Conquering Pandemic Flu by Non-Pharmaceutical Means, and Other Thoughts on Health Care

by
Richard L. Garwin
IBM Fellow Emeritus
IBM Thomas J. Watson Research Center
P.O. Box 218, Yorktown Heights, NY 10598
RLG2@us.ibm.com, www.fas.org/RLG/, www.garwin.us

Presented at the Weekly Seminar of the Department of Microbiology
Mt. Sinai School of Medicine, New York, NY 10029
February 16, 2010
Some of you will think that I am carrying coals to Newcastle, while others will not even recognize that metaphor. In any case, you are all aware of the potential for hundreds of millions of deaths if we had a virus with the infectivity of the 1918 strain, and the near-50% mortality exhibited in humans by the H5N1 avian flu, in the rare cases in which humans have been infected and the even rarer cases of human-to-human transmission.

Of course, the solution to this epidemic of unprecedented consequence would be a rapid cycle to define and produce billions of doses of a vaccine, or even a routine vaccine that would recognize a non-mutating portion of the virus. And if I were the Gates Foundation or the WHO, I would not rely on Big Pharma but would be spending a lot of money with little groups in academe and industry to perfect cell culture in general for the production of influenza vaccine.

But until that remedy is available, we should consider the fundamentals of epidemics and, in my opinion, understand that we might actually conquer such epidemics by non-pharmaceutical means.

An epidemic is generally characterized by a reproduction factor $R_o$, a serial interval $I$, and mortality $M$. The reproduction factor is the ratio of the number of those newly infected in one generation to the number in the previous generation, and the serial interval is the number of days between generations, on average. Mortality is the fraction of those infected who die under the conditions of the epidemic. Simple differential equations in terms of the fraction of population Susceptible,
fraction Infectious, and fraction Recovered (or dead) allow one to derive consequences from these assumptions via the “S-I-R” model. For smallpox, $Ro$ is about 3 and $I$ about 14 days$^1$.

Without any intervention, though, it is remarkable how small $Ro$ is for influenza—between 2 and 3, it is said. Let’s take $Ro = 2.0$ and $I = 4$ days. Under these circumstances, if there are 100 cases on day zero, there will be 200 newly infected on day 4. The next generation will be 400 on day 8 and 800 on day 12, 1000 on day 13, and one million on day 53. And so on? Yes, until the Susceptible population is depleted by 50%, in this case. But before that, social behavior might change to reduce transmission through better hygiene, social distancing, and the like.

In contrast, if it were possible to reduce $Ro$ by a factor 3 so that it is no longer $Ro$ but simply $R = 2/3$, then on the same days, 0, 4, 8, 12, those newly infected would be 100, 67, 44, 30, etc, The total number infected would be a good fraction of the population with $Ro = 2.0$, but only the number of index cases multiplied by $1/(1-R) = 3.0$ for an $R$ of $2/3$. So instead of 100,000,000 or so cases, the total number with 100 index cases would be 300. The task, then, is to reduce the infectivity by a factor 3. This is clearly possible for many individuals by reducing the occasions for viral transfer and reducing the efficiency of viral transfer.

Since we do believe in the germ theory of disease, the virus is communicated from one person to another either by direct contact, by transfer through the air in the form of droplets or aerosol, or by indirect transfer through solids—fomites. It is a shame that we don’t have a better idea, for ordinary seasonal flu, the portion of individuals who are infected by one route or another.

---

I have been interested in this low-tech approach to vanquishing epidemics since at least 2001, when I published a paper in The New York Review of Books in response to the 9/11 attacks.\textsuperscript{2} I greatly fear the use of communicable disease as a terrorist weapon, and ever since my service on the President’s Science Advisory Committee in 1972, at which time I opposed the elimination of routine smallpox vaccination for Americans, I have been concerned about the implications of vulnerability of a naïve population. Of course, that is what we have to various influenza strains, because of the incessant mutation of the bug. In 2002 I introduced this to the sessions of the World Federation of Scientists—WFS—meeting in Erice, Sicily, and since then I chaired for some years a “Permanent Monitoring Panel” for the Mitigation of Terrorist Acts, a principal concern of which has been the combating of terrorist-induced pandemics.

