

Target Audience: Emergency Medicine Residents

Primary Learning Objectives:

1. Demonstrate an appropriate initial approach to a pediatric patient with status epilepticus secondary to isoniazid toxicity
2. Identify symptoms of generalized convulsive status epilepticus, and recognize non-convulsive status epilepticus when it occurs (as evidenced by coma with fluctuating neurologic findings, subtle nystagmus, or focal twitching)
3. Consider toxicological causes for the patient's presentation
4. Demonstrate appropriate management of status epilepticus and isoniazid toxicity
5. Consider administration of other specific treatments as clinically warranted for the patient with undifferentiated status epilepticus or seizure, including, but not limited to: naloxone (narcotic overdose); pyridoxine (possible dependency, deficiency, or isoniazid toxicity); antibiotics (meningitis); magnesium and antihypertensive (e.g., hydralazine or labetalol) for eclampsia; dextrose (hypoglycemia); CT (trauma, intracerebral hemorrhage, possible abuse/violence); reversal agents for drug-associated or congenital coagulopathy

Secondary Learning Objectives: detailed technical/behavioral goals, didactic points

1. Develop a differential diagnosis for status epilepticus in a pediatric patient
2. Identify treatment failure of standard therapies such as benzodiazepines and anticonvulsants
3. Describe treatment options for status epilepticus

Critical actions checklist:

1. Obtain IV access
2. Place on continuous cardiac and respiratory monitoring
3. Check point-of-care glucose
4. Administer antiepileptic agents for status epilepticus
5. Administer pyridoxine for presumed INH toxicity
6. Perform endotracheal intubation
7. Request specialty consultation(s)
8. Administer/transfer to the PICU

Environment and Resources

1. Location – Emergency Department bed in a simulation facility
2. Manikin Set-Up – The participant(s) will find a pediatric manikin reclined on an ED stretcher wearing street clothes. Initially, there will be neither cardiac monitor leads attached nor an IV line placed unless requested by the physician.
3. Props – Available for use will be a cardiac monitor with leads, blood pressure cuff, and pulse oximeter, along with supplemental oxygen by nasal cannula and/or 15-liter facemask. There will be a medicine cart or tray with a full complement of vasoactive agents, ACLS medications, and medicines necessary for sedation, rapid sequence intubation, and analgesia. In addition, a fully stocked code cart with defibrillator will be available for use, along with a selection of direct laryngoscopes and intubation supplies.
4. Distractors – None.
5. Roles – The case can be run with a minimum of two participants—one to play the role of physician and the other to play the case director/simulation operator. Additional roles may consist of EMS personnel, nurses, co-residents, an attending physician, and patient's family members.
6. Participants – Actors may include resident physicians, medical students, nurses, and/or attending physicians.
7. Actions for the designate roles
 - a) Primary physician - The main scenario participant will perform the primary evaluation of the patient. This includes obtaining a history and conducting a physical exam, while also ordering any diagnostic tests, medications, procedures, and/or interventions. He/she can choose to perform any tasks or procedures on his/her own, or delegate them to another medical provider.
 - b) Secondary physicians - Other participants in the scenario will serve as collaborators, consultants, and assistants for any procedures.
 - c) Nursing staff - The role of the nurse will be to administer medications, verify orders, and perform other tasks as directed by the physician. The nurse can also make observations as needed to stimulate case progression.

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CASE SUMMARY

SYNOPSIS OF HISTORY/ Scenario Background

Chief Complaint: "seizure"

EMS report: Patient is a 5-year-old girl with no known medical history brought in from the babysitter's house after a seizure. The babysitter called 911 after she found the patient unresponsive on the bathroom floor with mild tremors across her trunk and upper extremities. The babysitter witnessed these movements for 10 seconds before the tremors stopped, at which point the patient had her eyes open but was unresponsive to her voice. The patient's mental status improved to the point of drowsy responsiveness until midway through the EMS ride to the hospital, at which point she suffered another 15-second episode similar to the one prior. If asked for, **EMS will report the finger stick glucose to be 125 mg/dL**. They were unable to start an IV and gave no medications prior to arrival to the ED.

