Pediatric Neurology

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Exam Content for Neurology (5 %)

Clinical presentation
- Headache
- Altered mental status
- Seizures
- Muscle weakness

Brain Disorders
- Migraine syndromes
- Post-concussion syndrome
- Seizure disorders
- Hydrocephalus
- Static encephalopathy
- Stroke
- Vascular anomalies

Spinal cord Disorders
- Inflammatory/infectious
- Anatomic

Peripheral nervous system
- Muscular dystrophies
- Neurocutaneous disorders
- Degenerative neurologic disorders (genetic)
- Movement disorders
HEADACHE / ALTERED MENTAL STATUS

**Benign Headache**

Most MIGRAINE or TENSION

Uncommon < 4 years

Prevalence increases with age

Female predisposition increases with puberty

< 10-12 years girls = boys (1 : 1)

> 10-12 years girls > boys (1.5 : 1)

Remission occurs in 70% of cases by 9-16 yo

NORMAL EXAM = NO NEUROIMAGING

**Migraine**

- **Anterior** (frontotemporal, retro-orbital, uni > bilateral)
- **Pulsating** (throbbing, pounding, heartbeat)
- **Autonomic symptoms required**
  - nausea / vomiting, photo- or phono-phobia, pallor
- “Common migraine” - no aura (70-85 % children)
- “Classic migraine” - begins with a transient aura
  - **Visual** aura most common (15-30 min)
  - Genetically predisposed
- **Triggers** - poor sleep, hunger, illness, travel, stress
  - only 50 % migraineurs can identify trigger
Migraine common with other conditions:
- Somatic pain complaints
  - non-localizing abdominal discomfort
- Epilepsy
- Psychiatric
  - depression
  - anxiety

Migraine-related syndromes (variants)
- Benign paroxysmal vertigo (usually < 3 yo)
  - suddenly look scared, grab onto someone
  - nausea/vomiting, horizontal nystagmus, ataxia
- Paroxysmal torticollis
  - start in 1st year of life, resolve by age 5 years
  - benign self-limited episodes of head tilt lasting hours-to-days
- Cyclic vomiting
  - recurring episodes separated weeks-to-months
  - last hours-to-days
  - symptom-free between attacks

“Chronic Daily Headaches”
Migraines that have changed character due to
- Poor pain control
- Psychosocial stressors
- Medication overuse ("rebound headaches")

5+ per week, 15+ per month

No underlying pathology

Require daily prophylactic medication
Tension

- Posterior > anterior, or band-like
- Squeezing quality (tight, vice-like)
- Neck muscles sore
- Common trigger: STRESS!
- NO autonomic symptoms
  - NO nausea / vomiting / photo- or phonophobia
- NO aura
- Best treatments:
  - NSAIDs, relaxation / biofeedback

Dx / Work-Up of chronic headache

- Diagnosis based on H & P
- No neuroimaging if exam normal
- Inadequate evidence to support the value of routine labs or CSF analysis
- EEG may show non-specific abnormalities (focal slowing, occipital spikes after migraine)
  - Does not distinguish headache types
  - Does not distinguish headache cause
  - NOT RECOMMENDED for routine evaluation

Treatment for benign headaches

- Avoid / minimize triggers (MIGRAINES)
  - Optimize hydration
  - Good sleep hygiene / avoid sleep deprivation
  - Avoid hunger
  - Avoid food triggers (aged cheeses, chocolate, caffeine/ soda, processed deli meats, MSG, red wine)
- Mind-Body approach - minimize stress (TENSION)
  - Biofeedback / relaxation
  - Acupuncture
  - Self-hypnosis
ACUTE treatments for migraines

- Treat at onset
- Avoid medication overuse (meds \(\leq 2-3 \times \) per week)
- Anti-emetics (if nausea / vomiting):
  - metoclopramide (Reglan)
  - prochlorperazine (Compazine)
  - promethazine (Phenergan)
- NSAIDs 1st line med
- Triptans (serotonin 1B/1D receptor agonists)
  - sumatriptan (Imitrex) intranasal or oral tablets

CHRONIC (prophylactic) treatment of migraines

- If headaches \(\geq\) weekly or prolonged/ debilitating
- propranolol (Inderal)
  - side effects – hypotension, bradycardia
  - avoid in asthmatics, depressed
- amitriptyline (Elavil) – may take 6 weeks to work
  - side effects – orthostasis, dysrhythmia (EKG)
- anti-epileptics (topiramate, valproic acid, carbamazepine, neurontin)
- calcium channel blockers (verapamil)
- serotonin agonists (cyproheptadine, methysergide)
- vitamins (B2 / riboflavin, magnesium)

Worrisome headaches if:

- bulging fontanelle, cranial sutures separating
- ‘sun setting’ eyes
- always same location
- not responding to medical therapies
- progressive worsening in frequency / severity
- focal neurologic signs appear
  - 6th nerve palsy / horiz diplopia, new onset strabismus, papilledema\(^*\), hemiparesis, ataxia
  - awakens from sleep, worse in the morning, AM vomiting
- worse with valsalva (coughing, straining)
- has at-risk condition: VPS, neurocutaneous disorder (brain tumors)

\(^*\)late finding
“Sunsetting Eyes” - clinical sign of increased intracranial pressure

Ominous headaches (ICP) if:
- One or both pupils dilating, becoming non-reactive
- Emergent treatments
  - Mannitol, Lasix
  - Intubation / hyperventilation
  - VP Shunt
- Cushing Triad
  - Increased Systolic BP
  - Bradycardia
  - Irregular / fast breathing

“Minor” Head Trauma?
- No neuroimaging required if:
  - No focal neurologic signs
  - No LOC
  - Minimal vomiting (0-1 times)
- **Be aware an epidural hematoma (arterial bleed) can present hours-to-days after a LUCID INTERVAL with subsequent rapid deterioration and death – so if you see a patient for minor head trauma several days after the trauma but there was LOC, get the CT! Requires surgery!**
Subdural Hemorrhage
- Shearing of bridging VEINS between dural sinuses
- Associated with high speed acceleration-deceleration
- Mental status changes may be rapid or slow in onset
- NO lucid interval
- Can turn into chronic subdurals

Subdural Hemorrhage
- Surgical evacuation needed only if:
  - Increased ICP
  - Increasing size on CT
- In infant, think Shaken Baby Syndrome and look for retinal hemorrhages!

Subarachnoid Hemorrhage
- Sudden, extremely painful headache
- “Worst headache of my life”
- From trauma
- From spontaneous rupture of cerebral aneurysm or AVM
- Neurologic deficits, like stroke + headache
- Diagnose with non-contrast CT (SAH blood)
- If CT normal, do LP to check for RBCs that are the same count in all tubes (traumatic tap has fewer RBCs in each tube as the sequence of collection continues)
Get CT or MRI brain for headache before LP if:

Abnormal neurologic exam (may be FOCAL MASS) 
- altered mental status
- papilledema, VI nerve palsy, diplopia, new onset strabismus
- focal findings (hemiparesis)
- nuchal rigidity, fever

CT – BONE (skull fracture), BLOOD (intracranial hemorrhage), EMERGENCY (altered MS); also ventricles (hydrocephalus), sinuses, mass lesions (less detailed, but faster)

MRI – acute STROKE, vascular malformation; also ventricles (hydrocephalus), sinuses, mass lesions (more detailed, takes longer)

LP – OK for pseudotumor, meningitis, SAH hemorrhage after CT

Headache due to focal mass (focal exam)

CT brain + contrast:
- Enhancing tumor (white mass)
- Surrounding edema (darkened region surrounding the tumor)

Effacement of ventricle

Meningitis causing Communicating Hydrocephalus (arachnoid granulations inflamed / fibrosed)

CT brain: all ventricles enlarged

Headache, photophobia, fever, nuchal rigidity, altered mental status (increased ICP)

With encephalitis, also Seizures

*SKIP CT and do LP if patient stable and exam non-focal!*

Then start antibiotics
Reasons to skip LP with Meningitis and Just Give Antibiotics

- Hx coagulopathy / bleeding
- Nuchal rigidity already present
- Seizures
- Signs of increased ICP
  - High BP
  - Low HR
  - Irregular breathing

