

## Benenson Lecture

Let me begin by wishing all of you, the School, the faculty, students and friends a happy 25<sup>th</sup> birthday. I recall well the launching of this School with its remarkable starting core of veteran faculty – including Bud Benenson. Their attract is not difficult to understand, what with the opportunity to be part of the birthing of a new baby and to do so in a climate like this in San Diego. After 2 cold weeks and nightly freeze warnings in Baltimore, it is refreshing to come here and to know that yes, spring will eventually come –even to Maryland.

You accord me a very great honor in asking me to present this first Benenson lecture. To me, Bud was a Renaissance type of man in my infectious disease world -- from “bench to bush”, broadly knowledgeable of the entire field, ever inquisitive, always approachable and more than willing to offer a point of view and ideas. Unquestionably, he was one of the most important, yet one of the least heralded, professionals in the public health infectious disease field throughout the course of his career. From the late 1950s through the mid-1980s, there was a prevalent view, indeed a degree of hubris, that we had conquered the infectious diseases. And this, I will comment upon later. Bud was one of a comparative few who continued to focus on the infectious diseases; who was knowledgeable of contemporary developments in microbiology and in the pathogenesis of disease; and, at the same time, was concerned about the translation of this into public health practice. Even today, regrettably, the Benenson species is still all too rare as witness so many of the current hysterical and ill-founded injunctions about controlling a possible pandemic of avian influenza epidemic. But more on this later.

This was the man who served for 25 years as editor of a reference book that we all kept on our shelves, the *Control of Communicable Diseases in Man*. He served as a burr under the saddle of more committees than one can imagine. He had a unique ability to see practical applications, to ask critical questions and to play an effective advocacy role. He played an essential part in the smallpox eradication program, roles unknown to most. I will cite only one apparently simple set of observations that had profound implications in the program—the proper technique for interpreting the reaction to a smallpox vaccination. Just to remind you – the smallpox vaccine is a living virus; it is scratched into the superficial layers of skin; and it is expected to multiply and so induce immunity.

How to interpret the reactions to vaccination was ingrained through years of medical practice. It was dead wrong. As of 50 years ago, it was assumed by most that if, following vaccination, there was erythema at the site during the first two to three days, it indicated that the vaccinia virus had grown (proliferated) and that the vaccination was successful. If no reaction was seen, it was assumed that the person was immune. As of the 1950s, my own son was vaccinated three times with no cutaneous reaction. I was solemnly informed that he must have a natural immunity to the disease!

Bud performed a series of carefully planned, well-controlled studies that showed that if, before inoculation, one destroyed the vaccinia virus by heat, an erythematous reaction occurred that could last for 2 to 3 days. It was simply a foreign body reaction. It usually meant that the vaccine was no good. If there was no reaction, it indicated, in fact, that a poor vaccination technique was responsible. Only if the cutaneous reaction lasted for at least 5 to 7 days could one be confident that the virus had multiplied producing or reinforcing protection. He presented his studies in 1951 and pressed the case repeatedly

to an all too complacent community. So complacent, in fact, that even in the 1960s, probably a third of the supposedly vaccinated US Peace Corps Volunteers who came to work in the WHO program had primary vaccination responses when we revaccinated them on arrival. However, Bud prevailed in the 1964 WHO Expert Smallpox Committee; its report reflected his findings; and thus, throughout the program, in field testing and quality control team, we were on the right track.

Was Bud ever really given credit for this discovery? I don't think so. Did his observations warrant a Nobel Prize in Medicine? No, but then there is no Nobel Prize in Public Health.

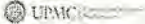
Bud spent a good portion of his time working on diseases of global concern – what have begun to be called “New and Emerging Infections”. They were little studied in the industrialized world except in a few small but unique laboratories, among the most important being those at Walter Reed, Fort Detrick and at a very few military research installations in such as Thailand, Taiwan and Egypt. With small budgets and staffs, the military scientists made enormously important contributions to the third world and to the US. Today, there is a clamor to considerably expand the research capabilities of these and similar laboratories. It was in these settings that Bud spent many years working.

Let me elaborate on our concerns about new and emerging infections. Some of these are well known to you now but unknown until comparatively recently.

