Recognizing testing pitfalls and optimizing test selection for common infectious diseases in Urgent Care clinics

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Disclosures

I have no actual or potential conflict of interest in relation to this program/presentation

I will not be discussing “off-label” uses of medications

Disclosures

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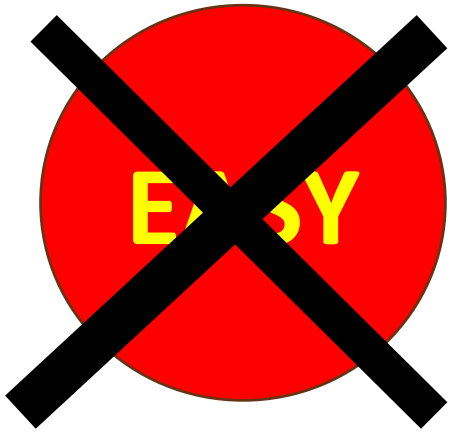
Learning objectives

- Describe the key differences between antigen and molecular testing in the urgent care setting
- Describe the limitations of serology testing for acute disease diagnosis
- Recognize pitfalls of laboratory testing and avoid clinical misinterpretation of test results
- Choose appropriate testing for common infectious disease presentations in the urgent care environment
- Develop an evidence-based approach to laboratory testing.

The perfect diagnostic test

- Correctly identifies all individuals with disease (100% sensitive)
- Correctly rules out all individuals without disease (100% specific)
- Fast (instant results)
- Non-invasive
- Ease of use
- Low cost
- Widely available



There is no easy button!

Unfortunately, the “perfect” test does not exist!

Appropriate test selection

- Laboratory testing technology and best practice guidelines change!
  - Keeping up-to-date avoids reliance on outdated, inferior or wrong tests
- Interpretation of results requires **clinical and epidemiological context**
- Test results should provide **clinical value**
  - Will the test result change clinical management?
  - Will the test result improve clinical outcomes?
  - Is there an action plan for an unexpected result?

Avoid a “spray and pray” approach

Patient expectations

Patients are repeatedly advised by public health campaigns, social media, news media to get tested …

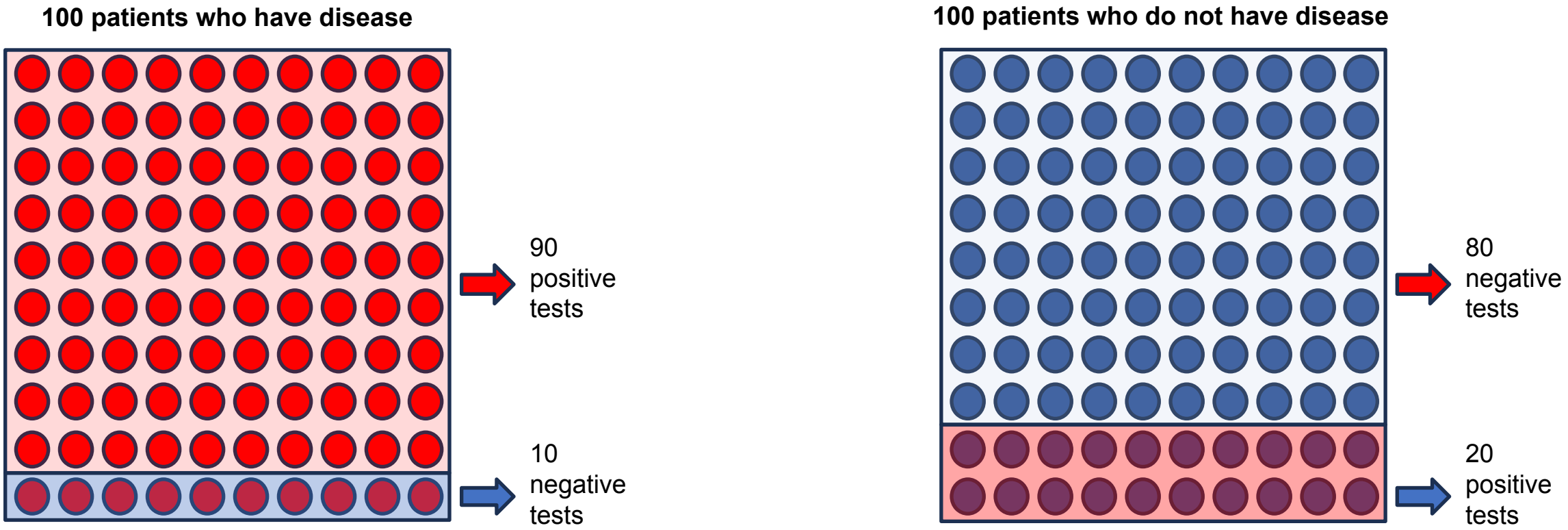
BUT

Patients may not understand the limitations of testing

INCORRECT test utilization => BAD information => RISK
(incorrect diagnosis, unnecessary additional workup, patient anxiety)

Test characteristics

Sensitivity and Specificity measure the test's ability to rule in or rule out disease



Sensitivity: 90% **Specificity 80%**

Note: sensitivity does not account for false positive tests

Test characteristics

- But it is the predictive value that is clinically important
  - Positive predictive value (PPV): How likely does the patient have disease, given a positive test result
  - Negative predictive value (NPV): How likely does the patient not have disease given a negative test result

- **Predictive value is strongly influenced by the pre-test probability**
- **Negative results, even on a highly sensitive test cannot rule out infection if the pretest probability is high!**

Diagnostic Test characteristics

	Gold standard		
Test	Positive	Negative	Total
Positive	TP	FP	TP + FP
Negative	FN	TN	FN + TN
Total	TP + FN	FP + TN	N

$$Sensitivity = \frac{TP}{TP + FN} \qquad Specificity = \frac{TN}{TN + FP}$$

$$PPV = \frac{TP}{TP + FP} \qquad NPV = \frac{TN}{TN + FN}$$

$$Accuracy = \frac{TP + TN}{N} \qquad OR = \frac{TPR/(1 - TPR)}{FPR/(1 - FPR)}$$

Sens = 60%, spec = 95%
Influenza RIDT, prevalence 5%

	Flu	No Flu	Total
Pos	300	475	775
Neg	200	9025	9225
Total	500	9500	10000

Sens = 300/300+200 = 0.60
Spec = 9025/9025+475 = 0.95
PPV = 300/300+475 = 0.387 (38.7%)
NPV = 9025/9025+200 = 0.978
False neg 200/500 = 40%

RIDT (antigen test) influenza A

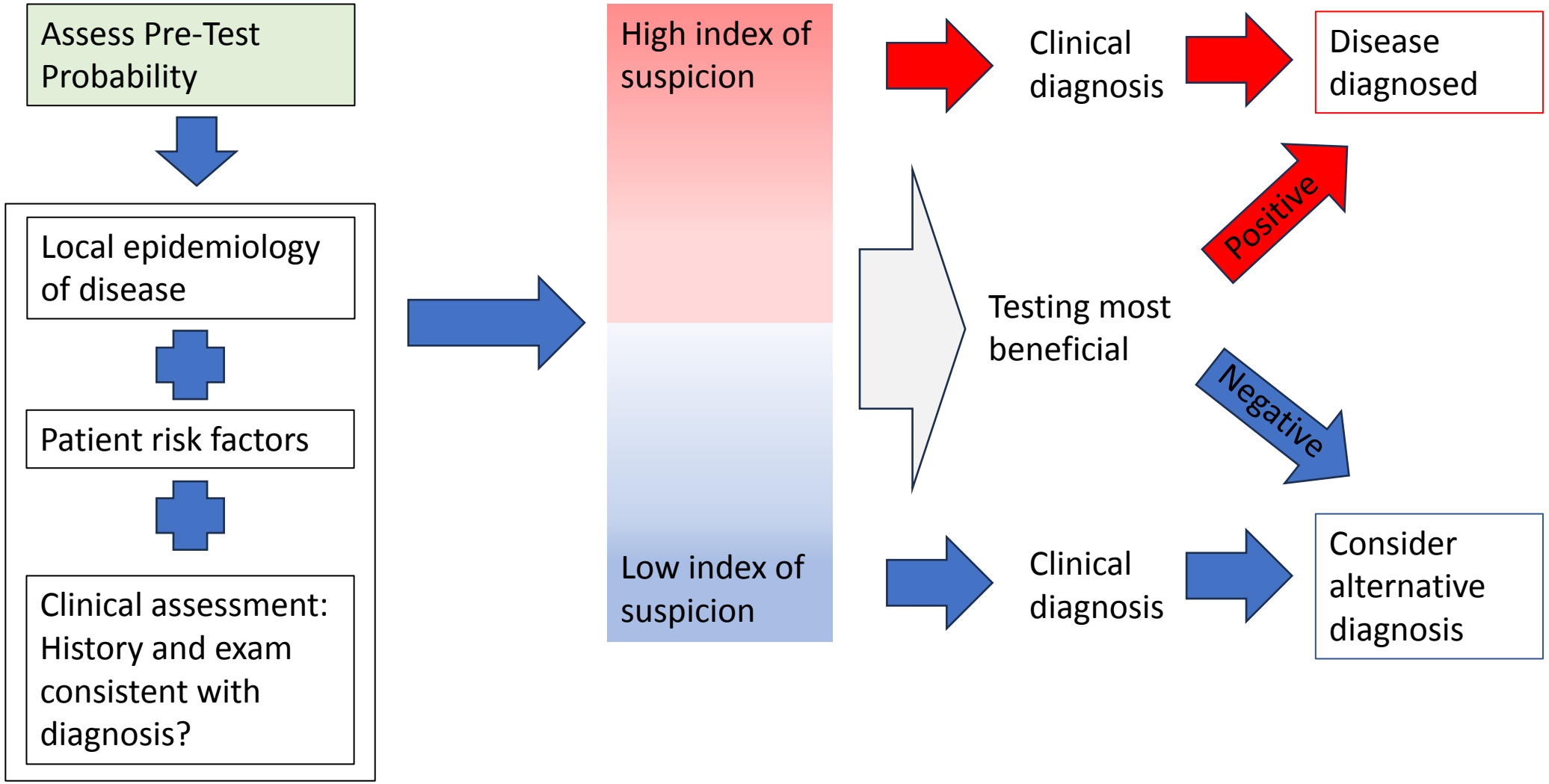
Sens = 96.2%, spec = 98.9%
Influenza PCR test, prevalence 5%

