Who Holds the Key?
Developing Antiviral Treatment Strategies for Healthcare Workers During an Influenza Pandemic

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Key Questions

- What are antivirals and how do they work?
- What does the World Health Organization (WHO), Health and Human Services (HHS), and the Centers for Disease Control and Prevention (CDC) recommend for use of antivirals?
- How do we apply information and recommendations about antivirals for use with healthcare workers?

What are antivirals and how do they work?

"***Antiviral medications:***
Medications presumed to be effective against potential pandemic influenza virus strains and which may prove useful for treatment of influenza-infected persons or for prophylactic treatment of persons exposed to influenza to prevent them from becoming ill. These antiviral medications include the neuraminidase inhibitors oseltamivir (Tamiflu) and zanamirivir (Relenza)" (Interim pre-pandemic planning, 2007).

What are antivirals and how do they work?

TABLE 1. CHARACTERISTICS OF ANTI-INFLUENZA ANTIVIRAL DRUGS

	Inhibits	Acts on	Administration	Common Side Effects
Amantadine	M2 ion channel	Influenza A	Oral	CNS, GI
Rimantadine	M2 ion channel	Influenza A	Oral	CNS, GI (less often than amantadine)
Oseltamivir	Neuraminidase	Influenza A and B	Oral	GI
Zanamivir	Neuraminidase	Influenza A and B	Inhaler	Bronchospasm

These agents differ in mechanisms of action, pharmokinetics, FDA-approved indications, dosages, cost, and potential for emergence of drug resistance (see July 2005 recommendations of the AHIC (http://www.cdc.gov/mmwr/PDF/rr/rr5408.pdf).

The neuraminidase inhibitors and rimantadine are superior to amantadine with regard to the frequency of serious side effects.

The use of M2 inhibitors, particularly for treatment, is likely to lead to the emergence and spread of drug-resistant influenza viruses.

(HHS Pandemic Influenza Plan, 2005)

What are antivirals and how do they work?

Adamantanes

Due to widespread resistance, ACIP recommends against treatment and prophylaxis for Influenza A in U.S.

Amantadine (Symmetrel) & Rimantadine (Flumadine) –

Dose: 100 mg PO bid x 3-5days (Both)

Mechanism of Action: Not completely understood; prevents penetration of virus into host cells; can inhibit viral uncoating

Pharmacokinetics: Amantadine – not metabolized; Rimantadine – metabolized extensively; (Both) excreted in urine

Adverse Effects: CNS effects (10-30% patients), CV effects (rarely), crosses placental barrier

(Lehne, 2007 & Epocrates Essentials, 2008)

What are antivirals and how do they work?

Neuraminidase Inhibitors

Oseltamivir (Tamiflu) -

Dose: Tx – 75 mg PO bid x 5 days

Mechanism of Action: Inhibits neuraminidase (viral enzyme for replication)

Pharmacokinetics: Well absorbed; liver converts to oseltamivir carboxylate; excreted in the urine

Adverse Effects: Well tolerated

Zanamivir (Relenza) –

Dose: Tx - 10 mg INH q12h x 5 days

Mechanism of Action: Same as Tamiflu

Pharmacokinetics: Poorly absorbed in the GI tract; inhaled as a dry powder; excreted in the urine

Adverse Effects: May cause bronchospasm in patients with existing lung disorders

(Lehne, 2007 & Epocrates Essentials, 2008)

What are antivirals and how do they work?