At least for advanced nations, nothing is simpler than near-universal vaccination, but in the modern world there can be very little time for prophylactic vaccination, because of the rapidity of spread of an infection carried by air travel.

Although the three-parameter model of an epidemic—$R,I,M$—is gross, it indicates what could be done essentially to eliminate the epidemic and explains why epidemics eventually burn out. At the next level of detail, one can write differential equations among three compartments—the susceptible, infectious, and recovered—$S, I, R$ model--and at an increasing level of detail, one can determine various populations with their own transition probabilities among the compartments, this


Conquering Pandemic Flu by Non-Pharmaceutical Means, and Other Thoughts on Health Care
accounting for the greater cross-infectivity of children, and the transfer of disease from children to their own households, for instance.

After some years of providing various commentaries and hortatory material and posting such on my website www.fas.org/RLG/, I had the good fortune to team with Paula Olsiewski of the Alfred P. Sloan Foundation and with Dr. Stephen S. Morse as co-director of a workshop at Columbia University in June 2006, a brief report of which was published in *Science*. We convened about 40 participants, from the public-health community, business, academe, and the national laboratories. I found two contributions particularly interesting. One of them was from T.C. Germann with a detailed model of the spread of pandemic influenza. A second was a presentation by Lawrence Wein, that has since been published in modified form.

In particular Germann showed his team’s highly detailed supercomputer simulation of the spread of a pandemic that allowed the modification of parameters such as degree of vaccination, effectiveness of vaccine, reduction in air travel, and the like.

Unfortunately, there are major unknowns in this modeling. I began with the observation that if one had a nominal influenza epidemic with an $Ro = 2.0$ and could by Draconian measures reduce that by a factor 3 to $R = 2/3$, an epidemic that could infect tens of millions of people in the United States could be limited to infecting a mere three times the index number of cases—say 3000 altogether for an index number of 1000 cases by the time the epidemic was recognized. Of course, if only a fraction of the population took such effective measures, the reduction of infectivity would have to be more substantial among those complying in order to achieve the same results.


On the other hand, if measures to limit infection were not evenly applied, but were implemented in a most-effective-first approach, a greater reduction in the average $R$ could be obtained for a given effort.

This approach would not necessarily vaccinate first those who are most susceptible to disease—those who are weakest or (for normal seasonal flu) oldest. It would concentrate on those who most effectively spread the disease, even if they themselves might have a low mortality. It would take me too far afield to comment on the detailed simulation by Germann. I show here a few figures from the paper, but the dynamical simulation is available on-line.
Day 50

[Map of the United States with different color intensities indicating a spread or distribution, likely related to a pandemic flu situation.]

Conquering Pandemic Flu by Non-Pharmaceutical Means, and Other Thoughts on Health Care
“It's probably not going to be practical to contain a potential pandemic by merely trying to limit contact between people (such as by travel restrictions, quarantine or even closing schools), but we find that these measures are useful in buying time to produce and distribute sufficient quantities of vaccine and antiviral drugs,” said Germann of Los Alamos’ Applied Physics Division.

Based on our results, combinations of mitigation strategies such as stockpiling vaccines or antiviral agents, along with social distancing measures could be particularly effective in slowing pandemic flu spread in the U.S.,” added Longini.

But exactly what measures are optimum and most compatible with the behavior of people and with the conduct of essential activities in modern society? Here it is hardly forgivable that we know so little, as commented in our 2006 Science article, confirmed by many participants at the workshop, and finally by the publication of a “Major Article” in CID of February, 2009 on hand hygiene.
Epidemic curves (note the logarithmic scale) demonstrating the effectiveness of several different mitigation strategies, as compared to the baseline scenario without any intervention, for different values of $R_0$.

Germann TC et al. PNAS 2006;103:5935-5940

NOTE the logarithmic scale for “Current Incidence”
Economists are largely undeterred by lack of facts, which only make their job more difficult. But I mean this as approbation for the presentation and papers of Wein, in this case. First, Larry Wein judges (without much experimental confirmation) that influenza is communicated in large part by aerosol transmission and not by droplets or by fomites. His prescription, therefore, is that individuals wear N95 masks, capable of trapping 95% of aerosols of diameter 0.3 micron or larger. There are, of course, many problems with such a prescription. The masks are uncomfortable and warm or even stifling. They are often not fitted very well, and there are, by far, insufficient masks and money to pay for them if they are used by the public as they are in the hospital surroundings, with a new mask for every encounter. So I long ago set out with my friend Stirling Colgate to encourage simple experimental determination of the possibility of multiple reuse of N95 masks. I referred to this in my presentation to an Institute of Medicine panel and, of course, made it a point to bring up at our 2006 workshop.

