

Better Living Through Chemistry

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The Plan

- Case based
 - Presentation
 - Pathophysiology
 - Diagnosis
 - Management
- Some of the common

Emergency Medicine Approach to a Patient

Chief Complaint

History

Physical

Ancillary tests

→ → → → → Differential Diagnosis → → → → →



Treatment

Chest Pain



Treatment



Treatment

Heart Attack

Aortic Dissection

Pulmonary Embolism

Pneumonia

Pericarditis

Muscle strain



Pneumonia

Pericarditis

Muscle strain

Pulmonary Embolism

Heart Attack

Aortic Dissection



Muscle Strain

Emergency Medicine Approach to a Patient

- How sure am I of my diagnosis?
 - History 80%
 - Physical 90%
 - Ancillary tests 95%
- EM providers are pessimists
- Sometimes we are given the diagnosis...
then must know what to do with it

Case 1

- **History:** 16 y/o male brought by his parents. Chief complaint is weakness; especially in his legs. Can't stand up. Began this morning. Not feeling ill o/w.
- **PMH:** None
- **Medications:** None
- **Social History:** ∅ alcohol, tobacco, other drugs

Differential Diagnosis

Muscle infection

Stroke

Trauma

Thyroid problem

Electrolyte

Botulism

Peripheral nerve

Spinal cord problem

Case 1

- **Physical Exam**

- HR 80 (60-100) RR 16 (16-20)
- BP 110/70 Temp 97°F
- Oxygen Saturation 98% (> 95%)
- Diffusely weak with 3/5 strength
- Facial muscles are normal strength
- Coordination intact
- Sensation intact
- Muscles are non-tender

So then we got mom and dad out of the room...and talked some more

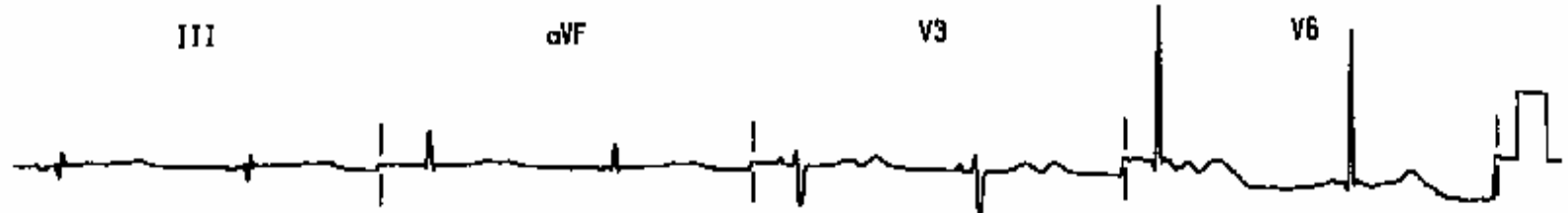
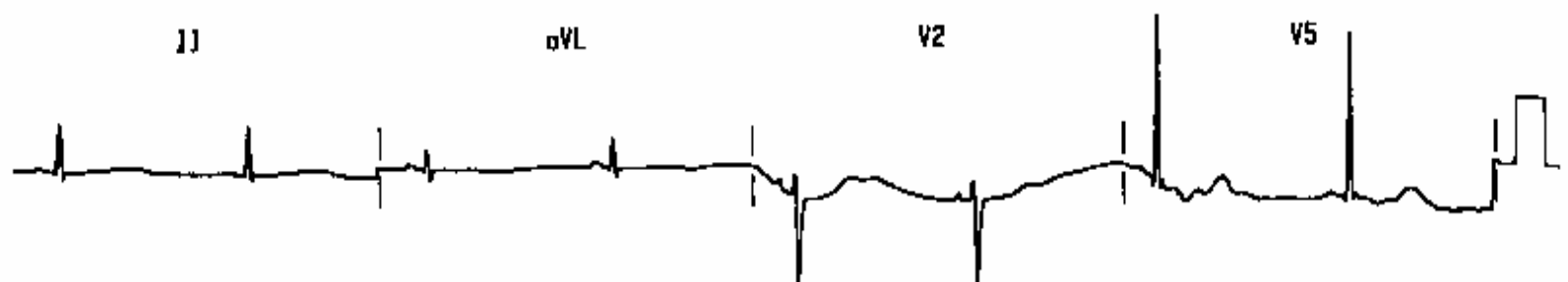
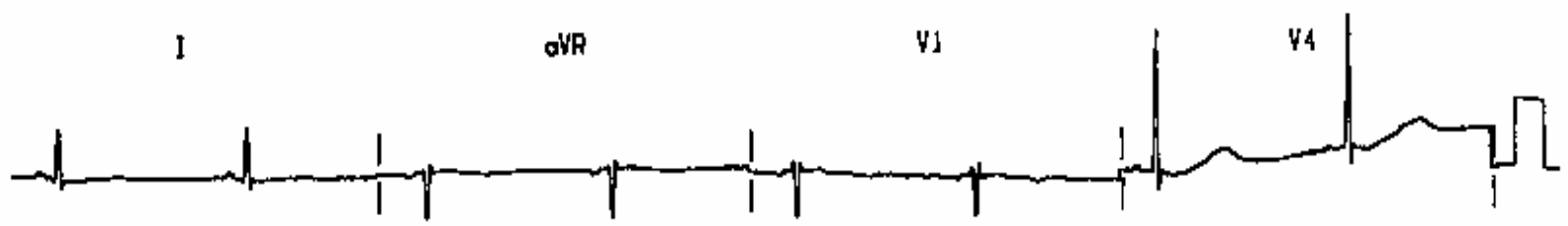
...and the rest of the story

- Sniffer
- Been doing more over recent weeks
- Last night was a big night...

Thus, suspect he is hypokalemic (Low potassium)

Potassium 2.4

Bicarbonate 15



RHYTHM STRIP: II
25 mm/sec; 1 cm/mV



Hypokalemic Periodic Paralysis

- Condition associated with low potassium
- Weakness is the usual presentation
- Toluene...a classic cause...
 - Common hydrocarbon solvent
 - Replaced benzene (ass with leukemia)
 - Paints, varnishes, glues

Toluene

- Highly fat soluble
- Highly volatile
- Stimulates gamma aminobutyric acid (GABA)...the primary CNS inhibitory neurotransmitter
- Inhibits glutamate NMDA receptors (a stimulatory neurotransmitter)
- Renal tubular effects
 - Acidosis
 - Loss of potassium
 - Chronic use causes leukoencephalopathy

Case 1 Conclusion

- Ensured he was breathing OK (ABC's!!!)
- Admitted to hospital
- Potassium supplementation by intravenous route
- Good news...strength improved to normal
- Bad news...grounded for life

