Digoxin Toxicity
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Target Audience: Emergency Medicine Residents (junior and senior level postgraduate learners), Medical Students

Primary Learning Objectives:
1. Recognize signs and symptoms of digoxin toxicity in a complex patient.
2. Recognize the indications for administering digoxin antibody fragments.
3. Consider alternate diagnoses and toxicities.

Secondary Learning Objectives: detailed technical/behavioral goals, didactic points
1. Appropriately uses available resources (poison center)
2. Communicates clearly and effectively while resuscitating a sick patient

Critical actions checklist:
1. Provide crystalloid fluid bolus
2. Place on cardiac monitor
3. Order serum digoxin and basic metabolic panel
4. Place pacing pads for undifferentiated symptomatic bradycardia
5. Give atropine
6. Administer digoxin antibody fragments
7. Consult Poison Center/Toxicologist
8. Admit to the MICU

Environment: Emergency Department treatment area
    1. Room Set Up – ED critical care area
        a. Manikin Set Up – Mid or high fidelity simulator
        b. Props – Standard ED equipment
    2. Distractors – ED noise, alarming monitor

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CASE SUMMARY

SYNOPSIS OF HISTORY/ Scenario Background

Chief Complaint: Altered mental status

This is a case of a 69-year-old woman who is brought in by EMS after her husband called 911 for increasing confusion, vomiting, and reduced level of consciousness. On ED arrival, she is altered, hypotensive, and bradycardic. She should be initially resuscitated by the learners. Her medication list includes digoxin and diltiazem, and her ECG will show slow atrial fib. When back, her digoxin level will be high. The learners should administer digoxin antibody fragments which will stabilize the patient. If not administered, the patient deteriorates into bidirectional VT.

PMHx:
atrial fibrillation
congestive heart failure
osteoarthritis
hypothyroidism
peptic ulcer disease
bipolar disorder
recent urinary tract infection

PSHx: None

Medications:

rivaroxaban	diltiazem
digoxin	nitroglycerin patch
spironolactone	furosemide
celecoxib	levothyroxine
lansoprazole	escitalopram
amitriptyline	quetiapine
olanzapine	nitrofurantoin
zopiclone	

Allergies: None

SH:
Lives at home with husband.
No formal social supports in place.
Husband denies ethanol or tobacco use.

FH: None

Onset of Symptoms: 2-3 days

Background Info: Her husband reports increasing confusion and vomiting for the past 2-3 days. He called EMS today because she was becoming less responsive over the last few hours. On arrival EMS found her to be bradycardic, hypotensive, and altered. No sick contacts. No trauma. No previous episodes. No new medication changes. Unknown last dose times of medications.

Review of Systems:

CNS: Patient unable to answer questions. Husband reports recent confusion and decreasing LOC.

HEENT: Recently complaining of worsening vision.

CVS: None

RESP: None

GI: Vomiting at home earlier today and complaining of abdominal pain for the last few days.

GU: None

MSK: None

Required Actions within the First Two Minutes

- Obtain HPI and essential ROS
- Establish safety net (IV, oxygen, cardiac monitor, two large bore IVs, draw blood for labs)
- A/B – Provide supplemental oxygen
- C – Cardiac monitor; NS IV bolus; ECG; place pacing pads on patient (with identification of significant bradycardia)
- D – Point-of-care glucose = 137 mg/dL

CASE CONTINUATION - PHYSICAL EXAM

General Appearance: Decreased level of consciousness, appears unwell.

Vital Signs: BP: 85/60 mmHg P: 30/minute, irregularly irregular R: 14/minute T: 36.5C (97.7F) POx: 95% (FiO_2=0.21)

HEENT: Normal

Neck: No tenderness or deformity on exam, full range of motion, no JVD

Skin: Warm and well-perfused, no rash.

Chest/CVS: HR slow and irregular. Normal heart sounds, no murmurs.

