Syphilis in Hospitalized Patients

Syphilis, caused by the spirochete Treponema pallidum, is a sexually transmitted infection that can lead to severe systemic complications if untreated. This guide provides students with a comprehensive framework to evaluate, diagnose, and manage syphilis in the hospital setting, with case scenarios to apply the knowledge.

Introduction and Pathophysiology

Syphilis is caused by Treponema pallidum, a gram-negative spirochete that cannot be cultured in vitro. It is primarily transmitted through sexual contact, including vaginal, anal, or oral sex, and can also be transmitted vertically from mother to child (congenital syphilis). The bacterium penetrates mucous membranes or broken skin, disseminating systemically via the bloodstream and lymphatic system.

- The natural history of syphilis progresses through distinct stages:
  - **Primary Syphilis:** Characterized by a painless chancre at the site of inoculation, typically 2-6 weeks after exposure.
  - **Secondary Syphilis:** Systemic dissemination 4-10 weeks after the primary stage, presenting with rash, fever, and lymphadenopathy.
  - **Latent Syphilis:** Asymptomatic phase; early latent (<1 year) can still be infectious, while late latent (>1 year) is typically non-infectious.
  - **Tertiary Syphilis:** Occurs years to decades later, involving gummas (granulomatous lesions), cardiovascular syphilis, or neurosyphilis.
  - **Neurosyphilis:** Can occur at any stage, involving the central nervous system (CNS) with meningitis, stroke, or tabes dorsalis.
- Syphilis requires careful diagnosis and management, especially in hospitalized patients where severe manifestations like neurosyphilis or cardiovascular complications may necessitate inpatient care.

Indications for Hospital Management

Severe Manifestations:

- **Neurosyphilis:** Meningitis, stroke, cranial nerve deficits, tabes dorsalis, or general paresis.
- **Cardiovascular Syphilis:** Aortitis, aortic aneurysm, or aortic regurgitation.
- **Ocular Syphilis:** Uveitis, optic neuritis, or vision loss.

- **Severe Secondary Syphilis:** Extensive rash, hepatitis, or renal involvement (e.g., glomerulonephritis).

Complications:

- **Jarisch-Herxheimer Reaction:** Fever, chills, and worsening symptoms post-treatment due to spirochete lysis; may require monitoring.
- **Pregnancy Complications:** Risk of congenital syphilis (e.g., stillbirth, neonatal infection) necessitating maternal treatment.

Other:

- **Inability to Take Oral Medications:** Patients with severe nausea, vomiting, or altered mental status may require IV therapy.
- **Co-Infections:** Syphilis often coexists with HIV, complicating management and requiring inpatient oversight.

Evaluation

History:

- **Symptoms:** Painless genital ulcer (primary), diffuse rash, fever, lymphadenopathy (secondary), neurological symptoms (neurosyphilis), or vision changes (ocular syphilis).
- **Risk Factors:** Unprotected sex, multiple partners, men who have sex with men (MSM), history of STIs, HIV co-infection.
- **Systemic Symptoms:** Weight loss, fatigue, neurological deficits (e.g., hearing loss, gait instability), or cardiovascular symptoms (e.g., chest pain, dyspnea).
- **Pregnancy:** Assess for congenital syphilis risk in pregnant patients.

Physical Exam:

- **Primary Syphilis:** Painless chancre (genital, anal, or oral), regional lymphadenopathy.
- **Secondary Syphilis:** Maculopapular rash (palms/soles), mucous patches, condyloma lata, generalized lymphadenopathy.
- **Neurosyphilis:** Cranial nerve deficits (e.g., hearing loss, vision loss), altered mental status, tabes dorsalis (lightning pains, sensory ataxia).
- **Ocular Syphilis:** Redness, vision loss, photophobia, uveitis on slit-lamp exam.
- **Cardiovascular Syphilis:** Aortic regurgitation murmur, widened pulse pressure, signs of heart failure.

- **General:** Fever, weight loss, signs of co-infections (e.g., HIV-related findings).

Initial Labs:

- **Serologic Tests:** Non-treponemal (RPR/VDRL) and treponemal (FTA-ABS, TP-PA) tests for diagnosis.
- **CSF Analysis:** If neurosyphilis suspected (e.g., CSF VDRL, cell count, protein, glucose).
- **HIV Testing:** Co-infection common; impacts treatment (e.g., longer duration for neurosyphilis).
- **CBC/CMP:** Assess for anemia, renal involvement (glomerulonephritis), or hepatitis.

