UNDERSTANDING SEIZURES

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Overview

• Definition of epilepsy
• Different types of seizures and epilepsies
• Medical treatment options
• Surgical treatments
• Neuromodulation options
• Other alternative therapies, including diet
• Status Epilepticus: Recognition and treatment
What is epilepsy?

- **Two or more unprovoked seizures**
  - Recently the definition has been broadened to include 1 seizure with a high (75%) chance for an additional seizure (e.g. EEG with spikes or MRI with abnormalities; strong family history, etc.)

- Incidence/Prevalence: Latest statistics suggest that **1 in 26 people** have/will develop epilepsy (3.8% of people!)

- An estimated **10%** will have at least 1 seizure at some point.
What is a seizure?

- Misfiring of brain cells, hypersychronization of neurons
- “A storm in the brain”
- May involve part or all of the brain
- Usually brief lasting less than a minute
- Typically has a clear beginning and an end
Parts of a Seizure

• **BEFORE**: Aura/Warning
  - More common in certain types of epilepsy
  - May give clues to where the seizure is coming from

• **DURING**: Ictal event (starring, shaking, loss of consciousness; etc.)

• **AFTER**: Post-ictal
  - Confusion or fatigue lasting several minutes to hours
  - Some types of seizures have no warning
What are various seizure symptoms?

• Usually **stereotyped**: each event is similar
• May or may not impair level of **consciousness**
• Feelings
  • **Déjà vu**: Feeling strange/weird; tingling/numbness in one area
• **Shaking** in an isolated body part
• Automatisms: **semi-purposeful behaviors**—picking, chewing/lip smacking
• **Staring**
• **Confusion**
• **Convulsions**
Why does epilepsy happen?

- **Genetics**
- **Idiopathic/Unknown**—probably a lot of these cases will be genetic
- **Lesions**
  - Focal cortical dysplasia
  - Mesial temporal sclerosis
  - Slow growing tumors
  - Prior stroke
  - Birth injury
- **Brain trauma** (usually prolonged loss of consciousness and/or displaced skull fracture)
- **Other**: Brain infection ETC.
Who gets epilepsy?

• Peak in young children and elderly.

• Any age!

• Man or Woman

• Anybody with something wrong with the brain

• Higher percentages in cognitive disorders, mental retardation, autism

• Depression increases risk for epilepsy and epilepsy increases the risk of depression

• ANYONE!
Is Epilepsy a **Single Disease**?

- No! Probably better described as a *spectrum of diseases*, or even, several diseases under the same name
- **Wide range** of seizure frequency—several dozen per day (even 100s) to once every several years
- **Wide range of symptoms** (isolated feelings or sensations to confusion to convulsion)
Epilepsy Mimickers?

- Syncope/Fainting
- Tremor
- Cardiac arrhythmias
- Migraine
- Psychogenic non-epileptic attacks
  - "Pseudoseizures": A derogatory term
  - *Rarely malingerers*
Seizure Types

• 2 main categories:
  • **Primary general epilepsies**
  • **Focal/Partial epilepsies**
  • **Mixed**: Both generalized and focal
  • **Non-epileptic**: Many people may carry the diagnosis of seizures when something else is going on (see epilepsy mimickers)
  • **Mixed epileptic and non-epileptic**: up to 20% of patients with epilepsy may have non-epileptic events also.
Seizure Names

• Old and new classifications
  • I will list both name types (e.g. complex partial vs focal dyscognitive seizures)
  • Descriptive names
  • Not yet official...because...it’s complicated!!

• Medical and non-medical
  • Absence/staring vs. petit mal
  • Convulsion/Tonic-clonic vs grand mal
Primary Generalized Epilepsy

- Most frequently onset in **young childhood/adolescence** (but may be later)

- Thought to be the **WHOLE brain** misfiring at once, rather than just a portion of the brain

- Most of these probably have some sort of **genetic** roots
  - Genetic may be a **NEW mutation** and not necessarily inherited

- Usually no seizure aura
  - …Though some do: e.g build up of myoclonic jerks; irritability; just a feeling they are going to have a seizure that day.
Types of **Primary Generalized Seizures**

- **Absence**
- **Myoclonic/myoclonic jerks**
- **Atonic** (loss of tone/collapse)
- **Tonic**
- **Tonic-clonic/convulsions**
Absence seizures

