VIRGINIA
EPIDEMIOLOGY BULLETIN

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Prevention and Control of Influenza - Part II

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

This article is based on the 2004 recommendations by the Advisory Committee on Immunization Practices (ACIP) for the use of influenza antiviral medications (Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR: May 28, 2004 / 53 (RR06);1-40). The complete report is available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5306a1.htm.

Background

The concern over influenza comes from its ability to spread rapidly and cause significant morbidity, as well as the seriousness of its complications (especially in the elderly and in people with chronic illnesses). The primary methods of controlling the spread of influenza consist of immunization and good respiratory etiquette. However, influenza antiviral medications can play an important role in the management of influenza both as chemoprophylaxis to prevent illness and as treatment of influenza infection. This article reviews the current indications for the use of influenza antiviral medications based on the 2004 Advisory Committee on Immunization Practices' (ACIP) recommendations.

In This Issue:

Diagnosis

Appropriate treatment of patients with respiratory illness, including the use of influenza antiviral medications, depends on accurate and timely diagnosis. State and local health departments, as well as the Centers for Disease Control and Prevention (CDC) supply feedback to healthcare providers on the presence and type of influenza viruses circulating in the community that can affect decisions on the use of influenza antivirals.

Healthcare providers also obtain information on influenza in their community through diagnostic tests during patient management. Available tests for influenza include viral culture, serology, polymerase chain reaction (PCR) and immunofluorescence. One recent development has been commercial rapid (within 30 minutes) diagnostic tests that can be used by laboratories in outpatient settings to detect influenza viruses. This can enable healthcare providers to more precisely direct therapy. However, the results of these tests should still be evaluated in the context of the clinical situation. In addition, the cost-effectiveness of using the rapid flu tests depends in part on the prevalence of influenza as well as the type of antiviral (if any) that may be used for treatment.[1]

Overall, influenza surveillance information and diagnostic testing can aid clinical judgment and help guide treatment decisions, including the potential value of antiviral therapy.

Influenza Antiviral Agents

Currently, four influenza antiviral agents are licensed and available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir.

Amantadine and rimantadine are chemically related drugs known as adamantanes (or M2 inhibitors)—this class has activity **only** against **influenza A viruses**. Amantadine is approved for the treatment and chemoprophylaxis of influenza type A virus infections among adults and children aged ≥1 year. Rimantadine is approved for treatment and chemoprophylaxis of influenza A infection among adults and prophylaxis among children (although some specialists consider it appropriate for treatment of influenza A among children).

Zanamivir and oseltamivir belong to the class of drugs known as neuraminidase inhibitors—they have activity against **both influenza A and B viruses**. Zanamivir is approved for treating persons aged ≥7 years with uncomplicated influenza infections. Oseltamivir is approved for the treatment of persons with uncomplicated influenza infections aged ≥1 year, and is also approved for chemoprophylaxis of influenza among persons aged ≥13 years.

An overview of these medications is presented below. However, package inserts should be consulted for additional information as needed.

Treatment

When administered within 2 days of illness onset to otherwise healthy adults, amantadine and rimantadine can reduce the duration of uncomplicated influenza A illness, and zanamivir and oseltamivir can reduce the duration of uncomplicated influenza A and B illness, by approximately 1 day.

Data are limited regarding the effectiveness of these agents in preventing serious influenza-related complications or their effectiveness for the treatment of influenza among persons at high risk for serious complications of influenza. One study assessing oseltamivir treatment primarily among adults reported a reduction in complications requiring antibiotic therapy compared with placebo. Even fewer studies of the efficacy of influenza antivirals have been conducted among pediatric populations. However, one study documented a decreased incidence of otitis media among children taking oseltamivir.

To reduce the emergence of antiviral drug-resistant viruses, amantadine or rimantadine therapy for persons with influenza A illness should be discontinued as soon as clinically warranted, typically after 3-5 days of treatment or within 24-48 hours after the resolution of signs and symptoms. The recommended duration of treatment with either zanamivir or oseltamivir is 5 days.