**Vital Signs: BP: 117/72 mmHg P: 117/minute R: 24/minute T: 36.7C (98.0F)
POx: 97% (FiO₂=0.21) Wt: 14.9 kg**

Past Medical History: unknown

Medications and Allergies: unknown

Family and Social History: lives with parents, attends kindergarten, and was born in Russia

History provided by babysitter: The patient had been in her usual state of health when the babysitter went to the bathroom and found her on the floor unresponsive, with subtle shaking more pronounced in her trunk and upper extremities. She did not see any medications or medication bottles on the floor, but given that events occurred so quickly and EMS arrived promptly, she admits not being completely sure. During the day prior to this episode, the patient herself had not been complaining of any fever, headache, rhinorrhea, cough, shortness of breath, nausea, vomiting, rash, or fatigue.

Review of Systems: unobtainable from patient, though EMS reports that the patient had been incontinent of urine when found on the bathroom floor of the babysitter's house.

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CRITICAL ACTIONS

1. Obtain IV access

Obtain IV access. Participant may need to demonstrate how to escalate to IO or other means (central venous access, intranasal administration) if, at faculty discretion, peripheral IV catheter placement is not achievable.

Cueing Guideline: The nurse can ask if the doctor by what means medication can be administered if IV access has not yet been achieved or is not possible.

2. Place on continuous cardiac and respiratory monitoring

Order continuous cardiac and respiratory monitoring, including continuous rhythm strip and pulse oximetry. May consider end-tidal capnometry as indicated.

Cueing Guideline: The nurse can ask if the doctor would like to do anything to “keep an eye on the patient’s status.”

3. Check point-of-care serum glucose

Check point-of-care serum glucose. Alternatively, the participant could empirically administer dextrose for suspected hypoglycemia (although this patient is not hypoglycemic; this is less preferred surrogate action, and, if selected, requires that the participant use the appropriate formulation and volume of dextrose (high-concentration dextrose solutions – 50%, etc. – should not be used in pediatric patients).

Cueing Guideline: The nurse can ask the doctor if there are reversible causes for status epilepticus.

4. Administer antiepileptic agents for status epilepticus

Administer antiepileptic agents for status epilepticus. Demonstrate the need for escalation of therapy as clinically warranted. In this case, typical antiepileptic agents will not be effective. Recommended escalation sequence: benzodiazepines > phenytoin or fos-phenytoin or levetiracetam or barbiturates > propofol.

Cueing Guideline: The nurse can ask if the doctor would like to consult the Poison Center or Toxicologist.

5. Administer pyridoxine for presumed INH toxicity

Pyridoxine (vitamin B6) is the only agent that will definitely resolve this patient’s status epilepticus. The empiric dose of pyridoxine is 5 grams. A weight-based dose could also be administered (see debriefing notes).

Cueing Guideline: Nurse asks if the doctor would like to provide any interventions to this otherwise stable-appearing patient.

6. Perform endotracheal intubation

Perform endotracheal intubation. Participant is expected to use modified rapid sequence intubation and demonstrate in-line manual stabilization.

Cueing Guideline: The nurse can ask the doctor if there are any specific tests that should be repeated if the patient is to remain under observation or is admitted, and at what time these should be performed.

7. Request specialty consultation(s).

Participants should consult either Neurology – **OR** – the Poison Center/Toxicologist – **AND** – the Pediatric Critical Care Intensivist.

Cueing Guideline: The nurse can ask if the doctor wants to consult a specialist to assist with this patient's care.

8. Admit/transfer the patient to the PICU

Depending on institutional capabilities, this may include admission or transfer to a tertiary pediatric hospital for admission to the PICU.

Cueing Guideline: Nurse asks the doctor where this patient will need to be admitted.

