

# Influenza, RSV, and SARS: What Every Laboratory Should Know

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# Objectives

At the end of the session, the participant will be able to:

- Describe the epidemiology and clinical presentations of influenza, respiratory syncytial virus, and the SARS-coronavirus.
- Discuss the importance of disease prevalence on test predictive values and test result interpretation.
- Summarize the current CDC recommendations for specimen testing and laboratory safety.

# Overview

- Clinical presentations of influenza, respiratory syncytial virus (RSV) and SARS.
- Epidemiology of influenza, RSV and SARS.
- Laboratory diagnostic methods for influenza, RSV and SARS-coronavirus.
- Predictive values, test performance characteristics, disease prevalence, and result interpretation.
- CDC recommendations for specimen collection, testing and laboratory safety for SARS
- Closing comments.

# Human Respiratory Viruses

## Orthomyxoviridae

**INFLUENZA TYPE A** (*2 subtypes, new strains each year*)

**INFLUENZA TYPE B** (*new strains each year*)

## Paramyxoviridae

**RESPIRATORY SYNCYTIAL VIRUS** (*2 subgroups*)

**PARAINFLUENZA VIRUS** (*4 serotypes*)

**HUMAN METAPNEUMOVIRUS**

## Picornaviridae

**RHINOVIRUSES** (*at least 113 serotypes*)

**ENTEROVIRUSES** (*68 serotypes*)

## Adenoviridae

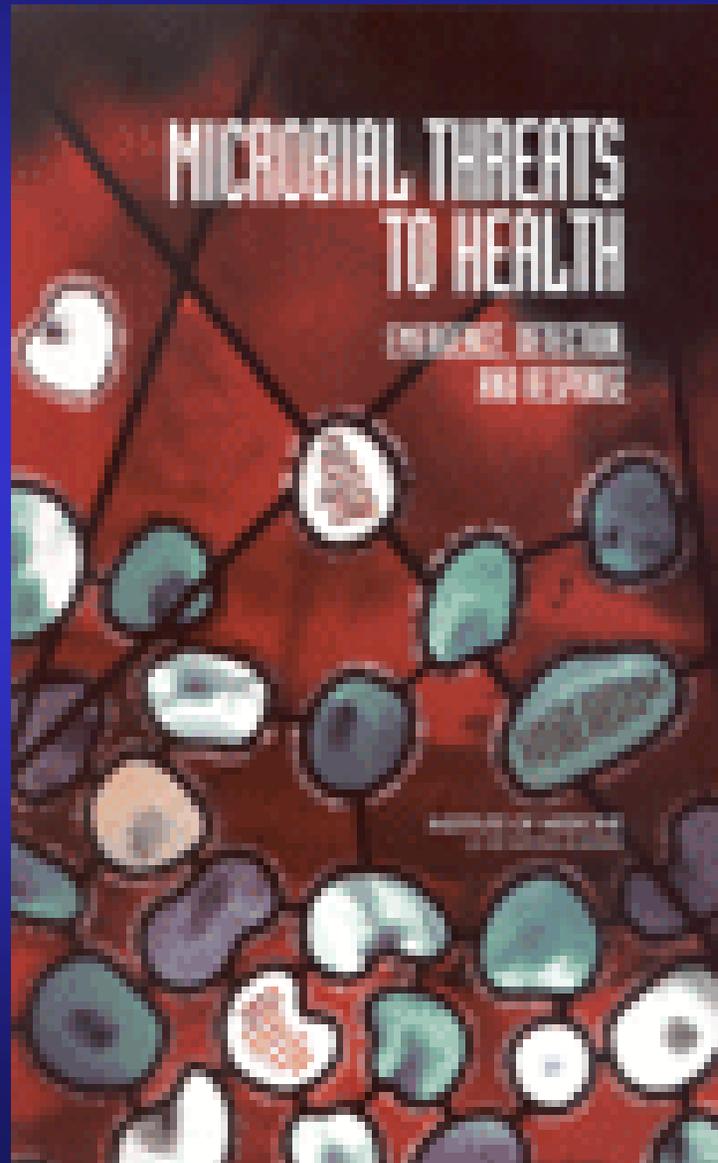
**ADENOVIRUSES** (*49 serotypes*)

## Coronaviridae

**CORONAVIRUSES** (*2 subgroups, unknown # of strains*)

## Resource:

<http://www.nap.edu/books/030908864X/html/>



Epidemiology, Clinical  
Presentations, and Public Health  
Importance

# Influenza: Resources (I)

- CDC home page for influenza

<http://www.cdc.gov/ncidod/diseases/flu/overview.htm>

- ACIP recommendations

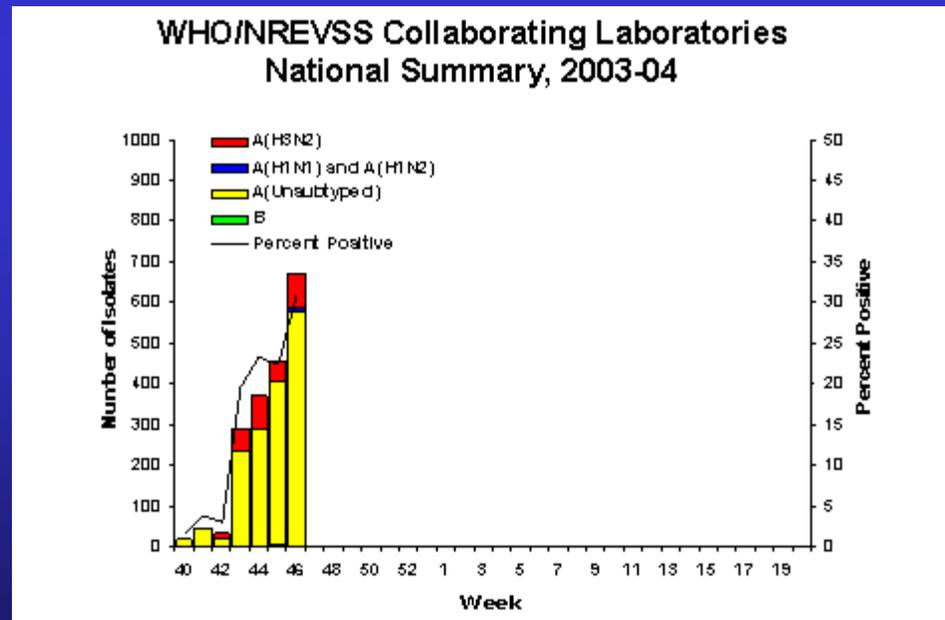
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5208a1.htm>

