BIRD FLU: FACTS AND FICTION

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TWO KINDS OF VIRUSES
WHAT IS INFLUENZA?

- Influenza A, B, and C
- RNA viruses that come from birds
- Waterfowl as reservoirs
- How is influenza transmitted?
- How does it spread from cell to cell?
- From animal to animal?
- How does it mutate?
SPREAD FROM CELL TO CELL
Avian receptors versus human

- the influenza virus is "looking for" a point of attachment preparatory to entering a cell and infecting it. That sugar, sialic acid (or neuraminic acid), attaches to another sugar (galactose) closer in through its own #2 carbon to either the #3 carbon (birds) or #6 carbon (humans) via a link that hooks in below the plane of the sialic acid ring (an Î±-linkage). The difference between hooking to either #3 or #6 of galactose makes the sugar chain look different to the virus.
Human versus Avian flu virus

• Human influenza viruses bind preferentially sialic acid containing N-acetylmuraminic acid alpha2,6-galactose (SAalpha2,6Gal) linkages while avian and equine viruses bind preferentially those containing N-acetylmuraminic acid alpha2,3-galactose (SAalpha2,3Gal) linkages.
The viral key to the lock

- HA – receptor binding site
THE FOLDING AND BINDING OF HEMAGGLUTININ

• When we look at the sequence of amino acids in avian flu viruses (the ones that bind efficiently to Î±-2,3 linkages), we find that amino acids at certain positions are important. One of these is the position numbered 223.

• When this is the amino acid serine, the HA binds nicely to Î±-2,3. But if it changes to asparagine, it switches its allegiance to Î±-2,6 linkages.
Antigenic Shift versus Drift

- Migratory waterfowl, especially ducks, are the natural reservoir of the avian influenza virus. Since no one is checking or treating them for diseases, viruses, especially non-fatal ones, spread unchecked throughout their population, harbored in their gastrointestinal tracts. As birds make antibodies to protect them against flu, at the same time the influenza virus continues to adapt and may change rapidly. These mutations sometimes become new forms of the virus, in a process that is known as antigenic drift.

- Most influenza epidemics among birds occur when ducks or geese with a new strain of virus come into contact with poultry. Domestic poultry are carefully monitored for influenza, even the mildest cases, because their lower tolerance means one infection can quickly become a highly fatal epidemic. This is especially true for H5 or H7 varieties of avian flu, which tend to be the most deadly among birds – HIGHLY PATHOGENIC STRAINS.

- If a mutation occurs to allow an influenza A to pass among humans, it can become our yearly flu strain (Influenza B occurs natively in humans, but influenza A has to mutate first). Antigenic drift keeps scientists and vaccine makers on their toes, trying to match the yearly vaccine with the yearly antigenic variety of human flu.

- There are thousands of bird flus that never make the jump. For a bird flu subtype to become a true human virus, one that can be passed from person to person, requires antigenic drift, or a more unusual process where bird and human viruses merge, known as antigenic shift.

- Pigs make an excellent mixing bowl for influenza, because they are actually susceptible to both bird and mammal varieties. A pig infected with both a human and bird virus at the same time can develop a hybrid. But what sort of hybrid? This is very difficult to predict. Remember Vincent Price as The Fly? – he went into a molecule mixer with an unnoticed fly and came out a monstrous killer with a fly’s head and human body. Meanwhile, out in the garden somewhere, was a fly body with a human head that became the helpless victim of a spider. Similarly, if a hybrid flu bug manages to connect the deadly aspects of a bird bug with the “legs” of a human flu, it could become a monstrous human killer. However, this new subtype, being a mix of the two, could exhibit completely different qualities than the original two. A deadly bird flu could become a mild human flu. A mild bird flu could become a deadly human one.
What is bird flu?

- 1 – what is influenza A?
- 2 – what is the role of the viral envelope?
- 3 – what is hemagglutinin?
- 4 – what is neuraminidase?
- 5 – what are the role of proteases?
- 6 – is there any immunity to this virus?
- 7 - Why H5N1? What about the other 144?
Since 1959, the world has seen 21 new strains of avian influenza viruses, mostly in Europe and the Americas, not Asia. Of those new strains, only five spread to numerous chicken farms, and only one of those spread to other countries.

