Herpes Viral Infections of the Central and Peripheral Nervous System

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Viruses in May, 2010

Or: as Bill says

- Ramsay Hunt Syndrome and post zoster syndromes
  - Pathogenesis and Treatment

Herpes Virus and the Nervous System

- Herpes Zoster
  - Primary infection
  - Post herpetic neuralgia
  - Ramsay-Hunt syndrome
  - Vasculitis
  - Myelitis
  - Cerebellitis
- Herpes Simplex
  - Primary infection
  - Encephalitis
  - Transverse Myelitis

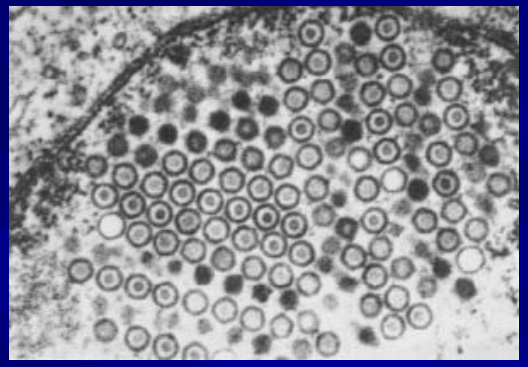
Varicella-Zoster Infection

- Exclusively human neurotropic alpha-herpesvirus.
- Primary infection causes varicella (chickenpox)

- Then: virus latent in cranial nerve ganglia, dorsal root ganglia, and autonomic ganglia along entire neuraxis

- Years later: reactivation of VZV to cause a wide range of neurological disorders

- Herpes simplex virions in nucleus of an infected cell



ZOSTER

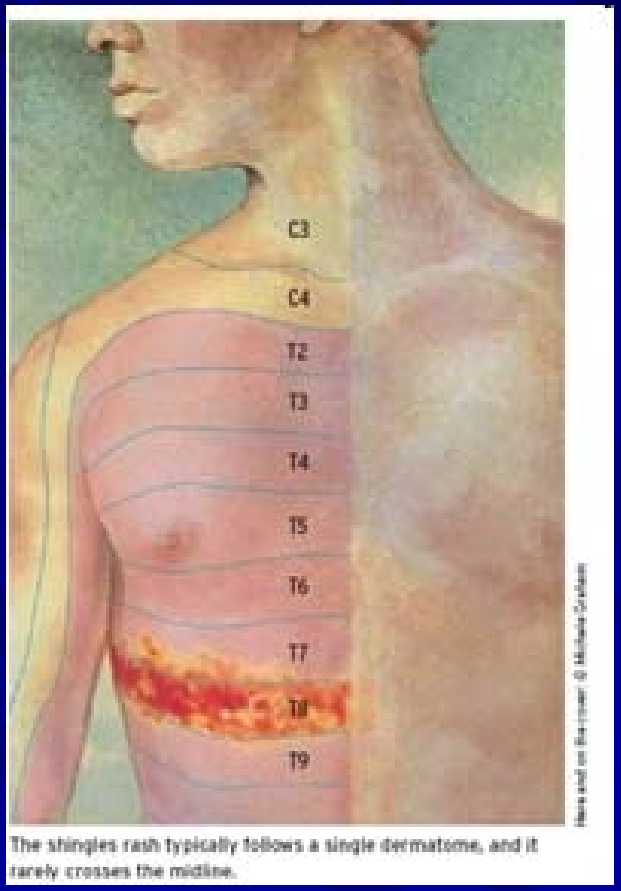
- 1. Ramsay-Hunt Syndrome
- 2. Post herpetic neuralgia
- 3. Vasculopathy
- 4. Myelopathy
- Retinal Necrosis
- 5. Cerebellitis

Herpes Zoster

- Any level of neuraxis
- Most common chest

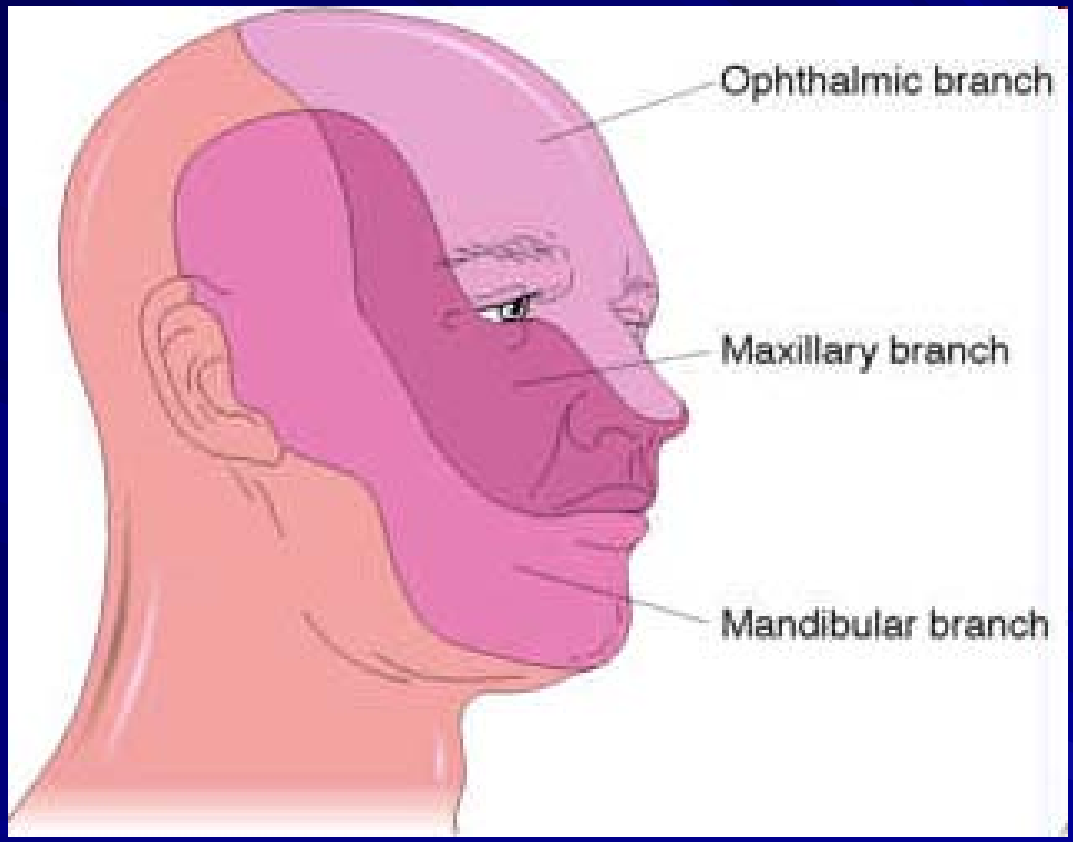
Herpes zoster lesion along the thoracic dermatome seen on the 6 th day of the development of lesion