*Can't skip CT if exam focal

Aqueductal Stenosis causing Non-Communicating (Obstructive) Hydrocephalus

CT of the brain:
- Large frontal and temporal horns of lateral ventricles
- Large third ventricle
- 4th ventricle small
- Obstruction of CSF Flow from 3rd to 4th ventricle

Chiari II Malformation causing Non-Communicating (Obstructive) Hydrocephalus

Obstruction of CSF flow due to low lying cerebellar tonsils

Chiari I

Chiari II (lumbosacral myelomeningocele)
Dandy-Walker Malformation causing Non-Communicating (Obstructive) Hydrocephalus

Posterior fossa abnormality
- missing/small cerebellar vermis
- underdeveloped foramina (lateral Luschka and medial Magendie)
  obstructing flow of CSF out of 4th ventricle (enlarged)

Dandy-Walker Malformation

- presents with motor delay, enlarging head circumference, signs of increased ICP (nausea, vomiting), and breathing problems
- may have seizures if additional cortical malformations
- associated with PHACES SYNDROME and Congenital Melanocytic Nevi

Dandy-Walker + PHACES

- PHACES SYNDROME = large hemangioma of face/neck + one of following:
  - Posterior fossa malformation (Dandy Walker)
  - Hemangioma (along facial nerve distribution)
  - Arterial cerebrovascular anomaly
  - Cardiac anomalies (esp Coarctation of Aorta)
  - Eye anomalies (microphthalmia/smaller eye, strabismus)
  - Sternal defect
CSF-secreting Tumor Causing Hydrocephalus

Choroid Plexus Papilloma

Carotid Artery Dissection leading to Stroke

- Running with pencil in mouth
- Whiplash injury
- Blunt force chest trauma (aortic forces transmitted to carotid artery)

Angio reveals ‘string sign’

Other Stroke Risk Factors

- Congenital heart defects
- Sickle Cell anemia
- Prothrombotic disorders
- Polycythemia (ex. chronic hypoxia)
- G6PD deficiency
- Cancer
- Autoimmune / Inflammatory (Lupus)
- Polycythemia due to chronic hypoxia

Best Stroke work-up: 1) MRI, 2) Angio (CT shows only hemorrhagic stroke)
Sickle Cell Disease leading to Stroke

MRI of the brain revealing posterior circulation strokes (occipital cortex, cerebellum and brainstem)

Child with sickle cell anemia presenting with headache, ataxia and cranial nerve palsies.

Pseudotumor Cerebri

• aka Idiopathic or Benign Intracranial Hypertension
• NOT BENIGN if untreated – Can go blind!
• presents with headache, vision changes, signs increased ICP
• late findings include papilledema and vision loss
• CT or MRI brain NORMAL

Pseudotumor Cerebri

• Requires LP to document increased opening pressure
• CSF analysis normal
• Causes
  • excess vitamin A
  • isotretinoin (vitamin A derivative to treat acne)
  • tetracycline
  • thyroxine
Pseudotumor Cerebri

- Treatment
  - **Diamox** (acetazolamide)
  - Diuretics
- If vision compromised, **surgical fenestration of the optic nerve sheath**
- Uncommonly needs VP Shunt

**Question 1:**

An 8 year old boy presents with **blurry vision**, difficulty seeing the blackboard in school, and trouble watching television for **about 1 week**. He also has **headache** in the back of his head. On exam, he has a **right esotropia** (right eye deviates medially). There is no papilledema. The rest of the exam is normal.

The test MOST likely to establish the diagnosis is:

- A. CT of the head
- B. Electroretinography
- C. Lumbar puncture
- D. Radiographs of the cervical spine and skull base
- E. Visual evoked response (VER)
• **A. CT of the head** – pt has sixth nerve palsy with recent onset of headache (ominous signs)

• **B. Electroretinography** – for retinal problems; boy’s visual complaints are due to diplopia / VI nerve palsy

• **C. Lumbar puncture** – not safe to do unless mass lesion ruled out by CT (but if CT were normal, could be pseudotumor although patient has no stated risk factors for pseudotumor)

• **D. Radiographs of the cervical spine and skull base** – only for headaches associated with base of skull problems (e.g., platybasia, Klippel-Feil deformity) but these conditions can be associated with hydrocephalus so CT of the head still preferable

• **E. Visual evoked responses** – for optic nerve problems which could present with blurry vision, but patient has VI nerve palsy

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**Question 2:**

A 17 year old boy reports constant headaches since suffering a minor laceration to his right frontal scalp 5 months ago. There was no LOC. Now he has daily frontotemporal headaches for which he frequently takes acetaminophen, ibuprofen or naproxen, but obtains little relief. His exam is normal. A urine tox screen is negative.

Of the following, the MOST appropriate next step in the management of this child is:

• **A. initiate sumatriptan and propranolol**

• **B. obtain computed tomography (CT) of the head**

• **C. perform a lumbar puncture**

• **D. refer the patient to a psychiatrist**

• **E. stop all analgesics and start amitriptyline**
A. initiate sumatriptan and propranolol – no; sumatriptan will contribute more to medication overuse (propranolol prophylaxis OK)

B. obtain computed tomography (CT) of the head – no; exam is normal; not likely to have an injury due to trauma becoming symptomatic after 5 months

C. perform a lumbar puncture – no; no papilledema and exam is normal (but if papilledema without fever, think pseudotumor)

D. refer the patient to a psychiatrist – may be needed in the future, but first must address medication overuse

E. stop all analgesics and start amitriptyline – need to stop acute abortive medications to recover from “chronic daily headaches” caused by medication overuse; initiating prophylactic medication (amitriptyline) will begin to decrease headache

Question 3:
A 15 year old boy who has cystic acne has experienced a frontal headache for 1 week. He reports that the only drug he takes is isoretinoin. Seen in the emergency room overnight, a CT of the brain was normal. He was given meperidine and discharged home. He presents to your office today for follow-up. The boy has papilledema, but his neurologic exam is otherwise normal.

Of the following, the MOST appropriate next step in the evaluation of this patient is:

- A. lumbar puncture
- B. MRI of the brain with gadolinium contrast
- C. neurosurgery consultation
- D. ophthalmology consultation
- E. urine toxicology screen
**A. Lumbar puncture** – headache and papilledema suggest increased intracranial pressure, but the CT of the head ruled out mass lesion. No MRI is needed as a lesion big enough to cause papilledema would be evident on CT. With normal CT of the brain, increased intracranial pressure headache suggests pseudotumor. Lumbar puncture would be both diagnostic and therapeutic. Follow-up with an ophthalmologist is reasonable, but is not needed before the LP because papilledema was already detected and the LP is necessary to make the diagnosis. Uncomplicated pseudotumor does not require neurosurgical consultation unless medical therapies are ineffective and the ongoing increased intracranial pressure jeopardizes (chokes) the optic nerves. Other causes of pseudotumor include: hyper- or hypo vitamin A, Addison disease, hypoparathyroidism, iron deficiency, polycythemia, otitis, mastoiditis, SLE, pregnancy, obesity, steroids, retinoids, OCPs, tetracycline, minocycline.

**Question 4:**

You are counselling the parents of a 3 month old girl who just underwent placement of a ventriculoperitoneal shunt for obstructive hydrocephalus secondary to aqueductal stenosis.

While talking with this family, you are most likely to state that:

- **A. antibiotic prophylaxis will be required before all dental procedures**
- **B. lethargy and decreased spontaneity are sensitive indicators of shunt malfunction**
- **C. most shunt infections with coagulase negative staphylococci occur between 3-12 months after shunt placement**
- **D. the child will need to wear a helmet while she is learning to walk**
- **E. the parents should depress the shunt bulb (or reservoir) daily to observe its refill and ensure the device works properly**
B. Lethargy and decreased spontaneity are the most sensitive indicators of shunt malfunction. Most shunt infections arise from coagulase-negative staph epidermidis in the first 3 months after surgical placement. Whenever a child with a shunt presents with fever, a shunt infection must be considered. Signs of shunt infection or malfunction include fever, malaise, headache, irritability, anorexia and vomiting. Shunt malfunction is evaluated by CT of the head and radiographs along the path of the catheter tubing to confirm its continuity. Needle access to the bulb (reservoir) or manipulation of the bulb is best done by a neurosurgeon. Children with shunts do NOT require a helmet nor antibiotic prophylaxis.