Critical Actions Checklist¹

Resident Name								
Case Description								
Skills measured <small>Core competencies: PC Patient care, MK Medical knowledge, IC Interpersonal and communication skills P Professionalism, PB Practice-based learning and improvement SB Systems-based practice</small>	Very Unacceptable		Unacceptable		Acceptable		Very Acceptable	
Data Acquisition (D) PC MK I	1	2	3	4	5	6	7	8
Problem Solving (S) PC MK PB	1	2	3	4	5	6	7	8
Patient Management (M) PC MK IC P PB SB	1	2	3	4	5	6	7	8
Resource Utilization (R) PC PB SB	1	2	3	4	5	6	7	8
Health Care Provided (H) PC SB	1	2	3	4	5	6	7	8
Interpersonal Relations (I) IC P	1	2	3	4	5	6	7	8
Comprehension of Pathophysiology (P) MK PB	1	2	3	4	5	6	7	8
Clinical Competence (C) PC MK IC P PB SB	1	2	3	4	5	6	7	8
Critical Actions								
Yes	No				Comments:			
		Obtain IV access						
		Place on continuous cardiac and respiratory monitoring						
		Check point-of-care glucose						
		Administer antiepileptic agents for status epilepticus						
		Administer pyridoxine for presumed INH toxicity						
		Perform endotracheal intubation						
		Request specialty consultation(s)						
		Admit/transfer to the PICU for observation			Yes	No	Dangerous actions	

¹ Modified ABEM Oral Certification Examination checklist and scoresheet

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INITIAL PHYSICAL EXAM

Vital Signs: BP: 117/72 mmHg P: 117/minute R: 24/minute T: 36.7C (98.0F)
POx: 97% (FiO₂=0.21) Wt: 14.9 kg

General Appearance: The patient appears to be a well-nourished child with normal growth development. At this time, she is reclined on the stretcher with her eyes open. She is drowsy and responding intermittently to basic questions and commands.

HEENT: There are no scalp deformities, wounds, or lacerations. Ears are grossly normal with clear pearly tympanic membranes, no hemotympanum. Pupils are equal, round, and reactive to light. Nares are patent, with no epistaxis.

Skin: Normal color and turgor. No diaphoresis. No rash.

Cardiovascular: Regular rate and rhythm. No murmurs, rubs, or gallops. Palpable pulses in all four extremities distally.

Respiratory: Tachypneic. Clear to auscultation bilaterally, with no rales or rhonchi.

Abdomen: Soft, non-tender, and non-distended. Normal bowel sounds. No masses or organomegaly.

Extremities: No edema, rashes, or wounds. Full active range of motion in all four extremities. Moving all fingers, warm and well perfused distally.

Neurological: Eyes open, gaze oriented to person, responding intermittently to basic questions or commands. Pupils equal, round, and reactive to light and accommodation. No sensory or motor deficits. Normal muscle tone and +2 deep tendon reflexes in all extremities. Normal finger-to-nose movements. Gait not assessed secondary to patient drowsiness.

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PLAY OF CASE GUIDELINES

The patient is a 5-year-old girl

1. Instructors will guide the initial patient course based on the physician's chosen diagnostic and therapeutic interventions. Feedback on these choices will come from: 1) the patient's responses. She will initially be able to respond drowsily to physical and verbal stimuli but will soon thereafter decompensate. 2) The patient's clinical condition, as reported by the simulation director and/or manikin's dynamic physical exam changes (if possible). 3) Imaging and laboratory values, as presented by the simulation director in a timely manner as requested (i.e., there should be a window period from the time that blood samples are collected and laboratory values result). 4) Nursing staff, who may provide real-time observational feedback to the physician.
2. The patient's condition will deteriorate one minute into the patient's arrival via EMS. At this point, she develops tonic-clonic movements, and becomes unresponsive and apneic. Her pulse oximetry readings will decrease to 80%. If the correct interventions are not initiated in a timely fashion, she will go into status epilepticus. Seizures will not cease until pyridoxine is given. Despite the patient's initial well-appearing appearance, the patient should be observed for several hours.
3. If requested, a complete medical history will not be available (parents not present; no records in computer).

