A Vision for Transforming Medicine in the 21st Century

Elias A. Zerhouni, M.D., Director
National Institutes of Health
The Promise of “Scientific” Medicine

Louis Pasteur (1822-1895)

Shibasaburo Kitasato
Current Public Health Challenges:
We Need a Global Culture of Science

- Acute to Chronic Conditions
- Aging Population
- Health Disparities
- Emerging and Re-emerging Infectious Diseases
- Emerging Non-communicable Diseases
The Shape of Things to Come

The Economist, Dec 13-19, 2003
Obesity: A Worldwide Issue

**Land of the Fry**

<table>
<thead>
<tr>
<th>Country</th>
<th>Overweight* men</th>
<th>Overweight* women</th>
<th>Obese* men</th>
<th>Obese* women</th>
</tr>
</thead>
<tbody>
<tr>
<td>England</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Russia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI = Weight in kilograms divided by the square of height in metres
*BMI of 25-29.9
**BMI of 30 or more

Sources: International Obesity Task force; Barry Popkin

---

Obesity Health Risks

- Cancer
- Hypertension
- Kidney Failure
- Stroke
- Diabetes
- Heart Failure
- Gall-bladder Disease
- Atherosclerosis
We Need a Global Culture of Science

- Emerging and re-emerging diseases create social instability

http://www.ecdgroup.com
Global Examples of Emerging and Re-Emerging Infectious Diseases

- Vancomycin-resistant *Staphylococcus aureus*
- Cryptosporidiosis
- Multidrug-resistant tuberculosis
- Drug-resistant malaria
- E. coli O157:H7
- Hepatitis C
- vCJD
- Lyme disease
- Typhoid fever
- Diphtheria
- SARS
- H5N1 influenza
- Rift Valley fever
- HIV
- Vancomycin-resistant *Staphylococcus aureus*
- Nipah virus
- Hendra virus
- Enterovirus 71
- Plague
- Human monkeypox

Legend:
- Newly emerging
- Re-emerging/resurfacing
- “Deliberately emerging”

Elias A. Zerhouni, M.D.
September 13, 2006
H5N1 Influenza Cases, 2003-2006

Total: 236 WHO laboratory-confirmed cases including 138 deaths

Toward a “Universal” Influenza Vaccine?

- DNA prime-recombinant adenoviral boost immunization to nucleoprotein (NP).
- Strong antibody and T cell responses were induced.
- Vaccination protected against lethal challenge with highly pathogenic H5N1 virus.

PROTECTION AGAINST MULTIPLE INFLUENZA A SUBTYPES BY VACCINATION WITH HIGHLY CONSERVED NUCLEOPROTEIN

SL Epstein, WP Kong, JA Misplon, CY Lo, TM Tumpey, L Xu, GJ Nabel
NIH Increased International Research Expenditures

Source: Fogarty International Center, Nov. 2005
U.S.-Japan Cooperative Medical Science Program (USJCMSP)

**U.S.**
- Department of State
- NIH

**Joint Committee**
est. 1965

**Japan**
- Ministry of Foreign Affairs
- MHLW*
- MEXT**

USJCMSP Panels and Boards

* Ministry of Health, Labour, and Welfare
** Ministry of Education, Culture, Sports, Science, and Technology
# Need to Transform Health and Medicine in the 21st Century

<table>
<thead>
<tr>
<th>20th Century</th>
<th>21st Century</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat disease when symptoms appear and normal function is lost</td>
<td>Intervene before symptoms appear and preserve normal function for as long as possible</td>
</tr>
<tr>
<td>Did not understand the molecular and cellular events that lead to disease</td>
<td>Understanding preclinical molecular events and ability to detect patients at risk</td>
</tr>
<tr>
<td>Expensive in financial and disability costs</td>
<td>Orders of magnitude more effective</td>
</tr>
</tbody>
</table>
The Future Paradigm: The 4 P’s

Transform Medicine from Curative to Preemptive
Today, a fundamental scientific barrier is our limited ability to study complex and dynamic biological systems in health or disease!
New Pathways to Discovery

- Building blocks, biological pathways, and networks
- Molecular tools libraries
- Structural biology
- Bioinformatics and computational biology
- Systems biology
- Molecular reclassification of diseases
Human Genome Project and HapMap Are Complete: *Where Do We Go From Here?*

- Plummeting cost of DNA sequencing
- New discoveries accelerating revolution of the practice of medicine
- **Genes, Environment, and Health Initiative**
  - Identify roots of 10 most common diseases
  - Devise new ways of monitoring personal environmental exposures

September 13, 2006
Discoveries in Age-related Macular Degeneration can **PREDICT** who is at risk of developing the diseases.

- **AMD** is the leading cause of blindness in people over age 60.

- Variations in genes involved in inflammation can predict the risk of developing AMD:
  - 56% of the unaffected individuals had a variant that conferred protection to AMD.
  - 74% of those with AMD had no protective variants.
  - **THOSE WITH THE “WRONG” GENES HAVE 100 FOLD GREATER RISK**
Pharmacogenomics Discoveries Make it Possible to “Personalize” Treatment

- Warfarin: An anticoagulant drug used to reduce the risk of clots causing strokes or heart attacks
- Effective daily dose ranges from 0.5 mg to 60 mg
- Too little: clots, stroke
- Too much: bleeding/death
- Genomic experiments revealed mutations that help predict best dose for individual patients
Cancer Treatment Gets Personal: Potential New Model of Cancer Treatment

“Advances in understanding genetic basis of cancer have led to promising new therapies, which have fueled discussions about a future model of cancer care-- treatment decisions are guided by the molecular attributes of the individual patient.”

CANCER GENOME PROJECT

http://www.sciencemag.org/sciext/cancer/
New Discoveries Make it Possible to “Personalize” Cancer Treatment

Identified 16 informative genes

Test tumor samples for mutations in these genes

Recurrence Score helps predict which patients need chemotherapy

Impact:

- 100,000 women each year can make a more informed choice
- 70,000 women may not have to undergo chemotherapy
- Reduces routine cost of treating these patients
Preemptive: HPV Vaccine

- Human Papillomavirus (HPV) infects over 80% of 15-50 year old women and can cause cervical cancer
- Prevent sexually transmitted HPV infection = prevent cervical cancer
- Anti-Viral Vaccines are among the most cost effective public health interventions (e.g., smallpox, polio, & measles)
- NIH has two vaccines currently in clinical trials
Participatory: Community Involvement

Jackson Heart Study
- Community participation
- Community education
  - Health awareness
  - Student outreach
  - Encourage involvement
- Identify minority risk factors for cardiovascular disease
NIH
Transforming medicine and health through discovery