1년차가 알아야 할 신경근육질환

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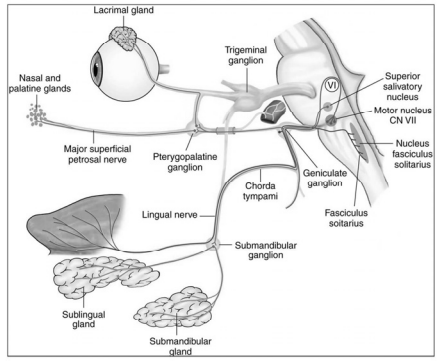
이 강의가 끝나면 여러분들은,

1. Facial palsy를 진단하고 치료할 수 있다.
2. Guillain-Barré syndrome을 진단하고 치료할 수 있다.
3. Myasthenia gravis를 진단할 수 있다.
4. Wrist drop과 foot drop의 원인을 감별할 수 있다.
5. 스테로이드와 면역글로불린을 올바로 사용할 수 있다.

Anatomy of Facial Nerve



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Treatment of Bell's palsy

- Prednisolone 1 mg/kg/day (up to 70 mg/day) for 6 days, then tapering off over subsequent 4 days
- Antiviral agent (?)

- Variable results in electrical stimulation
- Minimal positive evidence for facial exercise

- No well-designed studies

- Facial nerve decompression

Treatment of Bell's palsy

For new-onset (72-hrs of symptoms) patients,

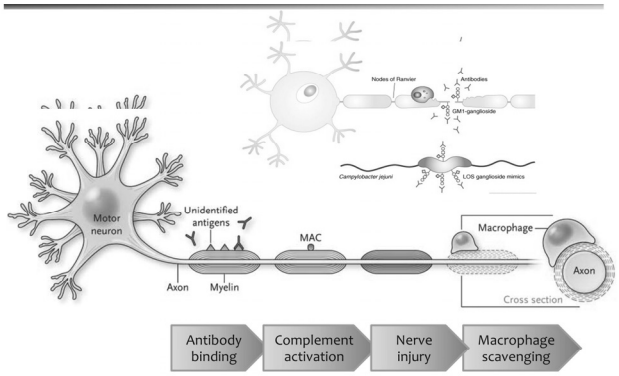
- **Steroids** are highly likely to be effective and should be offered to increase the possibility of recovery of facial nerve function.
- Antiviral agents in combination with steroids do not increase the probability of facial function recovery by > 7%. Patients **might be offered antivirals in addition to steroid**, and should be counseled that the benefit has not been established and its benefit id modest at best.

AAN. Neurology (2012)

Clinical Vignette (1)

- M/ 40
- 주호소: 3일 전부터 진행하는 사지 위약감
- 병력
  2 주전 제주도 여행 중 감기가 심하게 걸려 일주일간 앓음
  3 일전 발가락 끝이 저리면서 걸을 때 발목을 자주 접지름
  전일부터는 양 손아귀 힘이 빠지면서 물건을 자꾸 놓침
- 신경계진찰
  Symmetric distal and proximal weakness with bilateral facial palsy
  Generalized areflexia
  Normal sensory and cerebellar function

Guillain-Barré syndrome



Guillain-Barré syndrome

- Demonstration of elevated spinal fluid protein without cells (***albuminocytologic dissociation***) in the two paralyzed French soldiers

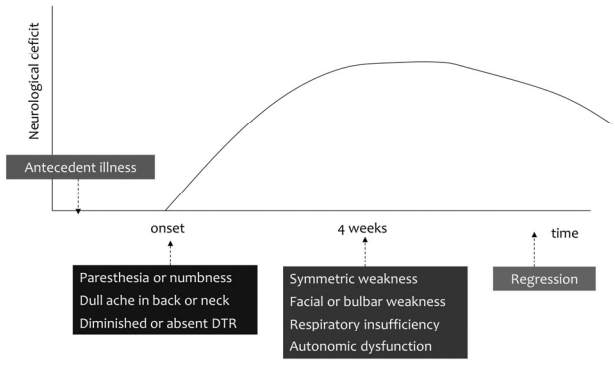
- Georges Guillain, Jean-Alexandre Barré, Andre Strohl (1916)


Guillain


Barré


Strohl

Typical time course of GBS



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Clinical criteria for GBS

- **Symmetric weakness** of more than one limb
- **Absent or reduced tendon reflexes**
- Progression over maximum **4 weeks**
- Mild sensory involvement
- Cranial nerve involvement (60 %)
- Autonomic dysfunction (15 %)
- Respiratory failure (up to 25 %)
- **NO** sensory level, sphincter dysfunction, persistent asymmetry