SEIZURES AND EPILEPSY IN CHILDREN

Seizures and Epilepsy

- Neonatal Seizures (not epilepsy)
- Febrile Seizures (not epilepsy)
- Infantile Spasms (epilepsy)
- Lennox-Gastaut Syndrome (epilepsy)
- Childhood Absence (Petit Mal) Epilepsy
- Juvenile Absence Epilepsy
- Juvenile Myoclonic Epilepsy
- Benign Rolandic Epilepsy
- Complex Partial Epilepsy
Epidemiology of Epilepsy in Children

- EEG predicts seizure recurrence after the 1st unprovoked seizure:
  - If EEG normal, up to ~40% recurrence risk
  - If EEG abnormal, up to ~80% recurrence risk
- ~50% of 2nd epileptic seizures occur within 6 months of the 1st
- 70-80% achieve remission (“outgrow” seizures)

Epidemiology of Seizures and Epilepsy

- Increased recurrence risk if:
  - “symptomatic” etiology (dev delay, MR / CP)
  - abnormal EEG
  - complex febrile seizures
  - Todd’s paresis (focal epilepsy)
  - nocturnal seizures (genetic epilepsy)
  - + FHx childhood onset epileptic seizures
- Factors that do NOT influence recurrence risk:
  - age
  - seizure duration / status epilepticus !!

First Time Seizure

- If GTC seizure in > 1 year old (healthy), no further work up if seizure < 5 minutes
- Chance of future epilepsy > 30%
- If neurologic deficits >> 30%
- If seizing in the ER
  - check glucose
  - if glucose normal, give IV Ativan (acts fast, longer half life than Valium); if no IV, give rectal Valium
  - if seizure recurs, give long acting anti-seizure med
Possible seizure?

- Todd’s paralysis
  - **acute unilateral weakness** that remains after a seizure and resolves over time
  - Think unwitnessed focal seizure!

Neonatal Seizures (not epilepsy)

- Benign Neonatal Convulsions/Seizures
  - Onset usually around DOL 5 (4-6 common range, can occur DOL 1-7)
  - No perinatal complications, 39+ wks GA
  - Autosomal dominant condition (+FHx)
    - Potassium channelopathy (KCNQ2 > KCNQ3 mutation)
  - Apneic and/or Focal clonic most common
    - Increase in frequency over 1-3 days to status epilepticus
  - Typically easy to control with medication; resolve in 1st year of life
  - Neuroimaging and etiologic work up negative

Neonatal Seizures that may progress to epilepsy

Multiple Causes

- Hypoxia-Ischemia (HIE)
- Infection (meningitis, sepsis)
- Hemorrhage (IVH, subarachnoid, intraparenchymal)
- Infarction (thrombotic, hemorrhagic)
- Metabolic derangement (low sodium, low calcium, glucose)
- Inborn errors of metabolism
- CNS malformation

- Treatments: IV phenobarbital → Keppra, Dilantin → Benzo / Versed → Pentobarbital, Lidocaine
- If seizures do not respond to conventional meds above, trial of IV pyridoxine 100 mg (pyridoxine deficiency)
**Febrile Seizures (not epilepsy)**

- 2-5% of children age ~ 6 months – 6 years
  - Provoked by a sudden spike in temp
  - Usually with URI, acute OM, AGE (genetic predisposition)

- “Simple”
  - Generalized convulsion (whole body shaking)
  - Brief (< 15-20 minutes)
  - Only one in the course of an illness
  - Future risk of epilepsy 1% like other children

- “Complex”
  - Focal seizure (one side of body shaking, staring)
  - Prolonged (> 15-20 minutes)
  - Multiple in 24 hours

**Febrile Seizures**

- Highest risk for recurrence if:
  - 1st febrile seizure < 18 months
  - +FHx febrile seizures
  - Febrile seizure is the first sign of an illness
  - Low grade fever

- Prolonged initial febrile seizure does NOT substantially boost the risk of febrile seizure recurrence. However, if another does occur, it is more likely to be prolonged.

- Prolonged > 30 minute febrile seizure may predict increased risk (30-40%) of future epilepsy

**Epilepsy that mimics Febrile Seizures**

- Generalized Epilepsy Febrile Seizure Plus (GEFS+)
  - May initially present as febrile seizures prior to the onset of afebrile seizures
  - Genetic etiology – ex. SCN1A gene mutation
Treatment of Febrile Seizures (not epilepsy)

- Considered benign, not warranting daily anti-seizure medication
- Phenobarbital or valproic acid provide partial prevention but not routinely recommended

- Rectal Diastat (valium gel) may be used to:
  - Abort prolonged complex febrile seizure
  - Prevent complex febrile seizure clusters (if child known to cluster)
  - Prevent febrile seizure recurrence during a febrile illness

- Anti-pyretics have NOT been proven to decrease the risk of recurrent febrile seizures

Infantile Spasms (West Syndrome) – a severe epilepsy

- Severe abnormal EEG pattern: disorganized, discontinuous, high amplitude, multifocal spikes called HYPSSARRHYTHMIA

Clinical spasms (1-2 secs):
- A subtle momentary flexion or extension of the body
- Occur in clusters when drowsy (waking or falling asleep)

Treatment: ACTH (Vigabatrin if tuberous sclerosis)

Infantile spasms

- May be mistaken for colic, reflux, hiccups, or a startle

- Common etiologies:
  - Perinatal insults (ex. hypoxia-ischemia, meningitis)
  - Brain malformation
  - Neurocutaneous disorder (Tuberous Sclerosis)
  - Metabolic disorder
  - Gene mutations (ARX, COKL5, FOXG1, GRIN1, GRIN2A, MAGI2, MEF2C, SLC25A22, SPTAN1, STXBP1)

- Prognosis best (10% good outcome) if idiopathic
  - Normal development at onset of infantile spasms
  - Extensive etiology testing negative

- Prognosis poor for:
  - Seizure control (infantile spasms and future seizures)
  - Future neurocognitive and developmental abilities
Lennox-Gastaut Syndrome – a severe epilepsy

- Often evolves from infantile spasms
- Syndrome defined by a TRIAD of:
  - Multiple seizure types (atonic, atypical absence, myoclonic, tonic-clonic, partial)
  - Developmental delay
  - Slow spike-wave” EEG pattern (< 2.5 Hz)
- Prognosis poor

Childhood Absence (Petit Mal) Epilepsy
a genetically predetermined generalized epilepsy = a ‘primary generalized’ epilepsy

- Sudden onset of staring, interrupting speech or activity
- Occurs multiple times per day
- Short duration (seconds)
- Occurs in school aged children ~ 4-12 years, otherwise normal

Childhood Absence (Petit Mal) Epilepsy (continued)

EEG findings characteristic:
- bilateral generalized 3 Hz spike-and-wave discharges
- provoked by hyperventilation and photic stimulation

Treatment: ethosuximide (Zarontin) = valproic acid (Depakote)

Commonly resolves by adolescence

Etiologic gene mutations – include GABA<sub>a</sub>-Receptor mutations
(GABRA1, GABRB3, GABRG2, CACNA1H, JRK)
Juvenile Absence Epilepsy
(another ‘primary generalized’ epilepsy)

- onset a bit older than childhood absence epilepsy
  - in adolescence (closer to middle school than elementary school)
- similar staring seizures but:
  - longer duration
  - fewer (less frequent)
- higher risk for other generalized seizures:
  - GTC
  - Myoclonic
- less likely to outgrow
- EEG generalized spike wave discharges:
  - Faster than 3 Hz (4-6 Hz)

Juvenile Myoclonic Epilepsy (JME)
(another ‘primary generalized’ epilepsy)

- Seizure types:
  - myoclonic in AM
  - “grand mal”
  - absence

EEG: bilateral generalized 4-6 Hz spike-wave or polyspike-wave activity

Genetic mutations with CACNB4, CLCN2, EFHC1, GABRA1, GABRD

Juvenile Myoclonic Epilepsy (JME)
(continued)