	Flu	No flu	Total
Pos	481	105	586
Neg	19	9395	9414
Total	500	9500	10000

Sens = 481/481+19 = 0.962
Spec = 9395/9395+105 = 0.989
PPV = 481/481+105 = 0.82 (82%)
NPV = 9395/9395+19 = 0.998 (99.8%)
False neg 19/500 = 4%

PCR (molecular test) influenza A

Diagnostic testing is a PROCESS



Diagnostic testing options

Direct testing
Tests that detect the pathogen in a specified sample

- Direct visualization
- Culture
- Antigen test
- Molecular test

Indirect testing
Tests that detect immunological response to a pathogen

- Antibody testing (IgG, IgM)

Home testing

Home tests: self collection by patient → Test kit or Collection with sendout to reference lab

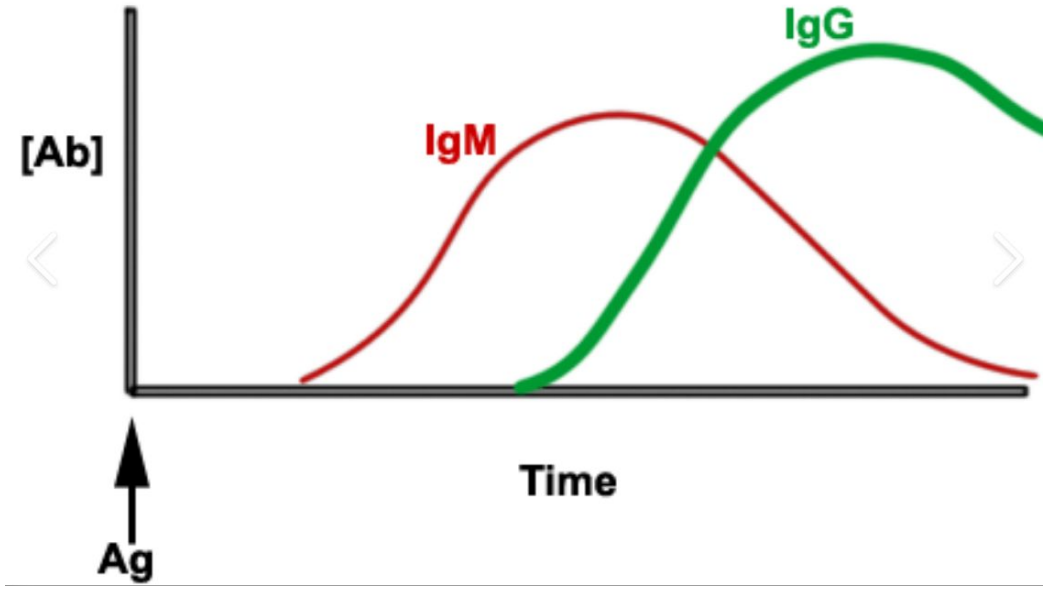
Clinic performed testing

Point of Care (POCT): tests performed at time of patient care → Results at time of visit (~< 30 min)

Reference lab: Specimen sent to reference lab → Results take hours to days

Diagnostic testing options

- Antibody testing aka serology testing
  - Measures antibodies produced by the body in response to an infection
  - **Antibodies take days to weeks to develop.**
  - Antibody testing is not appropriate for evaluation of ACUTE disease
  - Cross reaction with other antigens may result in false positive results



Diagnostic testing options

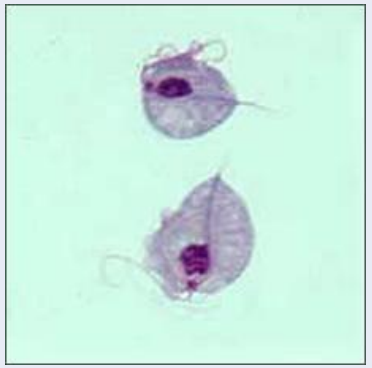
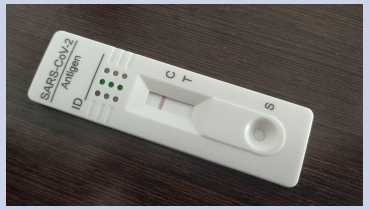
Direct Visualization of pathogen	Culture
Example: Wet Prep	Example: Bacterial culture
Quick, easy, low cost Immediate results	Historically the gold standard for many pathogens
Poor sensitivity (compared to culture) **Interpretation is skill dependent** Provider Provided Microscopy (PPM) waiver may be required	Requires incubation period Labor intensive (requires laboratory personnel) Expensive Prone to contamination
	

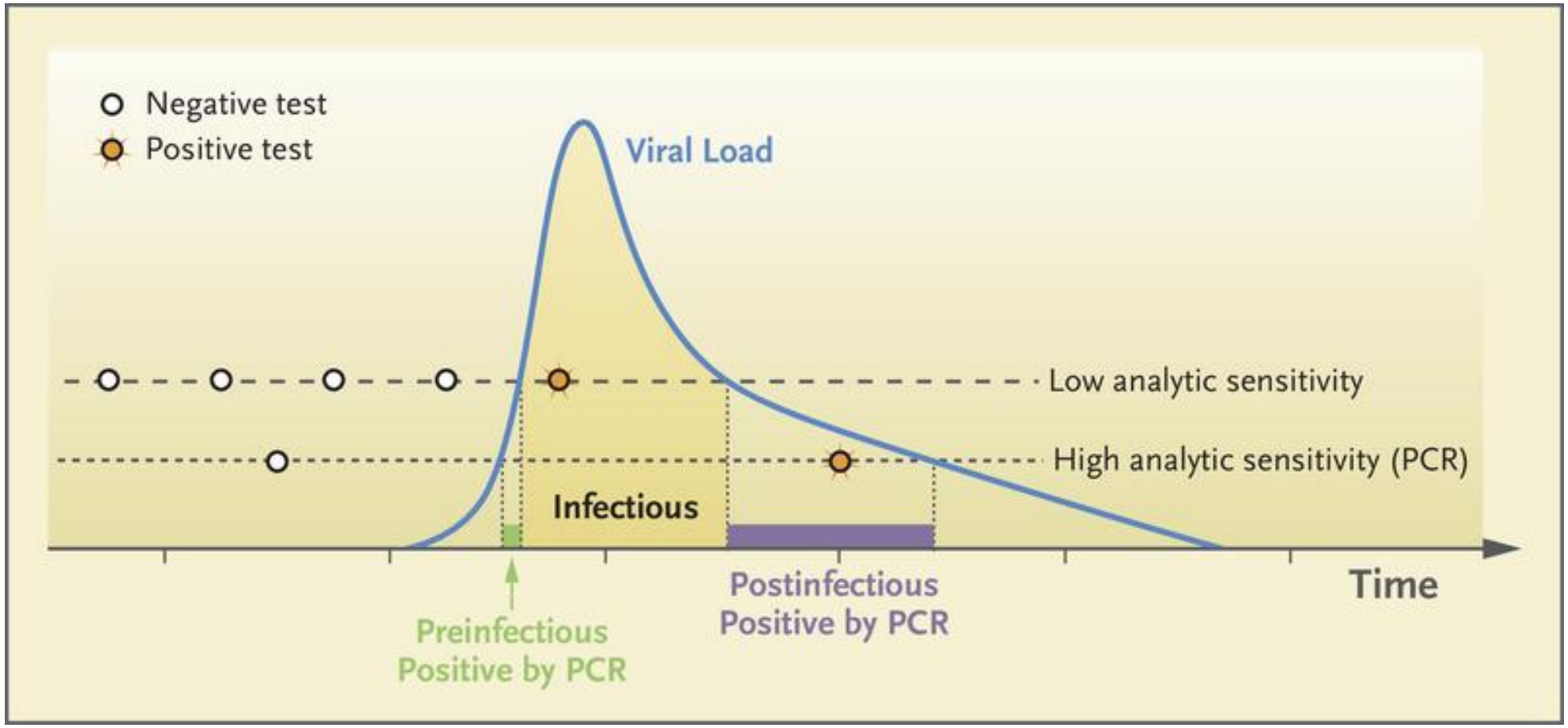
Image credit: CDC website STD Facts - Trichomoniasis (cdc.gov)