- National Immunization Program

<http://www.cdc.gov/nip/Flu/default.htm>

# Influenza: Resources (II)

- National Influenza Summary – Weekly Update  
<http://www.cdc.gov/ncidod/diseases/flu/weekly.htm>



# Influenza

Family: Orthomyxoviridae

- segmented (8), ssRNA genome
- lipid envelop

Genera: Influenzavirus Types A, B and C

Subtypes: Human -  $H_1N_1$ ,  $H_2N_2$ ,  $H_3N_2$ ,  $H_5N_1$ ,  
 $H_9N_2$ ,  $H_1N_2$ ,  $H_7N_7$

Animals –  $H_1$  to  $H_{15}$ ,  $N_1$  to  $N_9$

Strains: A/Moscow/10/99 ( $H_3N_2$ ) - like

(2003) A/New Caledonia/20/99 ( $H_1N_1$ ) - like

B/Hong Kong/330/2001- like

# Influenza: Clinical Syndrome

- Incubation period 1 to 3 days
- Abrupt onset of high fever and chills
- Associated symptoms
  - headache, malaise, myalgia, cough, sore throat, nasal congestion
- Duration of intense symptoms 3 to 5 days
- Prolonged recovery
- Note: CDC definition of *influenza-like illness*
  - Temp > 100°F orally and either cough or sore throat

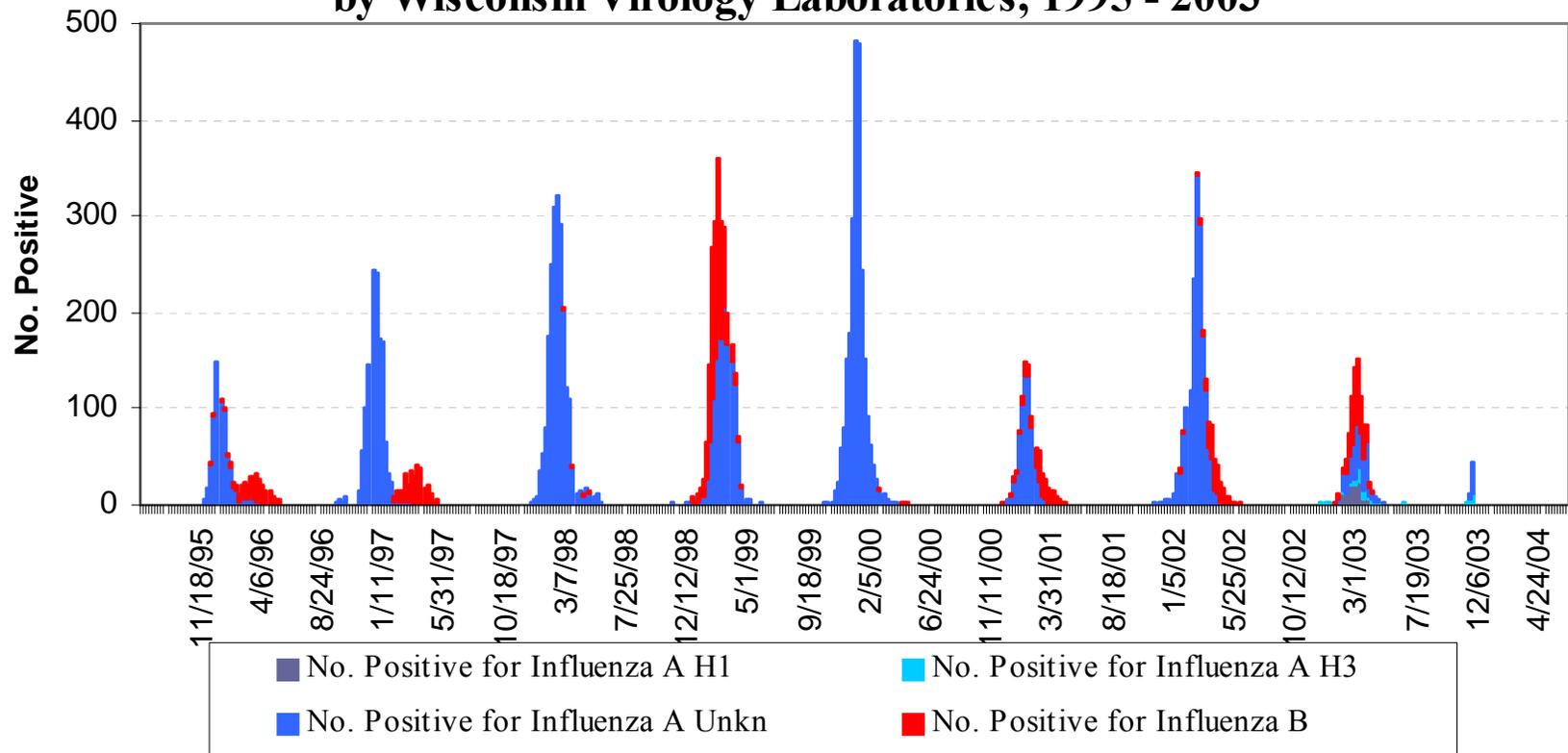
# Influenza: Potential Complications

- Pneumonia: primary viral  
secondary bacterial
- Exacerbations of asthma, chronic bronchitis
- Myocarditis and pericarditis
- Meningitis/encephalitis
- Reye's syndrome
- Guillain-barre syndrome
- Myositis, myoglobinuria

