking In Right Hemisphere Language Comprehension: Perspectives from Cognitive Neuroscience (Beeman, M. and Chiarello, C., eds). pp. 255–284, Erlbaum Pub. Philadelphia, PA, 1998

[284] Seger, C.A. et al. FMRI evidence for right hemisphere involvement in processing unusual semantic relationships. Neuropsychology 2000;14, 361–369

[285] Bowden EM. New approaches to demystifying insight. TRENDS in Cognitive Sciences 2005;9(7):322-28.

[286] Jung-Beeman, M. et al. Neural activity observed in people solving verbal problems with insight. PLOS Biol. 2004; 2, 500–510

[287] Chronicle, E. P. et al. What makes an insight problem? The roles of heuristics, goal conception, and solution recoding in knowledge-lean problems. J. Exp. Psychol. Learn. Mem. Cogn. 2004; 30, 14–27.

[288] Luo, J. and Niki, K. Function of hippocampus in 'insight' of problem solving. Hippocampus 2003, 13, 316–323

[289] Siegler, R. Unconscious insights. Curr. Dir. Psychol. Sci. 2000; 9, 79–83

[290] Bowden EM. New approaches to demystifying insight. TRENDS in Cognitive Sciences 2005;9(7).322-28.

[291] Bowden, E.M. and Jung-Beeman, M. Getting the right idea: semantic activation in the right hemisphere may help solve insight problems. Psychol. Sci. 1998, 6. 435–440.

[292] John Kounios J. et al. The origins of insight in resting-state brain activity Neuropsychologia 2008; 46:281–291.

[293] Jonah Lehrer. The Annals of Science: The Eureka Hunt The New Yorker, July 28, 2008: pgs 40-45

[202] Jung-Beeman, M. et al Neural activity observed in people solving verbal problems with insight. PLOS Biol. 2004; 2, 500–510.

[203] Smith, R. W., & Kounios, J. Sudden insight: All-or-none processing revealed by speed-accuracy decomposition. Journal of Experimental Psychology: Learning, Memory, and Cognition. 1996;22: 1443–1462.

[204] Jonah Lehrer. The Annals of Science: The Eureka Hunt The New Yorker, July 28, 2008: pgs 40-45.

[205] Jonah Lehrer. The Annals of Science: The Eureka Hunt. The New Yorker, July 28, 2008: pgs 40-45

[206] Rhoades DR, McFarland KF, Finch WH, Johnson AO Speaking and interruptions during primary care office visits. Fam Med. 2001 Jul-Aug;33(7):528-32.

[207] Beckman DB, et al. The effect of physician behavior on the collection of data. Ann Intern Med 1984,101:692-96.

[208] Magid CS. Developing tolerance for ambiguity. JAMA 2001,285(1):88.

[209] Rees J. Complex disease and the new clinical sciences. Science. 2002; 296:698-701.

[210] Radford T. Top scientist warns of "sickness" in US health system. BMJ. 2003;326.416.

[211] Vioxx: lessons for Health Canada and the FDA. CMAJ. 2005;172(11):5.

[212] Juni P, Nartey L, Reichenbach S, et al Risk of cardiovascular events and rofecoxib: cumulative meta-analysis The Lancet. 2004;364:2021-29.

[213] Yu SL, Ho LM, Lim BC, Sim ML. Urinary deoxypyridinoline is a useful biochemical bone marker for the management of postmenopausal osteoporosis. Ann Acad Med Singapore. 1998;27(4):527-29.

[214] Palomba S, Orio F, Colao A, et al. Effect of estrogen replacement plus low-dose alendronate treatment on bone density in surgically postmenopausal women with osteoporosis. J Clin Endocrinol Metab 2002;87(4):1502-1508.

[215] Moya-Camarena SY, Vanden Heuvel JP, Blanchard SG, et al Conjugated linoleic acid is a potent naturally occurring ligand and activator of PPARa. J Lipid Res. 1999;40:1426-33.

[216] Gaullier JM, Halse J, Hoye K, et al Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. Am J Clin Nutr. 2004;79:1118-25.

[217] O'Shea M, Bassaganya-Riera J, Mohede IC. Immunomodulatory properties of conjugated linoleic acid. Am J Clin Nutr. 2004:79(S):1199S-206S.

[218] Malloney F, Yeow TP, Mullen A, et al Conjugated linoleic acid supplementation, insulin sensitivity, and lipoprotein metabolism in patients with type 2 DM. Am J Clin Nutr. 2004;80(4):887-95.

[219] Riserus U, Vessby B, Arner P, Zethelius B. Supplementation with CLA induces hyperproinsulinaemia in obese men: close association with impaired insulin sensitivity. Diabetalogia 2004;47(6):1016-19.

[220] Ames, BN The metabolic tune-up: metabolic harmony and disease prevention J Nutr. 2003,133:1544S-48S.

[221] Ames BN, et al. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased Km): relevance to genetic disease and polymorphisms Am J Clin Nutr. 2002;75(4):616-58.

[222] Ames BN, et al. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased Km): relevance to genetic disease and polymorphisms Am J Clin Nutr 2002,75(4):616-58.

[223] Bralley JA, Lord RS: Laboratory Evaluations in Molecular Medicine. 2001 In Organic Acids, Chapter 6, p. 181

[224] Bralley JA, Lord RS: Laboratory Evaluations in Molecular Medicine. 2001. In Organic Acids, Chapter 6, p 181.

[225] Yamamoto Y, Gaynor RB. Therapeutic potential of inhibition of the NF-kB pathway in the treatment of inflammation and cancer. J Clin Invest. 2001;107(2):135-42.

[226] Tak PP, Firestein GS. NF-kB: a key role in inflammatory disease. J Clin Invest 2001,107(1):7-11.

[227] Yamamoto Y, Gaynor RB. Therapeutic potential of inhibition of the NF-kB pathway in the treatment of inflammation and cancer. J Clin Invest. 2001;107(2):135-42.

[228] Balmer JE, Blomhoff R. Gene expression regulation by retinoic acid J Lipid Res 2002;43:1773-808.

[229] Holick MF Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular diseases. Am J Clin Nutr 2004,80(6 Suppl).1678S-88S.

[230] Holick MF Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular diseases. Am J Clin Nutr. 2004,80(6 Suppl).1678S-88S

[231] Brown MM, et al Evidence-Based to Value-Based Medicine. AMA Press. USA 2005: pp 3-5

[232] Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-Based Medicine: How to Practice and Teach EBM. New York: Churchill Livingstone, 2000.

[233] Jerome Groopman. How Doctors Think. Houghton Mifflin. NY, NY 2007.

[234] Fiore, S and Schooler, J. Right hemisphere contributions to creative problem solving: Converging evidence for divergent thinking. In Right Hemisphere Language Comprehension: Perspectives from Cognitive Neuroscience (Beeman, M. and Chiarello, C., eds), pp. 255–284, Erlbaum Pub Philadelphia, PA, 1998.

[235] Seger, C.A. et al FMRI evidence for right hemisphere involvement in processing unusual semantic relationships. Neuropsychology 2000,14, 361–369.

[236] Scott JG, et al Understanding Healing Relationships in Primary Care Ann Fam Med 2008,6(4):315-22.

[237] Miller WL, et al. Research guidelines for assessing the impact of healing relationships in clinical medicine. Altern Ther Health Med. 2003,9(3)(Suppl).A80-A95.

[238] Jackson C. Healing ourselves, healing other: first in a series. Holist Nurs Pract 2004,18(2):67-81

[239] Acheson L. Community Care, Healing. Annals Fam Med 2008,6:290.

[240] Hsu C, et al Healing in Primary Care. A Vision Shared by Patients, Physicians, Nurses, and Clinical Staff. Ann Fam Med. 2008,6(4):307-14.

[241] Egnew TR. The Meaning of Healing: Transcending Suffering. Ann Fam Med. 2005;3(3):255-62.

[242] Scott JG, et al. Understanding Healing Relationships in Primary Care. Ann Fam Med 2008,6(4):315-22.

[243] Scott JG, et al Understanding Healing Relationships in Primary Care. Ann Fam Med 2008,6(4):315-22.

[244] Jonah Lehrer. The Annals of Science: The Eureka Hunt The New Yorker, July 28, 2008. pgs 40-45

[245] Galland L. "Person-Centered Diagnosis," in Power Healing. New York: Random House, 1997, pp 52-97.

[246] Lukaczer D. The 4R Program. In Ch 28, Clinical Approaches to Gastrointestinal Imbalance. The Textbook of Functional Medicine Gig Harbor, WA: The Institute for Functional Medicine, 2005.

[247] Silver SM, Rogers S, Russell M. Eye movement desensitization and reprocessing (EMDR) in the treatment of war veterans. J Clin Psychol. 2008,64(8):947-57.

[248] Jonah Lehrer. The Annals of Science The Eureka Hunt. The New Yorker, July 28, 2008 pgs 40-45.

[249] Gerd Gigerenzer. Rationality for Mortals: How people cope with Uncertainty. Oxford: Oxford University Press: 2008. pg v.

21ST CENTURY MEDICINE:
A New Model for Medical Education and Practice

APPENDIX
Table of Contents

21ST CENTURY MEDICINE:

A New Model for Medical Education and Practice

Recommendations from the Future of Family Medicine Project

(http://www.futurefamilymed.org/x24873.html)

New Model of Family Medicine

Family medicine will redesign the work and workplaces of family physicians. This redesign will foster a New Model of Care based on the concept of a relationship-centered personal medical home, which serves as the focal point through which all individuals — regardless of age, gender, race, ethnicity, or socioeconomic status participate in health care. In this new medical home, patients receive a basket of services of acute, chronic, and preventive medical care services that are accessible, accountable, comprehensive, integrated, patient-centered, safe, scientifically valid, and satisfying to both patients and their physicians. This New Model will include technologies that enhance diagnosis and treatment for a large portion of problems that people bring to their family physicians. Business plans and reimbursement models will be developed to enable the reengineered practices of family physicians to thrive as personal medical homes, and resources will be developed to help patients make informed decisions about choosing a personal medical home. A financially self-sustaining national resource will be implemented to provide practices with ongoing support in transitioning to the New Model of Family Medicine.

Communications

A unified communications strategy will be developed to promote an awareness and understanding of the New Model of Family Medicine and the concept of a Personal Medical Home. As part of this strategy, a new symbol for family physicians will be created, and consistent terminology will be established for the specialty ("family medicine" rather than "family practice" and "family physician" rather than "family practitioner"). In addition, a system will be developed to communicate and implement best practices within family medicine.

Electronic Health Records

Electronic health records that support the New Model of family medicine will be implemented. The electronic health record will enhance and integrate communication, diagnosis and treatment, measurement of processes and results, analyses of the effects of co-morbidity, recording and coding elements of whole-person care, and promoting ongoing, healing relationships between family physicians and their patients.

Family Medicine Education

Family medicine will oversee the training of family physicians who are committed to excellence, steeped in the core values of the discipline, expert in providing family medicine's basket of services within the New Model of Family Medicine, skilled at adapting to varying patient and community needs, and prepared to embrace new evidence-based technologies. Family medicine education will continue to include training in maternity care, the care of hospitalized patients, community and population health, and culturally effective and proficient care. Innovation in family medicine residency programs will be supported by the Residency Review Committee for Family Practice through 5-10 years of curricular flexibility to permit active experimentation and ongoing critical evaluation of competency-based education, expanded training programs and other strategies to prepare graduates for the New Model. In preparation for this process, every family medicine residency will implement electronic health records by 2006.

Life-Long Learning

The discipline of family medicine will develop a comprehensive, life-long learning program. This program will provide the tools for each family physician to create a continuous personal, professional, and clinical practice assessment and improvement plan that supports a succession of career stages. This personalized learning and professional development will include self-assessment and learning modules directed at individual physicians and group practices that incorporate science-based knowledge into educational interventions that foster improved patient outcomes. Family medicine residency programs and departments will incorporate continuing professional development into their curricula and will initiate and model the support process for life-long learning and maintenance of certification.

Enhancing the Science of Family Medicine

Participation in the generation of new knowledge will be integral to the activities of all family physicians and will be incorporated into family medicine training. Practice-based research will be integrated into the values, structures and processes of family medicine practice... Departments of family medicine will engage in highly collaborative research that produces new knowledge about the origins of disease and illness, how health is gained and lost, and how the provision of care can be improved. A national entity should be established to lead and fund research on the health and health care of whole people. Funding for the Agency for Healthcare Research and Quality should be increased to at least $1 billion per year.

Quality of Care

Close working partnerships will be developed between academic family medicine, community-based family physicians and other partners in order to address the quality goals specified in the IOM's Quality Chasm report. Family physicians and their practice partners will have support systems to measure and report regularly their performance on the 6 IOM aims of quality health care (safe, timely, effective, equitable, patient-centered, and efficient). Family med residency programs will track and report

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regularly the performance of their residents during their training on the 6 IOM quality measures and will modify their training programs as necessary to improve performance.

Role of Family Medicine in Academic Health Centers

Departments of family medicine will individually and collectively analyze their position within the academic health center setting and will take steps to enhance their contribution to the advancement and rejuvenation of the AHC to meet the needs of the American people. A summit of policymakers and family medicine leaders in academia and private practice will be convened to review the role of and make recommendations on the future of family medicine in academia.

Developing a Sufficient Family Medicine Workforce

A comprehensive Family Medicine Career Development Program and other strategies will be implemented to recruit and train a culturally diverse family physician workforce that meets the needs of the evolving US population for integrated health care for whole people, families and communities. Departments of family medicine will continue to develop, implement, disseminate and evaluate best practices in expanding student interest in the specialty.

Leadership and Advocacy

Recommendation #10 from the Future of Family Medicine Report concerned Leadership and Advocacy. The Strategic Initiative calls for: A Leadership Center for Family Medicine and Primary Care will be established which will develop strategies to promote family physicians and other primary care physicians as health policy and research leaders in their communities, in government, and in other influential groups. In their capacity as leaders, family physicians will convene leaders to identify and develop implementation strategies for several major policy initiatives, including assuring that every American has access to basic health care services. Family physicians will partner with others at the local, state and national levels to engage patients, clinicians and payers in advocating for a redesigned system of integrated, personalized, equitable and sustainable health care.

American Academy of Family Physicians (AAFP)
American Academy of Pediatrics (AAP)
American College of Physicians (ACP)
American Osteopathic Association (AOA)

Joint Principles of the Patient-Centered Medical Home

February 2007

Introduction

The Patient-Centered Medical Home (PC-MH) is an approach to providing comprehensive primary care for children, youth and adults. The PC-MH is a health care setting that facilitates partnerships between individual patients, and their personal physicians, and when appropriate, the patient's family. The AAP, AAFP, ACP, and AOA, representing approximately 333,000+ physicians, have developed the following joint principles to describe the characteristics of the PC-MH.

Principles

Personal physician – each patient has an ongoing relationship with a personal physician trained to provide first contact, continuous and comprehensive care.

Physician directed medical practice – the personal physician leads a team of individuals at the practice level who collectively take responsibility for the ongoing care of patients.

Whole person orientation – the personal physician is responsible for providing for all the patient's health care needs or taking responsibility for appropriately arranging care with other qualified professionals. This includes care for all stages of life; acute care; chronic care; preventive services; and end of life care.

Care is coordinated and/or integrated across all elements of the complex health care system (e.g., subspecialty care, hospitals, home health agencies, nursing homes) and the patient's community (e.g., family, public and private community-based services). Care is facilitated by registries, information technology, health information exchange and other means to assure that patients get the indicated care when and where they need and want it in a culturally and linguistically appropriate manner.