- **Staring** spells.
- Classically “petit-mals” though many patients use this term for other seizure types
- Brief staring usually **10-15 seconds**
- May have subtle features like eye rolling or automatic movements
- **Can typically induce with hyperventilation for 2 minutes**
- No recovery period—right back to self
- Usually in **children or teenagers** (childhood vs. juvenile), and frequently grow out of it
- Can happen **several hundred times per day!!**
Myoclonic Seizures

• Myoclonic jerks, twitchiness
• Everyone gets occasional myoclonic jerks—jerk as you are falling asleep
• In epilepsy, jerks may cluster in the morning
• May be isolated jerks, or associated with other seizure types, e.g. absence or convulsions
Atonic Seizures

• Suddenly go **limp**
• Crumble to the ground
• Brief, lasting 1-2 seconds
• May require a **helmet** to prevent injury
Tonic Seizures

- **Stiffening** events
- Usually extension of limbs
- ** Brief** event lasting 2-10 seconds
- An important seizure type in Lennox-Gastaut
Tonic-Clonic Seizures

- Convulsions; **Grand mal**
- May or may not have warning
- **Stiffening** followed by **jerking**
- Ictal cry
- Most last **30-60 seconds**
- Sometimes focal/partial seizures can spread and become a convulsion
Primary Generalized Epilepsies

- Overall category is Primary Generalized Epilepsy, and sometimes people are diagnosed with a specific type in the category
- EEG shows generalized discharges
- Most Common:
  - **Absence epilepsy**; childhood or juvenile
    - May grow out of it
    - May have occasional convulsions
  - **Juvenile myoclonic epilepsy**
    - Myoclonic jerks and convulsions
    - Typically don’t grow out of it
Focal Epilepsy

- Epilepsy is coming from one or more specific areas in the brain.
- Usually people have a spectrum of seizure types
  - Aura/Simple partial
  - Small/Complex partial
  - Big/GTC
- More common due to a lesions
- May have more treatment possibilities (e.g. surgery)
- More common to onset in adults
- May or may not have lesion/lesions on MRI
- Many patients will have an aura/warning before an event
Focal Seizure Types

- Simple Partial
- Complex Partial
- Convulsions “secondarily generalized”
Simple Partial Seizures

• Proposed name: **Focal seizure without dyscognitive features**; Focal **motor** vs. Focal **sensory**

• *Doesn’t* involve alteration in level of awareness

• **Stereotyped** symptoms: feelings or shaking in a specific limb; *déjà vu*

• **Awake walking and talking** and can describe what is going on
Complex Partial Seizures

- Proposed name: **Focal dyscognitive seizures**
- Some patients call this *petit mals* (which historically would be absence seizures)
- Involves some type of **confusion or loss of awareness**—not responding or staring
- May involve **automatisms**—picking, chewing
- Generally lasts **30-60 seconds**
- May be preceded by a simple partial seizure
Secondarily Generalized Seizures

• Occasionally a simple partial or complex partial seizure spreads into whole-brain involvement manifesting as a convulsion

• Spectrum of simple to complex to convulsion
Focal Epilepsy Types

- Many **childhood types**: Infantile Spasms; Lennox Gastaut; Rasmussens

- **Mesial temporal sclerosis** (MTS): most amenable to good surgical outcomes

- **Focal cortical dysplasia**—a abnormal “tuft” of brain cells that may or may not be seen on MRI

- Due to **any other brain lesion**: Tumors, strokes, traumas, etc.
What about the psychogenic non-epileptic patients??
Psychogenic Non-Epileptic Attacks

- Up to 30% of the patients in epilepsy monitoring units across the country have PNES.
- Some patients may have 30 events in a single day.
- Events can be prolonged lasting several minutes and usually have atypical features.
- **Warning:** PNES patients frequently also have epilepsy!
Mesial Temporal Sclerosis
Focal Cortical Dysplasia
What are treatment options for epilepsy?

- **First seizure**: watch and wait; no medications, seizure precautions/driving for 3 months

- **Medications**

- **Surgeries**

- **Neuromodulation**: Brain/nerve stimulators

- **Diets**
Medication Options

• In the beginning….very few options

• Early players: Bromides, Phenobarbital, Phenytoin (Dilantin)

• A little later: Valproic acid (Depakote), Carbamazepine (Tegretol)

• Drug explosion: Several new medications since the 1990s. Currently there are 1-2 medications coming out nearly yearly.

