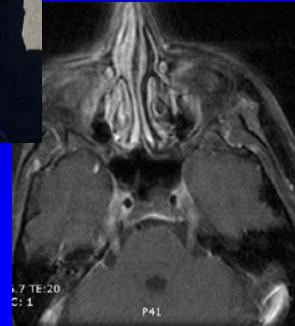


## NeuroAIDS, 2007: Sore Feet & Neurosyphilis



*Cheryl A. Jay, MD  
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UCSF Department of Neurology  
SFGH Neurology Service &  
Positive Health Program*

UCSF/SFGH

## NeuroAIDS, 2007

*Painful feet & twitching calves*

*Bell's palsy & a whole lot more*

*Neurosyphilis with persistently  
abnormal CSF*

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## Painful Feet & Twitching Calves

**44 y/o man admitted for AIDS & neutropenia:**

“His pain seems like neuropathy, but he has fasciculations... I think.”

**History:** 10 years ago (5 years after HIV diagnosis), he developed numbness & tingling in the soles of both feet

- CD<sub>4</sub> ~200
- Treatment-naïve

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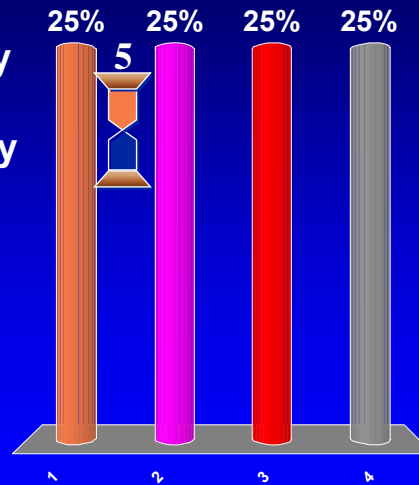
## Which diagnosis is LEAST likely?

1. Peripheral neuropathy
  2. Bilateral radiculopathy
  3. Cryptococcal meningitis
- Cervical spondylosis with myelopathy

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## Which diagnosis is **LEAST** likely?

1. Peripheral neuropathy
2. Bilateral radiculopathy
3. Cryptococcal meningitis
4. Cervical spondylosis with myelopathy



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## More Information

### **Interval history:**

Neurologically stable for the next 4-5 years

- ddl-containing regimen for 18 months
- Drug holiday for 3 years

CD<sub>4</sub> 80: HAART started, including d4T 40mg bid

- 1 month later: "walking on balloons," cramps, minor tingling in fingers
- 4 months later: amitryptiline for worsening pain, new ARVs without d-drug

**Exam:** WDNW man with healing abscesses

### • Motor

No atrophy, normal strength  
Occasional calf fasciculations  
Absent Achilles' reflexes (normal @ knees & in arms), toes down

### • Sensory

Vibration absent in toes, slightly diminished in fingers  
Cold decreased to mid-calf, normal in fingers

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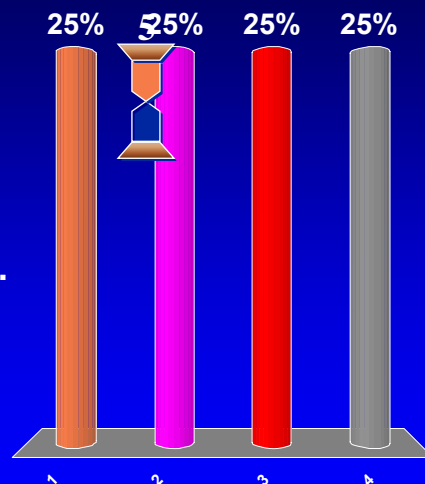
## At this point, I would:

1. Not worry too much about a drug-induced neuropathy.
  - Order an EMG.
  - Schedule a spine MRI.
  - Screen for diabetes and alcoholism, and check a B<sub>12</sub>, RPR & maybe a TSH.