In December, 2009, Stirling Colgate and his colleagues at New Mexico Institute of Technology—NMIT—published on YouTube a simple experiment showing that aerosol droplets of 3-micron diameter are in fact quantitatively trapped by the N95 mask reused 16 times and perhaps good for 100 cycles of use and washing. Here are the current opening and closing slides from that presentation.

---

6 “Face Masks in Context for Fighting Flu—Health Care Workers and the General Public,” by R.L. Garwin, presentation to the IOM Study of Reusable Facemasks for Protection in Pandemic Influenza, March 6, 2006, Washington, DC.

7 [http://www.youtube.com/watch?v=JLeDf0dHg4M&feature=channel](http://www.youtube.com/watch?v=JLeDf0dHg4M&feature=channel) (Not there, on 02/15/2010)
The Multiple Re-use of Face Masks

Stirling Colgate; Los Alamos Nat.Lab. & NMIMT: physicist
David Westpfahl; Phys. Dept., NMIMT: physicist
Video: R.Hepler; Educational Outreach and Distance Instruction; NMIMT

• Question: How many times can a cheap face mask be reused effectively in the event of a pandemic flu?
• Answer: Probably 100 times (with rinsing in Clorox) and drying.
• Method: Fluorescent dye in water of a nebulizer, black lights, and two masks in series.
• Results

Inner, mask, in series, dim, no fluorescent drops.

Inner mask

Outer mask

Outer mask bright, yellow, fluorescent, 3-micron drops (nebulizer). Washed 16 times.
The Multiple Re-use of Face Masks

Stirling Colgate; Los Alamos Nat.Lab. & NMIMT: physicist
David Westpfahl; Phys. Dept., NMIMT: physicist
Video: R.Hepler; Educational Outreach and Distance Instruction; NMIMT

We have shown that droplets that can carry virus are stopped by a mask even after multiple disinfectant washings. We have not demonstrated that virus is actually stopped.

Questions for funded research:
• What percentage of flu infections is caused by pneumonic drops carrying virus and what fraction is caused by virus alone?
• What fraction of active virus passes through a (new or washed) mask when water drops are stopped?
• What fraction of infections is caused by manual contact?
Note, however, that this shows only that droplets are not to a significant extent transmitted by the mask, because a single secondary N95 mask beneath the one under test for multiple reuse shows a vast reduction in fluorescein content. These masks were reused by washing in household Clorox (5.25% chlorine) diluted 100-fold, and then dried. Although not mentioned, it can be assumed that the elastic ties and other gross properties of the masks remain unchanged during this time.

Note also that this experiment did not check the fit of the mask, which could be improved as indicated by other experiments by the use of nylon stocking material to provide a resilient cushion around the edge of the mask.

Wein prescribes that in a time of flu contagion, under his assumptions, sleeping in the same room with a person who is infected but does not yet show symptoms greatly reduces the overall effectiveness of the mask as a prophylactic against infection. Relatively few households have the luxury of spare rooms or beds, nor the desire to implement this particular measure. Other approaches may be predicted to be useful.

For instance, in 2002 Ralph Gomory, Matt Meselson and I published in the Washington Post an OpEd[^8] “How to Fight Bioterrorism” advocating air filtration for reducing airborne infection in the workplace, school, or home. For this there are at last two approaches. One is to assume (and even to ensure) that air in a room is thoroughly mixed, and then ensure that it is gulped by a filter or inactivation device much more rapidly than it is by the people in the room. If this is done so that

the purification of the air overwhelms the natural leakage of the air (typically two air changes per hour), then the infection rate from aerosol-borne bugs would be reduced in the same proportion.