Even though these outbreaks were more limited and less formidable than H5N1 has become, it took a significant effort to control them in birds. Even well-managed, well-resourced efforts can take as much as two years to curb an outbreak of a new avian flu strain.

Quarantining farms and destroying exposed flocks has become the standard, primary measure for combating the spread of virus among birds. However, since the highly pathogenic viruses can survive long periods in the environment, especially in low temperatures, farmers need to closely disinfect any farm equipment, cages, or clothing that may have become contaminated.

The last large scale outbreak of highly pathogenic avian influenza in the US took place in 1983, in Pennsylvania. This strain took two years to control. More than 17 million birds were destroyed, at direct cost of $62 million, with an estimated related cost of $250 million. If you ponder how complicated and expensive this was for a developed nation, with a less pernicious strain of flu, you begin to understand the momentous economic challenge facing Asia today.

The last major international outbreak among poultry occurred in Mexico in 1995 (the H5N2 strain). Though it has been brought under control, despite years of intense efforts, and more than 2 billion doses of vaccines administered, the H5N2 subtype also has yet to be eradicated.
The Spread of H5N1 Influenza Virus and Time Line Showing Its Emergence

THE SPREAD OF H5N1 IN BIRDS

• The Spread of H5N1 Influenza Virus and Time Line Showing Its Emergence. The shaded area across southern China is the hypothetical epicenter for the emergence of H5N1 clades and subclades. The H5N1 viruses are being perpetuated in the domestic birds of the region, despite the use of universal vaccination of all domestic poultry. The red dot in the time line denotes the occurrence of the first human case, followed by the number of confirmed human cases in that country. The green and blue solid bars represent documented H5N1 infection in domestic poultry and wild birds, and dashed bars indicate that H5N1 in the avian population is suspected. These limited surveillance data are adapted from the World Health Organization and the U.N. Food and Agriculture Organization (www.fao.org). HA denotes hemagglutinin.
HISTORY OF H5N1

• The Asian H5N1 virus was first detected in Guangdong Province, China, in 1996, when it killed some geese, but it received little attention until it spread through live-poultry markets in Hong Kong to humans in May 1997, killing 6 of 18 infected persons (see map and time line). The culling of all poultry in Hong Kong ended the first wave of H5N1, but the virus continued to circulate among apparently healthy ducks in the coastal provinces of China.
HISTORY OF H5N1 SINCE 1997

- From 1997 to May 2005, H5N1 viruses were largely confined to Southeast Asia, but after they had infected wild birds in Qinghai Lake, China, they rapidly spread westward. The deaths of swans and geese marked H5N1's spread into Europe, India, and Africa. Infections with highly pathogenic H5N1 viruses were confirmed in poultry in Turkey in mid-October 2005, and the first confirmed human cases in Turkey occurred in early January 2006. Thus, H5N1 influenza viruses continue to emerge from the epicenter.

- The H5N1 viruses can be divided into clade 1 and clade 2; the latter can be further subdivided into three subclades. These clades and subclades probably differ sufficiently in their antigenic structure to warrant the preparation of different vaccines. Studies in ferrets suggest that vaccine against one clade will not protect against infection with another clade, though it will protect against influenza-associated death.
Will H5N1 Cause a Massive Pandemic??

- DOOMSAYERS –
  - Osterholm, Garrett, Webster

- NAYSAYERS –
  - Palese, Butcher, Orent/Ewald, Siegel

- SCIENTISTS – Taubenberger, Fauci
A BIRD’S EYE VIEW

• David Swayne – Director Southeast Poultry Research Lab – “New Strategies need to be developed…to protect birds from infection.”

• Elizabeth Krushinskie – President, Society of Avian Pathologists – “There is no selective pressure to drive it (H5N1) towards humans. It could just as easily move away.”
Attempts to control H5N1 in birds

- Controlling H5N1 influenza by eradicating it at the source in domestic poultry has worked for some wealthy countries: in 2003, Japan and South Korea eradicated H5N1 through a strategy of quarantine and culling of poultry and implementation of improved biosecurity measures for poultry facilities. In Thailand, however, the same strategy resulted in only a temporary respite; after nearly a year with no H5N1 activity, new cases in humans in July 2006 heralded the resurgence of H5N1 in domestic poultry.