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# DSP: Diagnoses & Plan

## *AIDS (HIV) neuropathy*

- Tx naïve, no other evident cause, CD<sub>4</sub> ~200
- Paresthesias > pain, nonprogressive

## *Uneventful 18 months of ddl*

## *d4T neuropathy*

- Foot pain
- Symptoms & signs to just below knees, also fingers
- Cramps & fasciculations

## *No further W/U unless worsens; taper TCA*

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# Painful Neuropathy & HIV

## *Distal symmetric polyneuropathy*

Hx: positive (pain, paresthesias) and negative (numbness) sensory sx

Exam: depressed or absent ankle reflexes, distal sensory loss (vibration, temperature, pain)

Symmetric, feet first

**Consider:** HIV (especially uncontrolled), d-drugs

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## *Atypical features*

prominent weakness  
hands ≥ feet  
proximal features  
asymmetry  
sphincter dysfunction

## *If typical features:*

Med hx: d-drugs, INH, dapsone, hydroxyurea, metronidazole, vincristine, thalidomide

Screening: DM, B<sub>12</sub>, RPR, TSH

# Neuropathy in HIV, 2007

## **New risk factor: protease inhibitors?**

*Khanlou H, Valdes-Sueiras M, Farthing C: Peripheral Neuropathy Induced by Lopinavir-Saquinavir-Ritonavir Combination Therapy in an HIV-Infected Patient, J Int Assoc Physicians AIDS Care 6:155 (2007)*

## **Symptomatic treatment trials:**

### **Negative: prosaptide**

*Evans SR et al: A randomized trial evaluating Prosaptide for HIV-associated sensory neuropathies: use of an electronic diary to record neuropathic pain, PLoS ONE 2:e551 (2007)  
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0000551>*

### **Positive: cannabis**

*Abrams DI et al: Cannabis in painful HIV-associated sensory neuropathy: a randomized placebo-controlled trial, Neurology 68:515(2007)*

### **Promising?: high-dose capsaicin patch**

*Simpson DM et al: An open-label study of high-concentration capsaicin patch in painful HIV neuropathy, J Pain Symptom Management, Oct 22 (2007)*

### **Pending: acetyl-L-carnitine for nucleoside neuropathy, pregabalin**

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# Bell's Palsy & a Whole Lot More

**39 y/o man with AIDS (CD<sub>4</sub> 101, VL >500K) admitted with HA, dysphagia, L hand weakness, unsteady gait & above symptoms**

**History:** off ARVs for a year, HBV/HCV, psoriasis

Rx for 2° syphilis 3 months ago; unprotected sex since 2 weeks ago: abrupt R facial weakness after 3 weeks of R ear pain, hearing loss, tinnitus; rx valacyclovir & artificial tears

**Exam:** afebrile, mildly stiff neck

Alert, conversant with moderate palatal dysarthria

Mild R V<sub>1-3</sub> sensory loss, R hearing loss, severe R LMN facial weakness, R palatal weakness

? L hand weakness, ? gait ataxia

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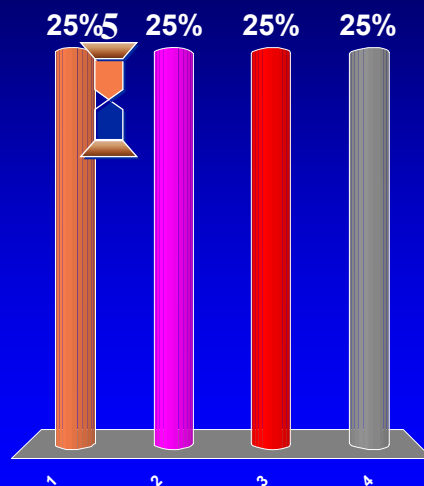
**Clinically, there is involvement all of the following EXCEPT:**