Even better would be a kind of laminar airflow so that the expired air from each individual is carried to the air purifier without largely mixing with the rest of the air in the room. Exhaled air is warmer and more humid, so it will typically rise in the room, and could be preferentially ingested by an air purification system.

Early on in our work in the Terrorism Mitigation Panel at Erice, Sicily, we realized that even if we could define measures to contain an epidemic, such would need to be put into an appropriate message. The message would need to be distributed, and the populace would need to be motivated to learn and follow the procedures.

In February 2009 there was published an evidence-based report on the effectiveness of alcohol-based hand sanitizers and of soap and water, against live H1N1 virus, with assay both by PCR and by infectivity.

In brief,

---


May 22, 2006

Conquering Pandemic Flu by Practical Measures

Over the past year, much public attention has focused on pandemic influenza, such as might arise from reassortment of the Type A (H5N1) avian flu that has been spreading from Southeast Asia, but expert consensus is stronger that a flu pandemic is likely than is the judgment that it will derive from H5N1. Even a recurrence or an image of the 1917-18 H1N1 "Spanish flu" that killed some 50 million people world wide would be a disaster in the modern age of specialization and globalization, and such a pandemic that occurred in the next few years could not be much eased by available stocks of vaccine or antiviral drugs. If the pandemic had the lethality (perhaps overestimated at 50%) of the present H5N1 for which there is no evidence of human-to-human transmission, it could kill a billion people or more, but there is no reason to believe that this lethality would be preserved in the transformed virus capable of such transmission and hence pandemic behavior.

Because there is a receptive audience to measures against pandemic flu, and because we have some novel and important perceptions to counter this serious and likely threat to health, life, and society, we present our analysis and recommendations for countering pandemic flu by nonpharmaceutical means. We speak of an epidemic in terms of a single reproductive actor $R_0$ ("R-naught") and a serial interval $\nu$ ("nu"). For the SARS epidemic, $R_0$ is about 3 and $\nu$ about 8 days. For smallpox, $R_0$ is about 3 and $\nu \approx 14$ days. And for influenza, $R_0 \approx 1.7\text{-}2.4$ and $\nu \approx 4$ days. In what follows we take for flu $R_0 = 2$, although we recognize that it will vary from society to society and in various groups within society. Unchecked, an epidemic that begins with $N$ "index cases" would give rise $\nu \approx 4$
days later to 2N additional cases, \( \nu \) days later to 4N more, 8N more, and so on, so that after \( M \) serial intervals there will be \( N(1 + R_0 + R_0^2 + R_0^3 + \ldots + R_0^M) \) cases altogether, until the susceptible population is exhausted and a substantial fraction of the population is resistant or even dead.

On the other hand, if by the nature of the germ or of population density or other measures to reduce the transfer of germs to additional victims, \( R_0 \) can be reduced below 1.0 (i.e., \( R_0 < 1.0 \)) the sum of successive generations is finite, even for \( M \) very large. Then the number of cases \( C \) totals \( N(1/(1-R_0)) \). If we use an example a reduction of \( R_0 = 2.0 \) by a factor 3, so that \( R_0 = 2/3 \), \( C = 3N \). We identify important measures that we believe may, if practiced, achieve this factor 3 reduction, so that a society in which 60 infective index cases enter per day would thus experience a total of 180 cases per day, or 65,700 flu cases per year—less than the normal seasonal flu that results in some 36,000 deaths each year from influenza in the United States alone. In the absence of such assumed effective measures, recent detailed modeling results\(^{11} \) [T.C. Germann, et al, 04/11/06] show on the order of 50% of the 281 M people in the US infected with pandemic flu—2000 times as many.

**Personal protective measures—PPM:**

These personal protective measures—PPM— that would appear to "protect" an individual by an assumed factor 3 would instead protect each individual in the society by a factor 2000. Under these circumstances, note that reducing or increasing the influx of infected persons (index cases) by a factor 3 would change \( C \) down or up by a factor 3 only—very different from the dramatic effect of a threefold reduction in the flu transmission factor \( R_0 \) within the society

---

Efforts to reduce the delay and to increase the rate of production of an effective vaccine are important, as are those to increase the production and protection from anti-viral drugs, but a pandemic in the next year or two would find inadequate vaccine and anti-virals for the population as a whole. This early pandemic would need to be met and might be vanquished by PPM in groups or societies which practiced such measures effectively in the face of contagion. Simply put, without such effective PPM, antiviral drugs and vaccines will be exhausted and a pandemic would infect most people and kill many; the assumed effectiveness of PPM in a society would reduce the pandemic to the status of seasonal flu and allow the protection of hospital and health care workers by such pharmaceuticals, even if there were insufficient stocks for the general population.