Required Actions within the First Two Minutes

- Initial assessment and stabilization measures should be performed during this time
- Place on continuous cardiac and respiratory monitoring
- A/B: Provide supplemental oxygen – **OR** – prepare for endotracheal intubation
- C: Obtain IV access (see note below); initial diagnostics should be ordered
- D: Check point-of-care glucose
- When seizures begin, provide antiepileptic therapy (demonstrate ability to escalate as clinically indicated according to the play of the case)

Branch Points

- **IF THE PATIENT IS NOT PLACED ON SUPPLEMENTAL OXYGEN**, then the patient will become more hypoxic once the seizures begin.
- **ATTEMPTS AT STOPPING THE SEIZURE (WHEN IT OCCURS) WITH CONVENTIONAL ANTIEPILEPTICS WILL NOT BE SUCCESSFUL.**
- **AT FACULTY REQUEST, IV ACCESS MAY BE DIFFICULT TO ACHIEVE BY PERIPHERAL VENOUS CATHETERIZATION.** The participant should demonstrate the ability to escalate to intraosseous or intranasal antiepileptic administration if this faculty option in the case play is selected.

Required Actions over the Next Four Minutes

- Patient should be placed on continuous cardiac and respiratory monitoring by this time
- Diagnostics should be returned as ordered
- Consideration of empiric pyridoxine (vitamin B6) administration in the context of status epilepticus refractory to escalation of conventional antiepileptic therapy should be made by this time
- Toxicology consultation should be considered at this time

Branch Points

- **IF EMPIRIC PYRIDOXINE (VITAMIN B6) IS NOT ADMINISTERED BY THIS TIME**, then the patient will continue to seize.
- **IF THE PATIENT IS NOT ENDOTRACHEALLY INTUBATED BY THIS TIME**, then the patient will demonstrate hypercarbia, hypoxia, and bradypnea in the postictal period.

Required Actions over the Remainder of the Case

- Consultation with either Neurology or the Poison Center/Toxicologist should be made by this time
- Consultation with the Pediatric Critical Care Intensivist should be made by this time
- Decision for definitive disposition (transfer to a tertiary care pediatric hospital and/or admission to the PICU for observation) should be made by this time

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STIMULUS INVENTORY

- #1 Complete blood count
- #2 Basic metabolic panel
- #3 Urinalysis
- #4 Liver function tests
- #5 Venous blood gas
- #6 Point-of-care glucose
- #7 Toxicology
- #8 Coagulation studies
- #9 CPK
- #10 Lactate

For Examiner Only**LAB DATA & IMAGING RESULTS**

Stimulus #1	
Complete Blood Count (CBC)	
WBC	16,000/mm ³
Hemoglobin	12.5 g/dL
Hematocrit	36%
Platelets	115,000/mm ³
Differential	
PMNLs	80%
Lymphocytes	9%
Monocytes	7%
Eosinophils	4%

Stimulus #2	
Basic Metabolic Profile (BMP)	
Sodium	138 mEq/L
Potassium	4 mEq/L
Chloride	102 mEq/L
Bicarbonate	12 mEq/L
Glucose	110 mg/dL
BUN	25 mg/dL
Creatinine	0.9 mg/dL

Stimulus #3	
Urinalysis	
Color	Yellow
Specific gravity	1.030
Glucose	Negative
Protein	Negative
Ketones	Negative
Leuk. Esterase	Negative
Nitrites	Negative
WBC	0/hpf
RBC	0/hpf

Stimulus #4	
Liver Function Tests	
AST	35 U/L
ALT	38 U/L
Alk Phos	110 U/L
Total Bilirubin	0.8 mg/dL
Direct Bilirubin	0.2 mg/dL
Albumin	4.3 mg/dL
Protein	7 g/dL

Stimulus #5	
Venous Blood Gas	
pH	7.28
pCO ₂	34 mm Hg
pO ₂	40 mm Hg
SaO ₂	97%

Stimulus #6	
Point-of-care glucose	
Value	115 mg/dL

Stimulus #7	
Toxicology	
Salicylate	< 2.5 mg/dL
Acetaminophen	< 10 mcg/mL
Ethanol	< 10 mg/dL
Urine drug screen	
Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Negative
Opiates	Negative
TCA's	Negative
THC	Negative

