VARICELLA INFECTION

What kind of virus is it? How does it get around?
- Herpesvirus (similar to other herpesviruses such as HSV-1, HSV-2, CMV and EBV)
  - Icosahedral ds DNA core, surrounded by lipoprotein envelope
  - No viral DNA or RNA polymerase
  - Viral DNA enters cell nucleus and uses host RNA polymerase to make DNA polymerase and tyrosine kinase protein which then replicates viral DNA, new virion buds off with nuclear membrane.
  - Transmitted through respiratory droplets or direct contact with non-crusted lesions. Virus enters through mucosal or conjunctival surfaces and travels to local lymph nodes for primary replication, then proceeds through initial viremia to invade the spleen and liver for secondary replication, followed by secondary viremia which distributes virus to skin to create a rash.
  - After the primary clinical infection of acute chicken pox, virus withdraws to sensory ganglia of CN V, VII, VIII, IX, X or dorsal root ganglia of peripheral afferent sensory nerves.
  - Virus remains latent in these ganglia until conditions that impair cell mediated immunity (advanced age, malignancies, AIDS, s/p transplant, immunosuppressive therapy with chemotherapy or steroids), occur which allow its reactivation, replication and travel outwards along the sensory neurons.
  - Reactivation of infection results in inflammation and necrosis of ganglia which spreads peripherally along sensory neurons to epidermis to form rash and also centrally into spinal cord motor neuron cells (anterior horn), posterior column tracts; as well from cranial nerves into brain.

How common is it?
- 90 % chicken pox cases in children, thus 10 % adults susceptible to infection
- Endemic in population at large, but epidemics in winters and early spring in temperate climate
- Highly contagious with attack rate of 70-90% in susceptible individuals
- 4 million cases a year, 4000 hospitalizations, 100 deaths (55% of these in adults)
- 300,000 cases of zoster a year

Primary varicella infections: Chicken pox
- Incubation period 10-21 days, prodromal non-specific symptoms of fever, malaise, nausea, headache,
- Typical rash described as small (5mm-10mm) erythematous macules that quickly progress into papules, then vesicles and ultimately pustules that crust over; rash begin on face and trunk and spreads outwardly and is extremely pruritic. Hallmark of rash: successive crops of lesions in different stages which lasts 3-5 days.
- Systemic complications include:
  - Encephalitis, meningitis, myelitis, hepatitis, acute GN, thromocytopenia, coagulopathy, myocarditis and arthritis.
  - Pneumonia- 1/500 adults, most lethal complication, onset within 3-5 days of rash, presents with cough and tachypnea, CXR reveals diffuse nodules or interstitial infiltrates, risk factors associated with severe disease include pregnancy, smoking and chronic lung disease.
  - Bacterial superinfection of skin with staph and strep species-impetigo, cellulitis, necrotizing fasciitis.

Secondary varicella infections: zoster
- Prodromal severe, sharp, lancinating pain in distribution of sensory dermatome followed by the eruption of small erythematous macules along the same dermatome, that progress into vesicle and pustules, lasting 14 days.
- Dermatomal distribution is hallmark of disease: most commonly from thoracic or trigeminal ganglia
  - Ophthalmic zoster: first branch of CN V, 7% cases, 20-70 % associated with severe ocular complications of keratitis, scleritis, uveitis; look for Hutchinson’s sign (lesion at tip of nose)
  - Maxillary and mandibular zoster: CN V branches 1 and 2, look for osteonecrosis of mandible and exfoliation of teeth.
• **Ramsey Hunt syndrome:** CN VII and VIII, associated with tinitus, vertigo, hearing loss, facial palsy, anterior 2/3 of tongue taste abnormalities; look at external ear canal and TM for vesicles.

• **Rarer manifestations:** CN palsies (CN III), cervical and lumbar zoster associated with weakness.

• **Zoster sine herpete:** dermatomal distribution of pain without antecedent rash;

• **Complications:**
  - Dissemination: more than 20 vesicles just outside, usually adjacent to affected dermatome, 10 case associated with visceral involvement
  - Post herpetic neuralgia: very common, 10-15% incidence increases with age, affects >50% patients > 60 yo, severe pain syndrome that persists more than 6 weeks post zoster resolution.

**Varicella CNS Infections**

• **Myelitis:** onset 1-2 weeks post primary or secondary infection, presents with paraparesis and sensory level decreased sensation and incontinence; usually self-limited in immunocompetent patients.

• **Large vessel encephalitis:** uncommon, seen in elderly patients, onset is weeks to months post zoster infection; patients present with stroke like syndromes with infarcts, pathology reveals a granulomatous vasculitis, 25% mortality.

• **Small vessel encephalitis:** most common in immunocompromised patients; onset weeks to months post zoster infection; patients present with chronic progressive encephalitis

• **Meningitis:** less common, but seen in primary and secondary infections.

**How to Diagnose?**

• Vesicle specimen: Tzanck smear reveals multi nucleated giant cells with intranuclear inclusions on acidophilic stains (not available at SFGH, also positive with HSV), direct immunofluorescence antibody detects VZV antigen, viral culture.

• CSF: PCR (1 ml send out lab, takes more than one week for results), viral culture

• Serology: IgG specific antibodies detected within 4-5 days of infection, good to check immune status.

**Treatment**

• **Primary infection:**
  - Uncomplicated infection in immunocompetent: NO indication for anti-virals post >24 hrs.
  - Immunocompromised patients or complicated infections (pulmonary and CNS): 10 mg/kg IV acyclovir q8h.

• **Secondary infection:**
  - Uncomplicated dermatomal zoster: PO acyclovir 800 mg 5xd, valacyclovir 1000mg TID, famciclovir 500 mg TID; all agents decrease formation of new lesions and reduces acute pain; controversial evidence if decrease PHN.
  - Complicated zoster: IV acyclovir 10 mg/kg Q8H for 7-14 days, prednisone 30 mg BID slow taper for 21 days, one DBRCT reports decrease in in acute pain and rash resolution.
  - PHN: TCA’s nortriptyline or amitriptyline at 25-100 mg relieve pain, possibly gabapentin and carbamezapine as well.

**Vaccination**

• Live attenuated vaccine; efficacy reported in NEJM 3/2001 as significant decrease in incidence of infection and severity of symptoms, CDC 85% effective in preventing infections, 100% in preventing serious disease.

• ACP recommends universal vaccination to children between 12-18 months, all susceptible children by 13 years of age; and immunocompetent adults who are in close contacts of people at risk for serious complications (such as health care workers, workers in day care, college students, family contacts of immunocompromised individuals).

**References:**