- Meninges
- Cranial nerves
- Cerebral cortex
- Cerebellum or posterior columns

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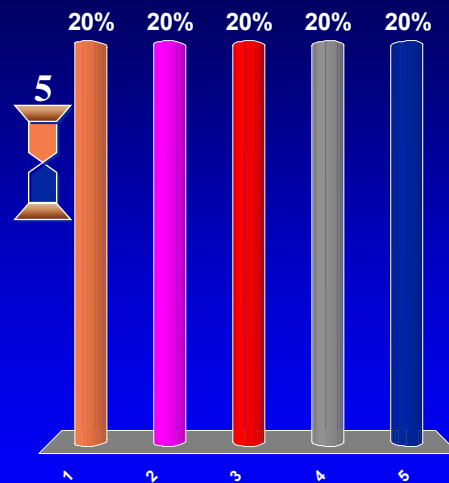
# I would:

- Order a CT or MRI.
- Do an LP.
- Get an RPR.
- Consider neuroTB or cryptococcosis.
- All of the above.

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# I would:

1. Order a CT or MRI.
2. Do an LP.
3. Get an RPR.
4. Consider neuroTB or cryptococcosis.
5. All of the above.



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# Meningitis?

**Head CT, noncontrast:** normal

## CSF

Protein 177, glucose 44 (serum 98)

3 rbc, 193 wbc (90% lymphocytes)

Gram stain, CrAg negative

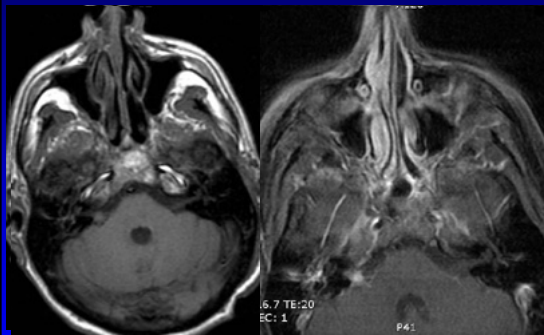
**Rx in ED:** ceftriaxone, vancomycin, ampicillin

**Differential dx:** Listeria, TB, syphilis, VZV, cocci

**IV acyclovir added the next day**

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# Further Workup



**Treatment failure or reinfection?**

**Rx:** IV PCN G x 14 days

**Followup:**

- Persistent R HL, facial weakness
- Serum RPR 1:128
- Audiogram, repeat LP not done (lost to followup)

**Serum RPR:** 1:1024 (was 1:16)

**CSF VDRL:** 1:32

**Dx:** syphilitic meningitis

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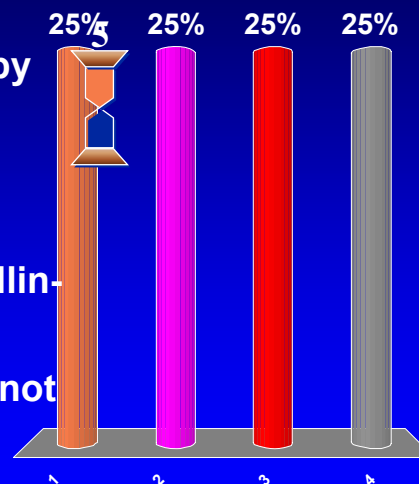
**Per CDC guidelines, management of neurosyphilis includes all of the following EXCEPT:**

1. Benzathine penicillin IM weekly x 3 as sole therapy
2. Repeat CSF exam in 6 months
3. Consideration of desensitization in penicillin-allergic patients
4. Retreatment of CSF has not normalized by 2 years