# Influenza – Seasonality/Epidemicity

## Wisconsin, 1995-2003

**Number of Specimens Tested and Positive for Influenza  
by Wisconsin Virology Laboratories, 1995 - 2003**



# Influenza: Public Health Importance

- Pandemic potential
- Significant annual (inter-pandemic) morbidity and mortality
- Prophylactic and therapeutic measures available
  - Advent of rapid diagnostic methods

# Influenza: Epidemic (Inter-Pandemic) Influenza

Disease caused by a new strain of influenza virus that has evolved gradually by **point mutations within the hemagglutinin or neuraminidase or both** such that preexisting antibody cannot completely neutralize the new strain.

The mechanism: **ANTIGENIC DRIFT**

# Influenza: Annual (Inter - pandemic) Morbidity and Mortality

- Greater than 35,000 deaths in US each year
  - 90% of mortality among elderly
  - Increased mortality in other risk groups
- From 15,000 to >200,000 flu-associated hospitalizations per epidemic
- Nursing home attack rate of 60%
- Attack rates of 5-20% in general population
- A significant childhood pathogen

# Pandemic Influenza

Disease caused by a **reassortment of Influenza A subtypes** that results in the emergence of a new virus containing a novel hemagglutinin and/or neuraminidase that is immunologically distinct from previously circulating strains.

The mechanism: **ANTIGENIC SHIFT**

Resource: <http://www.cdc.gov/od/nvpo/pandemics/>

# Influenza: Noteworthy events

1997: “Avian flu” (H5N1)

1997: “A/Sydney” (H3N2)

1999: Influenza A (H9N2)

2003: H5N1 strikes again

2003: Avian influenza A (H7N7)

2003: “A/Fujian” (H3N2)