• More than 30 choices now…about 10-15 used commonly
Does Seizure Medication Work?

• Generally, **YES**.
• **First** medication trial works around **50%** of the time
  • Need to tolerate medication in the therapeutic range or doesn’t count as a try
• Need to try a **2nd** medication the other 50% of the time, and this works about **50%** of the time
• Translation: The **first 1 or 2** medications will control seizures in about **65 to 75%** of patients
• This also means that about **25 to 30%** of epilepsy patients are in a “**difficult to treat**” category, also called **medically-refractory epilepsy**
How do you choose a seizure medication?

- Ideally, the **lowest dose** of medication that works with the **least side effects**

- Consider: are we trying to **treat anything else**?
  - e.g. Topamax and Depakote treat **migraines**
  - Lamictal and Depakote treat **bipolar/mood problems**
  - Lyrica/Neurontin have some anti-**pain** properties

- **Avoid drug interactions**
  - Some medications are less likely to interact with other medications, some are more likely
  - More important for people already on medications
How do you choose a seizure medication? (cont.)

- Consider: **Anything we are trying to avoid?**
  - Changes in weight
    - Topamax/Zonisamide lead to **weight loss** (avoid in thin patient, use in obese/overweight patients)
    - Depakote causes **weight gain** (avoid in obese)
  - Pregnancy or potential to become **pregnant**
    - Avoid Depakote. Probably Topamax. Lamictal or Keppra may be ideal
    - Be on only 1 medication, if possible
  - **Psychiatric problems**: Psychosis or depression
    - Avoid Keppra; monitor worsened mood/psychosis in other medications
Managing side effects?

- The goal is to be side effect free.
- Most seizure medications cause sleepiness, mental slowing for the first few weeks.
- Typically you need to give a seizure medication at least 2-4 weeks before judging if it is really intolerable.
- Some side effects need immediate discontinuation, e.g. rash in Lamictal, psychosis.
- Timing and dose.
- Frequently medications will be stopped for side effect reasons.
Medication failure?

- Seizures still occurring
- If patient is on a full dose of medication and still having seizures, either switch medications or sometimes add a 2nd medication.

**Sometimes 2 is better than 1**

- 2 medications may have different mechanisms and may work better together
- Occasionally we need to have 3 medications at once
- Usually a patient shouldn’t be on more than 3 seizure medications and the team needs to get rid of the one that never helped
Difficult to treat epilepsy?

- Patients who have been on 2 adequate doses of medications still have seizures, this is called **medically-refractory epilepsy** (about 1/3 of cases)

- Keep trying **different medications**—the next one may be the effective medication; however each additional medication <10% chance of working.

- Start investigating other options...surgery, stimulators: refer to an **epileptologist**
What is epilepsy surgery?

- Epilepsy surgery is when a neurosurgeon is able to surgically remove the part of the brain causing seizures.

- Some people become completely seizure free and are able to stop medications after a surgery takes place.

- Surgery success varies on the area of the brain affected and the type of lesions (best outcome: temporal lobe surgeries (>70% seizure free); poorer outcome: frontal/parietal lobe surgeries without a clear lesion on MRI; ~50% seizure free).

- Neurological impact of surgery will vary due to the location of the epilepsy. Sometimes if the brain tissue is in an essential area, then surgery is not an option.
Epilepsy Surgery Candidates

- About **10% of patients with epilepsy** would be good candidates for epilepsy surgery (however, very few of these are offered surgery).

- **Who is a good candidate?**
  - Anyone with **hard to treat epilepsy** should find out what type of epilepsy they have and if they are candidates for surgery
  - **Focal epilepsy** (potentially good candidate) vs. generalized epilepsy (poor candidate) vs. missed diagnosis (most commonly psychogenic non-epileptic episodes)

- Evaluation should be done with **MRI** and **video-EEG** at an epilepsy center
Surgical Evaluation

- Includes high resolution (3-Tesla) MRI, seizure protocol
- Inpatient video-EEG monitoring
- Wada/Cerebral angiogram to determine which side of the brain is important for language and memory
- Neuropsychological evaluation
- May include: PET scan, MEG (magnetoencephalogram), SPECT imaging
Who is **NOT** a candidate for surgery?