Quality and safety are hallmarks of the medical home:

- Practices advocate for their patients to support the attainment of optimal, patient-centered outcomes that are defined by a care planning process driven by a compassionate, robust partnership between physicians, patients, and the patient's family.
- Evidence-based medicine and clinical decision-support tools guide decision making.
- Physicians in the practice accept accountability for continuous quality improvement through voluntary engagement in performance measurement and improvement.

- Patients actively participate in decision-making and feedback is sought to ensure patients' expectations are being met
- Information technology is utilized appropriately to support optimal patient care, performance measurement, patient education, and enhanced communication
- Practices go through a voluntary recognition process by an appropriate non-governmental entity to demonstrate that they have the capabilities to provide patient centered services consistent with the medical home model.
- Patients and families participate in quality improvement activities at the practice level.

Enhanced access to care is available through systems such as open scheduling, expanded hours and new options for communication between patients, their personal physician, and practice staff.

Payment appropriately recognizes the added value provided to patients who have a patient centered medical home. The payment structure should be based on the following framework.

- It should reflect the value of physician and non-physician staff patient-centered care management work that falls outside of the face-to-face visit.
- It should pay for services associated with coordination of care both within a given practice and between consultants, ancillary providers, and community resources.
- It should support adoption and use of health information technology for quality improvement.
- It should support provision of enhanced communication access such as secure e-mail and telephone consultation.
- It should recognize the value of physician work associated with remote monitoring of clinical data using technology.
- It should allow for separate fee-for-service payments for face-to-face visits. (Payments for care management services that fall outside of the face-to-face visit, as described above, should not result in a reduction in the payments for face-to-face visits).
- It should recognize case mix differences in the patient population being treated within the practice.
- It should allow physicians to share in savings from reduced hospitalizations associated with physician-guided care management in the office setting.
- It should allow for additional payments for achieving measurable and continuous quality improvements.

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Background of the Medical Home Concept

The American Academy of Pediatrics (AAP) introduced the medical home concept in 1967, initially referring to a central location for archiving a child's medical record. In its 2002 policy statement, the AAP expanded the medical home concept to include these operational characteristics: accessible, continuous, comprehensive, family-centered, coordinated, compassionate, and culturally effective care. The American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP) have since developed their own models for improving patient care called the "medical home." (AAFP 2004) or "advanced medical home" (ACP 2006).

For More Information:

American Academy of Family Physicians (http://www.futurefamilymed.org)

List of Members of the Consortium of Academic Health Centers for Integrative Medicine (CAHCIM)

United States

Arizona

University of Arizona
Program in Integrative Medicine
www.integrativemedicine.arizona.edu

California

Stanford University
Stanford Center for Integrative Medicine
http://www.stanfordhospital.com/clinicsmedServices/clinics/complementaryMedicine/default

University of California, Irvine
Susan Samueli Center for Integrative Medicine
www.sscim.uci.edu

University of California, Los Angeles
Collaborative Centers for Integrative Medicine
www.uclamindbody.org

University of California, San Francisco
Osher Center for Integrative Medicine
www.osher.ucsf.edu

Colorado

University of Colorado at Denver School of Medicine
The Center for Integrative Medicine
www.uch.edu/integrativemed

Connecticut

University of Connecticut
School of Medicine
www.uchc.edu

Yale University
Integrative Medicine @ Yale
cam.yale.edu

Integrative Medicine Center at Griffin Hospital
www.griffinhospital.org

Hawaii

University of Hawaii-Manoa
John A. Burns School of Medicine
Department of Complementary and Alternative Medicine
www.jabsom.hawaii.edu/jabsom

Illinois

Northwestern University Feinberg School of Medicine
Northwestern Memorial Physician's Group Center for Integrative Medicine
www.nmpg.com

Kansas

University of Kansas
Program in Integrative Medicine
http://integrativemed.kumc.edu/

Maryland

Johns Hopkins University
School of Medicine
Center for Complementary and Alternative Medicine www.hopkinsmedicine.org/cam

University of Maryland
Center for Integrative Medicine
www.compmed.umm.edu

Massachusetts

Boston University School of Medicine
Program in Integrative Cross Cultural Care
www.bumc.bu.edu

Harvard Medical School
Osher Institute
www.osher.hms.harvard.edu

University of Massachusetts
Center for Mindfulness
www.umassmed.edu/cfm/index.aspx

Michigan

University of Michigan
Integrative Medicine
www.med.umich.edu/umim

Minnesota

Mayo Clinic
Complementary and Integrative Medicine Program
www.mayoclinic.org/general-internal-medicine-rst/cimc.html
Research
http://mayoresearch.mayo.edu/mayo/research/cimp/

University of Minnesota
Center for Spirituality and Healing
www.csh.umn.edu

New Jersey

University of Medicine and Dentistry of New Jersey
Institute for Complementary & Alternative Medicine
www.umdnj.edu/icam

New Mexico

University of New Mexico
Health Science Center
hsc.unm.edu/som/cfh

New York

Albert Einstein College of Medicine of Yeshiva University
Continuum Center for Health and Healing
www.healthandhealingny.org

Columbia University
Richard and Hinda Rosenthal Center for Complementary & Alternative Medicine
www.rosenthal.hs.columbia.edu

North Carolina

Duke University
Duke Integrative Medicine
www.dukeintegrativemedicine.org

University of North Carolina at Chapel Hill
Program on Integrative Medicine
pim.med.unc.edu

Wake Forest University School of Medicine
Program for Holistic & Integrative Medicine
http://www1.wfubmc.edu/phim/

Oregon

Oregon Health and Science University
Women's Primary Care and Integrative Medicine, Center for Women's Health
www.ohsu.edu/cam
www.ohsuwomenshealth.com/services/doctors/integrative.html

Pennsylvania

Thomas Jefferson University
Jefferson Myrna Brind Center of Integrative Medicine
jeffline.jefferson.edu/jubcim
www.jeffersonhospital.org/cim

University of Pennsylvania
CAM at Penn
www.med.upenn.edu/penncam

University of Pittsburgh
Center for Integrative Medicine
http://integrativemedicine.upmc.com

Tennessee

Vanderbilt University
Vanderbilt Center for Integrative Health
www.vcih.org

Texas

University of Texas Medical Branch
UTMB Integrative Health Care
http://cam.utmb.edu/

Vermont

University of Vermont College of Medicine
Program in Integrative Medicine
www.med.uvm.edu/integrativemedicine

Washington

University of Washington
UW Integrative Health Program
www.uwcam.org

Washington, DC

George Washington University
Center for Integrative Medicine
www.integrativemedicinedc.com

Georgetown University
School of Medicine
http://www8.georgetown.edu/departments/physiology/cam/index.html
http://som.georgetown.edu/

Wisconsin

University of Wisconsin-Madison
UW Integrative Medicine Program
www.uwhealth.org/integrativemed
www.fammed.wisc.edu/integrative

Canada

Alberta

University of Alberta
Complementary and Alternative Research and Education (CARE)
www.care.ualberta.ca/

University of Calgary

Canadian Institute of Natural & Integrative Medicine
www.cinim.org

Ontario

McMaster University
Family Practice Centre of Integrative Health and Healing
www.fpcihh.com

Institute for Systems Biology, Seattle, WA

From their website: http://www.systemsbiology.org/Intro_to_ISB_and_Systems_Biology/Predictive_Preventive_Personalized_and_Participatory

The goal of systems biology is to fundamentally transform the practice of medicine, and ISB researchers have taken the leadership role in catalyzing this transformation. We are developing tools and techniques, and pursuing research that will usher in a new era of predictive, preventive, and personalized medicine.

Today's medicine is reactive: we wait until someone is sick before administering treatment. Medicine of the future will be predictive and preventive, examining the unique biology of an individual to assess their probability of developing various diseases and then designing appropriate treatments, even before the onset of a disease. Today's medicine is also myopic: we use only a few measurements to diagnose disease and are generally unable to make fine distinctions between individuals or between subtle variations of the same disease. Medicine of the future will use more sophisticated measurements, as well as more measurements overall, thereby yielding accurate health assessments for truly personalized treatments.

Improved personal measurements and personalized treatments are the keys to improving health care. Diseases arise from either genetic abnormalities, detrimental environmental factors (poor diet, infectious organisms, or toxins), or a combination of these. We know certain genetic patterns can make a person unusually susceptible to factors in their environment. We also know certain defective genes will increase the probability of an individual having certain health problems. For example, a woman with a single copy of the mutant breast cancer 1 gene (BRCA-1) has a 70 percent chance of developing breast cancer by the time she's 65 years old. Unfortunately, today there is no practical way for each of us to determine our genetic makeup and, more important, to understand the likely health consequences. However, in the future individuals will be able to easily obtain such information, and then work closely with their health practitioner to develop a predictive, preventive and personalized health-care program.

Prediction. The technologies and tools of systems biology will provide medical practitioners with two exciting sources of health-related diagnostic data: By examining an individual's complete genetic makeup, a physician will be able to generate comprehensive predictions about the patient's health prospects. And by examining protein markers which naturally occur in an individual's blood, a physician will be able to accurately determine a person's health status, including both the current effects of any abnormal genes and the current reactions to any environmental toxins or infectious pathogens.

Prevention. The new approach to medicine, based on each individual's genetic makeup, will help us determine the probability of an individual contracting certain diseases, as well as reveal how an individual may respond to various treatments, thereby providing guidance for developing customized therapeutic drugs. Thus another use of the technologies and tools of systems biology will be to develop preventive treatments for individuals, based on their potential health problems, as indicated by their genetic makeup and current blood protein markers.

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The goal of this new approach to medicine will be to use the most fundamental health-related information—an individual's genetic makeup plus current health status as identified by blood protein markers—to prescribe appropriate preventive drugs. For example, given your genetic makeup, you may have a 10% chance of developing breast cancer by age 50, but if you start taking a certain drug at age 35, that chance could drop to 5% at age 50.

In fact, scientists at ISB are currently involved in several research programs involving blood diagnosis of complex diseases, including type 1 diabetes, breast cancer, and prostate cancer. Cancer is the second leading cause of death in the United States, with prostate cancer accounting for one third of all cancer cases among men, and breast cancer accounting for approximately half of all cancer cases among women. ISB scientists are currently researching protein markers which occur in blood to better identify the onset, metastatic potential, and probable course of these cancers in individuals, with the eventual goal of developing more effective treatments.

The common theme running through all of this research and its application to medicine—the predictive and preventive potential of systems biology—is ***personalization***. On average, each human differs from another by less than one percent of their genetic makeup. But these genetic differences give rise to our physical differences, including our potential predisposition to various diseases. So the ability to examine each individual's unique genetic makeup and thereby customize our approaches to medical treatment is at the heart of this new era of predictive, preventive, personalized medicine.

As a result of this personalization, medicine will become ***participatory***. Patients will actively participate in personal choices about illness and well-being. Participatory medicine will require the development of powerful new approaches for securely handling enormous amounts of personal information and for educating both patients and their physicians.

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http://www.systemsbiology.org/Systems_Biology_in_Depth/Premise_of_Systems_Biology

The true test of a good system model is successful prediction of the system's behavior under targeted alterations (genetic or environmental perturbations) of experimental conditions. But the very properties that make biological systems interesting and worthwhile to study their emergent properties, robustness, stability, modularity and adaptability to change, also make their behavior hard to predict at the molecular level. Confounding factors include functional redundancy (i.e., a given process might be accomplished by several different molecular mechanisms), and the stochasticity of cell populations (what is measured, e.g., gene expression, could be an average of a wide range of discrete responses among individual cells).

Systems biologists approach this conundrum by adopting the following principles:

1. Global approaches should be taken to data collection and analyses. Ideally, high-throughput platforms are used to collect accurate measurements under multiple sets of well-defined experimental conditions. Technologies for performing quantitative, multi parameter measurements on a single sample need to be developed. To add value to the analyses of data

obtained from multiplex technologies such as chips and panels of gene deletion mutants or RNAi gene knockouts, global approaches will incorporate relevant findings from curated databases and the published literature.

2. Information derived from diverse data types should be integrated. Systems biology derives power from the leveraging of pre-existing biochemical and cell biology knowledge with the various interaction network models inferred from the global datasets. Even though each source of data type might be sparse, noisy, or contain systematic errors, a meaningful pattern among the diverse data might become apparent and further analysis made possible if the network models are integrated.

3. Mathematical and statistical modeling is essential to the quantitative analysis of a system's properties. Based on a working model and relevant assumptions, computer simulations are used to probe the probable effects of perturbations on a system's components and interactions in the interest of making predictions that can be validated by the collection of more data. Thus, there is a tight integration of computer modeling with experimental design.

4. Biology should drive technology which, in turn, makes better biology possible. Invention of novel or more sophisticated data collection, analysis and modeling tools is motivated by the need to solve a real-world biological problem. As a paradigm case, the Human Genome Project forced the development of high-throughput DNA sequencing methodologies. The need to perform multiparameter measurements on single cells is currently driving the invention of microfluidics/nanotechnology devices.

5. Systems biology research should create an interactive inter-disciplinary scientific culture. For progress to occur, experts in engineering, physics, mathematics, and computer science must join biochemists, cell biologists, and physiologists in the effort to figure out how to obtain the required data and develop the sophisticated computational approaches that will be needed to make viable predictions. For scientists who have been trained primarily in one of these disciplines, doing systems biology research involves stepping outside one's comfort zone to learn new concepts and methodologies. Systems biology-focused institutions accept that cross-disciplinary training from the get-go is the best way for new investigators to embrace the field.

6. The results of research should be freely disseminated. The Human Genome Project has revealed the enormous benefit that derives from the public release of data to the community of researchers. While not as easy to work with as genomic sequence, available microarray datasets, yeast two-hybrid analyses, collections of gene knockout strains and the like have accelerated progress in systems biology research. Similarly, computational biology is facilitated by the sharing of open-source software.

Definition of Evidence-Based Medicine

Extracted from the Centre for Evidence-Based Medicine website; used by permission http://www.cebm.net/index.aspx?o=1014

What is EBM?

This article is based on an editorial from the British Medical Journal on 13th January 1996 (BMJ 1996; 312: 71-2)

Brief definition:

Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.

Expanded definition:

Evidence-Based Medicine, whose philosophical origins extend back to mid-19th century Paris and earlier, remains a hot topic for clinicians, public health practitioners, purchasers, planners, and the public. There are now frequent workshops in how to practice and teach it (one sponsored by this journal will be held in London on April 24th); undergraduate [1] and post-graduate training programmes [2] are incorporating it [3] (or pondering how to do so); British centres for evidence-based practice have been established or planned in adult medicine, child health, surgery, pathology, pharmacotherapy, nursing, general practice, and dentistry; the Cochrane Collaboration and the York Centre for Review and Dissemination in York are providing systematic reviews of the effects of health care; new evidence-based practice journals are being launched; and it has become a common topic in the lay media. But enthusiasm has been mixed with some negative reaction [4-6]. Criticism has ranged from evidence-based medicine being old-hat to it being a dangerous innovation, perpetrated by the arrogant to serve cost-cutters and suppress clinical freedom. As evidence-based medicine continues to evolve and adapt, now is a useful time to refine the discussion of what it is and what it is not.

Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise we mean the proficiency and judgement that individual clinicians acquire through clinical experience and clinical practice. Increased expertise is reflected in many ways, but especially in more effective and efficient diagnosis and in the more thoughtful identification and compassionate use of individual patients' predicaments, rights, and preferences in making clinical decisions about their care. By best available external clinical evidence we mean clinically relevant research, often from the basic sciences of medicine, but especially from patient centred clinical research into the accuracy and precision of diagnostic tests (including the clinical

examination), the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative, and preventive regimens. External clinical evidence both invalidates previously accepted diagnostic tests and treatments and replaces them with new ones that are more powerful, more accurate, more efficacious, and safer.

Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current best evidence, practice risks becoming rapidly out of date, to the detriment of patients.