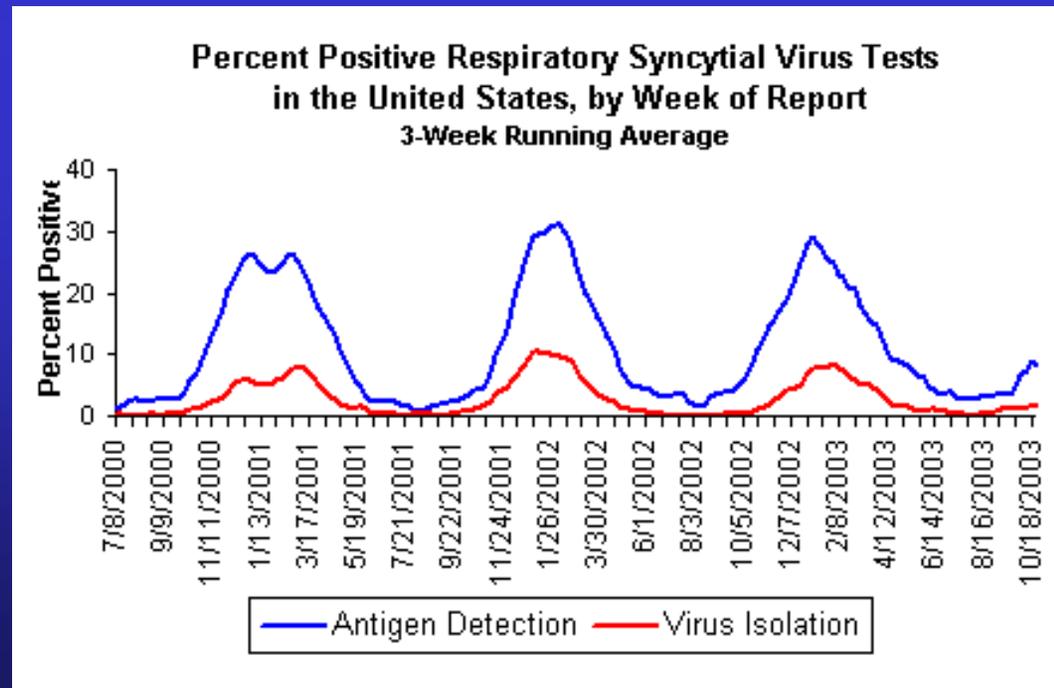
2001-03: H1N2

# hRSV: Resources

- National Respiratory and Enteric Virus Surveillance System (NREVSS) home page

<http://www.cdc.gov/ncidod/dvrd/revb/nrevss/index.htm>

## National RSV Data



# hRSV: Clinical Syndrome (I)

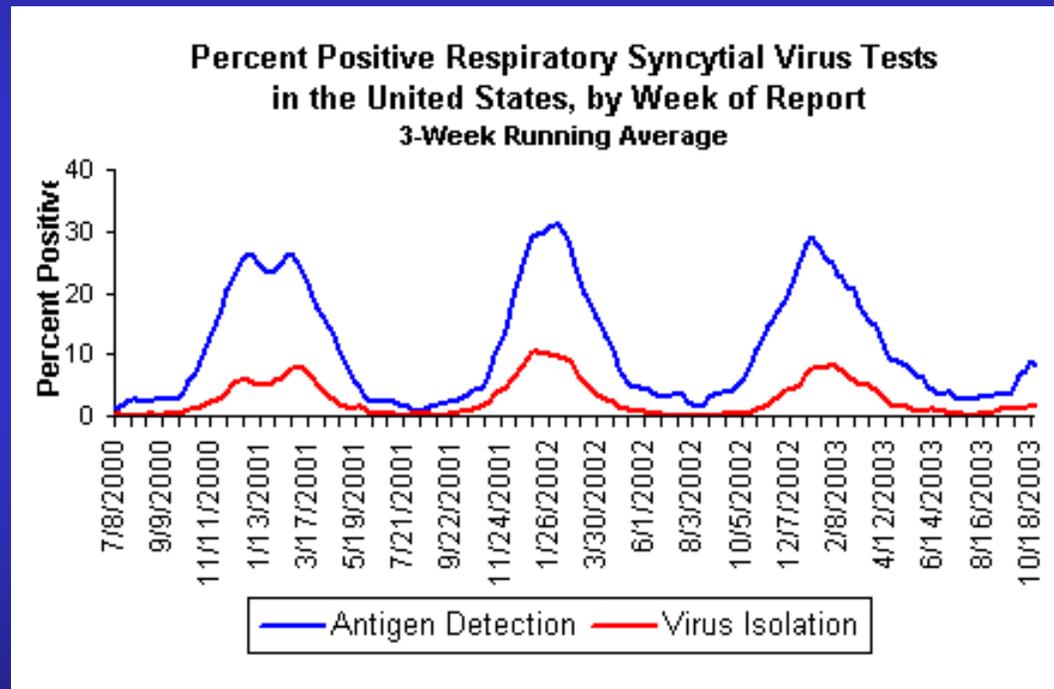
- Incubation period of 2-8 days
- Acute respiratory illness
  - Fever
  - Cough
  - Copious nasal discharge
  - Malaise
  - Respiratory distress and decreased feeding
- Leading cause of severe lower respiratory tract illness (bronchiolitis/pneumonia) in infants
  - Infants with underlying cardiopulmonary disease are at particularly high risk

## hRSV: Clinical Syndrome(II)

- Otitis media is a major complication
- **Highly contagious**-a leading cause of nosocomial infections in infants and the elderly
- Symptomatic re-infections occur throughout life:
  - Upper respiratory tract illness (URI)/bronchitis in adults
  - Severe lower respiratory illness in the elderly
- May be important precursor to asthma in later life

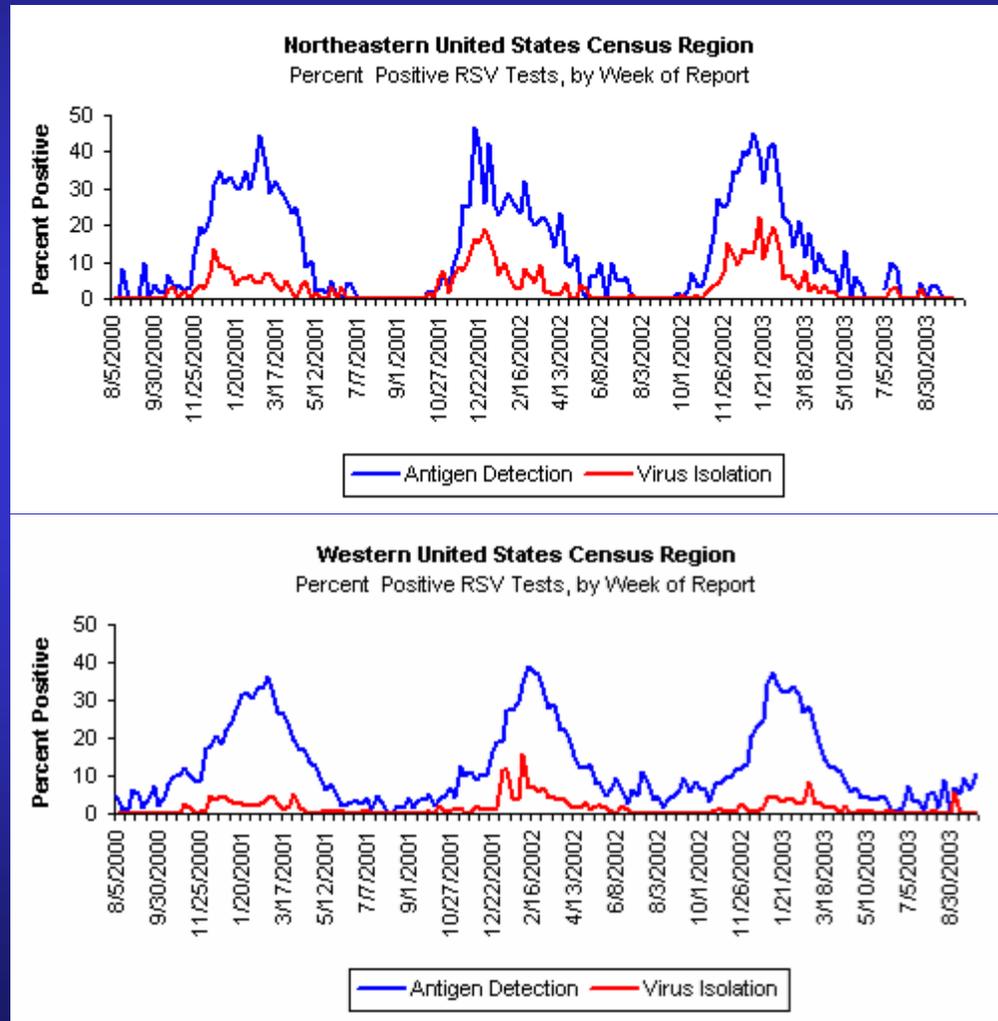
# hRSV: Epidemicity/Seasonality

## NREVSS National RSV Data



# hRSV

## NREVSS Regional RSV Data Examples



# hRSV: Public Health Importance

- Virtually all children are infected with RSV during the first 3 years
- The major viral cause of serious life-threatening lower respiratory tract illness (LRI) in infants worldwide
- Significant morbidity and mortality in U.S.
  - 1-2% hospitalization rate of infants
  - many others with LRI not hospitalized
  - up to 5,000 deaths/yr in US