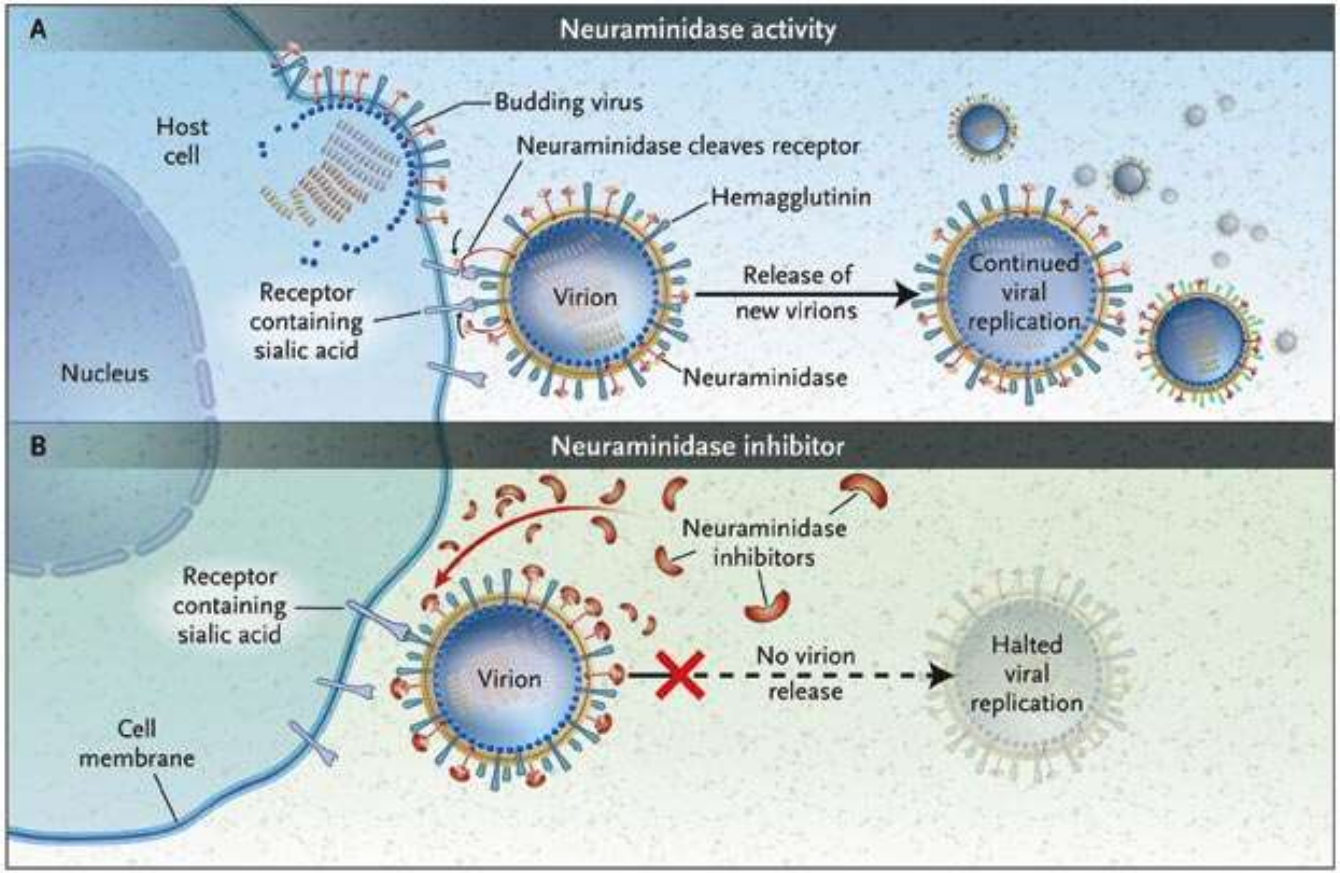

Figure 1. Mechanism of Action of Neuraminidase Inhibitors. Panel A shows the action of neuraminidase in the continued replication of virions in influenza infection. The replication is blocked by neuraminidase inhibitors (Panel B), which prevent virions from being released from the surface of infected cells.
Source: Moscona, A. (2005). Neuraminidase Inhibitors for Influenza. N Engl J Med 353: 1363-1373

What does the World Health Organization (WHO), Health and Human Services (HHS), and the Centers for Disease Control and Prevention (CDC) recommend for use of antivirals?

- *"**Prophylaxis**: Prevention of disease or of a process that can lead to disease. With respect to pandemic influenza this specifically refers to the administration of antiviral medications to healthy individuals for the prevention of influenza"* (Interim pre-pandemic planning, 2007).

