

Updates in Infectious Disease for the Outpatient Internist

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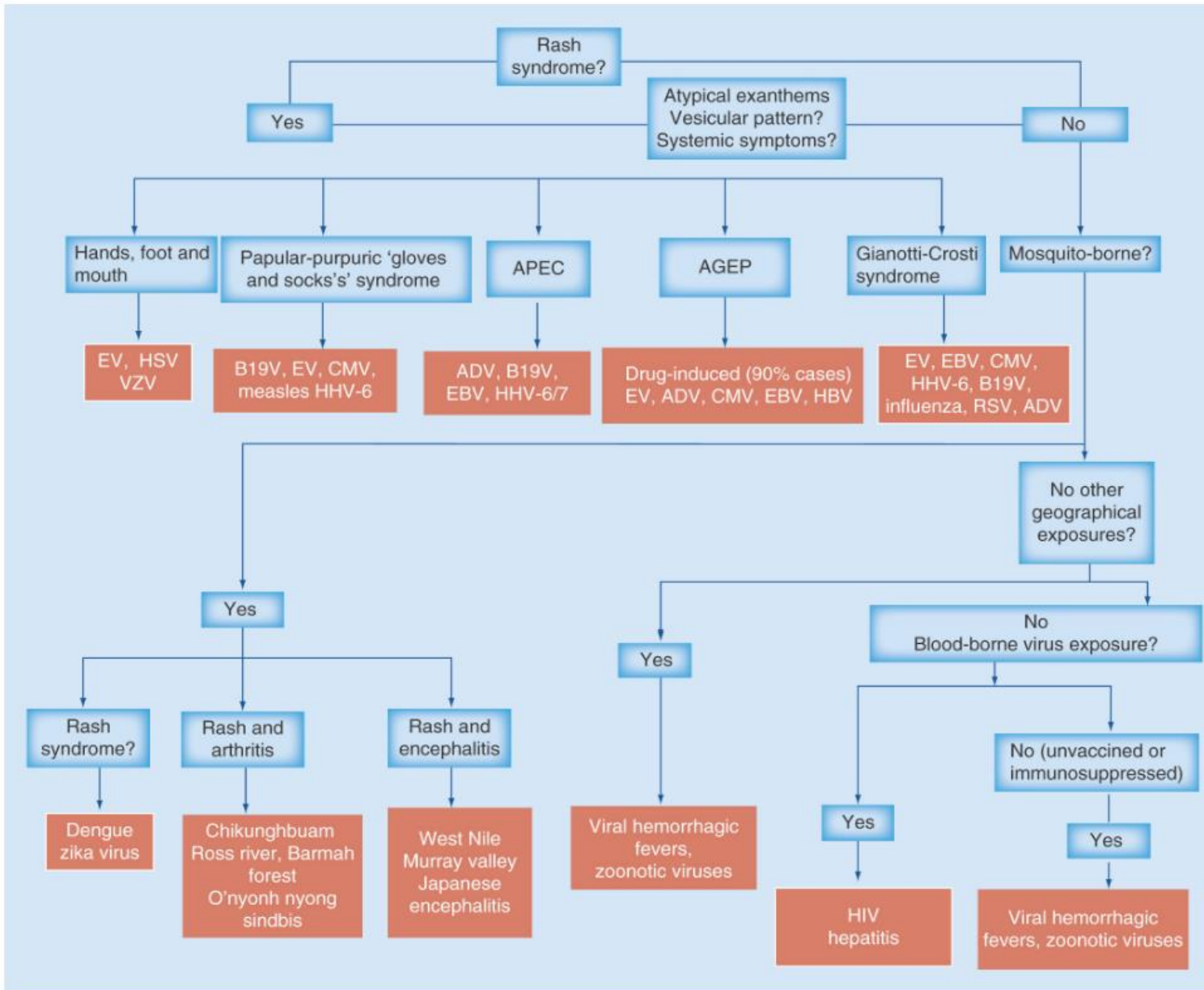
Disclosures

- I have no disclosures to report.

Objectives

- Identify potential infectious causes of rash in adult patients including Measles, CMV, Group A Streptococcus, syphilis.
- Identify the appropriate testing, treatment and prevention of infectious causes of rash in adults.
- Describe the updated treatment guidelines for community pneumonia.
- Identify the appropriate treatment for complicated UTIs.

Approach to Evaluation of Rashes



AGEP: Acute generalized exanthematous pustolosis; APEC: Asymmetric periflexural exanthem of childhood; B19V: Parvovirus B19; CMV: Cytomegalovirus; EBV: Epstein–Barr virus; EV: Erythematovesicular; HHV: Human herpesvirus; HSV: Herpes simplex virus; VZV: Varicella zoster virus.

Approach to Evaluation of Rashes

- Important to ask about:
 - Location and distribution of rash including where it started, how it has spread, and has it become confluent
 - Absence or presence of systemic symptoms
 - Changes to medications, detergents, etc.
 - Geographic exposures – certain infections are more common in certain countries or even in certain regions of the US
 - Environmental exposures including water sports or exposures to hot tubs, dust storms, chemicals, etc.
 - Recent travel (including travel in US)
 - Exposure to animals, insects, or ticks, and any known bites
 - Sexual history or other blood borne pathogen exposures

Examples Exanthems With an Infectious Etiology



Maculopapular rash due to Echovirus infection



Macular rash due to Rocky Mountain Spotted Fever



Disseminated pruritic papules and pustules (hot tub folliculitis) due to *Pseudomonas*

Case Presentation

- 55-year-old female with asthma and hypothyroidism presented to clinic with fever and sharp lower back pain that started about 5 days prior to visit
 - Mild nausea but no vomiting and no dysuria
 - Exam notable for mildly erythematous throat but otherwise negative
 - Testing including Grp A Strep pcr negative, FLUVID negative, CXR negative, UA with trace blood and trace ketones
 - Given Rx for cephalexin

Case Presentation

- Presents to the ED later that evening with fevers, anorexia, myalgias, and cough with some congestion
 - Traveled to Omaha, NE a week before but no sick contacts. No family members ill. States she is up-to-date on her vaccines.
 - Labs: WBC 4.2, H/H 14.8/44.6, Plts 187, UA negative, Cr 0.76, lactate 0.9, Alk phos 395, AST 718, ALT 843, Tbili 2.1
 - CT abd/pelvis negative

Case Presentation

- Patient admitted to the hospital for further evaluation
- Felt better with IV fluids
- Prior to discharge, developed a rash



