Clinical Cases

- Goals and Objectives
 - Provide an overview of common syndromes
 - Acute v chronic
 - Dose makes a poison
 - Dose related v idiosyncratic
 - Immediate action needed
 - Limited antidotes
 - Consult the Poison Center (1-800-222-1222)



DPPT Case Series

We will present a series of clinical vignettes and problem solve with you.

If you recognize the case and know the diagnosis, please do not spoil it for the others!

Case #1

A 17 year old argues with her mother and locks herself in the bathroom. She admits to ingesting a full bottle of Tylenol.[®] Two hours later she develops vomiting and goes to the ED.

A Very Common Overdose

- 2005: AAPCC reports 2,424,180 exposures
- #1 Category: Analgesics 283,253
- About 80% are for Acetaminophen – (226,000 reported cases per year)

Treatment is Based on Metabolism



The Rumack-Mathew Nomogram



Treatment is Based on Metabolism



Prognostic Indicators King's College Criteria pH < 7.3or Grade 3 or 4 encephalopathy and Creatinine > 2.3and PT > 100 seconds



The Case

<u>Call to PCC</u>: 75 year old woman was admitted to the hospital with what was thought to be a stroke. She was placed on a ventilator and the ABGS revealed:

> pH=7.02 pO2=100 pCO2=9 HCO3 = < 5

Is this consistent with a stroke?

The Case

Prior to becoming sick she and her husband were at a garage sale and drank "Twister". He didn't like it and only had a "swig" she drank the entire bottle

Does this help in the differential?



Repeat ABGs: pH=6.53, pO2 161, pCO2 16 Lytes: Na=141 K=4.7 CI=109 Co2=7 (Gap) BUN=11 Cr=0.9 Serum osmolarity=338 (Gap)

Crystals in urine

Wide Anion-gap Metabolic Acidosis

- Aspirin
- Methanol
- Uremia
- Diabetes
- Paraldehyde/Phenformin
- Isoniazide/Idiopathic
- Ethylene glycol

The Case

EtOH therapy/fomepizole therapy instituted Dialysis performed

Ethylene glycol level 12 hrs after the original call and prior to the first dialysis= 233 mg/liter





Ethylene glycol 77 mg/dl Glycolic acid 860 mg/L



Case 3



33 yo Princeton Univ graduate student presents to ED at around midnight with symptoms of nausea, diarrhea.

What information do you want?

What labs would you request?

Anything else?

12 hrs prior to the onset of the symptoms she ate some mushroom soup with her parents, visitors to the US from china. Daughter: ate some of the soup

Mother: ate all of her soup but no sauteed mushrooms

Father: ate sauteed mushrooms, his soup and finished the daughter's soup On arrival into the ED, both the father and mother are still complaining of diarrhea and abdominal cramps.

Both have elevations in the liver function studies. The father appears worse than the others in both symptoms and laboratory analyses.

	Peak transaminase	Peak INR
Daughter	102	1.0
Mother	150	1.1
Father	9900	2.3

Mushroom Ingestion Toxidromes

- Group I Cyclopeptides:
- Group II Gyromytrin
- Group III Muscarinic Poisoning
- Group IV Coprine poisoning
- Group V Ibotenic Acid and Muscimol
- Group VI Psylocibin
- Group VII GI irritants
- Group VIII Cortinarius
- Group IX Smithiana

Amanita virosa



Amanita phalloides





Amatoxin/Phallotoxins/Virotoxins all cyclic peptides

- Amatoxin: RNA polymerase II: prevents DNA transcription
- Phallotoxin: interferes with actin polymerization and impairs cell membrane activity

Treatment questions:

Gastrointestinal decontamination

Penicillin

Cimetidine

NAC

Milk Thistle: Silybin/silymarin

Extra-corporeal removal

Anti-oxidant and free radical scavenger, more potent than vitamin e

Increase intracellular glutathione and superoxide desmutase

Inhibit prostaglandin and leukotriene production

Stimulate hepatocyte regeneration

stimulates protein synthesis

Membrane stabilization and inhibition of cyclic AMP phosphodiesterase



Would you bet your life?







GOURMAND TASTING MENU

Charlotte of asparagus with Maine crabmeat and leek vinaigrette Champagne, Laurent Perrier 'Brut', NV • Champagne Laurent Perrier "Brut Rosé", NV •• Halibut with white asparagus, cockles, periwinkles and watercress 2001 Domaine Phillipe Plantevin, Cote du Phone • 1993 Château de Fieuzal, Graves •• Butter braised Maine lobster with garden asparagus, morrels and Sancerre 1999 Candela Chardonnay, Central Coast California • 1999 Chardonnay, Miura Vineyards, Cameros •• Canadian foie gras with green papaya, sassafras, crayfish and Thai basil 1998 Riesling, Josmeyer, Alsace • 1999 Riesling Grand Cru "Geisberg", Kientzler •• Roasted squab with gyromitre mushrooms, cippolini onions and fava beans 2001 Saintsbury, Pinot Noir, Carneros • 2000 Gevrey-Chambertin I^e Cru La Petite-Chapelle, Jean Michel Guillian •• Tataki of beef with wild asparagus, mustard, pickled ramps and lotus root 2000 Cabernet Sauvignon, Lolonis, Napa Valley • 2000 Spelletich Cellars, Cabernet Sauvignon, Napa •• Valrhona Gianduja, hazelnut feuilletine, white chocolate and tart cherries 2002 Vignaioli di S. Stefano, Moscato d' Asti •/•• Chocolate souffle coulant with Maldon salt gelee and Chai tea ice cream Grahams "Six Grapes" Unfiltered Reserve 1993 Banyuls "Clos Chatart" ... MENU <u>WITHOUT</u> WINES \$ 110- PER PERSON WINE PACKAGE #1 • \$70- PER PERSON (Supp.)/WINE PACKAGE #2 • \$ 140- PER PERSON (Supp.)

