AMPLIFY

Diagnostic Testing in Urgent Care Part 1: Respiratory Infections

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Learning Objectives

- Describe the key differences between antigen and molecular testing in the urgent care setting
- List common pitfalls with diagnostic respiratory testing
- Select the most appropriate tests for common infectious disease presentations based on the availability of your point of care tests
- Apply the recommendations for group A strep confirmatory testing
- Explain the age restrictions for RSV antigen testing

2 scenarios: negative test -> different outcomes

Case 1

53 y/o female presents with flu symptoms x2 days requesting oseltamivir. She is a teacher and several students in her classroom have been out with "influenza." Symptoms include chills, nausea and vomiting. She does not have any nasal congestion, sore throat or cough. She is otherwise healthy.

On examination, she is febrile with a temperature of 101.6F, BP 118/74, HR 104, POX 98% on RA.
ENT: unremarkable. Lungs CTA bilaterally. Mild suprapubic tenderness with mild flank pain.

Influenza/COVID antigen test is NEGATIVE

Case 2

91 y/o nursing home resident presents for febrile URI illness. He was at baseline health until 8 hours ago when he developed chills, decreased appetite, nasal congestion, runny nose, cough and chest congestion. Medical history significant for COPD, T2DM and CAD. There is influenza circulating in the facility and his family is requesting oseltamivir.

On examination, he is febrile with a temperature of 102.2F, BP 140/78, HR 106, POX 95% on RA.
ENT: nasal erythema, turbinate swelling. Lungs: rhonchi

Influenza/COVID antigen test is NEGATIVE

2 scenarios: negative test -> different outcomes

Case 1	Case 2
Patient discharged with a clinical diagnosis of influenza and started on oseltamivir. Patient calls the next day complaining of worsening vomiting, advised to discontinue oseltamivir. Patient return to UC 48 hours later, appears ill, temp of 104.2. Is the nausea caused by oseltamivir? Is influenza the correct diagnosis?	Based on the negative influenza antigen test, patient D/C'ed with DX viral URI, and advised on supportive care. Family advised "test is negative, he doesn't have flu" 2 days later, the patient's family took him to the Emergency Department, where a NAA respiratory antigen panel is positive for influenza A. Family is upset because they feel like patient was misdiagnosed in Urgent Care. Is this a failure of the influenza antigen test?

2 scenarios: negative test -> different outcomes

Case 1	Case 2
UA: SG 1.030, 2+ blood, 3+ leu est, 2+ pos nitrites Patient diagnosed with pyelonephritis. She was transferred to the Emergency Department.	Should oseltamivir have been initiated on the initial visit? Does initial testing platform (molecular vs antigen) make a difference?

Case 1: Test result correct
Expectation bias, tunnel vision

Case 2: Test result misinterpreted
Low negative predictive value

Introduction

- Respiratory tract infections (RTIs) are by far the most common presentation in urgent care
- Clinicians must be equipped to understand the types of tests at their disposal and how to determine which tests to utilize for each patient encounter

References

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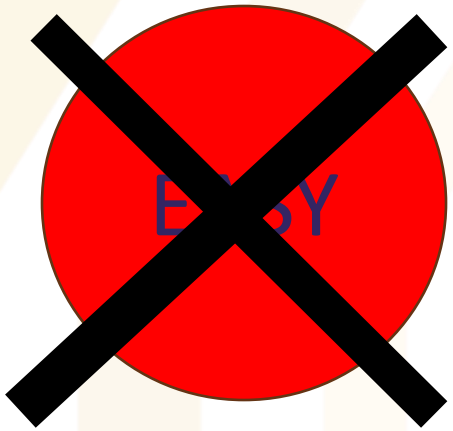
- Sociodemographic differences in treatment of acute respiratory infections in pediatric urgent cares. *Infect Control Hosp Epidemiol*. 2024.
- Ray KN, Shi Z, Gidengil CA, et al. *Health Aff (Millwood)*. 2019.

Introduction

- Inappropriate testing and incorrect interpretation drives up healthcare costs, may result in additional testing, can result in false positives (patient anxiety, unnecessary treatment, additional costly interventions) and false negatives (missed or delayed diagnosis).