Influenza is transmitted primarily by the virus in droplets accompanying coughs and sneezes, by persistent aerosols (droplets too small to fall out of the air in a few minutes), and by virus transferred to the hand of the infected person and thence to doorknobs, support poles in public conveyances, hand shakes, or via other surfaces. The hand of a susceptible person acquires the virus, which then enters the body through contact of the hand with the mouth, nose, or eye.

**Primary PPM:**

1. Wash the hands after contact with potential contagion—e.g., when returning home, to the workplace, or frequently in space shared with others who may be symptomatic. If hand washing is inconvenient, use a 60+% alcohol-content hand sanitizing gel.

2. When in the presence of others, use a surgical mask or an N95 filter mask to protect against droplets or aerosols respectively. If masks are not available, improvise a mask such as a scarf over the eyes and mouth.
3. Don't shake hands; bump elbows in greeting.

4. Keep hands away from your face—especially eyes, nose, and mouth.

5. Don't infect others; use a tissue or piece of paper towel for sneezes and coughs and have a bag for used tissues.

6. Eliminate or reduce unnecessary trips, even local ones.

7. If you need to care for a person who might be sick with flu, use additional precautions such as diluted household bleach for bed clothes and for cleaning surfaces.

8. Practice these procedures at least one day every two weeks.

9. Clean and circulate air where people are in proximity, e.g., in transport, offices, assembly work.

**Communicating the measures:**

Communicating these measures should be considered an important part of training in public health. International, national, state, and local organizations (including businesses, schools, lodges, and faith-based organizations) should adopt and make available information and training, including check lists, bulletins, and web-based materials. Showing is superior to telling. Simulation games are likely to be made available on the web so that children and web-adept adults can see the effectiveness of PPM in vanquishing epidemics, as well as the impact of non-compliance by some.
Communications should be grounded in scientific evidence (or else identified as speculation). They should be empirically evaluated for effectiveness prior to dissemination. These evaluations will provide effectiveness estimates for the modeling. Communications need to be adapted to the culture and circumstances of their audience; they should be created well in advance of a pandemic, and then updated as needed. In some societies one must begin with mass education that the cause of this disease is germs—not evil magic or God.

**Motivating individuals, families, and groups to practice and evaluate the measures:**

Businesses and public-interest groups have an evident incentive to preserve the health and effectiveness of their members. Still, it will take staff, effort, and funds to adopt such programs, to reach the individuals through their various intersecting affiliations, and to ensure that PPM are practiced on schedule before any pandemic occurs. Examples might be: no access to public transportation on Thursdays without an improvised mask; posted public health rules requiring employers to have dispensers of hand sanitizing gel available in the workplace.

**Validating the personal protective measures:**

Large-scale and simplified computer models are an essential tool for understanding and communication. They should clearly identify assumptions made about human behavior. Results of research regarding that behavior should be reflected in the model, rather than relying on intuition. Where such research is lacking and the model is sensitive to the assumed specific value, then research to establish the correct value should be a priority. Research needs and results should be shared on the web. For a strategy that depends on masks and bleach, ensure that suppliers have planned for rapid transition to manufacture and distribution of such supplies on a timely basis.
Real-time modeling of the emergence of pandemics in one's society and elsewhere:

WHO, aided by country teams and international business should make available on the web current and accurate information to guide action by individuals and groups everywhere. Measurements of $R_0$ in one society will need to be interpreted by a model to give characteristics of the virus that a similar model will translate into $R_0$ values for other societies and groups, thereby guiding the intensity of PPM required. Note that only a factor 3 reduction in $R_0$ is required, but if 1 of 3 people don't comply, then even perfect compliance by the rest will not reach the goal. And universal noncompliance by a compact subgroup would allow a pandemic to rage in that subgroup.