This description of what evidence-based medicine is helps clarify what evidence-based medicine is not. Evidence-based medicine is neither old-hat nor impossible to practice. The argument that everyone already is doing it falls before evidence of striking variations in both the integration of patient values into our clinical behaviour [7] and in the rates with which clinicians provide interventions to their patients [8]. The difficulties that clinicians face in keeping abreast of all the medical advances reported in primary journals are obvious from a comparison of the time required for reading (for general medicine, enough to examine 19 articles per day, 365 days per year [9]) with the time available (well under an hour per week by British medical consultants, even on self-reports [10]).

The argument that evidence-based medicine can be conducted only from ivory towers and armchairs is refuted by audits in the front lines of clinical care where at least some inpatient clinical teams in general medicine [11], psychiatry (JR Geddes, et al. Royal College of Psychiatrists winter meeting, January 1996), and surgery (P McCulloch, personal communication) have provided evidence-based care to the vast majority of their patients. Such studies show that busy clinicians who devote their scarce reading time to selective, efficient, patient-driven searching, appraisal and incorporation of the best available evidence can practice evidence-based medicine.

Evidence-based medicine is not "cook-book" medicine. Because it requires a bottom-up approach that integrates the best external evidence with individual clinical expertise and patient choice, it cannot result in slavish, cook-book approaches to individual patient care. External clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patient at all and, if so, how it should be integrated into a clinical decision. Similarly, any external guideline must be integrated with individual clinical expertise in deciding whether and how it matches the patient's clinical state, predicament, and preferences, and thus whether it should be applied. Clinicians who fear top-down cook-books will find the advocates of evidence-based medicine joining them at the barricades.

Evidence-based medicine is not cost-cutting medicine. Some fear that evidence-based medicine will be hijacked by purchasers and managers to cut the costs of health care. This would not only be a misuse of evidence-based medicine but suggests a fundamental misunderstanding of its financial consequences. Doctors practising evidence-based medicine will identify and apply the most efficacious interventions to maximise the quality and quantity of life for individual patients: this may raise rather than lower the cost of their care.

Evidence-based medicine is not restricted to randomised trials and meta-analyses. It involves tracking down the best external evidence with which to answer our clinical questions. To find out about the accuracy of a diagnostic test, we need to find proper cross-sectional studies of patients clinically suspected of harbouring the relevant disorder, not a randomised trial. For a question about prognosis, we need proper follow-up studies of patients assembled at a uniform, early point in the clinical course of their disease. And sometimes the evidence we need will come from the basic sciences such as genetics or immunology. It is when asking questions about therapy that we should try to avoid the non-experimental approaches, since these routinely lead to false-positive conclusions about efficacy. Because the randomised trial, and especially the systematic review of several randomised trials, is so much more likely to inform us and so much less likely to mislead us, it has become the "gold standard" for judging whether a treatment does more good than harm. However, some questions about therapy do not require randomised trials (successful interventions for otherwise fatal conditions) or cannot wait for the trials to be conducted. And if no randomised trial has been carried out for our patient's predicament, we follow the trail to the next best external evidence and work from there.

Despite its ancient origins, evidence-based medicine remains a relatively young discipline whose positive impacts are just beginning to be validated [12, 13], and it will continue to evolve. This evolution will be enhanced as several undergraduate, post-graduate and continuing medical education programmes adopt and adapt it to their learners' needs. These programmes, and their evaluations, will provide further information and understanding about what evidence-based medicine is, and what it is not.

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References:

1. British Medical Association: Report of the working party on medical education. London: British Medical Association, 1965.
2. Standing Committee on Postgraduate Medical and Dental Education: Creating a better learning environment in hospitals: 1/Teaching hospital doctors and dentists to teach. London: SCOPMF, 1994.
3. General Medical Council: Education Committee Report. London: General Medical Council, 1994.
4. Grahame-Smith D: Evidence-based medicine: Socratic dissent. BMJ 1995;310:1126-7.
5. Evidence-based medicine, in its place (editorial). Lancet 1995;346:785.
6. Correspondence. Evidence-Based Medicine. Lancet 1995;346:1171-2.
7. Weatherall DJ: The inhumanity of medicine. BMJ 1994;308:1671-2.
8. House of Commons Health Committee. Priority setting in the NHS: purchasing. First report sessions 1994-95. London: HMSO, 1995, (HC 134-1.)
9. Davidoff F, Haynes B, Sackett D, Smith R: Evidence-based medicine: a new journal to help doctors identify the information they need. BMJ 1995;310:1085-6.
10. Sackett DL: Surveys of self-reported reading times of consultants in Oxford, Birmingham, Milton-Keynes, Bristol, Leicester, and Glasgow, 1995. In Rosenberg WMC, Richardson WS, Haynes RB, Sackett DL: Evidence-Based Medicine. London: Churchill-Livingstone (in press).
11. Ellis J, Mulligan I, Rowe J, Sackett DL: Inpatient general medicine is evidence based. Lancet 1995;346:407-10.
12. Bennett RJ, Sackett DL, Haynes RB, Neufeld VR: A controlled trial of teaching critical appraisal of the clinical literature to medical students. JAMA 1987;257:2451-4.
13. Shuo JH, Haynes RB, Johnston ME: Effect of problem-based, self-directed undergraduate education on life-long learning. Can Med Assoc J 1993;148:969-76.

Information about the Chronic Care Model

from www.improvingchroniccare.org

[Permission will be needed if we wish to include the graphic of the model; for the content, permission is not required.]

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Dona Gatsegeorge, M.A., *Web Writer* | Tel 206.287-2092

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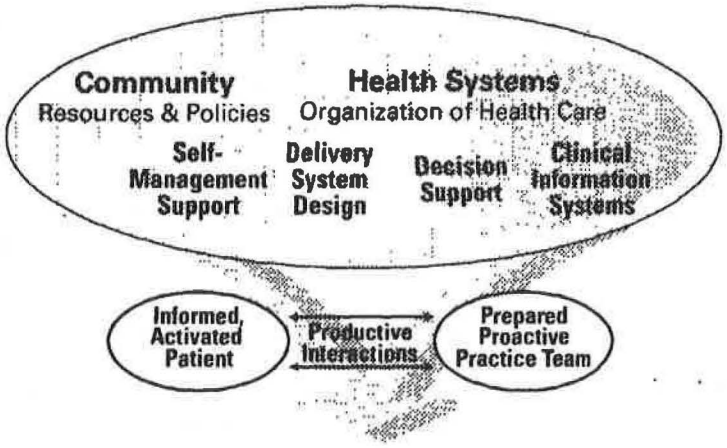
Reprint permission is required for use of the Chronic Care Model image. The copyright holder of the Chronic Care Model image is the American College of Physicians (ACP), which publishes the *Annals of Internal Medicine* journal. All usage of the CCM image requires copyright clearance from ACP. The CCM image first appeared in its current format in this article:

The Chronic Care Model



Improved Outcomes

Promoting effective change in provider groups to support evidence-based clinical and quality improvement across a wide variety of health care settings.

There are many definitions of "chronic conditions," some more expansive than others. We characterize it as any condition that requires ongoing adjustments by the affected person and interactions with the health care system.

133 million people, or almost half of all Americans, live with a chronic condition. 1 That number is projected to increase by more than one percent per year by 2030, resulting in an estimated chronically ill population of 171 million.

Almost half of all people with chronic illness have multiple conditions. As a result, many managed care and integrated delivery systems have taken a great interest in correcting the many deficiencies in current management of diseases such as diabetes, heart disease, depression, asthma and others. 2, 3, 4

Those deficiencies include:

- Rushed practitioners not following established practice guidelines
- Lack of care coordination
- Lack of active follow-up to ensure the best outcomes
- Patients inadequately trained to manage their illnesses

Overcoming these deficiencies will require nothing less than a transformation of health care, from a system that is essentially reactive - responding mainly when a person is sick - to one that is proactive and focused on keeping a person as healthy as possible. (5, 6, 7) To speed the transition, Improving Chronic Illness Care created the Chronic Care Model, which summarizes the basic elements for improving care in health systems at the community, organization, practice and patient levels.

Model Elements

The Chronic Care Model (CCM) identifies the essential elements of a health care system that encourage high-quality chronic disease care. These elements are the community, the health system, self-management support, delivery system design, decision support and clinical information systems. Evidence-based change concepts under each element, in combination, foster productive interactions between informed patients who take an active part in their care and providers with resources and expertise.

The Model can be applied to a variety of chronic illnesses, health care settings and target populations. The bottom line is healthier patients, more satisfied providers, and cost savings.

Development of the Chronic Care Model

The staff at the MacColl Institute for Healthcare Innovation developed the CCM by drawing on available literature about promising strategies for chronic illness management, and organizing that literature in a new more accessible way. The Model was further refined during a nine-month planning project supported by The Robert Wood Johnson Foundation, and revised based on input from a large panel of national experts. It was then used to collect data and analyze innovative programs recommended by experts. RWJF funded the MacColl Institute to test the Model nationally across varied health care settings, creating the national program, "Improving Chronic Illness Care" (ICIC).

Refinements to the Chronic Care Model

In 2003, ICIC and a small group of experts updated the CCM to reflect advances in the field of chronic care both from the research literature and from the scores of health care systems that implemented the Model in their improvement efforts. We list more specific concepts under each of the six elements. Based on more recent evidence, five new themes were incorporated into the CCM:

- Patient Safety (in Health System);
- Cultural competency (in Delivery System Design);
- Care coordination (in Health System and Clinical Information Systems);
- Community policies (in Community Resources and Policies); and
- Care management (in Delivery System Design).

The Model element pages have been redesigned to reflect these updates. Each page describes the overall strategy for each element, and the health system change concepts necessary to achieve improvement in that component. The refinements have been emphasized in bold typeface for ready identification.

Health System

Create a culture, organization and mechanisms that promote safe, high quality care

- Visibly support improvement at all levels of the organization, beginning with the senior leader
- Promote effective improvement strategies aimed at comprehensive system change
- Encourage open and systematic handling of errors and quality problems to improve care
- Provide incentives based on quality of care
- Develop agreements that facilitate care coordination within and across organizations

A system seeking to improve chronic illness care must be motivated and prepared for change throughout the organization. Senior leadership must identify care improvement as important work, and translate it into clear improvement goals and policies that are addressed through application of effective improvement strategies, including use of incentives, that encourage comprehensive system change. Effective organizations try to prevent errors and care problems by reporting and studying mistakes and making appropriate changes to their systems. Breakdowns in communication and care coordination can be prevented through agreements that facilitate communication and data-sharing as patients navigate across settings and providers.

Delivery System Design

Assure the delivery of effective, efficient clinical care and self-management support

- Define roles and distribute tasks among team members
- Use planned interactions to support evidence-based care
- Provide clinical case management services for complex patients
- Ensure regular follow-up by the care team
- Give care that patients understand and that fits with their cultural background

Improving the health of people with chronic illness requires transforming a system that is essentially reactive - responding mainly when a person is sick - to one that is proactive and focused on keeping a person as healthy as possible. That requires not only determining what care is needed, but spelling out roles and tasks for ensuring the patient gets care using structured, planned interactions. And it requires making follow-up a part of standard procedure, so patients aren't left on their own once they leave the doctor's office.[5,6,7] More complex patients may need more intensive management (care or case management) for a period of time to optimize clinic care and self-management. Health literacy and cultural sensitivity are two important emerging concepts in health care. Providers are increasingly being called upon to respond effectively to the diverse cultural and linguistic needs of patients.

Decision Support

Promote clinical care that is consistent with scientific evidence and patient preferences

- Embed evidence-based guidelines into daily clinical practice
- Share evidence-based guidelines and information with patients to encourage their participation
- Use proven provider education methods
- Integrate specialist expertise and primary care

Treatment decisions need to be based on explicit, proven guidelines supported by clinical research. Guidelines should also be discussed with patients so they can understand the principles behind their care. Those who make treatment decisions need ongoing training to stay up-to-date on the latest evidence, using new models of provider education that improve upon traditional continuing medical education. To change practice, guidelines must be integrated through timely reminders, feedback, standing orders and other methods that increase their visibility at the time that clinical decisions are made. The involvement of supportive specialists in the primary care of more complex patients is an important educational modality.

Clinical Information Systems

Organize patient and population data to facilitate efficient and effective care

- Provide timely reminders for providers and patients
- Identify relevant subpopulations for proactive care
- Facilitate individual patient care planning
- Share information with patients and providers to coordinate care
- Monitor performance of practice team and care system

Effective chronic illness care is virtually impossible without information systems that assure ready access to key data on individual patients as well as populations of patients. 11, 12 A comprehensive clinical information system can enhance the care of individual patients by providing timely reminders for needed services, with the summarized data helping to track and plan care. At the practice population level, an information system can identify groups of patients needing additional care as well as facilitate performance monitoring and quality improvement efforts.

Self-Management Support

Empower and prepare patients to manage their health and health care

- Emphasize the patient's central role in managing their health
- Use effective self-management support strategies that include assessment, goal-setting, action planning, problem-solving and follow-up
- Organize internal and community resources to provide ongoing self-management support to patients

All patients with chronic illness make decisions and engage in behaviors that affect their health (self-management). Disease control and outcomes depend to a significant degree on the effectiveness of self-management.

Effective self-management support means more than telling patients what to do. It means acknowledging the patients' central role in their care, one that fosters a sense of responsibility for their own health. It includes the use of proven programs that provide basic information, emotional support, and strategies for living with chronic illness. Self-management support can't begin and end with a class. Using a collaborative approach, providers and patients work together to define problems, set priorities, establish goals, create treatment plans and solve problems along the way.[9]

The Community

Mobilize community resources to meet needs of patients

- Encourage patients to participate in effective community programs
- Form partnerships with community organizations to support and develop interventions that fill gaps in needed services
- Advocate for policies to improve patient care

By looking outside of itself, the health care system can enhance care for its patients and avoid duplicating effort. Community programs can support or expand a health system's care for chronically ill patients, but systems often don't make the most of such resources. A health system might form a partnership with a local senior center that provides exercise classes as an option for elderly patients. State departments of health and other agencies often have a wealth of helpful material available for the asking – wallet cards with tips for controlling diabetes, for example. National patient organizations such as the American Diabetes Association can help by promoting self-help strategies.

Local and state health policies, insurance benefits, civil rights laws for persons with disabilities, and other health-related regulations also play a critical role in chronic illness care. Advocacy by medical organizations on behalf of their patients can make a difference.