- An alternative strategy adopted by China, Indonesia, and Vietnam has been to vaccinate uninfected poultry in conjunction with the quarantine and culling of infected birds. This approach has failed, however, and its critics explain that poultry vaccines are largely of poor quality, do not provide sterilizing immunity, and promote antigenic drift. Yet vaccines against H5N1 influenza virus have been used successfully since 2004 on all poultry sold in Hong Kong, where no H5N1 virus has been isolated from fowl in live-bird markets despite extensive prospective surveillance.

- In Vietnam, there is an important test strategy underway, since starting vaccinating all poultry with inactivated, oil-emulsion H5N1 vaccine, there have been no additional cases in humans and no reported H5N1 infections in chickens. But in September 2006, H5N1 was reported to have reemerged in ducks and geese in Vietnam. Thus, H5N1 influenza vaccine seems to protect chickens and, indirectly, humans, but probably not waterfowl.

- In China, where the same vaccine is given to all poultry, H5N1 is not under control. The problem may be the lack of protection in waterfowl. Ducks may be the stealth carriers, for wild mallard ducks do not always show signs of disease when infected with any of a range of highly pathogenic H5N1 viruses. Our knowledge about the efficacy of H5N1 influenza vaccines in domestic waterfowl is limited, and highly pathogenic H5N1 viruses continue to be isolated from waterfowl in the epicenter of the epidemic. If the reservoir of highly pathogenic H5N1 virus is domestic waterfowl, the virus should theoretically be eradicable, but eliminating it would require improved vaccines for waterfowl and draconian prospective surveillance and culling.
HOW DOES BIRD FLU SPREAD?

- SCIENCE - REVIEW - Global Patterns of Influenza A Virus in Wild Birds Björn Olsen,1,2 Vincent J. Munster,3 Anders Wallensten,4,5 Jonas Waldenström,6 Albert D. M. E. Osterhaus,3 Ron A. M. Fouchier3

- It is most likely that the H5N1 virus has circulated continuously in domestic birds in Southeast Asia since 1997 and, as a consequence, has evolved substantially…and that multiple genetic lineages of the virus are cocirculating…For the H5N1 virus, it is without doubt that domestic waterfowl, specific farming practices, and agroecological environments played a key role in the occurrence, maintenance, and spread of HPAI for many affected countries. Finally, recent studies suggest that HPAI viruses may become less pathogenic to ducks infected experimentally, while retaining high pathogenicity for chickens. The present situation in Europe, where infected wild birds have been found in several countries that have not reported outbreaks among poultry, suggests that wild birds can indeed carry the virus to previously unaffected areas.
H5N1 HUMAN CASES –
AGE DISTRIBUTION

Source: WHO Western Office for the Regional Pacific
A New Language of Risk

• Fear is a warning system.
• Emotions increase perceived risk.
• Fear of the unknown and new diseases.
• Avoiding zero sum arguments.
• Preparing for the worst case versus long term preparation.
How to Prepare?

- Do I need stockpiles or emergency supplies?
- Do I need a plan?
- Is the government prepared?
SHORT TERM PREPAREDNESS

• Pandemic preparation tips
• Some tips from the government for preparing for a potential flu pandemic:
  — Stock a supply of water and nonperishable food, which can be useful in other types of emergencies.
  — Cover your mouth and nose with a tissue when you cough or sneeze.
  — Cough or sneeze into your upper sleeve if you don’t have a tissue.
  — Stay at home if you are sick.
  — Plan home learning activities and exercises. Have materials such as books on hand.
  — Prepare backup plans for taking care of loved ones who are far away.
  — Consider working at home.
  — Ask your employer about how business will continue during a pandemic.
  — Check with your employer or union about leave policies.
  — Create a family emergency health plan that includes information such as blood types of family members, past and current medical conditions, medications and important phone numbers.
LONG TERM PREPAREDNESS

• 1 – Food, Energy, Medication independence.
• 2 – Improve infrastructure – hospital surge capacity, emergency response system.
• 3 – Anticipate and assimilate fear component.
• 4 – Vaccine upgrades – reverse genetics, cell culture, adenovirus vector.
• 5 – Computer models? Quarantine?
**Weak spots.** A universal flu vaccine would target "conserved" proteins, such as M2 or NP, an inner protein.