Stimulus #8	
Coagulation Studies	
INR	1
PTT	32 seconds

Stimulus #9	
CPK	250 U/L

Stimulus #10	
Lactate	6.4 mmol/L

Stimulus #1**Complete Blood Count (CBC)**

WBC	18,500/mm ³
Hemoglobin	13.2 g/dL
Hematocrit	40%
Platelets	219,000/mm ³
Differential	
PMNLs	70%
Lymphocytes	26%
Monocytes	2%
Eosinophils	1%

Stimulus #2**Basic Metabolic Profile (BMP)**

Sodium	145mEq/L
Potassium	3.6mEq/L
Chloride	110 mEq/L
Bicarbonate	20 mEq/L
Glucose	129 mg/dL
BUN	8 mg/dL
Creatinine	0.4 mg/dL

Stimulus #3**Urinalysis**

Color	Yellow
Specific gravity	1.030
Glucose	Negative
Protein	Negative
Ketones	Negative
Leuk. Esterase	Negative
Nitrites	Negative
WBC	0/hpf
RBC	0/hpf

Stimulus #4**Liver Function Tests**

AST	23 U/L
ALT	21 U/L
Alk Phos	110 U/L
Total Bilirubin	1.2 mg/dL
Direct Bilirubin	0.2 mg/dL
Albumin	4.3 mg/dL
Protein	8 g/dL

Stimulus #5

Venous Blood Gas

pH	7.30
pCO ₂	27 mm Hg
pO ₂	40 mm Hg
HCO ₃ base deficit	16 mEq/L 9

Stimulus #6

Point-of-care glucose

Value	129 mg/dL
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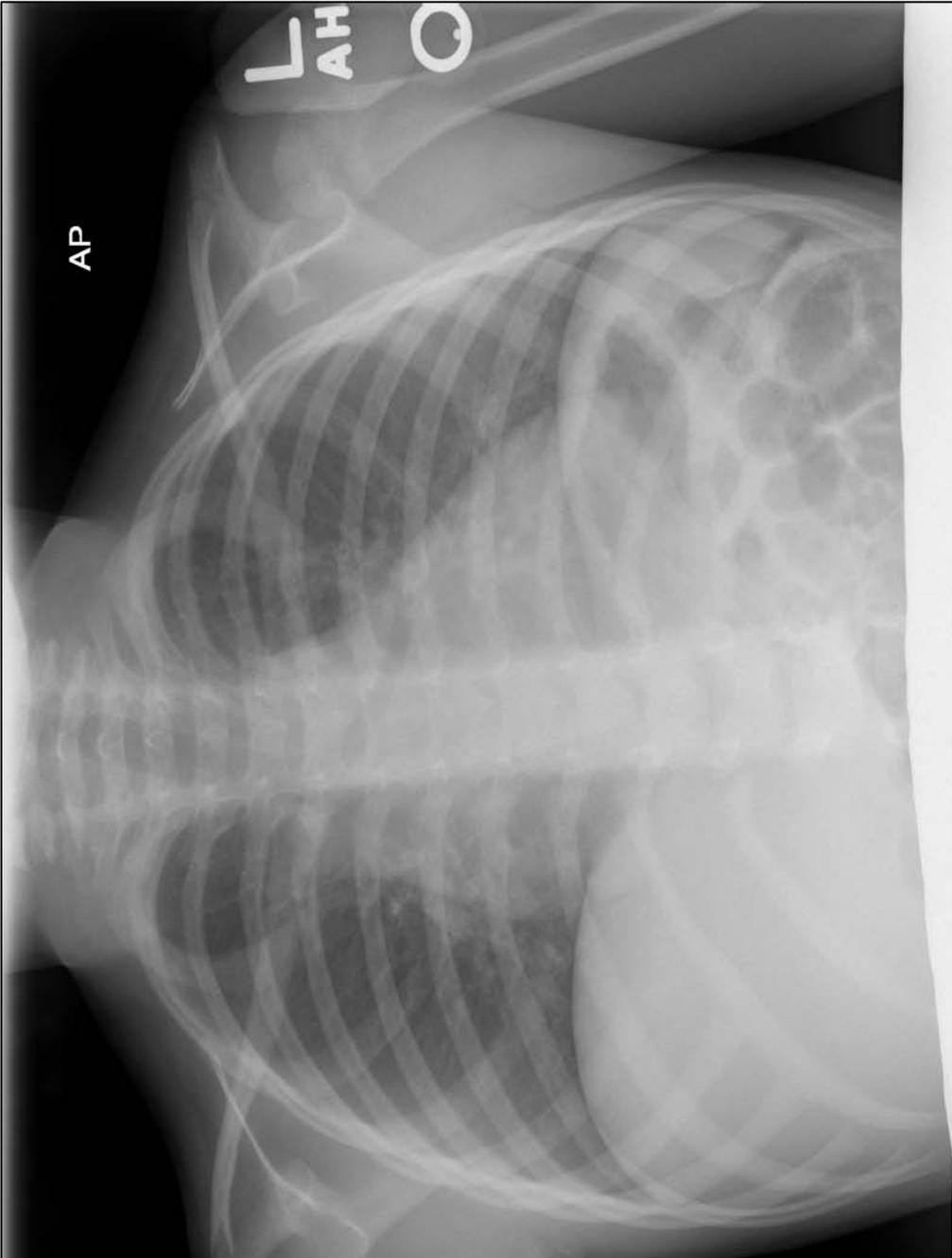
Stimulus #7**Toxicology**