- **Primary generalized epilepsies** (should be confirmed by EEG)

- **Multifocal epilepsy**—seizures coming from both sides of the brain....sometimes “palliative surgery” is pursued

- Brain lesion that is in an **eloquent part of the brain**—sometimes the risk for neurological deficit after a surgery outweighs the benefit of getting the surgery
What is done during the surgery?

- **If there is a clear lesion**, the neurosurgeon may just directly go in to remove that lesion.

- **If there is not a clear lesion** or there is debate about whether your seizures are coming from a specific lesion, they may do EEG monitoring directly on the brain, before removing a lesion.
  - This is called Phase II/III or **Grid Monitoring** and is only done at epilepsy centers.
What is expected after the surgery?

• **Ideal outcome:**
  • Seizure freedom and after 1 year, consideration of coming of medications.
  • No noticeable neurological deficits
  • Return to driving and working

• **Less ideal outcome:**
  • Less frequent seizures but still occasional seizures
  • May need to still remain on medications long term
  • Neurological complications from surgery
Alternatives to medications and resective surgery?

- Keep trying different medications.
- Consider vagal nerve stimulator.
- Consider Reactive Neurostimulation (RNS or Neuropace)
- Consider dietary options (Modified Atkins or Ketogenic diet)
- Canniboidoil?
Vagal Nerve Stimulator (VNS)

- **Battery pack** is inserted under skin in the left chest wall.

- A **wire/lead** connects this to the vagus nerve (travels from the body organs to the brain).

- **Stimulation** is titrated upwards over months and goes off automatically at least every 5 minutes.

- A **magnet** can be “swiped” to activate the magnet at any sign of a seizure.
Vagal Nerve Stimulator Benefits

• As effective OR more effective than a medication but **without drowsiness/cognitive side effects**

• About 50% of patients will have their seizures decrease by 50% or more

• Also an approved treatment for **depression**

• May be beneficial for generalized or focal epilepsy

• Becomes **more effective with time**
VNS Disadvantages

• **Not curative**—need to still continue medications

• Change in **voice**

• **Battery** pack needs to be changed every 5-10 years

• Some limitations on **MRI** scans
Neuropace: Responsive Neurostimulation (RNS)

- New neuromodulation device just approved for clinical use over the past year

- Battery pack is put into the **skull** and 2 wires can go directly to 1 or 2 places in the brain causing seizures.

- Only good for **focal and multifocal** epilepsy

- **Personalized**: The device is trained to recognize and activate when it sees your seizure waves
Neuropace Benefits

• Clinical trials have similar or better than VNS (may be able to use both devices)

• Stimulation not felt and does not interrupt speech

• Custom tailored to an individual’s epilepsy

• Personalized
Neuropace Disadvantages

- Focal epilepsy only

- More intensive investigations (may require intracranial monitoring)

- Battery pack change after time
Dietary Options

• Ketogenic diet

• Modified Atkins diet

• The idea is appealing…but living the diet may be very hard to maintain—Cut out SUGAR and CARBS!!

• Only considered in medically-refractory epilepsy (failed 2 or more medications)
Ketogenic Diet

- Very few/no carbohydrates or sugars
  - 90% fat; 8% protein; 2% sugars

- Diet is composed of cholesterol/fats with some protein and fewer carbohydrates

- Very strict diet to maintain ketosis and need close follow-up with a dietician

- Made popular by the Charlie Foundation—an example of parent advocacy!
Modified Atkins Diet

• **20 grams of carbs** a day; unlimited fat/protein/water

• Initiated at John’s Hopkins in 2003

• Mom of a 7 yr old who was already on the Ketogenic diet “loosened” up the regimen and had no change in seizure control.

• Studies so far have seen the same response as the Ketogenic diet.

• Much easier to follow long-term….still low sugars/carbs
WHAT IS STATUS EPILEPTICUS (SE)?
Definition

• An evolving definition!

• Historically:
  • A single generalized seizure lasting greater than 30 minutes
  • Group of repetitive seizures between which the patient had not fully recovered.