# Metapneumovirus: *“The new kid on the block”*

*References*

www.cdc.gov



Homepage



Click on search



Enter: metapneumovirus

# Metapneumovirus: Clinical Syndrome

## *Similarities To and Differences From RSV*

- Presumed similar incubation period
- Similar clinical spectrum and risk groups
  - Wide range of illness severity
- Lower incidence of clinically significant disease than hRSV
  - 1.5-7% RTI; year-to year variability; similar to PIV
- Asymptomatic and mild illness much more common, especially in older children and adults
- Reinfections???
- Age extremes and immunocompromised may experience severe LRI with hospitalization
- Similar relationship to asthma: initiation & exacerbation

# Metapneumovirus: *Epidemiological Characteristics*

- 2 genetic lineages with 2 subgroups each
- World-wide distribution
- Similar age/infection profile
  - Seroprevalence: 70-80% - < 5 yrs  
100% in adults
- Similar seasonality; however, summer infections may occur
- Serologic studies indicate hMPV circulation at least 50 years ago

# SARS-Coronavirus: Resources

- CDC's Home Page on Severe Acute Respiratory Syndrome (SARS)

<http://www.cdc.gov/ncidod/sars/>

- CDC's Draft Plan for Preparedness and Response to Severe Acute Respiratory Syndrome (SARS)

<http://www.cdc.gov/ncidod/sars/sarsprepplan.htm>

- CDC's archived webcasts (September 23 & 30, 2003 - Parts 1 & 2) "Preparing for the Return of SARS: Are we ready?"

<http://www.phppo.cdc.gov/PHTN/webcast/sars-return/>

- WHO

<http://www.who.int/csr/sars/en/index.html>

[http://www.who.int/csr/sarsarchive/2003\\_04\\_11/en/print.html](http://www.who.int/csr/sarsarchive/2003_04_11/en/print.html)

# SARS – What is it?

- Severe Acute Respiratory Syndrome
- Often severe influenza-like illness
  - Fever, chills, headache, malaise, myalgia, respiratory symptoms
  - Development of dry cough, 2-7 days
  - Diarrhea (10-20%)
  - Most develop pneumonia
    - Mechanical ventilation required (10-20%)
- Mortality rate ~15%; >50% in elderly
- Etiology: Novel, previously unrecognized coronavirus
  - **SARS-CoV**

# SARS – Key Epidemiologic Features

- Incubation period: 2 - 7 days; as long as 10d
- Transmission: Close person - to - person contact
  - Droplet spread, fomite
  - Mechanism of community spread?
- Infectivity: <sup>[www.who.int/csr/sars/en/index.html](http://www.who.int/csr/sars/en/index.html)</sup> Maximum with symptoms (fever, cough)
  - Asymptomatic virus shedding?
- Duration and scope of immunity?
  - Good antibody response; often delayed
  - Re - infection possible?

# The SARS Outbreak: 2002-03

- First cases: 11/16/02, Quangdong Province, China
- **First cases reported: 02/11/03, China**

**Singapore**



- Initial spread: **China → Hong Kong → Vietnam**



**Toronto**

- Initial “hot zones” with rapid increase in cases
  - 1° Tx in healthcare settings
  - 2° community chains of Tx
- Final totals - World: 8422 cases; 916 deaths; 30 countries

U.S.: 33 cases; 0 deaths

## - SARS -

“ A particular threat to international health”

- Pathogenicity; high mortality
- Human - to - human spread; no vector
- Initial sxs non-specific, common
- Targets healthcare workers
- Relatively long incubation period
- High proportion of patients requiring intensive care
- Possible zoonotic source
- No vaccine or treatment

# Laboratory Diagnostic Methods

# Influenza: Laboratory Diagnosis

- Culture
  - 1-5 days
  - “Gold standard”
- Direct Specimen Immunofluorescence
  - Dependent on reader expertise
  - Limited to laboratories with IF capability
  - Variable sensitivity & specificity
- Molecular
  - Not yet widely available/used
- Serology
  - Retrospective
- Rapid EIA and “EIA-Like” Tests
- **Note: The nasal mist vaccine may replicate in cell cultures and produce a positive result in rapid tests up to 3 weeks post-immunization.**

## Influenza: Rapid EIA and “EIA-Like” Tests

<b>Test</b>	<b>CLIA Status</b>	<b>Antigen Detected</b>
Directigen Flu A	Moderate	A
Directigen Flu A & B	Moderate	A & B
Flu OIA	Moderate	A / B
Flu OIA A/B	Moderate	A & B
NOW Flu A	Waived	A
NOW Flu A/B	Waived	A & B
QuickVue Influenza	Waived	A / B
Xpect Flu A/B	Pending (interim moderate)	A & B
ZstatFlu	Waived	A / B

# Influenza: Rapid EIA and “EIA-Like” Test - Specimens & Storage

Test	Specimen Type	Specimen Storage
Directigen Flu A	NP wash/asp, NP Sw, Throat Sw	2-8°C/72 hr.
Directigen Flu A+B	NP wash/asp, NP Sw, Nasal wash, Th Sw, BAL	2-8°C/72 hr.
Flu OIA	Nasal asp, NP Sw, Th Sw, Sputum	2-8°C/24 hr.
Flu OIA A/B	Nasal aspirate, nasopharyngeal swab, throat swab, or sputum	2-8°C/24 hr.
NOW Flu A	Nasal wash, NP Sw	2-8°C/24 hr. (elute swabs)
NOW Flu A/B	Nasal wash, NP Sw	2-8°C/24 hr. (elute swabs)
QuickVue Influenza	Nasal Sw, wash, asp	2-30°C/8 hr.
Xpect Flu A/B	Nasal wash, swab, Th Sw	2-8°C/72 hr (in transport medium) or -20°C/6 mo.
ZstatFlu	Th Sw	0-40°C/24 hr.