Salicylate	< 4 mg/dL
Acetaminophen	< 10 mcg/mL
Ethanol	< 10 mg/dL

Urine drug screen

Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Negative
Opiates	Negative
TCAs	Negative
THC	Negative

Stimulus #8

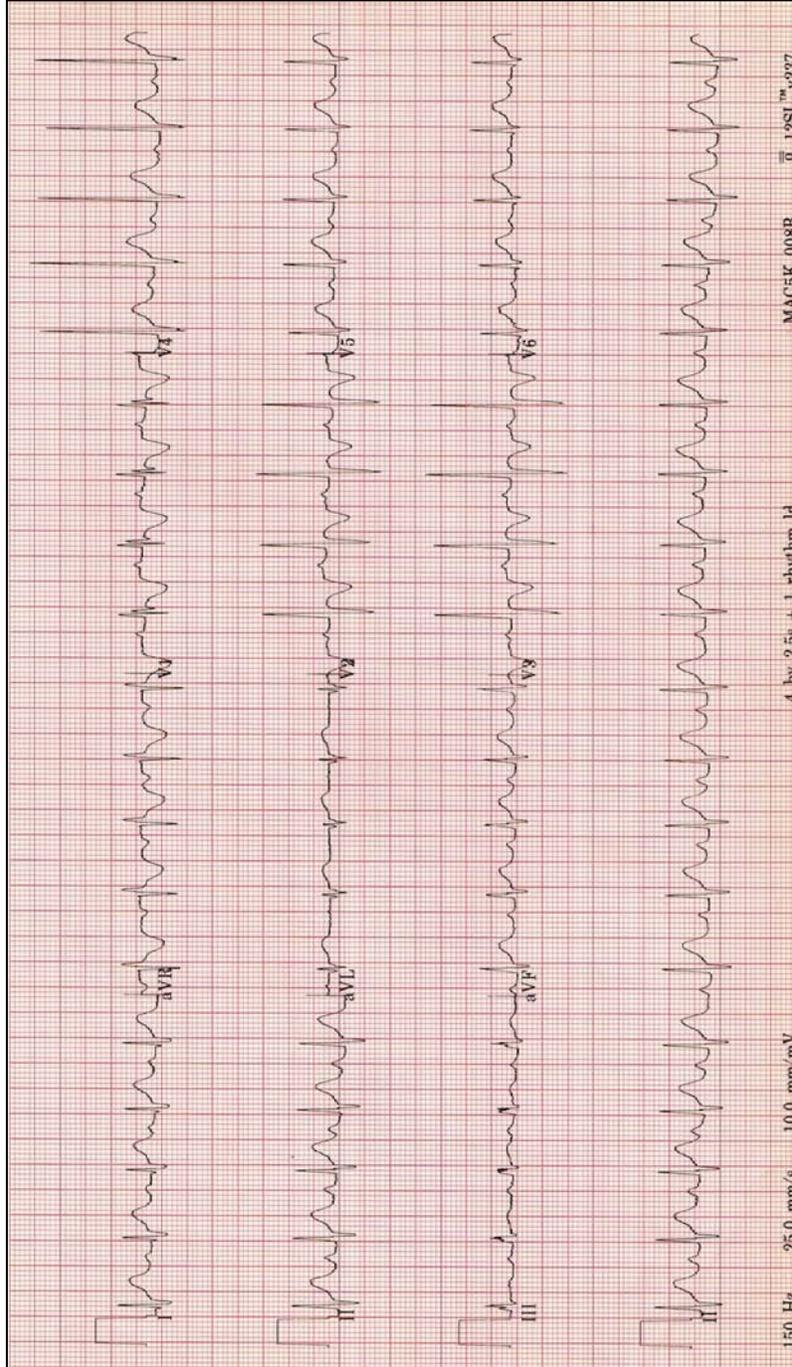


Stimulus #9



Stimulus #10

Source: <http://dontforgetthebubbles.com/ecg-quiz/>



Stimulus #11

Lactate	1.8 mmol/L
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Stimulus #12

Isoniazid (INH) Toxicity Teaching Note

Background

Seizures are episodes of abnormal brain function caused by excessive and aberrant electrical neuronal discharge that usually result in characteristic motor findings. Seizures occur when there is an imbalance of excitatory (glutamate) & inhibitory (GABA) neurotransmitters present. Toxicological causes include INH, TCA's, hypoglycemia from sulfonylureas, and many other etiologies. Status epilepticus is a classic presentation for INH overdose. Suspect INH in immigrants from SE Asia, Western Pacific, and Africa.

Treatment includes ABCs and supportive care. Benzodiazepines are the first line of treatment for seizures. When resistant, other medications can be used. The outline for treating status epilepticus is above but starts with sufficient doses of benzodiazepines, and moves through second-line agents (phenytoin/phosfenytoin, Levetiracetam (Keppra), barbiturates), and to third-line (propofol and others).