Footnotes

1. Partnership for Solutions: Johns Hopkins University, Baltimore, MD for the Robert Wood Johnson Foundation (September 2001 Update). "Chronic Conditions: Making the Case for Ongoing Care"
2. D.H. Stockwell, S. Madhavan, H. Cohen, G. Gibson and M.H. Alderman. "The determinants of hypertension awareness, treatment, and control in an insured population". American Journal of Public Health 84 (1994): 1768-1774
3. S.J. Kenny et al., "Survey of physician practice behaviors related to diabetes mellitus in the U.S.: Physician adherence to consensus recommendations", Diabetes Care 16 (1993): 1507-1510
4. J.M. Perrin, Homer CJ, Berwick DM, Woolf AD, Freeman JL, Wennberg JE. "Variations in rates of hospitalization of children in three urban communities". New England Journal of Medicine 320: 1183-1187
5. E.H. Wagner, B.T. Austin and M. Von Korff. "Improving outcomes in chronic illness". Managed Care Quarterly 4 (1996): (2) 12-25
6. E.H. Wagner, B.T. Austin and M. Von Korff, "Organizing care for patients with chronic illness", Milbank Quarterly 74 (1996): 511-544

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7. E. Calkins, C. Boult, E.H. Wagner and J. Pacala, "New Ways to Care for Older People: Building Systems Based on Evidence", New York: Springer; (1998)

8. D.K. McCulloch, M.J. Price, M. Hindmarsh and E.H. Wagner, "A population-based approach to diabetes management in a primary care setting: early results and lessons learned", Effective Clinical Practice (1998);1:2-22

9. M. Von Korff, J. Gruman, J.K. Schaefer, S.J. Curry and E.H. Wagner, "Collaborative management of chronic illness", Annals of Internal Medicine 127 (1997): 1097-1102

10. W. Katon, M. Von Korff, E. Lin, E. Walker, G.E. Simon, T. Bush, P. Robinson and J. Russo, "Collaborative management to achieve treatment guidelines", Journal of the American Medical Association 275 (1995): 1026-1031

11. M.R. Greenlick, "The emergence of population-based medicine", HMO Practice 9 (1995): 120-122

12. E.H. Wagner, "Population-based management of diabetes care," Patient Education and Counseling 16 (1995): 225-230

13. E.H. Wagner, C. Davis, J. Schaefer, M. Von Korff, B. Austin, "A survey of leading chronic disease management programs: are they consistent with the literature?", Managed Care Quarterly 7 (1999): (3): 56-66

14. Narayan KM, Boyle JP, Geiss LS, Saaddine JB, Thompson TJ. "Impact of Recent Increase in Incidence on Future Diabetes Burden, U.S., 2005-2050", Diabetes Care, 2006, 29 (9), 2114-2116

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EXCERPTS FROM *Patient-Centered Care: Antecedents, Triggers, and Mediators*

Chapter 8, Textbook of Functional Medicine

By Leo Galland, MD

The goal of person-centered diagnosis is to enable healers to develop individualized treatment plans that are based upon an understanding of the physiological, environmental, and psychosocial contexts within which each person's illnesses or dysfunctions occur.... you must start by eliciting all of the patient's concerns. In actively listening to the patient's story, you attempt to discover the **antecedents, triggers** and **mediators** that underlie symptoms, signs, illness behaviors, and demonstrable pathology. Functional medicine is based upon treatment that is collaborative, flexible, and focused on the control or reversal of each person's individual antecedents, triggers and mediators, rather than the treatment of disease entities.

It is the functional medicine practitioner's job to know not just the ailments or their diagnoses, but the physical and social environment in which sickness occurs, the dietary habits of the person who is sick (present diet and pre-illness diet), his beliefs about the illness, the impact of illness on social and psychological function, factors that aggravate or ameliorate symptoms, and factors that predispose to illness or facilitate recovery. This information is necessary for establishing a functional treatment plan.

What modern science has taught us about the genesis of disease can be represented by three words: triggers, mediators, and antecedents. Triggers are discrete entities or events that provoke disease or its symptoms. Microbes are an example. The greatest scientific discovery of the 19th century was the microbial etiology of the major epidemic diseases. Triggers are usually insufficient in and of themselves for disease formation, however. Host response is an essential component.

Identifying the biochemical mediators that underlie host responses was the most productive field of biomedical research during the second half of the 20th century. Mediators, as the word implies, do not "cause" disease. They are intermediaries that contribute to the manifestations of disease. Antecedents are factors that predispose to acute or chronic illness. For a person who is ill, they form the illness diathesis. From the perspective of prevention, they are risk factors. Knowledge of antecedents has provided a rational structure for the organization of preventive medicine and public health.

Medical genomics seeks to better understand disease by identifying the phenotypic expression of disease-related genes and their products. The application of genomic science to clinical medicine requires the integration of antecedents (genes and the factors controlling their expression) with mediators (the downstream products of gene activation). Mediators, triggers, and antecedents are not only key biomedical concepts, they are also important psychosocial concepts. In person-centered diagnosis, the mediators, triggers, and antecedents for each person's illness form the focus of clinical investigation.

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Antecedents and the Origins of Illness

Understanding the antecedents of illness helps the physician understand the unique characteristics of each patient as they relate to his or her current health status. Antecedents may be thought of as congenital or developmental. The most important congenital factor is gender: women and men differ markedly in susceptibility to many disorders. The most important developmental factor is age: what ails children is rarely the same as what ails the elderly. Beyond these obvious factors lies a diversity as complex as the genetic differences and separate life experiences that distinguish one person from another.

Triggers and the Provocation of Illness

A trigger is anything that initiates an acute illness or the emergence of symptoms. The distinction between a trigger and a precipitating event is relative, not absolute; the distinction helps organize the patient's story. As a general rule, triggers only provoke illness as long as the person is exposed to them (or for a short while afterward), whereas a precipitating event initiates a change in health status that persists long after the exposure ends.

Common triggers include physical or psychic trauma, microbes, drugs, allergens, foods (or even the act of eating or drinking), environmental toxins, temperature change, stressful life events, adverse social interactions, and powerful memories. For some conditions, the trigger is such an essential part of our concept of the disease that the two cannot be separated: the disease is either named after the trigger (e.g., "Strep throat") or the absence of the trigger negates the diagnosis (e.g., concussion cannot occur without head trauma). For chronic ailments like asthma, arthritis, or migraine headaches, multiple interacting triggers may be present. All triggers, however, exert their effects through the activation of host-derived mediators. In closed-head trauma, for example, activation of NMDA receptors, induction of nitric oxide synthase (iNOS), and liberation of free intraneuronal calcium determine the late effects. Intravenous magnesium at the time of trauma attenuates severity by altering the mediator response.[2] Sensitivity to different triggers often varies among persons with similar ailments. A prime task of the functional practitioner is to help patients identify important triggers for their ailments and develop strategies for eliminating them or diminishing their virulence.

Mediators and the Formation of Illness

A mediator is anything that produces symptoms, damage to tissues of the body, or the types of behaviors associated with being sick. Mediators vary in form and substance. They may be biochemical (like prostanoids and cytokines), ionic (like hydrogen ions), social (like reinforcement for staying ill), psychological (like fear), or cultural (like beliefs about the nature of illness). A list of common mediators is presented in Table 8.1. Illness in any single person usually involves multiple interacting mediators. Biochemical, psychosocial, and cultural mediators interact continuously in the formation of illness.

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[1] Cernak I, Savic VJ, Kotur J, et al. Characterization of plasma magnesium concentration and oxidative stress following graded traumatic brain injury in humans. J Neurotrauma. 2000;17(1):53-68.

[2] Vink R, Nimmo AJ, Cernak I. An overview of new and novel pharmacotherapies for use in traumatic brain injury. Clin Exp Pharmacol Physiol. 2001;28(1-2):119-121.

Table 8.1 Common Illness Mediators

Biochemical Hormones
- Neurotransmitters
- Neuropeptides
- Cytokines
- Free radicals
- Transcription factors

Subatomic
- Ions
- Electrons
- Electrical and magnetic fields

Cognitive/emotional
- Fear of pain or loss
- Feelings or personal beliefs about illness
- Poor self-esteem, low perceived self-efficacy
- Learned helplessness
- Lack of relevant health information

Social/cultural
- Reinforcement for staying sick
- Behavioral conditioning
- Lack of resources due to social isolation or poverty
- The nature of the sick role and the doctor/patient relationship
- Sample Form used by Functional Medicine Practitioners to Enhance Pattern Recognition

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Immune Surveillance			**Practitioner's Notes**
1	☐	Breastfed How long?	
2	☐	Vaccinated Adverse reactions?	
3	☐	Skin rashes	
	☐	Reaction to contact with significant redness (dermatographia)?	
4	☐	Joint swelling, redness	
5	☐	Dry mouth, lack of salivation	
6	☐	Dry eyes	
7	☐	Migraines Triggered by foods _____ odors _____	
8	☐	Cravings Fatigue after eating certain foods?	
9	☐	Illness, dysfunction after flu-like or GI flu illness	
10	☐	Neurological symptoms that developed slowly over the course of a day and then resolved after several weeks to months, clearing slowly ☐ Change in vision ☐ Coordination ☐ Numbness ☐ Cognitive problems	
11	☐	Family history of autoimmune disease	
12	☐	Multiple infections	
13	☐	Non-specific increased mucus / allergic symptoms	
14	☐	Fatigue	
15	☐	Other:	

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Inflammatory Process			**Practitioner's Notes**
1	☐	Swelling ☐ Diffuse (edema) ☐ Localized (angioedema, papules, eucarin)	
2	☐	Erthema (hyperemia, rashes, erysipelas)	
3	☐	Heat ☐ systemic (fever) ☐ localized (warmth,	
4	☐	Pain (arthralgias, neuralgias, cramping)	
5	☐	Irritation (pruritis, sneezing, etc.)	
6	☐	Loss of function ☐ Associated with pain or scarring ☐ Cognitive impairment (neurodegeneration)	
7	☐	Excessive mucus or fluid production (includes bronchospasm, diarrhea, etc.)	
8	☐	Inflammatory markers ☐ Elevated CRP, ESR, WBC (microscopic or gross purulence) ☐ thrombocytosis ☐ fibrinogen ☐ inflammatory cytokines (IL-1, IL-6, TNF alpha, ☐ decreased complement split products, ☐ homocysteine ☐ lipoprotein A2 (LPA2) ☐ calprotectin (fecal or serum)	
9	☐	Autoantibodies (ANA, RF, or elevated immunoglobulins (abnormal SPEP, tissue transglutaminase IgG, etc.	
10	☐	Elevated free radical markers (lipid peroxides, F2 isoprostanes, 8-OH-d-G)	
11	☐	Hypercoagulability	
12	☐	Other:	

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Digestion, Absorption, Barrier Integrity			**Practitioner's Notes**
1	☐	Symptoms that arise around eating	
2	☐ ☐	Chew your food thoroughly and east slowly or East quickly or on the run	
3	☐	Problems with saliva, such as dry mouth or drooling?	
4	☐ ☐	Experience early satiety, fullness with small portions Consistent discomfort after eating a typical meal	
5	☐	Frequent nauseas Triggered by:_____	
6	☐	Gas or bloating	
7	☐	Burping, belching, gurgling, rumbling	
8	☐	Diagnosed with reflux disease (GERD)? Medication_____ x day, week	
9	☐	Diagnosed with peptic ulcers Antacids_____ x day, week	
10	☐	Tend toward either diarrhea (loose stools) or constipation? If so, which is more typical? Bowel movements_____ x day, week	
11	☐	Stool consistency varies_____ If so, which is more typical? Bowel movements_____ x day / week	
12	☐	Ever sweat intensely after eating certain foods or after meals?	
13	☐	Camp, raft or spend time in wilderness areas and if so, do you drink stream water?	
14	☐	Live with pets? If so, have they had gastrointenstinal infections?	
15	☐	Other:	

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Detoxification and Biotransformation			**Practitioner's Notes**
1	☐ ☐	Smoke ..... how much x day / week..... Exposed regularly to secondhand smoke	
2	☐	Mercury amalgam fillings	
3	☐	Live or work in a densely populated area or near an industrial plant	
4	☐ ☐	Use of pesticides, herbicides, insecticides in the home or garden	
5	☐	Use of chemical preparations at work or as hobby	
6	☐	Breathe toxic elements in the air, fumes or other petrochemicals	
7	☐	Symptoms (fatigue, headaches, nausea) upon exposure to various chemicals (such as perfume, smoke, diesel or gas fumes, etc.)	
8	☐	Eat fish three times a week or more	
9	☐	Prone to problems taking most medications (overly sensitive to most medication and experience numerous side effects)	
10	☐ ☐ ☐	React quickly to dental anesthetics Require repeated administraiton of anesthetic Numbness of one shot lasts a long time	
11	☐	Other:	

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Oxidative/Reductive			**Practitioner's Notes**
1	☐	Smoke ..... how much x day / week..... ..... Exposed regularly to secondhand smoke	
2	☐	Has chronic inflammatory condition or an autoimmune disease	
3	☐	Exercise intolerance	
4	☐	Easily fatigued	
5	☐	Regularly feels 'foggy headed' or mentally fatigued for no apparent reason	
6	☐	Live or work in a densely populated area or near an industrial plant	
7	☐	Use of pesticides, herbicides, insecticides in the home or garden	
8	☐	Breathe toxic elements in the air, fumes or other petrochemicals	
9	☐	Unpleasant or worrisome symptoms at higher altitudes	
10	☐	Radiation exposure ☐ extensive medical radiation ☐ environmental exposure	
11	☐	Fly regularly	
12	☐	Other:	

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Hormone, Neurotransmitter Regulation			**Practitioner's Notes**
1	☐ ☐	Sluggish and unable to get started Agitated/anxious, difficulty slowing down, relax	
2	☐ ☐	Difficulty falling asleep Awaken frequently during the night x _____ Typical reason for waking up_____	
3	☐ ☐ ☐ ☐	Change in metabolism, in weight or energy levels Loss of stamina with weight gain Increased nervousness with weight loss, or A different combination of these problems	
4	☐ ☐	More likely to be calm in a crisis Completely disheveled and agitated even in mildly stressful circumstances	
5	☐	Temperature intolerant: ☐ More often colder than others ☐ More often hotter than others ☐ Variable sensitivity to temperature ☐ Experience hot flashes	
6	☐	Heavy or irregular periods	
7	☐ ☐ ☐	Loss of libido Erectile dysfunction Inability to achieve orgasm	
8	☐	Memory loss or brain fog	
9	☐	Signs or insulin resistance/metabolic syndrome	
10	☐	Problems with mood or lability of emotional responses (rapid mood swings)	
11	☐ ☐	Emotionally stable Emotionally labile	
12	☐	Other:	

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Psychological and Spoiritual Equilibrium			**Practitioner's Notes**
1	☐ ☐	Feeling stressed Problems with acute or chronic stress	
2	☐ ☐	Sadness, depression, emotional lability, anxiety as ☐ current symptoms or ☐ in the past Mood disorders (current or post diagnosis)	
3	☐	Psychiatric diseases: thought disorders, character disorders, neuroses (as a current symptom as well as any history of). Symptoms as well as a formal diagnosis.	
4	☐	Addictions (food, alcohol, drugs, cigarettes)	
5	☐	Problems with body weight (over or under) or image: eating disorders	
6	☐	Self destructive behavior (defined by practitioner or patient)	
7	☐	History of trauma, abuse neglect	
8	☐	Chronic or serious illness or pain in patient, family or friend	
9	☐	Allergies to food/environment that create difficulties (serious issues avoiding allergens) in living	
10	☐	Grief, mourning, loss	
11	☐	Caregiver for a disable, sick or elderly person	
12	☐	Feeling unhappiness with life situation (job, family, friends)	
13	☐	Loss or meaning, faith	
14	☐	Lack or social support	
15	☐	Other:	

PATTERN RECOGNITION: ULCERATIVE COLITIS			
Structural Integrity			**Practitioner's Notes**
1	☐	Joint pain	
2	☐	Pain impacted by movement (better or worse)	
3	☐ ☐	Pains that diminish as the day progresses, returning the next AM Pains that increase as the day progresses, minimized the next AM	
4	☐	Pains impacted by posture	
5	☐	Pains impacted by repositioning the body (worse or better)	
6	☐	Postural abnormalities (head anterior to shoulders, swayback, tilted head, elevated shoulder, hip sway with gait, awkward gait)	
7	☐	Abnormal wear pattern of shoes	
8	☐	Abnormal (awkward) gait patterns	
9	☐	Stiffness in AM getting out of bed, relieved by a hot shower	
10	☐	Other:	

Reforming the United States Health Care System: Implementing an Effective Approach to Chronic Disease

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The Challenge

It is widely acknowledged that the future of the United States health care system is challenged with the rising prevalence of chronic disease (1). The cost of health care per capita is increasing, but there is evidence that children born today will have on average a shorter life expectancy than their parents due to the rising incidence and subsequent burden of chronic disease (2). Thus, the United States health care system is facing a looming crisis. Medicine is in need of a new form of clinical education for physicians as well as an alteration in the health care delivery system that provides more effective preventive care and chronic disease management (3)

Disease Diagnosis versus Early Assessment

The origin of the problem lies in part with the emphasis on disease diagnosis and treatment. This coupled with the absence of an effective system that assesses and intervenes at an early state of illness before the onset of a disease has resulted in the increasing application of ever more expensive intervention and hospitalization (4). Presently the majority of the financial incentives in the health care system are focused on disease diagnosis and treatment by specialists. This translates into less than 10% of students in United States medical schools presently planning on going into the primary component of the health care system for the prevention and management of chronic disease: family practice.