The “perfect” diagnostic test

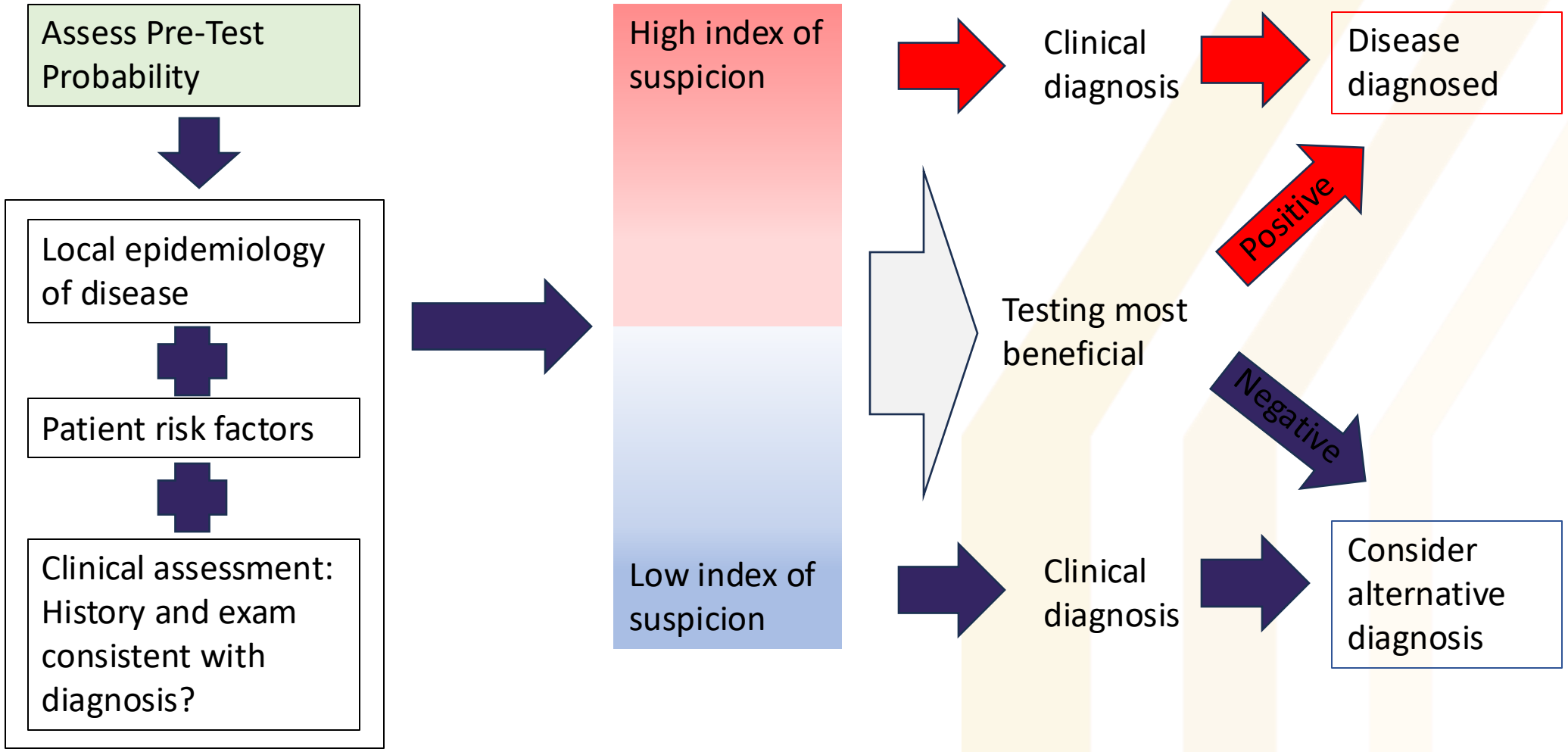
- Correctly identifies all individuals with disease (100% sensitive)
- Correctly rules out all individuals without disease (100% specific)
- Fast (instant results)
- Non-invasive
- Ease of use
- Low cost
- Widely available



There is no easy button!

