Protecting the Innocent Bystander
The Importance of Vaccination During Pregnancy

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Disclosures

• Consultant
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  – OR Patient Safety Commission
  – RTI International

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  – Éclair Medical Systems
Objectives: Pertussis and seasonal influenza

• Know clinical characteristics of pertussis and seasonal influenza
• Understand recent epidemiology of both diseases
• Be able to recommend effective disease prevention strategies to pregnant women and their newborns through immunization
**Bordatella pertussis**

- Fastidious gram negative bacillus causing respiratory tract disease
- Highly contagious
- Significant infant morbidity and mortality
- Called the “Hundred Day Cough” or “Whooping Cough”
- Prior to Tdap, the last pediatric pertussis vaccine was given at 4-6 years of age
Pertussis Disease Manifestations

- Incubation period: 7-10 days (range 4-21)
- Three clinical stages
  1. **Catarrhal**: Rhinorrhea, sneezing, low-grade fever, mild cough
    - Contagious period!
  2. **Paroxysmal**: severe spasms of cough, thick mucous, classic “whoop,” vomiting, exhaustion
  3. **Convalescent**: gradual recovery with less frequent & less severe coughing
Incidence by age and sex

Incidence of pertussis by age and sex: Oregon, 2014

Cases per 100,000

Age group

From 2014 Oregon Communicable Disease Summary
Oregon compared to rest of the country

Incidence of pertussis: Oregon vs. nationwide, 2000–2014

- FIVE infant deaths since 2003
- 2015-16: 28 infant hospitalizations

From 2014 Oregon Communicable Disease Summary
Reported Pertussis Incidence, by Age and Ethnicity Oregon, 2012

Age Group

- <6 mths
- ≥6 mths – 1yr
- 1–4 yrs
- 5–9 yrs
- 10–19 yrs
- ≥20 yrs

Incidence (per 1,000,000)

- Hispanic
- Non-Hispanic
Risk Factors for Pertussis in Hispanic Infants
Metropolitan Portland, Oregon, 2010–2012

Pertussis rates among Hispanic infants were greater than non-Hispanic infants aged <6 months

Similar vaccination rates among Hispanic and non-Hispanic infants aged <6 months

Household size of >4 persons is a potential risk factor for pertussis

Greater proportion Hispanic infants in households >4

Pertussis deaths by age group, 2000-2015*

*2015 data are provisional

Reported Pertussis Cases In The US: Then

Routine pertussis immunization begins

MMWR 2002;51:73-76
Reported Pertussis Cases In The US: Now

Reported NNDSS pertussis cases: 1922-2015

Year


Number of cases

0 50,000 100,000 150,000 200,000 250,000 300,000

0 10,000 20,000 30,000 40,000 50,000 60,000

DTP

DTaP

Tdap

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Increasing cases in adolescents and young adults

FIGURE 3
Differences in relationship of identified S0ls, by case infant age, 2006–2013.
Outbreaks of Pertussis Associated with Hospitals --- Kentucky, Pennsylvania, and Oregon, 2003

Please note: An erratum has been published for this article. To view the erratum, please click here.

Pertussis outbreaks have been reported in various settings, including sports facilities, summer camps, schools, and health-care facilities. Mild and atypical manifestations of pertussis among infected persons and the lack of quick and accurate diagnostic tests can make pertussis outbreaks difficult to recognize and therefore difficult to control. Outbreaks among health-care workers (HCWs) are of special concern because of the risk for transmission to vulnerable patients (1). This report describes three pertussis outbreaks among HCWs and patients that occurred in hospitals in Kentucky, Pennsylvania, and Oregon in 2003. These outbreaks illustrate the importance of complying with measures to reduce nosocomial infection when evaluating or caring for patients with acute respiratory distress or cough illness of unknown etiology.