What is Missing

The United States health care system is a very effective provider of hospital-based, specialty disease care, but is not as effective in providing intervention related to the prevention of disease. In 1983 Lewis Thomas, M.D. and past editor of the *New England of Medicine* authored a book entitled "*The Youngest Science*" in which he described how medicine was evolving from a descriptive science where disease diagnosis was the most important feature of medicine to a predictive science based upon the understanding of the etiology of disease. He predicted that by the start of the 21st century the biomedical sciences would have discovered enough about the origin of chronic disease to treat the early cause of the disease, and not just its late state effects (5). His prediction has proven to be largely correct. Over the past thirty years the underlying physiological dysfunctions that give rise to later disease have been discovered. We are witnessing the transition in medical thinking from that which is *reactive* (i.e. pathology-based) to that which is *proactive* (i.e. prognostic-based) based on the understanding of the early alterations in physiological function (6). The emerging understanding of the origin of chronic diseases is that they result from a complex interaction between the genetic uniqueness of the individual with their lifestyle and environment (7). Chronic disease is therefore the result of an alteration in physiological function in the individual that reflects the translation of

genetic susceptibilities through the exposure to specific lifestyle and environmental factors (8).

Functional Prospective Medicine

The present debate surrounding health care reform has focused heavily on universal access to health care and the institutional and financial implications of this objective. These are important objectives, but absent in this dialog has been a discussion concerning the type of health care that will be provided. A continued dominant focus on access to disease treatment in the absence of an equally serious discussion as to how lifestyle medicine will be effectively implemented in medicine to improve physiological function will result in a continued perpetuation of the costly disease intervention focused model.

Synderman and Hood have termed the medicine focused on improving the functional health of the individual as "Prospective Medicine" which has the four characteristics of personalized, predictive, preventive and participatory (9,10,11,12). This medical approach is built upon the emergent science of systems biology which focuses on the underlying functional disturbances in physiology at an early stage in its development prior to the onset of severe pathology (13).

Improved Clinical Outcome with Functional Predictive Medicine

A clinical example of the application of this type of medicine comes from a patient at the Functional Medicine Research Center in Gig Harbor, Washington which I oversee. John H was a 53 year old who has type 2 diabetes. He also has early stage cardiac disease. He was being seen by three different medical specialists each of which was treating under accepted standards of practice one aspect of his complex chronic disease presentation. His diabetes was being managed through the use of insulin injections and insulin stimulating medications, his elevated cholesterol and triglycerides were being managed by another physician with the administration of a statin and fibrate medication, and his hypertension and erectile dysfunction was being managed by a third physician with an angiotensin converting enzyme inhibitor and nitric oxide modulating medications. When he presented to our clinic he was still feeling poorly and his disease indicators were still significant. Using a systems biology, functional approach to his condition the underlying antecedents and lifestyle/environmental factors that underlie his diseases were identified. Using this patient-focused rather than disease-focused approach he was then given a treatment program that fulfills the criteria of personalized, predictive, preventive and participatory. His outcome on this program over twelve weeks was outstanding with an improvement in all his disease indicators, and a concomitant reduction or elimination of all the medications that he was initially taking.

This is a representative example of the type of outcome that can be achieved through the effective application of a systems biology-based intervention program. This is but one of countless hundreds of clinical outcome examples that have been achieved in patients with a variety of chronic diseases through the application of a functional prospective medicine approach.

The cost-effectiveness of this program is enhanced by the use of health extenders in its clinical application. A physician's time is a limited resource. Improvement in both patient outcome and a reduction in the cost of the delivery of a prospective, functional medicine approach to chronic disease have been achieved by the use of health care extenders such as nurses, dietitians, physician assistants and certified lifestyle educators. The use of such resources within the health care team has been demonstrated to improve compliance and personalization of the program to the patient's needs (14).

Recently, Elias Zerhouni, M.D. described in an article in the *New England Journal of Medicine* the importance of translating the latest in biomedical research progress into clinical practice to improve patient outcomes (15) He stated that it is "time for a new vision". This concept is applicable for both the management of chronic as well as acute diseases. The *Textbook of Functional Medicine* describes a successful way of introducing systems biology thinking and prospective medicine into clinical practice for the management of complex chronic diseases (16). In a recent article in the *New England Journal of Medicine* AL Barabasi indicated that the future of medicine will be in the implementation of a system that incorporates the understanding that disease arises from a complex alteration in the physiological network that connects genetic uniqueness to environmental and social factors (17). The Institute for Functional Medicine has been providing continuing medical education courses surrounding the concept of a patient-centered, systems biology approach to the management of chronic disease since 1991. There are presently more than 10,000 physicians who have attended the Institute for Functional Medicine courses, and are utilizing aspects of this patient-centered, prospective approach to health care for the successful management of their patients.

The Tools We Need Are Available Now

We are standing at the frontier of a new medicine based upon the recent biomedical discoveries of the origin of chronic diseases, and the recognition that they are rooted in the gene-environment interaction. This new medicine is systems biology rather than disease focused (18). It is a medicine that takes its lead from the understanding of the human disease network that connects the individual's genetic uniqueness with their lifestyle, environment and social network (19). It redefines chronic disease as a functional alteration in the physiological network that requires a system approach to clinical intervention to improve both the safety and effectiveness of therapy (20,21).

We have the tools to create a more effective health care delivery system today. We need to seriously address how to implement a nationwide clinical training program in prospective, functional medicine. We need to develop reimbursement procedures for prospective, functional interventions that provide support for assessment, patient education, and therapy. We need to harness the talents and expertise of health care extenders to provide patient services in the delivery of a personalized, predictive, preventive and participatory medicine for the reduction in the burden of chronic disease.

The tools we need are available, the effectiveness of the approach has been demonstrated through the successful clinical application of this model by thousands of health care providers over the past fifteen years, and the development of many of the clinical

biomarkers for the functional assessment of patients has been accomplished (22). What is now needed is a fundamental paradigm shift in the way regulators, overseers of institutional medicine, and third party payers think about the origin of chronic disease from a systems biology, functional perspective (23).

References

1. Bar-Yam Y, "Improving the effectiveness of health care and public health: A multiscale complex systems analysis", American Journal of Public Health 2006; 96: 459-466.
2. Olshansky SJ, Passaro DJ, Heshaw RC, Layden J, Carnes BA, Brody J, Hayflick L, Butler RN, and Ludwig DS, "A potential decline in life expectancy in the United States in the 21st century", N Engl J Med 2005; 352: 1138-1145.
3. Holman H, "Chronic disease-the need for a new clinical education", JAMA 2004; 292: 1057-1059.
4 Bland JS, "Functional somatic syndromes, stress pathologies and epigenetics", Alter Ther Health Med 2008; 14 (1): 14-16.
5. Thomas L, "The youngest science: notes of a biology watcher", Penguin Books 1983, New York.
6. Bland JS, "Systems biology, functional medicine and folates", Alter Ther Health Med 2008; 14 (3): 18-20.
7. Ordovas J, "Gene-environment interaction and susceptibility to metabolic syndrome and other chronic diseases", J Periodontology 2008; 79: 1508-1513.
8. Coyle YM, "Lifestyle, genes and cancer", Methods Mol Biol 2009; 472: 25-56.
9. Snyderman R and Williams, RS, "Prospective medicine: the next health care transformation", Academic Medicine 2003; 78: 1079-1084.
10. Auffray C, Zhu C, and Hood L, "Systems medicine: the future of medical genomics and health", Genome Medicine 2009; 1: 2-26.
11. Weston AD, and Hood L, "Systems biology, proteomics and the future of health care: toward predictive, preventative, and personalized medicine", J Proteome Res 2004; 3: 179-196.
12. Snyderman R, and Langheier J, "Prospective health care: the second transformation of medicine", Genome Biol 2006; 7: 104-112.
13. Hood L, Heath J, Phelps M, and Lin B, "Systems biology and new technologies enable predictive and preventative medicine", Science 2004; 306: 640-643.
14. Dagogo-Jack S, "Preventing diabetes-related morbidity and mortality in a primary care setting", J Natl Med Assoc 2002; 94: 549-560.
15. Zerhouni EA, "Translational and clinical science-time for a new vision", N Engl J Med 2005; 353: 1621-1623.
16. "Textbook of Functional Medicine", 2005, Jones D, editor, Institute for Functional Medicine, Gig Harbor, Washington.
17. Barabasi AL, "Network medicine-from obesity to the 'diseasome'", N Engl J Med 2007; 357. 37-379.
18. Aderem A, "Systems biology: its practice and challenges", Cell 2005; 121: 511-513.
19. Goh K, Cusick ME, Valle D, Childs B, Vidal M, and Barabasi A, "The human disease network", Proc Natl Acad Sci 2007; 104: 8685-8690.

20. Nicholson JK, "Global systems biology: personalized medicine and molecular epidemiology", Mol Systems Biol 2006; 10: 1-6.
21. Ahn AC, Tewari M, Poon C, and Phillips RS, "The clinical application of a systems approach", Plos Medicine 2006; 3: 956-959.
22. Bland JS, "Importance of functional biomarkers in the management of chronic disease", Alter Ther Health Med 2008, 14(4):18-21.
23. Ahn AC, Tewari M, Poon C, and Phillips RS, "The limits of reductionism in medicine: could systems biology offer an alternative?", PlosMedicine 2006; 3: 709-712.

RELEASE IN FULL

A WELLNESS INITIATIVE FOR THE NATION

SUMMARY DOCUMENT

PURPOSE

The purpose of the Wellness Initiative for the Nation (WIN) is to **proactively prevent disease and illness, promote health and productivity, and create well-being and flourishing for the people of America.** WIN can also prevent the looming fiscal disaster in our health care system. In fact, effectively addressing preventable chronic illness and creating a productive, self-care society is our only long-term hope for changing a system that costs too much and is delivering less health and little care to fewer people. [1, 3]

OVERVIEW AND RECOMMENDATIONS

★ The overarching recommendation is to **create a Wellness Initiative for the Nation focused on promotion of health through lifestyle change and integrative health practices.** WIN would be overseen by the White House, with a Director and staff to guide relevant aspects of health reform, as described in the recent report, *The Health Care Delivery System: A Blueprint for Reform (the "Blueprint").* [4]

★ WIN will focus primarily on **accomplishing goal three of the Obama/Biden Health Reform Plan** – "improve prevention and public health" – and support development of an educational workforce and informational toolkit for delivery of this goal in local populations. WIN leadership will provide program analysis, develop policies, guide curriculum and evidence standards, and establish incentives and mechanisms that support these efforts in national health care reform.

★ **WIN will align with overarching goals** of the "Blueprint" and Healthy People 2010 (Increasing Quality and Years of Healthy Life and Eliminating Health Disparities) [5] and link to recommendations such as the "Wellness Trust," [6] a "Federal Health Reserve," [7] the Institute of Medicine's reports on health care quality, [8] transformation, [9] integrative medicine, [10] and the White House Commission on Complementary and Alternative Medicine Policy. [11]

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The initial step towards a Wellness Initiative for the Nation (WIN) is to create a White House office, with a Director and staff, specifically focused on developing policies and programs for lifestyle-based chronic disease prevention and management, integrative health care practices and health promotion.

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★ The initial step of WIN is to **create a White House office,** with a Director and staff, specifically focused on developing policies and programs for lifestyle-based chronic disease prevention and management, integrative health care practices and health promotion.

★ The policies and programs of WIN would be grounded in the **continuity of health and the prevention of illness throughout the human lifecycle** and would approach this continuity through comprehensive lifestyle and integrative health care approaches that have demonstrated effectiveness.

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Other specific recommendations are as follows:

1. SYSTEMS WELLNESS ADVANCEMENT TEAMS NETWORK *("THE INNOVATORS")*

★ Establish a network of Systems Wellness Advancement Teams (SWAT) with national and then local leaders in health promotion/disease prevention and integrative practices to maintain the wellness vision and guide the White House in the implementation of this new paradigm.

★ Empower the SWAT network to continuously evaluate and translate effective prevention and health promotion practices into local delivery tools and policy changes.

★ Create learning communities that evaluate and translate innovations in lifestyle and integrative health practices into new settings and populations across the network.

2. HEALTH AND WELLNESS PROFESSIONAL COACH TRAINING *("THE ADVOCATES")*

★ Establish educational and practice standards in delivery of effective, comprehensive lifestyle and integrative health care approaches, and train individuals qualified to focus full-time on prevention, creating health and healing, and enhancing productivity and flourishing.

★ Facilitate any qualified and state licensed health care practitioner or educator to gain specialist certification in prevention, health and wellness delivery, or attain sub-specialist status for integrative health care delivery in specific settings and populations--for example, schools, worksites, health care settings, and long-term care facilities.

★ Create a Health Corps to provide an army of young and older people that would learn and model wellness behavior and support delivery of wellness education and training by the coaches.

3. HEALTH AND WELLNESS INFORMATION TECHNOLOGY TOOLKIT *("THE AVATARS")*

★ Create an advanced information tracking and feedback system (an applied health promotion technology toolkit) for delivery of personalized wellness education, customized to each person's level of readiness, IT capabilities and stage of life.

★ Interface this applied wellness toolkit with electronic health records for use by the public, the health and wellness coaches, the Health Corps, and the medical and health care delivery systems.

★ Coalesce current health promotion/prevention knowledge into a science-based Health Quotient Index (HQI) for personalized delivery of information to individuals and communities through multiple interface.

4. ECONOMIC AND SOCIAL INCENTIVES *("THE INDUSTRY")*

★ Create economic incentives (through bundling, capitation, premium reductions, tax reductions and other methods) for individuals, communities, and public and private sector institutions to create and deliver self-care training, wellness products and preventive health care practices.

★ Establish intellectual property protection policies that reward wellness innovations, using the latest technologies with evidence-based and comparative cost-value determinations.

★ Establish incentives for both personal and community activities that establish social and cultural change, which creates public wellness values and a flourishing society.

These recommendations are designed to work in a coordinated fashion on the specific leverage points of cultural and institutional change. If applied in concert, theses recommendations are a "triple multiplier" of health, productivity and economic stimulus for the country by: 1) creating new jobs in the educational, health and technology sectors; 2) increasing health and productivity across the population in both the short and long-run; and, 3) stimulating innovation and investment by the private sector into the creation of a health and wellness industry and society.

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The United States is first in spending for health care but 37th in health status among industrialized nations. If applied in concert, theses recommendations are a "triple multiplier" of health, productivity and economic stimulus for our nation.