CREDIT: C. BICKEL/SCIENCE
Japanese Experience vaccinating schoolchildren against FLU

Figure 3. The Five-Year Moving Average of Excess Deaths Attributed to Both Pneumonia and Influenza and All Causes, for Japan and the United States. Tick marks represent the beginning of the years indicated.
What is the role of anti-viral drugs?

• Another key question is whether these clades and subclades vary in sensitivity to available anti-influenza drugs. The majority of H5N1 clade 1 viruses (e.g., A/Vietnam/1203/2004) are resistant to the adamantanes (amantadine and rimantadine), but the majority of clade 2 viruses (e.g., A/Indonesia/5/2005) are sensitive. All H5N1 viruses that have been tested are sensitive to the neuraminidase inhibitors; these drugs may be effective when used prophylactically, but the window for effective treatment will probably be limited to 1 to 2 days after initial infection.

• The use of rapid diagnostics for H5N1 virus infection can permit specific antiviral treatments to be initiated early. Oner et al. report that in a human outbreak of H5N1 in Turkey, it was difficult to detect H5N1 virus infection with standard techniques; the authors found that a real-time polymerase-chain-reaction assay performed on nasopharyngeal specimens had the best diagnostic value.
What is a pandemic?

### Flu Factor

Estimated deaths caused by major flu pandemics of the 20th century, in millions:

- **1918 Spanish flu**: 50.0
- **1957 Asian flu**: 0.7
- **1968 Hong Kong flu**: 0.6
- **Annual seasonal flu**: 0.4

*1918 number represents world-wide deaths; other data are for U.S.*

Source: Centers for Disease Control and Prevention
FLU Pandemics Vary

• A major human influenza A pandemic—which could start as a mutated bird or pig virus—seems to occur, on average, three to four times each century. But no one can be certain when that pandemic will happen – or which virus will be involved.

• Fortunately, the last three pandemics in the U.S. have been getting progressively milder. From over 500,000 dead in 1918 to 50-100,000 in 1957 to 25-50,000 in 1968. Both these pandemics involved hybrids which included previous human strains, which tend to be milder. Both were also affected by the use of a rapidly made vaccine.
...the relative rarity of successful species jumps testifies to the complex adaptations often required to achieve sustained transmission in a new species... Influenza species barriers can be categorized into virus-host interactions occurring within individuals and host-host interactions, either within or between species, that affect transmission between individuals. Viral evolution can help surmount species barriers, principally by affecting virus-host interactions; however, evolving the capability for sustained transmission in a new host species represents a major adaptive challenge because the number of mutations required is often large... Which genetic changes would allow the currently circulating H5N1 virus to acquire the characteristic to spread efficiently among humans? Such a study would require a combination of reverse genetics to generate potential virus candidates and a suitable animal model to simulate human-to-human transmission. If such a virus were to evolve, which factors at the population level would allow it to cause a pandemic? Investigating this requires epidemiological models that take into account not only the properties of the donor and recipient populations but also the characteristics of the newly emerged virus.
HUMAN TO HUMAN?