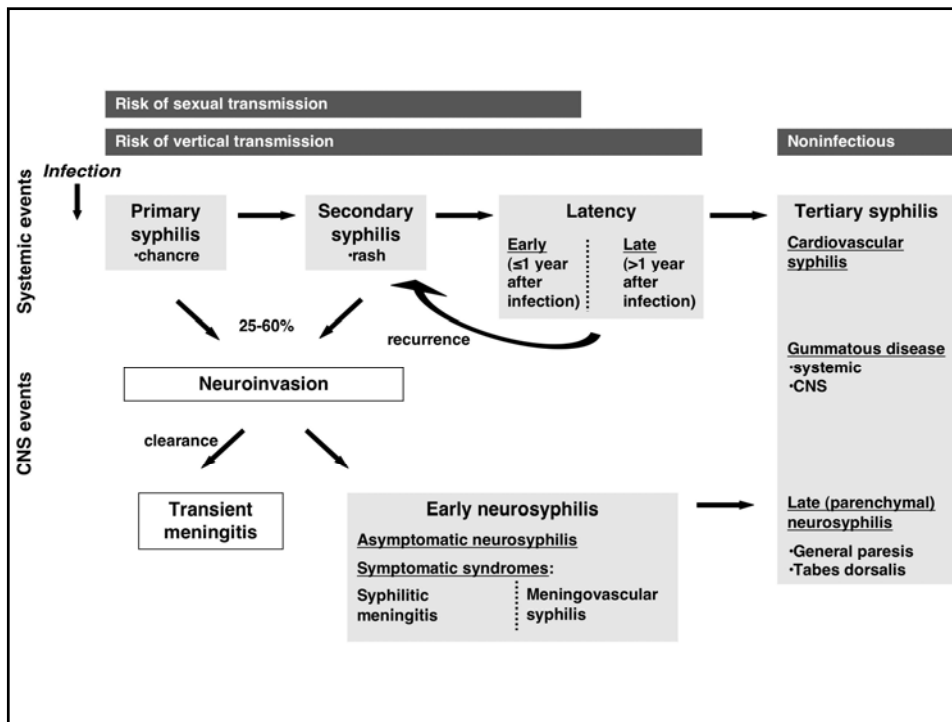
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# Neurosyphilis

**Failure of clearance after neuroinvasion:** may be asymptomatic, with increased risk to become symptomatic (the great imitator of neurologic disease)