**Abram Benenson Lecture**

**D.A. Henderson, MD, MPH**  
*Professor of Medicine and Public Health  
 University of Pittsburgh Medical Center*

University of California/San Diego  
 School of Public Health  
 13 April 2007


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*Abram for this lecture  
 Sobering thought*

**New and Emerging Infections**


*Man's only competitors for the  
 dominion of the planet are the viruses  
 – and the ultimate outcome is not  
 foreordained.*

*Joshua Lederberg*  
 Nobel Laureate

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**“Conquest” of the infectious diseases**  
 1950s-70s

- Dramatic changes post WW II
  - Vaccines
  - Antibiotics
  - Nutrition
  - Housing
  - Sanitation
- Decline or elimination of many diseases in the industrialized world
  - Smallpox, diphtheria, whooping cough, tetanus, polio, measles, *et alia*

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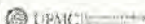
- *“One can think of the middle of the 20<sup>th</sup> century as the end of one of the most important social revolutions in history, the virtual elimination of the infectious diseases as a significant factor in social life”*

*Sir Macfarland Burnet*  
 Nobel Laureate, Australia, 1962

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**A cloud on the horizon**

- June, 1981 – first cases of AIDS diagnosed
- April, 1984 – HIV is identified  
*“the triumph of science over a dread disease”  
 “a vaccine will be available in 2 years”*
- 2007 - a world-wide pandemic in progress
  - 4<sup>th</sup> leading cause of death world-wide
  - No vaccine
  - No curative drug

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*1989 - 1999. Other threats*

- More than 30 new agents in 25 years
  - SARS – from Asia
  - West Nile encephallitis – from Middle East
  - Monkeypox – from Africa *PARV E Davis*
  - TSE – “mad cow” disease – from UK
  - Hanta virus pulmonary syndrome – U.S.
  - H5N1 influenza – from Asia
- IOM Committee on Emerging Infections
  - 1991-92 – *National Academy Press, 1992*

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*Other threats*

### Why now?

- Growth in urban populations
  - Population of cities
    - 1950 – 2 with more than 5,000,000
    - 2004 – 6 with more than 15,000,000
  - By 2015
    - 5 cities with more than 20,000,000 persons
    - 55% of world's population in urban areas

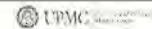
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### Why now?

- Growth in urban populations
- International travel
  - Volume
    - 18 million commercial air flights yearly
    - 1.6 billion air passengers per year
  - Remote destinations – tropics, rain forest
  - All cities less than 36 hours from all others

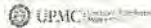
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### Why now?

- Growth in urban populations
- Travel
- Growth of hospitals in endemic areas
  - Major sites for disease distribution
  - Problem of blood borne diseases
  - Development of antibiotic resistance

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### Why now?

- Growth in urban populations
- Travel
- Growth of hospitals in endemic areas
- Food supply
  - Internationalized
  - Industrialized
    - Animal husbandry
    - Food processors

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### The future

- The threat of new and emerging infections is increasing
- Sources of the threat:
  - Natural mutation of microbes
  - Emergence of organisms from remote areas
  - Biological terrorism
- The threats are international

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### Concerns about terrorism –pre 1995

- Little concern about terrorism
- Control of nuclear arms believed to be effective
- Unwarranted confidence in the Biological Weapons Convention of 1972
- Intelligence capabilities limited

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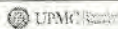


## Intentional release of biological agents

*Morally argument.*

- Rationale for ignoring the threat until mid -1990s
  - Too difficult to grow organisms
  - Technologically difficult to disseminate
  - Not used because of a moral barrier

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*Bw morally argument*

## Watershed events

Iraq -- 1995

- Papers of Iraqi bioweapons program became available
- Production and testing of anthrax
  - Aerosol studies
  - Use of drone aircraft

*Concern: Deliberate development of anthrax as a weapon by a nation-state*

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## Watershed events

Aum Shinrikyo -- Japan

- Religious cult released Sarin gas in Tokyo subway (1995)
- Cult - previously unknown to intelligence
  - Thousands of members, well-funded
  - Tried to aerosolize anthrax and botulinum toxin throughout Tokyo at least 8 times
- *Concern - unknown, large, non-state sponsored organization, acting without concern for moral deterrents*