Chemoprophylaxis

Influenza chemoprophylaxis is not generally a substitute for vaccination, although antivirals are critical adjuncts in the prevention and control of influenza. They may be used, for example, as a component of influenza outbreak-control programs to limit the spread of influenza within chronic care institutions.

Amantadine and rimantadine are indicated for chemoprophylaxis of influenza A infection (not influenza B), and are approximately 70%-90% effective in preventing illness. These antivirals may still permit subclinical infection and the development of protective antibody against circulating influenza viruses. These agents do not interfere with the antibody response to the inactivated vaccine.

Rimantadine

Among the neuraminidase inhibitors, only oseltamivir has been approved for prophylaxis, but community studies of healthy adults indicate that both oseltamivir and zanamivir are similarly effective in preventing febrile, laboratory-confirmed influenza illness (efficacy: zanamivir, 84%; oseltamivir, 82%). Both agents have also been reported to prevent influenza illness among persons administered chemoprophylaxis after a household member was diagnosed with influenza. Experience with prophylactic use of these agents in institutional settings or among patients with chronic medical conditions is limited, but one 6-week study of oseltamivir prophylaxis among nursing home residents reported a 92% reduction in influenza illness. Use of zanamivir has not been reported to impair the immunologic response to the inactiviated influenza vaccine.

Amantadine

Of note, because influenza antivirals reduce replication of influenza viruses, the Live Attenuated Influenza Vaccine (LAIV) should not be administered until 48 hours after cessation of influenza antiviral therapy, and influenza antiviral medications should not be administered for 2 weeks after receipt of LAIV.

To be maximally effective as prophylaxis, antivirals must be taken each day for the duration of influenza activity in the community. However, to be most cost-effective, one study of amantadine or rimantadine reported that the drugs should be taken only during the period of peak influenza activity in a community.

Appropriate use of Chemoprophylaxis:

- Persons at High Risk Who Are Vaccinated **After** Influenza Activity Has Begun. Persons at high risk for complications of influenza can still be vaccinated after an outbreak of influenza has begun in a community. However, development of antibodies in adults after vaccination takes approximately 2 weeks. When influenza vaccine is administered while influenza viruses are circulating, chemoprophylaxis should be considered for persons at high risk during the time from vaccination until immunity has developed. Children aged <9 years who receive influenza vaccine for the first time require 6 weeks of prophylaxis (i.e., prophylaxis for 4 weeks after the first dose of vaccine and an additional 2 weeks of prophylaxis after the second dose).
- Persons Who Provide Care to Those at High Risk. To reduce the spread of virus to persons at high risk during community or institutional outbreaks, chemoprophylaxis during peak influenza activity can be considered for **unvaccinated** persons who have frequent contact with persons at high risk. This may include employees of hospitals, clinics, and chronic-care facilities, household members, visiting nurses, and volunteer workers. If an outbreak is caused by a variant strain of influenza that might not be controlled by the vaccine, chemoprophylaxis should be considered for all such persons, regardless of their vaccination status.
- Persons Who Have Immune Deficiencies. Chemoprophylaxis can be considered for persons at high risk who are expected to have an inadequate antibody response to influenza vaccine. This category includes persons infected with HIV, chiefly those with advanced HIV disease. Such patients should be monitored closely if chemoprophylaxis is administered. Data are not available regarding the efficacy of any of the 4 antiviral agents in preventing influenza among severely immunocompromised persons (e.g., hematopoietic stem cell transplant recipients).
- Other Persons. Chemoprophylaxis throughout the influenza season or during peak influenza activity might be appropriate for persons at high risk who should not be vaccinated. In general, chemoprophylaxis could be used by any person who wishes to avoid influenza illness, but healthcare providers and patients should make this decision on an individual basis.
- As an Adjunct in the Control of

Outbreaks in Institutions. Using antiviral drugs for the treatment and prophylaxis of influenza is a key component of influenza outbreak control in institutions in addition to other outbreak-control measures (e.g., droplet precautions, cohorting, vaccinations). When confirmed or suspected outbreaks of influenza occur in institutions that house persons at high risk, chemoprophylaxis should be started as early as possible to reduce the spread of the virus. In these situations, having preapproved orders from physicians or plans to obtain orders for antiviral medications on short notice can expedite administration of antiviral medications.