- Seizures provoked by sleep deprivation, photic stimulation, excess alcohol
- Mean age at onset 14 years
- EEG: 4-6 Hz spike wave provoked by photic stimulation
- Recent reports of relapse following med discontinuation if GTC + myoclonic + absence seizures in 1st year of dx
- Treatment with broad spectrum AED
  - Keppra (levetiracetam), Lamictal (lamotrigine), Depakote (valproic acid)
Benign Rolandic Epilepsy
(a genetically predetermined focal epilepsy)

- Onset 3-13 years old, boys > girls
- 15% of epileptic children
- Normal IQ, normal exam, normal MRI
- May have + FHx sz
  - Candidate gene mutations on chromosome 11 (11p13) and chromosome 15 (15q14)
- Seizure description:
  - When awake:
    - twitching and/or tingling on one side of body
    - speech difficulty, may drool / gag
    - no loss of consciousness, usually < 2 minutes
  - When asleep (nocturnal):
    - “grand mal” with focal features

Benign Rolandic Epilepsy
Aka Benign Focal Epilepsy of Childhood with Centrotemporal Spikes

EEG pattern has autosomal dominant inheritance
bilateral independent centrotemporal spikes

Benign Rolandic Epilepsy

- Treatment recommended only if:
  - Seizures frequent (which is unusual)
  - Socially stigmatizing if occur in wakefulness
  - Anxiety provoking for parents if occur in sleep
- Effective treatments:
  - Avoidance of sleep deprivation
  - Medications: carbamazepine, oxcarbazepine
  - Time (outgrown by adolescence)
- May have co-morbid learning disabilities
Other Epilepsy Syndromes

1) Landau-Kleffner Syndrome

- an acquired EPILEPTIC APHASIA in a PREVIOUSLY NORMAL child, usually 3-7 years old
- Gradual or sudden inability to understand or use spoken language ("word deafness")
- Must have EEG abnormalities in deep sleep (sleep activated)
- Additional behavioral and psychomotor disorders (hyperactivity, aggressiveness, depression, autistic features)
- May have additional overt clinical seizures (80%) in sleep

Other Epilepsy Syndromes

2) Rett Syndrome

- Occurs only in girls (X-linked lethal mutation) – MECP2 gene mutation
- Initial normal development → dev regression / autistic (loss of motor / language / social skills)
- Acquired microcephaly (deceleration of head growth)
- Hand wringing / alternating hand movements
- Irregular breathing patterns
  - Apnea
  - Hyperpnea
  - Breathholding
- Seizures

Complex Partial Epilepsy

- Impairment of consciousness (staring)
- Temporal lobe onset (80%) most common

Mesiotemporal sclerosis
Differentiating “Staring” Seizures

- Complex Partial Seizures
  - + aura
  - + incontinence
  - + postictal lethargy
  - EEG with focal spikes
  - lasts minutes
    (but can be shorter)
- Absence Seizures
  - NO aura
  - NO incontinence
  - NO postictal period
    (immediate recovery)
  - EEG with generalized 3 Hz
    spike wave activity
  - lasts seconds
    (but can be longer)

Spells that mimic seizures

- Apnea / ALTE
- GER
- Sleep disorders (nocturnal myoclonus, night terrors, narcolepsy/cataplexy)
- Migraine variants (esp. aura)
- Benign breathholding spells
  - No neuro consult / lab / EEG / CT, Fe for cyanotic type
- Syncope
- Movement Disorders (tics, tremor, dystonia)
- ADD
- Behavioral Stereotypies (PDD)
- Pseudoseizures (psychogenic seizures)
  - Strange posturing, back arching, writhing
  - Alternating L and R limb shaking during same seizure
  - Psychosocial stressor

Medical triggers of seizures (acute symptomatic seizures)

- ↓ or ↑ glucose
- ↓ calcium
- ↓ or ↑ sodium
- CNS infection (meningitis, encephalitis)
- acute trauma
- toxic exposure
- acute ↑ bp
Treatment of epileptic seizures

- After second unprovoked seizure (after 1st if EEG abnl)
- Choice of AED - maximum effectiveness for that particular seizure type, aiming for minimal side effects
- 70% become seizure free on monotherapy
- an additional 15% become seizure free on polypharmacy
- 15% remain intractable
- Discontinue AED after 2 years seizure free (exception: JME subclass with mixed myoclonic + absence + GTC sz in 1st year of presentation)
- Alternate treatments:
  - Ketogenic diet (high fat diet)
  - Vagal nerve stimulator implantation
  - Other Epilepsy Surgery
  - CBD oil (marijuana plant extract)

Pathognomonic side effects of AEDs

- valproic acid (Depakote): liver toxicity, weight gain, acute pancreatitis
- lamotrigine (Lamictal): Stevens-Johnson syndrome
- phenytoin (Dilantin): gingival hypertrophy, acute ataxia, osteoporosis
- phenobarbital: adverse behavior / hyperactivity
- carbamazepine (Tegretol): agranulocytosis, aplastic anemia
- oxcarbazepine (Trileptal): low sodium
- ethosuximide (Zarontin): lupus-like reaction (+ANA)
- topiramate (Topamax): weight loss, acidosis, renal stones, anhidrosis
- felbamate (Felbatol): aplastic anemia
- levetiracetam (Keppra): mood / behavioral changes

Status Epilepticus

- Def:
  - seizure lasting > 30 minutes or repeated seizures > 30 minutes without recovery in mental status between seizures
  - seizures > 1 hour associated with neuronal injury due to glutamate excitotoxicity
- Evaluation and treatment if seizure lasts > 5 minutes:
  - ABC’s (RR, HR, BP)
  - check temp, glucose, electrolytes, CBC, renal and hepatic function, AED levels
  - Benzodiazepine → phenytoin → phenobarbital
Question 5:

An 11 month old boy is brought to the ER because of a seizure. At home, he was “unresponsive and jerking all over” for 30 minutes. The father reports that he himself had febrile seizures as a child. On exam, the boy’s temperature is 103.5 F (39.7 C), HR 140, RR and BP normal. He is sleepy but arousable. The neuro exam is non-focal.

Of the following, the MOST likely factor to increase his chance of developing epilepsy is:

- A. his first complex febrile seizure
- B. family history of febrile seizure
- C. male sex
- D. onset of febrile seizures before 1 year of age
- E. temperature greater than 103 F (39.5 C)

- **A. His first complex febrile seizure.** Complex febrile seizures are 1) longer than 15 minutes in duration, or 2) more than one (multiple) within 24 hours or 3) focal in nature. Complex febrile seizures increase the risk of developing future epilepsy, particularly if other epilepsy risk factor is identified. Other risk factors for future epilepsy include: family history of epilepsy (NOT febrile seizures), and the presence of developmental or neurologic abnormalities at the time of the febrile seizure. Male sex is not a risk factor for future epilepsy.

  Risk factors for the recurrence of FEBRILE seizures (not epilepsy) include: family history of febrile seizures, onset of febrile seizures before 1 year of age, and a low grade fever with the febrile seizure.
Question 6:

A father brings his 6 year old daughter to you because her teacher has observed multiple daily episodes in which the child stares and is unresponsive to verbal cues. The teacher also noted facial twitching with some of these several second events. Her physical exam is normal.

Among the following, the MOST appropriate medication for this child is:

- A. atomoxetine (Strattera)
- B. carbamazepine
- C. clonidine
- D. ethosuximide
- E. methylphenidate

D. Ethosuximide (brand name Zarontin). The girl in the vignette has absence epilepsy (aka petit mal epilepsy). Alternative treatments include valproic acid or lamotrigine. Carbamazepine makes the absence seizures worse (though one might mistakenly prescribe carbamazepine on the basis of her seizure description; complex partial seizures mimic the staring of absence seizures though are prolonged in duration and commonly preceded by an aura; complex partial seizures are treated with carbamazepine). The differentiation between absence seizures and complex partial seizures requires EEG testing (absence seizures will be associated with generalized 3 cycle per second spike and wave activity; complex partial seizures will be associated with focal spikes, usually temporal lobe). Atomoxetine, clonidine and methylphenidate are treatments for ADD.
Question 7:

After a year long history of twitching upon waking, a 16 year old girl experiences a generalized tonic-clonic seizure. Subsequent EEG demonstrates 4-5 cycle per second (Hz) generalized polyspike and wave; myoclonic seizures occur with photic stimulation. She will see a neurologist later this week, but she and her parents present now to your office for initial counseling. Diagnosis?