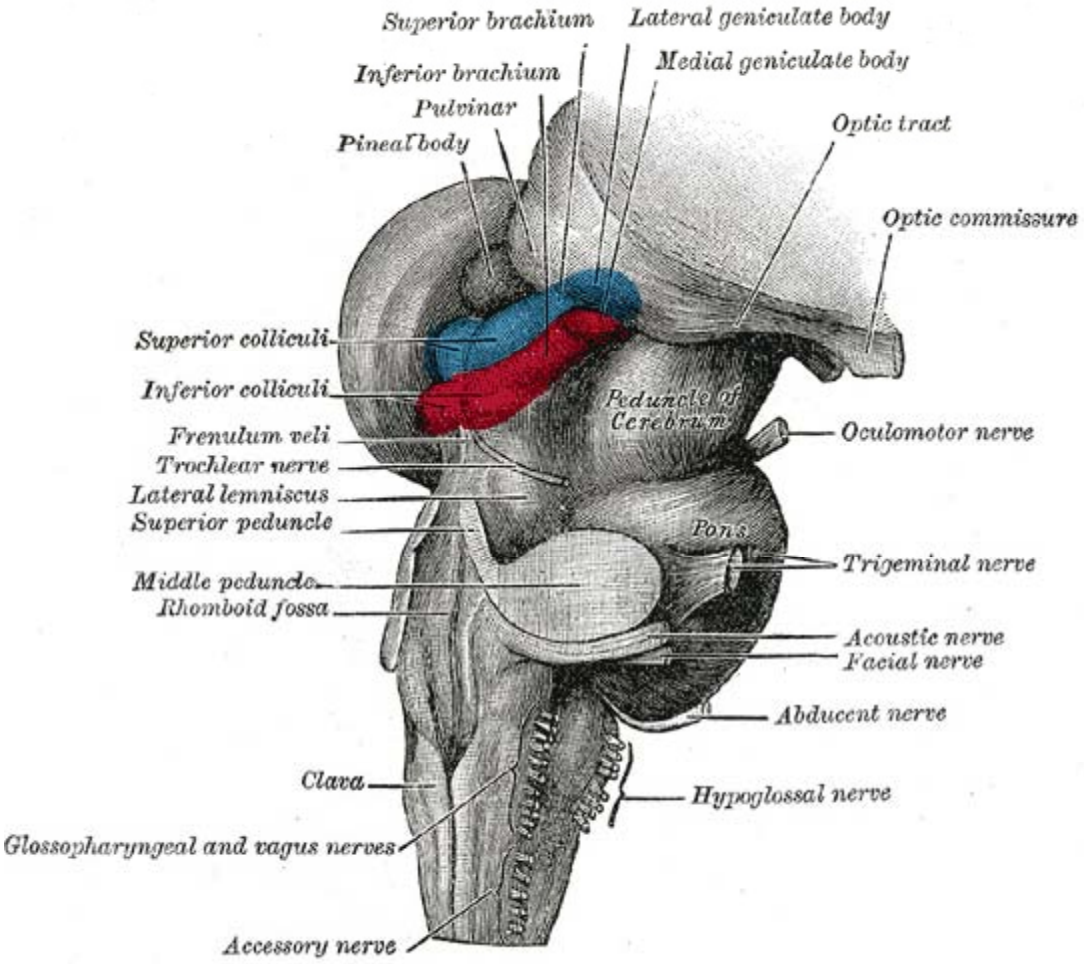
Figure 2: Healed lesion of herpes zoster seen on the 3 rd week of the illness

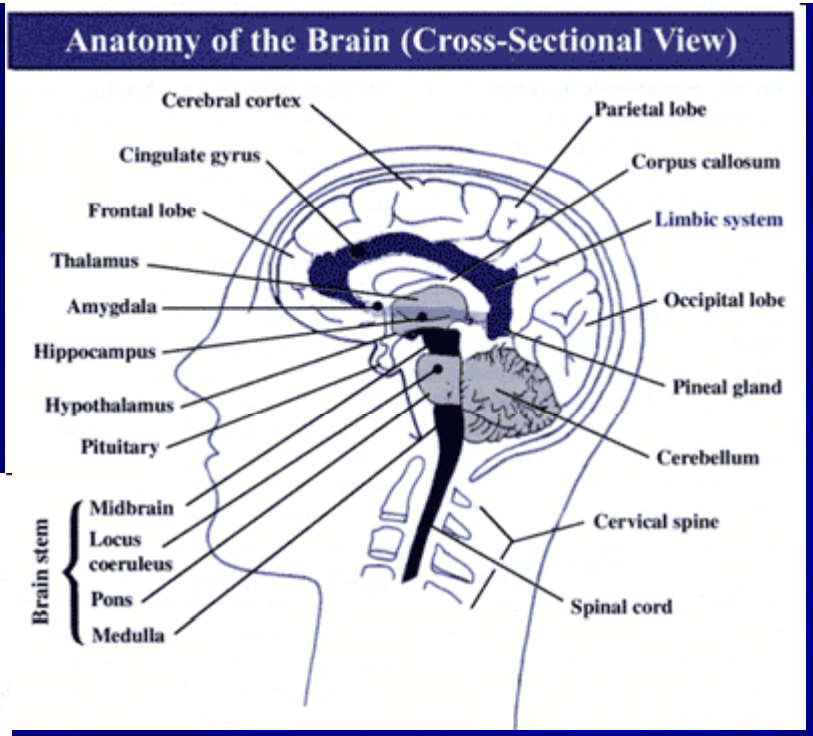


The shingles rash typically follows a single dermatome, and it rarely crosses the midline.