# Influenza: Rapid EIA and “EIA-Like” Test Performance Characteristics\*

Test	Sensitivity	Specificity
Directigen Flu A	91% (A)	95% (A)
Directigen Flu A+B	86% (A) 81% (B)	91% (A) 99.5% (B)
FLU OIA	62-88% (A/B)	52-80% (A/B)
FLU OIA A/B	62-88% (A/B)	52-80% (A/B)
NOW Flu A	78-82 (A)	92-94 (A)
NOW Flu A/B	78-82% (A) 58-71% (B)	92-94% (A) 97% (B)
QuickVue Influenza	73-81% (A/B)	96-99% (A/B)
Xpect Flu A/B	89-100% (A) 83-100% (B)	100% (A) 100% (B)
ZstatFlu	58-65% (A/B)	98-100% (A/B)

\* Per Manufacturer, without discrepant analysis

# hRSV: Laboratory Diagnosis

- Culture
  - 1-10 days
- Direct Specimen Immunofluorescence
  - Dependent on reader expertise
  - Limited to laboratories with IF capability
  - More sensitive than culture
- Molecular
  - Not yet widely available/used
- Serology
  - Retrospective
- Rapid EIA and “EIA-Like” Tests

## hRSV: Rapid EIA and “EIA-Like” Tests

Test	CLIA Status
Directigen RSV	Moderate
Directigen EZ RSV	Moderate
RSV OIA	Moderate
NOW RSV	Waived
Xpect RSV	Pending (interim moderate)

# hRSV: Rapid EIA and “EIA-Like” Tests - Specimens & Storage

<b>Test</b>	<b>Specimen Type</b>	<b>Specimen Storage</b>
<b>Directigen RSV</b>	NP wash/asp, NP Sw, Throat Sw	2-8°C/48 hr.
<b>Directigen EZ RSV</b>	NP wash/asp, NP Sw, Throat Sw	2-8°C/72 hr.
<b>RSV OIA</b>	Nasal wash, NP Sw	Room temp/2 hr 2-8°C/24 hr. Frozen
<b>NOW RSV</b>	Nasal wash	Room temp/4 hr 2-8°C/24 hr.
<b>Xpect RSV</b>	NP wash, asp., swab	2-8°C/48 hr -20°C/1 week

## hRSV: Rapid EIA and “EIA-Like” Test Performance Characteristics\*

Test	Sensitivity	Specificity
Directigen RSV	93-97%	90-97%
Directigen EZ RSV	67% (NPS) 87% (NPW)	92% (NPS) 86% (NPW)
RSV OIA	67% (NPS) 87% (NW)	96% (NPS) 83% (NW)
NOW RSV	89%	98-100%
Xpect RSV	96%	94%

\* Per Manufacturer, without discrepant analysis

# SARS-Coronavirus: Laboratory Diagnosis

- All methods developmental
- Culture
  - Not recommended
  - Test for other respiratory viruses
  - Strong evidence
- Direct Specimen Immunofluorescence
  - Not available
- Molecular
  - Real-time PCR
    - Available at CDC & state public health laboratories
    - Available as “home-brews”??, non-FDA approved kits??
- Serology
  - “Gold standard”
  - ELISA for total antibody (IgG, IgM, and IgA)
  - Retrospective

# SARS-CoV Laboratory Testing:

- Real-time RT-PCR
  - Good sensitivity (1-10 copies).
  - Highly specific for SARS-CoV, but <50% sensitive during 1<sup>st</sup> week of infection.
    - Low viral titers early in infection
    - Pathogenesis of disease may not allow a definitive diagnosis early in illness.
    - Changes in type, quality, and quantity of specimens and in specimen processing procedures may improve the detection of SARS-CoV infection in patients.
  - Potential for false negatives and false positives.
  - PPV low when prevalence is low.
  - Positive result considered presumptive until confirmed.
  - Negative result does not rule out SARS & should not affect patient management.
  - **Must be used and interpreted carefully.**

# SARS-CoV Laboratory Testing:

- Serology
  - Specific; no cross reactions with other coronavirus infections.
  - Serology can be positive 8-10 days after onset.
  - Serology cannot be considered negative until >28 days post onset
  - **Must be used and interpreted carefully.**

# Test Performance Characteristics

Appropriate use of the  
rapid tests requires the  
integration of knowledge of  
*epidemiology*  
with knowledge of  
*test performance*  
*characteristics.*

# Test Performance Characteristics: Definitions

## Sensitivity

- The probability of a positive test result given the presence of disease
- How good is the test at detecting infection in those who have the disease?

## Specificity

- The probability of a negative test result given the absence of disease.
- How good is the test at calling uninfected people negative?

# Sensitivity and Specificity

## DISEASE

		DISEASE	
		Present	Absent
TEST	Positive	True Positive (TP)	False Positive (FP)
	Negative	False Negative (FN)	True Negative (TN)

$$\text{Sensitivity} = \text{TP} / \text{TP} + \text{FN}$$

$$\text{Specificity} = \text{TN} / \text{TN} + \text{FP}$$

# Predictive Value

- The probability of the presence or absence of disease given the results of a test
  - PVP is the probability of disease in a patient with a positive test result.
  - PVN is the probability of not having disease when the test result is negative.

# Predictive Value

## DISEASE

		DISEASE	
		Present	Absent
TEST	Positive	True Positive (TP)	False Positive (FP)
	Negative	False Negative (FN)	True Negative (TN)

Predictive Value Positive (PVP) =  $TP / (TP + FP)$

Predictive Value Negative (PVN) =  $TN / (TN + FN)$ <sub>49</sub>

# Predictive Value

- How predictive is this test result for this particular patient?
- Determined by the **sensitivity and specificity** of the test, *and* the **prevalence rate** of disease in the population being tested.