The most likely statement you will make to the family is:

- A. oxcarbazepine should be started, but can be stopped after a 2 year period free of seizures
- B. oral contraceptives are contraindicated while she is receiving gabapentin
- C. the girl may not drive a motor vehicle for 18 months
- D. the girl must quit her school swim team
- E. valproic acid will be required lifelong

E. Valproic acid will be required lifelong.

The patient in the vignette has juvenile myoclonic epilepsy, possibly the only epilepsy that requires lifelong treatment despite achieving a 2 year seizure free interval. Risk factors for seizure recurrence after a prolonged seizure free interval include mental or motor handicap, onset of seizures after age 12 years, and multiple medications needed to control the seizures. The girl should be encouraged to lead a normal life, including swimming (under direct adult supervision) or driving unaccompanied (which in most states requires only 3-12 months seizure free interval on medication). Girls who are sexually active should be counselled about the risk of fetal malformations associated with most anti-convulsant medications, particularly neural tube defects associated with valproic acid or carbamazepine. Oxcarbazepine and gabapentin are not indicated for generalized seizures (best for focal onset epilepsy).
Question 8:
A 3 year old boy presents to the ER following a 2 minute seizure. The parents report that the seizure began with left upper extremity shaking, then shaking of the entire body with loss of consciousness. On exam, temp is 103 F (39.5 C). He remains lethargic for several hours. CT of the head with contrast is normal. LP reveals CSF with 62 WBC, 0 RBC, protein 72, glucose 46. Gram stain is negative.

The MOST appropriate next step in the management of this child is to:

- A. administer rectal diazepam
- B. initiate dexamethasone intravenously
- C. observe him
- D. provide a bolus of fosphenytoin intramuscularly
- E. start acyclovir intravenously

E. Start acyclovir intravenously – The child in the vignette continues to appear lethargic after a focal seizure in the setting of fever. This is unusual for a febrile seizure so herpes encephalitis must be considered and promptly treated while tests (LP) are being obtained. IV dexamethasone is indicated for bacterial H. flu meningitis (not supported by the LP) or brain tumor (not supported by the CT). Because the child is not presently seizing, there is no need for rectal diazepam or fosphenytoin. To do nothing (observe him) is not prudent in view of the mental status change. The hallmark clinical features of HSV encephalitis include fever, altered mental status, and focal neurologic signs (on exam or during a seizure). Abnormal findings on CT of the brain (localized cerebral edema and hemorrhage in the temporal lobes) comes late in the clinical course and therefore, normal CT does not exclude the diagnosis.
PERIPHERAL NERVOUS SYSTEM DISORDERS

Presents as WEAKNESS with lower motor neuron signs

REFLEXES ABSENT or DIMINISHED
NO clonus
NO upgoing toes

If Weakness is Progressive….

- Evaluate for RESPIRATORY COMPROMISE!
  - TACHYPNEA
  - ACCESSORY MUSCLE USE
  - PARADOXICAL (BELLY) BREATHING
  - SHALLOW RESPIRATIONS

- Pulse Ox is useless! Poor indicator of neuromuscular compromise to breathing

Tests for Muscle, Nerve, and Myelin

- Electromyogram (EMG) – you suspect a muscular dystrophy > neuropathy

- Nerve Conduction Velocity (NCV) – you suspect neuropathy or nerve demyelination

- Somato-sensory Evoked Potentials (SEP) – you suspect a brain or spinal cord demyelinating process
1. **ANTERIOR HORN CELL**
   A. Spinal Muscular Atrophy (genetic)
   B. Poliomyelitis (acquired)

2. Peripheral nerve

3. Neuromuscular junction

4. Muscle

**A. Spinal muscular atrophy (SMA)**

**Type 1 SMA - Werdnig-Hoffman**
- Prenatal – decreased fetal movements
- Neonatal / early infancy
  - severe hypotonia
  - tongue fasciculations***
  - absent reflexes
  - breathing difficulties (die of respiratory failure)
  - Poor suck
- Motor milestones: never sit
- Autosomal recessive - SMN (survival motor neuron) gene mutation, chromosome 5

**Type 2** less severe, typically sit, don’t walk

**Type 3** (Kugelberg-Welander) least severe, may walk, ultimately wheelchair bound

**Diagnosis of SMA:**
- Normal CPK (this is NOT a muscle problem; nerve problem)
- Genetic analysis – highly sensitive and specific
- If gene study positive, no additional testing required
- If gene study negative,
  - EMG → fibrillations (muscle denervation)
  - Muscle biopsy
Treatment of SMA:
- aggressive and early respiratory toilet
- assisted ventilation for most type 1 SMA + many type 2 SMA
- physical therapy to avoid / minimize contractures
- encouragement of full educational pursuits—intellect unaffected

B. Poliomyelitis (infantile paralysis)
- viral infection (fever, headache, sore throat, N/V, muscle aches) -- destruction of anterior horn cells (motor neurons) in spinal cord
- asymmetric flaccid paralysis, legs worse than arms
- may involve face (bulbar muscles)
- reflexes initially increased → then decrease to become absent reflexes
- CSF – increased WBCs (lymphocytes), mildly elevated protein (difficult to detect virus)

1. Anterior horn cell
2. PERIPHERAL NERVE
   A. Guillain-Barre Syndrome (acquired)
   B. Charcot-Marie-Tooth disease (genetic)
3. Neuromuscular junction
4. Muscle
A. Guillain-Barre Syndrome (GBS)

- Most common ACUTE neuropathy in children
- Most common cause of rapidly progressive weakness
  - early “pins and needles” in hands and feet
  - early back and hip pain common
  - ascending bilateral paralysis (days-to-weeks)
  - absent reflexes
- ICU observation if:
  - autonomic nerves affected → cardiac dysrhythmia
  - respiration affected → may need intubation/ventilation
- symptoms may worsen in 1st 4 weeks
- normal sensation, bowel/bladder fxn, rectal tone
- Miller-Fisher variant = Areflexia + Ataxia + CN palsies
  (CN palsies = abnormal eye movements, facial paralysis
described as “flat affect”, “decreased facial movements”)

Guillain-Barre Syndrome (GBS)

- aka Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP)
- 2/3 report antecedent infection 1-3 weeks prior
  - Campylobacter jejuni (esp. China) (diarrhea)
  - CMV
  - EBV
  - Hepatitis
  - Flu or vaccine
  - mycoplasma
  - HSV

- Diagnosis of GBS:
  - CSF (> 1 week)
    - increased protein + normal cells
    - “albumino-cytologic dissociation”
  - NCV (Nerve Conduction Velocity) – slowing
  - MRI – gadolinium enhancement of spinal roots
  - Send titers for suspected pathogens

- Management:
  - Look for tick and pull off
  - IVIG or plasmapharesis if ventilation affected, or
    rapidly worsening and has not nadired
  - OT/PT
  - Steroids NOT helpful
Differential Diagnosis of GBS

- Spinal Cord Disorders (but GBS has ABSENT REFLEXES)
- Tick paralysis - summer time, recent vacation, playing in the woods
  - no fever, normal CSF (normal protein)
  - caused by neurotoxin produced by tick
  - progresses faster than GBS (hours-to-2 days)
  - ABSENT REFLEXES
  - Remove the tick and the patient improves!