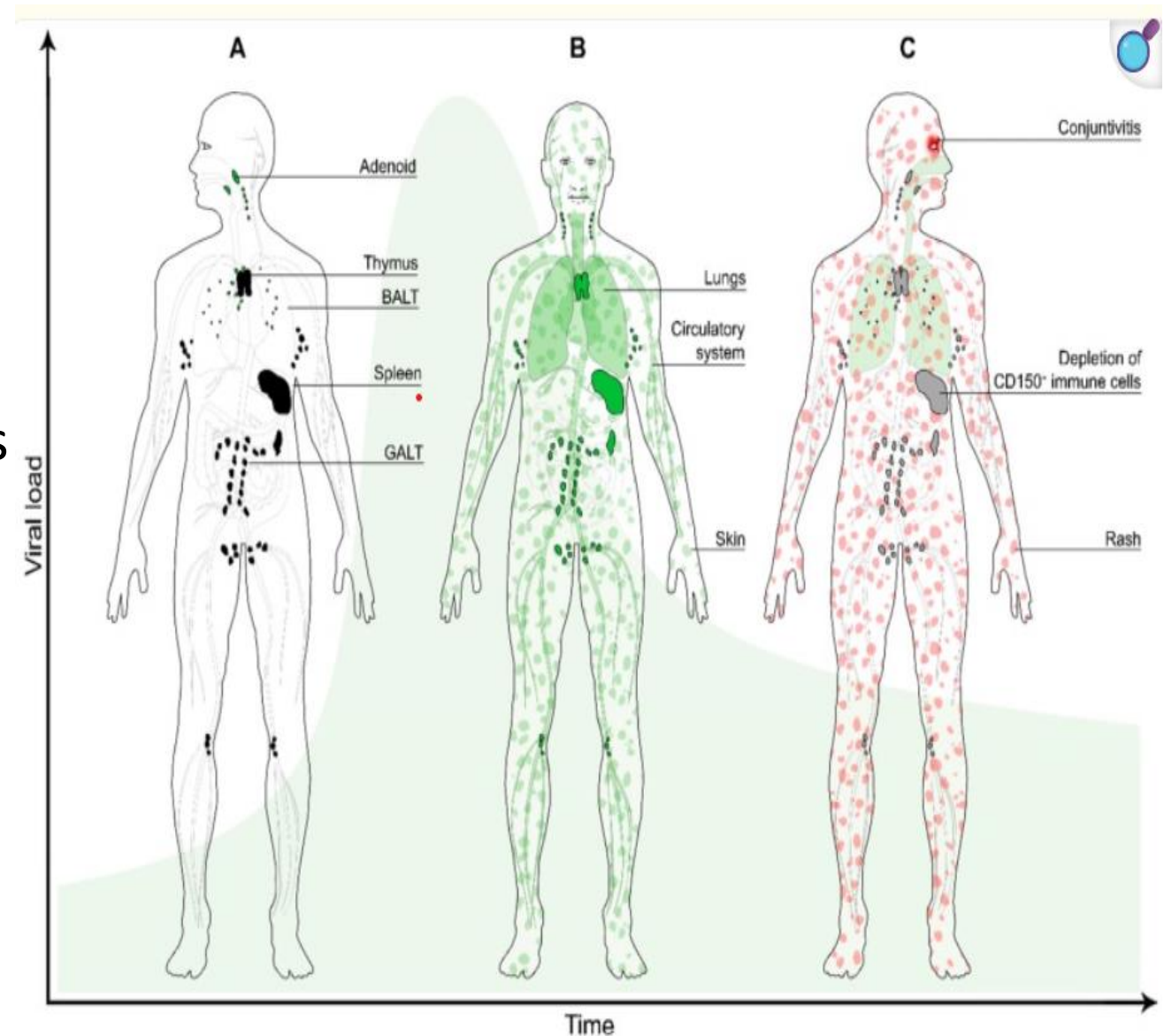
What is the Cause of the Symptoms and Rash?

- A) Mononucleosis secondary to EBV or CMV
- B) Group A Streptococcus (with scarlatina)
- C) Measles
- D) Neisseria meningitides

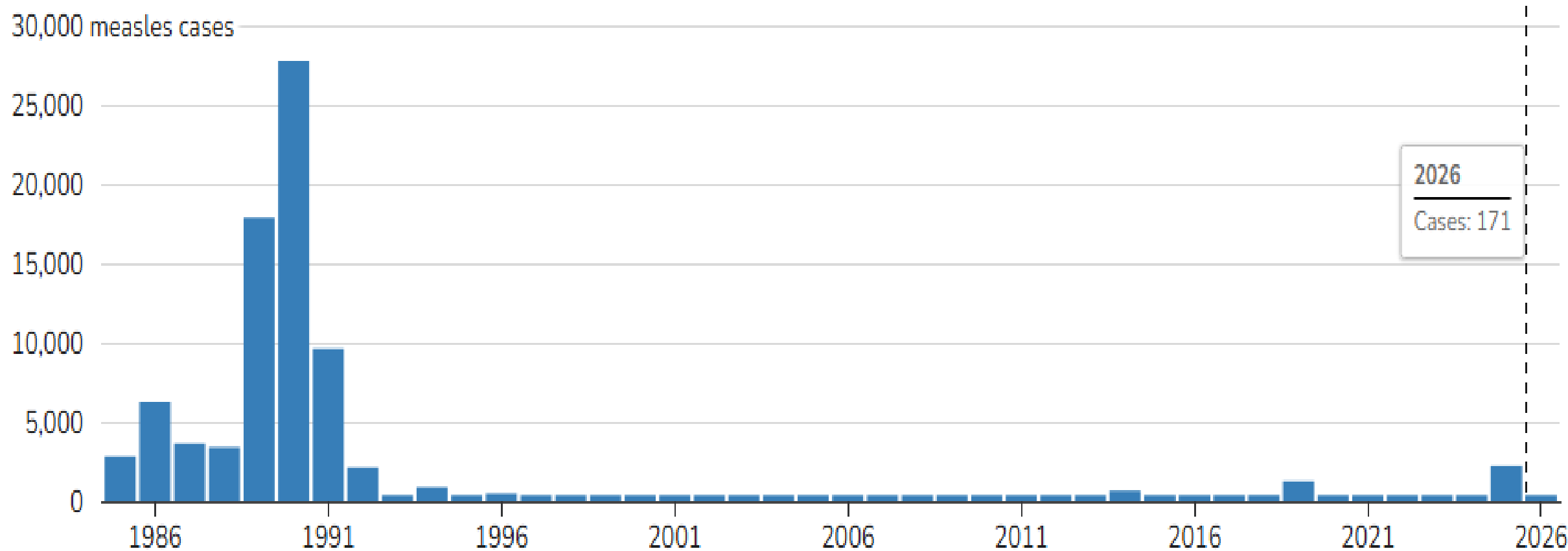
Answer is C

Measles Virology and Pathogenesis

- Genus *Morbillivirus*, the subfamily *Paramyxovirinae* and the family *Paramyxoviridae*
- It is an enveloped virus with a single strand, non-segmented negative sense RNA genome
- The first stage of measles involves infection of the respiratory tract
- The second stage involves systemic dissemination and leads to immune depletion and transient immune suppression
- The third stage involves transmission of new virus particles and infectivity