When outbreaks occur in institutions, chemoprophylaxis should be administered to all residents, regardless of whether they received influenza vaccinations during the previous fall, and should continue for a minimum of 2 weeks. If surveillance indicates that new cases continue to occur, chemoprophylaxis should be continued until approximately 1 week after the end of the outbreak. The dosage for each resident should be determined individually. Chemoprophylaxis also can be offered to unvaccinated staff who provide care to persons at high risk. Prophylaxis should be considered for all employees, regardless of their vaccination status, if the outbreak is caused by a variant strain of influenza that is not well-matched by the vaccine.

To limit the potential transmission of drug-resistant virus during outbreaks in institutions, whether in chronic or acute-care settings or other closed settings, measures should be taken to reduce contact as much as possible between persons taking antiviral drugs for treatment and other persons, including those taking chemoprophylaxis.

Dosage

Dosage recommendations vary by age group and medical conditions (e.g., impaired renal function, or liver disease) (Table 1).

Zanamivir inhaler device

Children

Oseltamivir

- **Amantadine**. Use of amantadine among children aged <1 year has not been adequately evaluated. The FDA-approved dosage for children aged 1-9 years for treatment and prophylaxis is 4.4-8.8 mg/kg body weight/day (maximum 150 mg/day), however, healthcare providers should consider prescribing only 5 mg/kg body weight/day (maximum 150 mg/day) to reduce the risk for toxicity. The approved dosage for children aged ≥10 years is 200 mg/day (100 mg twice a day); however, for children weighing <40 kg, prescribing 5 mg/kg body weight/day, regardless of age, is advisable.
- **Rimantadine**. Rimantadine is approved for prophylaxis among children aged ≥1 year. Although it has not been approved, some specialists in the management of influenza consider rimantadine appropriate for the treatment of influenza infection among children. Use of rimantadine among children aged <1 year has not been adequately evaluated. Rimantadine should be administered in 1 or 2 divided doses at a dosage of 5 mg/kg body weight/day, not to exceed 150 mg/day for children aged 1-9 years. The approved dosage for children aged ≥10 years is 200 mg/day (100 mg twice a day); however, for children weighing <40 kg, prescribing 5 mg/kg body weight/day, regardless of age, is recommended.
- **Zanamivir**. Zanamivir is approved for treatment among children aged ≥7 years. The recommended dosage of zanamivir for treatment of influenza is 2 inhalations (one 5-mg blister per inhalation for a total dose of 10 mg) twice daily (approximately 12 hours apart).
- **Oseltamivir**. Oseltamivir is approved for treatment among persons aged ≥1 year and for chemoprophylaxis among persons aged ≥13 years. Recommended treatment dosages for children vary by the weight of the child:
  - ✧ ≤15 kg: 30 mg twice a day
  - ✧ >15-23 kg: 45 mg twice a day
  - ✧ >23-40 kg: 60 mg twice a day
  - ✧ >40 kg: 75 mg twice a day

  The treatment dosage for persons aged ≥13 years is 75 mg twice daily. For children aged ≥13 years, the recommended dose for prophylaxis is 75 mg once a day.

Persons Aged ≥65 Years

- **Amantadine**. The daily dosage of amantadine for persons aged ≥65 years should not exceed 100 mg for prophylaxis or treatment because renal function declines with increasing age. For certain older persons, the dose should be further reduced.
- **Rimantadine**. Among older persons, the incidence and severity of central nervous system (CNS) side effects are substantially lower among those taking rimantadine at a dosage of 100 mg/day than among those taking amantadine at dosages adjusted for estimated renal clearance. However, chronically ill older persons have had a higher incidence of CNS and gastrointestinal symptoms than among healthy, younger persons when rimantadine has been administered at a dosage of 200 mg/day. Therefore, for prophylaxis among persons aged ≥65 years, the recommended dosage is 100 mg/day. For treatment of older persons in the community, a reduction in dosage to 100 mg/day should be considered if they experience side effects when taking a dosage of 200 mg/day. For treatment of older nursing home residents, the dosage of rimantadine should be reduced to 100 mg/day.
- **Zanamivir and Oseltamivir**. No reduction in dosage is recommended on the basis of age alone.