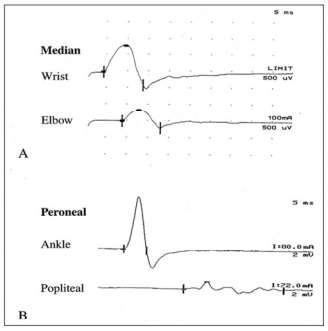
(*Asbury AK, et al. Ann Neurol 1990*)

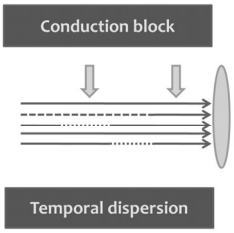
Laboratory criteria for GBS

- **CSF cell**
  Acellular or mild lymphocyte-dominant pleocytosis (<50/mm^3)
  Rapid decrease in the disease course
  Persistent pleocytosis refer alternative or additional diagnosis

- **CSF Protein**
  Albumino-cytologic dissociation
  Normal during the first few days of symptom
  80 % one week or more after onset
  Peak in 4 to 6 weeks

Nerve conduction study in GBS





Treatment of GBS

- **Give general good care**
- Frequent watch for respiratory failure
  ⇒ parallel with weakness of shoulder elevation and neck flexion
- **IV immunoglobulin** (0.4g/kg/day for 5 days) within first two weeks
  Severely affected patients (inability to walk unaided)
  Secondary deterioration after initial improvement or stabilization
- **Plasma exchange**
  200 mL/kg/ day E.O.D 4-5 times
  Sepsis, shock, air embolism

Signs and symptoms of respiratory failure

- Morning headaches
- Excessive daytime sleepiness
- Frequent nocturnal arousals
- Lack of restful sleep
- Dyspnea on exertion
- Orthopnea
- Staccato speech
- Weak cough
- Difficulties handling secretions
- Restlessness
- Hyperhidrosis
- Tachypnea
- Tachycardia
- Weak neck flexion/extension
- Accessory muscle use
- Paradoxical breathing

Objective measure of respiratory failure

- Breath count < 20 (< 2 L)
- FVC < 20 mL/kg
- MIP (NIF) > - 30 cm H_2O
- MEp < 40 cm H_2O
- Hypoxemia (late sign)
- Hypercapnia (late sign)

FVC, forced vital capacity; MEP, maximal expiratory pressure;
MIP, maximal inspiratory pressure; NIF, negative inspiratory force

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Interventions of respiratory failure

- NPO for patients with dysphagia/risk of aspiration
- Noninvasive ventilation, typically BiPAP with adequate airway protection
- Invasive ventilation
- Serial MIP/NIF and FVC monitoring to aid in decisions on extubation

BiPAP, bilevel positive airway pressure

Prognosis of GBS

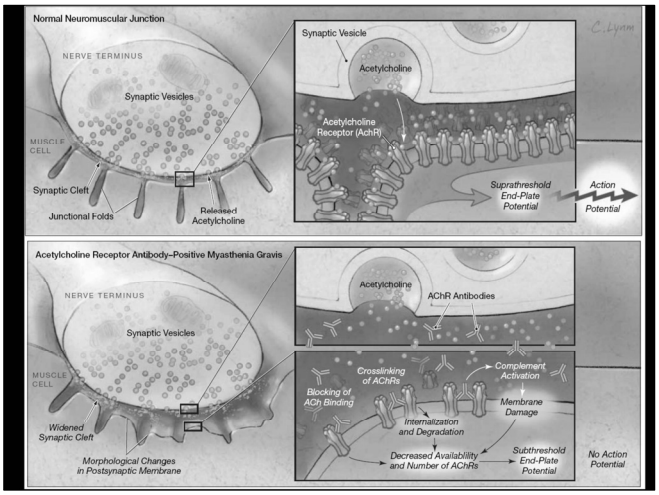
- Two thirds of patients are unable to walk in maximum weakness
- 20 % of patients remain unable to walk 6 months after onset
- Adverse prognostic factor

  Older age onset (> 50 yrs)
  Bed-ridden or mechanical ventilation at nadir
  Rapid progression
  Preceding diarrhea
  Axonal loss in electrophysiological study
  Low serum IgG level after IVIg administration

Clinical Vignette (2)