Lungs: Breath sounds present in all anterior and posterior lung fields. No adventitious sounds.

Back: Normal

Abdomen: Soft, non-tender, and non-distended. No guarding, rebound, or rigidity.

Extremities: Normal

Neurologic: Decreased level of consciousness. Sedated. Rouses to touch, but markedly confused (groaning and garbled words only) GCS 10 (E2 / V3 / M5)

Required Actions within the Next Two Minutes

- Laboratory studies (especially BMP and digoxin level) should be ordered and sent by this time
- Resuscitation with IV crystalloid fluids should have started by this time
- An ECG should have been obtained by this time
- Pacing pads should be placed on the patient, and pacing should be considered at this time. Atropine should be considered at this time.

Branch Point

- **IF PATIENT RECEIVES ATROPINE,** there will be a minimal response to HR and blood pressure (HR increases to 50/minute and BP increases to 98/62 mmHg).
- **IF IV FLUID BOLUSES ARE GIVEN,** here will be a minimal response to blood pressure (BP increases to 98/63 mmHg).
- **IF TRANSCUTANEOUS PACING IS ATTEMPTED PRIOR TO DIGOXIN ANTIBODY FRAGMENT ADMINISTRATION,** there will be a minimal response to BP (increases to 98/62 mmHg) and the patient begins to moan.
- **IF TRANSVENOUS PACING IS ATTEMPTED PRIOR TO DIGOXIN ANTIBODY FRAGMENT ADMINISTRATION, THEN THE PATIENT WILL DEVELOP VENTRICULAR FIBRILLATION AND SUFFER CARDIAC ARREST.**
- **IF ACTIVATED CHARCOAL IS GIVEN, THEN THE PATIENT VOMITS.**

Required Actions within the Next Several Minutes

- Labs return, notable for elevated digoxin level and potassium
- Poison Center/Toxicologist consultation should be obtained by this time
- Administration of digoxin antibody fragments should be considered and started by this time

Branch Points

- **IF DIGOXIN ANTIBODY FRAGMENTS ARE NOT ADMINISTERED AT THIS TIME, THEN THE PATIENT WILL DETERIORATE AND DEVELOP BIDIRECTIONAL VENTRICULAR TACHYCARDIA (VT).**
    - **Vital Signs: BP: 70/42 mmHg P: 120/minute R: 10/minute POx: 92%**
- **IF PARTICIPANTS CORRECT POTASSIUM WITHOUT TREATING THE DIGOXIN TOXICITY,** then the patient's status will not improve.
- **IF CALCIUM IS GIVEN,** then the patient's status will remain unchanged (remains in VT). (NOTE: a digoxin-toxic heart is "irritable" from relative intracellular hypercalcemia)
- **NOTE: PARTICIPANTS MAY EXPERIENCE THE CASE AS A CALCIUM CHANNEL BLOCKER OT BETA-BLOCKER TOXICITY, AND GIVE EMPIRIC CALCIUM OR GLUCAGON. THESE INTERVENTIONS WILL HAVE NO EFFECTS.**
- **IF DEFIBRILLATION IS ATTEMPTED (WITH PATIENT DETERIORATION TO BIDIRECTIONAL VT OR VF AS NOTED ABOVE) PRIOR TO THE ADMINISTRATION OF DIGOXIN ANTIBODY FRAGMENTS, THEN THERE WILL BE NO RESPONSE.**