Persons with Impaired Renal Function

- **Amantadine**. A reduction in dosage is recommended for patients with

Table 1. Recommended daily dosage of influenza antiviral medications for treatment and prophylaxis

	Age group (yrs)				
Antiviral agent	**1-6**	**7-9**	**10-12**	**13-64**	**≥65**
Amantadine*					
Treatment, influenza A	5 mg/kg body weight/day up to 150 mg per day in 2 divided doses†	5 mg/kg body weight/day up to 150 mg per day in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/day up to 150 mg per day in 2 divided doses†	5 mg/kg body weight/day up to 150 mg per day in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Rimantadine¶					
Treatment,** influenza A	NA††	NA	NA	100 mg twice daily§§	100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/day up to 150 mg per day in 2 divided doses†	5 mg/kg body weight/day up to 150 mg per day in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	100 mg/day¶¶
Zanamivir*†††					
Treatment, influenza A and B	NA	10 mg twice daily	10 mg twice daily	10 mg twice daily	10 mg twice daily
Oseltamivir					
Treatment,§§§ influenza A and B	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	75 mg twice daily	75 mg twice daily
Prophylaxis, influenza A and B	NA	NA	NA	75 mg/day	75 mg/day

NOTE: Amantadine manufacturers include Endo Pharmaceuticals (Symmetrel®, tablet and syrup); Geneva Pharms Tech and Rosemont (Amantadine HCL, capsule); USL Pharma (Amantadine HCL, capsule and tablet); and Alpharma, Copley Pharmaceutical, HiTech Pharma, Mikart, Morton Grove, Carolina Medical, and Pharmaceutical Associates (Amantadine HCL, syrup). Rimantadine is manufactured by Forest Laboratories (Flumadine®, tablet and syrup) and Corepharma, Impax Labs (Rimantadine HCL, tablet), and Amide Pharmaceuticals (Rimantadine ACL, tablet). Zanamivir is manufactured by GlaxoSmithKline (Relenza®, inhaled powder). Oseltamivir is manufactured by Hoffman-LaRoche, Inc. (Tamiflu®, tablet). This information is based on data published by the Food and Drug Administration (FDA), which is available at http://www.fda.gov.

** The drug package insert should be consulted for dosage recommendations for administering amantadine to persons with creatinine clearance ≤50 mL/min/1.73m^2.*

† 5 mg/kg body weight of amantadine or rimantadine syrup = 1 tsp/22 lbs.

§ Children aged ≥10 years who weigh <40 kg should be administered amantadine or rimantadine at a dosage of 5 mg/kg body weight/day.

¶ A reduction in dosage to 100 mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

*** Only approved by FDA for treatment among adults.*

†† Not applicable.

§§ Rimantadine is approved by FDA for treatment among adults. However, certain specialists in the management of influenza consider rimantadine appropriate for treatment among children (see American Academy of Pediatrics. 2000 red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2000).

¶¶ Older nursing-home residents should be administered only 100 mg/day of rimantadine. A reduction in dosage to 100 mg/day should be considered for all persons aged ≥65 years, if they experience possible side effects when taking 200 mg/day.

**** Zanamivir is administered through inhalation by using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of correct use of the device.*

††† Zanamivir is not approved for prophylaxis.

§§§ A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance <30 mL/min.

¶¶¶ The dose recommendation for children who weigh ≤15 kg is 30 mg twice a day. For children who weigh >15–23 kg, the dose is 45 mg twice a day. For children who weigh >23–40 kg, the dose is 60 mg twice a day. And, for children who weigh >40 kg, the dose is 75 mg twice a day.

creatinine clearance ≤50 mL/min/1.73m^2. Guidelines for amantadine dosage on the basis of creatinine clearance are located in the package insert—however, such persons should still be observed carefully for adverse reactions. If necessary, further reduction in the dose or discontinuation of the drug might be indicated because of side effects. Hemodialysis contributes minimally to amantadine clearance.