- Then face (**ophthalmic div of V**)
  - Zoster keratitis
  - Hutchinson's sign
  - Eye signs (ophthalmoplegia esp. of cranial nerves III and VI)


Ophthalmic branch
Maxillary branch
Mandibular branch


Superior brachium
Lateral geniculate body
Inferior brachium
Medial geniculate body
Pulvinar
Pineal body
Optic tract
Optic commissure
Superior colliculi
Inferior colliculi
Peduncle of Cerebrum
Oculomotor nerve
Frenulum veli
Trochlear nerve
Lateral lemniscus
Superior peduncle
Pons
Trigeminal nerve
Middle peduncle
Rhomboid fossa
Acoustic nerve
Facial nerve
Abducent nerve
Clava
Hypoglossal nerve
Glossopharyngeal and vagus nerves
Accessory nerve


Anatomy of the Brain (Cross-Sectional View)
Cerebral cortex
Parietal lobe
Cingulate gyrus
Corpus callosum
Frontal lobe
Limbic system
Thalamus
Amygdala
Occipital lobe
Hippocampus
Pineal gland
Hypothalamus
Pituitary
Cerebellum
Brain stem
Midbrain
Locus coeruleus
Pons
Medulla
Cervical spine
Spinal cord

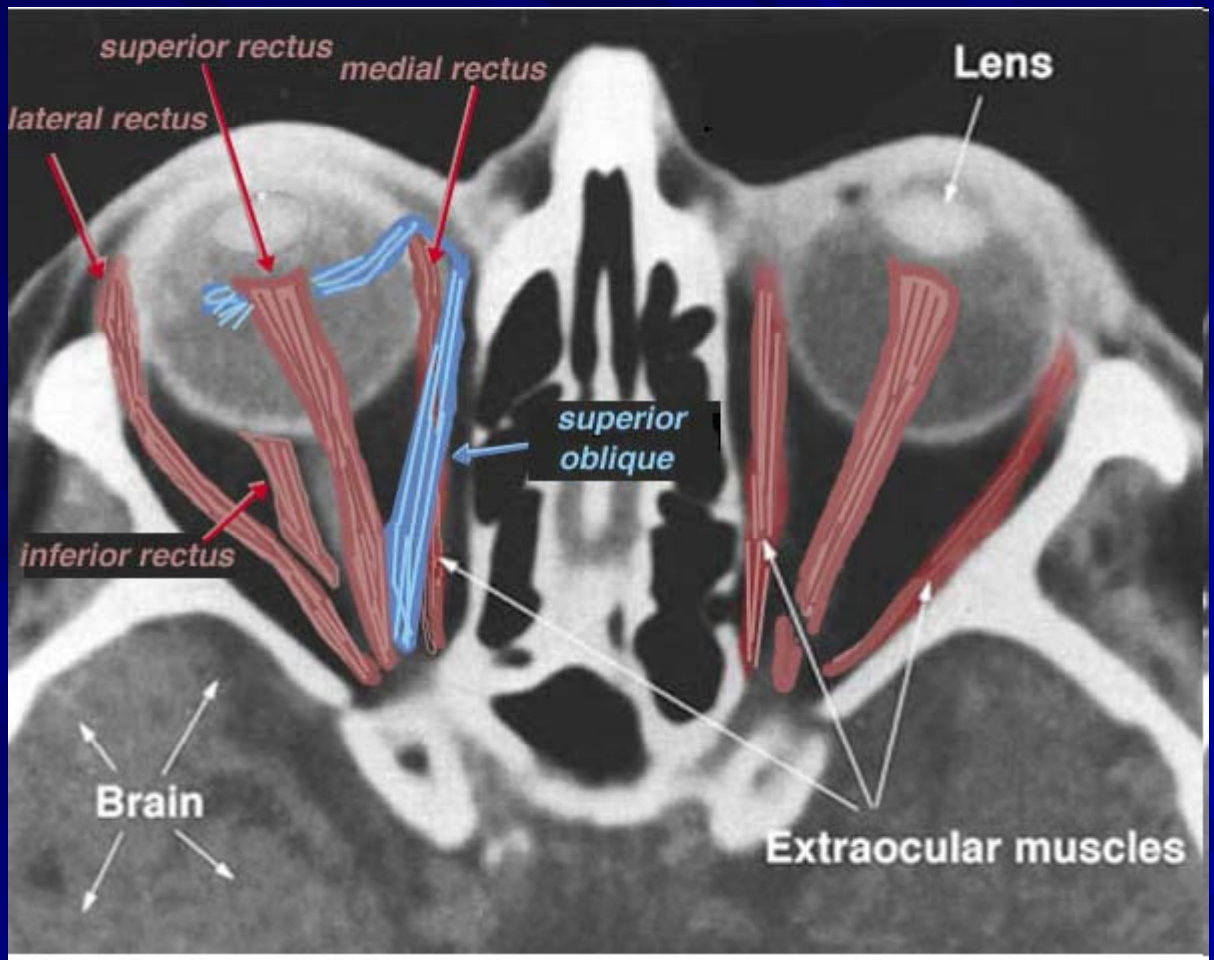
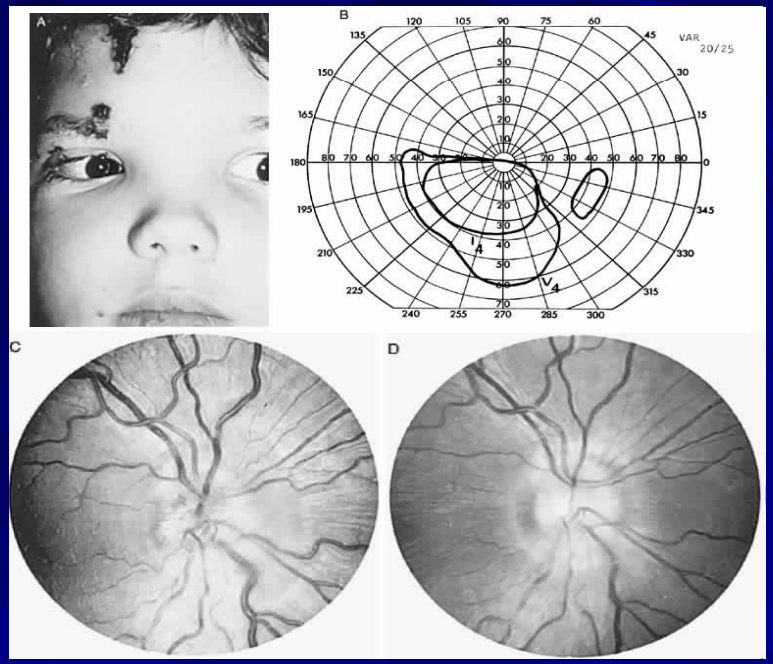


Fig. 3. CT Horizontal transverse scan at the plane of the brain, orbits and nose of the human head.