Case 2

- 17 y/o male comes home from an “evening out” with his buddies. He is agitated and confused. The buddies leave quickly and without explanation. Parental units bring him to the ER.
- PMH: None
- Medications: None
- Social History: Has used alcohol; Denies drugs

Case 2

Physical Exam

- Wide-eyed and agitated
- Confused, Hyper-religious
- Skin: Diaphoretic and warm
- HR 140 RR 30
 BP 220/120 Temp: 105°F
- Pupils: 6 mm (3-4 mm)
- Strength: Godzilla-like with all extremities

Differential Diagnosis

Cocaine

Theophylline

Hypoglycemic

Amphetamines

Cold pills

Psychodelics

Caffeine

Hallucinogens

Case 1

Impression

- Suspect drugs
 - Cough & Cold medicine abuse
 - Amphetamine-like (Ecstasy)
 - Cocaine
 - Doubt caffeine or theophylline
- Check glucose level
- Complications of the sympathomimetic state
 - Hyperthermia
 - Rhabdomyolysis
 - (Muscle breakdown → Myoglobin release → Kidney failure)
 - Seizures
 - Stroke



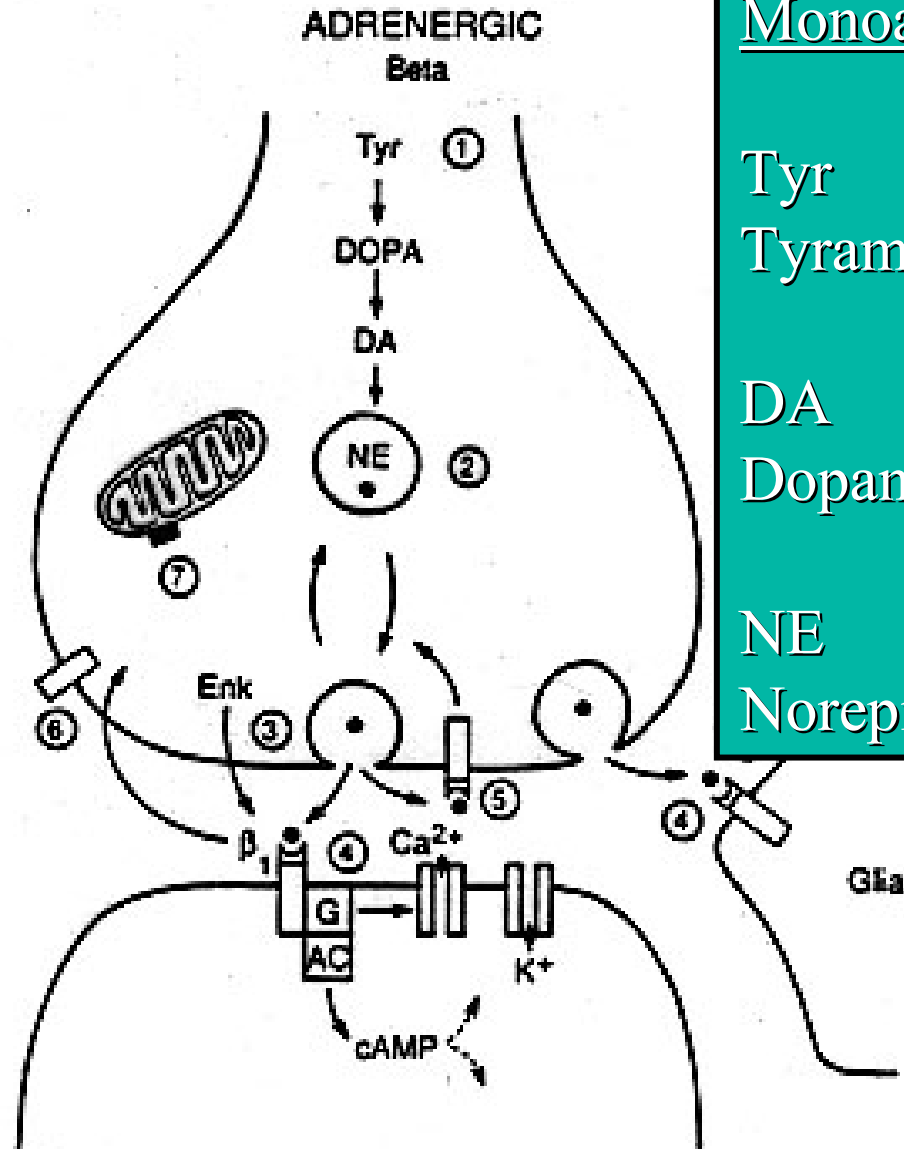
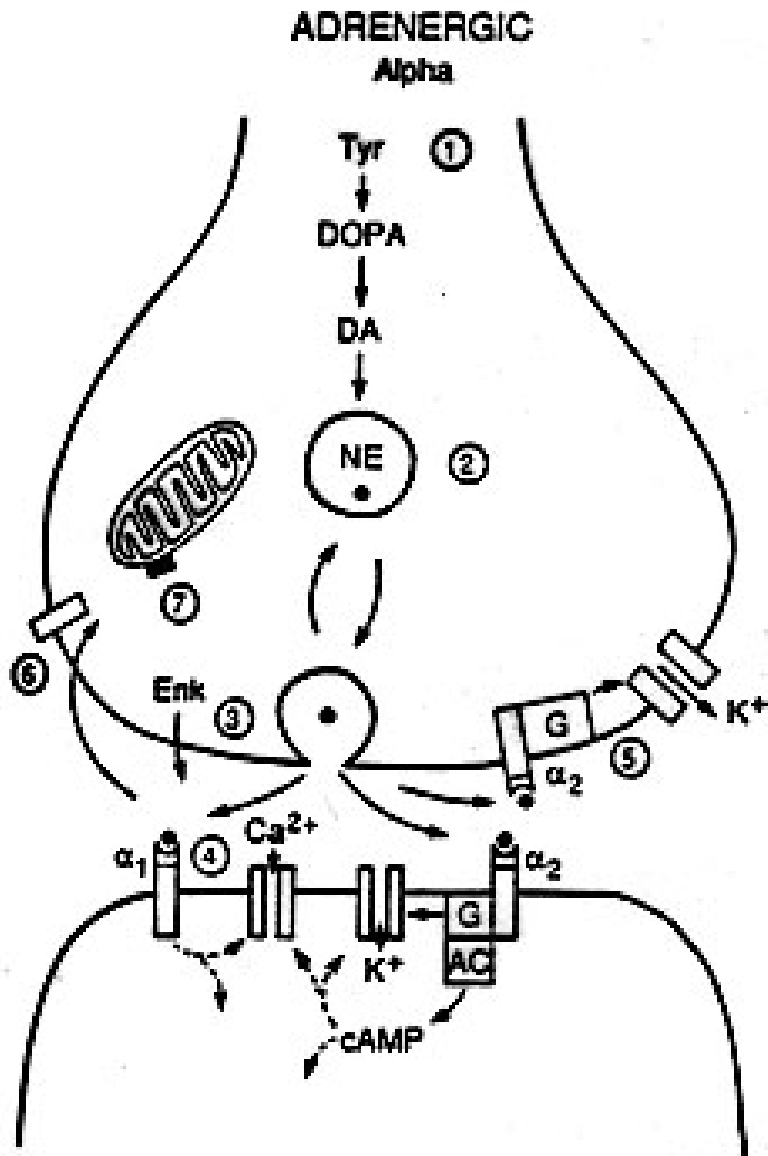
(CNN)