- *"**Post-exposure prophylaxis**: The use of antiviral medications in individuals exposed to others with influenza to prevent disease transmission"* (Interim pre-pandemic planning, 2007).

- ***"Countermeasures**: Refers to pre-pandemic and pandemic influenza vaccine and antiviral medications"* (Interim pre-pandemic planning, 2007).

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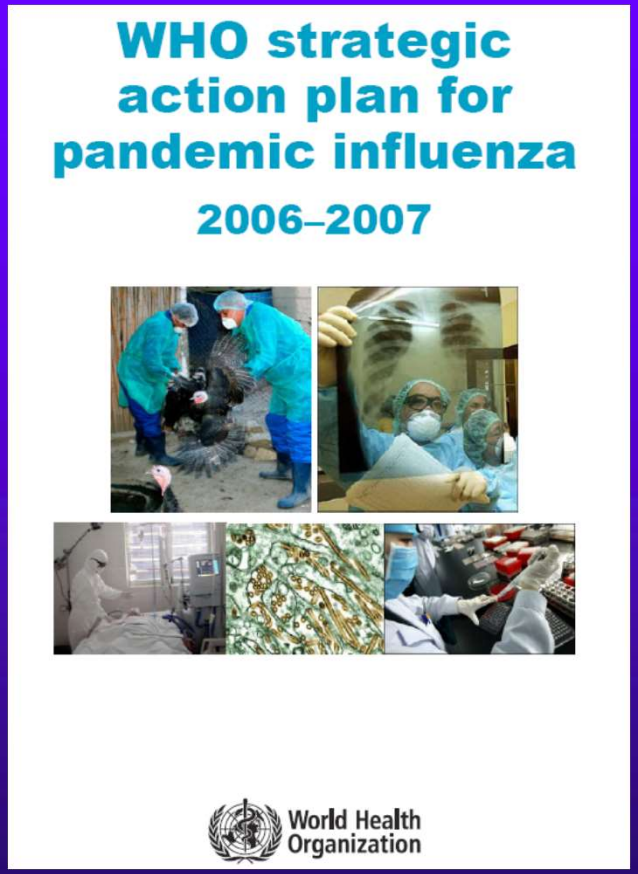
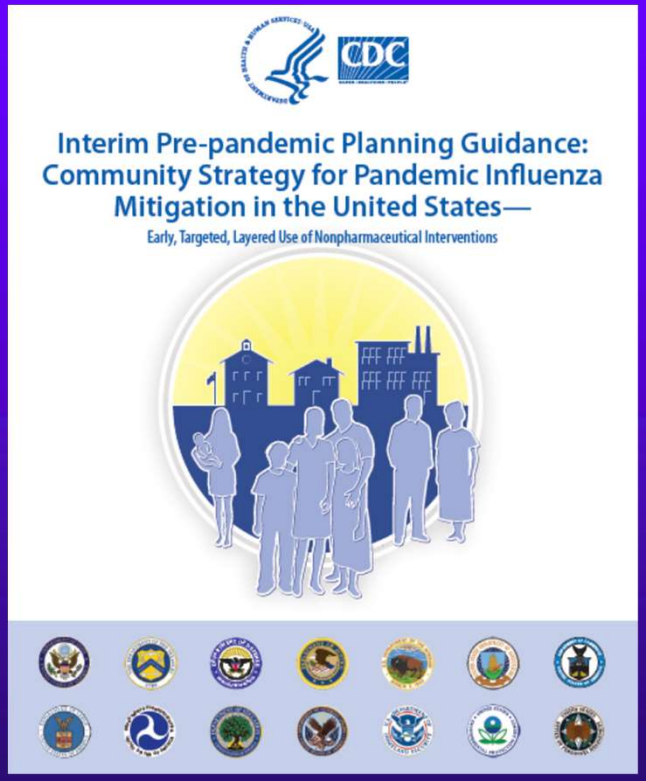


- Mass treatment with antivirals near the start of the pandemic could delay international spread
- WHO has a dedicated stockpile of antivirals reserved for early intervention in areas where the first signs of human to human transmission are noted
- Antiviral drugs have a critical role at the beginning of a pandemic to protect the frontline workers before a vaccine is developed

What does the World Health Organization (WHO), Health and Human Services (HHS), and the Centers for Disease Control and Prevention (CDC) recommend for use of antivirals?