Case Definitions

A clinical case of pertussis is defined as a cough illness lasting at least 2 weeks with one of the following: paroxysm of coughing, inspiratory "whoop," or posttussive vomiting, without other apparent cause (2). In addition, for the outbreaks described in this report, persons with cough lasting for ≥14 days were also considered to represent clinical cases of pertussis. A confirmed case was defined as 1) a cough illness of any duration with isolation of Bordetella pertussis, or 2) a case that met the clinical case definition and was either confirmed by a polymerase chain reaction (PCR) assay positive for B. pertussis DNA or had epidemiologic linkage to a confirmed case (2). In addition, sera from several patients with suspected pertussis were submitted to the Massachusetts State Laboratory Institute (MSLI) for serologic testing to support diagnoses.*
The “teaching hospital in Oregon”

- September 2003
  - “Physician C” treated 12 month old with confirmed pertussis in pediatric ICU
  - 2 weeks later physician had onset of cough
  - 2 weeks later pertussis confirmed in physician
  - Of 129 close contacts, 1 exposed patient had confirmed pertussis and 3 employees had pertussis-like illness.
  - Active case-finding identified 3 unrelated cases in hospital personnel, 2 of which had transmitted confirmed pertussis to family members
  - Cost to the hospital: $40,000 at minimum

DTaP versus Tdap

• DTaP
  – Can be used for children <7 years of age
  – 5 shot series: 2 mo, 4mo, 6mo, 15-18 mo, 4-6 yr

• Tdap
  – ACIP recommends: Minimum age is ≥7 years
  – Routine dose at 11-12 year of age
  – All people >12 yrs should receive a catch-up dose
  – ACIP recommends: No minimum interval between receipt of a tetanus- or diphtheria-toxoid-containing vaccine and Tdap, when Tdap is otherwise indicated (usually 5 yr interval since last Td)
Tdap Recommendations

• Initial CDC recommendation: March, 2006
• Persons ≥11yrs should routinely receive Tdap instead of Td
• Cocooning
  – Don’t forget everyone in the household, care providers
  – HCWs who provide direct care to infants should receive the vaccine as well
  – Still a one-time dose for non-pregnant
  – Helpful in prevention infant pertussis, but efficacy unclear

MMWR 2006; 55 (RR-3)
Antibodies don’t last long in adults

Persistence of pertussis antibodies 3 years after Tdap vaccination of adults

Anti-PT antibody GMCs (EU.L/mL)

Anti-FHA antibody GMCs (EU.L/mL)

### Mean Reduction in Infant Pertussis Morbidity and Mortality Relative to Base Case*

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy</th>
<th>Postpartum</th>
<th>+ Father</th>
<th>+ Grandparent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>33%</td>
<td>20%</td>
<td>29%</td>
<td>32%</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>38%</td>
<td>18%</td>
<td>28%</td>
<td>32%</td>
</tr>
<tr>
<td>Deaths</td>
<td>49%</td>
<td>16%</td>
<td>25%</td>
<td>29%</td>
</tr>
<tr>
<td>Program cost</td>
<td>$171 million</td>
<td>$171 million</td>
<td>$342 million</td>
<td>$513 million</td>
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<td>(72% coverage)</td>
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</tbody>
</table>

* Base case = DTaP series only
## Tdap vaccination leads to higher antibody levels in infants

<table>
<thead>
<tr>
<th>Outcome Antibodies</th>
<th>Mother did not receive Tdap, mean (SEM) n=52</th>
<th>Mother received Tdap, mean (SEM) n=52</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Pearson correlation coefficient (P value)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>11.010 (1.796)</td>
<td>28.220 (2.768)</td>
<td>&lt; .001</td>
<td>0.158 (.055)</td>
</tr>
<tr>
<td>FHA</td>
<td>26.830 (4.022)</td>
<td>104.15 (21.664)</td>
<td>.002</td>
<td>0.165 (.045)</td>
</tr>
<tr>
<td>PRN</td>
<td>24.700 (5.765)</td>
<td>333.01 (56.435)</td>
<td>&lt; .001</td>
<td>0.965 (&lt; .001)</td>
</tr>
<tr>
<td>FIM 2/3</td>
<td>82.83 (14.585)</td>
<td>1198.99 (189.937)</td>
<td>&lt; .001</td>
<td>0.293 (&lt; .001)</td>
</tr>
</tbody>
</table>

FHA, filamentous hemagglutinin; FIM, fimbriae; PRN, pertactin; PT, pertussis toxin;  
<sup>a</sup>Significant at .05 level.