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A PHASED PROGRAM

The WIN will use a phased approach to assure that prevention and health promotion programs are rolled out in a coordinated, systematic, stepwise and effective manner with full input from the public and stakeholders involved in wellness delivery. **Recommended phases** include:

Phase 1: ***Create a working group and coordinating office within the White House*** that is specifically focused on creating policies and programs for lifestyle-based chronic disease prevention and management, integrative health care practices and health promotion;

Phase 2: ***Establish a lead Systems Wellness Advancement Team (SWAT)*** of national leaders in health promotion, disease prevention, and integrative practices to guide the office;

Phase 3: ***Define the "new paradigm"*** – the key vision, strategies, and tactics and the effective elements and metrics of comprehensive lifestyle and integrative health care practices that will be the focus of WIN;

Phase 4: ***Collate, coordinate and align current health promotion and prevention policy efforts*** such as, House Concurrent Resolution 406, The Health Promotion First Act, the Healthy Workforce Act, The Health Project, the 1st Dollar Clinical Preventive Services Coverage, the Medicare Improvement Act, the Public Health Advisory Committee, and consensus statements by the Partnership for Prevention, the Prevention Institute, the American College of Occupational and Environmental Medicine, and other programs and recommendations;[12]

Phase 5: Use and evaluate current Department of Defense, Veterans Health Affairs, Medicare and workforce health, performance enhancement and wellness initiatives to rapidly ***establish models for delivery of national WIN projects;***

Phase 6: ***Create and evaluate new demonstration projects*** in each of the WIN lifecycle populations (e.g., children, worksites and aging; see below for details) to improve the cost-value of national programs created by the WIN; set up selection, modeling and evaluation parameters using indices such as COMPARE and Health Impact Assessment (HIA) processes;[13 14]

Phase 7: ***Create parallel legislative tracks*** to support and incentivize effective public and private wellness initiatives throughout the nation;

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BACKGROUND

Too many Americans go without high-value preventive services and health promotion practices. [5] As a result, they get sick and utilize expensive medical interventions. [1] Examples of underutilized preventive and health promotion practices include cancer screening to prevent advanced colon disease, immunizations to protect against flu or pneumonia, fitness and resilience training to enhance productivity and well-being, self-care and integrative health practices to treat chronic pain and enhance healing, and healthy lifestyle education to prevent diabetes, hypertension, stroke, cardiovascular disease and cancer.

The nation (and increasingly the world) faces epidemics of obesity, mental illness and chronic disease, as well as new threats of pandemic flu and bioterrorism. [15, 16] Yet despite all of this, less than four cents of every health care dollar is spent on prevention and public health. [17] We are first in spending for health care and 37th in health of the industrialized nations. [18] At current cost rates, health care will make up 25% of the GNP by 2025 and 49% by 2082! [19] The first of the "baby boomers" will turn 65 in 2011, creating an avalanche of aging care needs that will bury the current Medicare system. Our health care system is a broken disease treatment system, and the time for change is well overdue.

True prevention and health promotion requires something different than just access to current services. It requires a new vision of health and disease based on the primary components of human flourishing. Science has now clearly demonstrated a radically new view of chronic health and disease than the one developed over 100 years ago and currently in use. No longer is it reasonable to wait until disease reaches an advanced diagnostic threshold before our system provides expensive interventions.

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In his book The Power of Progress, John Podesta summarizes the situation succinctly. "It is not enough to merely expand access to the current system. Americans must also secure better value for their health care dollars through improved health care quality, outcomes, and efficiency. First, we must create a national focus on disease prevention and health promotion. The United States is plagued by preventable diseases that have a devastating impact on personal health and contribute to the nation's soaring health costs. Yet our current system focuses on treating these diseases after they occur, rather than promoting good health and reducing the incidence of disease in the first place." [2] *(pg. 182)*

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THE COST OF AVOIDABLE CHRONIC ILLNESS

★ A recent Milken Institute report showed that the combined cost of the top seven modifiable chronic diseases (cancer, diabetes, hypertension, stroke, heart disease, pulmonary conditions, and mental disorders) exceeds $270 billion per year in direct care costs and, with the addition of lost productivity, reaches over $1 trillion annually. [20]

★ These costs are largely avoidable by changes in behavior. A modest focus on prevention, early intervention and behavioral change could save annually in treatment and productivity loss costs an estimated $217 billion and $1.6 trillion, respectively. This could add over $6.9 trillion to the GDP between now and 2023—27% of the GDP's economic impact.

★ Modest gains in just smoking and obesity control, for example, would reduce illness in the top seven conditions by 24-30 million, save up to $100 billion in treatment costs, and add from $340-500 billion to the GDP in the next 15 years.

★ Application of the top 20 proven clinical preventive services (CPS) would save an additional $4 billion in treatment costs and increase quality of life years by over 2 million. [21] WIN will focus on effective delivery for the 10 CPS recommendations that address core primary prevention and lifestyle change factors. [21]

★ Suffering associated with chronic disease and pain produces an even greater burden, the cost of which is not quantifiable. Self-care practices can reduce pain, improve quality of life and enhance well-being. [22, 23, 24] Complementary health care practices are especially useful in this regard. [25,26]

CAUSES OF AVOIDABLE CHRONIC DISEASE

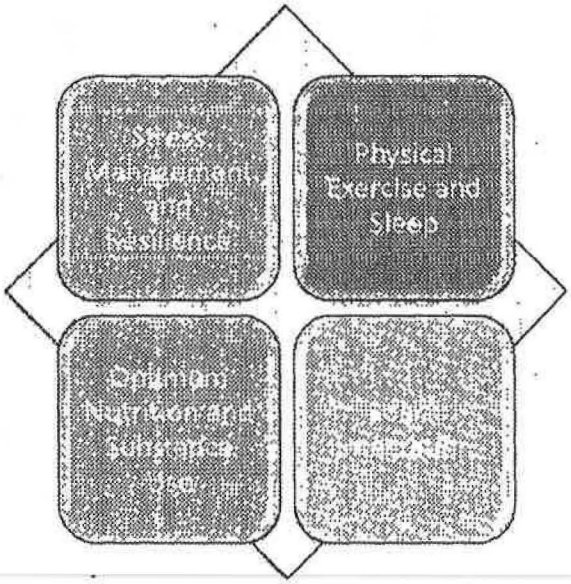
★ Seventy percent of avoidable costs could be mitigated by behavior changes that involve healthy lifestyle development, wellness enhancement, and early detection and intervention for the conditions listed above. Two-thirds of chronic illness is caused by lifestyle and behavioral factors that are influenced by our mental, social or physical environments. [27]

★ Five behavioral factors contribute the most to mitigating costs and to increasing sustainable wellness. These are: 1) reducing toxic substance exposure (smoking, alcohol, drugs and pollution); 2) sufficient exercise; 3) healthy diet; 4) psychosocial integration and stress management; and 5) early detection and intervention. [20, 28]

★ To achieve gains in wellness and productivity requires a change in the nature of the culture and services provided to our communities. Increased access to our current disease treatment system is not sufficient and will increase costs. We need a concerted investment in creating a flourishing human capital focused on prevention, productivity, healing and well-being. [29]

COMPONENTS OF HUMAN HEALTH BEHAVIOR AND PRODUCTIVITY OPTIMIZATION

We know now that health and disease are a continuum and we know the fundamental elements that move us along that continuum. Both before and after the threshold, between health and disease, the basic elements of health promotion can slow or prevent chronic disease progression and enhance function, productivity and well-being. No matter what the illness or stage of life we now know that the same components of human health behavior and productivity optimization apply. These components are:



1. ***Stress Management and Resilience.*** The first component is the induction of mind-body states known to counter the stress response and improve readiness and motivational factors for lifestyle change. Recent research has demonstrated that mind/body practices can be taught and can counter the physical and psychological effects of stress, prevent PTSD, increase fitness and weight management, and enhance cognitive and physical function.

2. ***Physical Exercise and Sleep.*** The second component is physical exercise. Optimum physical exercise can reduce stress hormone swings and improve brain function, improve fitness and enhance weight control. Fitness, along with proper rest and sleep, and rapid management of injury from physical training, will maintain functioning and productivity.

3. ***Optimum Nutrition and Substance Use.*** Third, ideal weight and optimal physiological function occurs best in the context of proper nutrition and reduced exposure to chemicals (such as smoking, alcohol and drugs) that impair

function. Food and substance management requires systematic motivational systems, environmental control, food and substance selection training, and family and community involvement.

4. ***Social Integration.*** Finally, the social environment is key. Social integration is not only health enhancing in its own right, but is essential for sustainability of behavior change. Health promotion is best achieved in a group and community context, in which common issues in the culture around behavior and lifestyle change are valued and shared with peers, friends and family. Both health and happiness are socially contagious. Social integration allows individuals, their families and communities the opportunity to spread healthy behavior and find day-to-day solutions for maintaining well-being and resilience.

A culture and industry that values and optimizes these components will produce a flourishing, productive society. In addition, the impending economic disaster of continuing to solely apply the current sickness treatment system to our rapidly aging population can be altered at its core. The policy recommendations of WIN are designed to focus directly on optimizing these components for individuals and communities.

CREATING SOURCES OF PREVENTION, PRODUCTIVITY, HEALING AND WELLNESS

★ Public policy should support, stimulate and enhance each individual's inherent wellness and healing capacities since this provides the most powerful force we have for maintaining health and productivity when well, and for enhancing recovery and well-being when ill. [30]

★ Approaches to the prevention of chronic disease, detection of early risk factors, and enhancement of well-being are well known but not done well or systemically by our health care system. [1]

★ Central to a new model of prevention and health care are the development of Optimal Healing Environments (OHE) [31] and integrative health care practices [26] that can support and stimulate inherent healing capacities on mental, social, spiritual and physical levels. As described below, many of these practices provide lower cost alternatives to current conventional practices. [32, 33]

★ Of the "Blueprint" recommendations, WIN will focus specifically on supporting areas in "Patient Activation" (pp 81-95) and "Public Health" (pp. 96-111) but also contribute to other areas, including nurse and geriatric training (p. 9, 23), wellness information technology (p. 27, 47), and developing bundling, capitation and tax relief approaches for delivery of evidence-based health promotion and integrative health care practices (p. 69-71).

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Public policy should support, stimulate and enhance each individual's inherent wellness and healing capacities since this provides the most powerful force we have for maintaining health and productivity when well, and for enhancing recovery and well-being when ill.

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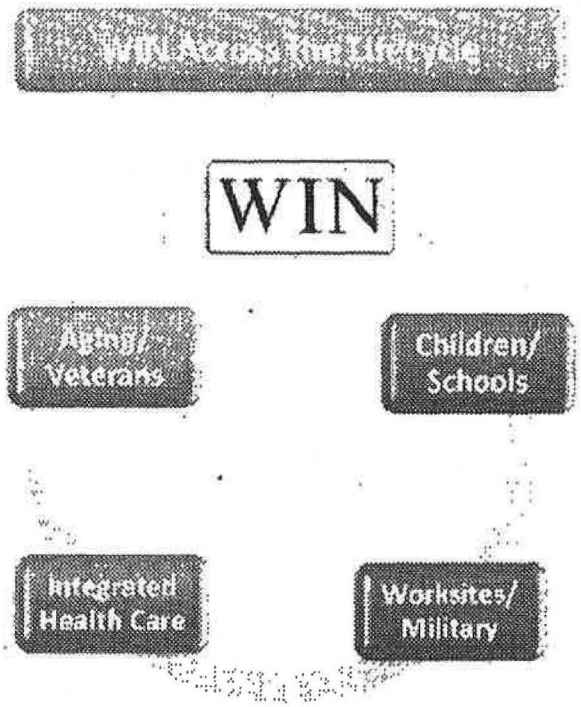
MODELS OF SUCCESSFUL PREVENTION AND HEALTH PROMOTION

THE MILITARY

The military has been at the forefront of health promotion and performance enhancement innovations for decades and has recently developed a renewed effort in "human performance optimization". [34] The non-profit Samueli Institute is working closely with a coalition of military partners to develop the next generation "Systems Wellness System" as a model for combining systems biology with lifestyle change to develop personalized prevention and health promotion tools. [35] This program could become a model for national application.

HEALTH CARE DELIVERY SYSTEMS

The health care delivery industry has a major role in advancing prevention and wellness and the "Blueprint" is primarily focused on this area. A recent study of eight "exemplar" OHE programs in health systems demonstrated the ways in which WIN could translate current innovations in health promotion and healing into our health care systems. [36] The use of health information technology could further extend skills in health promotion and self-care and disease management beyond the walls of the hospital and into communities and the home. [37]



SELF-CARE AND INTEGRATED CARE

The widespread application of selected, evidence-based integrated health care practices could markedly improve quality of life and reduce costs. [33] Behavioral and mind-body practices have been repeatedly demonstrated to enhance quality of life, improve self-care and reduce costs. [38] Acupuncture has now been definitively shown to improve chronic pain conditions (head, neck, knee and back) at almost twice the rate of guideline-based conventional treatment. [39, 40] Massage may be even more cost effective in back pain. [41] Massage has also been shown in multiple studies to accelerate recovery of premature babies, with projected cost savings of $4.7 billion per year if widely used. [42] Training retired persons to deliver this infant massage results in reduced depression and enhanced quality of life in those giving the massage – a double benefit. [43] Herbs and dietary supplements are widely used by the population but with little to no guidance on what is safe and effective. [44] Under current policies, these practices and products are not sufficiently profitable to provide economic incentives for research and investment. Thus, they remain under-investigated and unutilized at the expense of higher cost and more heroic treatment approaches. A properly focused wellness policy would change this situation.

WORKSITES

It is now well established that multi-component worksite wellness programs enhance productivity, well-being and return on investment (ROI) in industry. [45] For example, Procter and Gamble and the Dow Chemical Company have improved productivity and reduced health care costs, with a positive ROI for their programs at multiple sites. [46, 47] Companies are now extending these efforts to reducing costs of medical treatment and for chronic disease prevention and management. [48] Health promotion efforts for America's workers is a double multiplier for the economy by improving productivity and creating jobs. [49] The C. Everett Koop Awards of The Health Project have selected some of the most successful and innovative health promotion programs that could be applied nationally by the WIN. [50]

COMMUNITY-BASED PROGRAMS

Community-based, comprehensive lifestyle modification programs have demonstrated effectiveness for mitigating cardiovascular risk factors[51], stroke prevention[52], smoking cessation [53], treating obesity[54] and osteoporosis[55], and diabetes prevention[56], as well as other chronic conditions. [57] In Japan, comprehensive lifestyle modification programs including physical exercise and diet/nutrition education have been implemented and extensively evaluated in work sites and in elderly populations, and results have shown dramatic improvements for obesity and lifestyle-related disease. [58] The Centers for Disease Control and Prevention (CDC) has targeted community-based programs as an effective vehicle for delivering health promotion and disease prevention campaigns.

CHILDREN

Wellness must start with children by teaching them lifelong healthy habits. Healthy habits need to be a core competency delivered by our educational system. A number of exemplar programs in schools have produced major impacts on wellness behavior, including effects on obesity. For example, a school program in underserved elementary school children has demonstrated improved health behaviors that spread to families and the surrounding community. [59] Other examples are the *Planet Health Program, and the VERB Program.* [60, 61, 62, 63, 64] The *Wellspring Academy's* schools, camps and community programs have produced marked success in improved weight management, enhanced self-esteem and improved mental health during adolescence, a difficult time of life to affect change. [60, 65]

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The Wellness Initiative for the Nation will select the best of these programs and develop policies to establish them throughout the United States. The long-term impact of such policies would be a golden age of health, productivity and well-being; a flourishing and great society.

