



Protecting, Maintaining and Improving the Health of All Minnesota:

March 16, 2001

Ms. Donna Knutson
Council of State and Territorial Epidemiologists
2872 Woodcock Boulevard, Suite 303
Atlanta, Georgia 30341

Dear Ms. Knutson:

Enclosed, find a summary of the "Workshop on Antiviral Agents for Pandemic Influenza" held March 6-7, 2001, which I attended on behalf of the Council of State and Territorial Epidemiologists (CSTE). This 2-day workshop was convened for the purpose of developing strategies for the use of antiviral agents during an influenza pandemic.

Based on discussions we had at the workshop, it would be very useful for CSTE to send a letter to CDC stressing the importance of a strong federal role in vaccine and antiviral procurement and distribution as part of pandemic preparedness planning.

Thank you for the opportunity to represent CSTE at this workshop; I look forward to becoming more involved in CSTE activities in the future. If you have any questions about the report, I can be reached at 612-676-5707.

Sincerely,

A handwritten signature in cursive script that reads "Kristen Ehresmann".

Kristen Ehresmann, R.N., M.P.H.
Acting Manager
Acute Disease Prevention Services Section

cc: Matthew Carter, M.D., M.P.H.
C. Mack Sewell, M.D.
Kathy Gensheimer, M.D.

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Workshop on Antiviral Agents For Pandemic Influenza

Summary Report

This was a 2-day workshop convened by the National Vaccine Advisory Committee's working group on pandemic influenza for the purpose of developing strategies for the use of antiviral agents during the influenza pandemic. The objective of the workshop was to:

- To discuss issues and develop options for the potential uses of Antiviral Drugs during an Influenza Pandemic.
- 2. To identify knowledge gaps and research necessary for informed antiviral use planning.
- 3. To develop a limited number of realistic Antiviral Strategy options that can be presented to Interagency Work Groups and Advisory Committees for consideration.

During workshop presentations and discussions, two assumptions were used. First, the 1957 pandemic was used as a model framework for planning since it represented an intermediate situation midway between the extremes of 1918 and 1968.

Second, antiviral drugs were considered as classes (e.g., adamantane derivatives vs. neuraminidase inhibitors) rather than individual drugs in discussion.

The first day of the workshop consisted of presentations followed by large group discussions; a summary of the presentations follow.

Nancy Cox – History of the 1957 Pandemic

This presentation detailed the 1957 pandemic as a model for future pandemic preparedness planning. Key points:

- The 1957 pandemic represented a pandemic of intermediate severity
 - First pandemic after the development of virology
 - Global spread from this pandemic was well-documented
 - First pandemic for which vaccines were available
 - Within 6 months the pandemic had spread to all parts of the world
 - 25% of the population was ill
 - Attack rates were highest in school age kids
 - Mortality rates were highest in the very young and elderly
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Vaccine production began in late May (6 companies) with a cumulative total of 60 million doses released by early December.

Early use of antivirals could have impacted the pandemic.

Lone Simonsen – On the Age Shift in Mortality Attributable to Pandemic Influenza

Based on relative number of deaths, elderly are at less risk of death during a pandemic than during a severe non-pandemic.

- Younger persons are at up to 4-fold higher risk of death during a pandemic.
- 40-50% of excess deaths during a pandemic and early subsequent years occur in younger persons. In subsequent interpandemic years, fewer younger deaths occur until eventually interpandemic deaths occur exclusively in elderly populations.
- These pandemic age shifts in mortality may be due to recycling of the virus (H₁, H₂, H₃) and may not occur with novel virus introduction.
- Much discussion on relative mortality rates vs. absolute number of deaths.

Carol Glaser – The Impact of Influenza on Health Care Services

This presentation summarized the impact of influenza on LA County Health Services in 1997-98.

- In December 1997, LA County hospitals were overwhelmed with influenza patients; 65% of ERs were on diversion.
- A review of hours of ER diversion over time found that peaks in ER diversion matched the influenza season and correlated with influenza hospital data.
- Factors influencing the health system overload include: virus subtype (A Sydney), timing of peak cases (Christmas and New Year's), hospital downsizing (20% decrease in licensed bed capacity), and the nursing shortage.
- Even in interpandemic years, the health care system lacks "surge capacity."

Martin Meltzer – Social Disruption: Past Experience and Estimating Future Pandemics

A pandemic will have considerable social impact.

Attack rates/mortality will be dependent on whether the pandemic represents a recycled or novel viral strain.

- There is a great deal of uncertainty as to "who" will be affected, "what" strain will circulate, and "when" a pandemic will occur.
 - High risk populations will account for a high proportion of deaths.
 - It is possible that $\geq 50\%$ of deaths will occur in persons ≤ 65 years of age.
- The greatest economic burden will be due to death – therefore, intervene to save lives.

Thomas Tsang – H₅N₁ Hong Kong Experience

This presentation reviewed the H₅N₁ outbreak in Hong Kong and subsequent antiviral recommendations and stock piling.

- One study found giving antivirals to children resulted in direct protection of adults in the household.
- In reviewing adamantanes for pandemic planning must consider the following: side effects, selection of resistant variants when used in treatment, and high efficacy when used for prophylaxis.

Alan Hay – Resistance to Antiviral Drugs

- Adamantanes act on the M₂ protein during cell entry
- This table summarizes the presentation:

	<u>Drug Resistant Influenza Viruses</u>	
	<u>Adamantane</u>	<u>Neuraminidase Inhibitors</u>
Spectrum of Sensitivity	Most A sensitive B resistant European swine viruses resistant	Most A & B sensitive
Ease of emergence	easily selected (M ₂)	Not readily selected
Degree of resistance	total loss of sensitivity	Variable
Cross-resistance	complete	Partial
Biologic consequences	neutral? infectivity/transmission/virulence	Reduced infectivity
Spread	person-to-person swine-to-person	?

Ira Longini – Decision Analysis (for drug intervention)

- This presentation described the role that modeling could play in determining the best use of antivirals in a pandemic situation. Modeling may be most useful during the second wave, once certain data are available.

The second day consisted of small group discussions on the role of antivirals in pandemic influenza. Participants were divided into three groups for discussion. One group focused on the use of antivirals and prophylaxis only, one on use for treatment only and one on both prophylaxis and treatment.

Groups were to identify utilization of antivirals if a pandemic occurred in one year and if it occurred in 10 years.

Walt Dowdle – Overall Conclusions of Group Discussion

1. Overwhelming consensus that there is a role for antivirals
2. Clear priority group guidelines for antiviral use are needed.
3. A long-term (> 5 years) strategy is needed.
4. There is a major need for both public and provider education.
5. Surveillance of disease and antiviral resistance is critical to anti-viral use decision-making .
6. Two distribution systems exist: public and private.
7. More research is needed.

Martin Meyer – Final Summary of Policy Issues

1. Community readiness, ability to respond in the face of no drugs or vaccine, is critical.
2. Although vaccine is the primary interventional strategy, there is a role for antiviral drugs.
3. Objectives for antiviral use are needed, but will evolve as the pandemic evolves.
4. All proposed strategies for antiviral use will require a supplemental drug supply. Use of multiple rather than a single antiviral drug is planned.
5. A centralized distribution system is required for both antivirals and vaccine.
6. The anti-viral strategy involved targeted prophylaxis and targeted treatment. Amantadine is considered a second line drug (compared to NI) as a treatment strategy.
7. Important targeted research needed for developing an effective antiviral strategy.

Future plans include bringing the workgroup's recommendations to the NVAC working group to be incorporated into the pandemic plan. The NVPO will pursue funding for pandemic preparedness and a pandemic research agenda.