Image credit: Dr Graham Beards at en.wikipedia, CC BY-SA 4.0 <https://creativecommons.org/licenses/by-sa/4.0>, via Wikimedia Commons

Antigen vs Molecular testing

	How it works	Why use it?	Caveats	Notes
Antigen test	Antigen tests detect **protein** produced by a pathogen (ie, COVID-19 capsularprotein)	- Relatively inexpensive - Fast results **- Portability** 	- **Not as accurate as molecular** testing (higher risk of false negative vs molecular)	- Current home tests are antigen tests. - **Tests may be negative in early disease**
Molecular test	Molecular tests detect pathogen **nucleic acid** (RNA or DNA)	- Current gold standard for many common infections seen in UC. - Highest sensitivity **Can be point-of-care or reference lab**	- Relatively expensive, compared to antigen tests - Requires a device to perform and read the test.	- Presence of nucleic acid does not imply active infection. - **DNA/RNA can be detected for weeks or months after infection has resolved**

Diagnostic testing options



Source: Rethinking Covid-19 Test Sensitivity — A Strategy for Containment | NEJM

Residual nucleic acid fragments may result in a positive molecular test

- Viral shedding can persist for weeks (longer in immunodeficient patients). Shedding does not mean patient is contagious
- Nucleic acid can be detected for weeks to months

Pathogen	Duration of positive results attributable to residual nucleic acid
COVID-19	90 days or longer (CDC)
Chlamydia	3-4 weeks (mean time 9 days)
Gonorrhea	3-4 weeks (mean time 6 days)
Trichomonas	3-4 weeks (mean time 7 days)
Influenza	Up to 7 days or longer
Group A strep	~ 10 days (median time 4 days), 20% positive 14-18 days

Duration of Group A Streptococcus PCR positivity following antibiotic treatment of pharyngitis - ScienceDirect

Williams, James A. BS*; Ofner, Susan MS*; Batteiger, Byron E. MD*; Fortenberry, J. Dennis MD, MS*; Van Der Pol, Barbara PhD, MPH†. Duration of Polymerase Chain Reaction–Detectable DNA After Treatment of Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis Infections in Women. Sexually Transmitted Diseases 41(3):p 215-219, March 2014. | DOI: 10.1097/OLQ.0000000000000102

Even if a test is ideal, errors occur

- Testing errors occur due to:
  - Insufficient sampling
    - Incorrect collection technique
    - Non-cooperative patient
  - Not following manufacturers recommendations
    - Incorrect swab
    - Improper storage
    - Reading the test before or after the recommended time limit
      - Lateral flow tests: evaporation line
    - Use of an expired test
    - Machine incorrectly calibrated
  - Sample degradation during transport

Some common myths

1. **RT-PCR means "real time PCR"**
   - RT-PCR = reverse transcriptase polymerase chain reaction
     - As RNA is a single strand, it requires reverse transcriptase to complete the 2nd strand for the PCR process to complete
   - Rapid RT-PCR may be abbreviated as rRT-PCR

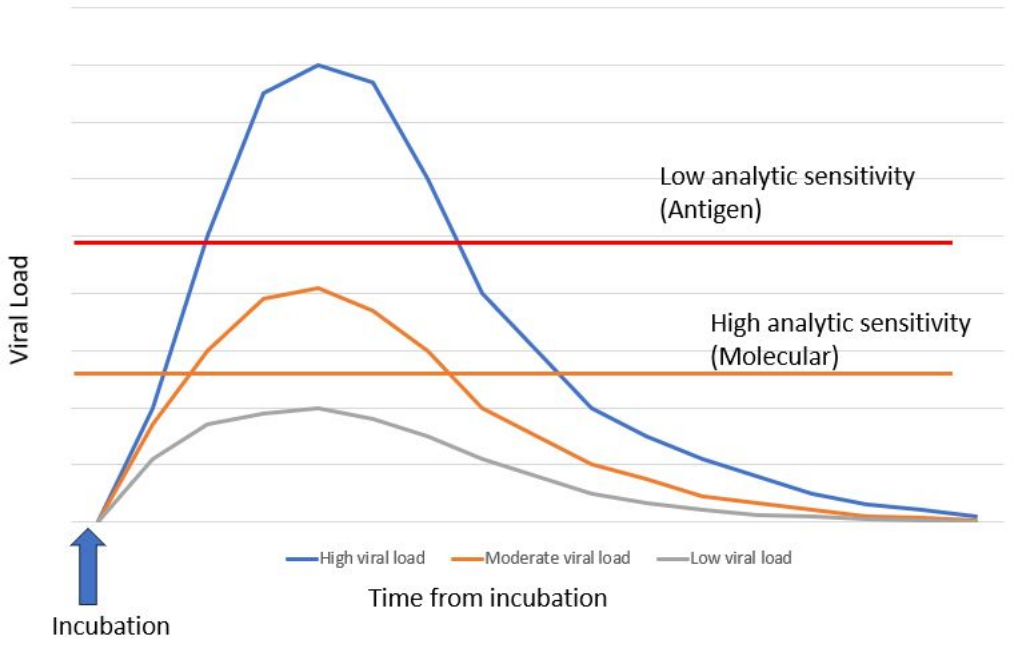
2. **All point of care tests are antigen tests**
   - Point-of-care tests may either be **antigen** or **molecular tests**

3. **All molecular tests are PCR tests**
   - PCR is a technique for NAA (nucleic acid amplification)
   - Other molecular tests include isothermal NAAT, LAMP, etc.

Myths

4. **A negative molecular test rules out disease**
    - There must be sufficient pathogen in the sample for the test to detect nucleic acid!
    - Using COVID-19 as an example, there is a time between exposure to when the viral load is detectable
    - If a test is performed too soon after exposure, insufficient viral load will result in a negative test.

If test result is unexpected, reassess the situation. Consider alternative diagnosis



Clinical scenario #1

CC : “I’m sick”

HPI: Patient is a 65 year old male presents with a 1 day history of URI symptoms including fever (up to 102 degrees F oral), chills, body aches, runny nose, sore throat and cough.

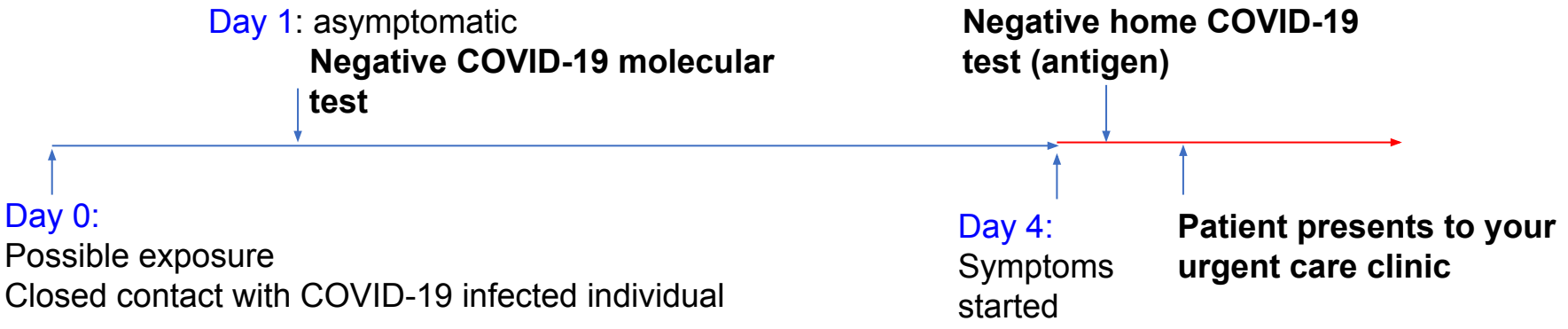
Patient states “I was exposed to COVID-19 from a co-worker 4 days ago. My co-worker had runny nose, and cough, but he attributed his symptoms to allergies. After work, he went to an urgent care clinic and tested positive for COVID-19”

Clinical scenario #1

CC : “I’m sick”

“I went to urgent care the next day and had a COVID-19 test. The test was negative and I was told ‘you don’t have COVID-19.’”

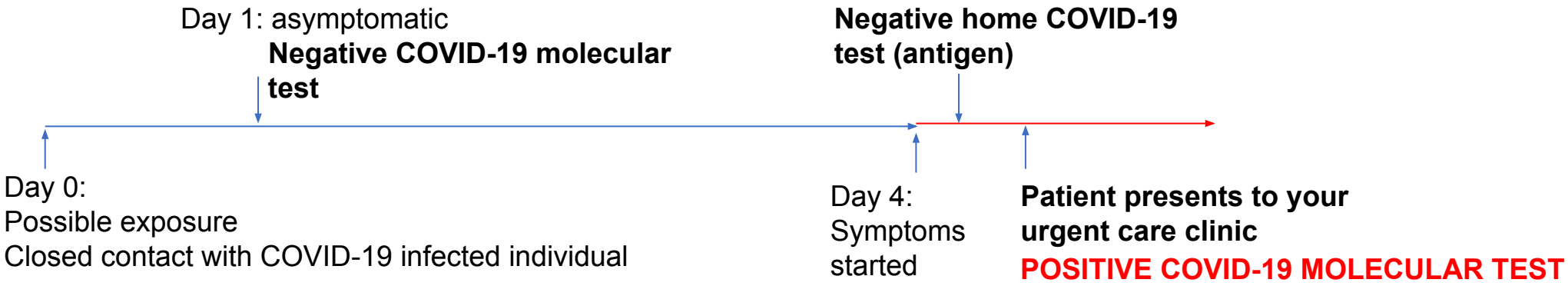
“I took a home antigen test this morning. It was negative. I think I need an antibiotic.”