Unfortunately, the “perfect” test does not exist!

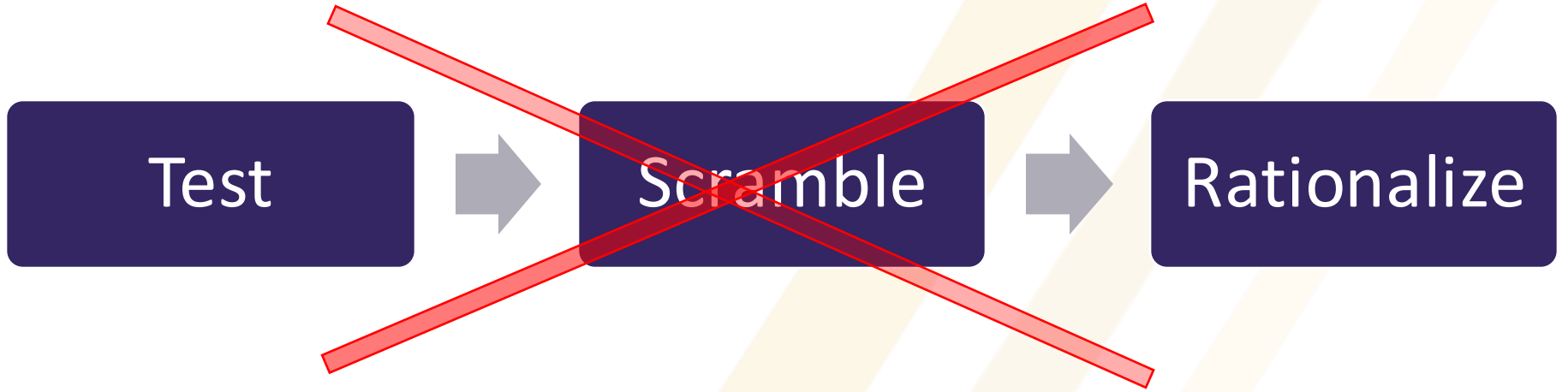
Diagnostic tests are part of the diagnostic PROCESS



Don’t “spray and pray”

- **Test to confirm your thinking, not to do your thinking.**

The wrong approach



The correct approach

What are the challenges in Urgent Care?

- Technology has increased diagnostic options available in Urgent Care clinics
- Patients are expecting and demanding tests
  - “I want to know now…”
  - COVID-19 changed “testing culture”
- Clinical stewardship “paradox”
  - Discouraging empiric treatment in lieu of a confirmed diagnosis
  - HEDIS/MIPS
- Defensive medicine

But how well do you know your tests?

- As an urgent care clinician, **the scope and quality of diagnostic decision-making are inherently constrained by the tests available at your center**.

- Know your testing platforms!
  - Is your diagnostic test validated for your patient population?
  - Will the test result change your clinical decision making?
  - Is the test capable of detecting the disease you are considering?

Diagnostic testing options for infectious disease

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)
- Biomarker testing
  - Emerging technology

Home testing

Home tests: self collection by patient → Test kit or Collection with send out 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

A tale of two clinics

Clinic A	Clinic B
Respiratory testing Point-of-care - Strep antigen test - Influenza A/B antigen - COVID-19 antigen - Monospot - RSV antigen Sendout - Molecular strep test - Molecular multiplex panel (Influenza A/B, COVID-19, RSV)	Respiratory testing Point-of-care - Molecular strep test - Molecular respiratory panel (Influenza A/B, COVID-19, RSV) - Monospot

Antigen vs Molecular – what's the difference?

	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)	- **Tests may be negative in early disease** - **Antigen tests may be "good enough"**
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**	- Higher cost, 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 (post infectious positive)**

Antigen vs Molecular

- Neither antigen tests nor molecular tests can differentiate between colonization vs true infection!