- Not known if antivirals will be effective against a pandemic strain
- May not have sufficient quantities of antivirals
- Antivirals are recommended for treatment and prophylaxis of infected and exposed individuals

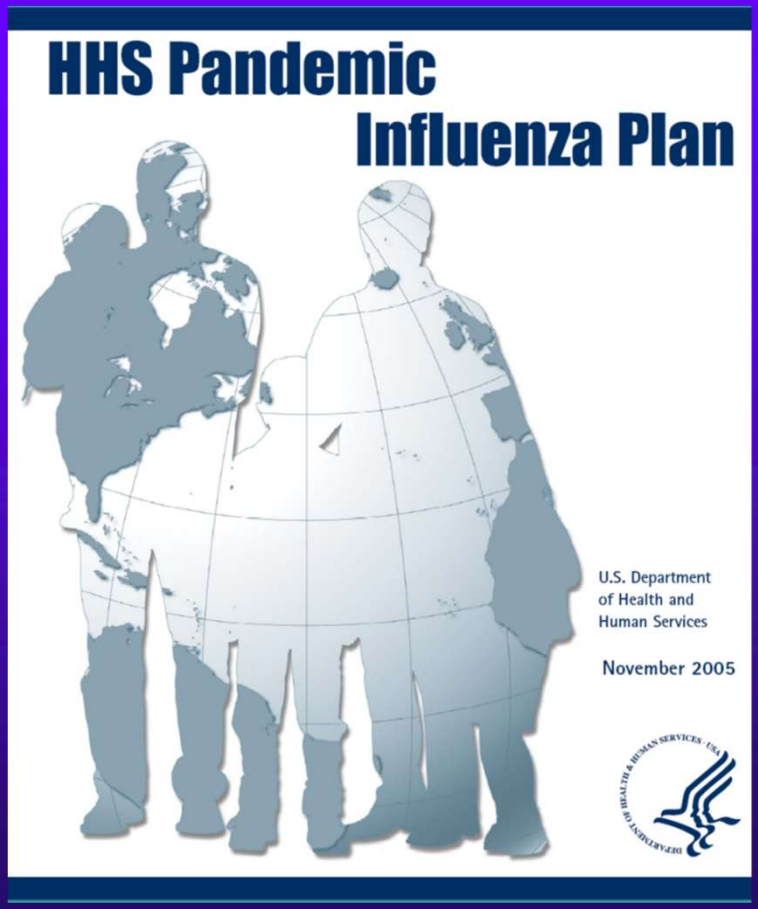


How do we apply information and recommendations about antivirals for use with healthcare workers?

- Healthcare workers may be key candidates for prophylaxis once supplies are sufficient to support this measure
- Using mitigation tactics early could delay the epidemic peak and allow more time for production of additional antivirals and vaccine development

What does the World Health Organization (WHO), Health and Human Services (HHS), and the Centers for Disease Control and Prevention (CDC) recommend for use of antivirals?

- The U.S. should stockpile enough antivirals to treat 25% of our population
- At the beginning of a pandemic, stockpiled antivirals will be distributed to healthcare facilities for treatment of priority groups



What does the World Health Organization (WHO), Health and Human Services (HHS), and the Centers for Disease Control and Prevention (CDC) recommend for use of antivirals?

- Antivirals are included in the Strategic National Stockpile (SNS) managed by HHS
- The Alabama Department of Public Health has 500,000 antiviral treatment courses stockpiled through CDC/HHS funding
- HHS will monitor the effectiveness and adverse events of antivirals during a pandemic

What does the World Health Organization (WHO), Health and Human Services (HHS), and the Centers for Disease Control and Prevention (CDC) recommend for use of antivirals?