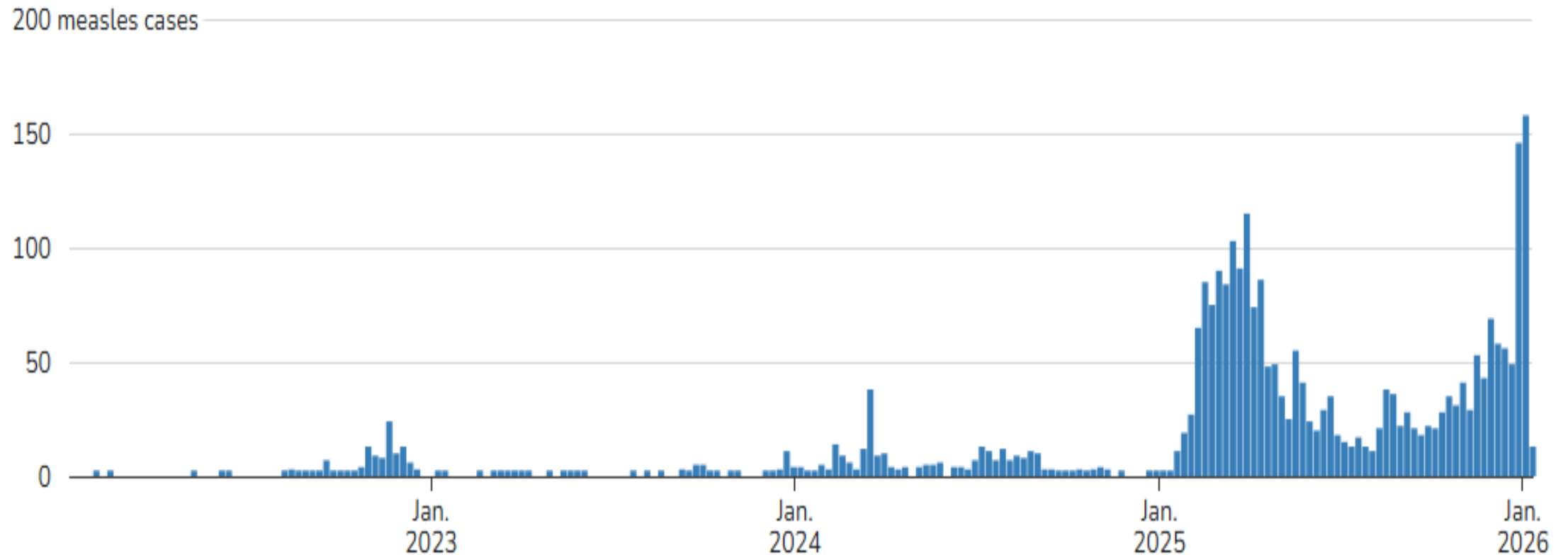


Epidemiology of Measles in the United States



Epidemiology of Measles in the United States

2023–2026* (as of January 13, 2026)



Clinical Presentation

- The incubation period is typically 11–12 days from exposure to measles virus until the first symptoms appear (prodromal symptoms)
 - **Prodromal:** Fever, cough, coryza, or conjunctivitis. Koplik spots may also appear 2–3 days after symptoms first appear.
- A rash follows the prodromal symptoms 2–4 days later and usually lasts 5–6 days. Measles is infectious 4 days before and 4 days after rash onset. Symptoms
 - **Rash:** A maculopapular rash begins on the head and face and then spreads downward to the neck, trunk, arms, legs, and feet and may become confluent. Temp may spike to more than 104° F when rash appears.

Measles Rash in Unvaccinated and Vaccinated Patients



Unvaccinated

Fully Vaccinated

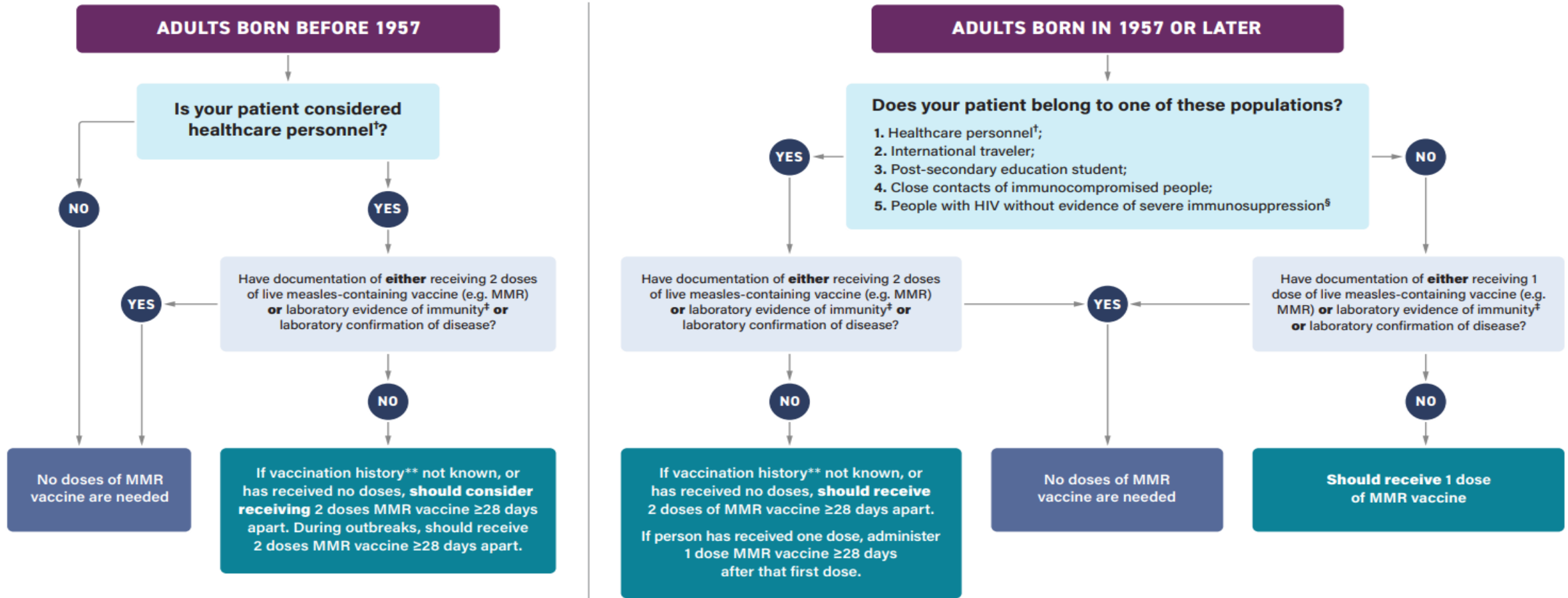
Measles Testing

- Serology
 - Rubeola IgM can be collected within a few days after rash onset and if positive, can provide presumptive evidence of active or recent infection
 - False positive Rubeola IgM can occur in patients with Parvovirus B19, Enterovirus, HHV-6. False positives can also occur with presence of RF.
 - Patients with throat or ear infections that develop a rash following administration of antibiotics may result in a false positive Rubeola IgM.
 - Rubeola IgG should be used for testing for immunity
- Measles NAAT pcr from nasal swab, throat swab, or urine is primary test for diagnosis

MMR Vaccine Recommendations

Measles vaccine recommendations for non-pregnant adults* aged ≥19 years by birth year—United States

This infographic for healthcare providers summarizes ACIP and CDC recommendations



*MMR vaccine should NOT be administered during pregnancy. Refer to Adult Immunization Schedule by Age | Vaccines & Immunizations | CDC (www.cdc.gov/vaccines/hcp/immunization-schedules/adult-age.html) for more contraindications and precautions, and other details.

[†]Healthcare personnel include all paid and unpaid persons working in healthcare settings who have the potential for exposure to patients and/or to infectious materials, including body substances, contaminated medical supplies and equipment, contaminated environmental surfaces, or contaminated air.

[‡]Acceptable laboratory evidence of immunity includes: measles IgG in serum (equivocal results should be considered negative).