Prognosis of GBS

- Usually good (~75%), may take weeks-to-months to recover
- Poor prognostic signs:
  - rapidly progressive weakness in < 7 days
  - assisted ventilation
  - Axonal involvement (not just demyelination) – seen on NCVs as decreased amplitudes

B. Charcot-Marie-Tooth (CMT) Disease

- the most common CHRONIC neuropathy in children, slowly progressive over decades
- a hereditary peripheral (sensory-motor) neuropathy (HSMN)
- Initial symptoms noted > 10 years:
  - "pes cavus" – high pedal arches
  - "champagne glass" or "stork" deformity - muscle atrophy below the knees
  - bilateral foot drops - slaps feet when walks, difficult to heel walk, tend to toe walk
  - poor or absent reflexes
CMT Disease

“Champagne Glass” or “Stork” Deformity
Distal Muscle Atrophy of
Lower Extremities

High Arched
Foot Deformity
“Pes Cavus”

- Diagnosis of CMT:
  - NCVs abnormal - conduction slowing
  - Genetic testing (autosomal dominant)
    - peripheral myelin protein 22 (PMP22) mutation

- Management:
  - PHYSICAL THERAPY
  - Bracing for the foot drop improves gait
  - Relatively rare to need a wheelchair later in life

1. Anterior horn cell
2. Peripheral nerve
3. NEUROMUSCULAR JUNCTION
   A. Myasthenia Gravis (autoimmune or genetic)
   B. Infant botulism (acquired)
4. Muscle
A. Myasthenia Gravis (MG) – 3 forms

- **Neonatal**
  - transplacental passage of maternal Ach-R antibodies
  - severe hypotonia at birth, but self-limited (days-to-weeks)
  - may require temporary feeding and respiratory support

- **Congenital – not autoimmune**
  - neonatal, infantile or very early childhood onset
  - ptosis constant (doesn't wax and wane)
  - anatomic or physiologic abnormality of NMJ (muscle bx)
    - abnormal presynaptic acetylcholine packaging
    - presynaptic acetylcholinesterase deficiency
    - abnormal post-synaptic Ach receptors

- **Autoimmune - most common; antibodies block post-synaptic acetylcholine receptors (Ach-R Ab)**

Autoimmune MG

- 2 subtypes recognized:
  - **Ocular** (ptosis, ophthalmoplegia)
  - **Generalized weakness**

- Onset acute or subacute:
  - varying ptosis, abnormal eye movements
  - difficulty swallowing, poor gag
  - varying weakness, DTRs diminished
  - diurnal fatigue (worse at night)
  - may require ventilatory support at presentation
  - symptoms exacerbated by infection, hot weather, medications

Autoimmune MG

- 1st best step in evaluation
  - check for respiratory compromise (tachypnea, shallow weak respirations)
  - may need to intubate

- **Medications that may worsen Myasthenia Gravis**
  - D-penicillamine
  - Aminoglycosides
  - beta-blockers
  - Ca channel blockers
  - laxatives / antacids (Mg salts)
  - iodinated contrast dyes (gad)
Autoimmune MG

- **Dx: Tensilon (edrophonium) test**

Edrophonium blocks / inhibits the enzyme acetylcholinesterase from metabolizing acetylcholine in the synaptic cleft so there is more acetylcholine available to bind to the acetylcholine receptors that are not blocked by antibody; a 'positive' test shows improved strength such as less ptosis / eyes more open

Autoimmune MG

Other important work-up:

- **Chest imaging** (x-ray, CT, MRI) to look for **thymoma (surgical removal could improve symptoms)**
- Send serum for:
  - quantitative immunoglobulins (increased in MG)
  - antibodies to acetylcholine receptors (Ach-R Ab)
  - antibodies to muscle specific receptor tyrosine kinase (MuSK Ab)

Autoimmune MG

- **Management:**
  - **Cholinesterase inhibitors**
    - Pyridostigmine (Mestinon)
      - inhibits the metabolism of Ach
      - monitor for hyper-cholinergic symptoms
      - increased lacrimation / salivation
      - bradycardia
      - stomach cramps
  - **Prednisone** to suppress antibody production
  - **Plasmapharesis** to filter off antibodies
    - for acute and severe weakness
    - for respiratory depression
  - **Thymectomy**
    - for medication refractory generalized MG
B. **Infant Botulism** (6 weeks – 6 months)

- **Toxin** of the gram+ bacteria *Clostridium botulinum* irreversibly binds to the acetylcholine receptor at the NMJ (bacterial spores grow in the intestine)
- Rapidly progressive DESCENDING paralysis (hours)
- **Symptoms:**
  - **Constipation, progressive ptosis**
  - descending paralysis, hypotonia, head lag
  - poor feeding/suck, absent gag, weak cry
  - reflexes reduced
  - respiratory failure, apnea

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**Infant Botulism**

- **Source of C. botulinum spores**
  - Soil
  - Foods
    - honey
    - corn syrups
- **Diagnosis**
  - Isolation of organism or toxin in stool
- **Treatment**
  - Supportive care (may require intubation)
  - IV anti-toxin Botulism Immune Globulin (BIG)

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**1. Anterior horn cell**
**2. Peripheral nerve**
**3. Neuromuscular junction**
**4. MUSCLE**
Duchenne and Becker Muscular Dystrophy
Duchenne Muscular Dystrophy
- X-linked (only boys) (Xp21) – mostly spontaneous mutations; FHx often negative; check Mom’s CPK
  - Preschool age of onset
  - Proximal muscle weakness – difficulty running, hopping, stair climbing, standing from sitting (“Gower”)
  - Face and eye weakness NOT present
  - Pseudohypertrophy of calf (gastroc) muscles
  - Toe walking, lordotic waddling gait
  - Wheelchair bound by 7-8, cant walk by 13
  - Progressive dilated cardiomyopathy occurs
  - Death by late teens-to-early 20s
    - resp failure due to chest weakness, scoliosis

BECKER Muscular Dystrophy (milder)
- slowly progressive
- onset after preschool (elementary or later)
- prognosis more variable
  - may live past middle age
  - may self-ambulate without a wheelchair for may decades
  - progressive dilated cardiomyopathy occurs
  - may result in end-stage cardiac failure
Diagnosis:
- Elevated CPK (always >10,000 in DMD)
- Genetic testing (dystrophin mutation)
- Muscle biopsy if genetic testing negative (unknown mutation) – stain for dystrophin (deficient)
  - absent staining in Duchenne MD
  - reduced staining in Becker MD
  - normal in all other muscle disorders

Optimal management:
- orthotics to preserve ambulation
- OT/PT to minimize contractures
- when non-ambulatory, prevent scoliosis with:
  - proper fitting wheelchair (by 7-8 years)
  - spinal fusion if necessary

Myotonic Dystrophy
- Autosomal Dominant (childhood form from mother)
- Distal weakness, especially face, hands, legs
  - Slow relaxation of muscle after contraction
  - Shake mother’s hand, unable to relax
- CPK usually normal
- Associated problems:
  - Endocrine
  - GI
  - Cognitive

Question 9:
A 6 year old girl is brought to your office for clumsy gait of 3 days duration. On exam, she is afebrile and ataxic. She has a full right facial palsy. Deep tendon reflexes are absent at the knees and ankles.

Of the following, the MOST appropriate next step in the evaluation of this child is:
- A. computed tomography (CT) of the head
- B. electroencephalography (EEG)
- C. lumbar puncture
- D. magnetic resonance imaging of the spine
- E. urine toxicology screen

C. Lumbar puncture – the ataxia plus areflexia plus facial palsy is pathognomonic for Guillain-Barre syndrome (Miller-Fisher variant). LP will reveal increased protein (due to breakdown of myelin proteins / demyelination of the nerve roots) with normal WBC count ("cytoalbuminemic dissociation").