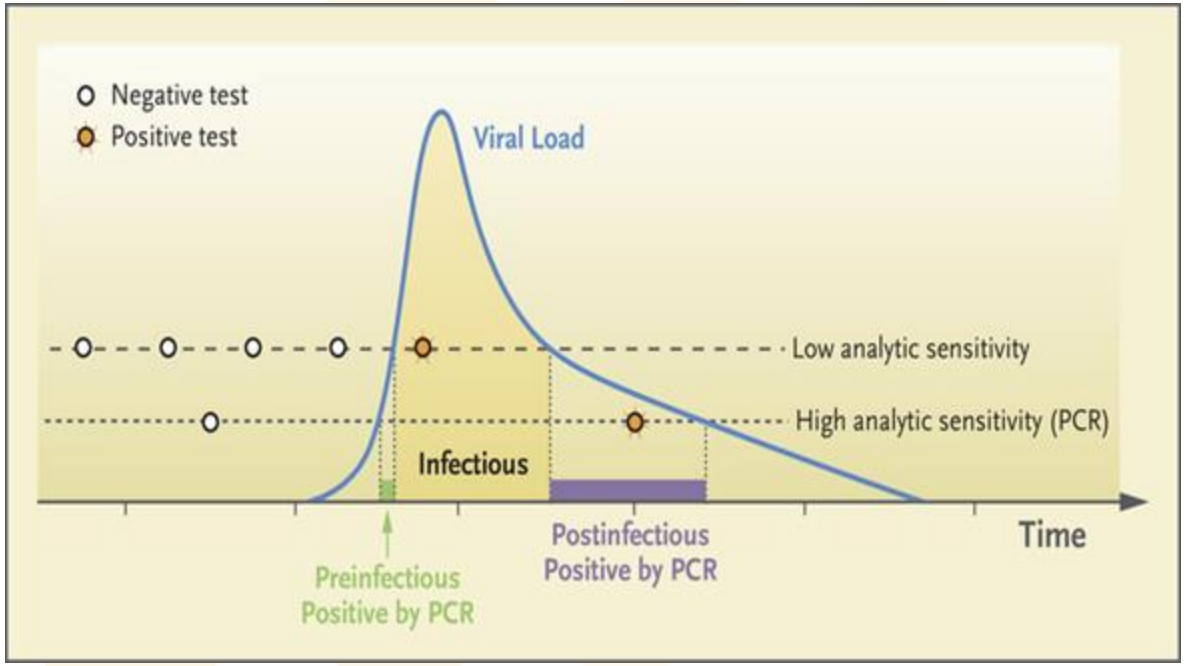
- Clinicians must interpret results in the context of:
  - **Symptoms**
  - **Pretest probability**
  - **Epidemiology**
  - **Physical exam**
  - **Alternative diagnoses**

Post-infectious positive test results with molecular testing

- 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)
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



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

Case 3 : Acute pharyngitis

- 8 y/o male presents for sore throat, fever, chills. There is strep reported at school. Mild cough. Exam: Temp 101.4, exudates present, uvula midline, anterior cervical nodes tender and enlarged, no posterior cervical nodes.

- **Is testing necessary?**
- Can empiric antibiotics be initiated based on the clinical picture?

Case 3 : Acute pharyngitis

- 8 y/o male presents for sore throat, fever, chills. There is strep reported at school. Mild cough. Exam: Temp 101.4, exudates present, uvula midline, anterior cervical nodes tender and enlarged, no posterior cervical nodes.

- HEDIS/MIPS
  - Quality metric: This measure addresses appropriate treatment for pharyngitis with a strep test and, if appropriate, prescription of an antibiotic within three days of the test.
- IDSA
  - Clinical judgment alone is unreliable for diagnosis GAS pharyngitis
  - Oct 2025 update: Use a clinical scoring system as part of the evaluation of children and adults with sore throat to help decide who should be tested for group A strep

Case 3 : Is strep testing necessary?