[§]Refer to Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013 (www.cdc.gov/mmwr/preview/mmwrhtml/r6204a1.htm) for details about absence of severe immunosuppression. In addition to the adults belonging to one of these population groups, health departments may consider a second dose for adults (including visitors) who have received one dose who are living in or traveling to domestic areas with sustained, community-wide measles transmission affecting adults where there is ongoing risk of exposure.

Refer to VPD surveillance manual (www.cdc.gov/surv-manual/php/table-of-contents/chapter-7-measles.html).

^{**}A small number (<5%) of adults vaccinated between 1963–1967 received an inactivated (killed) measles vaccine. Check documentation to ensure that the adult did not receive inactivated vaccine. Adults who received killed vaccine, or do not know what type of vaccine they received between 1963–1967,



Back to Case Presentation

- Other Potential Causes of Fever, Rash, and LFT abnormalities
 - EBV/CMV Infections
 - Group A Streptococcal Infections
 - *Neisseria meningitidis*

EBV/CMV Infection

- Mononucleosis classically presents with fever, LAD, and tonsillar pharyngitis and sometimes rash (typically after antibiotics)
- Peak incidence in 15-24 year olds
- Can be associated with hepatitis but generally LFTs much lower than seen with hepatitis A
- Diagnosis with monospot for EBV (average sensitivity from 80-85%) or serology (EBV/CMV IgM/IgG), or EBV/CMV blood pcr
- Treatment is supportive unless immunocompromised



EBV rash

Cleveland Clinic Journal of Medicine June 2025, 92 (6) 335-337



CMV rash

Future Micro, 2016. 12(2), 171–193.

Streptococcus pyogenes (Group A Strep)

- Presents with fevers, sore throat, and rash
- Most common in children 5-15 years old
 - In adults (5-15% of pharyngeal infections)[#]
- Testing:
 - Rapid Strep Ag (86% sensitivity/96% specific)
 - Strep PCR (97.5% sensitive/95.1% specific)
 - Culture (generally not recommended for adults)^{*}
- Treatment with penicillin or amoxicillin unless allergic and can treat with cephalosporin or azithromycin



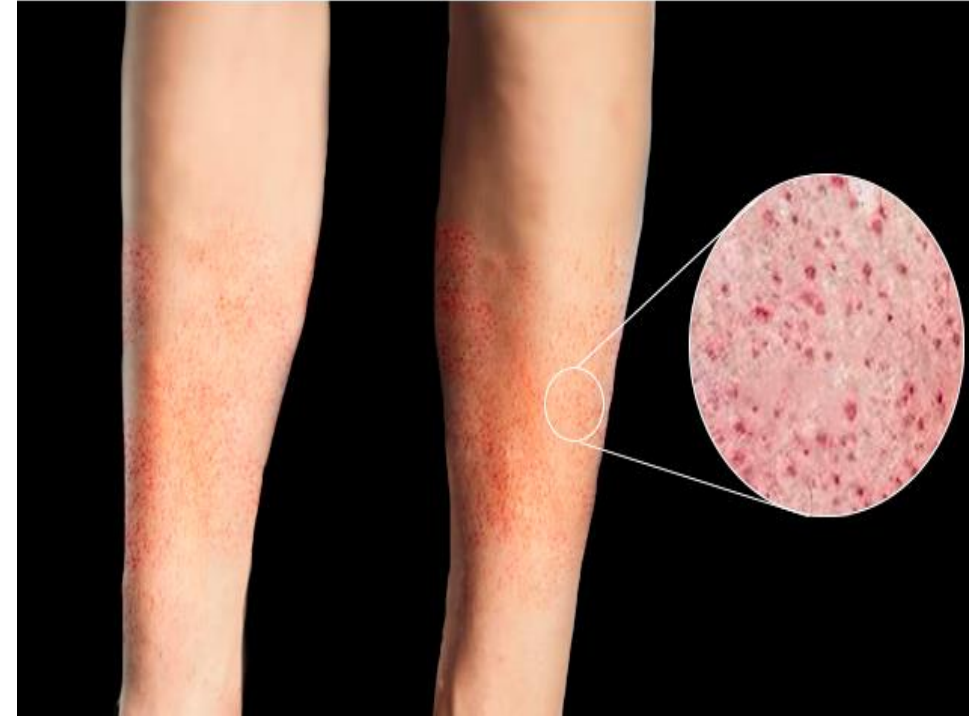
<https://phil.cdc.gov/Details.aspx?pid=3167>

[#]<https://www.cdc.gov/group-a-strep/hcp/clinical-guidance/strep-throat.html>

^{*}Pediatrics. 2014. 134(4):771-81

Neisseria meningitidis

- Presents with fever, headache, nausea, vomiting, sore throat, myalgias and rash
 - Triad of fever, altered mental status and nuchal rigidity only occurs in about 44% of cases
- In the US, disease is highest between November and March
- Increased transmission risk for household contacts, college students in dorms, military recruits, etc.
- 3 Vaccines (MenACWY, MenG, MenABCWY) recommended with age specific indications



<https://www.ncbi.nlm.nih.gov/books/NBK549849/#:~:text=History%20and%20Physical,any%20signs%20of%20a%20rash.>

Case Presentation

- A 39-year-old man presented to his PCP reporting several weeks of generalized weakness, headache, nausea, and migratory arthralgia.
- The patient had exclusively had sex with men and had been in a monogamous relationship during the past 6 months.
- He had an ulceration on his upper lip and a nonpruritic hyperkeratotic maculopapular palmar rash and bilateral submandibular lymphadenopathy.