- **Fig. 1.** Schematic illustrating phases in overcoming species barriers. (A) Interspecific host-host contact must allow transmission of virus from donor species to recipient species. (B) Virus-host interactions within an individual of recipient species affect the likelihood of the virus replicating and being shed sufficiently to infect another individual of recipient species. (C) Intraspecific host-host contact in recipient species must allow viral spread ($R_0 > 1$) in the presence of any preexisting immunity. Superspreader events (red asterisk) early in the transmission chain can help this process. (D) The pathogen must persist in the recipient species population even during epidemic troughs (after most susceptible individuals have had the disease) so that subsequent epidemics can be seeded: If few susceptibles are left, the virus may (stochastically) go extinct in epidemic troughs. Viral variation and evolution can aid invasion and persistence, particularly by affecting host-virus interactions.
Bird to Human versus Human to Human

Meanwhile, the number of infections in humans continues to increase. By mid-August, 97 humans had been infected in 2006 — the same number as in all of 2005. Perhaps the most surprising thing about highly pathogenic H5N1 is that although more than 230 million domestic birds have died or been killed, only 251 humans have become ill from H5N1 infection, and there has been little or no evidence of subclinical infection in humans. The current H5N1 virus is apparently not well "fitted" to replication in humans, although the genetic makeup of a small proportion of humans supports attachment and replication of the virus, if not its transmission. The specific receptor for the current avian influenza virus (2-3 sialic acid) is found deep in the respiratory tract of humans, but it seems likely that only a minority of people have receptors for avian influenza viruses in their upper respiratory tracts. Moreover, receptor specificity is only one of the requirements for human infection; the virus must also find compatible enzyme systems in the infected human cells if the viral polymerase complex is to function. Currently, these conditions are apparently met in only a few persons. But the virus is always changing, and mutations that make it more compatible with human transmission may occur at any time. – Robert Webster, et. al, NEJM November 23, 2006
CULTURAL DIFFERENCES

Sabah Arar / AFP - Getty Images file
You can't catch the bird flu by kissing someone. But you might from kissing an infected bird. Here, an Iraqi feeds his pigeon from his mouth in Baghdad, where birds have tested positive for the H5N1 strain.
Historical Differences

1 – 1918 – no antibiotics or other lifesaving medications. No vaccines or antivirals. Government suppressed information.


3 – 2006 – larger population, air travel, immunocompromised, public health, communications networks
THE SPANISH FLU

- This H1N1 strain is frequently referred to as the "Spanish Flu," even though it neither started in Spain, nor peaked there, though Spain did have one of the worst early outbreaks. And the Spanish discussed this strange flu more extensively than many other cultures. They were not drawn into the war; they didn’t censor their news to manipulate public morale; and they were able to devote more of the national debate to the topic.

- The first wave of infections was relatively mild. Though hundreds of men at Camp Funston became ill, only 38 died of pneumonia. Since this flu was not yet the terrifying killer it would become, it didn’t garner much attention, and it may have spread somewhat undetected among American troops preparing to leave for Europe.

- It seems these GIs must have brought it with them from home, because by April it had appeared in Western Europe. It spread quickly across the continent, reaching Poland by the summer.

- However, by August, the H1N1 strain appeared to have become more lethal. After passing once around the world, it has been speculated that it must have mutated into something more effective at reaching deep into the lungs of its victims, perhaps turning the immune systems of young and healthy victims against them as they choked on copious secretions. The virus spread more and more quickly, dashing around the globe to become a true pandemic. In the end, it swept across Europe and North America, down through Latin America, into Asia and Africa, and even to the most remote islands on the globe.

- To take just one example of its fury in an American military facility, one reported infection at Camp Devens in Massachusetts, became, in only six days, 6,674 cases. By 1919, the flu had killed a total of at least 550,000 Americans, and perhaps as many as 50 million or more across the rest of the world, wreaking the most havoc in India where it killed seventeen million people alone.

- The Spanish flu was easily the most destructive influenza outbreak in history. As has been widely reported, more United States soldiers died from the Spanish flu during World War I than from the war itself.
1976 SWINE FLU

Is yesterday's swine flu today's bird flu?
By Marc Siegel  USA TODAY

A newly mutated flu virus infects a man in New Jersey, and he dies within a day. Health officials fear that the general public has no immunity to this new strain and predict a severe pandemic on the order of the 1918 "Spanish flu." The president holds a news conference and recommends that all Americans be inoculated.

This scenario reads like something from our near future. Experts predict that the bird flu virus might hit our shores within a year. In fact, it's a news flash from three decades ago. The events of the so-called swine flu in the USA seem hauntingly familiar to those of us who are focused on the current bird flu, and they can serve as a useful guide on what to do now and — perhaps as important — what not to do.