Clinical scenario #1

Patient consents to a repeat point-of-care COVID-19 molecular test, which is **POSITIVE** for COVID-19

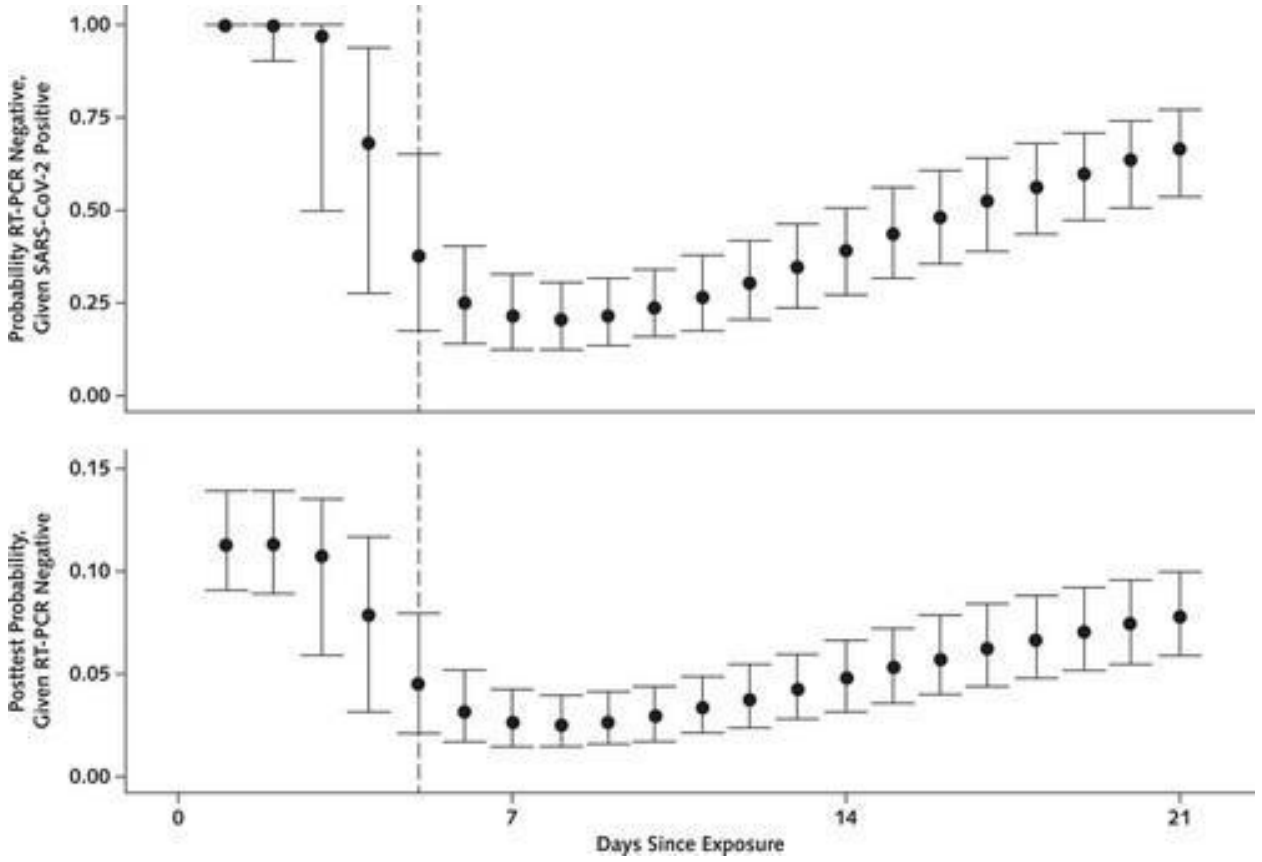
How do you explain the initial negative test results?



Sometimes, it is not the test's fault

False negative tests occur if testing **too early** after exposure or early in the course of illness!

- Insufficient viral load will not be detectable
- In COVID-19, risk of significant false negatives through day 5
- Incubation period (2-12 days), average 5 days +/- exposure

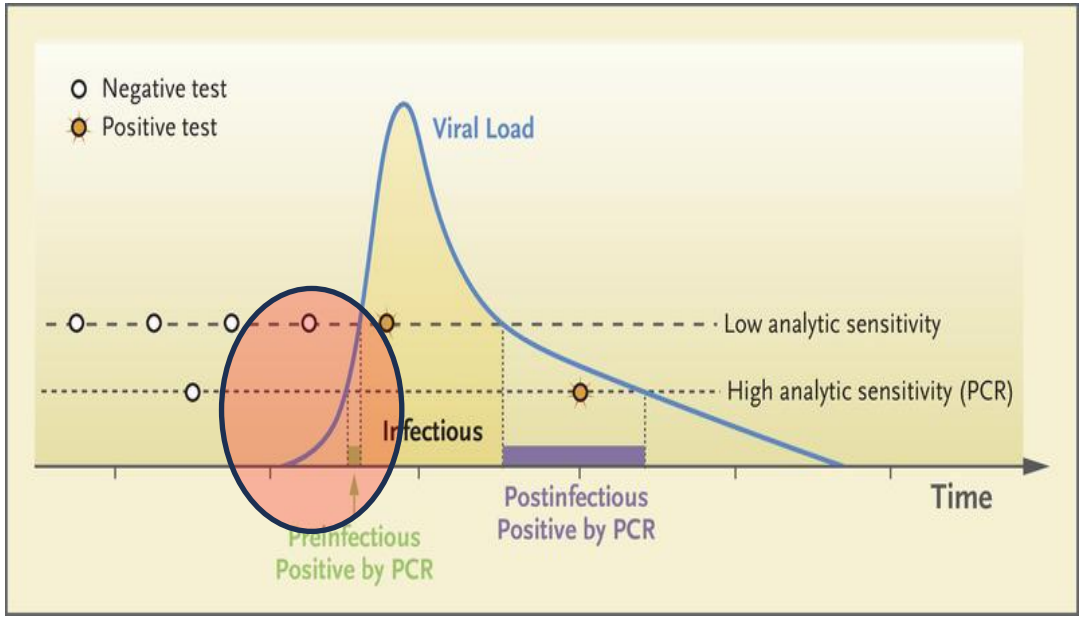


Lauren M. Kucirka, Stephen A. Lauer, Oliver Laeyendecker, et al. Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure. Ann Intern Med.2020;173:262-267. [Epub 13 May 2020]. doi:10.7326/M20-1495

Clinical scenario #1

Case conclusion:

A review of patient's history classified patient in a high risk category for progression to severe COVID-19 disease. Antiviral treatment was initiated, and patient was counseled on isolation and masking recommendations.



Source: Rethinking Covid-19 Test Sensitivity — A Strategy for Containment | NEJM

Clinical scenario #2

- Patient presents to urgent care requesting a COVID-19 test. He has mild URI symptoms for 3 days which he attributed to allergies.
- He took a “home COVID-19 test” today and it was positive.
- He is here because he wants a confirmatory test.

Is a repeat (antigen or molecular) COVID-19 test necessary at today’s visit?

Clinical scenario #2

- **No testing is clinically indicated**
  - He has symptoms consistent with acute COVID-19
  - He has a positive antigen test
  - Predictive value of the antigen test is high
- A negative test in urgent care does not have sufficient NPV to clear the patient

Clinical scenario #3

An 88-year-old nursing home patient presents to urgent care with fever of 102 degrees, cough, runny nose and nausea. Symptoms started 24 hours prior to arrival

The nursing home reports that there is both COVID-19 and influenza reported in the facility.

Can you clinically differentiate between COVID-19 and influenza?