- **Rimantadine**. A reduction in dosage to 100 mg/day is recommended for persons with creatinine clearance <10 mL/min. Because of the potential for accumulation of rimantadine and its metabolites, patients with any degree of renal insufficiency, including older persons, should be monitored for adverse effects, and either the dosage should be reduced or the drug should be discontinued, if necessary. Hemodialysis contributes minimally to drug clearance.
- **Zanamivir**. Limited data are available regarding the safety and efficacy of zanamivir for patients with impaired renal function. The manufacturer recommends no dose adjustment for inhaled zanamivir for a 5-day course of treatment for patients with either mild to moderate or severe impairment in renal function.
- **Oseltamivir**. Serum concentrations of oseltamivir carboxylate (GS4071), the active metabolite of oseltamivir, increase with declining renal function. For patients with creatinine clearance of 10-30 mL/min, a reduction of the treatment dosage of oseltamivir to 75 mg once daily and in the prophylaxis dosage to 75 mg every other day is recommended. No treatment or prophylaxis dosing recommendations are available for patients undergoing routine renal dialysis treatment.

Persons with Liver Disease

- **Amantadine**. No increase in adverse reactions to amantadine has been observed among persons with liver disease. Rare instances of a reversible elevation of liver enzymes among patients receiving amantadine have been reported, although the relation between the drug and such changes has not been established.
- **Rimantadine**. A reduction in dosage to 100 mg/day is recommended for persons with severe hepatic dysfunction.
- **Zanamivir and Oseltamivir**. Neither of these medications has been studied among persons with hepatic dysfunction.

Persons with Seizure Disorders

- **Amantadine**. An increased incidence of seizures has been reported among patients with a history of seizure disorders who have received amantadine. Patients with seizure disorders should be observed closely for possible increased seizure activity when taking amantadine.
- **Rimantadine**. Seizures (or seizure-like activity) have been reported among persons with a history of seizures who were not receiving anticonvulsant medication while taking rimantadine. The extent to which rimantadine might increase the incidence of seizures among persons with seizure disorders has not been adequately evaluated.
- **Zanamivir and Oseltamivir**. Seizure events have been reported during postmarketing use of zanamivir and oseltamivir, although no epidemiologic studies have reported any increased risk for seizures with either zanamivir or oseltamivir use.

Route

Amantadine, rimantadine, and oseltamivir are administered orally. Amantadine and rimantadine are available in tablet or syrup form, and oseltamivir is available in capsule or oral suspension form. Zanamivir is available as a dry powder that is self-administered via oral inhalation by using a plastic device included in the package with the medication. Patients benefit from instruction and demonstration of correct use of this device.

Side Effects and Adverse Reactions

When considering use of influenza antiviral medications (i.e., choice of antiviral drug, dosage, and duration of therapy), clinicians must consider the patient's age, weight, and renal function; presence of other medical conditions; indications for use (i.e., prophylaxis or therapy); and the potential for interaction with other medications.

Amantadine and Rimantadine

Both amantadine and rimantadine can cause CNS side effects (e.g., nervousness, anxiety, insomnia, difficulty concentrating, and lightheadedness), although rimantadine at a dosage of 200 mg/day causes fewer symptoms compared to the same dosage of amantadine. Gastrointestinal side effects (e.g., nausea and anorexia) occur among approximately 1%-3% of persons taking either drug.

Side effects associated with amantadine and rimantadine are usually mild and cease soon after discontinuing the drug. Side effects can diminish or disappear after the first week, despite continued drug ingestion. However, serious side effects have been observed (e.g., marked behavioral changes, delirium, hallucinations, agitation, and seizures). These more severe side effects have been associated with high plasma drug concentrations and have been observed most often among persons who have renal insufficiency, seizure disorders, or certain psychiatric disorders and among older persons who have been taking amantadine as prophylaxis at a dosage of 200 mg/day. Clinical observations and studies have indicated that lowering the dosage of amantadine among these persons reduces the incidence and severity of such side effects. In acute overdosage of amantadine, CNS, renal, respiratory, and cardiac toxicity, including arrhythmias, have been reported. Amantadine has anticholinergic effects and might cause mydriasis – therefore, it should not be used among patients with untreated angle closure glaucoma. Because rimantadine has been marketed for a shorter period than amantadine, its safety among certain patient populations (e.g., chronically ill and older persons) has been evaluated less frequently.