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AGING

Our population is rapidly aging, resulting in ballooning of chronic disease and illness. The majority of health care costs are expended in the last years of life. The older population is highly motivated for self-care and makes extensive use of complementary and alternative practices, some helpful and some harmful. [66, 67] Extending functional years through prevention (such as vaccination), early detection (such as screening), lifestyle and self-management training can also reduce costs of chronic disease treatment. For example, simple procedures (such as providing a health coach or call nurse) significantly reduce health care costs and mortality in cardiovascular disease. [68] Extension of health care into the home with TeleHealth (the delivery of health-related services and information via telecommunications technologies) could further maintain function and reduce costs in the senior population up to 70% with current technologies. [69, 70 71] A set of recently funded Centers for Medicare & Medicaid Services (CMS) demonstration projects of health promotion in older people are examples of programs that serve as national models under the WIN. [72]

THE UNDERSERVED

The widening gap in health disparities is one of the major moral failures of our society. [73] Social isolation and socio-economic class are major determinants of chronic disease and premature death. [27] The poor often seek out and use self-care and complementary medical practices, but get little guidance on which practices are effective or harmful. [74] Self-care and integrative health care approaches, when properly delivered, can significantly improve health in these populations. For example, a recent Medicaid demonstration project providing integrative health care found an 86% reduction in pain, 25% reduction in health care utilization and 20% reduction in prescription drug use in an underserved community. [75, 76] The Samueli Institute, along with the Institute for Alternative Futures and the Health Resources and Services Administration recently brought together integrated health care programs for the underserved as possible models for WIN. [74]

These examples are only a few of the practices that could improve health, productivity and well-being, and reduce costs from disease and disability in our nation. For other examples involving disease screening, vaccination, nutritional practices and educational programs, see the governmental summaries on those areas. [5, 77, 78-86]

REFERENCES

1. Editorial: Tackling the burden of chronic diseases in the USA. Lancet. 373; 981. Jan 17, 2009. See also: Park A. America's health check-up. *Time Magazine.* 2008; December 1:41-51.
2. Podesta J. *The Power of Progress: How America's Progressives Can (Once Again) Save Our Economy, Our Climate, And Our Country*: Crown / RandomHouse 2008.

3. Schoen C, Osborn R, How SK, Doty MM, Peugh J. In Chronic Condition: Experiences Of Patients With Complex Health Care Needs, In Eight Countries, 2008. *Health Aff (Millwood).* Nov 13 2008.
4. Center for American Progress and the Institute on Medicine as a Profession. *The Health Care Delivery System: A Blueprint for Reform* 2008. http://www.americanprogress.org/issues/2008/10/health_care_delivery.html Accessed January 2, 2009.
5. Healthy People. http://www.healthypeople.gov/ Accessed December 2, 2009.
6. Lambrew J, Podesta J, Center for American Progress. Promoting prevention and preempting costs: A new wellness trust for the United States. *Center for American Progress.* 2006; http://www.americanprogress.org/issues/2006/10/pdf/health_lambrew.pdf.
7. Daschle T, Lambrew J, Greenberger S. *Critical: What We Can Do About the Health Care Crisis.* New York: St. Martin's Press; 2008.
8. Institute of Medicine. *Crossing the Quality Chasm: A new health system for the 21st century.* Washington, DC: National Academic Press; 2001.
9. Adams K, Corrigan J. *Priority Areas for National Action: Transforming Health Care Quality.* Washington, DC: National Academies Press; 2003.
10. Institute of Medicine. *Complementary and Alternative Medicine in the United States.* Washington, DC: National Academies Press; 2005.
11. *White House Commission on Complementary and Alternative Medicine Policy: Final Report* 2002. www.whccamp.hhs.gov Accessed December 2, 2009.
12. Samueli Institute. Alignment of the WIN. http://www.siib.org/news/news-home/112-SIIB.html. 2009; Accessed January 21, 2009.
13. Cole B, Fielding J. Building Health Impact Assessment (HIA) Capacity: A strategy for Congress and Government Agencies. *A Prevention Policy Paper Commissioned by Partnership for Prevention* http://thehill.com/wppdf/PfP_HealthImpactAssessment.pdf. Accessed January 20, 2009.
14. RAND COMPARE. http://www.randcompare.org/ *Accessed January 20, 2009.*
15. World Health Organization. *Primary Health Care: Now More Than Ever.* Washington, DC: World Health Organization; 2008. http://www.who.int/whr/2008/en/index.html Accessed January 2, 2009.
16. Demyttenaere K, Bruffaerts R, Posada-Villa J, et al. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *JAMA.* Jun 2 2004;291(21):2581-2590.
17. Lambrew J. *A Wellness Trust to Prioritize Disease Prevention*: Brookings Institute; April 2007. www3.brookings.edu/views/papers/200704lambrew.pdf Accessed December 2, 2008.
18. World Health Organization. *Health Systems: Improving Performance.* Geneva: World Health Organization; 2000. www.who.int/whr/2000/en Accessed December 2, 2008.
19. Congressional Budget Office. *The Long-Term Outlook for Health Care Spending* November, 2007. www.cbo.gov/ftpdocs/87xx/doc8758/11-13-LT-Health.pdf Accessed December 2, 2008.
20. DeVol R, Bedroussian A, Charuworn A, et al. *An Unhealthy America: The Economic Burden of Chronic Disease -- Charting a New Course to Save Lives and Increase Productivity and Economic Growth.* Santa Monica, CA: Milken Institute; October 2007.
21. Partnership for Prevention. *Real Health Reform Starts with Prevention* December 2008. www.prevent.org/HealthReform Accessed January 2, 2009.
22. Lorig KR, Sobel DS, Ritter PL, Laurent D, Hobbs M. Effect of a self-management program on patients with chronic disease. *Eff Clin Pract.* Nov-Dec 2001;4(6):256-262.
23. Duensing L. Shifting the health care paradigm: An interview with Wayne Jonas, MD, President and Chief Executive Officer of the Samueli Institute. *The Pain Practitioner.* 2008;18(2):48-54.
24. Brown K. Biopsychosocial perspectives of chronic pain, depression and effective medical therapeutics. *The Pain Practitioner.* 2008;18(2):38-47.
25. Snyder M, Wieland J. Complementary and alternative therapies: what is their place in the management of chronic pain? *Nurs Clin North Am.* Sep 2003;38(3):495-508.
26. Jonas WB, Levin J. *Essentials of Complementary and Alternative Medicine.* Philadelphia: Lippincott Williams & Wilkins; 1999.
27. McGinnis JM, Russo P, Knickman J. The case for more active policy attention. *Health Affairs.* 2002;21(2):78-93.
28. McGinnis JM. A vision for health in our new century. *Am J Health Promot.* Nov-Dec 2003;18(2):146-150.
29. Schroder s. We can do better-improving the health of the American people. *N Engl J Med.* 2007;357:1221-1228.
30. Walach H, Jonas WB. Placebo research: the evidence base for harnessing self-healing capacities. *J Altern Complement Med.* 2004;10(Suppl):S103-S112.
31. Chez R, Pelletier K, Jonas WB. Toward optimal healing environments in health care: Second American Samueli Symposium. *J Altern Complement Ther.* 2004;10(Suppl 1).

32. Herman PM, Craig BM, Caspi O. Is complementary and alternative medicine (CAM) cost-effective? A systematic review. *BMC Complement Altern Med.* 2005;5:11.
33. Debas H, Laxminarayan R, Straus S. Complementary and alternative medicine. In: Jamison D, Breman J, Measham A, Alleyne G, Claeson M, eds. *Disease Control Priorities in Developing Countries.* 2nd Edition: The World Bank Group; 2006:1281-1291.
34. Deuster PA, O'Connor FG, Henry KA, et al. Human performance optimization: an evolving charge to the Department of Defense. *Mil Med.* Nov 2007;172(11):1133-1137.
35. Samueli Institute. Toward a Systems Wellness System. *http://www.siib.org/research/research-home/systems-wellness-system.html.* Accessed December 2, 2008.
36. Samueli Institute. Knowledge Center for Optimal Healing Environments. http://www.siib.org/research/research-home/optimal-healing.html Accessed December 2, 2008.
37. Eng T. *The eHealth landscape: a terrain map of an emerging information and communication technology in health and health care.* Princeton, NJ: Robert Wood Johnson Foundation; 2001.
38. Sobel DS. MSJAMA: mind matters, money matters: the cost-effectiveness of mind/body medicine. *JAMA.* Oct 4 2000;284(13):1705.
39. Haake M, Muller HH, Schade-Brittinger C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Arch Intern Med.* Sep 24 2007;167(17):1892-1898.
40. Diener HC, Kronfeld K, Boewing G, et al. Efficacy of acupuncture for the prophylaxis of migraine: a multicentre randomised controlled clinical trial. *Lancet Neurol.* Apr 2006;5(4):310-316.
41. Cherkin DC, Sherman KJ, Deyo RA, Shekelle PG. A review of the evidence for the effectiveness, safety, and cost of acupuncture, massage therapy, and spinal manipulation for back pain. *Ann Intern Med.* Jun 3 2003;138(11):898-906.
42. Scafidi F, Field T, Schanberg S. Factors that predict which preterm infants benefit most from massage therapy. *J Development Behav Pediatrics.* 1993;14(3):176–180.
43. Field T, Hernandez-Reif M, Quintino O, Schanberg S, C K. Elder retired volunteers benefit from giving massage therapy to infants. *J Appl Gerontology.* 1998b;17:229–239.
44. Barnes P, Bloom B, Nahin R. *Complementary and alternative medicine use among adults and children: United States, 2007.* Washington, DC: US Department of Health and Human Services; December 10, 2008. http://www.cdc.gov/nchs/data/nhsr/nhsr012.pdf Accessed January 2, 2009.
45. Pelletier KR. A review and analysis of the clinical and cost-effectiveness studies of comprehensive health promotion and disease management programs at the worksite: update VI 2000-2004. *J Occup Environ Med.* Oct 2005;47(10):1051-1058.
46. *The Business of Health-The Health of Business: Building the case for health, safety and wellness* 2006. http://www.iblf.org/docs/BizofHealth.pdf Accessed December 2, 2008.
47. Substance Abuse and Mental Health Services Administration. Fact Sheet: Workplace Health Promotion/Wellness. http://www.workplace.samhsa.gov/ResourceCenter/r305.pdf. 1998.
48. Pelletier KR. Corporate Health Improvement Program (CHIP). http://www.drpelletier.com/chip/index.html Accessed December 2, 2008.
49. Special Committee on Health, Productivity, and Disability Management. Healthy Workforce/Healthy Economy: The Role of Health, Productivity, and Disability Management in Addressing the Nation's Health Care Crisis: Why an emphasis on the Health of the Workforce is Vital to the Health of the Economy. *J Occupational and Environmental Medicine.* 2009;51(1):114-119.
50. The Health Project: Reducing health care costs through improved health behavior. http://healthproject.stanford.edu/ Accessed January 2, 2009.
51. Pazoki R, Nabipour I, Seyednezami N, Imami SR. Effects of a community-based healthy heart program on increasing healthy women's physical activity: a randomized controlled trial guided by Community-based Participatory Research (CBPR). *BMC Public Health.* 2007;7:216.
52. Sit JW, Yip VY, Ko SK, Gun AP, Lee JS. A quasi-experimental study on a community-based stroke prevention programme for clients with minor stroke. *J Clin Nurs.* Feb 2007;16(2):272-281.
53. Andrews J, Bentley G, Crawford S, Pretlow L, Tingen M. Using community-based participatory research to develop a culturally sensitive smoking cessation intervention with public housing neighborhoods. *Ethn Dis.* 2007;17(2):331-337.
54. Pettman TL, Misan GM, Owen K, et al. Self-management for obesity and cardio-metabolic fitness: Description and evaluation of the lifestyle modification program of a randomised controlled trial. *Int J Behav Nutr Phys Act.* 2008;5:53.
55. Pearson JA, Burkhart E, Pifalo WB, Palaggo-Toy T, Krohn K. A lifestyle modification intervention for the treatment of osteoporosis. *Am J Health Promot.* Sep-Oct 2005;20(1):28-33.
56. Satterfield DW, Volansky M, Caspersen CJ, et al. Community-based lifestyle interventions to prevent type 2 diabetes. *Diabetes Care.* Sep 2003;26(9):2643-2652.
57. Kerr J, ed. *Community Health Promotion: Challenges for Practice*: Bailliere Tindall; 2000.

58. Togami T. Interventions in local communities and work sites through Physical Activity and Nutrition Programme. *Obes Rev.* Mar 2008;9 Suppl 1:127-129.
59. Kain J, Uauy R, Albala, et al. School-based obesity prevention in Chilean primary school children: methodology and evaluation of a controlled study. *Int J Obesity.* 2004;28(4):483-493.
60. Wellspring Academies. *http://www.wellspringacademies.com/.* Accessed December 5, 2008.
61. Gortmaker SL, Peterson K, Wiecha J, et al. Reducing obesity via a school-based interdisciplinary intervention among youth: Planet Health. *Arch Pediatr Adolesc Med.* Apr 1999;153(4):409-418.
62. BMJ Health Intelligence 2007. http://healthintelligence.bmj.com/hi/do/home Accessed November 25, 2008.
63. van Sluijs EM, McMinn AM, Griffin SJ. Effectiveness of interventions to promote physical activity in children and adolescents: systematic review of controlled trials. *BMJ.* Oct 6 2007;335(7622):703.
64. Huhman ME, Potter LD, Duke JC, et al. Evaluation of a national physical activity intervention for children: VERB campaign, 2002-2004. *Am J Prev Med.* Jan 2007;32(1):38-43.
65. Kirschenbaum D, Craig R, Kelly K, Germann J. Treatment and innovation: Description and evaluation of new programs currently available for your patients. *Obesity Management.* 2007;DOI: 10.1089/obe.2007.0115:261-266.
66. Astin JA, Pelletier KR, Marie A, Haskell WL. Complementary and alternative medicine use among elderly persons: one-year analysis of a Blue Shield Medicare supplement. *J Gerontol A Biol Sci Med Sci.* Jan 2000;55(1):M4-9.
67. Najm W, Reinsch S, Hoehler F, Tobis J. Use of complementary and alternative medicine among the ethnic elderly. *Altern Ther Health Med.* May-Jun 2003;9(3):50-57.
68. Coleman MT, Newton KS. Supporting self-management in patients with chronic illness. *Am Fam Physician.* Oct 15 2005;72(8):1503-1510.
69. Martin EM, Coyle MK. Nursing protocol for telephonic supervision of clients. *Rehabil Nurs.* Mar-Apr 2006;31(2):54-57, 62.
70. Noel HC, Vogel DC, Erdos JJ, Cornwall D, Levin F. Home telehealth reduces healthcare costs. *Telemed J E Health.* Summer 2004;10(2):170-183.
71. Amarasingham R, Plantinga L, Diener-West M, Gaskin DJ, Powe NR. Clinical information technologies and inpatient outcomes: a multiple hospital study. *Arch Intern Med.* Jan 26 2009;169(2):108-114.
72. Goetzel RZ, Shechter D, Ozminkowski RJ, et al. Can health promotion programs save Medicare money? *Clin Interv Aging.* 2007;2(1):117-122.
73. Newsreel C. Unnatural Causes...is inequality making us sick? *http://www.unnaturalcauses.org/.* 2008; Accessed Dec 2, 2008.
74. Bezold C, Calvo A, Fritts M, Jonas WB. Integrative medicine and health disparities: A scoping meeting. *A report produced by the Institute of Alternative Futures, Health Resources and Services Administration and the Samueli Institute.* 2008.
75. Sarnat RL, Winterstein J, Cambron JA. Clinical utilization and cost outcomes from an integrative medicine independent physician association: an additional 3-year update. *J Manipulative Physiol Ther.* May 2007;30(4):263-269.
76. NCMIC. The Integrator Blog. *http://theintegratorblog.com/site/index.php?option=com_content&task=view&id.* Accessed December 2, 2008.
77. Center for Disease Control. *www.cdc.gov.* Accessed December 2, 2008.
78. *A series of issue briefs addressing many of the most important prevention policy issues facing the nation.* www.prevent.org/HealthReform/ Accessed January 21, 2009.
79. Recommendations from the US Preventive Services Task Force about effective clinical preventive services. www.ahrq.gov/clinic/prevenix.htm. Accessed January 2, 2009.
80. Recommendations from the Task Force on Community Preventive Services about effective community preventive services. www.thecommunityguide.org/ Accessed January 2, 2009.
81. Partnership for Prevention. http://www.prevent.org/component/option,com_frontpage/Itemid,1/.
82. Prevention Institute. http://www.preventioninstitute.org/ Accessed January 2, 2009.
83. The American College of Occupational and Environmental Medicine. http://www.acoem.org/ Accessed January 2, 2009.
84. Maciosek M, Coffield A, Edwards N, et al. Priorities among effective clinical preventive services: results of a systematic review and analysis. *Am J Prev Med.* 2006;31(1):52-61.
85. Partnership for Prevention. Principles for prevention-centered health reform. *www.prevent.org/HealthReform/.* 2007; Accessed January 20, 2008.
86. National Commission on Prevention Priorities. Preventive care: National profile on use, disparities, and health benefits. *Partnership for Prevention.* 2007;www.prevent.org/100,000Lives/ Accessed January 20, 2009.