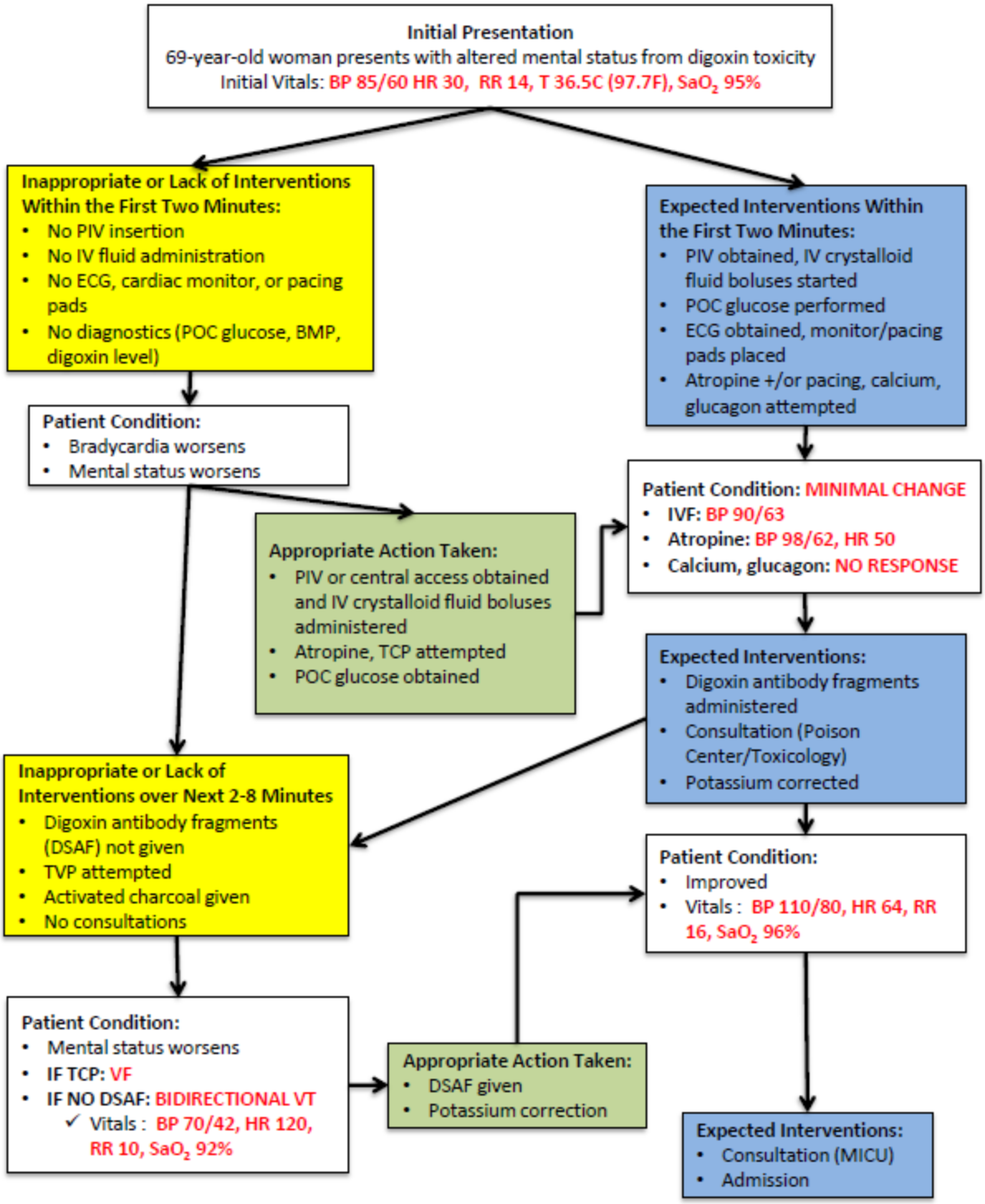
Required Actions within the Next Several Minutes

- Patient should have received therapies for symptomatic bradycardia, including digoxin antibody fragments, by this time
- Patient should receive additional IV crystalloid fluid boluses at this time
- Poison Center/Toxicologist and MICU should be consulted by this time for recommendations and definitive disposition

Branch Points

- **IF THERAPIES FOR THE DIGOXIN TOXICITY ARE GIVEN, THEN THE PATIENT'S CLINICAL STATUS WILL IMPROVE.**
    - **Vital Signs: BP: 100/80 mmHg P: 64/minute, irregularly irregular R: 16/minute T: 37C (98.6F) POx: 96%**
    - **Patient demonstrates improved level of consciousness, and opens eyes spontaneously**

Timeline and Branch Points for This Case



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CRITICAL ACTIONS

1. **Obtain peripheral IV access**

   Obtain peripheral IV access. Patient will require this access for medication and fluid boluses as the case progresses.
   Cueing Guideline: Nurse can ask if the doctor wants an IV inserted and blood for testing.