Tdap recommendations for pregnant women

• Postpartum vaccination is a suboptimal national strategy to prevent infant pertussis morbidity and mortality
• Vaccinating during late 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester recommended
  – Target: 27 to 36 weeks of pregnancy
• Late 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester maternal vaccination may prevent infant pertussis during the same pregnancy
• Antibodies decline quickly in adults. Tdap with each pregnancy will provide best protection to infant
Summary

• Pertussis activity in Oregon is high
  – Significant M&M in young
  – Have a high index of suspicion for pertussis
  – PCR is diagnostic test of choice
  – Wear a mask while examining pt & collecting sample!

• Know immunization recs for pregnant women

• Be familiar with Health Dept recommendations
  – Testing, prophylaxis, reporting, immunizations
  – Call for help whenever needed!
Pertussis
Suggested references & useful information


• http://www.cdc.gov/vaccines/recs/acip/

• AAP Red Book 2015
Seasonal Influenza: 2016-17 Recs
Influenza: Clinical Description/Diagnosis

• Incubation period
  – 1 to 4 days
  – Adults: infectious from day before to +5 days after illness onset
  – Children: infectious ≥ 10 days (can shed virus several days before onset)
  – Severely immunocompromised: Can shed virus for months

• Likely transmission paths
  – Coughing & sneezing → respiratory droplets
  – Aerosolization?
  – Contact with an infected person, not washing hands afterward

CDC. MMWR. Sept 20, 2013 / 62 (RR07)
Signs and Symptoms

• Abrupt onset:
  – Fever, myalgia, headache, malaise, nonproductive cough, sore throat
  – Rhinorrhea is minimal

• Differential diagnosis:
  – Can be difficult based on symptoms alone, unless influenza is already present in the community
  – Children and elderly can have different presentations

• Can last up through 7 days
Complications of Seasonal Influenza

• Most vulnerable patients
  – Age $\geq$ 65 yrs and children $\leq$ 2 yrs of age
  – Underlying chronic conditions at any age
    • Includes pregnant women and infants $<2$ yrs

• Secondary complications
  – Primary influenza viral pneumonia or secondary bacterial pneumonia
  – Exacerbation of underlying cardiac or pulmonary disease

CDC. MMWR. Sept 20, 2013 / 62 (RR07)
Groups Most Affected by Seasonal Influenza

• Adults
  – Older at greatest risk for death
    • ≥ age 65: 90% of influenza-related deaths
    • ≥ age 85: 32x more likely to die of influenza-related pneumonia than persons aged 65-69 years

• Children
  – Youngest at greater risk for hospitalization
    • Under age 2 yrs
  – Older children bear greater disease burden
    • School attendance increases disease transmission
    • Ill family members transmit disease
Influenza severity increases during pregnancy

- Physiologic changes increase susceptibility
  - Altered respiratory mechanics
  - Changes in cell mediated immunity
- Increased risk for hospitalization
- Compared to those without flu, higher risk:
  - Preterm labor
  - Fetal distress
  - C/S

CDC. MMWR. August 26, 2016 / 65(5);1–54
Why target pregnant women?

• Immunocompromised host
  – More severe influenza disease

• To decrease risk of preterm and complicated L&D

• Passive antibody transfer to fetus
  – Newborn too young to be vaccinated
  – Decreases infant risk of ILI, flu, hospitalizations
Decreased influenza in infants born to women vaccinated during pregnancy

• All women delivered from 12/05 to 3/2014 in healthcare system (n= 245,386)
• Infants born to women reporting flu immunization during pregnancy had:
  – 64% risk reduction for ILI
  – 70% risk reduction for lab-confirmed flu
  – 81% risk reduction of flu-related admissions
Why Target All Healthy Children?

- Children acquire and shed virus more frequently than adults.
- Role in transmission of virus in day care, school, and households.
- Significant socioeconomic effects of influenza on children and their household contacts.
- Presence of children the most important determinant of influenza within the family.

Major Academies and Associations recommend flu vaccination for pregnant women
Flu vaccine uptake in US pregnant women appears to be improving
Flu vaccine is safe in pregnancy

- VAERS review from 1990-2009
  - No unusual patterns of pregnancy complications or fetal outcomes
  - Rate of spontaneous abortion 1.9 per one million pregnant women vaccinated

AJOG February 2011 (204), 2: 146.e1–146.e7
Does flu vaccine increase risk for other complications during pregnancy?