For suspected INH toxicity, administer pyridoxine (vitamin B6) immediately. If the amount of INH ingested in overdose is known, administer a gram-per-gram equal amount of pyridoxine (max 5 gm) intravenously for the first dose. Benzodiazepines and barbiturates may be used to potentiate the anticonvulsant effect of pyridoxine. If the amount of INH ingested is unknown, empiric dosing of pyridoxine 70 mg/kg (max 5 gm) is recommended. Pyridoxine administration can be repeated if seizures persist or recur.

Although INH is dialyzable, dialysis is unnecessary if adequate doses of anticonvulsants and pyridoxine are administered. Hemodialysis may be indicated if the patient fails to improve with standard therapy or if adequate doses of pyridoxine cannot be obtained.

Mechanism of Action

INH interferes with the conversion of glutamate to GABA. INH inhibits pyridoxine phosphokinase, the enzyme required to form pyridoxal-5'-phosphate, which is the essential cofactor for glutamic acid decarboxylase to convert glutamate to GABA. Decreased GABA results in persistent seizure activity. Until the pyridoxine is replaced in sufficient quantities, seizures may continue unabated. The key is formation of pyridoxal-5'-phosphate from pyridoxine.

References:

1. American Epilepsy Society Algorithm for Convulsive Status Epilepticus. https://www.aesnet.org/about_aes/press_releases/guidelines2016. Accessed 30 May 2016.