2. **Place on cardiac monitor**

   Place on cardiac monitor
   Cueing Guideline: Nurse can ask if the doctor wants the patient placed on a cardiac monitor and other adjuncts.

3. **Order serum digoxin and basic metabolic panel**

   Order serum digoxin and basic metabolic panel. These are important for verifying the presence of digoxin (although this could be presumed and treatment started empirically with digoxin antibody fragments in the context of worsening clinical instability) and electrolyte derangements (e.g., hyperkalemia).
   Cueing Guideline: The nurse asks if the doctor wants to order any diagnostic tests.

4. **Place pacing pads for undifferentiated symptomatic bradycardia**

   Place pacing pads for undifferentiated symptomatic bradycardia.
   Cueing Guideline: The nurse asks if the doctor about the patient's concerning heart rate, and if anything could be done to improve the patient's status.

5. **Give atropine**

   Give atropine. Note that although this intervention is a critical action, there will be a minimal response resulting from its administration.
   Cueing Guideline: The nurse asks if the doctor about the patient's concerning heart rate, and if anything could be done to improve the patient's status.

6. **Administer digoxin antibody fragments**

   Administer digoxin antibody fragments.
   Cueing Guideline: The nurse asks if the doctor about the patient's concerning heart rate, and if anything could be done to improve the patient's status, especially if pacing, atropine, or other interventions (e.g., glucagon) have already been attempted.

7. Consult Poison Center/Toxicologist

The Poison Center or Toxicologist should be consulted for further management recommendations regarding digoxin toxicity.
Cueing Guideline: The nurse can ask if the doctor has called the Poison Center or Toxicologist yet.

8. Admit to the MICU

Admit to the MICU for continued critical care monitoring and reassessment. A discussion with intensivist regarding admission is required prior to the completion of the case.
Cueing Guideline: The nurse can ask if there is a definitive disposition for the patient yet.

Critical Actions Checklist[1]

Resident Name	
Case Description	

Skills measured **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	**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 peripheral IV access	
		Place on cardiac monitor	
		Order serum digoxin and basic metabolic panel	
		Place pacing pads for undifferentiated symptomatic bradycardia	
		Give atropine	
		Administer digoxin antibody fragments	
		Consult Poison Center/Toxicologist	
		Admit to the MICU	

Yes	No	
		Dangerous actions

[1] Modified ABEM Oral Certification Examination checklist and scoresheet

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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	Toxicology
#7	Coagulation studies
#8	Additional electrolytes
#9	Digoxin level
#10	ECG 1
#11	ECG 2

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LAB DATA & IMAGING RESULTS

Stimulus #1	
Complete Blood Count (CBC)	
WBC	9,700/mm^3
Hemoglobin	13.2 g/dL
Hematocrit	36%
Platelets	297,000/mm^3
Differential	
PMNLs	75%
Lymphocytes	22%
Monocytes	2%
Eosinophils	1%

Stimulus #2A	
Basic Metabolic Panel (BMP)	
Sodium	134 mEq/L
Potassium	6.9 mEq/L
Chloride	105 mEq/L
Bicarbonate	21 mEq/L
Glucose	117 mg/dL
BUN	32 mg/dL
Creatinine	2.1 mg/dL

Stimulus #3	
Urinalysis	
Color	Yellow
Specific gravity	1.030
Glucose	Negative
Protein	Negative
Ketones	Negative
LE/Nitrites	Negative
Blood	Negative
WBC/RBC	0/hpf / 0/hpf
Crystals/bacteria	Negative