Anterior segment photograph of the left eye showing the superotemporal area of scleromalacia.



Herpes zoster optic neuritis.

- **A.** Typical vesiculation in the ophthalmic division of the trigeminal nerve.
- **B.** Light perception only, returned to 20/25 vision and field as indicated.
- **C.** Acute disc swelling.
- **D.** Disc 5 days later, after orbital and systemic steroid therapy.

Ramsay-Hunt Syndrome

- Peripheral facial weakness and zoster oticus=Ramsay-Hunt
- Zoster affects the VII cranial nerve (geniculate ganglion) with rash on external auditory canal (zoster oticus) or pinna
- Also seen with rash on tympanic membrane, or ipsilat 2/3 of tongue, or hard palate
- Often also have tinnitus, vertigo, hearing loss, nausea, vomiting, nystagmus (ie not only geniculate ganglion but also VIII is involved.
- Weakness is often more dramatic and poorer prognosis than Bells palsy

Ramsay Hunt

- 1907, James Ramsay Hunt described syndrome
- Also described dyssynergia cerebellaris myoclonica, aut rec, myoclonic epilepsy
- Geniculate ganglionitis vs polycranial neuronitis

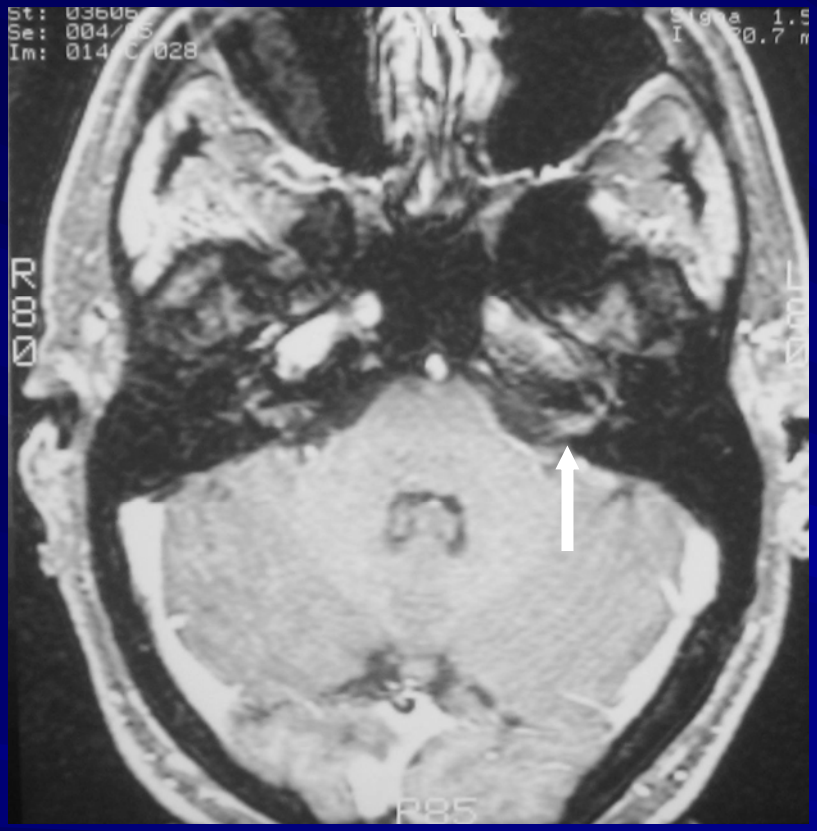
- Nervus intermedius: taste ant 2/3 tongue, and parasympathetic fibres to lacrimal, submandibular, and sublingual glands

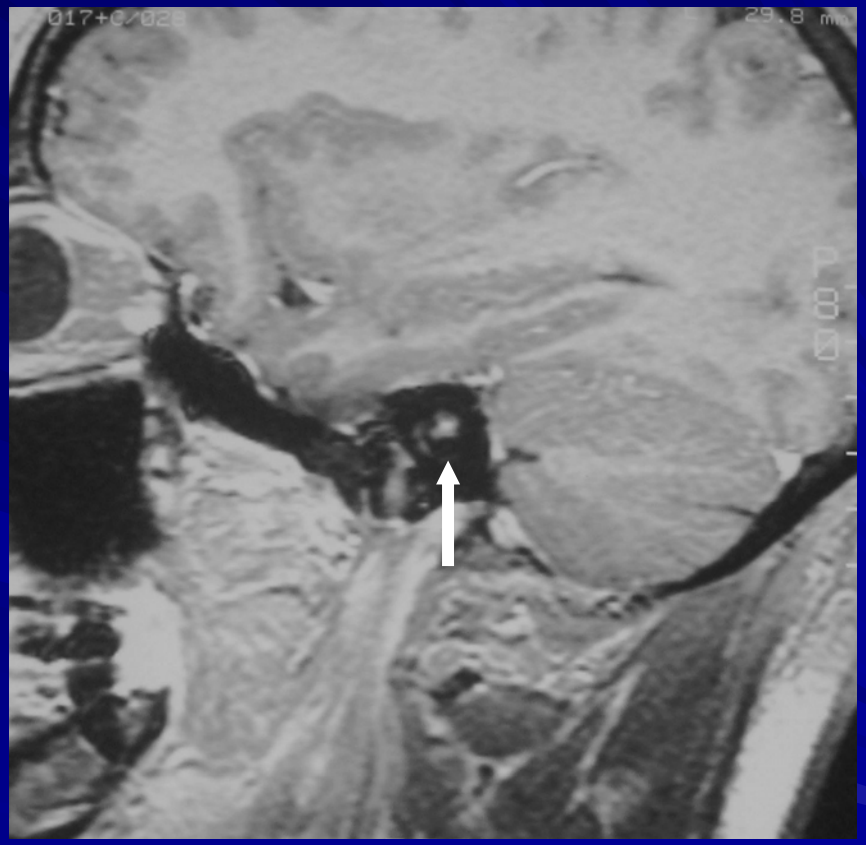
Unusual presentation of Ramsay Hunt syndrome in renal transplant patients:

Why does this happen?