**Increased risk with syphilitic eye disease**

**Early (weeks to years after 1<sup>o</sup> infection):** meningeal +/- cranial nerve, stroke (or both)

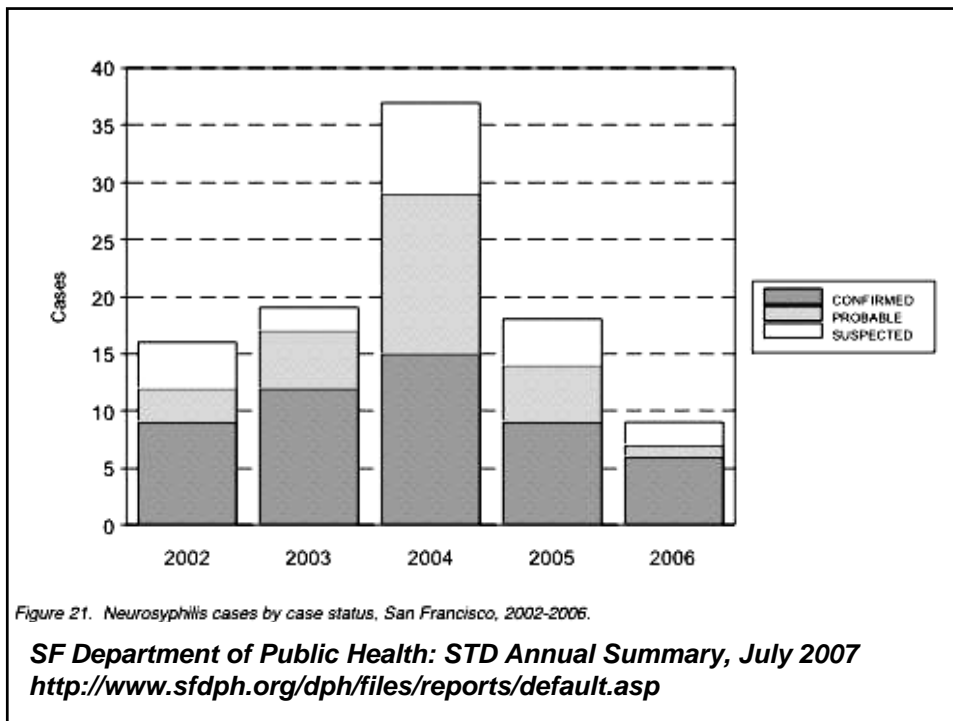
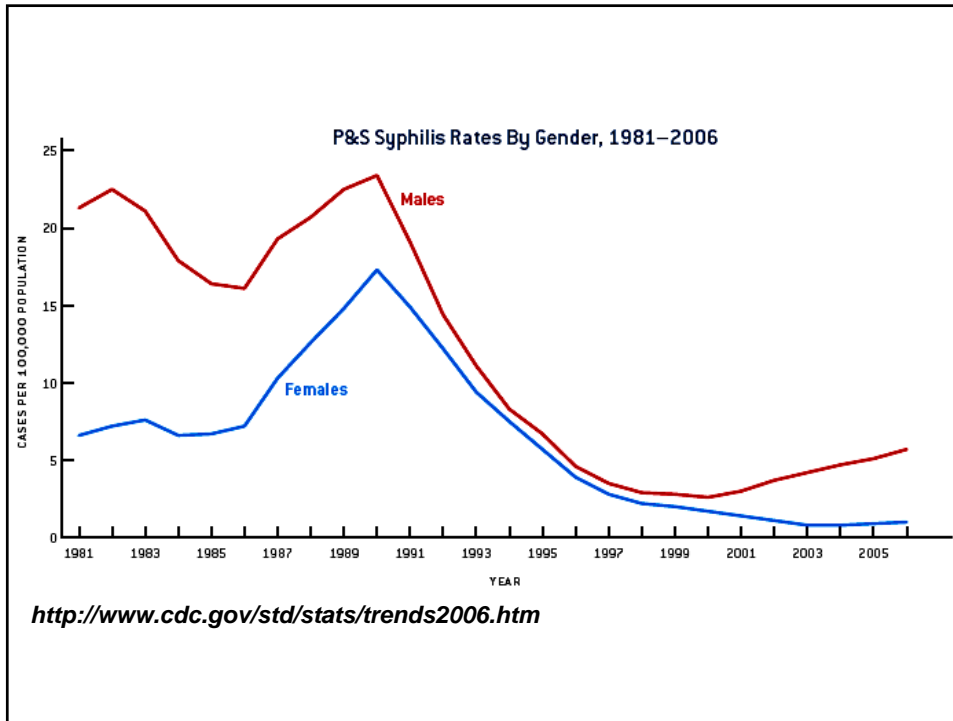
**Syphilitic meningitis:** HA, stiff neck, cranial nerve palsies (hydrocephalus, seizures, myelopathy)

**Meningovascular syphilis:** meningitis with ischemic stroke

**Late (years to decades after 1<sup>o</sup> infection):**

**Parenchymal**  
General paresis (brain)  
Tabes dorsalis (cord & nerve roots)

**Gummatous**  
Cerebral mass lesion  
Compressive myelopathy



# Syphilis & HIV: A Bad Combination

**Major global epidemics**  
**HIV augments syphilis transmission & vice versa**

**In HIV+ patients:**

Increased risk of neurosyphilis & treatment failure (?)

Syphilis: ↓CD<sub>4</sub> and ↑viral load

Zetola NM, Klausner JD: Syphilis and HIV infection: an update. *Clin Infect Dis* 44:1222 (2007)

**The Great Imitator:**

- Dementia
- Cranial neuropathies
- Meningitis
- Myeloradiculopathy
- Brain/spine mass
- Stroke in a young patient
- Eye/ear disease

**HIV-related neurologic disorders are also on the differential of these syndromes.**

**Serology & CSF**

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# Lumbar Puncture

**Indications:** CDC, 2006

- Syphilis and:  
Neurologic disease  
Syphilitic eye disease (otosyphilis?)
- 3° syphilis
- Treatment failure
- HIV+ and:  
Late latent syphilis  
Syphilis of unknown duration