Despite the fact that H5N1 — the bird flu virus — remains essentially a bird disease, Anthony Fauci, esteemed director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, has spoken of the need to make more than 100 million doses of a vaccine for H5N1 available to Americans.
THE SPECTOR OF 1918

• We've been here
  The rush to make vaccines for a flu virus to which we have no immunity is not a new concept. This is what happened during the swine flu fiasco of 1976, when the fear of another killer outbreak provoked a national political response and a rushed vaccination program. More than 40 million people received the swine flu vaccine that year against a new pig virus that ultimately never took hold.
  It was later determined that the swine flu wasn't as virulent or as deadly as originally thought. But more than 1,000 cases of Guillain-Barré syndrome, a life-threatening ascending paralysis, occurred in those who received the vaccine, which had been rushed into production. The public relations nightmare and lawsuits against the government helped to drive many drug companies away from making flu vaccine at all. (Of 27 companies that manufactured flu vaccines at the time, only three still do.)
  So what happened to ignite this overreaction? It all started when David Lewis, a military recruit at Fort Dix, N.J., became ill in February of that year and died within a day, apparently of a mysterious new flu virus. Over the next two weeks, more than 200 other recruits were found to have antibodies to this swine flu, meaning they had caught it and survived. At least one recruit became ill. Public health officials jumped to the conclusion that this was the first wave of flu, and that it would return with a vengeance in the fall. They feared millions of deaths.
  In 1976, health experts believed that history gave them plenty of reasons to be afraid. It was thought, incorrectly, as it turns out, that the Spanish flu had jumped from birds to pigs before mutating into a massive killer of humans. Nevertheless, there is a disturbing similarity between 1976 and today: A worst-case scenario, just a prevailing theory, is used to justify a massive public reaction.
FORECASTS OF DOOM

• David Sencer, then the head of the Centers for Disease Control, began to make proclamations and forecasts of doom. In a memo March 18, 1976, Sencer wrote, "The entire U.S. population under the age of 50 is probably susceptible to this new strain." Sencer still maintained, in a CDC publication earlier this year, that "when lives are at stake, it is better to err on the side of overreaction than underreaction."

• Sencer's recent statement shows a continuing lack of insight because it assumes that the only choices available to a public health official are either protecting all of civilization or not protecting it at all. In fact, decisions on potential health threats are never so clear-cut.

• Thirty years ago, Sencer headed a group of distinguished scientists (including the polio vaccine inventors Jonas Salk and Albert Sabin) who met in Washington with President Ford for the purpose of persuading the federal government to take action. Ford, with flagging public support and in the midst of a presidential election campaign, attached himself to the issue and held a national TV news conference announcing a plan to vaccinate every American by the fall.

• A similar scene played out late last year. President Bush, supported by several of today's greatest scientists and public health experts, responded to the risk of the bird flu virus by announcing a $7.1 billion plan for pandemic preparedness. At the time, Bush was reeling in the aftermath of Hurricane Katrina and found that linking the bird flu with the historical precedent of the 1918 "blue death" gave him an issue in which he could be perceived as our protector.
LESSONS FOR TODAY

• Short term preparedness for bird flu may divert money from other diseases such as HIV, tuberculosis, malaria, and malnutrition that are already killing millions.

• A rushed production of vaccines could lead to premature use. That could mean significant side effects, or perhaps worse, for any American who is inoculated.

• Currently, $3.8 billion of Bush's plan has been approved for this year and $2.6 billion budgeted for 2007. But the majority of the money is set aside for emergency stockpiles of vaccines and anti-virals. More money should be budgeted for upgrading how vaccines are made and for building a health care infrastructure designed to anticipate many scenarios.