Imaging/Other:

- **Neurosyphilis:** Brain MRI (meningeal enhancement, stroke), audiometry (hearing loss).
- **Cardiovascular Syphilis:** CT/MRI aorta (aneurysm), echocardiography (aortic regurgitation).
- **Ocular Syphilis:** Ophthalmologic exam (slit-lamp, fundoscopy).

Interpreting Labs and Titers

Serologic Testing:

- **Non-Treponemal Tests (RPR/VDRL):** Measure disease activity; titers rise with active infection, decline with treatment.
- **Treponemal Tests (FTA-ABS, TP-PA):** Confirmatory; remain positive for life, regardless of treatment.

Interpretation:

Diagnosis: Positive non-treponemal test + positive treponemal test = syphilis. False positives may occur (e.g., pregnancy, autoimmune disease); treponemal test confirms.

Titers:

- Active Disease: High titers (e.g., RPR ≥1:32) suggest active infection.
- Treatment Response: A 4-fold decrease in titer (e.g., 1:32 to 1:8) within 6-12 months indicates successful treatment.
- Persistent Titers: Low-level titers (e.g., 1:2) may persist post-treatment (serofast state); does not indicate treatment failure unless titers rise.

- **Neurosyphilis:** CSF VDRL specific but not sensitive; CSF pleocytosis (>5 WBCs/μL), elevated protein support diagnosis.
- **Table:** Interpreting Syphilis Serology

Test Type	Test Examples	Result Interpretation	Notes
Non-Treponemal	RPR, VDRL	Positive: Active infection; monitor titers	False positives (e.g., pregnancy, SLE)
Treponemal	FTA-ABS, TP-PA	Positive: Confirms syphilis diagnosis	Lifelong positive, even after treatment
CSF Analysis	CSF VDRL, cell count	CSF VDRL+: Neurosyphilis	CSF pleocytosis, high protein also support

Treatment

General Principles:

- Penicillin is the treatment of choice for all stages of syphilis; no documented resistance.
- Hospital management is indicated for severe manifestations requiring IV therapy or monitoring.
- Jarisch-Herxheimer reaction (fever, chills within 24 hours of treatment) may occur; manage with supportive care.

Specific Treatments:

- **Primary, Secondary, Early Latent (<1 year):**
  - **Treatment:** Benzathine penicillin G 2.4 million units IM x 1 dose.
  - **Alternative (Penicillin Allergy):** Doxycycline 100 mg PO BID x 14 days (outpatient); desensitize for inpatient IV therapy if severe allergy.
- Late Latent (>1 year), Unknown Duration, Tertiary (non-neurosyphilis):
  - **Treatment:** Benzathine penicillin G 2.4 million units IM weekly x 3 doses.
  - **Alternative:** Doxycycline 100 mg PO BID x 28 days.
    - **Neurosyphilis, Ocular Syphilis:**
      - **Treatment:** Aqueous crystalline penicillin G 18-24 million units/day IV (3-4 million units q4h) x 10-14 days, followed by benzathine penicillin G 2.4 million units IM x 1.
      - **Alternative:** Ceftriaxone 2 g IV daily x 10-14 days (if penicillin allergic, after desensitization failure).
    - **Cardiovascular Syphilis:**
      - **Treatment:** Same as neurosyphilis (IV penicillin), followed by surgical evaluation for aneurysms.

- **Pregnancy:**
  - **Treatment:** Benzathine penicillin G per stage; desensitize if allergic (no alternatives safe for fetus).
  - **Jarisch-Herxheimer Reaction:**
  - **Management:** Supportive (antipyretics, fluids); steroids not routinely recommended.

Follow-Up:

Monitor RPR titers at 6, 12, and 24 months; expect 4-fold decrease within 12 months.

Repeat CSF analysis at 6 months for neurosyphilis; persistent abnormalities may require retreatment.

Table: Syphilis Treatment Guidelines

Stage	Treatment	Agent/Dose	Notes
Primary/ Secondary	Penicillin IM	Benzathine penicillin G 2.4 million units IM x 1	Doxycycline if allergic (outpatient)
Late Latent/ Tertiary	Penicillin IM	Benzathine penicillin G 2.4 million units IM weekly x 3	Doxycycline 100 mg BID x 28 days if allergic
Neurosyphilis	Penicillin IV	Aqueous penicillin G 18-24 million units/day IV x 10-14 days	Ceftriaxone alternative if desensitization fails
Pregnancy	Penicillin IM	Benzathine penicillin G per stage	Desensitize if allergic; no alternatives

Complications

Acute:

Jarisch-Herxheimer Reaction: Fever, chills, headache within 24 hours of treatment; self-limiting but may require monitoring.