COVID-19 vs influenza vs Strep

	COVID-19	Influenza	Strep pharyngitis
Fever/chills	**Common**	**Common** (may be afebrile)	**Common**
Cough	**Common**	**Common**	Uncommon
Shortness of breath/dyspnea	**Common**	**Common**	Uncommon
Fatigue	**Common**	**Common**	**Common**
Sore throat	**Common**	**Common**	**Common**
Runny nose/congestion	**Common**	**Common**	Uncommon
Myalgias/body aches	**Common**	**Common**	**Common**
Headaches	**Common**	**Common**	**Common**
Diarrhea	**Common**	Peds >> adults	Uncommon
Loss of taste and smell	**Common**	Uncommon	Uncommon

COVID-19 vs influenza

- Historically influenza was a CLINICAL diagnosis
- Clinically differentiate between COVID-19 and influenza
  - Epidemiological trends may offer insight
    - If prevalence of COVID-19 is high and influenza is low, pre-test probability for COVID-19 is high
    - If prevalence of influenza is high and COVID-19 is low, pre-test probability for influenza is high

Testing may be necessary to differentiate between COVID-19 and influenza

Clinical scenario #3

Case Conclusion

- Clinical symptoms are common between flu and Covid
- **Molecular testing is appropriate**
  - POCT influenza A PCR/molecular is **positive**, influenza B is **negative**, COVID-19 is **negative**
- Patient is a high risk (age, co-morbidities) and is offered antiviral treatment

Multiplex testing/Respiratory panels

- Multiplex panels can test for 2 or more respiratory pathogens
  - Influenza A/Influenza B/COVID-19 (antigen or molecular)
  - Influenza A/Influenza B/COVID-19/RSV
  - Molecular testing includes panels of up to 19 or more respiratory viruses and bacteria pathogens

Component	Ref Range & Units
Adenovirus PCR	Not Detected
Coronavirus 229E PCR	Not Detected
Coronavirus HKU1 PCR	Not Detected
Coronavirus NL63 PCR	Not Detected
Coronavirus OC43	Not Detected
Coronavirus 19 PCR	Not Detected
Human Metapneumovirus PCR	Not Detected
Human Rhinovirus/Enterovirus PCR	Not Detected
Influenza A PCR	Not Detected
Influenza B PCR	Not Detected
Parainfluenza 1 PCR	Not Detected
Parainfluenza 2 PCR	Not Detected
Parainfluenza 3 PCR	Not Detected
Parainfluenza 4 PCR	Not Detected
Respiratory Syncytial Virus PCR	Not Detected
Bordetella parapertussis PCR	Not Detected
Bordetella pertussis PCR	Not Detected
Chlamydophila pneumoniae PCR	Not Detected
Mycoplasma Pneumoniae PCR	Not Detected

Multiplex testing/Respiratory panels

Is more “better?”

- Potential pitfalls of multiplex panels
  - Increased likelihood of at least one false positive, especially as number of targets increase
  - Not all positive results indicate current active infection
    - Previous infection
    - Non-pathological colonization
  - It is not possible to identify or test for every viral cause of respiratory tract infections
- Impact on antibiotic stewardship

Making Sense of Respiratory Viral Panel Results (asm.org)

Influenza testing (outpatient) recommendations

IDSA recommends molecular testing for influenza

FDA requires RIDT (rapid influenza diagnostic tests) to achieve a minimum sensitivity of 80%

If utilizing a RIDT (antigen) test, consider the context, with careful attention to the pre-test probability, influenza activity in the community and the clinical context.

Clinical scenario #4

- Patient is a 24-year-old female who presents to urgent care for “another antibiotic.”
- She was seen 1 week ago and diagnosed with an urinary tract infection. She was prescribed nitrofurantoin 100mg twice a day.
- She has taken the medication as directed without relief of her symptoms. She is here because she wants a different antibiotic.
  - Urine culture (1 week ago): No growth
  - Urinalysis today: 1+ leukocyte esterase, 1+ protein, neg nitrates, neg blood

Differential diagnosis?

Dysuria does not always mean UTI

Differential diagnosis of dysuria

- **Inflammatory**
  - Dermatologic — dermatitis, psoriasis
  - Infectious — cystitis, urethritis, pyelonephritis, STIs
    Women: vulvovaginitis, cervicitis,
    Men: prostatitis, epididymitis
  - Non-infectious — foreign body
- **Non-inflammatory**
  - Anatomic — stricture, spasms
  - Drug related — bladder-irritating foods or medications
  - Endocrine — atopic vaginitis, endometriosis
  - Neoplastic — TCC bladder, RCC
  - Traumatic — Foley catheter placement, instrumentation

Clinical scenario #4

Additional sexual history is obtained

- Patient is currently sexually active with a male partner
- She has been with her current partner for a few weeks
- She engages in unprotected receptive vaginal intercourse
- She reports **non-odorous vaginal discharge**
- No abdominal pain or flank pain

Clinical scenario #4

- Consider additional STI testing based on history and risk
  - Chlamydia/Gonorrhea
    - Oropharynx
    - Rectal
    - Endocervical/vaginal
  - Trichomonas
  - Syphilis
  - Herpes
  - HIV (4th generation)
    - ~ 14 days after exposure
  - Hepatitis B
  - Hepatitis C
  - Ureaplasma/Mycoplasma

Test results need to be interpreted within the context of the clinical presentation. Serological conversion may take weeks to months!

Clinical scenario #4

Case conclusion:

Sexual history is critical

- Wet Prep inconclusive (no clue cells, no trichomonas seen)
- **Point-of-care molecular testing is important for providing an immediate actionable result!**
  Point-of-care chlamydia/gonorrhea/trichomonas NAA test ordered
  - Chlamydia: negative
  - Gonorrhea: negative
  - Trichomonas: **POSITIVE**
- Patient was treated with metronidazole 500mg twice a day for 7 days
- Patient declined additional testing and opted to follow-up with her primary care provider.

Vaginitis/Vaginal discharge

90% of vaginitis is due to bacterial vaginosis, vaginal candidiasis and trichomonas

	How common?	Risks	Testing options
Bacterial vaginosis	Most common cause of vaginitis. 40-50% of cases in women of childbearing age	Risk for PROM and preterm labor. Increases risk of STI transmission	- pH > 4.5 - Wet Prep - Antigen testing - Molecular testing
Vulvovaginal candidiasis	~ 75% of women will have one episode in a lifetime	Complications are rare Sign of underlying DM or immunodeficiency?	- pH < 4.5 - Wet Prep - Molecular testing
Trichomonas	10-25% of vaginal infections ~ 30% symptomatic	Associated and as a vector for other STIs Transmitted sexually (STI)	- pH > 4.5 - Wet Prep - Antigen testing - Molecular testing

Vaginitis/Vaginal discharge

Chlamydia

- Most common bacterial STI in the United States
- Up to 1.8 million cases reported each year (2017-2021)
- Many cases are asymptomatic
  - Women:
    - Urethritis: dysuria, urgency, frequency
    - Cervicitis: vaginal discharge, vaginal bleeding, abdominal pain.
- May infect oral, rectal or vaginal tissue
- Complications include PID, infertility, increased risk of ectopic pregnancy, vertical transmission to newborn (conjunctivitis, pneumonia)

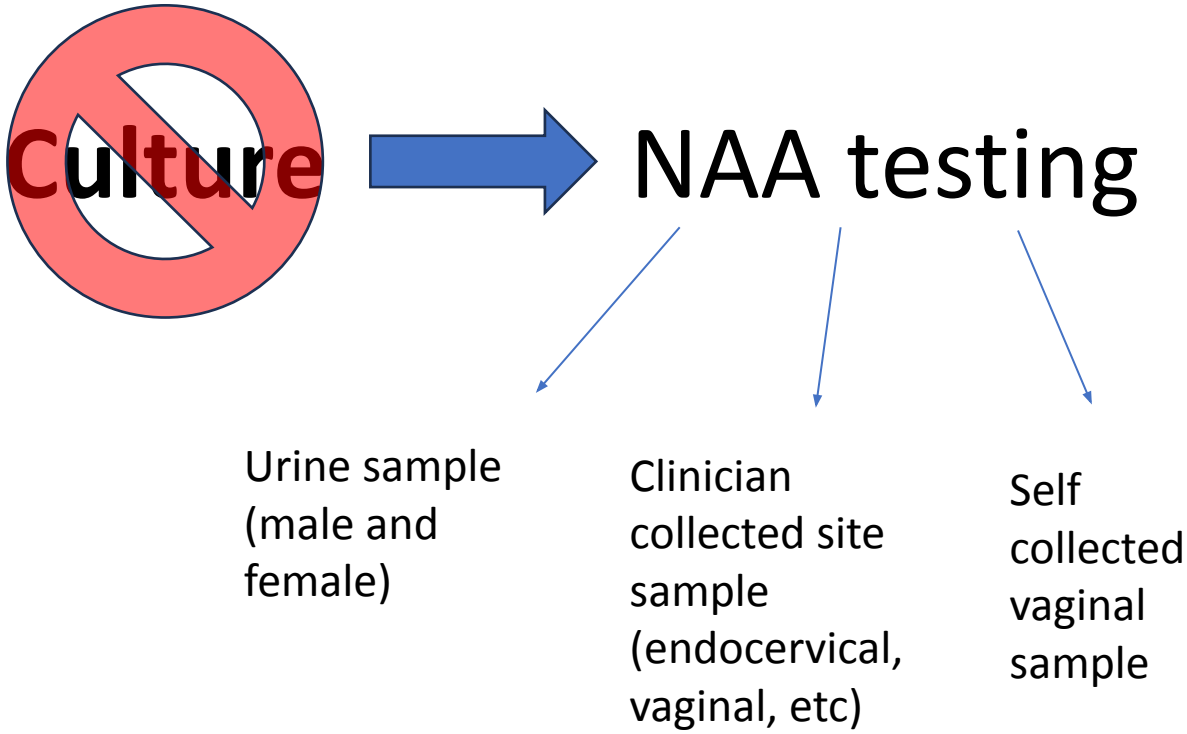
Vaginitis/Vaginal discharge

Gonorrhea

- Up to 700,000 cases reported each year (2017-2021)
- Many cases are asymptomatic
  - Women:
    - Urethritis: dysuria, urgency, frequency
    - Cervicitis: vaginal discharge, vaginal bleeding, abdominal pain.
- May infect oral, rectal or vaginal
- Complications include PID, infertility, increased risk of ectopic pregnancy, disseminated gonococcal infection (arthritis), vertical transmission to neonate