<https://consultqd.clevelandclinic.org/secondary-syphilis-a-case-report>

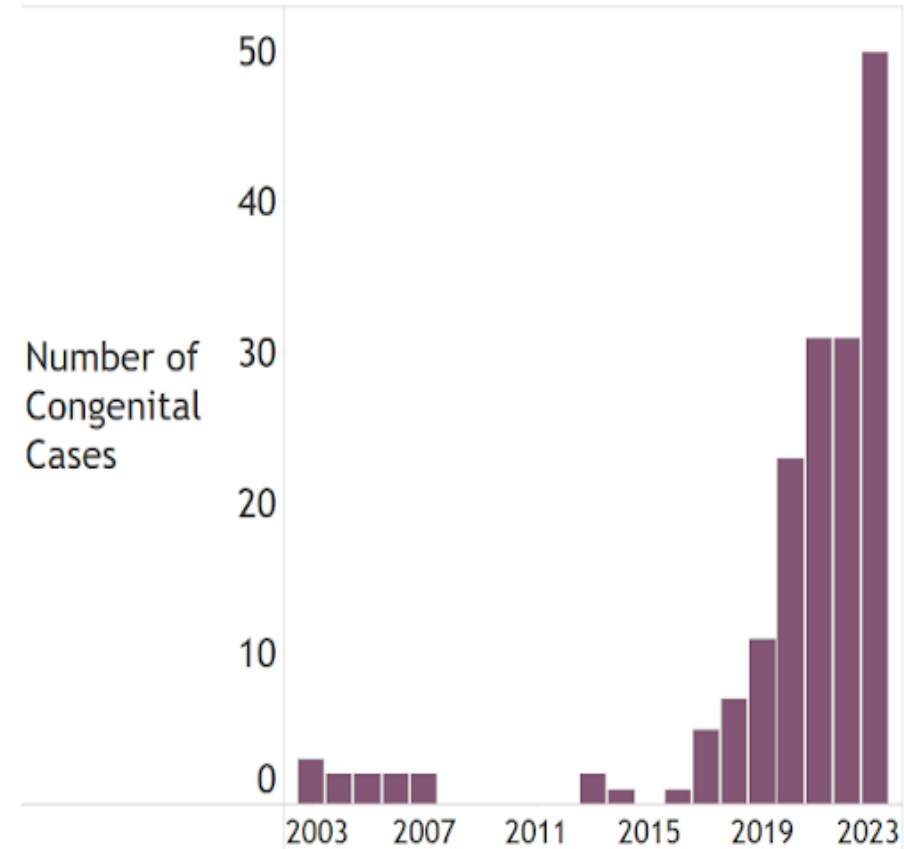
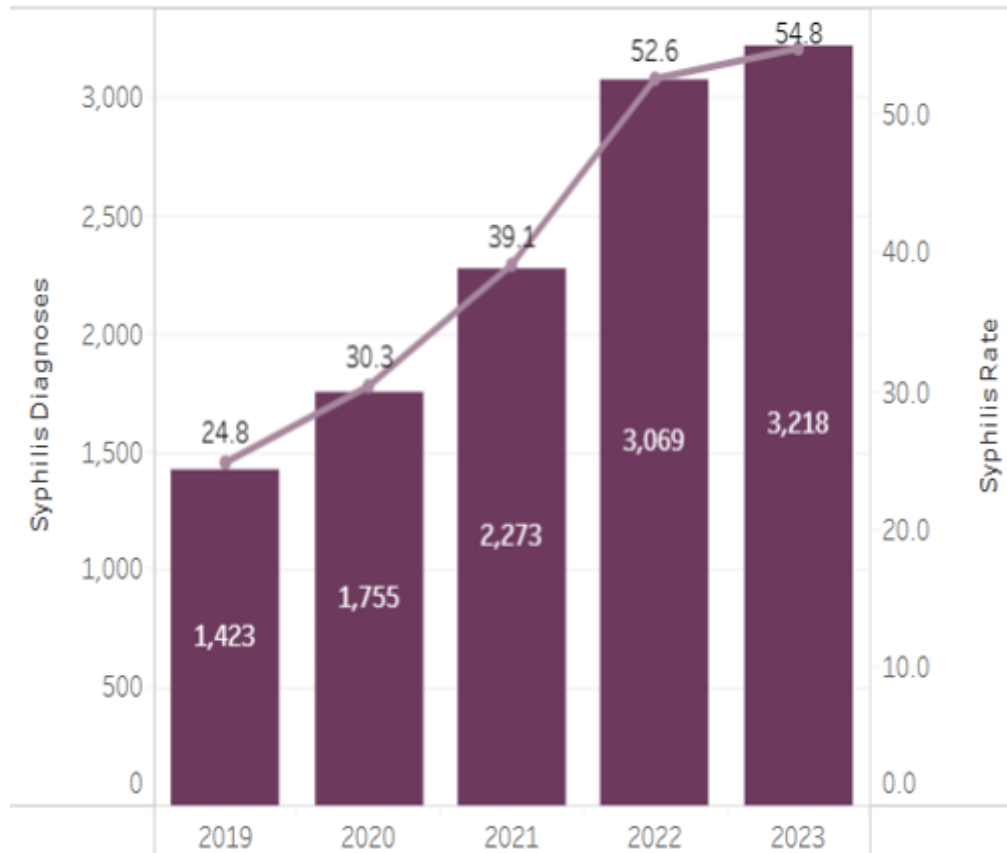
<https://www.cdc.gov/syphilis/hcp/images/index.html>

What is the Cause of the Symptoms and Rash?

- A) Acute HIV seroconversion
- B) Hand-Foot-Mouth Disease (Enterovirus)
- C) Mpox
- D) Syphilis

Answer is D

Epidemiology of Syphilis in Colorado



Rates of syphilis increased 120.7% from 2019-2023.

Rates among females have increased by 318.9% from 2019-2023.

Rates of Congenital syphilis increased more than 7 times.

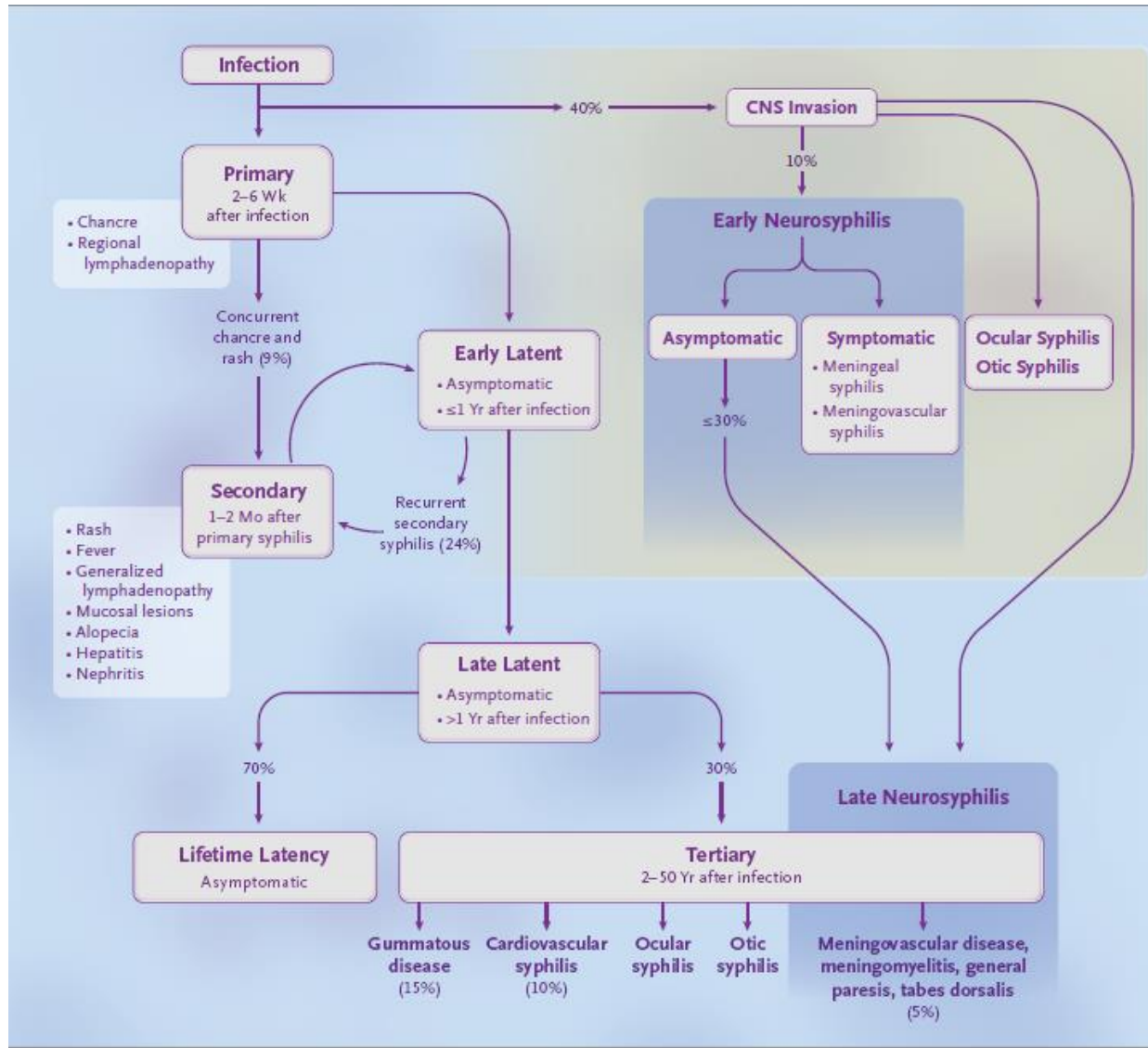
Clinical Manifestations of Syphilis

- Multiple stages of syphilis infection with asymptomatic or symptomatic neurologic involvement at any stage
 - Primary syphilis: Often manifests as a solitary chancre, indurated and ulcerative, with a clean base, at the site of contact with the sex partner's infectious lesion
 - Secondary syphilis: A mild non-pruritic rash, particularly on the palms and soles of the feet but can also include fever, LAD, mucosal lesions, alopecia, periostitis and occasionally hepatitis (often with high Alk phos)