**Monitoring adherence to PPM:**

Groups and public health officials should monitor training for PPM and the actual practice in the presence of flu in each group or country. Current and accurate data of case incidence should be made available on the web by responsible and credible groups for this purpose.

**Beyond personal protective measures:**

Prepare the population and groups for self reliance; prepare (and practice) the health care sector to do the greatest good in the face of overwhelming need.

Annexes (3):

**o- Pandemic Mitigation Factors By Population Sectors**

<table>
<thead>
<tr>
<th>Mitigation Factors</th>
<th>By Governments</th>
<th>By Industry</th>
<th>By Individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand washing or sanitization</td>
<td>Population education</td>
<td>Employee education and stock extra soap, gel</td>
<td>Family education and implementation</td>
</tr>
<tr>
<td>Use of masks</td>
<td>Population education</td>
<td>Employee education and stock</td>
<td>Family education and implementation</td>
</tr>
<tr>
<td>Reduced contact, elbow bump, cough etiquette</td>
<td>Population education</td>
<td>Employee education and stock</td>
<td>Family education and implementation</td>
</tr>
</tbody>
</table>
**Quick Availability of Vaccine**

Evidently real-time intelligence is needed on how a particular pandemic spreads. They are not all the same. Some flu strains provoke coughing or are more readily expired. There is, of course, a phenomenon of “super spreaders,” and such individuals should be identified and fitted with masks or particularly effective room purification systems. It remains that vaccination is by far the most cost effective solution. But not if it comes too late.

Clearly we need to characterize the germ more quickly than we do now, but then we need to have a vaccine design and production system that is far more responsive than is now the case. Large firms that can make more profit in other activities than in the low-profit vaccine field. Evidently the WHO and the Gates Foundation could fund appropriately chosen work on vaccines growing in cell culture, with rights acquired by the sponsoring...
Conquering Pandemic Flu by Non-Pharmaceutical Means, and Other Thoughts on Health Care

organization, even though some royalty might be paid to the groups whose approach is ultimately used for large-scale vaccine production. It is unlikely that U.S. government funds could be used to sponsor quick-response vaccine innovation in China and India, for instance.

Naturally, one should worry about such advances in applied virology increasing the capability of terrorists or terrorist collaborators. That is a matter for another day.

More General Remarks on Healthcare

While I am speaking, I thought I would mention a 1968 paper I published in Public Health Reports, as a result of my service on the New Technologies Panel of the National Commission on Health Manpower, the report of which was published by the GPO, 1967. I simply show a few slides and some excerpts of text here to indicate the substance of that paper, which is based on some of the earliest work I did at IBM in 1954 or thereabouts in connection with hospital information systems, and visits to Kaiser, the Karolinska, Los Angeles County Medical Center, and other establishments in the United States in the 1967 era, I was committed at that time to integrating the information to and from physicians, hospitals, testing laboratories, and the patient.

The paper addresses the requirement that any such system should not only be built but has to be built “for growth and with the aim of replacing (it) in 5 or 10 years.” And, the presentation emphasizes “self-norm” and overall system costs and benefits. It proposes at that time to spend “… at least 5% of the $43 billion expended annually for healthcare … to investigate and demonstrate ways in which healthcare can be less expensive and more widely and readily available.” It cautions “We should recognize the difference between a system in the process of development and one which has been fully developed and is ready for replication and use” and “We should also be ready and eager to spend money and time to develop a system to compete at some future specified time with continued use of an older, more expensive, and less efficient system.

Finally, in regard to cost minimization, it cautions against purely local decisions: “At present, no mechanism seems to exist to enable such decisions to be made easily, and while information systems may help medical economists understand better these interactions, the solution would seem to lie in part in proper incentives.”

Although 1968 was a time of the large and costly mainframe and the so-called mini-computer, far before the PC era, despite the 31% annual reduction in storage cost since then (something like a factor 3 million in 40 years) and enormous improvement in processing power per dollar, the system as proposed would have been feasible then, and it is not only feasible but demands to be build now. The problem, however, is to choose a single system with provision for growth and replacement, and to consider frankly the cost and requirements for the change of behavior that is required to achieve the enormous benefits of such a system.

Impact of Information-Handling Systems on Quality and Access to Health Care