# Prevalence Rate

Number of cases of illness existing at a given time divided by the population at risk

# Hypothetical Influenza Test Performance

Prevalence = 20.0%

**Disease**

		Disease	
		+	-
Test	+	380	64
	-	20	1536

Sensitivity =  $380/400 = 95.0\%$

Specificity =  $1536/1600 = 96.0\%$

Predictive Value Positive (PVP) =  $380/444 = 85.6\%$

Predictive Value Negative (PVN) =  $1536/1556 = 98.7\%$

# Hypothetical Influenza Test Performance

Prevalence = 1.0%

**Disease**

		Disease	
		+	-
Test	+	19	80
	-	1	1900

Sensitivity =  $19/20 = 95.0\%$

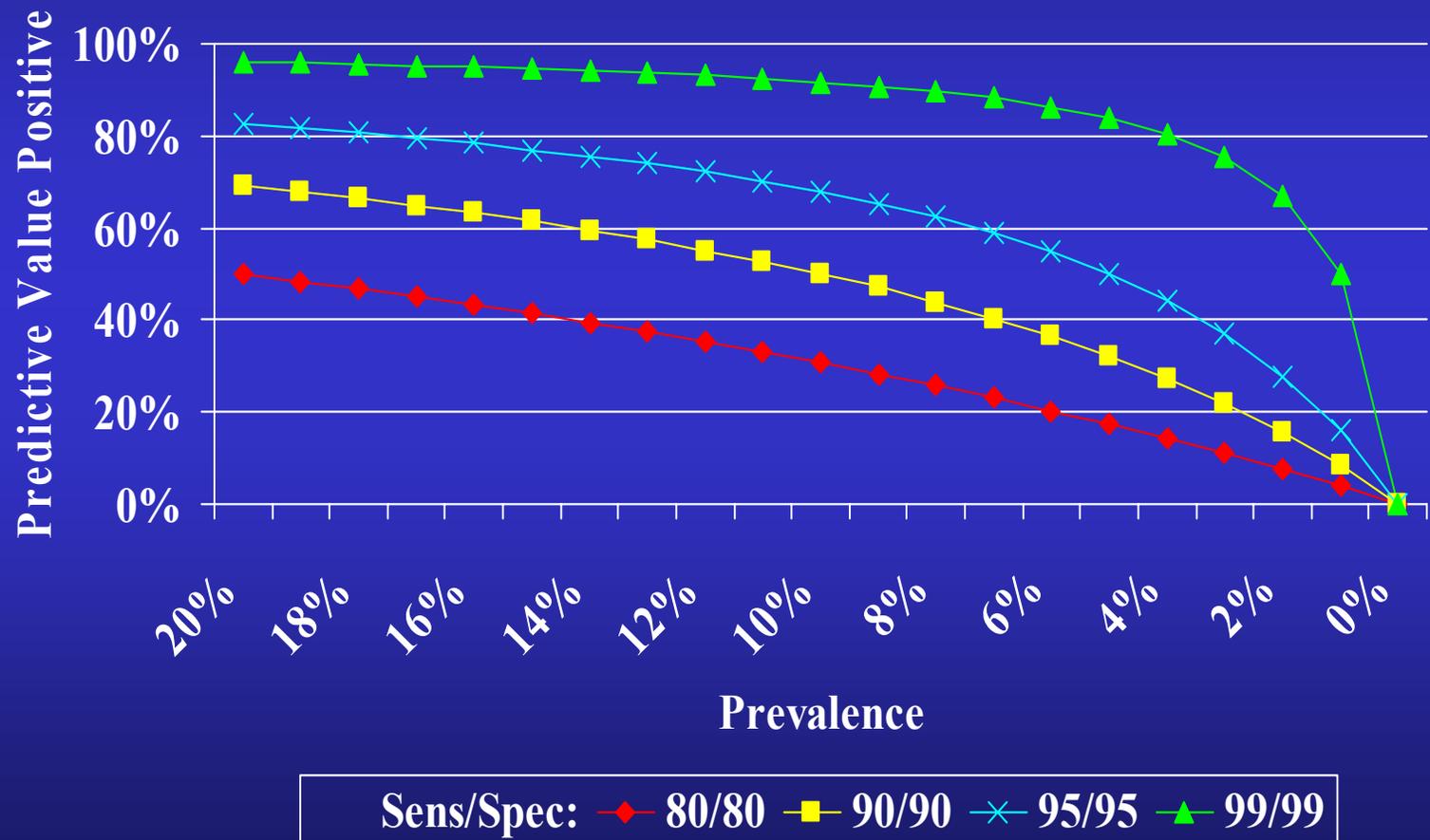
Specificity =  $1900/1980 = 96.0\%$

Predictive Value Positive (PVP) =  $19/99 = 19.2\%$

Predictive Value Negative (PVN) =  $1900/1901 = 99.9\%$

# Predictive Value Positive

## Dependence on Sensitivity, Specificity and Prevalence



# Recommendations for Use of Rapid Tests for Influenza or RSV

- Use prevalence indicators to decide:
  - When to test
  - Whether to qualify result
  - Whether to confirm results
  - Potential prevalence indicators:
    - Laboratory Detections
      - CDC
      - Statewide data
      - Your laboratory data
      - “Sister” laboratory’s data
- Culture confirm your first influenza positives, others as needed
- Educate clinicians on predictive values & limitations of tests

# CDC Recommendations for Specimen Collection, Testing and Laboratory Safety for SARS

# SARS-CoV Laboratory Testing: Specimen Submission

- Consult with your state health department for evaluation of case
- If possible, include informed consent form for serology testing
  - Testing will be performed if consent not obtained
  - FDA regulation for use of non-licensed test
  - **Allows use of patient specimen for future studies**

[http://www.](http://www.cdc.gov/ncidod/sars/specimen_collection_sars2.htm)

[cdc.gov/ncidod/sars/specimen\\_collection\\_sars2.htm](http://www.cdc.gov/ncidod/sars/specimen_collection_sars2.htm)