- F/ 35
- 주호소: 2달 전부터 시작된 피로감, 3일전부터 시작된 좌측 안검하수와 복시
- 병력, 과거력: 특이 사항 없음
- 신경계진찰

  Ptosis (OS)
  Isocoric pupil
  Limitation of extraocular movement – fluctuating
  Normal sensory function
  Normoactive tendon reflex



Clinical features of MG

- **Fluctuating weakness (fatigue),**
  worsened in the late of day or after exercise
- **Ocular** palsies
  diplopia, ptosis, Cogan's lid twitching
- **Facial** and **bulbar** weakness
  reduced facial expression
  difficulty in mastication and swallowing
- **Proximal muscle** weakness

Edrophonium (Tensilon®) test

- Improved strength after administration of anticholinesterase
- Positive more than 90% in generalized MG
- **Neostigmine** (1.0-1.5 mg) or **pyridostigmine** (2-3 mg)
- Compare pre- and post- (20-30 minutes) administration
- Pretreatment with atropine (0.5 mg) S.C
- False-positive : brain tumor, ALS, GBS
- False-negative : insufficient injection dosage

vs. Ice pack test

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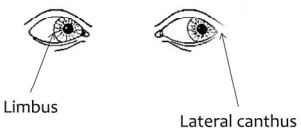
How to measure – Ocular

Normal eyelid and eye



Palpebral fissure

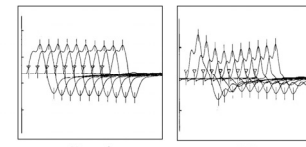
Normal when there is no ptosis or diplopia on the lateral gaze > **60 sec**

How to measure – Extraocular

Test Items Weakness (Score)	None (0)	Mild (1)	Moderate (2)	Severe (3)
Facial muscles	Normal lid closure	Complete, weak, some resistance	Complete, without resistance	Incomplete
Swallowing 4 Oz / 120 ml water		Minimal coughing or thoat cleaning	Severe coughing /choking or nasal regurgitation	Cannot swallow (Test not attempted)
Speech following counting aloud from 1-50 (onset of dysarthria)	None at #50	Dysarthria (#30-49)	Dysarthria at #10-29	Dysarthria at #9
Arm outstretched (90° sitting)	240	90-239	10-89	0-9
Head, lifted (45°supine)	120	30-119	1-29	0
Leg outstretched (45°supine)	100	31-99	1-30	0

Laboratory test for MG

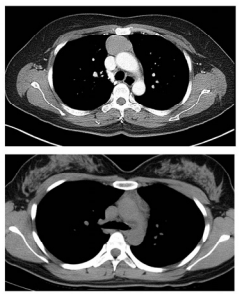
- **Acetylcholine receptor antibody**
  - 85 % of generalized MG and 60 % of ocular MG patients
  - No correlation with the severity of disease
  - Seronegative patients (anti-MuSK antibody)
- **Repetitive nerve stimulation test (Jolly test)**
  - Decremental response
  - Normal response in ocular MG



Thymus in MG

- Thymic hyperplasia (65 %)
- Thymoma (10-15 %)

- Thymectomy is never, never, never emergency!!!



Drugs inducing or exacerbating myasthenic weakness

Category	Drugs
Anesthetic agent	Nondepolarizing neuromuscular blocking agents Local anesthetics (e.g., procaine, xylocaine)
Antibiotics	Aminoglycosides (e.g., gentamycin, tobramycin) Beta-lactamase (e.g., ampicillin, penicillin) Fluoroquinolones (e.g., ciprofloxacin, norfloxacin) Macrolides (e.g., azithromycin, erythromycin) Sulfonamides, Tetracyclines, Clindamycin Others (e.g., polymyxin B, vancomycin)
Anti-rheumatic agents	Penicillamine, chloroquine
Cardiovascular agents	Antiarrhythmics (e.g., lidocaine, procainamide, quinidine) Beta-blockers (e.g., atenolol, propranolol) Calcium channel blockers (e.g., verapamil) Diuretics
Anticonvulsants	Barbiturates, benzodiazepines, gabapentin, phenytoin
Others	Magnesium salts, lithium, corticosteroid, estrogen, narcotics

Management of myasthenic Crisis

- General Airway assistance and ventilation
- Discontinue anticholinesterases and any offending drug (e.g. antibiotic, β-blocker)
- Cardiac monitoring Identify and treat infection
- Prophylaxis for deep vein thrombosis
- Initiate specific treatment
  Plasma exchange (removal of 1–1.5 times plasma volume on each session x5)
  Intravenous immunoglobulin (0.4 mg/kg/day x5)
  High dose corticosteroids (prednisolone 1 mg/kg/day)