Zanamivir

Because of the risk for serious adverse events and because the efficacy has not been demonstrated among this population, zanamivir is not recommended for treatment for patients with underlying airway disease. If healthcare providers decide to prescribe zanamivir to patients with underlying chronic respiratory disease after carefully considering potential risks and benefits, the drug should be used with caution under conditions of appropriate monitoring and supportive care, including the availability of short-acting bronchodilators. Patients with asthma or chronic obstructive pulmonary disease who use zanamivir are advised to 1) have a fast-acting inhaled bronchodilator available when inhaling zanamivir and 2) stop using zanamivir and contact their physician if they experience difficulty breathing. Allergic reactions, including oropharyngeal or facial edema, have also been reported.

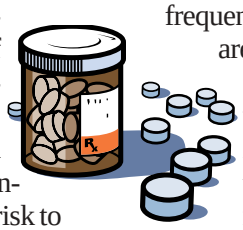
In clinical treatment studies of persons with uncomplicated influenza, the frequencies of adverse events were similar for persons receiving inhaled zanamivir and those receiving placebo (i.e., inhaled lactose vehicle alone). The most common adverse events reported by both groups were diarrhea; nausea; sinusitis; nasal signs and symptoms; bronchitis; cough; headache; dizziness; and ear, nose, and throat infections. Each of these symptoms was reported by <5% of persons in the clinical treatment studies combined.

Oseltamivir

Nausea and vomiting were reported more frequently among adults receiving oseltamivir for treatment. Among children treated with oseltamivir, 14.3% had vomiting, compared with 8.5% of placebo recipients. Similar types and rates of adverse events were reported in studies of oseltamivir prophylaxis. Nausea and vomiting might be less severe if oseltamivir is taken with food.

Use During Pregnancy

No clinical studies have been conducted regarding the safety or efficacy of amantadine, rimantadine, zanamivir, or oseltamivir for pregnant women. However, both amantadine and rimantadine have been demonstrated in animal studies to be teratogenic and embryotoxic when administered at high doses. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these four drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.



Drug Interactions

Careful observation is advised when amantadine is administered concurrently with drugs that affect the CNS, including CNS stimulants. Concomitant administration of antihistamines or anticholinergic drugs can increase the incidence of adverse CNS reactions. No clinically substantial interactions between rimantadine and other drugs have been identified.

Clinical data are limited regarding drug interactions with zanamivir. However, no known drug interactions have been reported, and no clinically critical drug interactions have been predicted on the basis of *in vitro* data and data from studies using rats.

Limited clinical data are available regarding drug interactions with oseltamivir. Because oseltamivir and oseltamivir carboxylate are excreted in the urine by glomerular filtration and tubular secretion via the anionic pathway, a potential exists for interaction with other agents excreted by this pathway. For example, coadministration of oseltamivir and probenecid resulted in reduced clearance of oseltamivir carboxylate by approximately 50% and a corresponding approximate twofold increase in the plasma levels of oseltamivir carboxylate.

Antiviral Drug-Resistant Strains of Influenza

Amantadine-resistant viruses are cross-resistant to rimantadine and vice versa. Drug-resistant viruses can appear in approximately one-third of patients when either amantadine or rimantadine is used for therapy. During the course of amantadine or rimantadine therapy, resistant influenza strains can replace susceptible strains within 2-3 days of starting therapy. Resistant viruses have been isolated from persons who live at home or in an institution where other residents are taking or have recently taken amantadine or rimantadine as therapy; however, the frequency with which resistant viruses are transmitted and their effect on efforts to control influenza are unknown. Epidemic strains of influenza A resistant to amantadine and rimantadine have rarely been detected. Amantadine- and rimantadine-resistant viruses are not more virulent or transmissible than susceptible viruses.