Age Group A streptococcus (GAS) rare under 3	**3-14 years**	**+1**
	15-44 years	0
	≥45 years	-1
Exudate or swelling on tonsils	No 0	**Yes +1**
Tender/swollen anterior cervical lymph nodes	No 0	**Yes +1**
Temp >38°C (100.4°F)	No 0	**Yes +1**
Cough	**Cough present**	**0**
	Cough absent	+1

Table 2. Clinical Scoring for Predicting Group A Streptococcal Pharyngitis

Feature	Centor	Score	Mclsaac	Score	FeverPAIN*	Score
Viral Symptoms	Absence of Cough	1	Absence of Cough	1	Absence of Cough or Coyrza	1
Cervical Adenopathy	Swollen tender anterior cervical nodes	1	Swollen tender anterior cervical nodes	1	N/A	
Fever	>100.4oF (38oC)	1	>100.4oF (38oC)	1	Febrile in past 24 h	1
Tonsillar Appearance	Tonsillar Exudate or swelling	1	Tonsillar Exudate or swelling	1	Inflamed Tonsils Purulent Tonsils	1 1
Duration	N/A		N/A		<3 days since symptom onset	1
Age	N/A		3 y – 14 y 15 y – 44 y >45 y	1 0 -1	N/A	
Risk Stratification	Points	% Strep	Points	% Strep	Points	% Strep
Low Risk	0-1	7-12%	0-1	7.6-13.1%	0-1	1-10%
Intermediate Risk	2-3	21-38%	2-3	20.8-33.6%	2-3	11-35%
High Risk	4	57%	4-5	50.7-69.3%	4-5	51%-53%

Case 3 : Acute pharyngitis

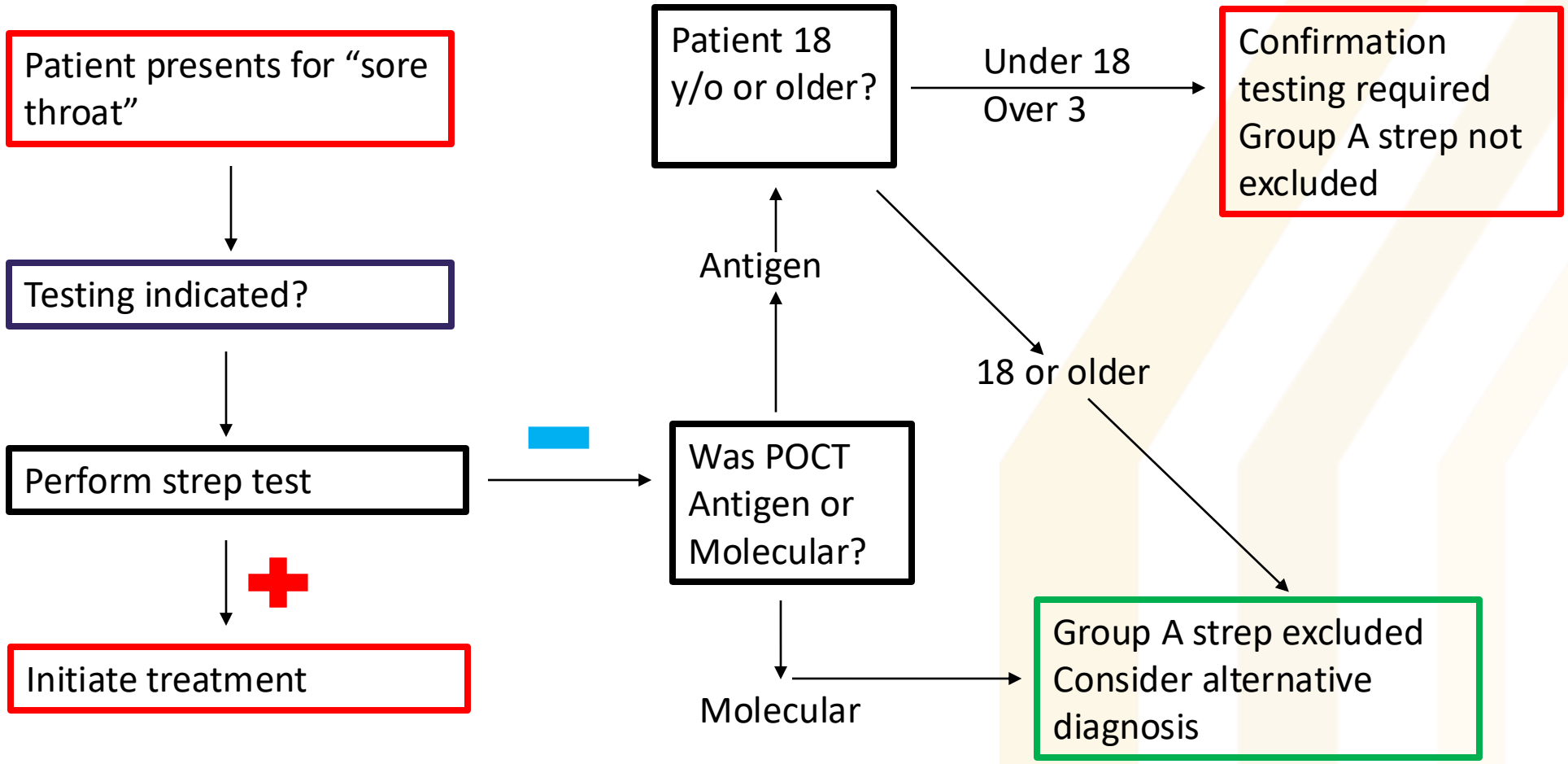
- 8 y/o male presents for sore throat, fever, chills. There is strep reported at school. Mild cough. Exam: Temp 101.4, exudates present, uvula midline, anterior cervical nodes tender and enlarged, no posterior cervical nodes.