• Even if the worst-case scenario occurs and the bird virus mutates into a form that can pass easily from human to human, it might still not signal the next pandemic. There is much about flu genetics that we don't know, such as whether the virus will cause the human population significant harm.
<table>
<thead>
<tr>
<th>FACTOR\ECOLOGICAL CHANGES (including those due to economic development and land use)</th>
<th>EXAMPLES OF SPECIFIC FACTORS: Agriculture; dams, changes in water ecosystems; deforestation/reforestation; flood/drought; famine; climate change</th>
<th>EXAMPLES: Rift Valley fever (dams, irrigation); Argentine hemorrhagic fever (agriculture); Hantaa (Korean hemorrhagic fever) (agriculture); Hantavirus pulmonary syndrome, southwestern US, 1993 (weather anomalies)</th>
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<tbody>
<tr>
<td>HUMAN DEMOGRAPHICS, BEHAVIOR</td>
<td>Societal events: Population migration (movement from rural areas to cities); war or civil conflict; economic impoverishment; urban decay; factors in human behavior such as commercial sex trade, intravenous drug use; outdoor recreation; use of child-care facilities and other high density settings</td>
<td>Spread of HIV and other sexually transmitted diseases; spread of dengue (urbanization)</td>
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<tr>
<td>INTERNATIONAL TRAVEL AND COMMERCE</td>
<td>Worldwide movement of goods and people; air travel</td>
<td>Dissemination of HIV; dissemination of mosquito vectors such as Aedes albopictus (Asian tiger mosquito); ratborne hantaviruses; introduction of cholera into South America, dissemination of O139 (non-O1) cholera bacteria (via ships)</td>
</tr>
<tr>
<td>TECHNOLOGY AND INDUSTRY</td>
<td>Food production and processing: Globalization of food supplies; changes in food processing and packaging. Health care: New medical devices; organ or tissue transplantation; drugs causing immunosuppression; widespread use of antibiotics</td>
<td>Food production processes: Hemolytic uremic syndrome (certain E. coli strains, from cattle, contaminating meat and other food products); Bovine spongiform encephalopathy; Nipah (pigs); avian influenza; SARS (probably)Health care and medical technology: Contaminated injection equipment (Ebola, HIV); opportunistic infections in immunosuppressed patients; Creutzfeldt-Jakob disease from contaminated batches of human growth hormone</td>
</tr>
<tr>
<td>MICROBIAL ADAPTATION AND CHANGE</td>
<td>Microbial evolution, response to selection in environment</td>
<td>&quot;Antigenic drift&quot; in influenza virus; possibly genetic changes in SARS coronavirus in humans; development of antimicrobial resistance (HIV, antibiotic resistance in numerous bacterial species, multi-drug resistant tuberculosis, chloroquine resistant malaria)</td>
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Disease in Perspective

WHAT WE FEAR VERSUS WHAT WE ACTUALLY DIE FROM

<table>
<thead>
<tr>
<th>Disease</th>
<th>Deaths in the U.S.</th>
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<tbody>
<tr>
<td>Smallpox</td>
<td>0</td>
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<td>Chemical Weapons</td>
<td>0</td>
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<tr>
<td>SARS</td>
<td>0</td>
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<td>Mad Cow Disease</td>
<td>0</td>
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<tr>
<td>Bird Flu</td>
<td>0</td>
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<tr>
<td>Anthrax</td>
<td>5 in 2001</td>
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<tr>
<td>Terrorism</td>
<td>2,978 in 2001</td>
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<td>West Nile Virus</td>
<td>200-300 yearly</td>
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<tr>
<td>FLU</td>
<td>36,000 yearly</td>
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<tr>
<td>Coronary Heart Disease</td>
<td>700,000 yearly</td>
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<tr>
<td>Cancer</td>
<td>500,000 yearly</td>
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<tr>
<td>Traffic Accidents</td>
<td>100,000 yearly</td>
</tr>
<tr>
<td>Infant mortality</td>
<td>25,000 yearly</td>
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Marc Siegel MD, author of *False Alarm: The Truth About the Epidemic of Fear*
Public Perception of Risk

• Smallpox – December, 2002 – NEJM survey shows 65% of public choose immediate vaccination for all

• Avian Flu – April, 2006 – AP/IPSOS Public Affairs Survey – 35% believe they are family member will get H5N1. 53% believe it would be fatal.
• BIRD FLU IN PERSPECTIVE