Testing for gonorrhea and chlamydia

- Historically, culture has been the diagnostic gold standard
- **Due to advances in molecular testing technology, NAA tests is now the standard of care, at the point of care**



Vaginal self-swabs for chlamydia and gonorrhea - PMC (nih.gov)

Testing for gonorrhea and chlamydia

NAAT: Collection options		
Urine Sample	**HCP obtained swab**	**Self-Swab**
First pass urine (FPU) aka “dirty urine”	Endocervical swab Blind swab (LVS)	Patient performed lower vaginal swab
Non-invasive	Chaperone required Exams are uncomfortable	Non-invasive
- Patient should not have voided 1-2 hours prior to collection May not be as sensitive compared to vaginal swabs - Cannot assess oropharyngeal or anal source	- If pelvic exam is indicated, swab can be obtained as part of the exam - **Pelvic exam may identify other pathologies**	- **Studies suggest equivalent or even superior sensitivity compared to urine or provider obtained swabs** - Patients need to be counseled on appropriate technique

Pelvic exam should always be performed if there is a suspicion of PID or intra-abdominal pathology

Vaginal self-swabs for chlamydia and gonorrhea - PMC (nih.gov)
Everything the emergency medicine physician needs to know about vaginal self swabbing for patients. — NUEM Blog
Assessment of self taken swabs versus clinician taken swab cultures for diagnosing gonorrhoea in women: single centre, diagnostic accuracy study | The BMJ

Loss to follow-up after STI testing is a concern

- Undertreated patients are often lost to follow-up
  - Up to 40% of patients (ED) who have a positive STI test are lost to follow-up

- Concerns:
  - Untreated patients at the time of visit can have disease progression and further transmit disease
  - Missed opportunity for expedited partner treatment
  - Lack of definitive diagnosis creates a missed opportunity for patient education
  - Disruption of clinical workflow including excessive time spent by clinical staff tracking down patient

Point-of-care STI testing

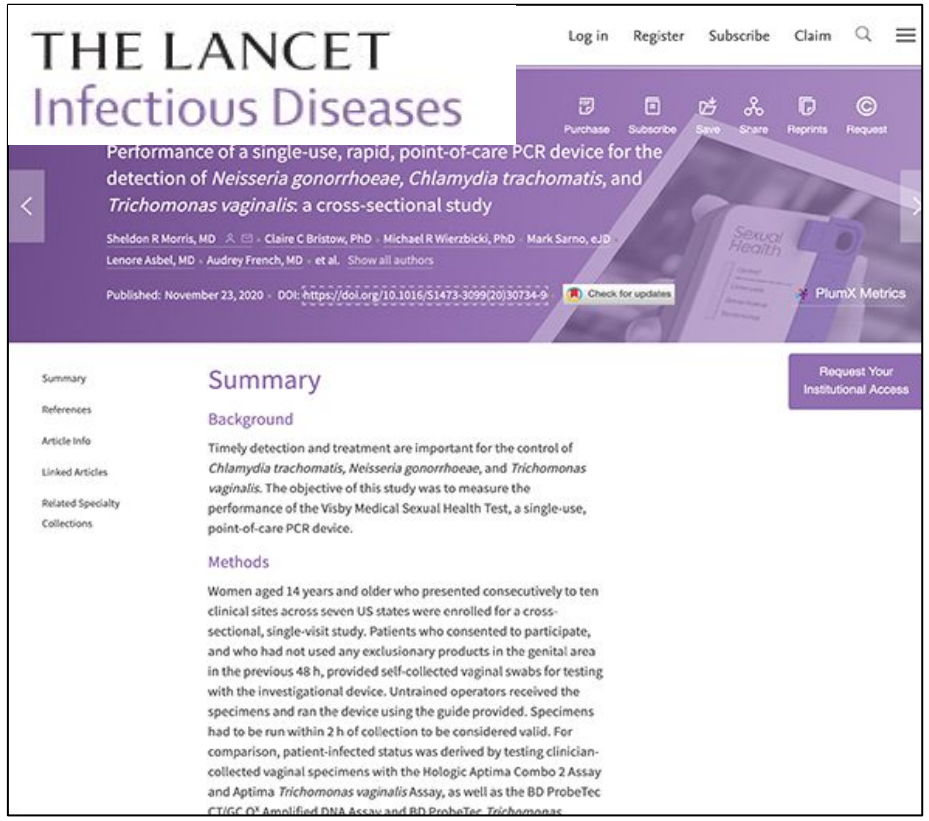
- March 2021: FDA cleared CLIA-waived point-of-care testing chlamydia and gonorrhea
- August 2021: FDA cleared CLIA-waived point-of-care testing for chlamydia/gonorrhea/trichomonas

- Allows an actionable result in as little as 30 minutes.
- Test results at the time of the ambulatory office visit will allow immediate patient counseling and treatment decisions

Positive Screening Tests for Gonorrhea and Chlamydial Infect... : Sexually Transmitted Diseases (lww.com)
The Rising Importance of Urgent Care in the Fight Against the STI Epidemic - Journal of Urgent Care Medicine (jucm.com)

Point-of-care vs Reference tests

Authors: Sheldon R Morris, MD Claire C Bristow, PhD Michael R Wierzbicki, PhD Mark Sarno, eJD Lenore Asbel, MD Audrey French, MD Charlotte A Gaydos, DrPH Lydie Hazan, MD Leandro Mena, MD Purnima Madhivanan, MD Susan Philip, MD Saara Schwartz, MD Constance Brown, MD David Styers, BS Toni Waymer, BA Jeffrey D Klausner, MD



Performance of a single-use, rapid, point-of-care PCR device for the detection of *Neisseria gonorrhoeae, Chlamydia trachomatis*, and *Trichomonas vaginalis*: a cross-sectional study

Published November 23, 2020

Findings

Between Feb 25, 2019, and Jan 6, 2020, 1585 participants aged between 14 years and 80 years (mean 34·8 [SD 14·2]) were enrolled. 1555 participants had tests run with the investigational device, of whom 1532 (98·5%) had a valid result on either the first or repeat test. Among the patients with evaluable results (including a determinate patient-infected status), the device had a sensitivity of 97·6% (95% CI 93·2–99·2) and specificity of 98·3% (97·5–98·9) for *C trachomatis* (n=1457), sensitivity of 97·4% (86·5–99·5) and specificity of 99·4% (98·9–99·7) for *N gonorrhoeae* (n=1468), and sensitivity of 99·2% (95·5–99·9) and specificity of 96·9% (95·8–97·7) for *T vaginalis* (n=1449).

Point-of-care vs Reference tests

JAMA Network Open

Original Investigation | Infectious Diseases

Evaluation of the Performance of a Point-of-Care Test for Chlamydia and Gonorrhea

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Abstract

IMPORTANCE Rates of chlamydial and gonococcal infection continue to increase in the United States, as do the associated costs of untreated infections. Improved diagnostic technologies that support testing and treating in 1 clinical visit are critical to advancing efforts to control the rates of chlamydial and gonococcal infection.

OBJECTIVE To evaluate the clinical performance of a point-of-care (POC) molecular diagnostic assay for the detection of chlamydia and gonorrhea.

DESIGN, SETTING, AND PARTICIPANTS A noninterventional, cross-sectional clinical study was conducted from September 18, 2018, through March 13, 2019, at sexually transmitted infection (STI), HIV, family planning, and obstetrics and gynecology clinics where STI screening is routine, using a convenience sample and comparing commercially available assays with a new 30-minute POC assay. Patients included were those eligible for STI screening or diagnostic testing who had not taken antibiotics effective against chlamydia or gonorrhea within the previous 28 days. Four vaginal swab samples were collected from women and a first-catch urine sample was obtained from men.

MAIN OUTCOMES AND MEASURES A composite infection status was used to classify participants as infected if 2 or more comparator results were positive, as not infected if 2 or more comparator samples were negative, and as unevaluable if 1 result was invalid and the other 2 results did not agree with each other.

RESULTS Swab samples from 1523 women (median age, 27 years [interquartile range, 17-37 years]), 817 (53.6%) of whom presented with symptoms, and 922 men (median age, 29 years [interquartile range, 17-41 years]), 308 (33.4%) of whom were symptomatic, were tested. For chlamydia, sensitivity of the new POC assay was 96.1% (95% CI, 91.2%-98.3%) for women and 92.5% (95% CI, 86.4%-96.0%) for men. For gonorrhea, sensitivity estimates were 100.0% (95% CI, 92.1%-100.0%) for women and 97.3% (95% CI, 90.7%-99.3%) for men. For chlamydia, specificity of the new POC assay was 99.1% (95% CI, 98.4%-99.5%) for women and 99.3% (95% CI, 98.4%-99.7%) for men. For gonorrhea, specificity estimates were 99.9% (95% CI, 99.5%-100%) for women and 100% (95% CI, 95.5%-100%) for men. Non-laboratory-trained personnel performed 94.8% of all tests (2318 of 2445) during the study.

Key Points

Question How does a new point-of-care assay for detection of chlamydia and gonorrhea compare with commercially available laboratory-based molecular diagnostics?