Chris' clinic
Point-of-care - Strep antigen test Sendout - Molecular strep test

Joe's clinic
Point-of-care - Molecular strep test

- How is the approach different between the clinics?

Case 3 : Acute pharyngitis – Strep testing



Case 3 : Acute pharyngitis – Strep testing

Chris' clinic

Point-of-care
- Strep antigen test

Sendout
- Molecular strep test

RST positive: Diagnosis of strep confirmed with testing

RST negative: Diagnosis of strep not ruled out Confirmation testing needed

Do you start antibiotics while awaiting for confirmation test result?

Joe's clinic

Point-of-care
- Molecular strep test

RST positive: Diagnosis of strep confirmed

RST negative: Diagnosis of strep ruled out. No confirmation testing recommended.

Case 3 : Acute pharyngitis

- Case conclusion:

Patient presented to clinic that utilized RST (antigen test)

RST negative, patient advised on supportive care. Confirmation test negative.

Strep ruled out

Who needs confirmation testing

- If antigen test is utilized, and the test is NEGATIVE then
  - age < 18, confirmatory testing is necessary
  - age ≥ 18, confirmatory testing is NOT necessary.
    - Confirmatory testing may be considered in the following special circumstances
      - Patients who are at higher risk for severe infection or complications from GAS pharyngitis (eg, patients with a history of acute rheumatic fever)
      - Patients living in areas where acute rheumatic fever is endemic or where there are active acute rheumatic fever epidemics.
- Clinical considerations
  - Rapid Antigen Diagnostic Test (RADT) is widely available in virtually every clinical setting
  - If your clinic population services a high percentage of pediatric patients, molecular testing may be advantageous due to the need for confirmation test for a negative Rapid Antigen Diagnostic Test (RADT)

Case 4 : RSV

- Case 5: 34 y/o female presents for cough, chest congestion, and low-grade fever. 2 y/o daughter diagnosed with RSV. Patient presents to urgent care requesting RSV testing.

Chris' clinic
Point-of-care - RSV antigen test Sendout - Molecular respiratory multiplex panel (includes RSV)