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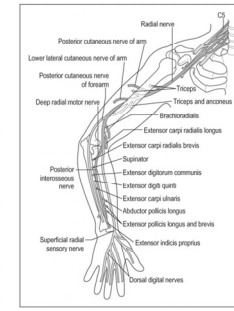
Focal neuropathies in ER

Acute compression	Entrapment neuropathy
Often abrupt onset	Slowly progressive
Severe weakness	Late feature of weakness
Less pain and sensory	Prominent pain and sensory

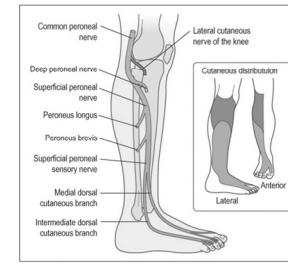
Radial neuropathy

- External compression at the spiral groove (Saturday night palsy)
- DDx with central lesion
- Supportive wrist and finger extension brace



Foot drop in Peroneal neuropathy

- External compression at the fibular head
- Weak ankle dorsiflexion and eversion with preserved plantar flexion and inversion
- Sensory abnormality in dorsum of foot



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Commonly prescribed steroid

Corticosteroids	Glucocorticoid potency	Equivalent dose (mg)	Minelarocorticoid potency
Short			
Cortisol (hydrocortisone)	1	20	Yes (1)
Prednisone	4	5	No
Prednisolone	4	5	No (0.8)
Methylprednisolone	5	4	No (0.5)
Intermediate			
Triamcinolone	5	4	No
Long			
Betamethasone	25	0.6	No
Dexamethasone	30	0.75	No (<0.2)

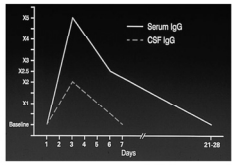
Methylprednisolone 1g = Prednisolone 800 mg, Dexamethasone 16 mg = Prednisolone 120 mg

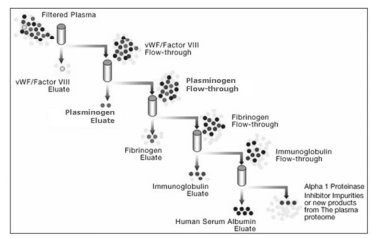
Steroid pulse therapy

- Infusion of a large dose of corticosteroid
  (1g **methylprednisolone over 30 min**)
- Adverse effect
  - Sudden death / ventricular dysrhythmia
  - Severe infection
  - Hyperglycemia / Pancreatitis
  - Gastrointestinal hemorrhage
  - Acute psychosis

IV Immunoglobulin

- Cold ethanol fraction of human plasma derived from pools of 3,000~10,000 donors → stabilized with glucose, maltose, glycine, sucrose, mannitol or albumin
- IgG (95%), IgA (2.5%), IgM
- Half life: 18-32 days





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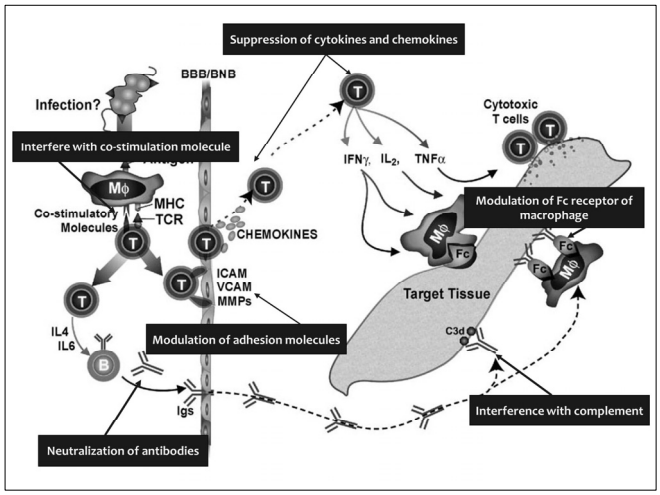

Administration of IVIg

- Dosage: 2g/kg (0.4g/kg for 5 days) or 1g/kg for 2 days
- Common minor adverse effect
  Headache, chill, myalgia, fever, fatigue
- Major adverse effect
  Thromboembolic event, aseptic meningitis
  Severe anaphylactic reaction (in case of severe deficiency of IgA)
  Renal tubular necrosis: reversible, pre-existing kidney disease or dehydration
- No need to pretreatment of steroid or antihistamine