Findings This cross-sectional study including 1523 women and 922 men found that a new molecular point-of-care assay was associated with excellent performance compared with laboratory-based molecular diagnostics for vaginal swab samples and has been cleared for use by the US Food and Drug Administration. Male urine samples were associated with good performance in this assay and are undergoing continuing evaluation.

Meaning Highly sensitive, rapid chlamydia and gonorrhea testing at the point of care is now a possibility that can support same-day testing and treatment strategies.

Supplemental content

Author affiliations and article information are listed at the end of this article.

Point-of-care STI testing

2019 John Hopkins Study

Rapid *C trachomatis* and *N gonorrhoeae* testing in the ED led to a **significant reduction in overtreatment for women** without infections compared with the standard-of-care control group.

- Rapid testing in this study = 90-100 minutes
- Current technology ~30 minutes
  - 100% of infected patients received treatment at time of discharge
  - **> 21% decrease in unnecessary antibiotics**
  - 0 patients were lost to follow-up

Randomized Controlled Trial > Ann Emerg Med. 2019 Jul;74(1):36-44.
doi: 10.1016/j.annemergmed.2018.09.012. Epub 2018 Nov 2.

Use of a Rapid Diagnostic for Chlamydia trachomatis and Neisseria gonorrhoeae for Women in the Emergency Department Can Improve Clinical Management: Report of a Randomized Clinical Trial

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Affiliations + expand

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Use of a Rapid Diagnostic for Chlamydia trachomatis and Neisseria gonorrhoeae for Women in the Emergency Department Can Improve Clinical Management: Report of a Randomized Clinical Trial - PubMed (nih.gov))

Molecular testing

- Molecular testing has revolutionized infectious disease diagnostic testing
- Historically, access to molecular testing was the challenge
  - Send-out to reference lab
  - Sample transport
  - Results not available at time of patient visit
- **Advances in technology now allow CLIA-waiver point-of-care options**
  - Fast results (< 30 minutes)
  - Improved sensitivity and specificity vs antigen test
  - Ability to make clinical decisions and initiate treatment at time of service

Final thoughts

- No perfect test exists!
- Diagnostic testing is a process!
  - Sensitivity/specificity helps the clinician choose a diagnostic test, but it is the predictive value impacts clinical decision making.
  - Improper test selection and interpretation can lead to adverse clinical outcomes
- Molecular tests are preferred over antigen tests!
- Point-of-care molecular tests are best!
- Have a plan.
  - Will the test result provide clinical value or change your management plan?
  - Do you know what to do with an unexpected result?

Questions?

Clinical scenario #5

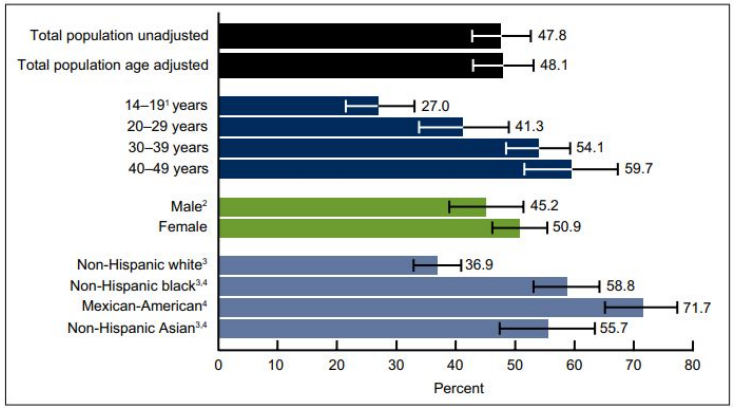
- Patient (34 y/o) presents to urgent care because “he has herpes.” 1 week prior to the visit, he had a “pimple” in his groin area. Because the pimple was crusted over, a blood test for herpes was ordered.
- Results:

Test	Result	
HSV-1 IgG	29.4 (Ref: < 0.9 NEG, 0.9-1.1 EQUIVACAL, > 1.1 POS)	POSITIVE
HSV-2 IgG	0.08 (Ref: < 0.9 NEG, 0.9-1.1 EQUIVACAL, > 1.1 POS)	NEGATIVE
HSV-1/2 IgM by ELISA	0.28 (Ref < 0.89 not detected)	NEGATIVE

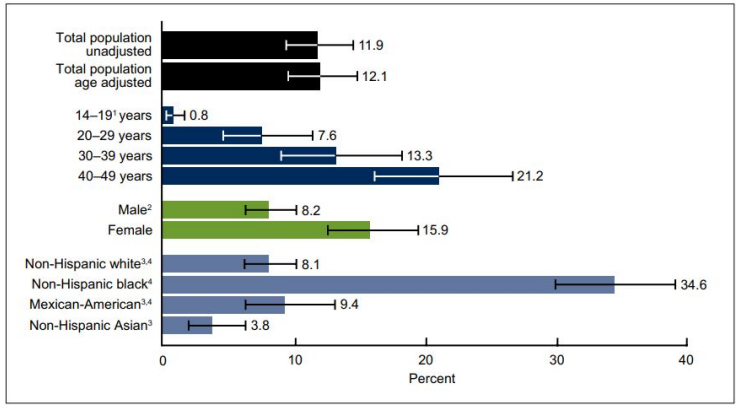
- When he called asking for the results he was told “you have herpes.”
- He is here for a second opinion

Genital Herpes

- Common, lifetime infections
- Many cases are asymptomatic
  - Herpes simplex virus type 1
    - Estimated to affect 67% of global population
    - Oral lesions
    - **Increasing prevalence as the cause of genital lesions**
  - Herpes simplex virus type 2
    - Estimated to affect 11% of global population
    - Women (15.8%) > Men (8.2%)

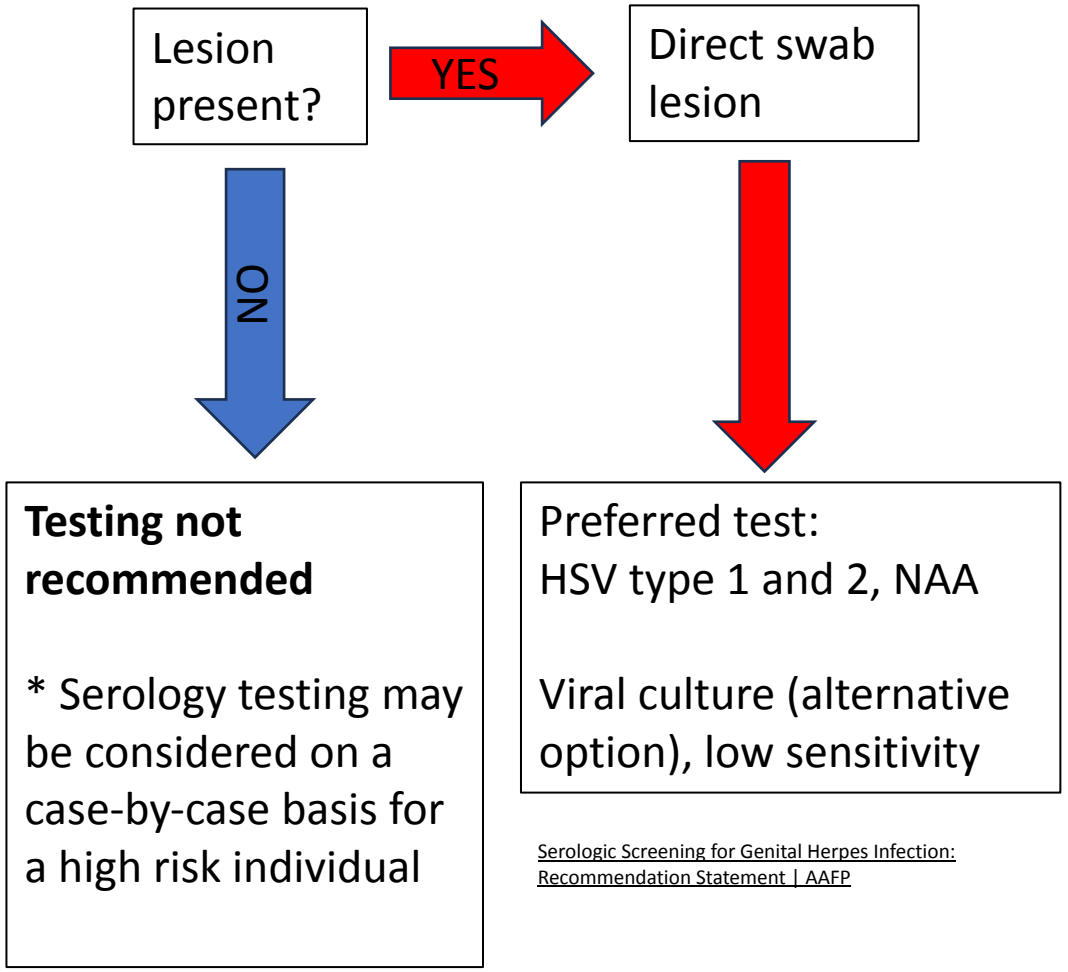


Prevalence of HSV-1 2015-2016



Prevalence of HSV-2 2015-2016

Testing for HSV



Serologic Screening for Genital Herpes Infection: Recommendation Statement | AAFP

- Limitations of serology testing:
  - Positive result
    - High false positive rates
    - Cross reactivity
    - Positive test does not indicate active infection or disease
      - IgM may be detectable following recurrent outbreaks
    - Positive HSV-1 cannot determine the site of infection (oral or genital)
  - Negative result
    - Does not rule out acute disease
    - May take 12 weeks for antibodies to be detectable

Clinical scenario #5

Case conclusion

- No clinical conclusion can be drawn from the serology test
  - Approximately 48% of the population has antibodies to HSV-1
  - Test cannot differentiate between oral and genital lesions
  - Since suspected lesion has healed, no further testing is indicated or recommended.