Stimulus #4	
Liver Function Tests	
AST	49 IU/L
ALT	32 IU/L
ALP	110 IU/L
T. Bilirubin	1.2 mg/dL
D. Bilirubin	0.2 mg/dL
Albumin	4.3 mg/dL

Stimulus #5	
Venous Blood Gas	
pH	7.31
pCO_2	47 mmHg
pO_2	36 mmHg
HCO_3	21 mEq/L
Lactate	4.5 mmol/L

Stimulus #6	
Toxicology	
APAP / ASA	Undetectable
Ethanol	Undetectable

Stimulus #7	
Coagulation Studies	
PTT	38 seconds
INR	1.7

Stimulus #8	
Additional Electrolytes	
Calcium	9.7 mEq/L
Magnesium	1.6 mEq/L
Phosphorous	2.8 mEq/L

Stimulus #9	
Digoxin level	
Value	5.5 ng/mL

Stimulus #10
ECG 1 Atrial fibrillation with slow ventricular response

Stimulus #11
ECG 2 Bidirectional VT

Stimulus #1

Complete Blood Count (CBC)

WBC	9,700/mm^3
Hemoglobin	13.2 g/dL
Hematocrit	36%
Platelets	297,000/mm^3
Differential	
PMNLs	75%
Lymphocytes	22%
Monocytes	2%
Eosinophils	1%

Stimulus #2

Basic Metabolic Panel (BMP)

Sodium	134 mEq/L
Potassium	6.9 mEq/L
Chloride	105 mEq/L
Bicarbonate	21 mEq/L
Glucose	117 mg/dL
BUN	32 mg/dL
Creatinine	2.1 mg/dL

Stimulus #3

Urinalysis

Color / pH	Yellow
Specific gravity	1.030
Glucose	Negative
Protein	Negative
Ketones	Negative
LE/Nitrites	Negative
Blood	Negative
WBC/RBC	0/hpf / 0/hpf
Crystals/bacteria	Negative

Stimulus #4

Liver Function Tests

AST	49 IU/L
ALT	32 IU/L
ALP	110 IU/L
T. Bilirubin	1.2 mg/dL
D. Bilirubin	0.2 mg/dL
Albumin	4.3 mg/dL