Clinical Manifestations of Syphilis (Continued)

- Latent syphilis: Asymptomatic stage that can occur between primary and secondary stages
 - Early latent: ≤ 1 year after infection or last known negative syphilis test or
 - Late latent: > 1 year after infection
- Tertiary syphilis: Neurologic manifestations manifesting as hemiplegia, aphasia, or seizures or general paresis (irritability and cognitive and memory impairment) and tabes dorsalis (lightning pains, ataxia, bladder disturbances, visceral crises, and rectal incontinence)

Clinical Manifestations of Syphilis



- Ocular syphilis – typically presents as uveitis but can affect any part of the eye
- Otic syphilis – Usually presents with hearing loss, tinnitus, or both
- Cardiovascular syphilis – may lead to aortic aneurysms, aortic insufficiency, coronary artery stenosis or myocarditis

Syphilis Testing

- Two stage testing algorithms
 - Standard screening with nontreponemal test (RPR) or VDRL and then confirmatory testing with specific treponemal test (TPPA or FTA)
 - Reverse screening with treponemal test and if positive, reflexed with a nontreponemal test with titers
- Serologic results are non-reactive in 30% of persons with primary syphilis so should repeat in 2 weeks if negative
- CSF testing not needed unless neurologic symptoms are present
- All pregnant patients should be screened for syphilis early in pregnancy
- Testing as part of dementia evaluation in elderly patients is not routinely recommended but if positive, attempt to get history and consider LP/CSF examination if have symptoms c/w general paresis

Syphilis Testing – Interpreting Results

Algorithm	NTT	TT	Confirmatory TT†	Interpretation‡
Traditional	Nonreactive			No serologic evidence of syphilis (most likely) Early primary syphilis (extremely recent infection cannot be ruled out) Treated or long-standing untreated syphilis
Traditional	Reactive	Nonreactive		Biologic false positive NTT§
Traditional and reverse-sequence	Reactive	Reactive		Untreated syphilis (likely) Treated syphilis (likely) Endemic treponematoses
Reverse-sequence	Nonreactive	Reactive	Nonreactive	Biologic false positive TT¶
Reverse-sequence	Nonreactive	Reactive	Reactive	Treated syphilis (most likely) Long-standing untreated syphilis Early primary syphilis (before NTT has turned positive) Prozone reaction (more common with VDRL test than with RPR test)
Reverse-sequence		Nonreactive		No serologic evidence of syphilis (most likely) Early primary syphilis (extremely recent infection cannot be ruled out) Long-standing treated syphilis if TT shows seroreversion

* The traditional algorithm starts with a nontreponemal test (NTT) followed, if reactive, by a confirmatory treponemal test (TT). The reverse-sequence algorithm starts with a TT (e.g., fluorescent treponemal-antibody absorption test, *Treponema pallidum* particle agglutination test, or automated enzyme or chemiluminescence immunoassay), followed, if reactive, by an NTT. RPR denotes rapid plasma reagin, and VDRL Venereal Disease Reference Laboratory.

† The confirmatory TT should be different from the TT performed initially.

‡ The likely or most likely interpretation of test results is noted for each algorithm.

§ Causes of a biologic false positive NTT include older age, autoimmune diseases, infections (e.g., human immunodeficiency virus infection), and drug use; pregnancy as a cause is controversial.

¶ Causes of a biologic false positive TT include infections (e.g., Lyme disease), autoimmune diseases, and older age.

Syphilis Treatment

For primary and secondary syphilis in nonpregnant adults, including HIV-infected adults:

Penicillin G benzathine, 2.4 million units in a single IM dose

Doxycycline, 100 mg orally twice a day for 14 days (first alternative)

Ceftriaxone, 1–2 g daily, IM or IV, for 10–14 days (second alternative)

For latent syphilis in nonpregnant adults, including HIV-infected adults:

Early latent: penicillin G benzathine, 2.4 million units in a single IM dose

Late latent: penicillin G benzathine, 7.2 million units total, administered in 3 IM doses of 2.4 million units each at 1-week intervals

Doxycycline, 100 mg orally twice a day for 28 days (alternative)

For late syphilis (gummas and cardiovascular manifestations) but not neurosyphilis:

Penicillin G benzathine, 7.2 million units total, administered in 3 IM doses of 2.4 million units each at 1-wk intervals

Syphilis Treatment

For neurosyphilis and ocular syphilis:

Aqueous crystalline penicillin G, 18–24 million units per day, administered in IV doses of 3–4 million units every 4 hr or as a continuous infusion, for 10–14 days

Penicillin G procaine, 2.4 million units in a single IM dose daily, plus probenecid, 500 mg administered orally four times a day, both for 10–14 days (alternative)

For primary and secondary syphilis in pregnancy:

Penicillin G benzathine, 2.4 million units in a single IM dose†

For latent syphilis in pregnancy:

Early latent: penicillin G benzathine, 2.4 million units in a single IM dose

Late latent: penicillin G benzathine, 7.2 million units total, administered in 3 IM doses of 2.4 million units each at 1-wk intervals

Case Presentation

30 yo WM with presents with 3-day history of cough, fevers, and increasing DOE

PMHx: asthma as child

Allergies: NKMA

Medications: none

Social Hx: Grew up in Denver. Lives alone with dog. No tobacco or IVDU. Occasional EtoH. No recent travel