• Now: Based on the typical seizure duration of 1 to 2 minutes, it is reasonable to consider SE as any seizure event greater than 5 minutes in length

• Spontaneous resolution of seizures of this duration is rare.
  • The benefit to treating patients with prolonged seizures as if they have SE seems to outweigh any risk associated with therapy. (Continuum, 2006)
**Types of SE**

- **Generalized convulsive SE (GCSE)** may be phenotypically overt in their expression, or they may have more subtle motor manifestations, which are particularly common if SE is prolonged. By far, GCSE is the most commonly reported SE subtype.

- **Nonconvulsive SE (NCSE)** continuous nonmotor seizures. Probably an under-recognized cause of altered mental status. Common in the ICU, however, possible on the floor.

- **Non-urgent:** **Focal motor SE (FMSE),** or **epilepsy partialis continua**, is relatively uncommon.
  - Continuous motor twitching of a single limb or side of face is most frequently observed.
  - These seizures can be difficult to control with medications.
  - It is not clear whether prolonged FMSE results in substantive injury to the cerebral cortex.
  - Thus, reasonable attempts at control are advocated, but high-risk therapies such as induced pharmacological coma are rarely considered appropriate.
Diagnosing Status

• Clinical observation.
• Urgent EEG if unsure.
• With high suspicion do not wait for EEG to start treatment!!!
Clinical Manifestations of Status

- **Generalized:**
  - Tonic-clonic convulsion
  - Myoclonic jerks in setting of myoclonic epilepsy or anoxic brain injury (initially may be conscious)

- **Partial:**
  - Epilepsy Partialis Continua: focal clonic jerking movements confined to a body part
  - Hemiconvulsive

- **Nonconvulsive:**
  - Absence: Activity arrest with continued blank staring; unresponsive/or slow to respond
  - Coma: With absent or subtle clinical signs: nystagmoid movements or twitching of face/limbs. EEG shows status.
  - Partial status in coma
  - Complex Partial Status: fluctuating level of awareness
20-40% of Neurological patients with unexplained alteration in mental status/coma have been shown to be having seizures!
Demographics

- SE is relatively frequent complication of epilepsy and also other medical conditions
- 152,000 cases of SE in USA yearly with 42,000 deaths
- Most common in children <1 or adults >60
- Nonconvulsive SE is more common than convulsive SE
A Neurological Emergency!

- One of the most common neurological emergencies.
- 40% of cases occur in patient’s with known epilepsy
- Convulsive SE is easily recognized….non-convulsive SE less-so=Need an index of suspicion
- There is a high morbidity/mortality risk and quicker reaction leads to quicker benefit
Time is Brain

“The longer it lasts the harder it is to treat.”
Mortality

- Independent predictors:
  - Older age (3% in children; 26% in adults <60; 39% in adults >60)
  - Longer duration (mortality rises steeply after 1hr 10x); Early treatment is more effective
  - Etiology (anoxia, hypoxia, stroke more likely to die than low AED)
- Myoclonic SE (50-86%); GTC SE (30%); Simple partial SE (17-24%)
Other Complications of Status

- **Respiratory**—hypoxia, aspiration, hypercapnia
- **Cardiovascular**—hypotension, tachycardia, arrhythmia
- **Renal**—myoglobinuria, rhabdomyolysis, acute tubular necrosis
- **Autonomic**—hyperthermia, impaired cerebral autoregulation
- **Metabolic**—lactic acidosis, hypoglycemia, electrolyte disturbances
- **Neurologic**—neuronal damage, increased intracranial pressure, decreased cerebral perfusion, cerebral edema
5 h's: Hypoxia hemodynamics

- **Hypoxia** increases mortality in SE
- **Hemodynamics**: sympathetic overdrive can lead to exhaustion and need for pressors
- **Hyperpyrexia**: treat aggressively with cooling
- **Hypothermia**: may be an effective treatment
- **Hyper- and hypoglycemia**: neuronal damage
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Cause of Status

• Low AED is #1 (induced by us in the EMU)
• Stroke (ischemic or hemorrhagic) causes 60% in older adults
• In children, infection with fever is the most common cause
What do we do to treat status?
1. ABCs

2. BZDs

3. PHT

If seizures still going at this point...Definite ICU

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Medical and Pharmacological Treatment for Status Epilepticus