Neurosyphilis: Stroke, seizures, meningitis, or cranial nerve deficits (e.g., hearing loss, vision loss).

Ocular Syphilis: Permanent vision loss if untreated.

Chronic:

Cardiovascular Syphilis: Aortic aneurysm, aortic regurgitation, coronary ostial stenosis.

Neurosyphilis: Tabes dorsalis (lightning pains, sensory ataxia), general paresis (dementia, personality changes).

Gummatous Syphilis: Destructive lesions in skin, bones, or organs.

Other:

Congenital Syphilis: Stillbirth, neonatal death, Hutchinson's triad (interstitial keratitis, notched teeth, deafness).

Co-Infections: Increased risk of HIV transmission/acquisition; alters treatment duration.

Key Pearls

- **Stages:** Primary (chancre), secondary (rash), latent (asymptomatic), tertiary (gummas, neurosyphilis).
- **Diagnosis:** Non-treponemal (RPR) + treponemal (FTA-ABS) tests; CSF analysis for neurosyphilis.
- **Titers:** 4-fold decrease post-treatment indicates success; persistent low titers may be serofast.
- **Treatment:** Penicillin for all stages; IV for neurosyphilis/ocular syphilis.
- **Hospital Indications:** Neurosyphilis, cardiovascular syphilis, severe secondary syphilis, or inability to take oral meds.
- **Follow-Up:** Monitor titers at 6, 12, 24 months; repeat CSF analysis for neurosyphilis.

References

UpToDate: "Syphilis: Epidemiology, Pathophysiology, and Clinical Manifestations" (2025). UpToDate Syphilis

CDC: "Syphilis Treatment Guidelines" (2024). CDC Syphilis Guidelines

NEJM: "Neurosyphilis: Diagnosis and Management" (2024). NEJM Neurosyphilis

IDSA: "Management of Syphilis in Persons with HIV" (2023). IDSA Syphilis Guidelines

Case Scenarios

Case 1: A 45-Year-Old Male with a Genital Ulcer

Presentation: A 45-year-old male presents with a painless genital ulcer for 2 weeks. He reports recent unprotected sex. Exam shows a 1 cm indurated, non-tender ulcer with raised borders and regional lymphadenopathy.

Labs: RPR 1:64, TP-PA positive. HIV test negative.

Diagnosis: Primary Syphilis → Painless chancre, positive serologies.

Management: Benzathine penicillin G 2.4 million units IM x 1 dose. Monitor for Jarisch-Herxheimer reaction (supportive care if occurs). Follow-up RPR at 6 and 12 months. Counsel on safe sex practices.

Case 2: A 50-Year-Old Female with Vision Loss

Presentation: A 50-year-old female with HIV presents with blurred vision and eye redness for 1 week. Exam shows anterior uveitis on slit-lamp exam, fundoscopy reveals optic disc swelling. She reports a history of untreated syphilis (RPR 1:32, TP-PA positive).

Labs: CSF VDRL positive, lymphocytic pleocytosis, high protein.

Diagnosis: Ocular Syphilis (Neurosyphilis) → Vision changes, uveitis, positive CSF findings.

Management: Admit for IV therapy. Aqueous penicillin G 18-24 million units/day IV x 14 days, followed by benzathine penicillin G 2.4 million units IM x 1. Consult ophthalmology and ID. Monitor for Jarisch-Herxheimer reaction. Repeat CSF analysis at 6 months.

Case 3: A 60-Year-Old Male with Chest Pain

Presentation: A 60-year-old male presents with chest pain and dyspnea. Exam shows a diastolic murmur (aortic regurgitation) and widened pulse pressure. History reveals untreated syphilis 20 years ago (RPR 1:16, TP-PA positive).

Labs: CT chest shows aortic root dilation (aneurysm). Echocardiogram confirms aortic regurgitation.

Diagnosis: Cardiovascular Syphilis → Aortitis, aortic regurgitation, aneurysm.

Management: Admit for IV therapy. Aqueous penicillin G 18-24 million units/day IV x 14 days. Consult cardiothoracic surgery for aneurysm management. Monitor for heart failure. Follow-up RPR at 6 and 12 months.

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