(c) Alya fra Norge

Case 2

Pathophysiology

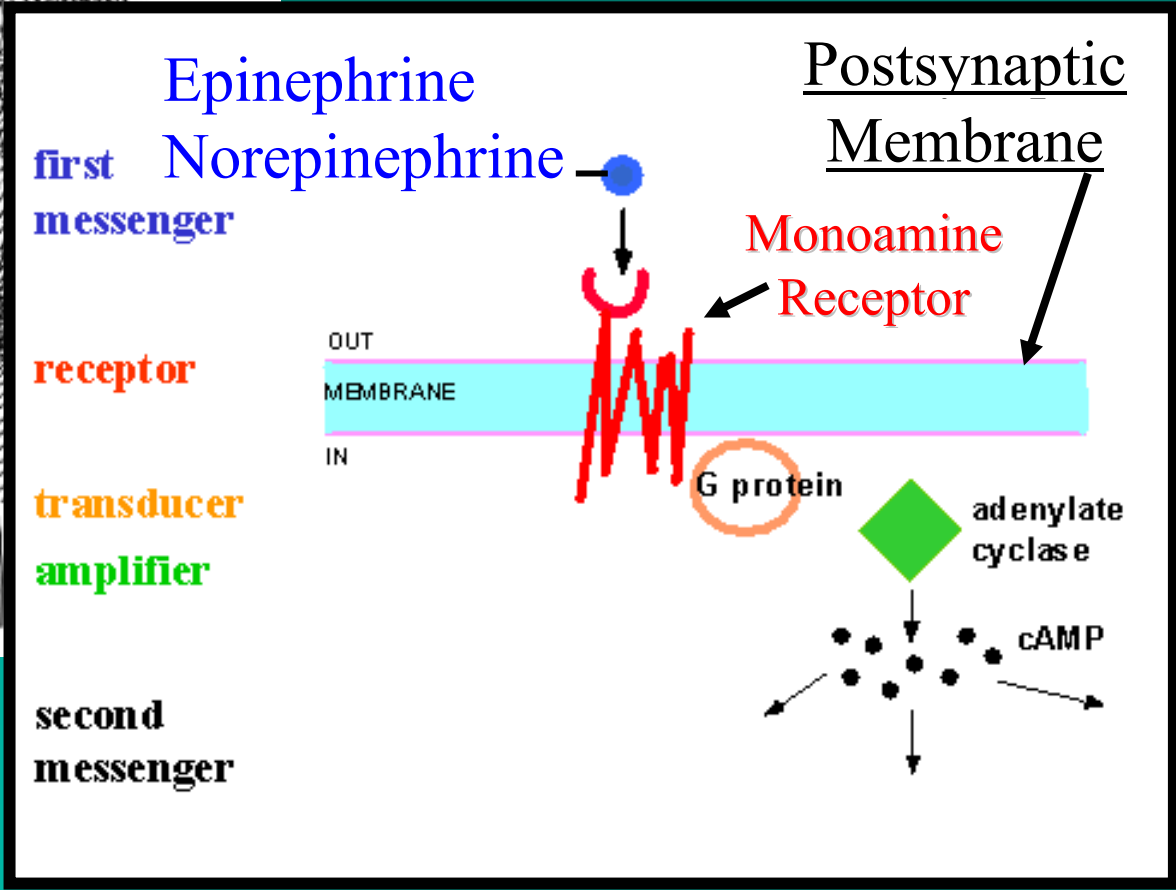
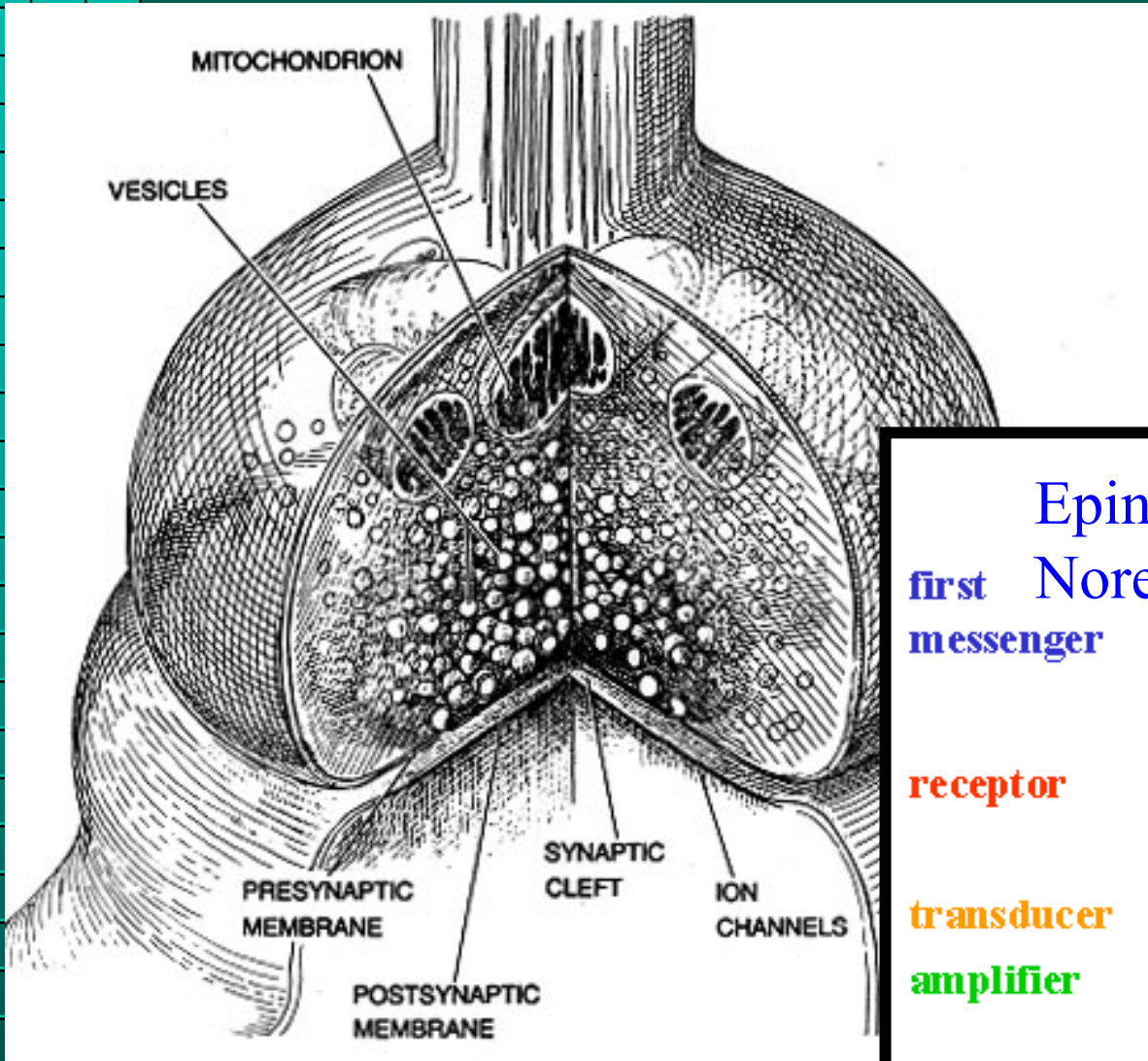