CDC: Sexually transmitted diseases: treatment guidelines, 2006. *MMWR* 55 (RR11):1(2006)

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**CSF findings:**

- ↑Protein
- ↑Cells (lymphs)
- CSF-VDRL  
Highly specific in atraumatic CSF  
30-70% sensitive
- CSF-FTA  
Sensitive, not specific  
Can exclude neurosyphilis

# Treatment of Neurosyphilis in Adults

**Aqueous crystalline penicillin G, 18-24 million units/day:** 3-4 million units IV q4h or continuous infusion, 10-14 days

**Alternate:** procaine penicillin G 2.4 million units IM daily with probenecid 500mg PO 4x/day, both for 10-14 days

**Desensitization if penicillin-allergic**

**Jarisch-Herxheimer reaction**

**Benzathine PCN IM weekly x 3 afterwards?**

**F/U:** serial serum serologies & CSF exams

CDC: Sexually transmitted diseases: treatment guidelines, 2006. MMWR 55 (RR11):1(2006)

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# Neurosyphilis, 2007

**Latest CDC guidelines (August 2006):**

**<http://www.cdc.gov/std/treatment/>**

**49 MSM (LA, SD, Chicago, NYC) meeting CDC criteria for early neurosyphilis**

**most also HIV+**

**1.7% risk for symptomatic neurosyphilis with early syphilis in this group**

Lee MA et al: Symptomatic Early Neurosyphilis Among HIV-Positive Men Who Have Sex with Men --- Four Cities, United States, January 2002--June 2004, MMWR (2007)

[http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5625a1.htm?s\\_cid=mm5625a1\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5625a1.htm?s_cid=mm5625a1_e)

**Cases continue to increase nationwide, but decrease in SF the past 2 years accompanied by a fall in neurosyphilis.**

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## HIV+ Man with Neurosyphilis & Persistently Abnormal CSF

*48 y/o homeless HIV+ man with prior alcohol withdrawal seizures c/o numbness, pain & weakness in his legs for 3 weeks*

- Began after bicycle accident—scalp laceration sutured & left arm cellulitis treated at outside hospital
- ? Bowel/bladder incontinence, minor tingling in his hands, no neck/back pain

**Exam:** tremulous, disheveled

- Anisocoria (R>L), no nystagmus
- Normal strength, generally hyperreflexic, including AJ, toes down
- Allodynia to thighs, decreased vibration in feet
- No ataxia

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## Neuropathy & EtOH Withdrawal

*Neuropathy due to EtOH +/- HIV*

Benzodiazepines, thiamine; antibiotics for UTI  
CD<sub>4</sub> 108, VL 55K, RPR 1:1024

**CSF:**

Protein 48, glucose 44 (serum 93)

#1: 10 rbc, 2 wbc

#4: 14 rbc, 5 wbc

VDRL 1:16

**Rx:** High-dose IV PCN G for 2 weeks

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# Neurosyphilis

*Symptomatic or asymptomatic?*

*Improving serologies, persistent pleocytosis:*

time (months)	RPR	protein	glucose	wbc #1	wbc #4	CSF-VDRL	CD <sub>4</sub>
0	1:1028	44	48	2	5	1:16	108
→ 6	1:2048	45	48	13	11	1:8	168
12	1:256	38	54	3	2	1:4	
18		48	58	6	4	1:4	
→ 24		47	56	11	13	1:4	108
34	1:128	39	57	6	3	1:128	186

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## Sore Feet & Syphilis: Some Perspectives

*Neuropathy is the predominant HIV-related neurologic complication in the US.*

- New risk factors: ? PIs, age, but not HCV (yet)
- Treatment trial results pending

*Neurosyphilis, symptomatic & asymptomatic, remains a challenging clinical problem in HIV+ patients.*

- In addition to the usual limits of serologic testing, CSF is difficult to interpret in the setting of HIV.
- Rising incidence of syphilis in the US, particularly among MSM

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