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## Watershed events

USSR Bioweapons Program

*Weapons Concerns*

- Secret program - not suspected until 1989
- 1992 - Ken Alibek, Deputy Director of bioweapons program, deserts
- 1995 - Full scope of program apparent
  - 60,000+ persons in 50 different labs
  - 30 metric tons of anthrax spores in storage
  - Large capacity to produce smallpox virus
- *Concern - Expertise and possibly specimens now dispersed world-wide. Still a secret program*

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## Civilian counter-terrorism initiatives

1995-99

- Presidential Decision Directive #39 - 1995
- For terrorist events-- emergency response *response*
  - First responders -- police, fire, emergency ~~medical~~
  - DoD to do the training
  - FBI to find the bad guys
  - Public health and medical treatment - ignored
- Assumption that chemical and biologic weapons required the same response
  - A new word "CHEMBIO"

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## Biological weapons

"the poor man's nuclear weapon"

- Growing number of labs and expertise
- Necessary ingredients available
- Production in small facilities
- Inexpensive
- Few technical staff required
- Small quantities produce a major effect
- Easily transported

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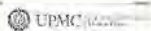


## New World Coming

- *Besides nuclear weapons, biological weapons are the only weapon class with the capacity to take the nation past the "point of non-recovery"*

*Admiral Stansfield Turner, former CIA Director*

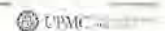
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## Medical and public health interest 1997

- Biological weapons a taboo subject in most of academia
- CDC/NIH – no program and no interest
- Research in potential weapons – nil
  - Smallpox, anthrax, tularemia, bot tox, etc
- Secretary of HHS – not involved
- Locus of competence – Fort Detrick

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## Reassessment of priorities – 1997-2001

- Plenary panel at IDSA – September 1997
- JHU Ctr for Civilian Biodefense Strategies--1998
  - Working group to decide priority (Class A) agents
  - Two national symposia for medical and public health professionals
  - HHS funding -- \$8m > \$173m > \$300m
  - The Dark Winter exercise (June 2001)
- The anthrax attacks (October 2001)

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## DHHS --Office of Public Health Emergency Preparedness-2001

Emergency appropriation – January 2002  
\$3 billion

- State directors for preparedness and planning
- Surveillance and epidemiologists
- Laboratory capacity
- IT systems
- Training and education
- Research on principal agents

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## Funds for Public Health Emergency Preparedness

- State and local health departments
  - \$1 billion with flexibility to allocate funds
- Schools of Public Health
  - Twenty grants of \$1 million each to strengthen education programs and work with state and local health departments
- Public health diagnostic laboratories

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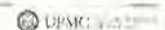


## Biological Agents of Greatest Concern

- Smallpox
- Anthrax
- Plague
- Tularemia
- Botulinum Toxin
- Hemorrhagic fevers

Agents that if released, could threaten the integrity of government

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## Smallpox – a serious but now diminished concern

- Risk is small but potential for global catastrophe
  - Acquisition of smallpox virus – Former Soviet labs
  - Dissemination as aerosol – not difficult
- Response
  - Educational programs on clinical features
  - Stockpile -- from 90,000 to 300 million doses
  - Diagnostic labs — 2 to >100

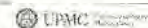
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## Anthrax – the greatest concern

- B. anthracis – easy to obtain
  - Former Soviet laboratories
  - Natural infections occur around the world
  - Until 2003 – 46 labs offered specimens
- Demonstrable intent and capability to use
  - Aum Shinrikyo
  - Iraq
  - Russia
  - U.S. terrorist "x" of 2001

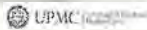
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## Production and dispersal of anthrax

- Methods of production widely known
  - Only a small lab needed
- Aerosols – either from powder or slurry
  - Crop dusters
  - Ambient sprayer s – easily obtained
  - Ventilation systems

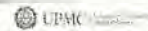
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## Anthrax detection

- Prevention
  - Interdiction of terrorists – unlikely
- Detection
  - Biowatch air sampling – technology inadequate
  - Biosense reporting -- unproven, untested
  - Early, rapid diagnosis – difficult

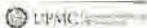
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## Response to anthrax release