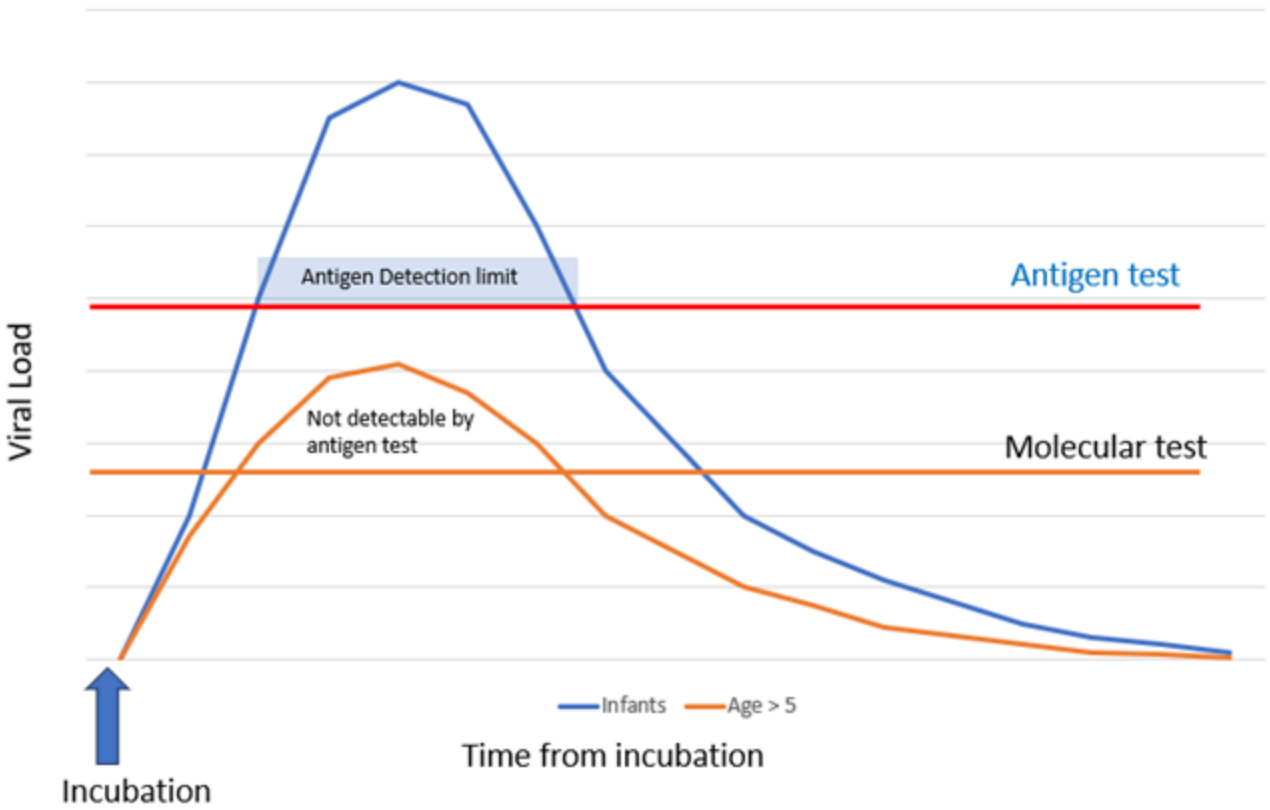
Joe's clinic
Point-of-care - Molecular respiratory multiplex panel (includes RSV)

RSV testing

- Is RSV antigen test appropriate?

RSV viral load

- 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 testing

- **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. RSV testing may be useful in special circumstances (e.g., HCW).

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!

Why this is hard

- Low clinical utility

  VS

- High perceived value
  - Patient reassurance
  - Antibiotic stewardship
  - Avoidance of further testing, or unnecessary treatment

The answer is not binary.

Case #5

- 11yo M presents with 2 days of low-grade fever (Tmax 99.9F), rhinorrhea, cough, fatigue, and mild body aches. He denies sore throat. Mom notes that he has been exposed to classmates with strep, flu, and walking pneumonia.

- Mom also notes he is prone to strep and often tests positive even when he does not have a sore throat. Physical exam is remarkable only for mild fatigue and mild rhinorrhea. There is no tonsillar or pharyngeal erythema or exudates and no palpable cervical LAD.

- What testing, if any, is warranted?

Case #5

- 11yo M presents with 2 days of low-grade fever (Tmax 99.9F), rhinorrhea, cough, fatigue, and mild body aches. He denies sore throat. Mom notes that he has been exposed to a classmates with strep, flu, and walking pneumonia.

Chris' clinic	Joe's clinic
Point-of-care - COVID-19/influenza A/B antigen test - Rapid strep test Sendout - Molecular strep test - Molecular respiratory multiplex panel (does not include *M pneumonia*)	Point-of-care - Molecular respiratory multiplex panel (does not include *M pneumonia*) Sendout - Respiratory panel (includes *M pneumonia*) - Pharyngitis panel

Can you clinically differentiate between COVID-19 and flu

	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

Case #5

- What if Covid/flu PCR is positive for Flu B and rapid strep is positive?