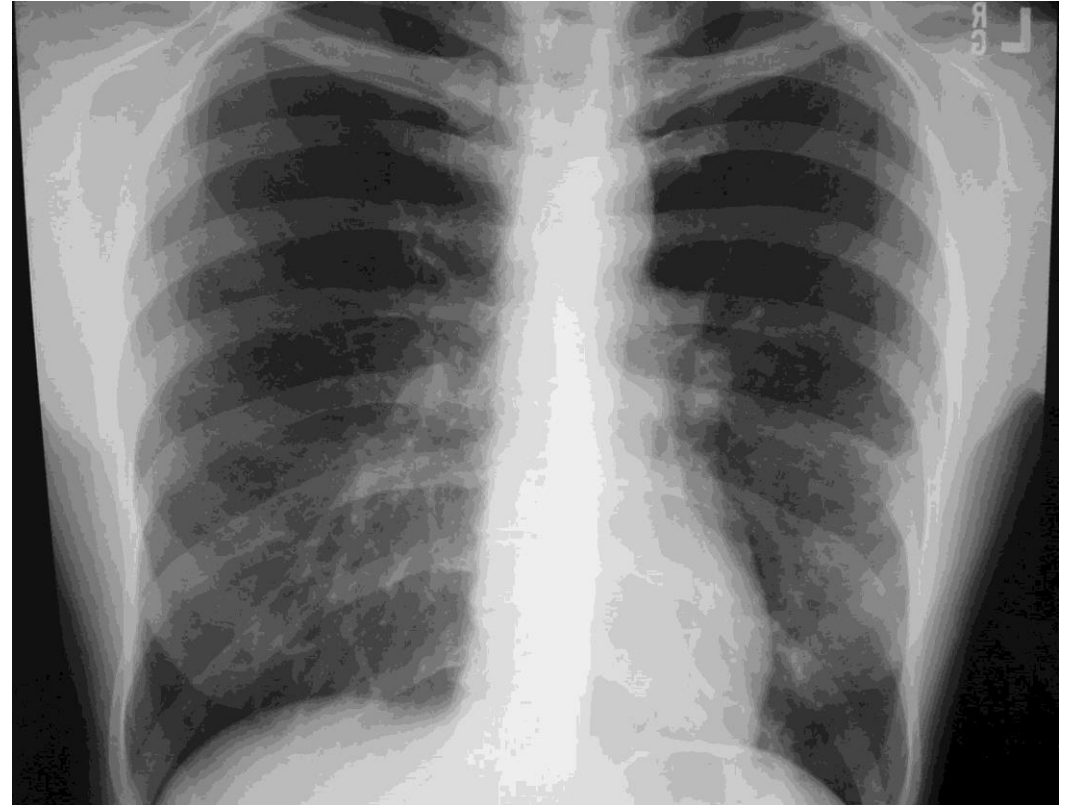
Exam: WD/WN WM in mild distress

VS: T 38.0°C, RR 20, HR 80, BP 100/60

HEENT: wnl; O/P without erythema or thrush

CV: RRR, tachy

Lungs: BLL crackles, expiratory wheezes



What Additional Work Up is Indicated?

- A) Respiratory gram stain and culture
- B) Respiratory Viral Pathogen PCR Panel
- C) Blood cultures
- D) Procalcitonin level
- E) None of the above

Answer is E

Evaluation of Community Acquired Pneumonia (CAP)

- Bacterial pathogens to consider
 - *Streptococcus pneumoniae*
 - *Haemophilus pneumoniae*
 - *Mycoplasma pneumoniae*
 - *Staphylococcus aureus* (especially post-viral)
 - *Legionella pneumophila*
 - *Chlamydia pneumoniae*
 - *Moraxella catarrhalis*
- Current guidelines do NOT recommend sputum gram stain/culture or blood cultures for non-severe CAP unless risk factors for *Pseudomonas* or *S. aureus*
 - Poor yield and does not impact outcomes

Evaluation of CAP – Lab and Radiographic Studies

- Legionella urine antigen testing should be reserved for severe CAP or for cases suspected as part of an exposure or outbreak
- No good procalcitonin threshold to distinguish between viral and bacterial causes of CAP so should not be routinely ordered
- Testing for influenza, if circulating, could be considered if would impact decision to give antiviral such as oseltamivir
- Chest radiograph is considered standard of care
- Lung Ultrasound is recommended as an alternative to CXR in 2025 ATS CAP guidelines
 - Meta-analysis: sensitivity 95% (68-100%) compared to CXR (median sensitivity 70% (16-94%))

Treatment of CAP – Inpatient vs Outpatient

- Clinical judgment + Pneumonia Severity Index preferred versus the CURB-65 (confusion, urea level, RR, BP, age ≥ 65)
- Compared with CURB-65, PSI identifies larger proportions of patients as low risk and has a higher discriminative power in predicting mortality
- Two multicenter, cluster-randomized trials demonstrated that use of the PSI safely increases the proportion of patients who can be treated in the outpatient setting
- Consistent evidence from three pre–post intervention studies and one prospective controlled observational study support the effectiveness and safety of using the PSI to guide the initial site of treatment

Pneumonia Severity Index (PSI)

Sex

- ☐ M (0 points)
- ☐ F (-10 points)

Demographic factors

- Age (1 point for each year)
- ☐ Nursing home resident (10 points)

Comorbid illnesses

- ☐ Neoplastic disease (30 points)
- ☐ Liver disease (20 points)
- ☐ Congestive heart failure (10 points)
- ☐ Cerebrovascular disease (10 points)

Physical examination findings

- ☐ Altered mental status (20 points)
- ☐ Respiratory rate ≥ 30 /minute (20 points)
- ☐ Systolic blood pressure < 90 mmHg (20 points)
- ☐ Temperature < 35 degrees C or ≥ 40 degrees C (15 points)
- ☐ Pulse ≥ 125 /minute (10 points)

Laboratory and radiographic findings

- ☐ Arterial pH < 7.35 (30 points)
- ☐ Blood urea nitrogen ≥ 30 mg/dL (11 mmol/L) (20 points)
- ☐ Sodium < 130 mEq/L (20 points)
- ☐ Glucose ≥ 250 mg/dL (14 mmol/L) (10 points)
- ☐ Hematocrit < 30 percent (10 points)
- ☐ Partial pressure of arterial oxygen < 60 mmHg or oxygen saturation $< 90\%$ (10 points)
- ☐ Pleural effusion (10 points)

Class I 0.1% Mortality
51 to 70 Points: Class II 0.6% Mortality
71 to 90 Points: Class III 0.9% Mortality
91 to 130 Points: Class IV 9.3% Mortality
131 to 395 Points: Class V 27.0% Mortality

<https://www.merckmanuals.com/en-ca/professional/multimedia/clinical-calculator/community-acquired-pneumonia-severity-index-psi-for-adults>

Treatment of CAP – Antibiotic Options

- Immunocompetent Hosts without co-morbidities
 - Amoxicillin 1 gram po tid or
 - Doxycycline 100 mg po bid or
 - Azithromycin 500 x1 day/250 mg qd x 4 days
- Immunocompetent Hosts with co-morbidities (lung, liver, cardiac or renal disease, DM)
 - Amoxicillin 500 mg po tid or Augmentin 875 mg po tid PLUS
 - Macrolide or respiratory FQ
- **Duration of minimum 3 days but if have good clinical response may stop before 5 days**
 - Contraindications to shorter courses includes severe chronic lung disease, evidence of necrotizing pneumonia, or confirmed infection with a necrotizing or resistant organism

Antibiotic Treatment for Patient with Positive Viral Test and Use of Steroids

- For outpatients, do NOT routinely recommend empiric antibiotic therapy in a patient with a positive viral pathogen test
- Controversy over whether underlying co-morbidities should weigh into decision to give empiric antibiotics
 - >50% committee agreement for chronic pulmonary disease (other than asthma), ESLD, ESRD, CV disease, alcoholism, or neoplastic disease
 - IDSA did not endorse guidelines based on this topic
- Steroids not routinely indicated

Clinical Case

- 44-year-old female with DM presents with urinary frequency and epigastric pain radiating to the left flank
- VS: T 38.0C HR 80 BP 128/84 RR 16
- Exam: L CVAT and mild LLQ pain
- UA: 1.018, pH 5.5, prot 100, large bld, >75 WBC, >75 RBC, large leukocyte esterase
- Urine culture pending

What is the Appropriate Management of this Patient?