• Large study compared risks for adverse OB events between vaccinated (n=74K) vs unvaccinated (n=144K) women
  – Observed for risks within 42d of vaccination for potential complications

• Vaccination during pregnancy was not associated with increased risk of adverse OB events
Testing for Flu

• Rapid flu tests lack sensitivity
  – Recent meta-analysis: 62% sensitive / 98% specificity
  – Negative rapid flu does not exclude diagnosis of flu
  – Influenza PCR is best, if available

• Know local epidemiology
  – When flu is highly prevalent, may not necessarily need to send a diagnostic test
# Weekly Oregon flu surveillance

## Data at a Glance

**January 15–January 21, 2017 (Week 3)**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Current Week (3)</th>
<th>Previous Week (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of emergency department visits for ILI(^1)</td>
<td>3.4%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Percentage positive influenza tests(^2)</td>
<td>25.2%</td>
<td>31.5%</td>
</tr>
<tr>
<td>Influenza-associated hospitalizations(^3)</td>
<td>129</td>
<td>236</td>
</tr>
<tr>
<td>Reported ILI/influenza outbreaks</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td>Influenza-associated pediatric mortality</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Percentage of outpatient visits for ILI</td>
<td>2.7%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Respiratory Syncytial Virus (RSV) activity(^4)</td>
<td>12%</td>
<td>10%</td>
</tr>
</tbody>
</table>

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\(^1\) Based on Oregon ESSENCE Syndromic Surveillance. Data represent statewide aggregate percent.

\(^2\) Percent positivity based on data from Oregon reporters to the National Respiratory and Enteric Virus Surveillance System (NREVSS)

\(^3\) Based on hospitalization surveillance in Clackamas, Multnomah, and Washington counties only.

\(^4\) Percent positivity based on data from Oregon’s RSV Laboratory Surveillance System.

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Google search: “Oregon Flu Bites!”
Figure 1. Percentage of ED Visits for ILI, Oregon ESSENCE Syndromic Surveillance, 2014–2015, 2015–2016, 2016–2017
Mostly Influenza A
Hospitalizations high among elderly
Flu resources on line:


http://www.cdc.gov/flu/
The best way to deal with pertussis and flu:

• Prevention by immunization!
  – Immunization of patients & families, healthcare providers
  – Improve immunization access in your community

• Education!
  – Respiratory etiquette: “Cover your cough” & clean hands
  – Keep babies, high-risk patients away from people with cough
  – Discuss vaccine benefits at every opportunity
Vaccination during pregnancy: Key message

Vaccines Routinely Recommended for Pregnant Women

It is safe for the flu vaccine and Tdap vaccine to be given to pregnant patients at the same time.

**Flu Vaccine**
- Is recommended for pregnant women and safe to administer during any trimester.
- Is the best way to protect pregnant women and their babies from the flu, and prevent possible flu-associated pregnancy complications.
- Is safe and can help protect the baby from flu for up to 6 months after birth. This is important because babies younger than 6 months of age are too young to get a flu vaccine.

**Tdap Vaccine**
- Is recommended during every pregnancy, ideally between 27 and 36 weeks gestation.
- When given during pregnancy, boosts antibodies in the mother, which are transplacentally transferred to her developing baby. Third trimester administration optimizes neonatal antibody levels.
- Helps protect infants, who are at greatest risk for developing pertussis and its life-threatening complications, until they are old enough to start the childhood pertussis vaccine series.

Immunize yourself, your patients, and your family!

Courtesy of Miles Cottrill, 2012
Diagnosing pertussis
Diagnosing Pertussis Infection

- Clinical specimen from the posterior nasopharynx
  - NP secretion aspirate
  - Insertion of a swab applicator
- Polymerase chain reaction (PCR)
  - Recommended in clinical practice
- Direct fluorescent antibody (DFA)
- Serology
  - Bordatella culture on selective media
Treatment of Infected Patients

- **Azithromycin**
  - <6 mos: 10 mg/kg/day once daily for 5 days
  - >6 mos: Usual “Z-Pak” dosing”

- **Erythromycin estolate or erythromycin ethylsuccinate (EES)**
  - 40-50 mg/kg/day (max 1 g/day) in 3 divided doses for 7 days
  - Minimum age: 1 month

- **Clarithromycin**
  - Not recommended for <1 month of age
  - >1 mos: 20 mg/kg/day (max 1 g/day) in 2 divided doses for 7 days
PEP is recommended for all household contacts in index case and other close contacts, including children in child care, regardless of immunization status.