- Preserve airway and oxygenation by intubation. Order EEG to be available during therapy.
- Measure finger-stick blood glucose and administer IV glucose if less than 40 mg/100 dL to 60 mg/100 dL.
- Immediate benzodiazepines—IV lorazepam 5 mg to 10 mg, diazepam 20 mg to 40 mg, or midazolam 5 mg to 20 mg over 5 minutes.
- Phenytoin loading dose 20 mg/kg at 50 mg/min or fosphenytoin 20 mg/kg PE (phenytoin equivalents) at 150 mg/min. Goal serum level 15 mg/dL to 20 mg/dL.
- Continuous EEG if available.
  - If seizures continue, phenytoin or fosphenytoin (additional 5 mg/kg to 10 mg/kg or 5 mg/kg PE to 10 mg/kg PE). Goal serum level 20 mg dL to 25 mg/dL.

Refractory Status Epilepticus—Several Options

- Rapid pharmacological burst suppression/coma with hemodynamic support—propofol 2 mg/kg and 150 μg/kg/min to 200 μg/kg/min infusion or thiopental 4.0 mg/kg and 0.3 mg/kg/min to 0.4 mg/kg/min.
- Midazolam 0.2 mg/kg followed by 0.1 mg/kg/h to 0.2 mg/kg/h may be used as an alternative to propofol or thiopental.
- Valproate 60 mg/kg to 70 mg/kg may be tried.
- Pentobarbital 5 mg/kg to 10 mg/kg followed by 1 mg/kg/h to 10 mg/kg/h is a common recipe for long-term burst-suppression.

Weaning From Electroencephalogram Seizure Suppression

- Using continuous EEG, maintain drug levels to suppress seizure activity (true burst suppression may be desirable but is not required) for 12 to 48 hours before attempting to withdraw from pharmacological coma.
- Ensure adequate anticonvulsant levels of selected agents for chronic seizure control. Aim for high levels of the fewest number of anticonvulsant agents. Most common agents are phenytoin and valproate.
- Wean infusion and follow EEG as background rhythm begins or increases. If breakthrough seizures recur, rebolus using 30% to 70% (as necessary) of original bolus amount.
- Readjust anticonvulsant serum level or add additional agents before another weaning attempt.
- It is not uncommon to make more than one adjustment before a successful wean.

EEG = electroencephalogram; IV = intravenous.

Adapted from with permission from Varelas PN, Mirski MA. Seizures in the adult intensive care unit. J Neurosurg Anesthesiol 2001;13:163–175. Lippincott Williams & Wilkins.
Reaction to Status

• Nurses may be the first person to recognize the status (especially if the patient isn’t in the epilepsy monitoring unit).
• If the seizure lasts longer than one minute, have Ativan ready.
• If the nurse finds a patient seizing in the epilepsy monitoring unit, would go ahead and prepare Ativan STAT.
Uses of EEG in Status Epilepticus

• Identify subtle or nonconvulsive seizure activity (sometimes convulsive morphs into non-convulsive—muscles fatigue)
• Monitor response to treatment
• Determine seizure type (focal vs. generalized)
• Suggest etiology or prognosis
• Differentiate seizures from nonepileptic events
CONCLUSION

• Epilepsy is 2 or more seizures and is actually several different diseases called by the same name
• Epilepsy can be grouped into Generalized or Focal or sometimes a mix
• Medical treatment works well and fast or about 65-75% of patients
• Epilepsy is hard to control for 25 to 30% of patients
• Patients will need to try multiple medications and sometimes combinations of medications.
CONCLUSION (cont.)

• When medication isn’t working, alternative treatments should be sought out.

• About 10% of all seizure patients would likely benefit from seizure surgery. Best case scenario is temporal lobe epilepsy where 70-80% of patients may become seizure free.

• Vagal nerve stimulation (VNS) and Neuropace (RNS) are 2 implanted devices that help a lot of patients.

• Diet options, including the Ketogenic diet or Modified Atkins diet may be good option for highly motivated patients and families.
CONCLUSION (cont)

• Canniboidoil or medical marijuana is not yet a proven treatment for epilepsy
• Status epilepticus is a medical emergency and early treatment leads to better outcomes.
References:

THANK YOU!

Any questions?