Herpes Simplex Virus

PCR is the test · and the one presentation you must never wait on is encephalitis

Start acyclovir
on suspicion

⚠ SUSPECTED HSV ENCEPHALITIS: START IV ACYCLOVIR IMMEDIATELY

Do not wait for the PCR, the MRI or the lumbar puncture. Untreated mortality is around 70%, and outcome depends almost entirely on how early treatment starts. **Acyclovir 10 mg/kg IV every 8 hours** (dosed on ideal body weight, adjusted for renal function) **for 14 to 21 days**. Suspect it with **fever, confusion, personality or behavioral change, seizures, or aphasia**; MRI shows **temporal and inferior frontal** involvement. **A normal early CSF PCR does not exclude it:** if suspicion is high, continue acyclovir and repeat the PCR after 3 to 7 days. **Hydrate well**, since acyclovir causes crystal nephropathy.

THE PRESENTATIONS *the same virus wearing very different clothes*

Presentation	What to know
Orolabial *usually HSV-1*	Primary **gingivostomatitis** in children with fever and diffuse painful ulcers, then recurrent **cold sores** with a tingling prodrome. Recurrences are triggered by sunlight, fever and stress
Genital *HSV-2, increasingly HSV-1*	**Painful grouped vesicles then shallow ulcers**, with tender lymphadenopathy and dysuria. **Painful is the discriminator from the syphilitic chancre.** First episodes are far more severe and more often systemic. **Type the virus**: HSV-1 genital disease recurs much less often, which changes the counseling
Herpetic whitlow	Painful vesicles on a finger, classically in health workers and children who suck their thumbs. **Do not incise it**, which is the usual error when it is mistaken for a bacterial felon
Eczema herpeticum	**An emergency.** Disseminated HSV over eczematous skin: monomorphic punched-out erosions, fever, unwell. **Treat systemically and urgently**, and beware bacterial superinfection
Keratitis	**Dendritic ulcer** on fluorescein staining, with pain and photophobia. **Same-day ophthalmology, and never give topical steroids without specialist supervision**: they can drive corneal perforation. A leading infectious cause of blindness
Neonatal	Skin-eye-mouth, CNS, or disseminated disease. **Highest risk when the mother acquires primary infection late in pregnancy**, and it is frequently non-specific, so a septic-looking neonate gets acyclovir empirically

DIAGNOSIS *and the two tests that no longer earn their place*

PCR IS THE TEST

PCR of a swabbed lesion, unroofing a vesicle to sample the base, or of CSF for encephalitis. Fast and by far the most sensitive. **Viral culture is much less sensitive**, especially once lesions crust, and delays the answer.

SEROLOGY HAS A NARROW ROLE

Type-specific IgG can confirm established infection in an asymptomatic partner or a recurrent unexplained syndrome. **It cannot diagnose an acute lesion**, since seroconversion lags, and **IgM is unreliable** and should not be ordered.

THE TZANCK SMEAR IS OBSOLETE

It shows multinucleated giant cells but **cannot distinguish HSV from VZV** and is far less sensitive than PCR. If a rapid answer is needed and PCR is unavailable, **direct fluorescent antibody** at least types the virus.

TREATMENT *the regimen depends on whether it is first, recurrent or being prevented*

Situation	Valacyclovir	Acyclovir
First episode, genital	**1 g twice daily for 7 to 10 days**	**400 mg three times daily for 7 to 10 days.** Extend if healing is incomplete
Recurrent episode	**500 mg twice daily for 3 days**, or 1 g daily for 5 days	**800 mg three times daily for 2 days**, or 800 mg twice daily for 5 days
Suppression	**500 mg to 1 g daily**	**400 mg twice daily.** Consider with 6 or more recurrences a year, severe episodes, or to **reduce transmission to a partner**
Severe or disseminated, immunocompromised	**Acyclovir 5 to 10 mg/kg IV every 8 hours**, stepping down to oral once improving. Treat until lesions have healed rather than for a fixed course	

Episodic treatment only works if it starts early. Give the patient a prescription to keep at home so they can start **within the prodrome or the first 24 hours**; started later it does very little, which is the usual reason patients report the drug "does not work". **Adjust every regimen for renal function**, and note famciclovir is an equivalent alternative throughout.

WHEN THE GENITAL ULCER IS NOT HSV *pain and number narrow it fast*

Cause	The ulcer	What settles it
HSV	**Multiple, small, PAINFUL**, grouped vesicles then shallow ulcers, often recurrent	**PCR of the lesion base.** Recurrence in the same site is highly suggestive
Syphilis	**Single, indurated, PAINLESS**, clean base	**RPR plus a treponemal test.** Painless plus indurated should trigger syphilis testing even when it looks atypical
Chancroid	**Deep, ragged, painful**, with suppurative lymphadenitis that can form a draining bubo	**Haemophilus ducreyi**. Rare in the US, but consider it in the painful-ulcer-plus-bubo picture
Lymphogranuloma venereum	A **transient painless ulcer** that is usually gone by presentation, followed by prominent lymphadenopathy or **proctocolitis**	**Chlamydia trachomatis** serovars L1 to L3. Consider it in proctitis in men who have sex with men, and note it needs **doxycycline for 21 days**, longer than ordinary chlamydia
Non-infectious	Recurrent oral **and** genital ulcers, or an ulcer recurring at the same site after a drug	**Behcet disease** and **fixed drug eruption**. Both are missed when every genital ulcer is assumed to be infectious

PEARLS & PITFALLS

- **Acyclovir resistance is essentially confined to the immunocompromised.** Suspect it when lesions fail to heal on adequate therapy in a transplant or advanced HIV patient, and treat with **foscarnet**, which does not need viral thymidine kinase.
- **Genital HSV in pregnancy:** suppression from around 36 weeks reduces recurrences and the need for cesarean delivery, and **active lesions or prodromal symptoms at labor are an indication for cesarean** to prevent neonatal disease.
- **Recurrent aseptic meningitis is HSV-2 until proven otherwise** (Mollaret meningitis), and it is easily missed because the episodes are self-limiting and the patient looks well between them.
- **Counseling matters as much as the prescription.** Asymptomatic viral shedding transmits infection, so condoms reduce but do not eliminate risk. Suppressive therapy plus condoms is the combination to recommend to serodiscordant couples.

References: CDC Sexually Transmitted Infections Treatment Guidelines, genital herpes section · IDSA practice guidelines for the management of encephalitis · standard antiviral prescribing references.

Educational aid; verify against current guidance, local formulary and patient factors.

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