- Cardinal features of zoster are:
  - Inflammation and haemorrhagic necrosis with neuritis
  - Localized leptomeningitis
  - Unilateral segmental poliomyelitis
  - Degeneration of motor and sensory roots
  - Demyelination also observed in areas of cns with microglial proliferation.

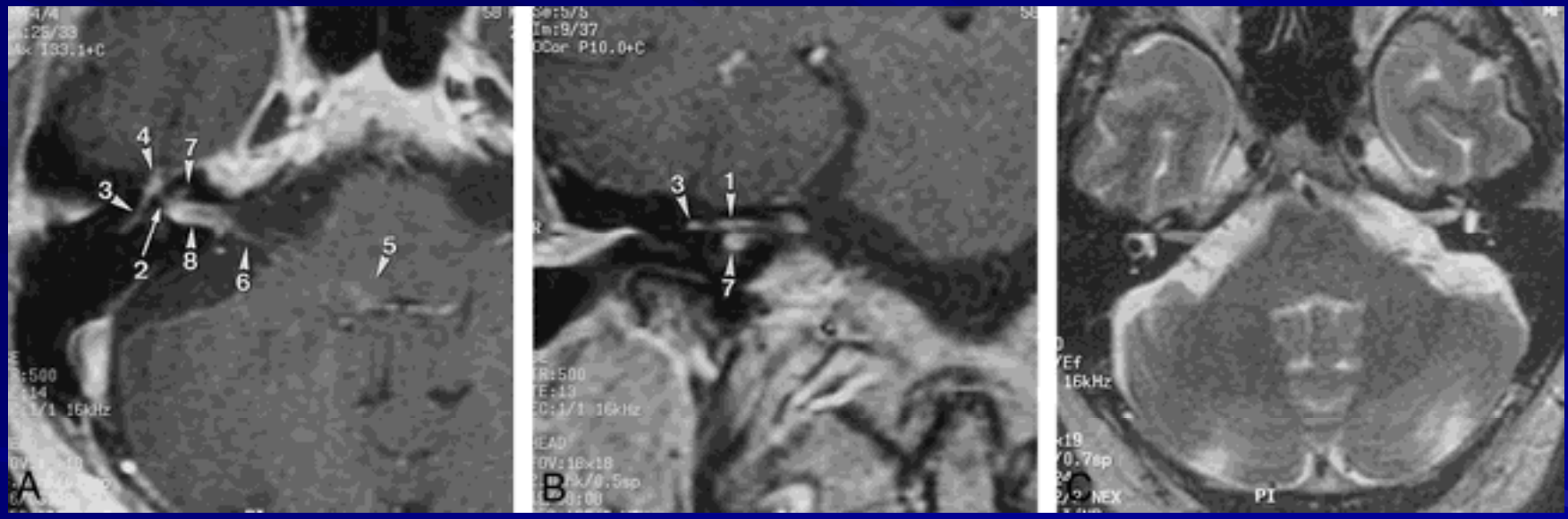
Ramsay Hunt





Enhancement 7th Nerve

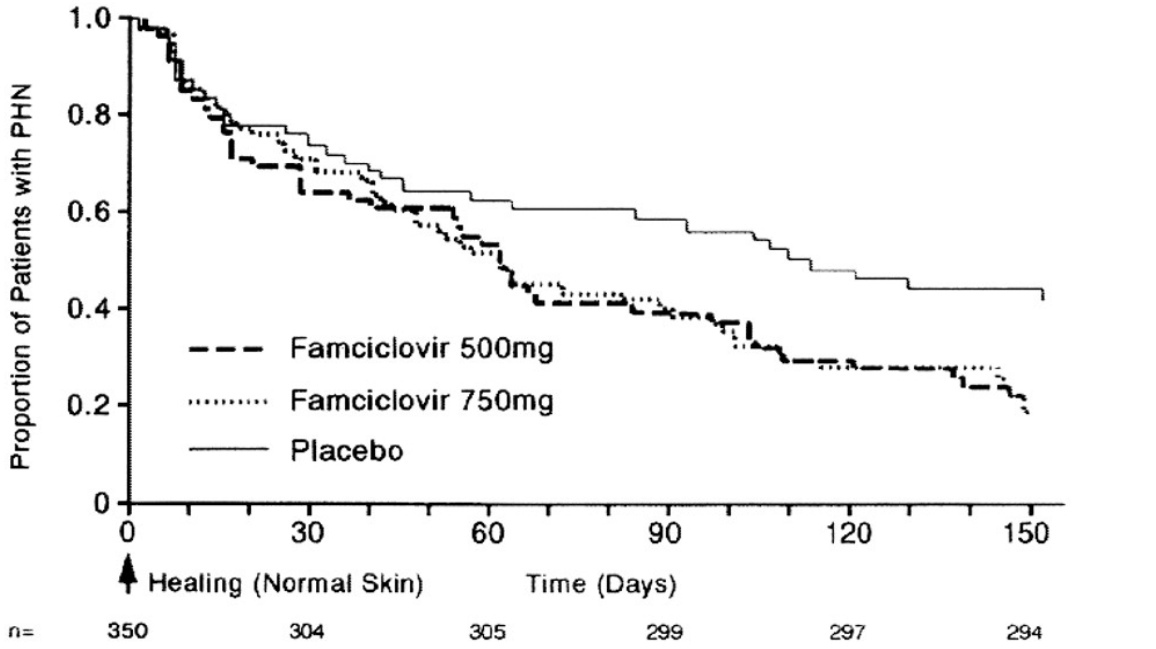
Ramsay Hunt Syndrome

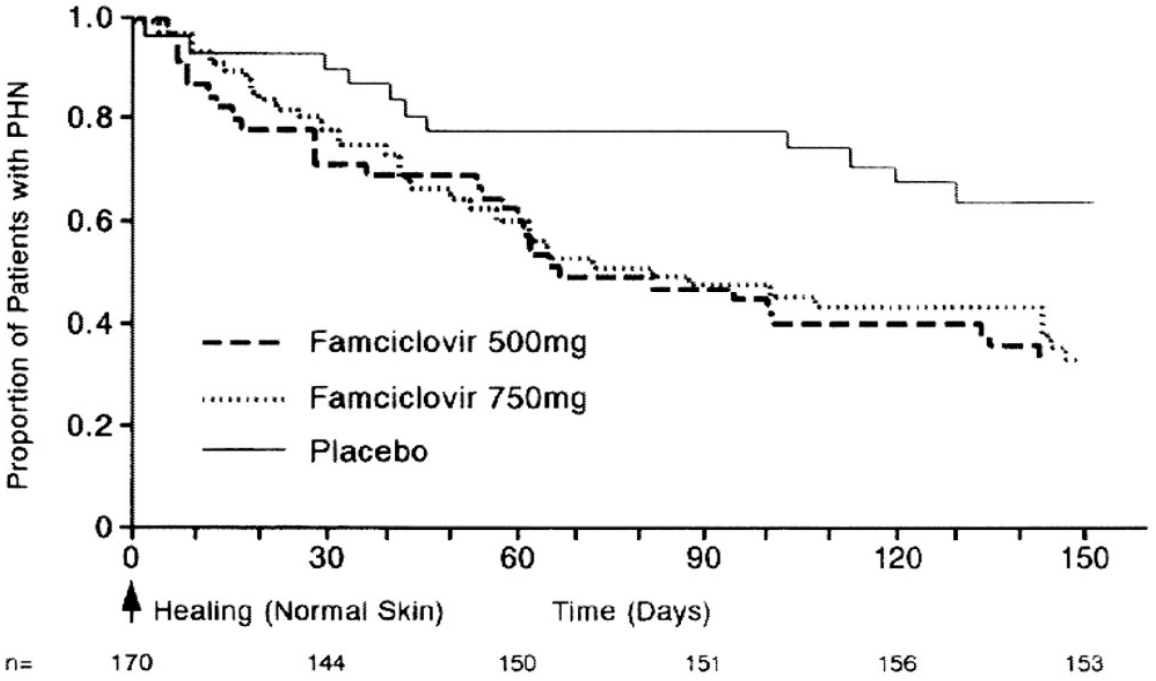


AJNR

Treatment

- Immunocompetent:
  - Analgesics
  - Antivirals: could use famciclovir 500mg tds or valacyclovir 1g tds
  - Ramsay_Hunt:
    - Antivirals +/- prednisone1mg/kg
- Immunosuppressed:
  - Intravenous antiviralagents


Proportion of Patients with PHN
1.0
0.8
0.6
0.4
0.2
0
Famciclovir 500mg
Famciclovir 750mg
Placebo
0
30
60
90
120
150
Healing (Normal Skin)
Time (Days)
n=
350
304
305
299
297
294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0
Famciclovir 500mg
Famciclovir 750mg
Placebo
0
30
60
90
120
150
Healing (Normal Skin)
Time (Days)
n=
170
144
150
151
156
153

ondary-amine TCAs				
Nortriptyline[b] or desipramine[b] (use tertiary amine TCA only if secondary amine TCA not available)	25 mg at bedtime	Increase by 25 mg/d every 3-7 d as tolerated	150 mg/d; if blood concentration of active medication and its metabolite is <100 ng/mL (mg/L), continue tritation with caution	6-8 wk with at least 2 wk at maximum tolerated dos
RIs				
Duloxetine	30 mg once daily	Increase to 60 mg once daily after 1 wk	60 mg twice daily	4 wk