Development of viral resistance to zanamivir and oseltamivir during treatment has been identified but does not appear to be frequent.

Conclusions

The appropriate use of antiviral agents in the treatment and prophylaxis of influenza can reduce influenza morbidity and mortality, especially in select populations. In particular, antivirals may significantly benefit people at risk for complications from influenza but who cannot take the vaccine, or in the prevention or control of an outbreak. However, the expense of these medications, as well as the risk of side effects, the risk of developing more wide-spread viral resistance, and the likely limited availability of such drugs during major outbreaks, makes judicious use important and reinforces the importance of primary prevention (through vaccination and respiratory etiquette).

Sources of Information Regarding Influenza and Its Surveillance

Information regarding influenza control is available on the CDC/National Immunization Program website at www.cdc.gov/nip/flu or by calling their hotline at 800-232-2522 (English) or 800-232-0233 (Spanish). **State and local health departments should be consulted concerning availability of influenza vaccine, access to vaccination programs, information related to state or local influenza activity, and for reporting influenza outbreaks and receiving advice concerning outbreak control.**

Reference

1. Hueston WJ and Benich JJ. A Cost-Benefit Analysis of Testing for Influenza A in High-Risk Adults. *Ann Fam Med.* 2:33-40 (2004).

West Nile Virus in Virginia

West Nile Virus (WNV) has not been as active in Virginia in 2004 as it was in 2002 or 2003. To date there have been 5 identified human cases (including 1 death), 9 WNV positive horses, 24 WNV positive birds, 2 WNV positive sentinel chickens, and 409 WNV positive mosquito pools.

During the past several weeks the infection rate among mosquitoes tested for WNV has taken a general downturn. Although the exact cause of this has not been determined, one hypothesis is that the many heavy rains Virginia has experienced starting in mid-August have disrupted the breeding habitats of the mosquitoes most likely to carry WNV (e.g., *Culex pipiens* prefer the stagnant water of storm water catch basins—heavy rains wash the eggs and larvae out).

The WNV human cases have occurred in:

- Roanoke (onset: July)
- Accomack County (Onley area; onset: August)
- Chesterfield County (Midlothian area; onset: August)
- Augusta County (onset: September), and
- Fairfax County (onset: September).

Despite the lower WNV activity, the Virginia Department of Health requests that healthcare providers continue to maintain a high level of suspicion for this disease in patients presenting with signs and symptoms compatible with viral encephalitis:

- Fever ≥38°C (100°F);
- Altered mental status and/or other evidence of cortical involvement such as focal neurologic findings or seizures; and
- Cerebral spinal fluid pleocytosis with predominant lymphocytes and/or elevated protein and a negative gram stain or culture.

Patients hospitalized with clinical evidence of viral encephalitis should be reported immediately to the local health department. The local health department and the Division of Consolidated Laboratory Services (DCLS) can advise on specimen collection and submission as needed.

In an effort to prevent mosquito-borne diseases such as WNV, physicians should remind their patients, especially the elderly who may be at increased risk for severe illness from WNV, of the importance of personal protection from mosquito bites and of removal of potential mosquito breeding sites from around their homes.

Submitted by:
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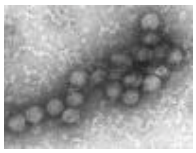

October: Antibiotic Awareness Month

Governor Warner has proclaimed October "Antibiotic Awareness Month." In conjunction with this proclamation, a mass media campaign supported by the *Get Smart Virginia* partners will run on television, radio, newspaper, and bus advertisments across much of Virginia.

Resources for Healthcare Providers

Materials are now available to help healthcare providers educate their patients about antibiotic resistance. These include an eye-catching brochure to inform patients about the importance of using antibiotics properly. A coordinating "prescription pad" is also available that provides a list of options patients have to treat the symptoms of colds and viruses. Physicians can check off the options that may apply and provide it to the patient instead of an unnecessary antibiotic prescription. Also available are waiting room posters and a CD-ROM to play on physician office telephone hold lines and/or on patient waiting room televisions.