Due to the limitations of serology test, CDC does not recommend serology tests for most clinical situations.

Clinical scenario #6

A 55-year-old presents to urgent care for cough, chest congestion and “wheezing.” He is otherwise in good health but is requesting RSV because he was the caregiver of his granddaughter who has tested positive for RSV. He is afebrile.

The urgent care clinic utilizes RSV antigen test.

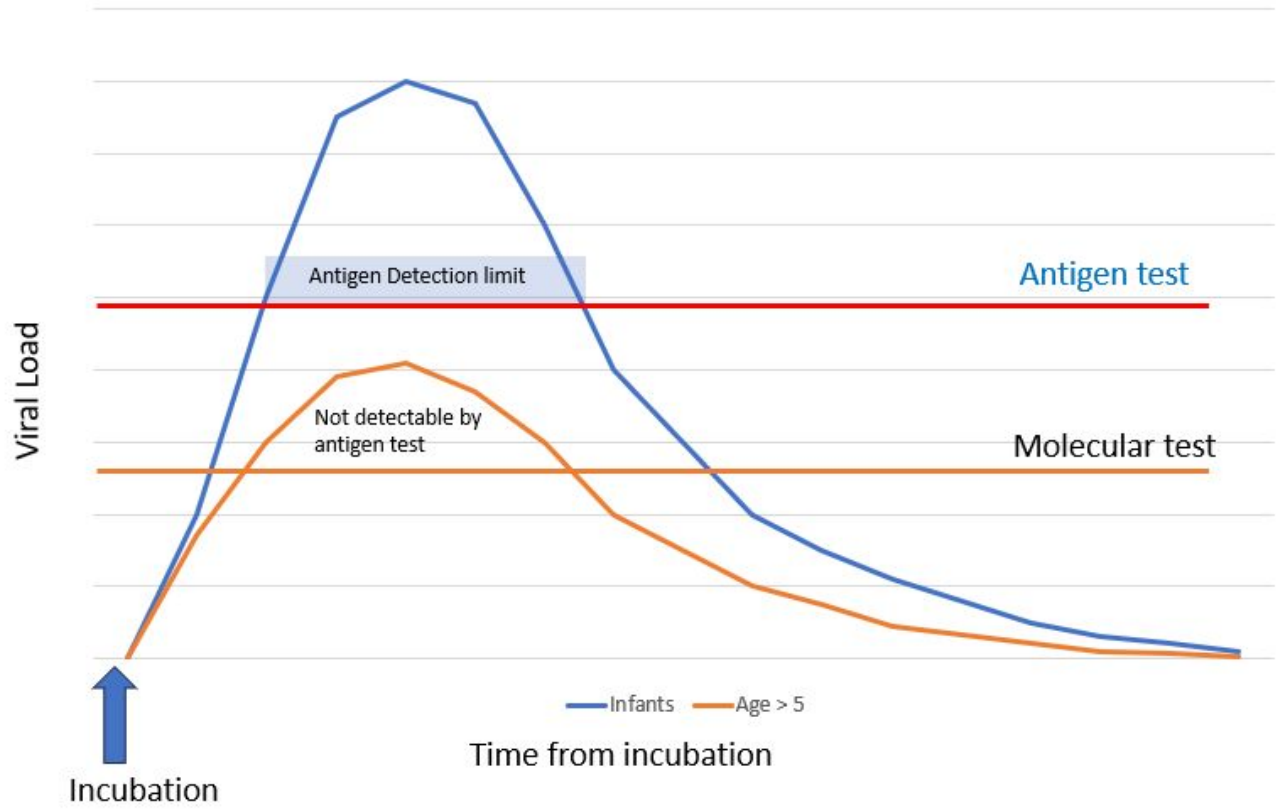
Do you proceed with the RSV antigen test?

RSV

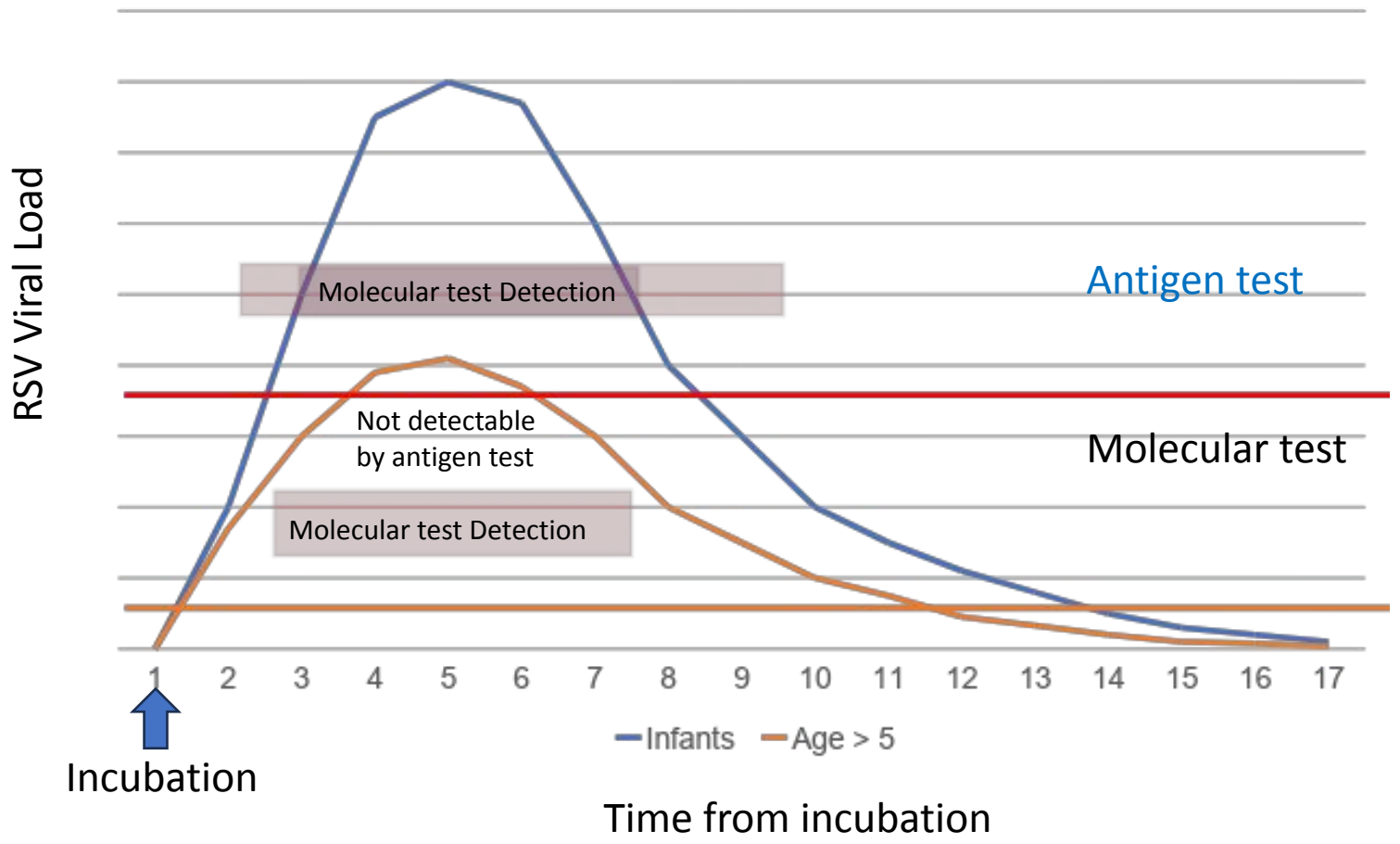
- Respiratory syncytial virus (RSV) is a common respiratory virus that usually causes mild, cold-like symptoms
  - Symptoms include runny nose, anorexia, cough, sneezing, fever and wheezing
- Most individuals recover within 1-2 weeks
- High risk patients include infants and older adults
  - May develop severe symptoms
  - May require hospitalization

RSV antigen testing vs molecular testing

- Viral load is age dependent. Infants and young children have high viral load. Adults have lower viral load
- Antigen test sensitivity 80-90% in children < 5 years old.



RSV antigen testing vs molecular testing



Clinical scenario #6

Is RSV testing even necessary?

Does the test result change your clinical management?

Patient is an otherwise healthy individual. RSV in adults is generally a self-limited disease and treatment is supportive care.

A positive RSV test in the general population would not change clinical management.

Patients who are symptomatic with ILI are potentially contagious, regardless of whether the specific viral pathogen is identified!

Clinical scenario #6

Case conclusion

- Patient was informed that the clinic point-of-care test for RSV is not validated for adults
- Exam was consistent with a mild upper respiratory infection. He declined further testing and verbalized agreement with supportive care and home observation.