Stimulus #5

Venous Blood Gas

pH	7.31
pCO_2	47 mmHg
pO_2	36 mmHg
HCO_3	21 mEq/L
Lactate	4.5 mmol/L

Stimulus #6

Toxicology

APAP / ASA	Undetectable
Ethanol	Undetectable

Stimulus #7

Coagulation Studies

PTT	38 seconds
INR	1.7

Stimulus #8

Additional Electrolytes

Calcium	9.7 mEq/L
Magnesium	1.6 mEq/L
Phosphorous	2.8 mEq/L

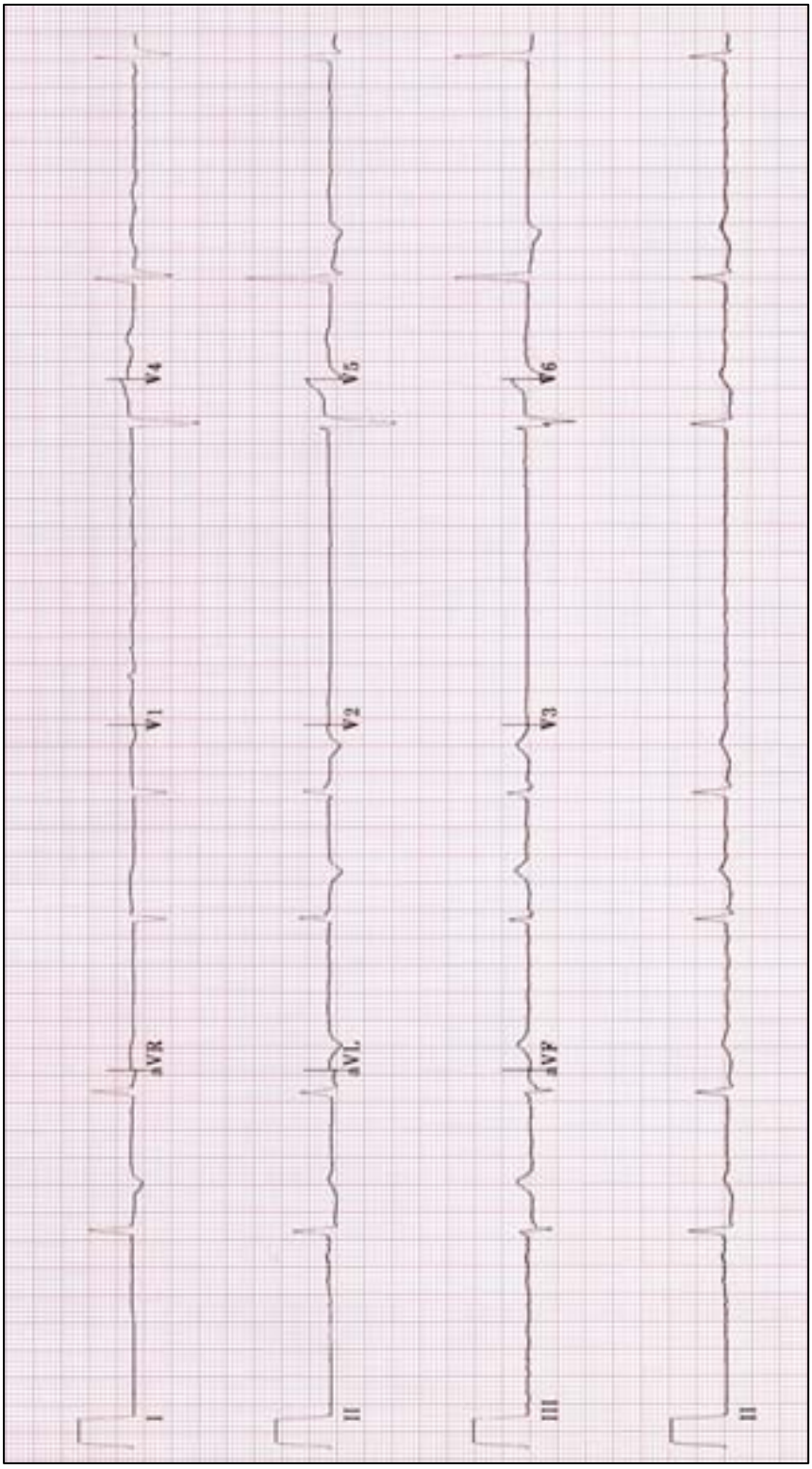
Stimulus #9

Digoxin level

Value	5.5 ng/mL

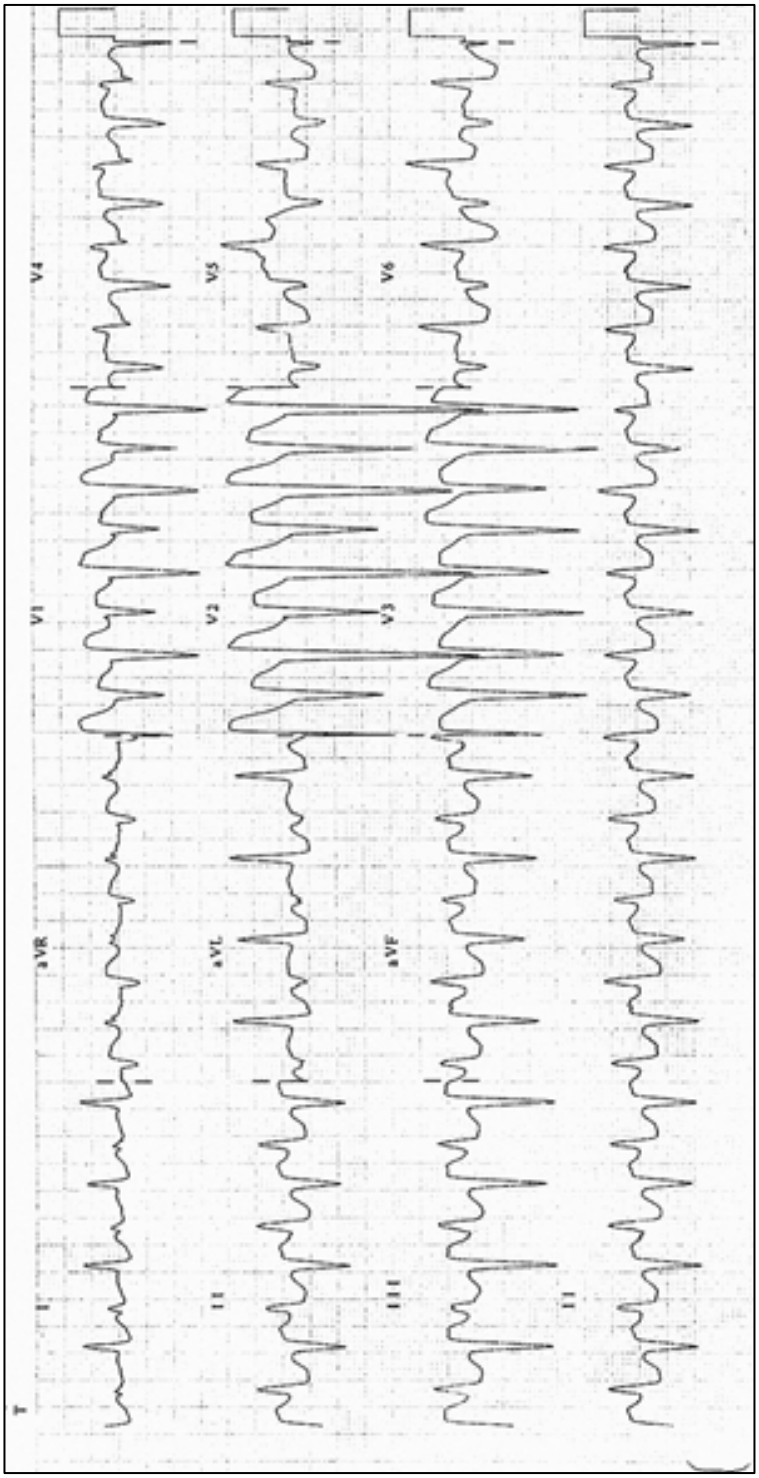
Stimulus #9

ECG 1 From Life in the Fast Lane:http://i1.wp.com/lifeinthefastlane.com/wp-content/uploads/2012/01/AF-slow-ventricular-response.jpg



Stimulus #10

ECG 2 From Life in the Fast Lane:http://i2.wp.com/lifeinthefastlane.com/wp-content/uploads/2011/01/ecg-exigency-010.jpg?w=1457



Debriefing Materials – <u>Digoxin Toxicity</u>

Educational Goal: To recognize and manage a patient with digoxin toxicity.

Sources of Exposure: Digoxin is a cardioactive steroid (CAS) used in the treatment of congestive heart failure and atrial fibrillation/flutter. Digitoxin is another CAS. Numerous plants contain cardioactive steroids including foxglove, oleander, red squill, and lily of the valley.