Monoamines

Tyr
Tyramine

DA
Dopamine

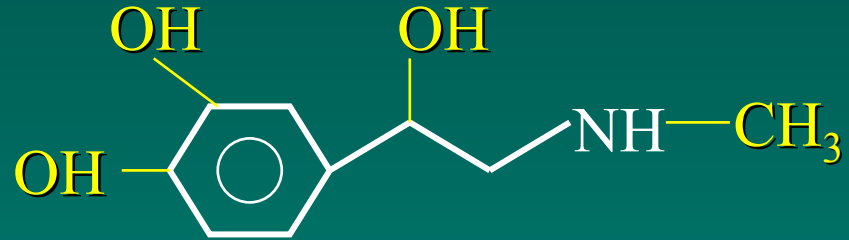
NE
Norepinephrine



Phenylethylamine Structures



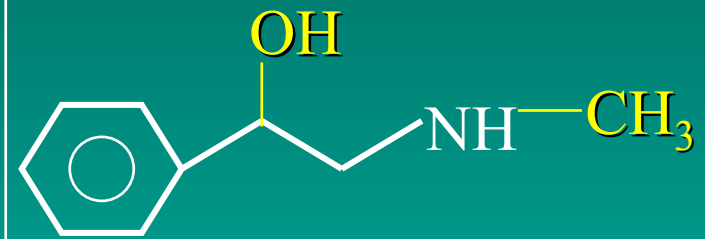
Phenylethylamine



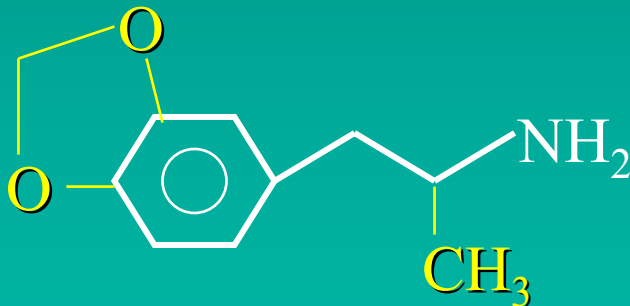
Epinephrine (Adrenaline)



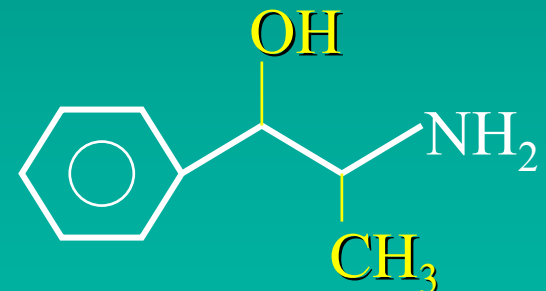
Amphetamine



Ephedrine



3,4-methylenedioxymethamphetamine
(MDMA) (Ecstasy)