From: H <hdr22@clintonemail.com>
Sent: Friday, March 6, 2009 8:26 PM
To: Cheryl Mills <CMills@hillaryclinton.com>
Subject: Can you talk?

RELEASE IN FULL

I just arrived in Ankara and would like to check in I would call thru Ops.

From: H <hdr22@clintonemail.com>
Sent: Friday, February 27, 2009 1:33 PM
To: Lauren Jiloty <JilotyLC@state.gov>
Subject: Fw: The Hearing and IOM Meeting
Attach: Hyman Senate Testimony Final.2.26.09.doc; 21stCentMed.pdf; 21stCentMed_Appendix.pdf; 2009 Functonal Prospective Medicine.doc; WIN Summary 19feb09.pdf

RELEASE IN PART
B6

Pls print all of this and hold for me. Thx.

From: "Mark Hyman, MD"
Date: Fri, 27 Feb 2009 07:45:48 -0500
To: Hillary Clinton<hr15@att.blackberry.net>; Hillary Clinton<hdr22@clintonemail.com>
Subject: The Hearing and IOM Meeting

Dear Hillary,

I thought you would also like to see some of the testimony submitted this week.

1. My testimony
2. Jeff Bland's testimony
3. The White Paper on A New Model for Education and Practice in the 21st Century from the Institute for Functional Medicine.
4. Dr. Wayne Jonas proposal for a White House wellness initiative to help the health care reform team and bring in key advisory leaders in this field.

Hope to see you soon!
–
Mark Hyman, MD
Founder and Medical Director
The UltraWellness Center
45 Walker Street
Lenox, MA 01240

B6

Mark

From: H <hdr22@clintonemail.com>
Sent: Friday, February 27, 2009 1:37 PM
To: Mark Hyman, MD [redacted] B6
Subject: Re: In Washington

RELEASE IN PART B6

Dear Mark,

I'm so sorry but I'm just seeing this (no blackberry contact permitted in my office) and I'm on the way to the shuttle to NY Tomorrow I leave for Egypt, Israel, Europe and Turkey for a week. I hope the meeting and the hearing goes well Let me know All the best

From "Mark Hyman, MD"
Date Fri, 27 Feb 2009 07:45:35 -0500
To: Hillary Clinton<hr15@att.blackberry net>; Hillary Clinton<hdr22@clintonemail.com>
Subject. In Washington

Dear Hillary,

I just wanted to thank you again so much for opening the door to Senator Harkin and helping me bring the concepts that will be the best hope for changing not only the way we do medicine but the medicine we do, into the conversation of health care reform. I am sending another email with the documents – in case attachments don't get through..

I am also at the Institute of Medicine meeting at the NAS on Integrative Medicine this week – 600 leaders –quite a gathering. I saw that the State Department was right across the street.

I know you are extremely busy – but if you are around I would love to pop by and say hi.... Just let me know if you have time and I will come over. I am here and mostly free all day - Friday Feb 27th.

Thinking of you!!

Be well,

Mark

–
Mark Hyman, MD
Founder and Medical Director
The UltraWellness Center
45 Walker Street
Lenox, MA 01240

[redacted]

HA 09/01/2015

From: H <hdr22@clintonemail.com>
Sent: Friday, February 27, 2009 1:38 PM
To: Marty Torrey
Subject: Re: Dave Stone, etc

RELEASE IN PART B6

B6

Thx so much. I look forward to seeing you two.
------Original Message------
From. Marty Torrey
To: hdr22@clintonemail.com
Sent: Feb 26, 2009 3:05 AM
Subject: Re: Dave Stone, etc

Great. Thanks. I imagine your body won't know what time zone it is in for a couple of years. (the exchange teacher who is back in China) reported that your trip to China was well received by the everyone she knows. Interesting to watch Washington I recall that a few months ago you said fixing the home owners problems was a vital step that had to be dealt with at the front end Now they're trying to fix it as a 4th or 5th priority because they finally see that element provides the basis for confidence in the economy, etc. That said, I'll connect with your office to arrange for sailors visit. A few minutes of your busy schedule most appreciated. While I doubt it is possible, hope you are getting a bit of rest Busy times
Marty
---- H <hdr22@clintonemail.com> wrote:
> I'd love to see you two sailors. Don't know when schedules will mesh, but contact Lauren or Lona in my office to try to coordinate the three of us. All the best from your jet-lagged friend.
> ------Original Message-----
> From: Marty Torrey
> To: hdr22@clintonemail.com
> Sent: Feb 25, 2009 2:08 AM
> Subject: Dave Stone, etc
>
> Dave Stone is in Bahrain for a bit. Any chance Dave and I could get 10 minutes just to say hello ? Either Washington or NY. We all recognize you're the planet's busiest lady... and doing great for sure. Everyone proud. Glad to see the Ann Lewis emails, site, etc underway. Best,
> Marty
>
>

From: H <hdr22@clintonemail com>
Sent: Friday, February 27, 2009 2:01 PM
To: Bill Owens [redacted] B6
Subject: Re:

RELEASE IN PART
B6

Dear Bill,

Thank you for coming to the Beijing Embassy to see me. You look as tho your new life is agreeing w you and I only regret we did not have more time together. I will follow up on in the next week on your memo about complementary engagements. All the best Hillary
------Original Message------
From Bill Owens
To: 'hdr22@clintonemail.com'
Sent: Feb 21, 2009 6:38 PM
Subject:

Dear Hillary,

I think your "listening tour" has been inspiring to all of us who have cared about our relationships with Asia I had dinner last night in Beijing with about a dozen very well placed senior generals and politicians You would have liked their comments about your visit. I'm proud of what you're doing and always here to help when I can. It was very nice to see you at the Embassy. After such an arduous trip, I thought you were great with the staff/Marines/Peace Corps (and the kids!).

I hope you'll have a chance to think about the "complementary engagement" one pager on mil/econ/political friendships (which I'm afraid I too quickly passed to you) I think the effort is helpful to what you're doing on a more formal level.

Warm best wishes, I'm cheering for you, Bill Owens

HA 09/01/2015

From: Huma Abedin [redacted] B6 RELEASE IN PART B6
Sent: Friday, February 27, 2009 3:13 PM
To: hdr22@clintonemail.com
Subject:

Call ops to connect you to susan rice
202-647-1512
And then call lauren 202-647-5298 if u want to be connected to mort zuckerman and chuck schumer

From: Huma Abedin [redacted]
Sent: Friday, February 27, 2009 9:40 PM
To: hdr22@clintonemail.com
Subject:

B6

RELEASE IN PART
B6

Can u call cheryl thru ops?
202-647-1512

From: H <hdr22@clintonemail com> B6
Sent: Saturday, February 28, 2009 7:29 AM
To: Huma Abedin
Subject: Re: Calls

Yes to both.
------Original Message------
From: Huma Abedin
To hdr22@clintonemail com
Sent: Feb 27, 2009 11:59 PM
Subject: Calls

B5

Ops can reach out tonite and suggest a time.

B5

From: Abedin, Huma <AbedinH@state.gov>
Sent: Saturday, February 28, 2009 9:58 AM B6
To: humamabedin
Subject: PrintFw: Final NEA/EUR Trip Schedule: 27 February p.m.
Attach: 090209 Sharm, J'salem, Bxl, Genf.doc

RELEASE IN PART
B6

From: Merten, Kenneth H
To: Ries, Marcie B; Lucas, William; Turner, Bruce I; Feltman, Jeffrey D; Hale, David M; Abedin, Huma; Valmoro, Lona J; McLean, Lori A; Shapiro, Andrew J; Muscatine, Lissa; Crocker, Bathsheba N; Russell, Daniel A; Shah, Khushali P; DeMarcellus, Roland F; Sullivan, Jacob J; Simon, Jessica L (PACE); Bennett, Virginia L; Goldberger, Thomas H; Adler, Caroline E (PACE); Wohlers, Laurence D; Arizu, Patricia A; Slaughter, Anne-Marie; Feinstein, Barbara (AID/A/COO); Thompson, Trent(AID/A); Silliman, Douglas A; Garbe, Danielle N; Bennett, Virginia L; Crocker, Bathsheba N; Wells, Alice G; Turner, Bruce I; Rana, Gautam A; Abedin, Huma; Fried, Daniel
Cc: SES_4; Inzerillo, Suzanne M; Ruggles, Taylor V; Piechowski, Jon E; Sindle, James M; Littlejohn, J.R.; Narain, Paul F; Mack, Jason R; S_SpecialAssistants; Russell, Daniel A; Lukens, Lewis A; Hunter, Theresa M
Sent: Fri Feb 27 18:23:28 2009
Subject: Final NEA/EUR Trip Schedule: 27 February p.m.

All,
This is my final trip schedule. From here on out we'll be producing them on the road. Jerusalem is pretty firm, and we have a few more details on Sharm. Still waiting on NATO-Georgia-Ukraine councils to firm up...

Kenneth Merten
Deputy Executive Secretary
Executive Secretariat
U.S. Department of State
Tel: 1-202-647-8448

From: Capricia Penavic Marshall [redacted] B6
Sent: Friday, March 6, 2009 9:58 PM
To: humamabedin [redacted] Huma Abedin [redacted]
Subject: Re: FW: Key Contact

RELEASE IN PART B5,B6

I did not say anything to him.

-----Original Message-----
From: huma abedin <humamabedin [redacted]
To: Huma Abedin; Capricia Penavic Marshall
Sent: Fri Mar 06 21:13:14 2009
Subject. Re FW: Key Contact

B5

just seeing this [redacted]
please reply all cause I'm only on my yhaioo account briefly.

--- On Fri, 3/6/09, Capricia Penavic Marshall [redacted] wrote:

> From: Capricia Penavic Marshall [redacted]
> Subject: FW: Key Contact
> To: "Huma Abedin" [redacted] humamabedin [redacted]
> Date: Friday, March 6, 2009, 12:15 PM
> On this matter – David called me again and I asked [redacted] to
> talk to [redacted] – this is what she learned
> [redacted]
> FYI!
>
>
>
> From: David Mercer [redacted]
> Sent: Friday, March 06, 2009 12:03 PM
> To: Capricia Penavic Marshall
> Subject: Fw: Key Contact
>
>
>
> Hi Capricia--Here's the email I sent to Huma regarding
> [redacted] Thanks very much for your help in all this.
> It would be great if Huma gave [redacted] a call prior to their
> arrival in Turkey which I believe is tomorrow David.
>
> David L Mercer
> President
> Mercer & Associates, Inc.
> 2550 M Street, NW
> Washington, DC 20037
> [redacted]
>
> ----- Original Message -----
> From: David Mercer
> To: 'abedinh@state.gov' <abedinh@state.gov>
> Sent: Wed Mar 04 12:33:07 2009
> Subject: Key Contact

HA 09/01/2015

> Hi Huma--Hope all's well and you're having a
> successful trip
>
> [redacted]
>
> [redacted]
>
> Could you please make contact with [redacted]? I greatly
> appreciate it If you need additional information,
> don't hesitate to email me or reach me by cell at [redacted]
> [redacted] All the best David
>
>
> David L. Mercer
> President
> Mercer & Associates, Inc.
> 2550 M Street, NW
> Washington, DC 20037
> [redacted]

HA 09/01/2015

B6

RELEASE IN PART B6

From: Burns Strider [redacted]
Sent: Saturday, March 7, 2009 11:07 AM
To: hdr22@clintonemail.com
Subject: I love running across your kiddies... FW: Vets Screening Bill and Hello from Naz Durakoglu

---

I don't even know what Naz did in the campaign... I just know she was energetic, full of excitement and totally loyal to you.. [redacted] I spoke yesterday to the House Demo Press Secretaries on Veterans message and communications and met one of her colleagues:

From: Durakoglu, Naz [mailto:Naz.Durakoglu@mail.house.gov]
Sent: Friday, March 06, 2009 5:27 PM
To: bstrider[redacted]
Subject: Vets Screening Bill and Hello from Naz Durakoglu

Dear Mr. Strider,
I heard that you ran into my co-worker, Lauren Amendolara today. It was a nice surprise to hear that she met you and discussed our bill. I wanted to send you the bill itself because I heard that you were interested in it. We are very excited about it, and the Congressman really hopes that it will make a difference in the horrific suicide statistics amongst the young vets returning home from OEF and OIF.

I would love to know what you think of it. Please keep in touch!

Thank you,

Naz Durakoglu
Legislative Assistant
The Office of Rep. Michael E. McMahon
CHOB Room 323
T: 202-225-3371
F: 202-226-1272

From: H <hdr22@clintonemail.com>
Sent: Sunday, March 8, 2009 12:59 PM
To: Huma Abedin
Subject: Re:

RELEASE IN PART B6

B6

Ok. Can Kristy come tomorrow for both?
------Original Message------
From Huma Abedin
To: hdr22@clintonemail com
Sent. Mar 8, 2009 12:14 PM
Subject: Re:

Sorry its ops 647-1512

-----Original Message----
From: Huma Abedin
To: 'hdr22@clintonemail.com' <hdr22@clintonemail com>
Sent: Sun Mar 08 12 13:54 2009

Richard holbrooke wants to talk at your convenience.
202-547-1512

From: H <hdr22@clintoncmail.com>
Sent: Sunday, March 8, 2009 12.59 PM
To: Cheryl Mills
Subject: Re: Are you up and about?

B6

RELEASE IN PART
B6

Yes--pls call the house in DC.
-----Original Message-----
From: Cheryl Mills
To: hdr22@clintonemail com
Sent: Mar 8, 2009 12:55 PM
Subject: Are you up and about?

From: H <hdr22@clintonemail.com>
Sent: Sunday, March 8, 2009 8:38 PM
To: Cheryl Mills [redacted] B6
Subject: Re: Maria Haley

RELEASE IN PART
B5,B6

Ok

From: "Cheryl Mills"
Date: Sun, 8 Mar 2009 20:31:54 -0400
To: <hdr22@clintonemail.com>
Subject: RE. Maria Haley

[redacted] B5

From: H [mailto:hdr22@clintonemail.com]
Sent: Sunday, March 08, 2009 8:31 PM
To: Cheryl Mills B5
Subject: Re: Maria Haley

[redacted]

From: "Cheryl Mills"
Date: Sun, 8 Mar 2009 20:23:22 -0400
To: <hdr22@clintonemail.com>; Hillary Clinton<hr15@att.blackberry.net>
Subject: Maria Haley
See below – thoughts before I answer?

From: Maria Luisa M. Haley [redacted]
Sent: Sunday, March 08, 2009 2:17 PM
To: millscd@state.gov B6
Cc: Cheryl Mills
Subject:

Cheryl:

Gary Locke has asked me to help him in his confirmation and personnel process so I am taking vacation from my present job in the Gov.'s Cabinet to go to DC for a week, week and a half. I was just talking to Ginger Lew. Can I help HRC and you?

Maria Haley