Pathophysiology:

- Cardioactive steroids are direct inhibitors of the sodium-potassium ATPase found in myocardiocytes
- This increases intracellular sodium, which prevents the antiporter from exchanging sodium for calcium
- The overall effect is increased intracellular calcium
- This results in enhanced inotropy at therapeutic levels
- In toxicity, excessive elevation of calcium elevates the resting membrane potential, producing myocardial sensitization and predisposing to dysrhythmias

Severity of Ingestion:

- Overall, digoxin use has been decreasing over time
- There are about 3,500 exposures to CAS medications per year, resulting in about 20 deaths. There are around 2000 exposures to CAS-containing plants per year with no reported attributable deaths during one study period.
- Severity of digoxin toxicity correlates with serum level.
- Severity of acute CAS toxicity correlates with elevation in potassium.

Organ System Effects:

- Ophthalmologic: photophobia, blurring, scotomata, decreased visual acuity, yellow halos around lights
- Cardiovascular: alterations in rate and rhythm resulting in nearly any dysrhythmia
- Neurologic: lethargy, confusion, and weakness
- Gastrointestinal: nausea, vomiting, and abdominal pain

Diagnostic Testing:

- Toxicity should be suspected by history and physical
- ECG findings suggestive of digoxin toxicity include paroxysmal atrial tachycardia with high-degree AV block, bidirectional ventricular tachycardia
- Serum digoxin level
    - Most accurate 6 hours after time of ingestion in acute overdose
    - Levels drawn earlier in acute overdose can be falsely elevated may not reflect steady state levels
    - Levels drawn after administration of digoxin-specific antibodies (DSFab) are difficult to interpret as they do not distinguish free versus bound digoxin levels
    - In general, a toxic digoxin level is considered to be above 2 ng/mL
- Chemistry panel: Repeat as needed, especially when monitoring potassium

Treatment:

- Definitive treatment: DSFab

- Indications for treatment
    - Any digoxin-related life-threatening dysrhythmias
    - K+ concentration > 5 mEq/L in acute overdose
    - Chronic elevation in serum digoxin concentration (SDC) with associated dysrhythmias, significant GI symptoms, or altered mental status
    - SDC ≥ 15 ng/mL at any time, or ≥ 10 ng/mL 6 h post ingestion
    - Ingestion of 10 mg in adults or 4 mg in children
    - Poisoning with non-digoxin cardioactive steroid

- Hyperkalemia: marker for severity of toxicity, especially in acute overdose
    - Debate regarding the treatment of hyperkalemia with calcium in CAS toxicity
    - Some animal studies and case reports suggest an increased risk for dysrhythmia and death with calcium administration
    - However, there are numerous case reports of successful treatment of hyperkalemia associated with CAS toxicity with calcium without harm
    - Treatment with DSFab is preferred and will resolve hyperkalemia
    - Insulin/glucose can also be an effective temporizing measure
- Cardiac dysrhythmias:
    - Symptomatic bradycardia generally resistant to pacing
    - Dysrhythmias resolve after treatment with DSFab
    - Treat hemodynamically unstable V-tach and V-fib with DSFab; cardioversion and defibrillation can be used but there is some thought that electricity may precipitate dysrhythmias as well.

Consultations:

- Consult the regional poison center or a local medical toxicologist for additional information and patient care recommendations

Disposition:

- Admit patients with major signs and symptoms to an ICU (cardiovascular ICU or medical ICU)

Take-Home Points:

- Cardioactive steroid toxicity can occur from exposure to medications (digoxin, digitoxin) as well as naturally occurring sources, such as foxglove
- CAS inhibit the cardiac myocyte sodium-potassium ATP-ase, causing an increase in intracellular calcium and increased inotropy
- In addition to cardiac effects, symptoms of toxicity can include nausea, vomiting, abdominal pain, fatigue, visual disturbances, and altered mental status
- In overdose, CAS can produce nearly any dysrhythmia on ECG, but A-fib, A-flutter, or PAT with AV block and bidirectional ventricular tachycardia are highly suggestive of toxicity
- Definitive treatment is with digoxin-specific antibody fragments, which can also be effective in non-digoxin CAS toxicity

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