Phenylpropanolamine

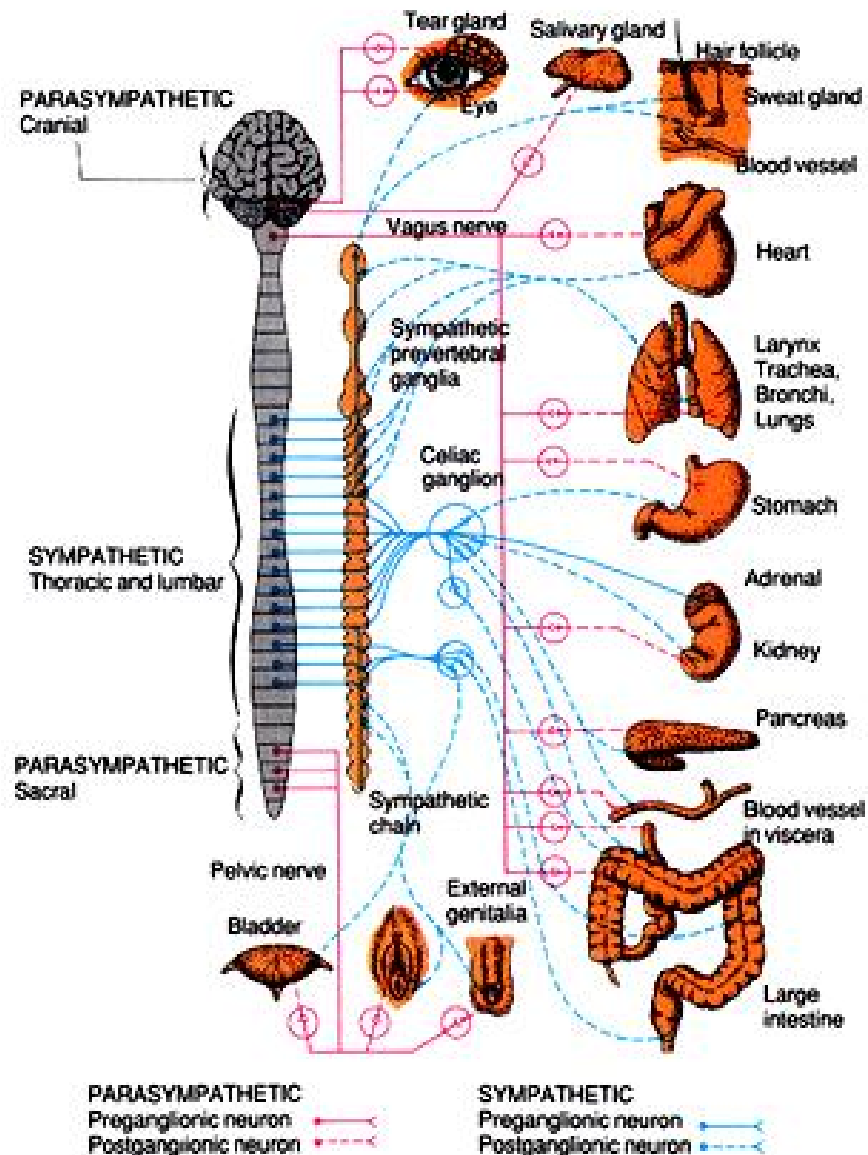
► The Autonomic Nervous System

Alpha

Vasoconstriction
 ↑ Urethral tone
 Mydriasis
 Diaphoresis

Beta

Vasodilation
 Intestinal Relaxation
 Uterus Relaxation
 Bronchodilation
 Glycogenolysis
 Tachycardia
 Heart Contractility
 Lipolysis



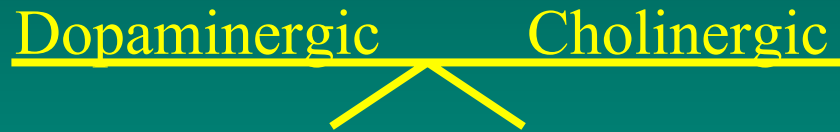
The Limbic System of the Brain

- Components:
 - Limbic lobes w/ Diencephalon, hemispheres
 - Ant. Nucleus of thalamus
 - Amygdaloid nucleus
 - Hypothalamus (Temperature Regulation)
- Effects:
 - Emotions (Fear, Excitement, Anger, etc)
 - Memory
 - Visceral brain (autonomic effects)

The Limbic System

Effects: Emotions (Fear, Excitement, Anger, etc) & Psychosis

Dopaminergic Cholinergic



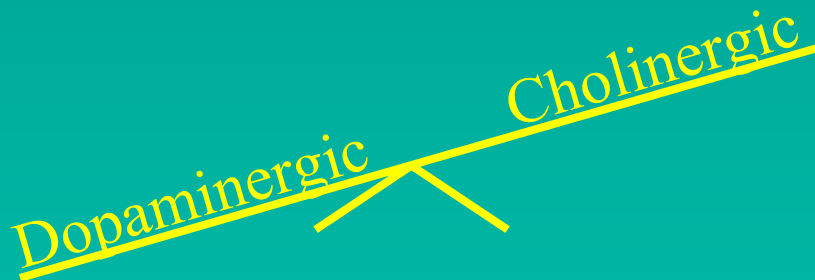
The desired balance...

Dopaminergic Cholinergic



Dopa (Monoamine) Excess...
...Psychosis...
...like Schizophrenia

Dopaminergic Cholinergic



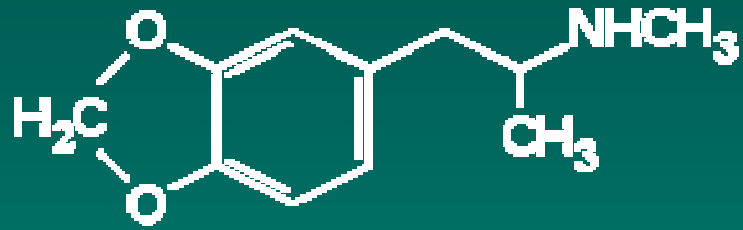
Dopamine much less
...Anti-Psychotic Med effect
...Parkinson's Syndrome

Cocaine

- Not a monoamine
- Pathophysiology
 - Uptake ↓ of monoamine neurotransmitters
→ ↑ Dopamine → Psychostimulant
 - Vasoconstrictor
 - CNS stimulation
 - Excitatory amino acids I.e. glutamate
- Clinical Effects
 - Sympathomimetic effects
 - Agitation (↑ Temperature)
 - Muscle damage (Rhabdomyolysis)

Amphetamines

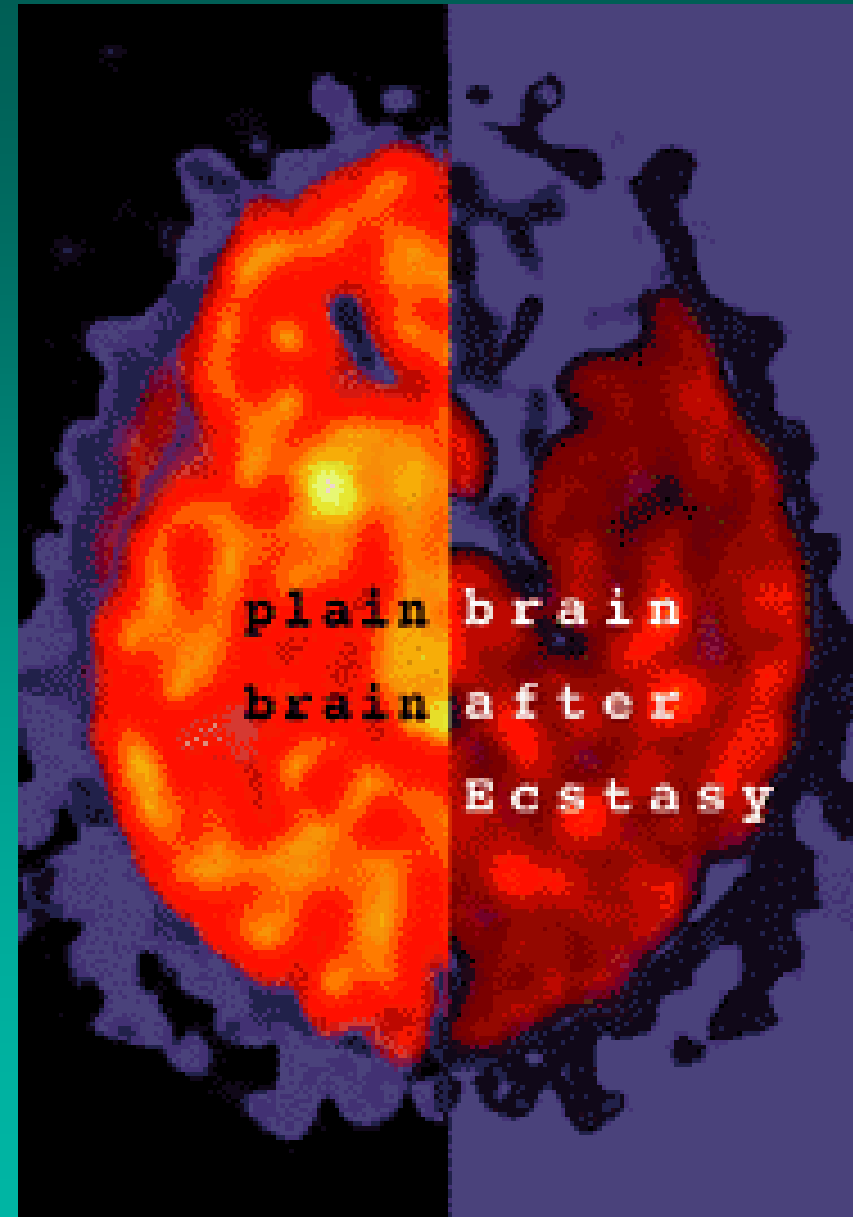
- Phenylethylamine derivatives
- Pathophysiology
 - Monamine Release ↑
 - Monoamine Reuptake ↓
 - Limbic effects prominent
- “Designer” Amphetamines big in 1980s
 - First done to avoid the law
 - MDMA / Adam / Ecstasy now a “rave” favorite
- Methamphetamine
 - Easy to make; Low cost
 - Most common illicit drug made in “labs” in the US
 - “Ice” is a high purity, crystalline form