Mycoplasma pneumoniae

- Most cases are mild, self-limited RTIs
- Symptoms often resolve without antibiotics
- Do not test reflexively
  - A positive test does not mean patient has pneumonia!
- Do not treat just because molecular test is positive
- Treat only if clinical syndrome supports pneumonia!

Case #5: Conclusion

- A covid/flu antigen test was positive for covid-19 and negative for Flu A&B.
- Strep testing was deferred because the patient did not have a sore throat, had predominantly viral symptoms, and the Centor score was 1 (for age).
- You discussed with mom that, since the patient only had URI symptoms, *M. pneumoniae* testing would not change treatment. Mom agreed to hold off on testing.
- The patient made a full recovery in 6 days with supportive treatment.

Actionable testing

- Treatment
  - COVID-19: nirmatrelvir/ritonavir started within 5 days
  - Influenza A/B: oseltamivir or baloxavir started as soon as possible, within 48 hours for optimal benefit

- Is there a timeframe after onset of symptoms when COVID-19/influenza testing is no longer actionable?
  - Patient presents with URI symptoms X 2 days? 4 days? 6 days?

Case #6

- 30yo F presents with fever (Tmax 101F), sore throat, body aches, cough, and rhinorrhea x 1 day. PMHx of hypertension, Type II DM, hyperlipidemia, rheumatoid arthritis. Child tested positive for mono in the past 2 weeks. Physical exam reveals an obese female with tonsillar exudates and bilateral tender anterior cervical lymphadenopathy.

- What testing is warranted?

Case #6

- Strep testing is negative
- No in house PCR option available
  - Negative covid/flu → molecular test warranted?
- Mono testing? Negative (too early?)
- Pharyngitis panel (contains EBV) → pos rhinovirus, *H. flu*, *M. cat*
  - Advantage of multiplex testing (can get covid, flu, strep, etc with 1 NP swab)
  - Disadvantage → cost, may detect pathogens that are not pathologic

Controversies: Multiplex testing (syndromic testing)

- Is more “better?”
  - Does it improve antibiotic stewardship?
  - Pitfalls of multiplex panels
    - 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

The ultimate question:

Does the result change clinical management or outcomes?

Common pitfalls

- Assuming all COVID/flu tests are equivalent
  - “Know what test you’re using, not just what you are testing for.”
  - Antigen vs molecular differences
  - Lateral flow vs IFA
- Over-reliance on negative results in high-risk patients
  - Negative RST without confirmation
  - Negative influenza antigen test in early illness
- Not applying the test in the context of the clinical presentation
  - Failure to consider alternative diagnoses in the context of a negative test

Common pitfalls

- Testing when it won’t change management
  - Ordering tests “just to be sure”
    - Are you prepared to explain an unexpected result?
  - Ordering tests because “the patient demanded it.”
  - Over-testing -> over-diagnosis -> Potential unnecessary treatment

Take-home points

- Know your testing platform
- Will your diagnostic test provide information that will meaningfully guide clinical decision making?
- Diagnostic testing should support and confirm clinical decision-making, not replace it
- Molecular tests detect lower viral loads and therefore may identify infection earlier than antigen tests
  - … but, that doesn't mean antigen tests aren't useful, they simply need to be interpreted within the appropriate clinical context.

Clinical pearls

- Negative strep antigen tests requires a confirmation test in patients ages 3 to 18 years old
- RSV antigen tests are primarily validated for use in young children, particularly infants and toddlers
- Diagnostic tests CANNOT differentiate between colonization and active infection
- Multiplex testing cannot test for every possible pathogen, they only identify the specific pathogen in the panel
- Trust your tests!

How to improve your practice

- “A good clinician interprets the test – the test does not interpret the patient.”

- Avoid the “spray and pray approach.”
- **EDUCATE PATIENTS (and staff)**
  - Set expectations
  - Explain why testing may not help
  - Reduce satisfaction-driven over-testing

Questions?

- Stay tuned for part 2: Diagnostic testing for STIs!

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