Venlafaxine	37.5 mg once or twice daily	Increase by 75 mg each week	225 mg/d	4-6 wk
ium channel α_2-δ ligands				
Gabapentin[b]	100-300 mg at bedtime or 100-300 mg 3 times daily	Increase by 100-300 mg 3 times daily every 1-7 d as tolerated	3600 mg/d (1200 mg 3 times daily); reduce if impaired renal function	3-8 wk for tritration plu 2 wk at maximum dc
Pregabalin[b]	50 mg 3 times daily or or 75 mg twice daily as tolerated	Increase to 300 mg/d after 3-7 d, then by 150 mg/d every 3-7 d as tolerated	600 mg/d (200 mg 3 times or 300 mg twice daily); reduce if impaired renal function	4 wk
cal lidocaine				
5% lidocaine patch	Maximum of 3 patches daily for a maximum of 12 h	None needed	Maximum of 3 patches daily for a maximum of 12-18 h	3 wk
oid agonists[c]				
Morphine, oxycodone, methadone, and levorphanol[b]	10-15 mg morphine every 4 h or as needed (equianalgesic dosages should be used for other opioid analgesics)	After 1-2 wk, convert total daily dosage to long-acting opioid analgesic and continue short-acting medication as needed	No maximum dosage with careful titration; consider evaluation by pain specialist at relatively high dosages (eg, morphine at 120-180 mg/d; equianalgesic dosages should be used for other opioid analgesics)	4-6 wk
Tramadol[d]	50 mg once or twice daily	Increase by 50-100 mg/d in divided doses every 3-7 d as tolerated	400 mg/d (100 mg 4 times daily); in patients >75 y, 300 mg/d	4 wk

NRI = selective serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant.

3. VZV Vasculopathy

- Viral production in large or small cerebral blood vessels
- Headache, fever, delerium, TIAs and strokes

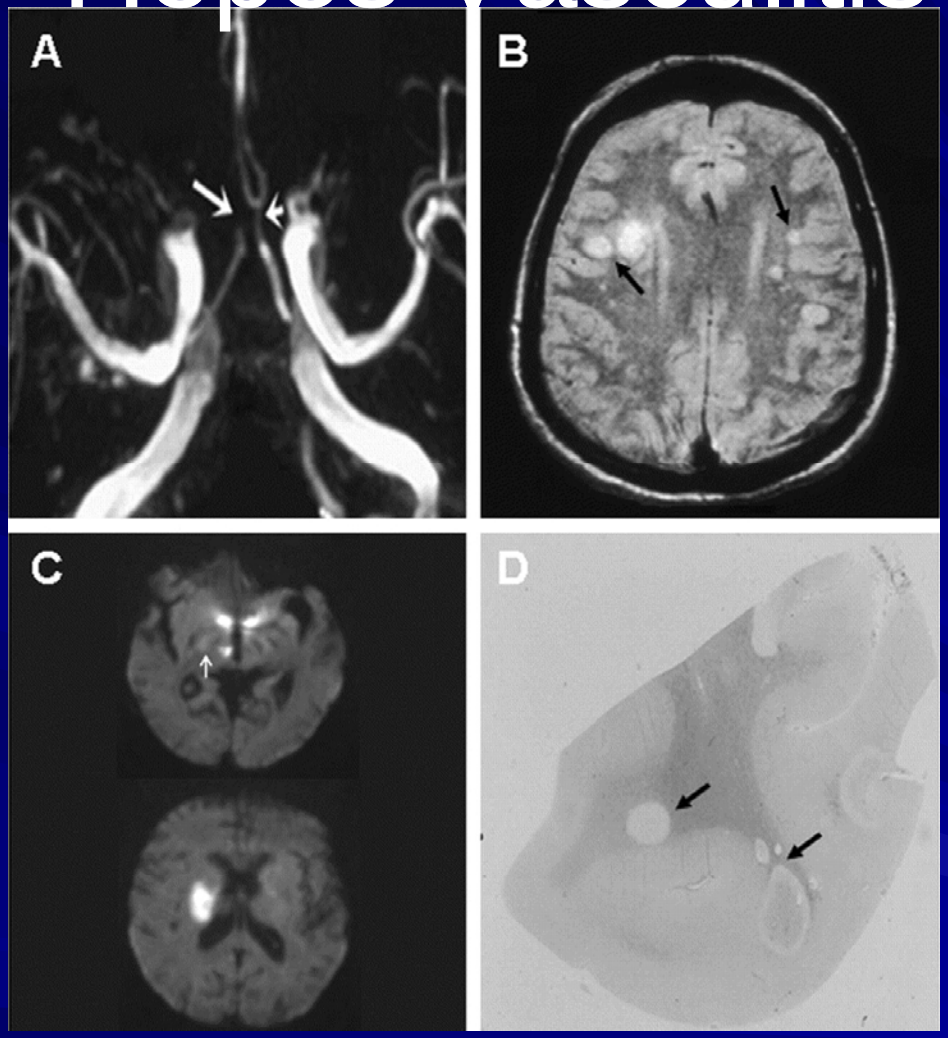
- Classic scenario: stroke in the ipsilateral middle cerebral artery, weeks or months after VZ of trigeminal nerve

- CSF: mononuclear pleocytosis
- MRI: stroke in affected territory
- Angiogram: focal stenosis

- 64 yo female
- Zoster R. trigeminal 6/12 prev
- Presented with left arm, leg weakness
- Headache
- Investigated with MRI
- Angiogram

- Treated with steroids, antiviral agents.

Hepes Vasculitis



Nagel, M. A. et al. Neurology 2008;70:853-860

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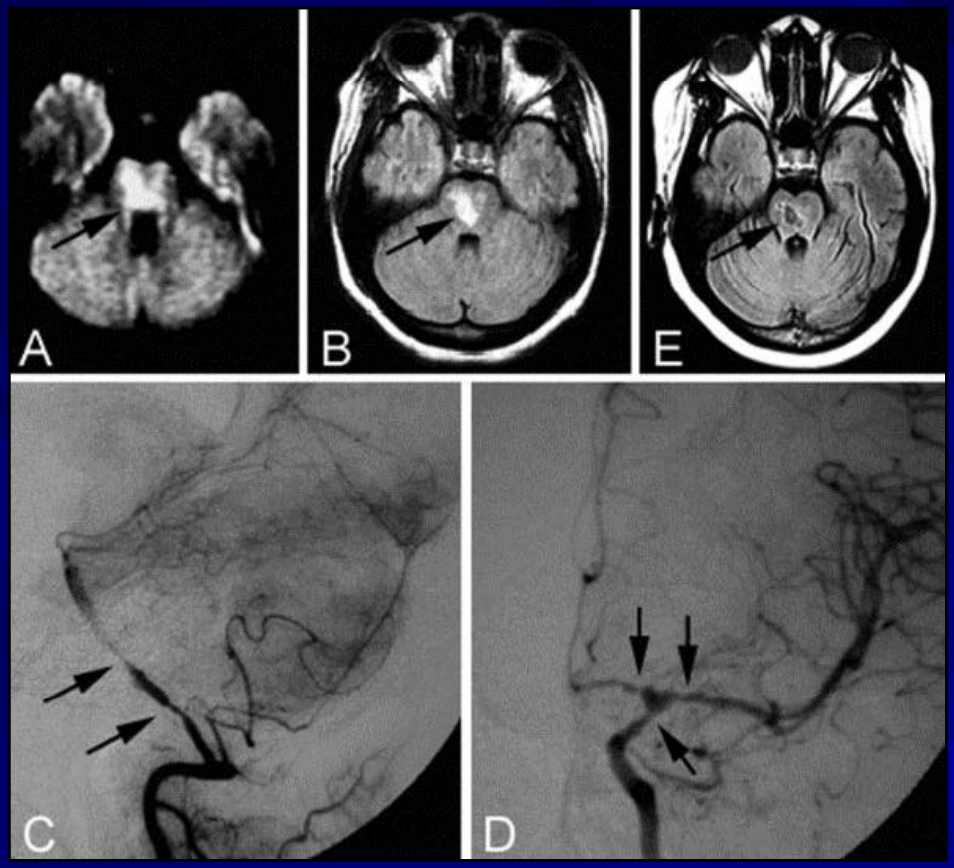


Figure Brain MRI and cerebral digital subtraction angiography (DSA)(A) Brain MRI, diffusion weighted imaging shows restricted diffusion at the level of right pons (arrow). (B) Brain MRI, initial FLAIR, with abnormal area of hyperintense signal at the level of the pons (arrow). (C) Cerebral DSA. Posterior circulation, with segmental caliber narrowing affecting distal vertebral arteries and mid-basilar artery (arrows). (D) Cerebral DSA. Anterior circulation. Segmental caliber narrowing and beading in distal left internal carotid artery, left middle cerebral artery, and anterior cerebral artery (arrows). (E) Brain MRI, follow-up FLAIR, 4 months later; area of hypointensity within the pons (arrow).

- Diagnosis:
  - Amplifiable VZV DNA or anti-VZV IgG antibodies or both in CSF
  - PCR amplifiable VZV DNA may be absent, so must always check IgG antibodies
  - Prognosis poor: mortality without treatment 25%
  - May occur without rash or months after the rash
  - Treatment: iv acyclovir

4. VZV Myelopathy

- 2 scenarios:
  - Immunocompetent
    - Monophasic, spastic paraparesis, some sensory changes, may have spincter changes
    - “postinfectious myelitis”
    - Days to weeks after VZV infection
    - CSF: mononuclear pleocytosis, elevated protein
    - Good prognosis, usually treated with steroids

Myelitis

66 yo male

Shingles of C7 region, 6 weeks before, a few vesicles, no treatment

Presented with stiffness of legs, urgency of bladder

Numbness of legs, slowly ascended to the mid thoracic region

Lasted 3 weeks

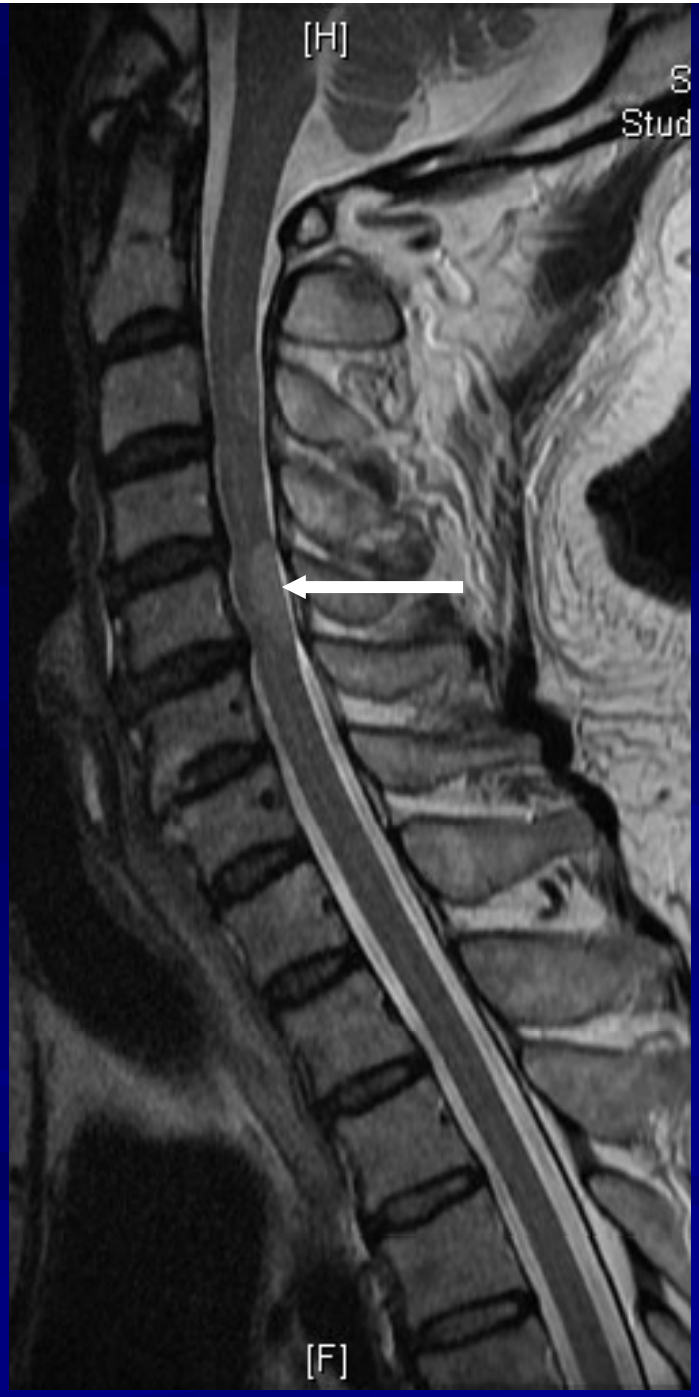
Slowly improving.

OE: brisk reflexes.

Extensor plantars

Sensory level to T2

Zoster Cord



– Immunocompromised

- Insidious, progressive myelitis, sometimes fatal
- Often HIV
- MRI: long enhancing lesions
- Frank invasion of virus into cord parenchyma
- Treatment iv acyclovir


Ex:4505
Se:5/7
Im:6/9
S120
01/25/95
L10.0+0
A
6
3
TR:3200
TE:96/Ef
4.0thk/0.5sp
W:436/L:124
I199

Cerebellitis

- In adults: most commonly seen with
  - EBV and mycoplasma
  - Also with Herpes zoster
  - Onset of ataxia of limbs and gait, dysarthria
  - Prognosis: reasonably good

Zoster sine herpete

- Pain without rash
- Reactivation of VZV
- Rare occurrence
- Detect VZV DNA and anti VZV antibody in people with
  - Meningoencephalitis
  - Myelitis
  - Cerebellar ataxia
  - Polyneuritis cranialis

Olny srmat poelpe can rae d tihs.

I cdnuolt blveiee taht I cluod aulaclty uesdnatnrd waht I was rdanieg.

The phaonmneal pweor of the hmuan mnid, aoccdrnig to a rscheearch at Cmabrigde Uinervtisy,
it deosn't mttaer in waht oredr the ltteers in a wrod are, the olny iprmoatnt tihng is taht the frist
and lsat ltteer be in the rghit pclae. The rset can be a taotl mses and you can sitll raed it wouthit a porbelm. Tihs is bcuseae the huamn mnid deos not raed ervey lteter by istlef, but the wrod as a wlohe.

Amzanig huh? yaeh and I awlyas tghuhot slpeling was ipmorantt! if you can raed tihs psas it on !!