- Vaccination and antibiotic distribution
  - A logistics nightmare
  - Available vaccine – reactogenic, limited supply
  - Limited tolerance of antibiotic for 60 days
- Clean-up of environment
  - Cumbersome, expensive, uncertain
- Hospital care
  - Limited capacity to care for casualties

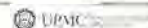
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## Pandemic Flu – a test for preparedness

- H5N1 -- unprecedented flu strain causing massive deaths in poultry and 50% death rate in humans
- Influenza – 1918 – H1N1
  - Case fatality rate – about 2%
  - Deaths U.S. 675,000  
World > 50,000,000
- H5N1 influenza – 2004-2007
  - >250 cases, about 125 deaths

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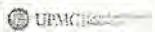




## Status – April 2007

- Infected wild fowl, chickens, ducks, turkeys
  - Asia
  - Much of Eastern Europe
  - Africa
- Human cases – contacts of birds (a few patients)
  - Asia and Africa
- Vaccination programs -- *VACCINATING PROGRAM*
- Massive slaughter of fowl in infected areas
- Embargo on fowl from infected areas

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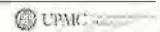


## Prospects for the U.S.

- Avian H5N1 – likely means of importation
  - Migratory birds
  - Bird smugglers
- Human pandemic flu
  - Will it occur?
  - When might it occur?
  - Can it be slowed or stopped?
- Reality and myth

*MODELING*

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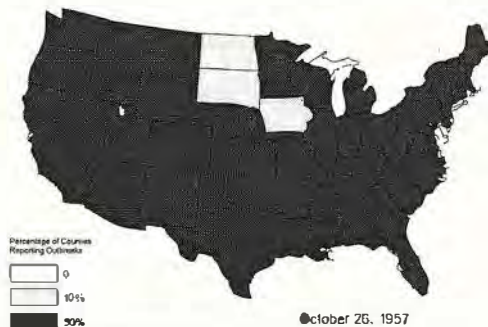
Influenza Outbreaks



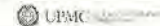
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Influenza Outbreaks



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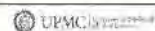


## Key assumptions

- Expected attack rate -- about 25 %
  - 75% do not develop illness
- Duration of outbreak in a city – 10-12 weeks
- Illness lasts ~10 days
  - Peak absentee rate because of illness = < 15%
- Patients with flu begin spreading virus one to two days before symptoms

*No quarantine measures have slowed the spread*

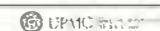
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## Actions to deal with pandemic flu recommended

- Vaccination – most important
  - No vaccine will be available until specific strain identified and produced in quantity – 6 months+
  - Research promises a more broad-based antigen
- Antiviral agents in treatment
  - Tamiflu – uncertainties about side-effects, development of resistance, utility
- Isolate sick patients
- Provide for care of large numbers of patients

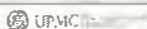
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### Other measures Impractical

- Close borders and/or screen arriving air passengers from abroad or ? other states
  - 317 ports of entry into the U.S.
  - 1.1 million passengers and pedestrians daily
- Screening in Asia for SARS
  - 3.5 million screened for temperature- 0 cases

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### Other measures Impractical

- Reduce contact among individuals
  - Quarantine infected households
  - Shelter in place – for 3 months?
  - Close churches, schools, malls, etc – for 3 months ?
  - Station workers 3 feet apart

*Risk—an otherwise manageable epidemic could be turned into a national catastrophe*

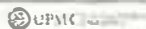
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### Principal tenets for dealing with pandemic flu -- 2006-2007

- Alleviate anxiety; avoid panic
- Change the normal social activities of the city as little as possible
- Provide care for those who are ill
  - Community-wide efforts are requisite to plan for the care of a tidal wave of patients

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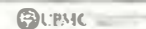


### Prospects for the future

- Influenza pandemics caused by new strains are certain. Not "if" but "when".
- New and emerging infections of unexpected types will occur.
- Sophisticated terrorist events are increasing

*Community-wide planning and preparation are essential. Public health should be taking a lead role. But is it?*

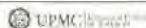
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### WANTED

A practical, experienced expert in public health practice and infectious diseases to assume national responsibility.

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### WANTED

- A practical, experienced expert in public health practice and infectious diseases to assume national responsibility.

*Someone like Bud Benenson*

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