# SARS-CoV Laboratory Testing: Specimens to collect during the course of illness

SPECIMEN	<1 week post symptom onset	1-3 weeks post symptom onset	>3 weeks post symptom onset
Serum	++	++	++
Blood (EDTA/purple top)	++		—
Respiratory (sputum, BAL, nasal aspirate/wash, NP swab, throat swab)	++	++	
Stool		++	++

++ Preferred specimen

- Not recommended

# SARS-CoV Laboratory Testing: Specimens for PCR

- Lower respiratory tract specimens
  - Sputum, bronchoalveolar lavage, tracheal aspirate, pleural tap
- Upper respiratory tract specimens
  - Nasopharyngeal aspirate/wash
  - Nasopharyngeal/oropharyngeal swab
    - Place in dry sterile container
    - Dacron or rayon with plastic shaft
    - NOT calcium alginate or wooden shafted swab
- Blood
  - 5-10ml in EDTA tube (Purple top)
- Stool
  - 10 - 50cc in stool cup or urine container, no preservatives
- Store all specimens at 4°C prior to shipping

# SARS-CoV Laboratory Testing: Specimens for Serology

- Acute and convalescent sera
  - Acute serum
    - Collect ASAP
    - approx. 30% positive within 6-10 days post-onset
  - Convalescent serum
    - Collect >28 days post-onset
    - Most patients positive at 2 weeks

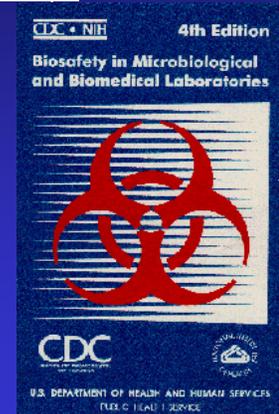
# SARS-CoV Laboratory Testing: Specimen Shipping and Transport

- Resource: <http://www.cdc.gov/ncidod/sars/packingspecimens-sars.htm>
  - Check with your state health department or laboratory for in-state guidance.
  - Proper packaging is the responsibility of the shipper.
- In brief: Package as “Diagnostic Specimens”
  - Primary receptacle: watertight; screw-capped closures wrapped with tape or parafilm; individually wrapped;
  - Secondary receptacle: watertight; include absorbent.
  - Outer packaging: dry ice or coolant outside secondary packaging; allow release of CO<sub>2</sub> gas if dry ice used.
  - At least 4 inches on smallest side & large enough for documents
  - Additional: Volume limits, container specifications, itemized list of contents, & labelling requirements based on mode of transport (ground, air, USPS)

# Biosafety in the Laboratory: Resources

- Biosafety in Microbiological and Biomedical Laboratories (BMBL),  
4<sup>th</sup> edition

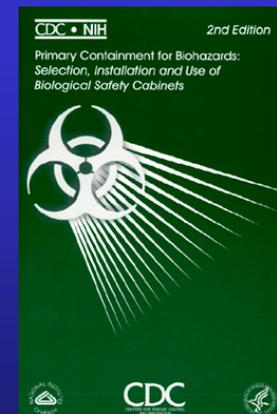
U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention  
and  
National Institutes of Health  
Fourth Edition, May 1999.  
US Government Printing Office  
Washington: 1999



<http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm>

- Primary Containment for Biohazards: Selection, Installation and  
Use of Biological Safety Cabinets, 2nd Edition

U.S. Department of Health and Human Services  
Public Health Service  
Centers for Disease Control and Prevention  
*And*  
National Institutes of Health  
September 2000



<http://www.cdc.gov/od/ohs/biosfty/bsc/bsc.htm>

# Biosafety in the Laboratory with SARS (I)

- Establish process to identify SARS specimens.
- If recommended safety equipment not available, reduce risk by other means.
  - Perform risk assessment
  - Consider referral to another laboratory
- Viral culture of suspect SARS specimens must only be performed in BSL-3 facility.

# Biosafety in the Laboratory with SARS (II)

- Blood and urine
  - Biosafety Level 2 (BSL-2)
  - PPE: gloves, laboratory coats, face shield or eye protection/surgical mask
  - BSC for aerosol potential
  - Sealed centrifuge rotors or sample cups, if available.
- Other untreated specimens
  - Biosafety Level 2 (BSL-2) facilities using BSL-3 practices
  - Use biosafety cabinet (BSC) with PPE: gloves, solid front gown, full face protection
    - If BSC not available/feasible, N-95 respirator, full face protection, other containment devices
  - Centrifuge using sealed rotors or sample cups
    - Unload in the BSC

## 2003-04 – What can we expect?

- The first SARS case of the season: Singapore, 9/9/03
- Developments to watch for:
  - Enhanced national and international surveillance
  - Stages/levels of activity to guide response
  - Enhanced public health laboratory testing capability and capacity
  - Enhanced public health response strategies
    - Isolation, quarantine, travel advisories
  - Updated specimen collection, lab testing, results interpretation and biosafety guidelines
  - Identification of natural reservoir

## Closing Comments (I)

- CDC and other response partners have developed a plan for SARS preparedness & response.
- The potential for global spread of SARS requires collaboration and communication between healthcare and public health communities.
- Early case detection and diagnosis of SARS cases is critical to prevent transmission and limit the outbreak.
- Because the signs and symptoms are similar, we may not be able to differentiate influenza and SARS clinically if they occur simultaneously.

## Closing Comments (II)

- Results of SARS laboratory tests in the clinical setting are only relevant IF SARS cases have been documented.
- Inappropriate laboratory testing that produces false positive or negative results will have adverse consequences.
- Identification of another respiratory pathogen in SARS-like illnesses can be significant.
- Current specimen collection and test procedures for SARS are interim guidelines that may change as we learn more.
- **A new model for biosafety in the laboratory?**
  - Universal precautions for blood in the 80's;  
respiratory precautions in the 2000's?