MDMA (Ecstasy, Adam)



ICE (Pure Methamphetamine)



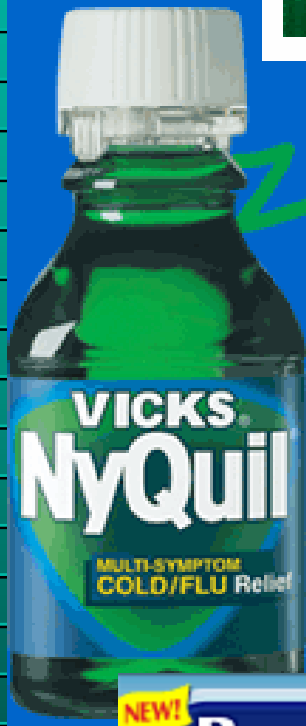
Dextromethorphan

- D-isomer of codeine analog
- Anti-tussive in many OTC cough medications
- No analgesic or CNS effects at therapeutic doses
- Other effects...
 - ↑ serotonin (a monoamine) release
 - Affects NMDA receptor at PCP site
(→ Hallucinations)
 - Sigma receptor → Psychotomimetic symptoms
(hallucinations, Delusions, Dysphoria, Depersonalization, Emotion lability)
- Toxicity: Hyperexcitable, lethargy, ataxia, seizures, diaphoresis, HTN, nystagmus, dystonia,

Cold Medicines

- “Decongestants”
 - Pseudoephedrine; phenylpropanolamine
 - Not commonly done
- Antihistamines “Allergy” meds
 - Older antihistamines are in the “combination” cough and cold medicines
 - Anticholinergic effects
 - Delerium
 - Dry skin (Can not sweat)

Cough and Cold Medications



Back to Case 2

- 17 y/o male
- Wide-eyed and agitated
- Confused, Hyper-religious
- Skin: Diaphoretic and warm
- HR 140 RR 30
 BP 220/120 Temp: 105°F
- Pupils: 6 mm (3-4 mm)
- Strength: Godzilla-like with all extremities

With all the different drug possibilities...

how do I know which one is the problem, and thus how to treat him?

Case 2 Diagnosis: Drug Screens

- Gas Chromatography / Mass Spectrometry
 - Detailed to the very specific drug
 - Expensive
 - Long time to do...
- Urine “Tox Screen”
 - Common
 - Relatively inexpensive
 - Tells if a drug “class” is present
 - Limited “sensitivity” and “specificity”
 - **Still takes an hour to do!!!**

Case 2 Treatment

It does not matter exactly which drug it is!!!

Treat...

- **Symptoms**

- Agitation
- Sympathetic
 - Fast Heart Rate
 - Hypertension

- **Complications**

- Hyperthermia
- Muscle breakdown → Renal Failure

Case 2 Treatment

- Hyperthermia
 - Stop new heat production (Agitation)
 - Cool him off...
 - Ice baths
 - Fans
 - Not acetaminophen or aspirin
 - Avoid medicines that affect body temperature regulation
- Muscle Breakdown
 - Aggressive IV fluids to keep urine output up

Case 2 Treatment

Benzodiazepines (i.e. Valium)

- Affects CNS (which → periphery)
- Mechanism: ↑ Gamma-aminobutyric acid
(the #1 CNS Inhibitory neurotransmitter)
- Decreases
 - Agitation
 - Heart Rate
 - Blood Pressure
- Aggressive use i.e. every five minutes until patient's agitation is stopped
- If overuse, can make patient stop breathing

Case 2 Closure

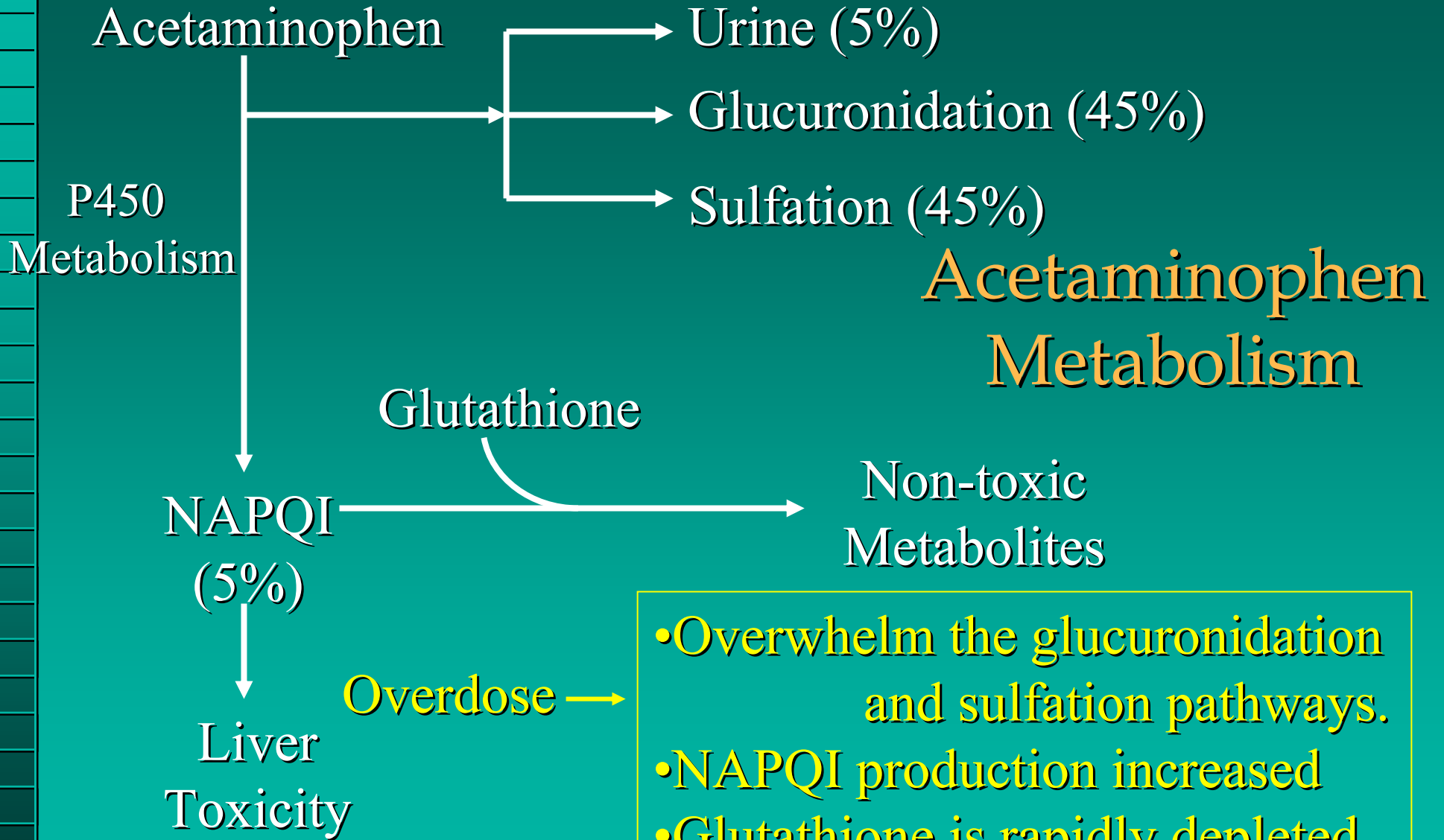
- Agitation resolved and temperature decreased
- Patient awoke and was normal
- The rest of the story...
 - Had been to a “little party”
 - Used Ecstasy
 - Promises he’ll never do it again
 - Grows up and becomes...?