- State and local health departments are responsible to develop statewide and local/regional plans to manage a pandemic
- State and local health departments are to assist healthcare facilities and build partnerships among healthcare
- Healthcare facilities are responsible for developing plans for use and administration of antivirals within the facility

Table D-2: Antiviral Drug Priority Group Recommendations*

	Group	Estimated population (millions)	Strategy**	# Courses (millions)		Rationale
				For target group	Cumulative	
1	Patients admitted to hospital***	10.0	T	7.5	7.5	Consistent with medical practice and ethics to treat those with serious illness and who are most likely to die
2	Health care workers (HCW) with direct patient contact and emergency medical service (EMS) providers*	9.2	T	2.4	9.9	Healthcare workers are required for quality medical care. There is little surge capacity among healthcare sector personnel to meet increased demand.
3	Highest risk outpatients—immunocompromised persons and pregnant women	2.5	T	0.7	10.6	Groups at greatest risk of hospitalization and death; immunocompromised cannot be protected by vaccination.
4	Pandemic health responders (public health, vaccinators, vaccine and antiviral manufacturers), public safety (police, fire, corrections), and government decision-makers	3.3	T	0.9	11.5	Groups are critical for an effective public health response to a pandemic.
5	Increased risk outpatients—young children 12-23 months old, persons ≥ 65 yrs old, and persons with underlying medical conditions	85.5	T	22.4	33.9	Groups are at high risk for hospitalization and death.
6	Outbreak response in nursing homes and other residential settings	NA	PEP	2.0	35.9	Treatment of patients and prophylaxis of contacts is effective in stopping outbreaks; vaccination priorities do not include nursing home residents
7	HCWs in emergency departments, intensive care units, dialysis centers, and EMS providers	1.2	P	4.8	40.7	These groups are most critical to an effective healthcare response and have limited surge capacity. Prophylaxis will best prevent absenteeism.
8	Pandemic societal responders (e.g., critical infrastructure groups as defined in the vaccine priorities) and HCW without direct patient contact	10.2	T	2.7	43.4	Infrastructure groups that have impact on maintaining health, implementing a pandemic response, and maintaining societal functions
9	Other outpatients	180	T	47.3	90.7	Includes others who develop influenza and do not fall within the above groups
10	Highest risk outpatients	2.5	P	10.0	100.7	Prevents illness in the highest risk groups for hospitalization and death.
11	Other HCWs with direct patient contact	8.0	P	32.0	132.7	Prevention would best reduce absenteeism and preserve optimal function.

* This is inclusive of Federal healthcare providers to Indian Nations and Tribes.

Tx = Treatment is 10 capsules

PEP = Post-exposure prophyaxis is 10 capsules

Px = Prophylaxis is 40 capsules

(Appendix D., 2005).

How do we apply information and recommendations about antivirals for use with healthcare workers?

NATIONAL VACCINE INFORMATION CENTER

National Vaccine Advisory Committee (NVAC) advises that "*additional work with public and private sector groups should be done to further hone definitions of target groups and their estimated population sizes, and to provide further guidance on antiviral drug distribution and dispensing*" (Appendix D., 2005).

How do we apply information and recommendations about antivirals for use with healthcare workers?

- The ADPH Healthcare Sector committee developed the following as one of it's goals: **Develop a template for antiviral treatment distribution plans for healthcare facility staff**
- **What are your suggestions/ideas to achieve this goal?**

Questions, Comments, and Discussion????

Healthcare workers could hold the **key** to solving this and other difficult issues facing the healthcare system during an influenza pandemic. Your suggestions and input are welcome!!

References

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Appendix D: NVAC/ACIP Recommendations for prioritization of Pandemic Influenza vaccine and NVAC recommendations on pandemic antiviral drug use. (2005). [Data File]. U.S. Department of Health and Human Services. Available from http://www.hhs.gov/pandemicflu/plan/pdf/AppD.pdf

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