Topic: Newborn/Infant Exam
- Clonus - normal in immature nervous system (newborn / young infants)
  - Jaw clonus
  - Bilateral ankle clonus

- Babinski reflex (upgoing toe) normal in immature nervous system (up to 2 yo)

- Upgoing toe > 2 yo is pathologic
**Topic: Erb vs Klumpe Palsy**

- Due to birth trauma / shoulder dystocia with:
  - BREECH delivery
  - LGA newborns (maternal diabetes)
  - FRACTURED CLAVICLE
  - C-SECTIONs

**Erb Palsy**

- UPPER brachial plexus injury (spinal roots C5-6, C5-7)
- If C5-6, paralysis of upper arm but able to GRASP and EXTEND the HAND
- If C7 involved, holds arm in 'waiter tip' posture (can grab the money!)
- 5% have **unilateral diaphragmatic paralysis** due to damaged **phrenic nerve** by fractured clavicle (only motor innervation of diaphragm)

**Klumpke Palsy**

- LOWER brachial plexus injury (spinal roots C8-T1)
- less common, worse prognosis (nerves are typically torn)
- paralysis of lower arm with CLAW hand and INABILITY TO GRASP; able to flex at elbow
- Commonly with **Horner's syndrome** (T1 lesion) = triad of PTOSIS + MIOSIS + ANHIDROSIS on same side
**Topic: Static Encephalopathy**

- disorder of BRAIN that does NOT progressively WORSEN
- Cerebral palsy (motor impairment due to brain insult) is an example
- Cause of brain insult over (not progressive) but motor spasticity may change (progress) with time

**Spastic Cerebral Palsy**

- Common etiologies
  - Prematurity, IUGR, Infections
  - Asphyxia much less common!
- Diagnosis usually by age 1
- Intelligence can be normal!
- INCREASED incidence due to IMPROVED SURVIVAL of PRETERM infants

**Spastic Cerebral Palsy subtypes**

- Spastic HEMIPLEGIA - unilateral arm > leg stiffness / weakness; good prognosis for cognition
- Spastic DIPLEGIA - both legs stiff / weak; great prognosis for cognition
- Spastic QUADRIPLEGIA – all extremities affected; poor prognosis for cognition
Spastic Cerebral Palsy subtypes

- Athetoid Cerebral Palsy
  - spastic CP
  - + dystonia (odd movements, twisting movements)

Topic: Spina Bifida

- Vertebral midline defects
- Potential for spinal cord to protrude out the spine
- May be asymptomatic
- May be associated with an overlying skin change/hair patch or cyst of the lower back
- Obtain neuroimaging
  - spinal ultrasound < 6 months old
  - MRI for older child

Spina Bifida subtypes

- Spina bifida OCCULTA
  - vertebra minimally split
  - no skin opening
  - may have dimple or tuft of hair on back
  - may have no symptoms
  - may have mild incontinence or mild sensory symptoms
Spina Bifida subtypes

- Spina bifida WITH MENINGOCELE
  - vertebra split enough for the meninges to protrude out of skin as a visible cyst
  - cyst contains only CSF (no nerves)
  - minimally symptomatic

Spina Bifida subtypes

- Spina bifida WITH MENINGOMYELOCELE
  - vertebra split wide enough for meninges and spinal cord to protrude out
  - all patients have some paralysis
  - common urologic issues (incontinence, retention, infections)
  - common orthopedic issues
  - needs STAT CT head to rule out associated CHIARI MALFORMATION

Spina Bifida with Chiari

- CHIARI MALFORMATION
  - downward displaced cerebellar tonsils
  - obstructive hydrocephalus
  - high mortality by age 2 if Chiari malformation associated with spina bifida / myelomeningocele
**Topic: Spinal Cord Disorders**

- Present with:
  - INCREASED reflexes
  - Weakness
  - Loss of sensation
  - Poor rectal tone
  - Bowel/bladder incontinence

- Needs STAT MRI; if FEVER, start anti-staphylococcal ANTIBIOTICS immediately; give dexamethasone (DECADRON) for suspected cord compression

**Spinal Cord Compression**

- Tumor disrupts spinal cord function causing:
  - INCREASED REFLEXES
  - Abnormal sensation
  - Weakness
  - Bowel/bladder incontinence

- May mimic Guillain Barre Syndrome but differentiated by INCREASED REFLEXES

**Spinal Cord Transverse Myelitis**

- Swollen inflammation of a cross section of the spinal cord (visible on MRI)

- Mimics cord compression:
  - INCREASED REFLEXES,
  - abnormal sensation
  - weakness
  - bowel/bladder incontinence

- Look for hx fever; CSF may show neutrophils
Spinal Cord Epidural Abscess

- Abscess compresses spinal cord
- Has FEVER and pain in addition to weakness-to-paralysis (legs or arms depending on spinal level), tingling, INCREASED REFLEXES

Question 10:
A 12 year old girl presents with paraparesis progressing over 2 days along with urinary incontinence and constipation. She complains of constant dull lower back pain. On physical exam, the child cannot move her lower extremities and has brisk knee and ankle deep tendon reflexes. She has loss of pain sensation below dermatome T10.

Of the following, the test MOST likely to lead to this child’s diagnosis is:

- A. edrophonium test (Tensilon test)
- B. lumbar puncture
- C. MRI of the spine
- D. nerve conduction velocities
- E. somatosensory evoked potentials
C. MRI of the spine – the differential diagnosis of low back pain with neurologic symptoms referable to the spinal cord (lower extremity weakness, bowel / bladder dysfunction, hyperreflexia and a sensory level) in children includes: spinal tumors, epidural abscess, diskitis, trauma, transverse myelitis, AVM, or Guillain-Barre syndrome. MRI of the spine helps to differentiate these entities. If the MRI was normal, LP would be obtained next to rule out transverse myelitis (associated with increased lymphocytic WBC and mildly elevated protein in CSF, due to post-infectious lymphocytic infiltration + demyelination of the spinal cord, usually at the thoracic level, triggered by EBV, HSV, flu, mumps, rubella, or varicella) or to suggest Guillain-Barre syndrome (increased protein and normal WBC in CSF). If the LP then suggested GBS, nerve conduction velocities would be obtained to confirm nerve conduction slowing of spinal nerves.

Topic: Movement Disorders

- Tics
- Stereotypy
- Dystonia
- Chorea

Movement Disorders STOP in SLEEP

Tics
- onset usually > 3 yo
- types change over time (various motor and vocal tics)
- may feel strong urge or need to do them
- can be suppressed temporarily (by biofeedback)
- rarely occur during purposeful voluntary activities
- no severe impact on daily living
- exacerbated by stress or excitement
Tics

- no required treatment
- treatments: clonidine, guanfacine, pimozide, haloperidol (NOT SSRIs as this is NOT an anxiety / nervous disorder)
- Tourettes = mixed motor (2) + vocal (1) tics
- Commonly with co-morbid ADHD / ADD
- **ADD medications can unmask a tic, but this is NOT a reason to stop the needed ADD medication! Continue ADD med!**

Stereotypy

- onset usually < 3 years old
- repeated pattern of movement or behavior (hand flapping, toe walking, rocking, head banging)
- do not change over time (different than tics)
- there is NO strong urge or need to do them
- may enjoy them (self-soothing/ self-stimulating)
- can be suppressed in older children
- no severe impact on daily living; no required treatment (SAME as tics)

Dystonia

- sudden muscle contractions with ODD POSTURES (twisting of limbs at their joints)
- medication causes – clonidine, phenothiazine, metoclopramide, promethazine
- also a subtype of cerebral palsy (no spasticity)
- treat medication-induced dystonia with BENADRYL (diphenhydramine)
Chorea

- random dance-like movements that suddenly occur
- age of onset depends on cause
- can NOT be suppressed
- often WORSENS with focused activities or purposeful movements
- extremely DISRUPTIVE to daily living

Chorea subtype – Sydenham’s

- Choreiform movements that follow Group A Strep infection
  - with hypotonia, emotional lability, milk maid’s grip
- **ASLO titer elevated** in acute/subacute phase
- **ASLO titer may become negative while chorea persists**
- May be associated with RHEUMATIC FEVER
  Carditis, Polyarthritis, Erythema marginatum, Subcutaneous nodules

Chorea subtype – Huntington

- Autosomal dominant, due to CAG repeats
- Can present at any age (though usually adults)
- Associated with cogwheel rigidity, chorea, and emotional lability (adults have dementia)
Other Brain Malformations

- Porencephaly
- Holoprosencephaly
- Anencephaly
- Encephalocele
- Agenesis of Corpus Callosum
- Lissencephaly
- Schizencephaly

- Encephalomalacia (loss of brain tissue due to anoxia or stroke)
Anencephaly

Agenesis of Corpus Callosum in Aicardi syndrome
- seizures (inf spasms), MR / dev delay, microcephaly
- retinal lesions
- symptom onset 3-5 months, only females