Case 3

- 15 y/o girl brought in after overdosing on Tylenol. Took a bottle. Occurred 8 hours ago. She has no complaints.
- PMH: Nothing
- Medications: Nothing
- Physical Exam:
 - Awake and alert
 - Vital signs are normal
 - Abdomen is normal

Acetaminophen

- Most commonly used analgesic medicine
 - Effective
 - Safe when used properly
- Common overdose
 - Available
 - Danger of it are not well known
- More hospitalizations with it than any other agent
- Liver toxin in overdose
 - Liver failure
 - #1 cause of need for liver transplant
 - Death



Acetaminophen Metabolism

- Overwhelm the glucuronidation and sulfation pathways.
- NAPQI production increased
- Glutathione is rapidly depleted
- Liver toxicity occurs

Acetaminophen Treatment

- Get it out of the stomach
- Get it through the intestines so fast that little is absorbed
- Decrease the absorption into the body from the intestines
- Prevent the effects
- Heal the injury that already exist

Acetaminophen Treatment

- Get it out of the stomach
 - Syrup of Ipecac → Vomit
 - Gastric Emptying (Hose down into stomach)
 - But...these have not been shown to change clinical outcomes (deaths, hospital length of stay)
- Get it through the intestines fast; little is absorbed
 - Sorbitol; Magnesium Citrate
 - No change in clinical outcomes

Acetaminophen Treatment

- Decrease the absorption into the body (**Charcoal**)
 - Decreases absorption a statistically significant amount
 - But no change in clinical outcomes
 - It has its own complications (Risk / Benefit Ratio)
 - Aspiration
 - Turn a benign OD into a 3 week hospital stay
 - Could absorb an antidote
 - Our approach
 - Using much less than we used to
 - Educate other physicians as to our concerns