- A) Send patient to the ED for admission and IV antibiotic therapy
- B) Start on nitrofurantoin and treat for 7 days
- C) Start a FQ and treat for 5-7 days as long as has clinical improvement
- D) Start a 3rd generation cephalosporin and treat for 14 days




Answer is C

Urinary Tract Infections (UTI)

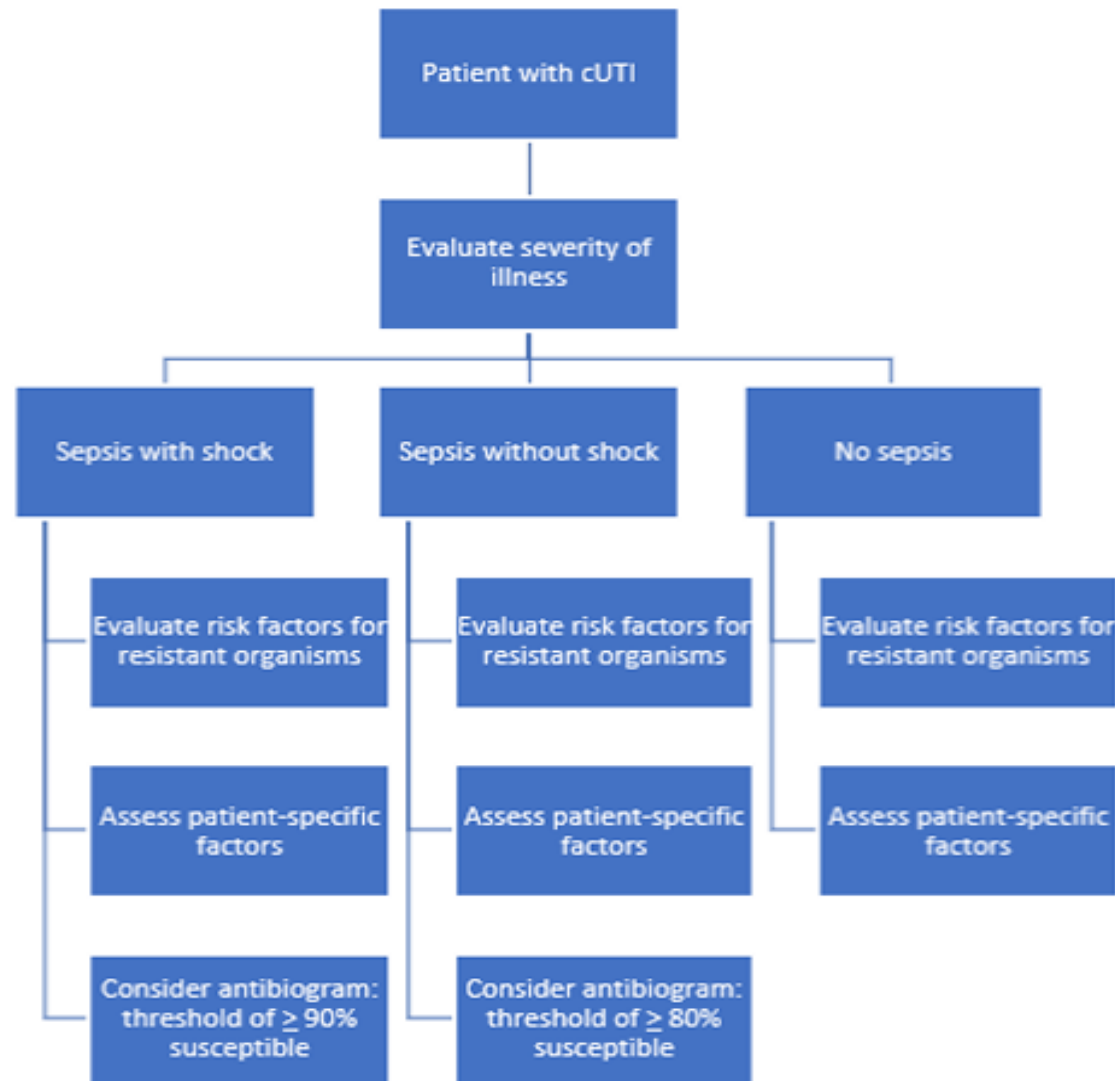
- Women have a lifetime risk of 53% of developing a UTI
- Men uncommonly have a UTI prior to the age of 50 years but have a lifetime risk of 14% of experiencing a UTI
- Risk for developing a UTI increases with age and also with procedures
- Resistance profiles of *Enterobacterales* urinary isolates in the US from 2018-2020 in out-patient settings
 - Fluorquinolones – 21.6%
 - Trimethoprim-sulfamethoxazole – 22.4%
 - Nitrofurantoin – 21.6%

2025 Updated IDSA Guidelines - UTI

New classifications of uUTI and cUTI

Old Classifications		New Classifications
Uncomplicated UTI: Acute cystitis in afebrile nonpregnant premenopausal women with no diabetes and no urologic abnormalities		Uncomplicated UTI: Infection confined to the bladder in afebrile women or men
Acute Pyelonephritis: Acute kidney infection in women otherwise meeting the definition of uncomplicated UTI above		Complicated UTI: infection beyond the bladder in women or men <ul style="list-style-type: none">• Pyelonephritis• Febrile or bacteremic UTI• Catheter-associated (CAUTI)• Prostatitis* (*not covered by these guidelines)
Complicated UTI: All other UTIs		

Approach to Empiric Antibiotics for Complicated UTI



- Achieves therapeutic levels in the urine and relevant tissue
- Avoid antibiotics to which the patient has had a resistant pathogen isolated from the urine previously
- Duration is counted from the first day of effective antibiotic therapy and depends on clinical response to treatment

Risk Factors for Resistance

- Prior exposure to fluoroquinolones and risk of FQ resistance
 - Prior month – aOR 4.62 (1.09-19.61), 15.73 (6.15-40.26), and 30.35 (5.82-158.42) based on 3 separate studies
 - Prior 3 months: aOR 23.35 (8.20-76.85)
 - Prior 6 months: aOR 21.8 (3.7 – 127.1)
 - Prior 12 months: aOR 7.6 (2.1-27.5) and 13.16 (3.11-68.43) in 2 studies
- Prior exposure to TMP/SMX and risk for resistance
 - Prior 12 Months: aOR 2.36 (1.94-2.88) and aOR 2.58 (1.13-5.89) in 2 studies
- Current resident in a NH or hospitalization in the 3 months prior is a weak predictor of antibiotic resistance

Treatment Duration

- Complicated UTI (including acute pyelonephritis) and who are improving clinically on effective therapy:
 - 5-7 days of a fluoroquinolone (i.e. ciprofloxacin or levofloxacin)
 - 7 days of a non-fluoroquinolone antibiotic (e.g. Bactrim, 3rd generation cephalosporin*, beta-lactams)
 - Higher doses of amoxicillin, amoxicillin/clavunate and cephalosporins may be needed to achieve appropriate levels in urine (amox 1000 mg po q8, amox-clav 875–1000 mg po q8, or cephalexin 1000 mg po q6)
- Men with febrile UTI and suspected bacterial prostatitis may benefit from a longer treatment duration (i.e., 10-14 days)



QUESTIONS