Lissencephaly = “smooth brain”
- achieve 3-5 month developmental milestones
- microcephaly, MR, seizures
- “Miller-Diecker syndrome” - when caused by the LIS-1 gene mutation
Schizencephaly: “clefted brain”

ATAXIA

Ataxia - diagnosed by the timeline of symptoms

- Acute Ataxia
- Episodic / Recurrent Ataxia
- Chronic or Progressive Ataxia

In vignettes, think ataxia if:
- problems walking in a coordinated way
- clumsy, difficulty with balance
- problems reaching for objects
ACUTE ATAXIA – other causes

- Drug Ingestion
  - alcohol, benzodiazepines, phenytoin, antihistamines
  - thallium / pesticides
- Brainstem encephalitis
  - fever, ataxia + cranial nerve palsies, abnormal CSF
- Metabolic causes
  - low glucose, low sodium, elevated ammonia
- Neuroblastoma
  - ataxia + opsoclonus (roving eye movements) + myoclonus
- Brain tumors
- Trauma
  - ataxia not uncommon with concussion

ACUTE ATAXIA – other causes

- Vascular lesions
  - hemorrhage of a cerebellar AVM
- Kawasaki disease
  - ataxia due to multiple brain infarcts
- Polyradiculopathy
  - Guillain-Barre syndrome (Miller-Fisher variant)
  - tick paralysis
- Biotinidase deficiency
  - ataxia + seizures + hypotonia (dry skin, alopecia)
- Conversion reaction
- Postinfectious cerebellitis – DX OF EXCLUSION
  - 1-3 year olds, 1-2 weeks after viral illness (varicella, coxsackie, echovirus), ataxia maximal at onset
  - CSF normal or mildly increased protein
  - ataxia resolves after several weeks-to-several months

EPISODIC / RECURRENT ATAXIA

- Basilar migraine
- Ataxia with occipital headache
- AVOID TRIPTANS
- Multiple sclerosis
  - Ataxia a common presentation of MS in children
- Epileptic pseudoataxia
  - Ataxia a rare seizure manifestation
- Metabolic disorders
  - Hartnup Disease—impaired tryptophan absorption
  - Maple Syrup Urine Disease (intermittent)
  - Pyruvate Dehydrogenase Deficiency-E1
### EPISODIC / RECURRENT ATAXIA

<table>
<thead>
<tr>
<th>Episodic Ataxia type 1 (EA1)</th>
<th>Episodic Ataxia type 2 (EA2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- K⁺ channel gene mutation</td>
<td>- Ca⁺ channel gene mutation</td>
</tr>
<tr>
<td>- autosomal dominant (chr 12)</td>
<td>- autosomal dominant (chr 19)</td>
</tr>
<tr>
<td>- duration seconds (to hours)</td>
<td>- duration minutes to days</td>
</tr>
<tr>
<td>- triggers: STARTLE, exercise</td>
<td>- triggers: stress, exercise</td>
</tr>
<tr>
<td>- tx: Diamox, phenytoin</td>
<td>- tx: Diamox</td>
</tr>
</tbody>
</table>

### CHRONIC OR PROGRESSIVE ATAXIA

**Friedrich Ataxia**
- most common hereditary progressive ataxia
- multiple GAA repeats in Frataxin gene, auto recessive
- progressive degeneration of mostly spinal tracts:
  - dorsal root ganglia → areflexia
  - posterior columns → decreased vibration / position sense
  - corticospinal tracts → upgoing toes (+Babinski’s)
  - spinocerebellar tracts + cerebellum → SLOW AND CLUMSY around the time of puberty
- scoliosis and pes cavus can occur
- With hypertrophic cardiomyopathy/congestive heart failure (need regular EKGs), Diabetes Mellitus, +/- hearing loss or optic atrophy, pes cavus (high pedal arches)

**Brain tumors**
- ataxia + signs of increased ICP / vomiting
- infratentorial > supratentorial tumors for ages 1-8 years
- common infratentorial types:
  - cerebellar astrocytoma
  - ependymoma
  - medulloblastoma
  - brainstem / pontine glioma (ICP elevation later in course)
CHRONIC OR PROGRESSIVE ATAXIA

- Congenital cerebellar hypoplasia (diagnosed with MRI)
- Dandy-Walker malformation (see above)
- Chiari malformation
  - Ataxia
  - Headache
  - Apnea
  - Spasticity
  - Bladder Dysfunction

CHRONIC OR PROGRESSIVE ATAXIA

- ATAXIA TELANGETASIA
  - Autosomal recessive gene - defective repair of DNA
  - Treatment:
    - prevent exposure to radiation
    - treat recurrent infections (pneumonia, sinusitis)
    - treat malignancy (in 3rd decade of life)
  - neurologic symptoms (primary presentation in children):
    - ataxic gait at onset of walking (1st sign)
    - unusual eye movements
    - peripheral neuropathy
    - dysphagia, choking
    - involuntary movements (dystonia, chorea, tics)
    - cognitive deficits

CHRONIC OR PROGRESSIVE ATAXIA

- Ataxia Telangiectasia (continued)
  - non-neurologic symptoms:
    - telangectasias (> 2 years old) esp. in conjunctiva
    - premature gray hair, senile keratosis (premature aging)
    - immune deficiencies (infections)
      - atrophy of thymus / lymphoid tissues
      - low WBC
      - low IgA / IgE / IgG
    - lymphoma, leukemia
    - elevated alpha fetoprotein (AFP)
CHRONIC OR PROGRESSIVE ATAXIA

- Spinocerebellar Ataxia
  - over 16 distinct genetic loci, mostly autosomal dominant
  - many due to CAG expansion repeats
  - the larger the expansion, the earlier the age at onset

- Vitamin E Deficiencies
  - Acquired – fat malabsorption
    - ataxia, peripheral neuropathy, retinitis pigmentosa
  - Abetalipoproteinemia (Bassen-Kornzweig disease)
    - mutations in microsomal triglyceride transfer protein gene (MTP gene), autosomal recessive
    - In infants, steatorrhea and malabsorption
    - Dx: absence of apolipoprotein B in plasma
    - Tx: fat restriction and large doses of vitamin E

Neurocutaneous Syndromes

- Neurofibromatosis
  - Autosomal dominant
  - NF 1
    - 1:3500 incidence
    - Mutation in Neurofibromin on chromosome 17

- NF 2
  - 1:40,000 incidence
  - Deafness (bilateral)
  - Higher incidence of CNS tumors
  - Mutation in Merlin on chromosome 22
Neurofibromatosis

- NF 1 criteria (need 2 of the following 9):
  - FHx (but ~1/2 cases sporadic mutation)
  - Skin criteria:
    - CAL (need 6+, >0.5 cm prepubertal, >1.5 cm post-pubertal)
    - Neurofibromas
    - Inguinal / axillary freckling
  - Bone criteria:
    - Pseudarthrosis (angulation deformity of long bone)
    - Scoliosis
    - Hypoplasia of sphenoid bone in base of skull
  - Eye criteria:
    - Lisch nodules (hamartomas in the iris)
    - Optic pallor (optic glioma)
Lisch Nodules
Optic Glioma

**Tuberous Sclerosis (systemic involvement)**
- Autosomal dominant (need only one mutation)
- TSC1 gene mutation on chromosome 9 (hamartin)
- TSC2 gene mutation on chromosome 16 (tuberin)
- Skin hypopigmentations (“Ash leaf” spots)
- Benign hamartomas:
  - skin
  - adenoma sebaceum on face
  - shagreen patch (brown leathery) on forehead or lower back
  - brain, retina, heart, kidney
- Seizures in 80-90%
Sturge Weber

- Unilateral port wine stain over upper face
  - 1 in 1000 born with port wine stain (most not S-W)
  - 6 % of newborns with port wine stain have S-W
- Buphthalmos (infantile glaucoma) → enlargement of globe, corneal clouding
- Intracranial leptomeningeal vascular anomaly and calcifications in 90 %
- Seizures (partial / focal onset)
- Random mutation in GNAQ gene (not inherited, but genetic)
Port Wine Stain

Buphthalmos with enlarged globe, corneal clouding

Leptomeningeal Vascular Anomaly