Other resources are also available for Virginia's healthcare providers. For example, GlaxoSmithKline has provided funding for a speakers bureau. Physician organizations, community clinics, and hospitals can request that an infectious disease expert come to their area to speak on the latest medical research on antibiotic use and resistant strains of bacterial infections. In addition, Pfizer is providing a "cold pack"—a zipper close pouch that contains tissues and samples of over-the-counter medicines to treat viral and cold symptoms for providers to give to their patients.

GET SMART VIRGINIA
Know When Antibiotics Work

Obtaining Materials

Materials can be viewed at www.vdh.virginia.gov/epi/getsmart/index.asp. Healthcare providers can also place orders without charge for these resources, including the cold pack and speakers, through the Medical Society of Virginia Foundation by contacting Melissa King, Director of Programs, Medical Society of Virginia Foundation (804-377-1053 or mking@msv.org).

Cases of Selected Notifiable Diseases Reported in Virginia*

Disease	Total Cases Reported, August 2004: State	Regions: NW	N	SW	C	E	Total Cases Reported Statewide, January through August: This Year	Last Year	5 Yr Avg
AIDS	40	5	13	5	4	13	473	543	551
Campylobacteriosis	86	16	29	13	11	17	433	565	425
E. coli O157:H7	8	0	3	3	1	1	25	28	37
Giardiasis	82	15	33	13	13	8	315	227	233
Gonorrhea	696	49	63	101	170	313	5,858	5,922	6,585
Hepatitis, Viral									
A, acute	20	1	14	2	1	2	76	52	84
B, acute	36	2	8	6	13	7	159	113	103
C, acute	1	0	0	0	1	0	15	6	5
HIV Infection	57	3	13	5	10	26	577	519	565
Lead in Children†	112	11	12	31	32	26	511	500	436
Legionellosis	8	2	1	4	1	0	31	64	26
Lyme Disease	38	4	23	0	6	5	94	52	77
Measles	0	0	0	0	0	0	0	0	1
Meningococcal Infection	2	0	1	0	0	1	12	19	30
Mumps	0	0	0	0	0	0	1	1	5
Pertussis	6	0	2	0	1	3	105	77	54
Rabies in Animals	52	11	17	9	8	7	326	384	360
Rocky Mountain Spotted Fever	6	0	3	2	0	1	17	14	13
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	211	23	58	31	41	58	768	643	729
Shigellosis	23	3	14	1	4	1	104	290	293
Syphilis, Early§	13	3	8	0	0	2	134	121	175
Tuberculosis	29	0	18	2	2	7	148	175	183

Localities Reporting Animal Rabies This Month: Accomack 1 raccoon, 1 skunk; Albemarle 1 fox; Amherst 1 raccoon; Bland 1 cow; Botetourt 1 bat, 1 raccoon; Campbell 1 raccoon; Charlotte 1 raccoon; Cumberland 1 skunk; Dinwiddie 1 skunk; Fairfax 1 cat, 2 foxes, 5 raccoons, 1 skunk; Fauquier 1 fox, 1 raccoon; Floyd 1 cat; Giles 1 fox; Goochland 1 groundhog; Hanover 1 raccoon; James City 1 raccoon; King and Queen 1 raccoon; King George 1 fox; Loudoun 1 cat, 1 groundhog, 3 raccoons; Lunenburg 1 skunk; Montgomery 1 bat; Nelson 1 raccoon, 1 skunk; New Kent 1 raccoon; Northampton 1 raccoon; Powhatan 1 raccoon; Prince William 2 foxes, 1 raccoon; Pulaski 1 raccoon; Rockingham 2 raccoons; Shenandoah 1 raccoon; Stafford 1 bat, 1 raccoon; Suffolk 1 skunk; Virginia Beach 1 raccoon.

Toxic Substance-related Illnesses: Asbestosis 2; Adult Lead Exposure 8; Mesothelioma 1; Pneumoconiosis 7.

*Data for 2004 are provisional. †Elevated blood lead levels ≥10µg/dL. §Includes primary, secondary, and early latent.

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