- If borderline exposure, PEP recommended if contact lives in household with a high-risk person (or if the contact is high-risk him/herself).

- If 21 days have elapsed since onset of index case’s cough, PEP should be considered only for households with high-risk contacts.

- PEP is recommended for all HCPs even if immunized with Tdap who have unprotected exposure to pertussis and are likely to expose a high-risk patients (e.g., infants, pregnant women).
Chemoprophylaxis

Most pertussis in adults and adolescents is neither diagnosed nor reported and antibiotic prophylaxis does not control the transmission of pertussis when it is widespread in the community. The effort to provide antibiotic prophylaxis for pertussis must focus on infants under age 1 year since serious complications and death are limited to this group. Recommend prompt antibiotic prophylaxis within 21 days of exposure for close contacts of confirmed, presumptive, and suspect cases who are:

- Infants
- Pregnant women in the 3rd trimester (since they will soon have contact with an infant)
- All household contacts of a case if there is an infant or a pregnant woman in the 3rd trimester in the household, even if the infant in the household is the case
- All those attending or working in a childcare setting (i.e., same room) of a case if there is an infant or one of those same third trimester women in the setting
- Other contacts at the discretion of the local health department (e.g. pediatric healthcare workers, unimmunized contacts, other pregnant women, high-risk contacts of suspect cases).
Who Should be Treated for Flu?

- Antiviral treatment is recommended **as early as possible** for any patient with confirmed or suspected influenza who
  - is hospitalized;
  - has severe, complicated, or progressive illness; or
  - is at higher risk for influenza complications.

- Persons at higher risk for influenza complications recommended for antiviral treatment include:
  - children aged younger than 2 years;*
  - adults aged 65 years and older;
  - persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopmental conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury);
  - persons with immunosuppression, including that caused by medications or by HIV infection;
  - women who are pregnant or postpartum (within 2 weeks after delivery);
# Treatment of Influenza: What Medication?

<table>
<thead>
<tr>
<th>Antiviral Agent</th>
<th>Use</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Oseltamivir</td>
<td>Treatment (5 days)</td>
<td>If younger than 1 yr old&lt;sup&gt;1&lt;/sup&gt;:</td>
<td>75 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 mg/kg/dose twice daily&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>If 1 yr or older, dose varies by child’s weight:</td>
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<tr>
<td></td>
<td></td>
<td>15 kg or less, the dose is 30 mg twice a day</td>
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<td>&gt;15 to 23 kg, the dose is 45 mg twice a day</td>
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<td>&gt;23 to 40 kg, the dose is 60 mg twice a day</td>
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<td></td>
<td>&gt;40 kg, the dose is 75 mg twice a day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chemoprophylaxis (7 days)</td>
<td>If child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not</td>
<td>75 mg once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>recommended unless situation is judged critical due to limited data in this age group.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>If child is 3 months or older and younger than 1 yr old&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 mg/kg/dose once daily&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>If 1 yr or older, dose varies by child’s weight:</td>
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<td>15 kg or less, the dose is 30 mg once a day</td>
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<td>&gt;15 to 23 kg, the dose is 45 mg once a day</td>
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<td></td>
<td>&gt;23 to 40 kg, the dose is 60 mg once a day</td>
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<tr>
<td></td>
<td></td>
<td>&gt;40 kg, the dose is 75 mg once a day</td>
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</tr>
</tbody>
</table>

## Zanamivir Dosing

| Inhaled Zanamivir<sup>4</sup> (5 days) | Treatment | 10 mg (two 5-mg inhalations) **twice** daily  
(FDA approved and recommended for use in children 7 yrs or older) | 10 mg (two 5-mg inhalations) **twice** daily  
(FDA approved and recommended for use in children 7 yrs or older) |
|--------------------------------------|-----------|-----------------------------------------------------------------|-----------------------------------------------------------------|
| Chemo-prophylaxis (7 days)           | 10 mg (two 5-mg inhalations) **once** daily  
(FDA approved for and recommended for use in children 5 yrs or older) | 10 mg (two 5-mg inhalations) **once** daily  
(FDA approved for and recommended for use in children 5 yrs or older) |

[https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm](https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm)