周围神经疾病

华山医院神经科

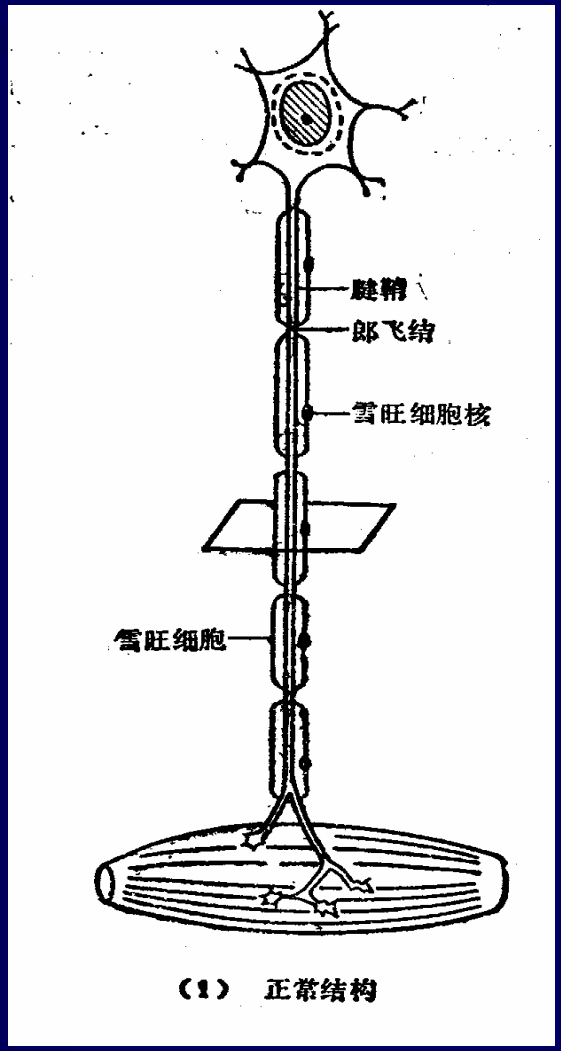
王　　毅

- 周围神经的解剖和生理
- 周围神经变性类型
- 周围神经病分类
- 颅神经疾病
  - 三叉神经痛
  - 面神经炎（**Bell's palsy**）
- 脊神经疾病
  - 急性感染性多发性神经炎
    （**Guillain-Barré Syndrome**）

周围神经解剖与生理

- 周围神经:
  - 颅神经
  - 脊神经
- 周围神经病
- 解剖生理

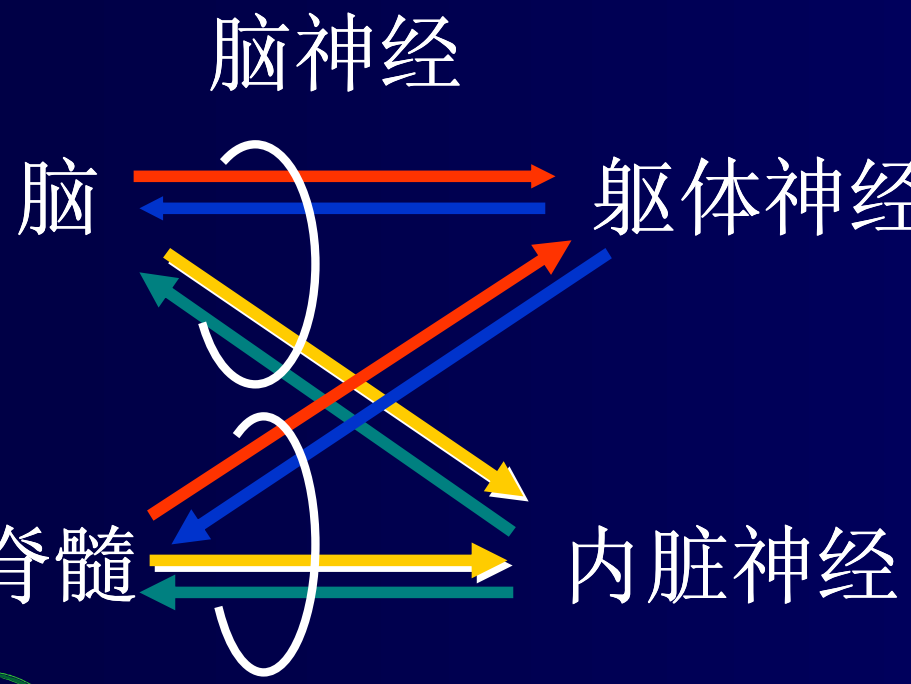
  神经纤维:
  - 有髓鞘
  - 无髓鞘纤维
  - 雪旺细胞
  - 髓鞘组成和作用



(1) 正常结构

中枢神经　　周围神经

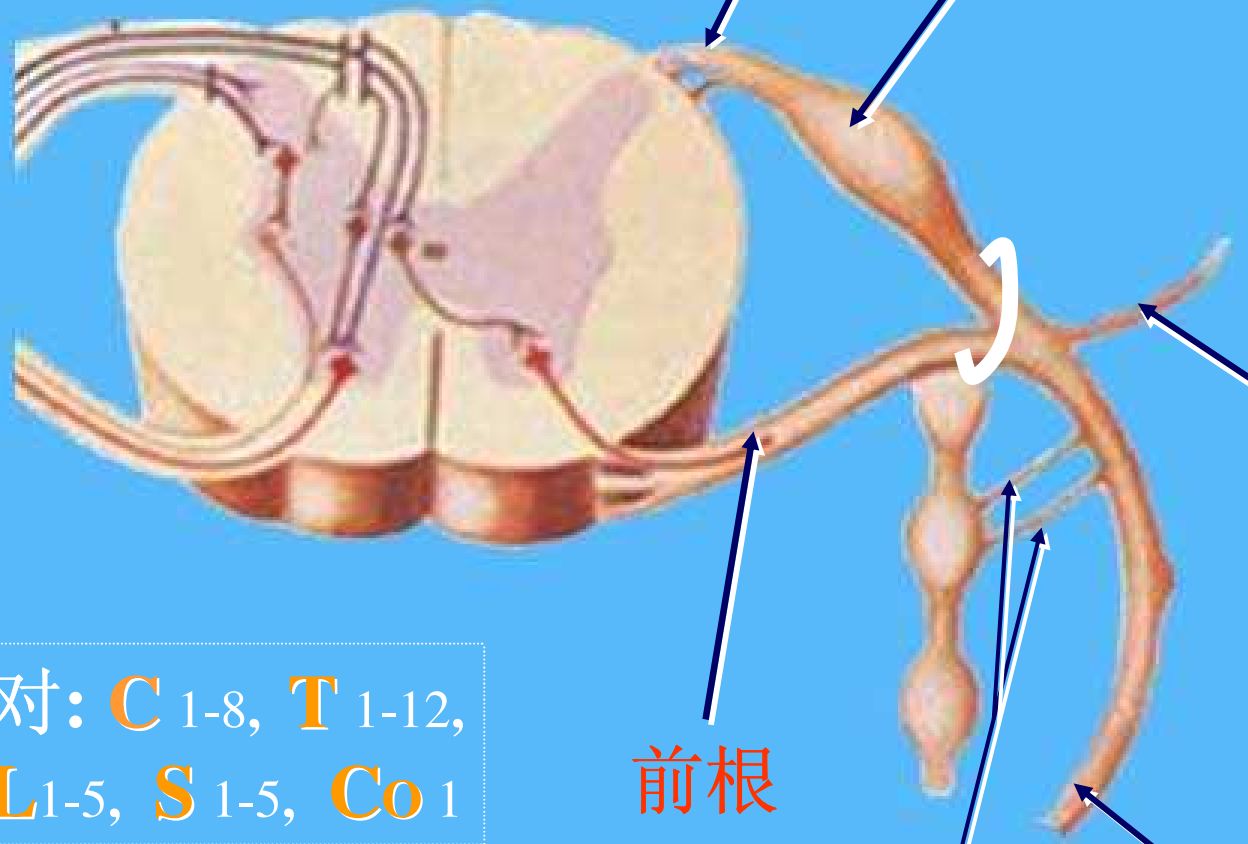
Peripheral nervous system



12对脑神经

1	嗅	不属周围神经系统
2	视	
3	动眼	中脑
4	滑车	
5	三叉	桥脑
6	外展	
7	面	
8	位听	
9	舌咽	延髓
10	迷走	
11	副	
12	舌下	

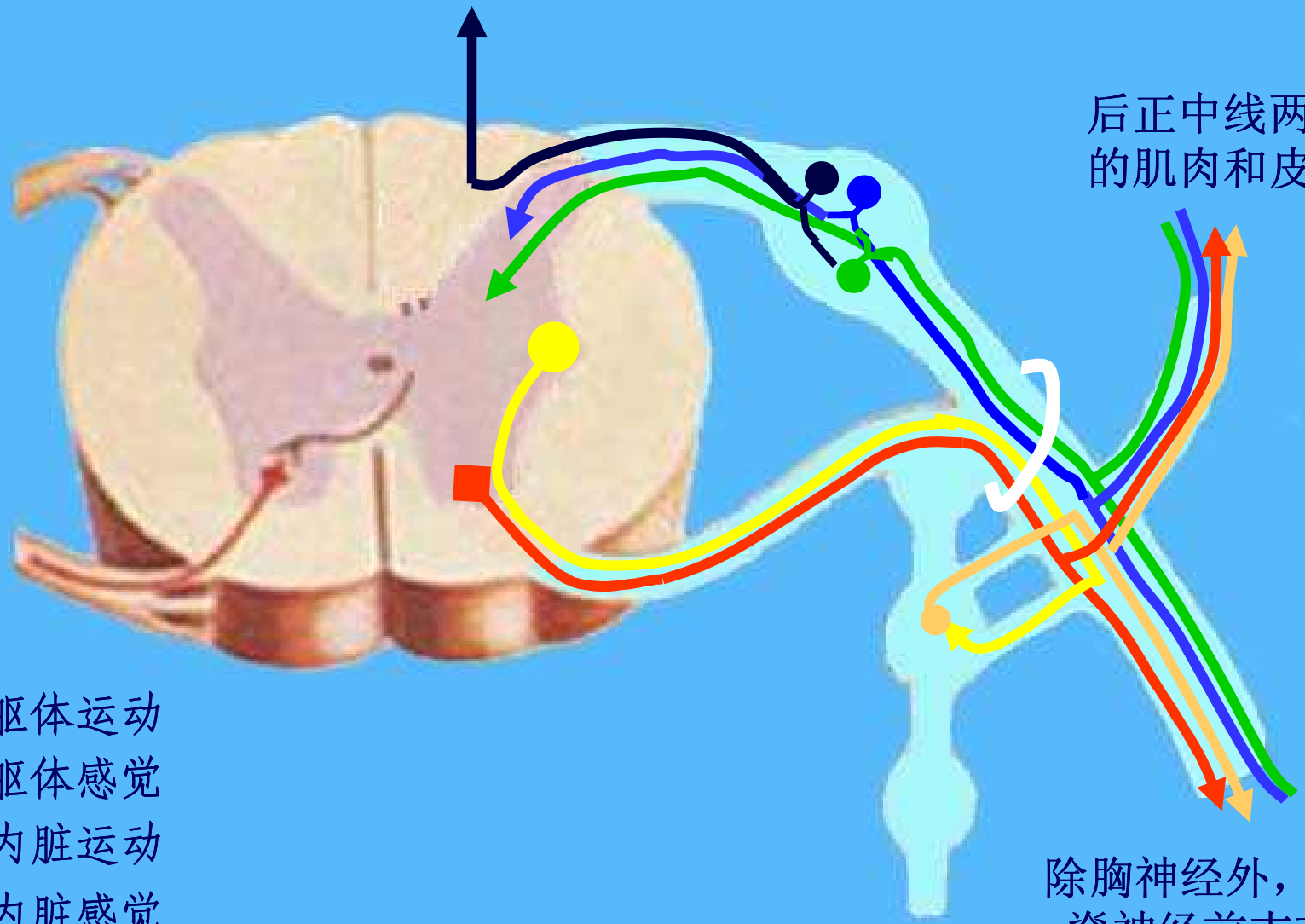
脊神经



31对：C 1-8, **T** 1-12,
L1-5, **S** 1-5, **Co** 1

- 组成
- 分支

脊神经



后正中线两侧
的肌肉和皮肤

成分

躯体运动
躯体感觉
内脏运动
内脏感觉

除胸神经外，其余
脊神经前支交织
成丛→相应部位

脊神经前支

组成

颈丛 C_1-C_4

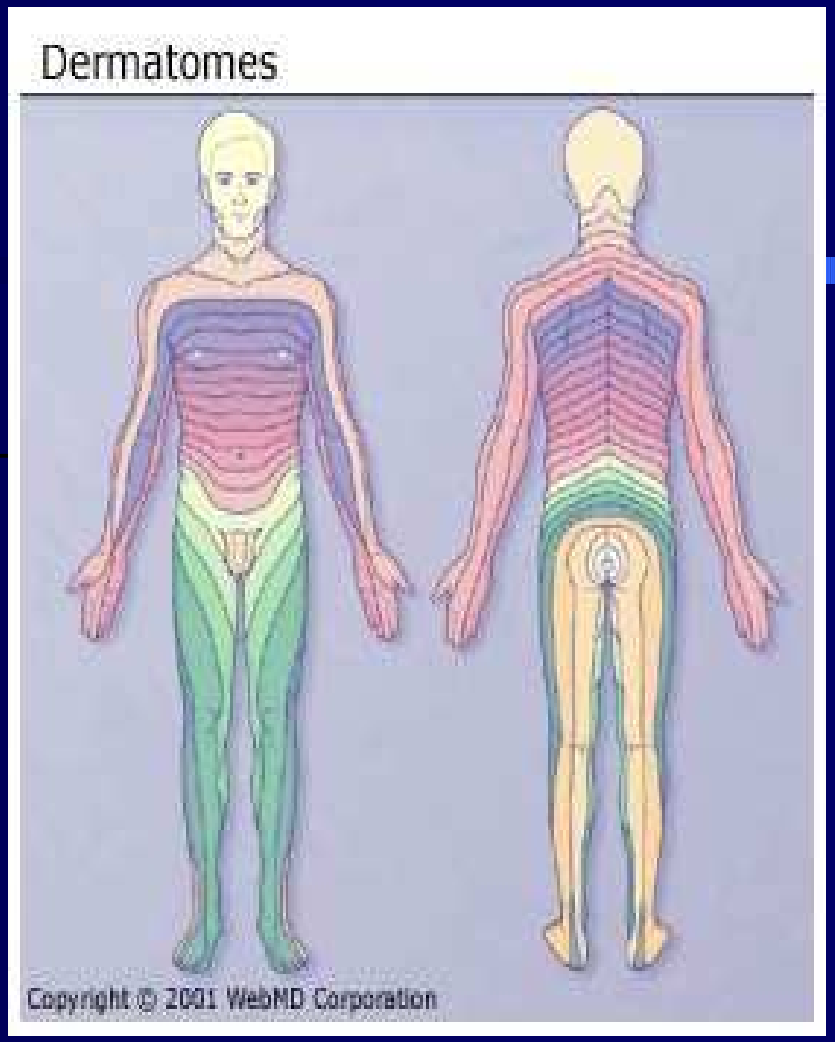
臂丛 C_5-T_1

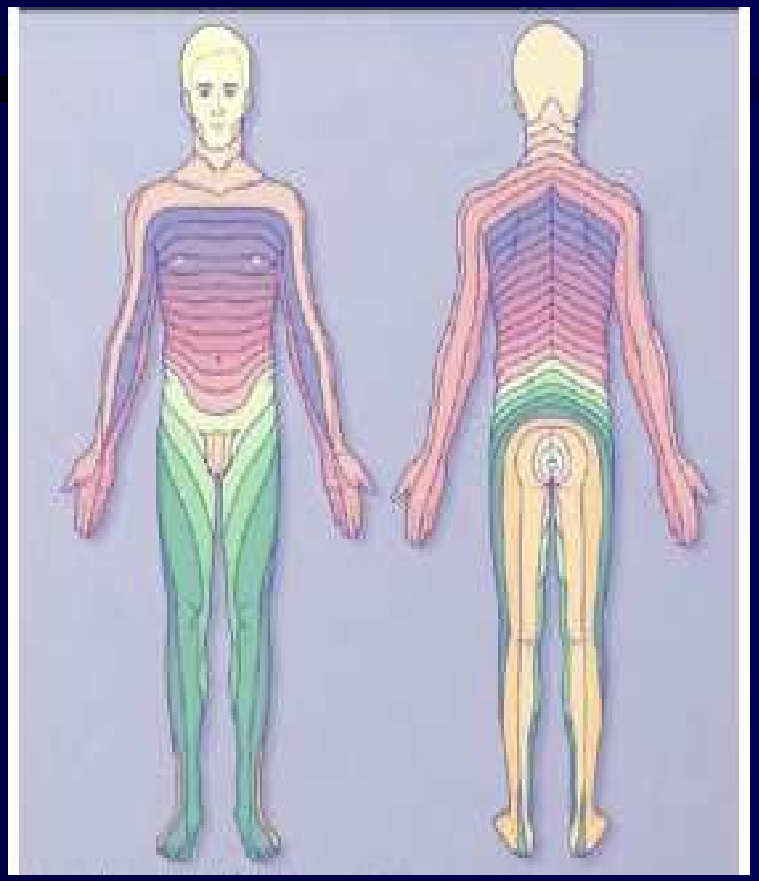
胸神经前支 T_1-T_{12}

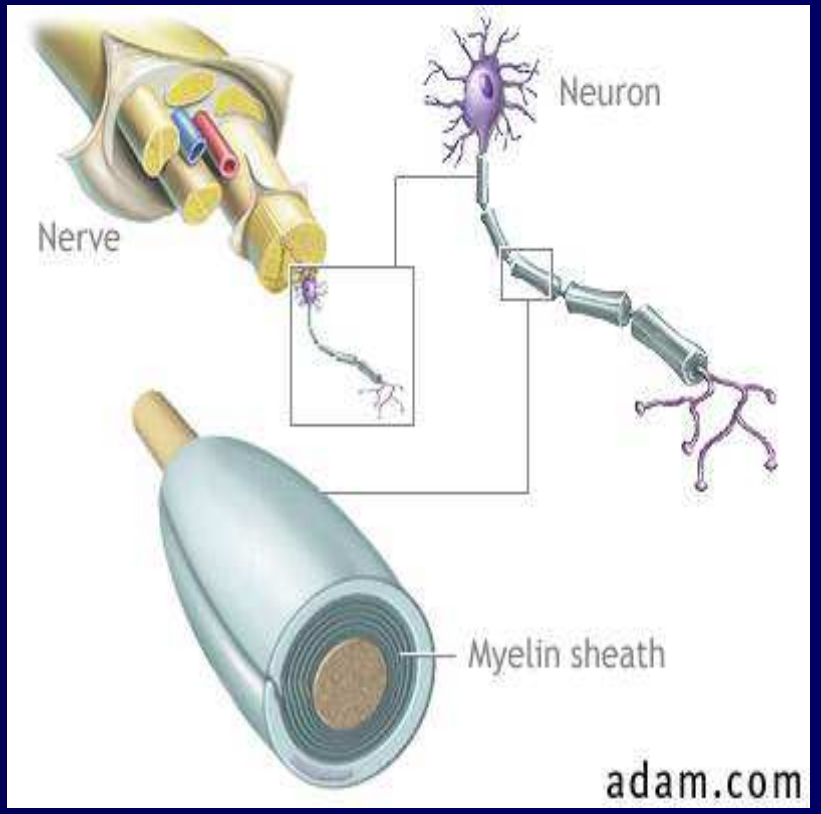
腰丛 $T_{12}-L_4$

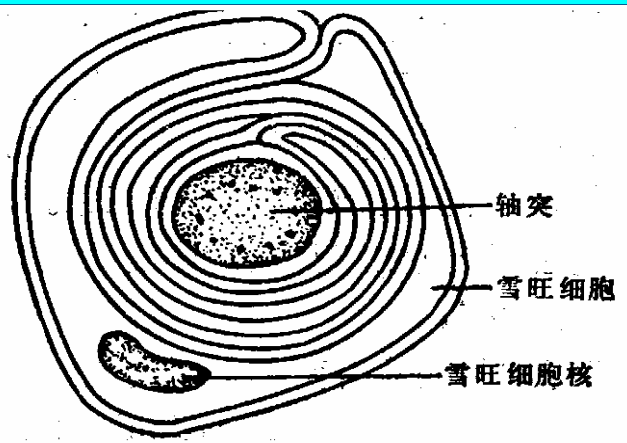
骶丛 L_4-L_5→腰骶干

全部S，Co



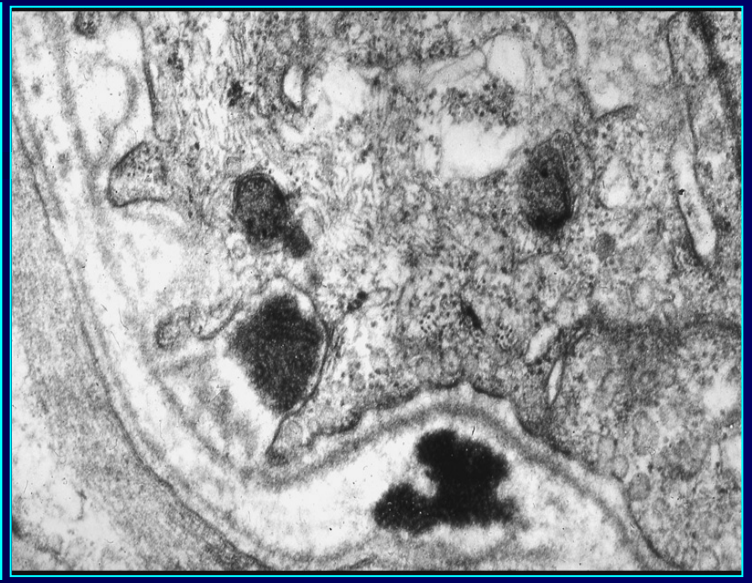


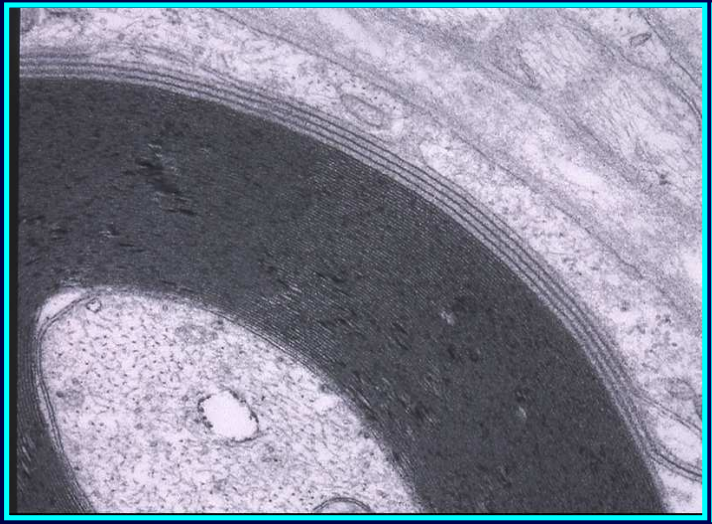

Neuron
Nerve
Myelin sheath
adam.com

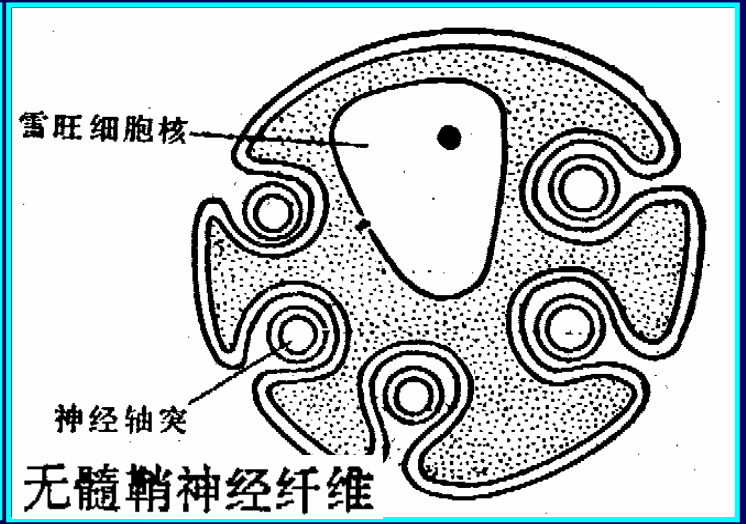


（2）横切面

有髓鞘神经纤维

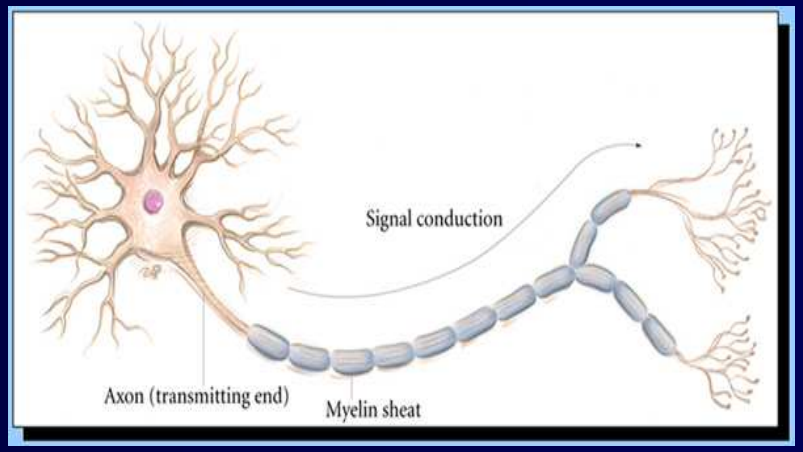


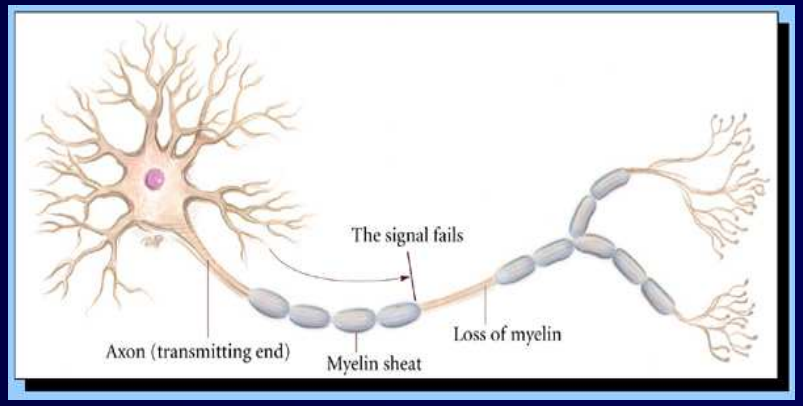




无髓鞘神经纤维

周围神经变性类型





- 节段性脱髓鞘
- 局限性雪旺细胞及髓鞘破坏－轴突正常

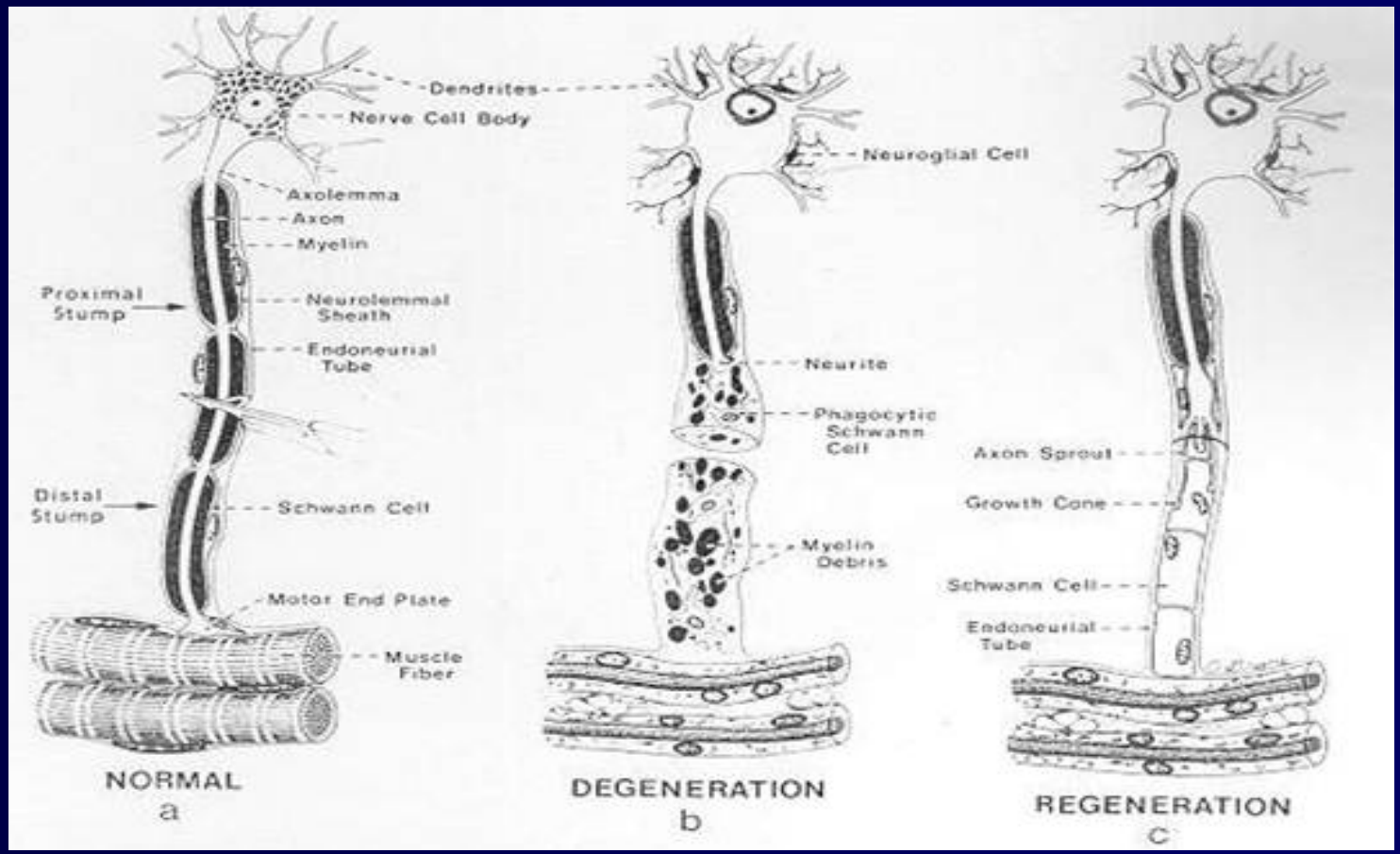
  节段性、斑点状病变
- 电生理:
  - 肌肉失神经不明显
  - 神经传导可减慢

周围神经变性类型

- 轴突变性
- 轴突病变 – 继而髓鞘或雪旺细胞破坏、神经传导阻滞、肌萎缩

- 电生理:
  - 肌肉失神经支配
  - 神经传导显著减慢

- 瓦勒变性（Wallarian degeneration）



周围神经病分类

- 神经痛:
  - 受累感觉神经分布区发生疼痛
  - 神经主质无明显变化
  - 神经传导正常
- 神经病或神经炎:
  - 各种原因引起的周围神经变性
  - 神经主质有改变
  - 神经传导异常

神经病或神经炎分类

- 分类的依据
  - 病理
  - 病程
  - 症状
  - 解剖部位
  - 神经数目
- 临床分类:
  - 对称性多发性神经病
  - 单神经病
  - 多数性单神经病

诊断和处理

- 电生理：肌电图、神经传导速度
- 处理：
  - 病因治疗
  - 对症治疗
  - 康复治疗

颅神经疾病

三叉神经痛

- 反复发作
- 短暂、阵发性
- 解剖

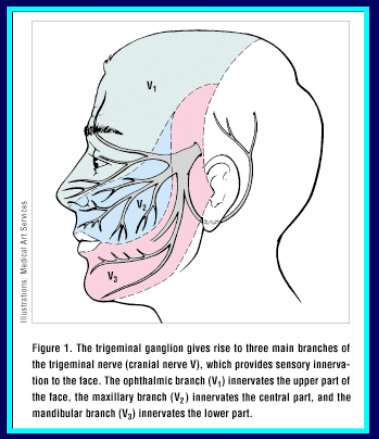
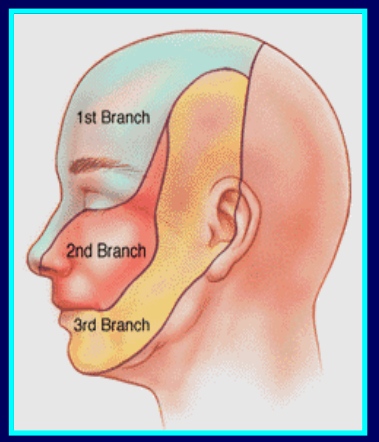


Figure 1. The trigeminal ganglion gives rise to three main branches of the trigeminal nerve (cranial nerve V), which provides sensory innervation to the face. The ophthalmic branch (V_1) innervates the upper part of the face, the maxillary branch (V_2) innervates the central part, and the mandibular branch (V_3) innervates the lower part.

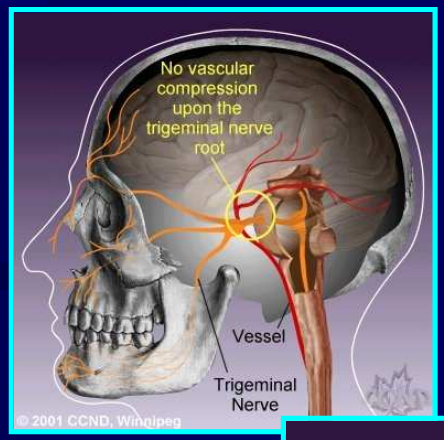


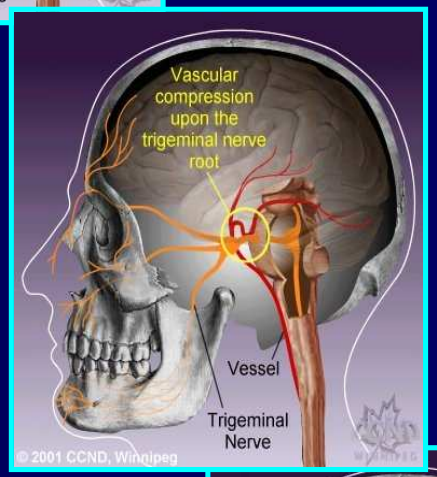
病因和病理

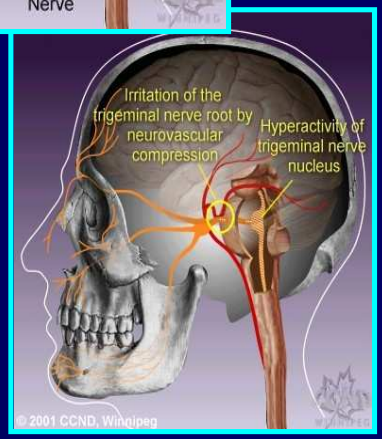
- 原发性三叉神经痛
  - 原因不明
  - 无明显病理改变
  - 无三叉神经功能异常

病因和病理

- 原发性三叉神经痛
  - 原因不明？？？
  - 无明显病理改变？？
  - 无三叉神经功能异常？







病因和病理

- 继发性三叉神经痛
  - 病因明确
  - 伴有邻近结构损害
  - 三叉神经功能丧失

临床表现

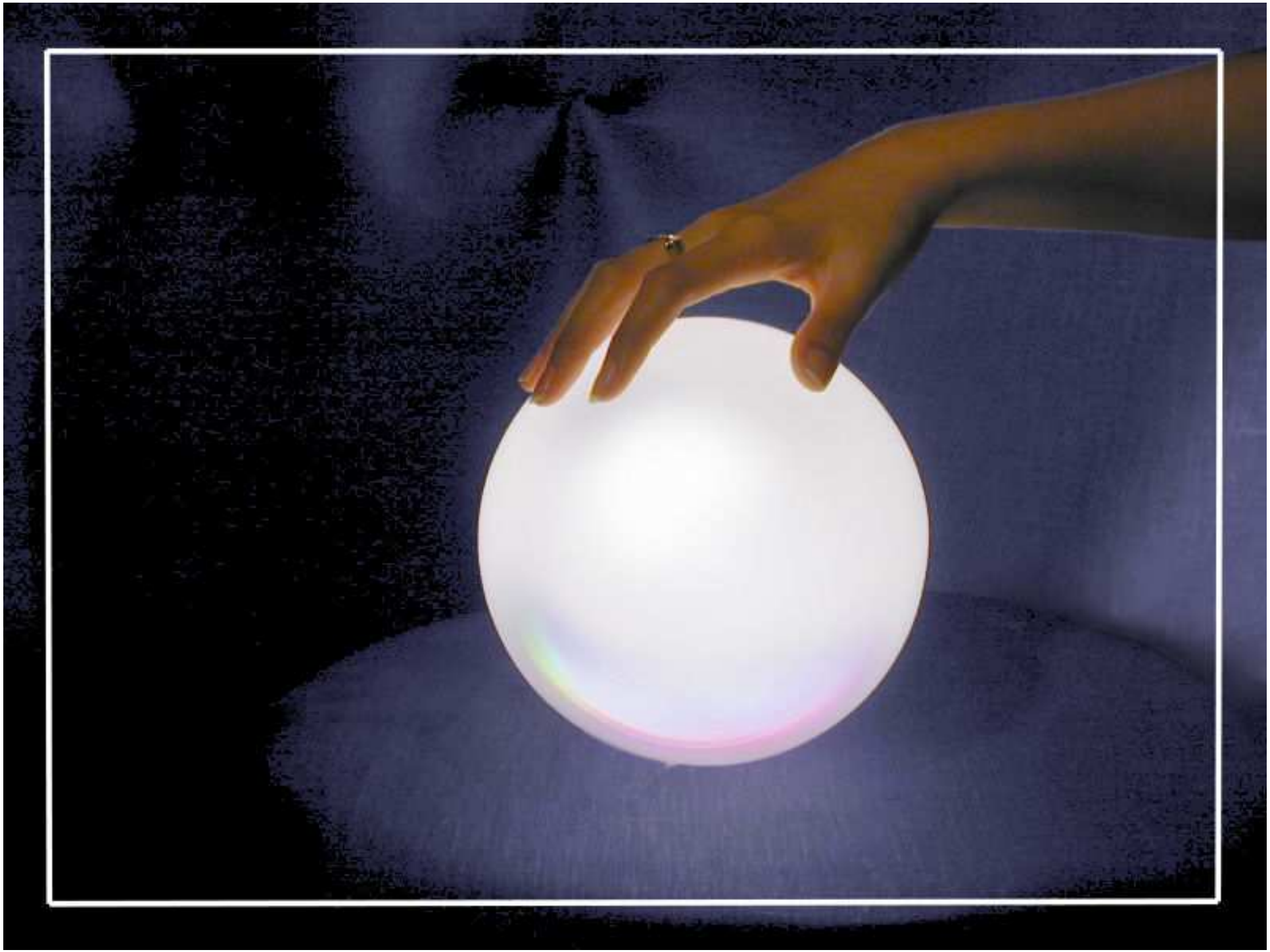
- 女性、多见于**40**岁后
- 单侧面部突发的剧痛（无先兆）
- 电击、针刺、刀割、撕裂、烧灼样
- 主要在第二、第三支分布区
- 有“触发点”，时间短暂（不超过**2**分钟）
- 神经系统检查无阳性发现*
- 发作间隙期如常人

诊断和鉴别诊断

- 鉴别继发性三叉神经痛
- 同一部位的面痛鉴别
  - 青光眼
  - 牙痛、额窦或颌窦炎
  - 颞颌关节综合征
  - 其他颅神经痛

治疗

- 病因治疗：继发性三叉神经痛
- 症状治疗：
  - 药物治疗
  - 神经阻滞（药物无效，而不宜手术）
  - 射频治疗*
  - 手术治疗



Bell's Palsy

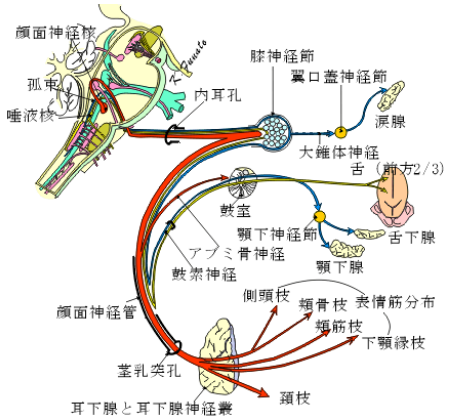
Sir Charles Bell

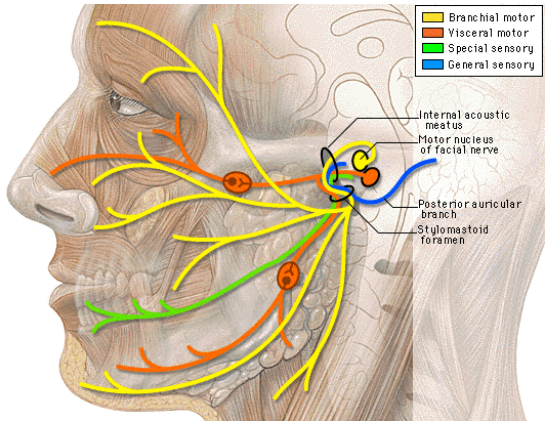
Epidemiology

- Lifetime prevalence: 6.4 to 20 per 1,000
- Incidence: Increased with age
  - Overall: 0.5 per year per 1,000
  - Age 20: 0.1 per year per 1,000
  - Age 80: 0.6 per year per 1,000
- Male = Female
- Recurrence: 7%
- Side: Right in 63%
- Increased incidence: Diabetes; Pregnant females

Pathogenesis

- Evidence for herpes simplex type 1 infection





Clinical Features

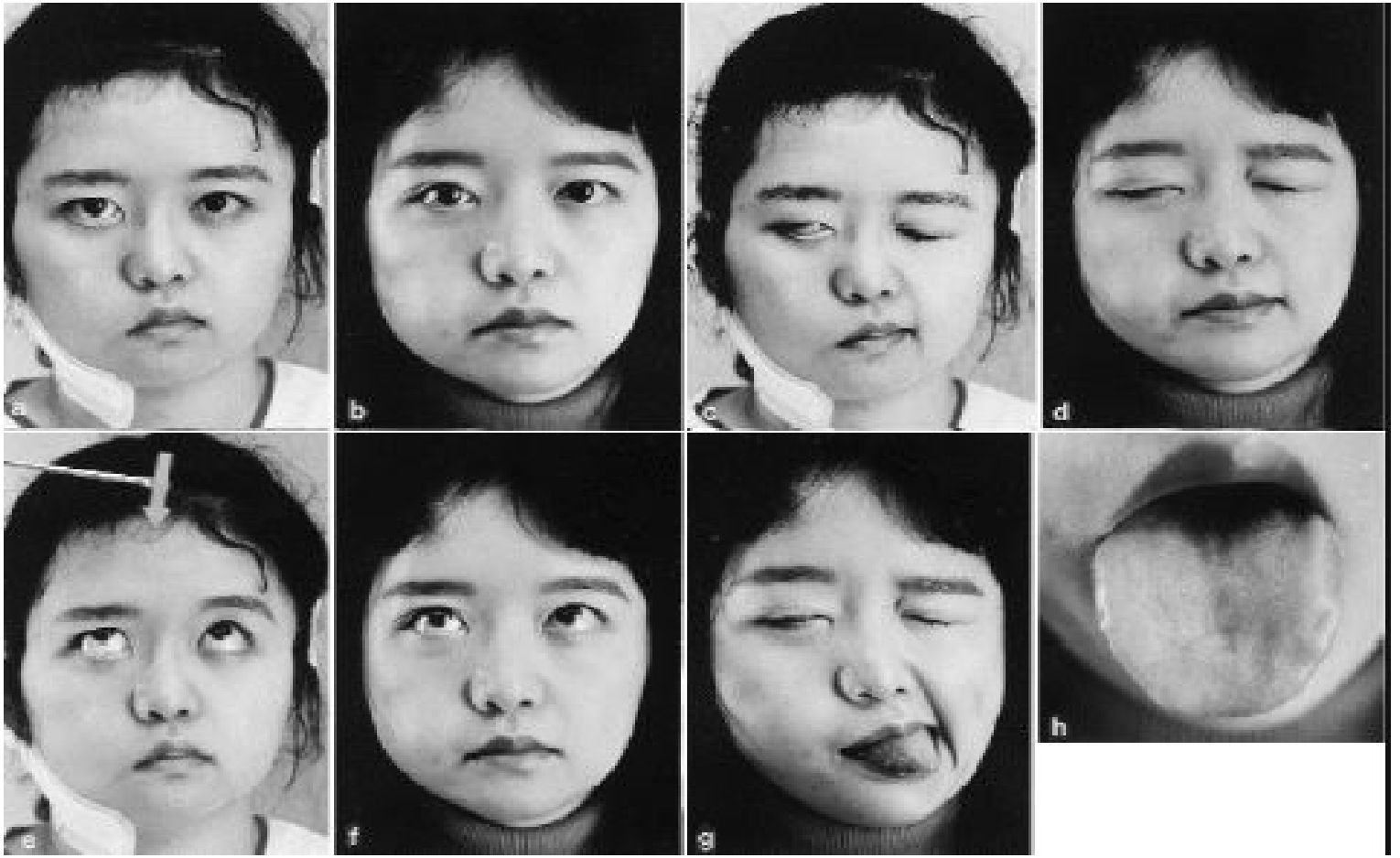
- **Onset**
  - Paralysis: Progresses to maximal defecit over 3 to 72 hours
  - Pain (50%): Near mastoid process
  - Excess tearing (33%)
  - Other: Hyperacusis; Dysgeusia

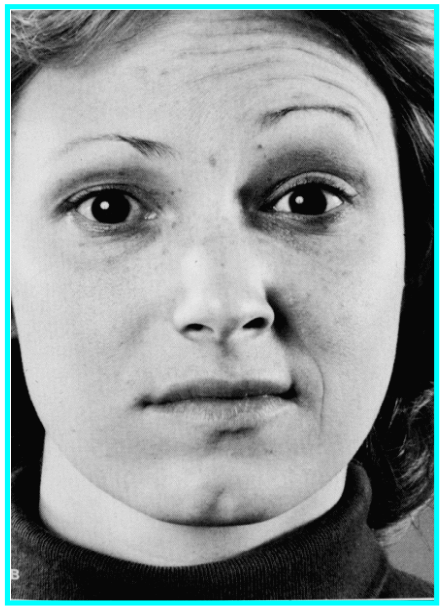
Clinical Features

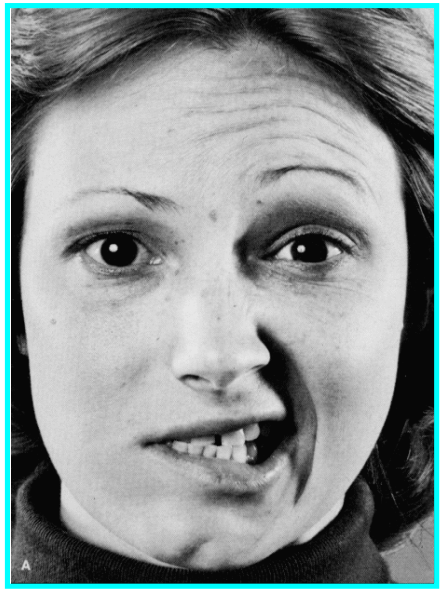
- **Signs**
  - Facial weakness
    - All branches of nerve: Upper & Lower
    - Unilateral， Bilateral in < 1%
    - Degree: Partial (30%); Complete (70%)
  - Stapedius dysfunction (33%): Hyperacusis

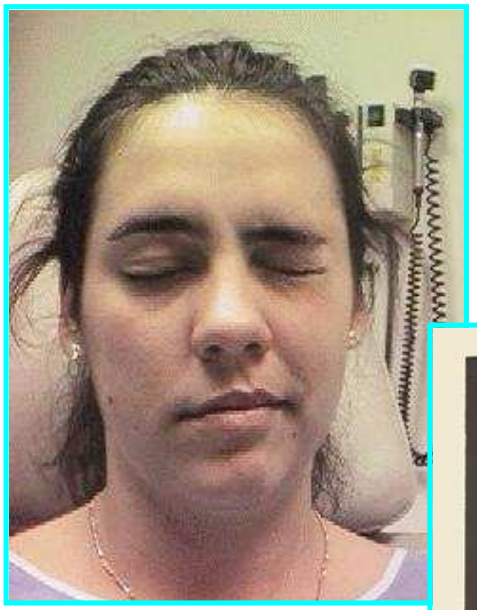
Clinical Features

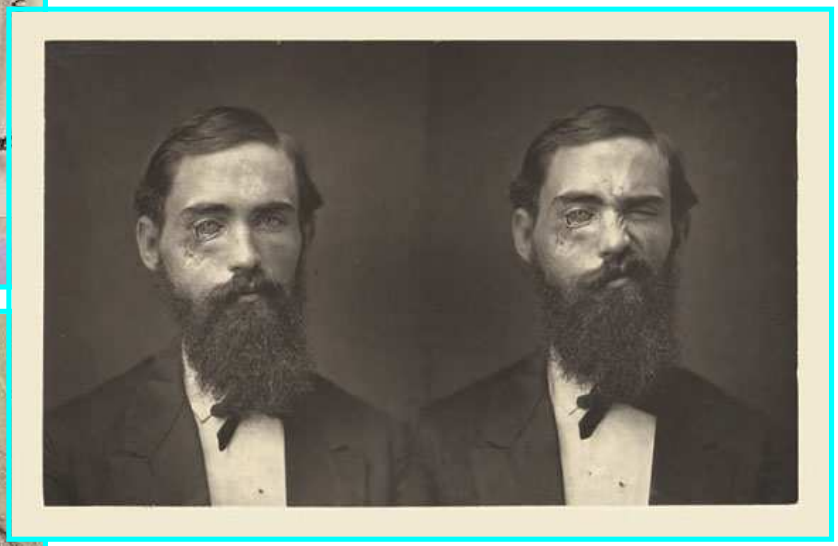
- **Signs**
  - Lacrimation: Mildly affected in some patients
  - Taste: No clinically significant changes in most patients
  - Sensory loss
    - Mild or None
    - May be present on face or tongue: On side of paralysis
    - Possibly related to involvement of greater superficial petrosal nerve


a
b
c
d
e
f
g
h









Prognosis

- **Prognosis better**
  - Incomplete paralysis
  - Early improvement
  - Slow progression
  - Younger age
  - Normal salivary flow
  - Normal taste
  - Electrodiagnostic tests normal
    - Nerve excitability
    - Electrogustometry

- Course

- Improvement onset: 10 days to 2 months
- Plateau: 6 weeks to 9 months

- Course
  - Residual signs
    - Synkinesis（联带运动）
      - » Frequency: ~50%; May be reduced by corticosteroid treatment
      - » May be treated with botulinum
      - » Probably due to misregeneration of nerve
    - Face weakness: 30%
    - Contracture: 20%
    - Crocodile tears: 6%
    - Blepharospasm: May occur years after paralysis

Treatment of Bell's palsy

- Statistical degrees of benefit from drug treatment
  - Prednisone + Acyclovir > Prednisone > Acyclovir
  - More benefit when treatment started within 3 days of onset
  - No benefit from treatment starting more than 10 days after onset

Treatment of Bell's palsy

- **Corticosteroids**
  - Use within one week of onset
  - Adults: Initial dose prednisone 80 mg qd x 5 days
  - Children: Initial dose prednisone 1 mg/kg/day
  - After initial dose: Taper off over 7 to 10 days

Treatment of Bell's palsy

- **Acyclovir**
  - Use within 3 days of onset
  - Adults
    - 2,000 mg per day (400 mg 5x/day) for 7 days
    - With varicella zoster 4,000 mg per day
  - Children: 80 mg/kg per day for 5 days
  - ? More effective in Ramsay-Hunt syndrome
  - Alternative anti-viral: Valacyclovir

Treatment of Bell's palsy

- Protect eye from exposure
- ? Facial exercise

Laboratory

- CSF: Protein high in 30%; Cells in 10%
- Calorics: Often reduced on affected side

Laboratory

- CNS imaging (MRI with gadolinium) indicated when
  - No improvement in facial paresis after 1 month
  - Hearing loss
  - Multiple cranial nerve deficits
  - Signs of limb paresis or sensory loss


7 4:13PM

Guillain-Barré Syndrome

Epidemiology

- Incidence: 1 to 2/100,000/year
- Male: Female = 1.25: 1
- Peak ages: Young adults & > 55 years
- Genetic risk factor: Fc γ RIIa-H131 allele homozygosity (vs R131)
  - More common than in healthy controls
  - Higher risk for severe disease than other genotypes
  - Same allele protective against lupus nephritis

Clinical features

- Weakness
- Cranial Nerves
- Sensory
- Tendon reflex loss
- Autonomic dysfunction

Clinical features

- **Weakness**
  - Distribution: Proximal + Distal; Symmetric
  - Severity:
    - Quadriplegia in 30%;
    - Bed bound another 30%

Clinical features

- **Weakness**
  - Distribution: Proximal + Distal; Symmetric
  - Severity:
    - Quadriplegia in 30%;
    - Bedbound another 30%

Clinical features

- **Respiratory failure**
  - Vital capacity < 1 liter: Observation in ICU necessary
  - ~33% of GBS require intubation
  - Indications for intubation
    - » Vital capacity < 12 to 15 ml/kg: Especially with rapid decline
    - » Negative inspiratory force (NIF) < 25 cm H_2O
    - » Hypoxemia: PaO_2 < 80 mm Hg (?)
    - » Difficulty with secretions

Clinical features

- **Respiratory failure**
  - Time of onset: 7 days
  - Time on respirator: 50% < 3 weeks
  - Usually 2° to muscle weakness
  - Occasionallly related to aspiration

Clinical features

- **Cranial Nerves (70%)**
  - VII
    - » Symmetric: Occurs early in parallel with weakness
    - » Asymmetric
    - » Occurs later in disease course
    - » Other weakness may be stable or improving
  - Extra-ocular: Overlap with Miller-Fisher
  - Tongue: Symmetric; Common (50%)

Clinical features

- **Sensory**
  - Paraesthesias:
    - Initial symptom in 50%; Eventually occur in 70% to 90%
  - Pain
    - Prominent in 70%
    - Associations
      - » Neuropathy: In back, hips & legs at onset; Myalgias; Occasional radicular
      - » Immobility: Myalgias
      - » Recovery phase: Distal; Legs > Hands; Dysesthesias
  - Loss(?)
    - Distal; Symmetric
    - All modalities involved

Clinical features

- **Tendon reflex loss**
  - Early in most (70%) but not all patients
  - Progressive reduction during 1st week
  - Distribution: Ankles most frequently lost; Biceps most frequently spared
  - Associations: Sensory loss; Weakest limbs; Distal
  - Spared reflexes all during disease course suggests another diagnosis

Clinical features

- **Autonomic dysfunction**
  - Frequency: 60%
    - More common in more severe syndromes
  - Blood pressure
    - Transient hypertension or, less often, hypotension
    - Increased sensitivity to anti-hypertensive medications
  - Cardiac arrhythmias:
    - Sinus tachycardia; Bradycardia

Clinical features

- **Autonomic dysfunction**
  - Bladder: Urinary retention; Sphincter symptoms in 10% to 15%
  - GI: Ileus
  - Test: Bilateral ocular pressure x 25 sec; Produces bradycardia (< 40 bpm)
  - Course
    - Usually improves in parallel with motor & sensory function
    - Rarely any long-term autonomic dysfunction

Clinical features

- **Progression**
  - Nadir: Mean at 9 days
  - General definition: Progression for < 4 weeks
  - 1% have acute onset of CIDP vs GBS: May need repeat treatment; ? Steroid responsive

Clinical features

- **Death**
  - Frequency: 3% to 10%
  - Causes: Pneumonia; Iatrogenic hypotension
  - Associations:
    - » Mechanical ventilation;
    - » ? Autonomic dysfunction

GBS Prodrome

- **Upper respiratory**: + CMV titers = 18%
  - Younger patients
  - More sensory loss & cranial nerve involvement
  - More severe disease
    - Respiratory insufficiency more common (65%)
    - Longer median time until independent locomotion
  - Antibodies
    - Higher Frequency of serum IgM vs GM2 ganglioside
    - Also see IgM vs GalNAc-GD1a ganglioside

（N-乙酰半乳糖胺）

GBS Prodrome

- **Gastrointestinal**:
  - + Campylobacter jejuni titers = 28%
  - Motor predominant
  - More severe outcome

GBS Prodrome

- Mycoplasma pneumonia
  - Associated with antibodies to galactocerebroside (GalC) （半乳糖脑苷脂）
  - Frequency: 5% of GBS patients in Japan

GBS Prodrome

- **Other infections**
  - Epstein-Barr virus;
  - HIV;
  - ? Hepatitis A

GBS Prodrome

- Vaccinations

- Tetanus toxoid; Influenza; ± Polio (oral)
- Rabies
  - Vaccines: Myelin-containing (Semple); Suckling mouse brain
  - Usually > 10 years old
  - Some cases associated with sensitization to myelin basic protein
  - Occurs in clusters

GBS Prodrome

- Surgery
- ? Graft vs Host disease
- Drugs: Zimeldine

Nerve conduction studies in GBS

- Demyelination ± Axonal loss
  - Common early (< 1 week from onset) features
    - Reduced H reflex (97%)
    - SNAPs: Upper extremity (61%); Sural may be preserved
    - Reduced F-waves (84%)

Nerve conduction studies in GBS

- Other electrodiagnostic features: Demyelination
  - Overall
    - Features less common in 1st 5 to 7 days of disease
    - Increased frequency when multiple nerves studied
  - Features of demyelination for more specific diagnosis
    - One abnormality in 2 different nerves
    - Nerves: Median & Ulnar or Peroneal

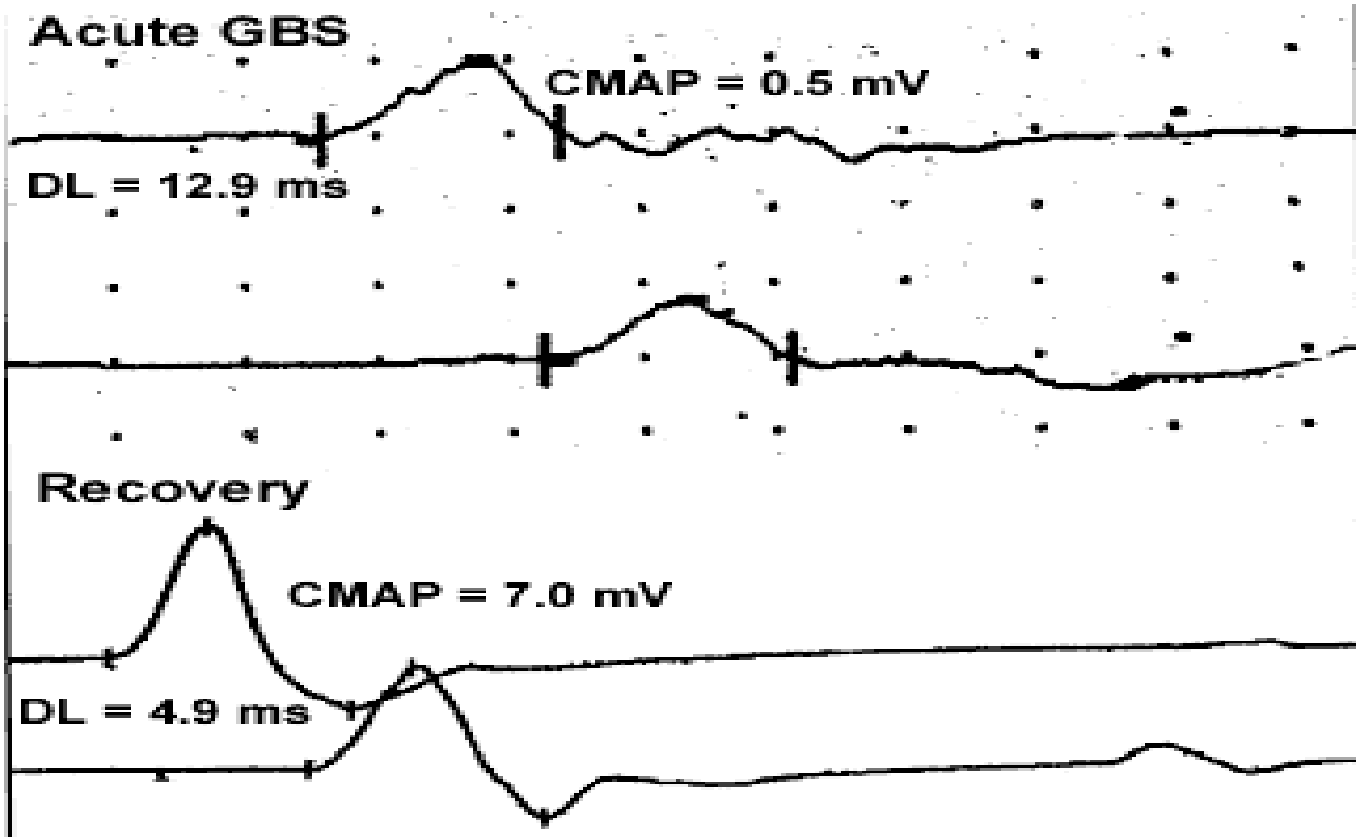
Nerve conduction studies in GBS

- Other electrodiagnostic features: Demyelination
  - Specific features
    - » Distal motor latency: > 150% upper limit of normal
    - » Motor NCV: < 70% lower limit of normal (? CIDP)
    - » F-wave latency: > 150% upper limit of normal
    - » CMAP amplitude decay: > 10% to 30%
    - » CMAP temporal dispersion
      > 300% upper limit of normal (Distal)
    - » CMAP temporal dispersion
    - » > 150% upper limit of normal
    - » Distal: Proximal

Nerve conduction studies in GBS

- Motor conduction block probably causes acute weakness
  - Locations
    - Proximal nerve roots
    - Along course of nerve
    - Distal near motor nerve terminals
- Compound motor action potentials (CMAPs):
  - Often become progressively small
  - Small CMAPs may indicate
    - Axonal loss or distal conduction block
    - Poor prognostic sign
- EMG: Fibrillations & Positive sharp waves
  - Onset: 2 to 4 weeks
  - Peak: 2 to 3 months

Nerve conduction studies in GBS



GBS: Humoral Immunity

- IgM or IgG vs Tubulin: 10%
- IgG vs GM1, GM1b or GalNAc-GD1a (N-乙酰半乳糖胺): Motor syndromes
- United States: < 2%
  - Japan, China, Australia & ? Europe: 10% to 20%

GBS: Humoral Immunity

- IgM or IgG vs Heparan sulfate: 35%
- IgG vs other glycolipids: 10% to 30%
- IgM or IgG vs PMP-22: Probably testing artefact; Not specific for GBS
- Tumor necrosis factor-α : High serum level correlates with demyelination

GBS: Laboratory

- **CSF: Albumino-cytological dissociation**
  (蛋白—细胞分离2～6周)
  - Protein
    - Early (1st 2 days): Usually (85%) normal
    - Later
      - » High; 66% in 1st week; 82% in 2nd week
      - » Highest with most slowing of NCV
  - Cells: Normal (~90%), unless associated disorder present
  - Oligoclonal bands: 10% to 30%

GBS: Laboratory

- Hematology: Only abnormal with associated infection or other disorder
- Serum CK: Higher in patients with pain
- ESR: Usually < 50 mm/hr
- Mild proteinuria: 25%
- Liver function test: Abnormal in 10%
- WBC: Most commonly normal; > 20,000 only with associated infections

GBS: Laboratory

- HLA types: Class II associations with AIDP in northern Chinese patients
  - General
    - Regions important in peptide binding and T cell recognition
    - Associated with other diseases with pathoimmunological basis
    - No class II associations found for AMAN
  - Susceptibility: DQ β RLD55–57/ED70–71 & DR β E9V11H13
  - Protection: DQ β RPD55–57 epitope

Causes of morbidity

- Weakness
  - Respiratory failure
  - Pneumonia or sepsis
  - Dysphagia
  - Thromboembolism
  - Corneal exposure

Causes of morbidity

- Sensory
  - Pain: 2° neuropathy or immobility
- Autonomic
  - Cardiac Arhythmias
  - Labile blood pressure
  - Hypersensitivity to cardiovascular medications

Associated Systemic Disorders

- Infections: Prodromes
  - Viral
    - Cytomegalovirus (CMV)
    - Epstein-Barr virus (EBV) ± Hemophagocytic syndrome
    - Human immunodeficiency
  - Bacterial
    - Campylobacter jejuni
    - Mycoplasma pneumoniae

Associated Systemic Disorders

- Porphyria
- Hyponatremia
  - Mildly reduced Na+ in 7% to 26%
  - Severely reduced Na+ (SIADH) (105 to 120 mEq/L) may occur
  - No relation to degree of severity of GBS

Associated Systemic Disorders

- Renal
  - Common: Mild transient proteinuria
  - Rare: Glomerulonephritis
- Cardiac
  - Arhythmias: 10% to 75%
  - EKG changes: > 50%
- Serum CK: High in 33%; Up to 4x normal

Prognostic factors

- **Mechanical ventilation needed**
  - Rapid disease progression
  - Bulbar dysfunction
  - Facial weakness: Bilateral

Prognostic factors

- **Mechanical ventilation needed**
  - Dysautonomia
  - Pulmonary function testing
    - Vital capacity < 20 ml/kg
    - Decrease from baseline > 30%: Vital capacity or Respiratory pressure

Prognostic factors

- **Residual disability greater**
  - Clinical prognostic factors for residual disability
    - Increasing age (especially > 40 to 60)
    - Weakness
      - » Severe
      - » Need for ventilatory support
      - » Rapid development

Prognostic factors

Residual disability greater

- *Clinical* prognostic factors for residual disability
  - **Complete areflexia** in the acute stage
  - **Diarrhea prodrome**: Especially with Plasma exchange treatment
  - Lack of treatment with **plasma exchange or IV Ig**
  - **Longer time to improvement**
    - » Initial improvement > 21 days
    - » Disability present at 12 to 18 months

Prognostic factors

- *Laboratory* prognostic factors for residual disability
  - Axonal loss
    - » Low compound motor action potential (CMAP) amplitudes
  - < 20% of normal
    - » ? Lack of demyelinating features
  - Serology
    - » ? Serum IgG vs GM1 ganglioside
    - » ? Preceding Campylobacter jejuni infection
    - » Recent CMV infection

Treatment

Immunomodulation

- Plasma Exchange or IV IgG definitely indicated
  - Patients with inability to walk
  - 1st 2 weeks of disease
  - Decision between IV IgG & PE: Depends on individual features of patient & disease
- Probably indicated: Milder weakness; Early in disease course

Treatment

Immunomodulation

- Plasma Exchange and IV IgG
  - Often provide similar degrees of benefit
  - Exception
    - » Associated IgG vs GM1, GM1b, or GalNAc-GD1a gangliosides: IVIg more effective
- **Not** Corticosteroids

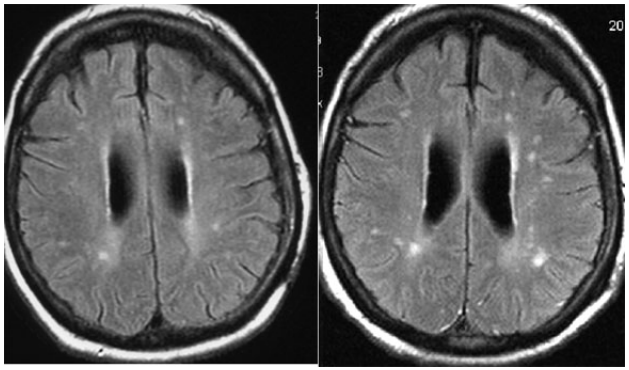
Treatment

- Ventilatory support
- Avoid anti-hypertensive medications
- Sub-cutaneous heparin with immobility: Lower Risk of thromboembolic events

Childhood GBS

- Ages: Neonatal to Teens
- Onset
  - Lower extremity Generalized weakness
  - Pain & Paresthesias (60%): Lower limbs or Back
- Miller-Fisher syndrome: 1% of childhood AIDP

Childhood GBS



- CNS signs: More frequent; At onset
- Bladder dysfunction
- Mental status changes & headache
- Pain & meningismus (30%)
- Ataxia: Gait
- Occasional: Papilledema (< 5%)

Childhood GBS

- Recovery
  - » Often more rapid than adults
  - » Disability at 1 year: Rarely full recovery
  - » Residual disability (~30)%:
  - » Foot drop, Pes cavus, Tremor

Miller Fisher Syndrome

- Epidemiology in Japan
  - Onset: Mean 40 years; Range 13 to 78 years
  - Seasonal: Higher frequency in Spring (March to May)
  - Clinical prodrome: Respiratory most common

Miller Fisher Syndrome

- Epidemiology in Japan
  - Frequency: 25% of GBS in Japan; 1% of GBS in US
  - Associated infections
    - Campylobacter jejuni: Often serotype O-2 or O-10
    - Hemophilus influenzae: 7% of MFS patients with positive serology[11]

Miller Fisher Syndrome —Clinical

- Onset
  - Diplopia (Asymmetric) (80%)
  - Myalgia & Paresthesias
  - Vertigo & Ataxia

Miller Fisher Syndrome – Clinical

- Eye
  - External ophthalmoplegia (100%): Symmetric or Asymmetric
  - Pupillary dysfunction (42%): Mydriasis
  - Ptosis (58%)

Miller Fisher Syndrome —Clinical

- **Ataxia** (100%): Dysmetria; Gait ataxia; Arms & Legs
- **Areflexia** (100%): By 1 week of disease
- **Sensory**
  - Distal & Facial paresthesias & dysesthesias (24%)
  - Sensory loss: Minimal; Definite in 20%
- **Weakness**: 20%
- **Autonomic**: Bladder disorders 16%

Miller Fisher Syndrome – Clinical

- Other Cranial nerve disorders
  - Oropharyngeal weakness (26%)
  - Facial weakness (32%)
- Progression
  - Over days to weeks
  - May progress to generalized weakness
  - Recovery
    - Onset: After 2 weeks to 2 months
    - Long term: Many with no residual defects

MFS-Cranial nerve variants

- Often associated with IgG vs GQ1b or GT1b gangliosides
- GBS overlap: Ophthalmoplegia; Weakness; ± Ataxia
- Internal ophthalmoplegia: Dilated pupils; Light-near dissociation
- Acute external ophthalmoplegia: Complete or partial

MFS-Cranial nerve variants

- Acute ataxia: May progress to Weakness & GBS
- Visual impairment
- Rule out: Neurosyphilis

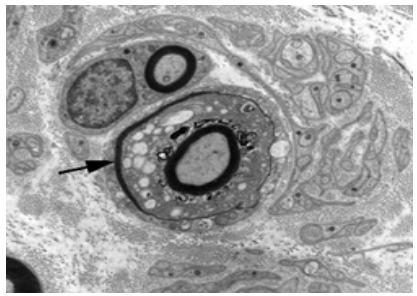
MFS-Cranial nerve variants

- Chronic ophthalmoplegia with serum IgG binding to GQ1b ganglioside
  - May be associated with vestibulopathy or demyelinating neuropathy
- Acute neuropathies with bulbar dysfunction: Pharyngo-cervical-brachial variants
- Bickerstaff brainstem encephalitis: Brainstem signs

Laboratory

- CSF
  - Protein: 20 to 60 mg/dl
  - Cells: Few or None; 0 to 5/mm3

Laboratory



- Nerve conduction studies
  - Sensory
    - Axonal loss
    - SNAPs: Reduced amplitude
  - Motor
    - Peripheral nerve: Normal CMAPs
    - Facial: Reduced CMAP amplitude
  - F-waves: Prolonged; Dispersed; Absent
  - H reflexes: Absent from soleus

Laboratory

- Serum antibodies
  - IgG vs GQ1b(80%)
  - IgG staining of cerebellar molecular layer

Laboratory

- MRI
  - Cranial nerve enhancement (gadolinium) may occur
  - Brainstem or Cerebellar lesions: Some patients

THANKS!

Q & A