Acetaminophen Treatment

- Prevent the effects
- Heal the injury that already exist

An Antidote

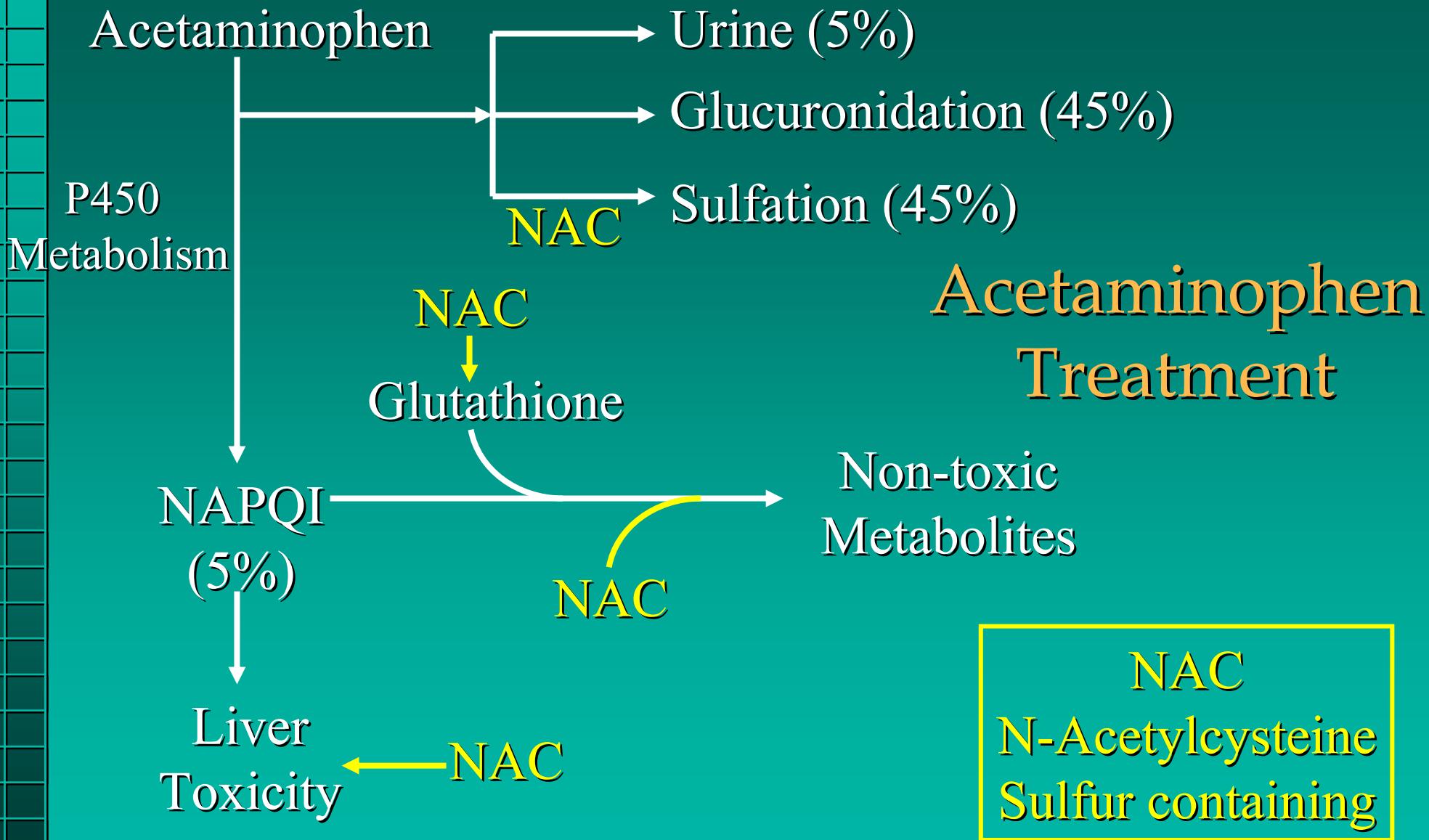
Antidotes

- Very few exist
- Most “poisonings” are treated with supportive care
- Some antidotes more dangerous than the “poison”
- Ideal Antidote
 - Safe
 - Effective
 - Inexpensive
 - Easy to use by the nurses
 - Easy to take by the patient

Acetaminophen Antidote

N-Acetylcysteine (NAC)

- Safe ✓
- Effective ✓
- Inexpensive ✓
- Easy to use by the nurses ✓
- Easy to take by the patient ±



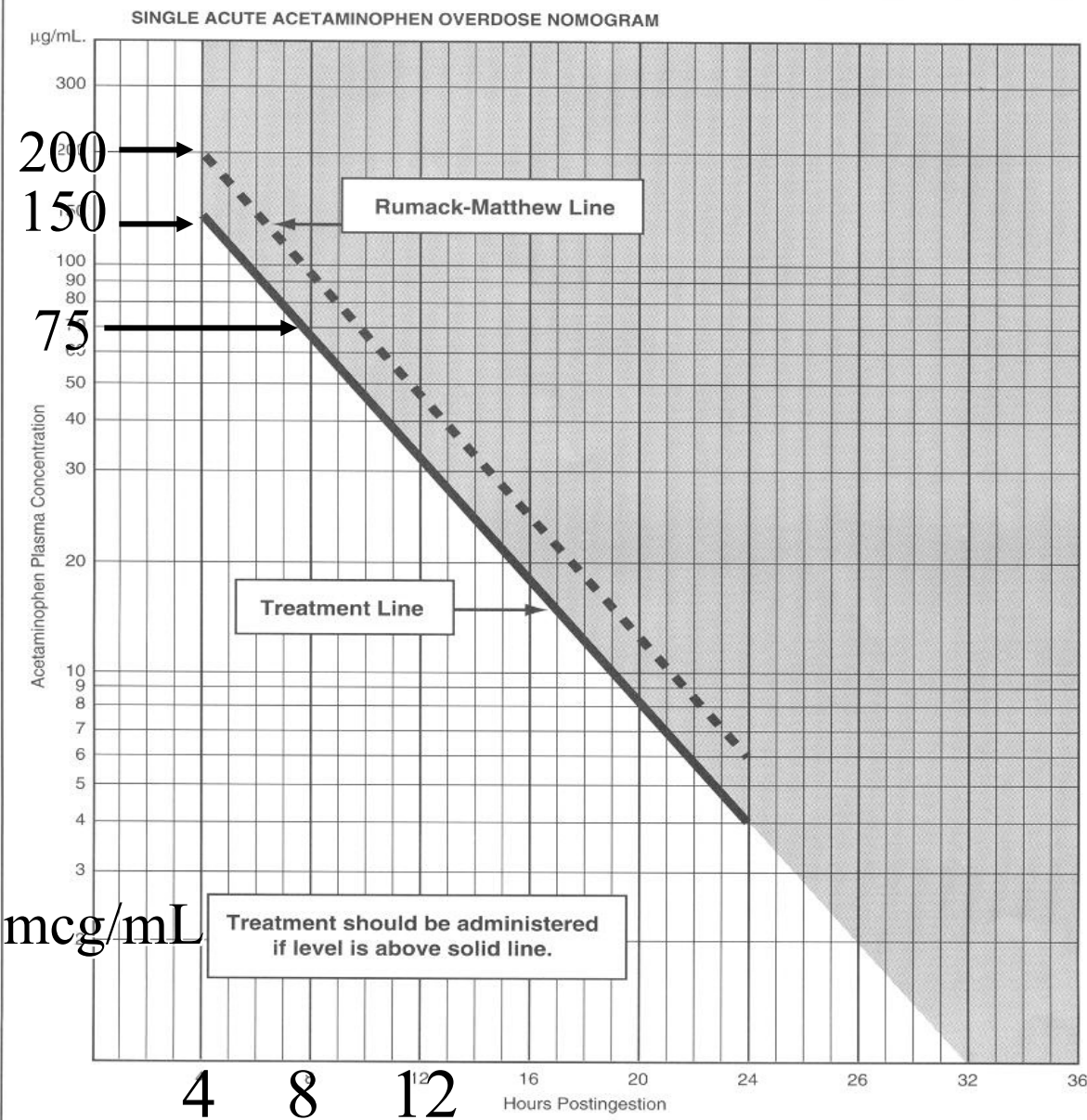
Does Every Acetaminophen Overdose Get NAC?

- No...Decision is based on...
 - Time of presentation
 - Acetaminophen Level in the blood
 - Single exposure of over a period of time (Chronic)

The Acetaminophen Nomogram

Single, acute overdose
 Original Work:
 200 was “toxic” at 4 hrs
 USA: Fudge Factor
 (150 is “toxic”)

Our patient’s 8 hour level
 175 mcg/mL



mcg/mL

Treatment should be administered if level is above solid line.

The nomogram has been constructed so that a plasma acetaminophen concentration of 200 µg/mL at 4 hours post-ingestion will result in a plasma acetaminophen concentration of 6 µg/mL at 24 hours post-ingestion. The shaded area represents the region where treatment should be administered. The Treatment Line is placed 25% below the Rumack-Matthew Line to allow for potential errors in plasma acetaminophen assays and estimated time from ingestion of an overdose.

Hours After Ingestion

CAUTIONS FOR USE OF

1. Time coordinates refer to hours post-ingestion.
2. Graph relates only to plasma acetaminophen concentration.
3. The Treatment Line is placed 25% below the Rumack-Matthew Line to allow for potential errors in plasma acetaminophen assays and estimated time from ingestion of an overdose.

Case 3

- Started NAC therapy while in the ER
- Checked Liver function tests
- Admit to hospital
- Psychiatric evaluation