ALA CARTE

APPETIZERS

Garbure of spring vegetables with herbs, smoked bacon and patranque	16-
Cannelloni of beef with Parma ham, micro lettuces and brioche	18
Artic char with mousserons, fava beans, Miner's lettuce, pinenuts and aged sherry	
Bluefin tuna tartare with radishes and micro greens	
Torchon of foie gras with Muscat grapes and black pepper gastrique	
Warm tart of Maine lobster with chanterelle mushrooms and saffron sauce	22

SALADS

Salad of organic baby lettuces and spring vegetables with black truffle *vinaigrette* 15-Smoked trout salad with watercress, *frisée*, apples, roasted beets and horseradish cream 16-

ENTRÉES

Black sea bass with sunchokes, peashoots, chanterelle mushrooms and Maine crabmeat	34
Day-boat halibut with English peas, morrel mushrooms, fingerlings and lobster	34
Roasted squab with gyromitre mushrooms, cippolini onions and fava beans	34
Roasted loin of yeal with artichokes, cippolini onions, fennel and ricotta gnocchi	36
Côte de bœuf with haricots verts, baby carrots, roasted shallots and aligot	38

June 14, 2003

65 Bergen Street

Telephone 908.534.4011 # Facsimile 908.534.6592

Box 284 Route 22 West Whitehouse New Jersey 08888

Steven M. Marcus, MD Executive Director New Jersey Poison Information & Education System

www.therylandinn.com

Newark, NJ 07107-3001 Dear Dr. Marcus,

Thank you for your letter of June 9th, 2003. I read the attachments and shared them with my staff. I have served gyromite mushrooms for over a decade at the Ryland Inn and used them when working in New York. Your letter raised the point of mushroom pickers and I have taken your comments seriously. I have instructed my sous chefs to discontinue the use of gyromite mushrooms. I would never want to endanger a customer and I have no control over the mushroom pickers.

Thank you for the "heads-up" and I look forward to your return visit to the Ryland Inn.

Respectfully yours, Craig C. Shelton Chef/Proprietor

There are old mushroom pickers,

There are bold mushroom pickers,

But, there are no old, bold, mushroom pickers!



Case #4

- 18 year-old woman is transported to the ED unconscious.
- Her family stated that their carbon monoxide detector at home had been going off for the past 3 days and they kept resetting it.
The most common inhaled poison

- U.S. averages about 500 deaths per year
- Contributes to annual 15,000 fire-related deaths
- Product of incomplete combustion of fossil fuels

Many Sources of CO

- Cookers/heaters
 - Gas, coal, wood, kerosene burning
- Automobile exhaust
- Engine powered tools, equipment
 - Gasoline, methane, propane
- Building fires



Clinical Effects

- Symptoms
 - Headache
 - Nausea
 - Dizziness
 - Confusion
 - Chest pain
 - Dyspnea
 - Weakness
 - Blurred vision
 - Disorientation

- Signs
 - Vomiting
 - Tachypnea
 - Tachycardia
 - Cognitive defects
 - Ataxia
 - Myocardial ischemia
 - Coma
 - Seizures
 - Hypotension

Pharmacokinetics

- Binds initially to HB with 200-250 times the affinity of oxygen
- Eventually 15% moves into tissue myoglobin
- Elimination:
 - Natural halflife: 5 hours
 - 100% oxygen: 50-80 minutes

CO Decreases Oxygen Unloading



Cardiovascular-Pathophysiology

- Myoglobin also binds CO with 60-times affinity of O₂
- Binding is enhanced with hypoxia
- Myocardial depression
- Displaced NO and vasodilation

Management

- Emergency Safety Net

 IV, Monitor, Fingerstick glucose
- Inotropes?
- Oxygen 1-3 ATA

Indications for HBO

- Definite
 - Loss of consciousness
 - Seizures
 - Coma
 - Altered mental status

- Relative
 - Persistent neurological symptoms after several hours oxygen
 - Pregnancy
 - Persistent cardiac ischemia
 - Increased CO levels

Case 5

- Cold October day
- First day of heating system
- Children went out for recess
- Children reported to nurse with blue lips, headache, some were vomiting

 There were no berries on bushes outside

There were no blue foods for lunch

The blue did not wash off

 Ten children were taken to one hospital

 Two of these children had blue lips and fingers

 Pulse oximetry showed O₂ saturation of 85%

 Children were started on oxygen therapy

 Laboratory values on the 2 sickest children revealed:

high pO₂, low pCO₂, normal pH

Dietary history:

All who became sick ate the soup, none of the non-soup eaters became sick, some of those who ate the soup stayed well

 All who became sick ate during the second lunch period

 Soup was a name brand product, heated out of the can









 High concentration of nitrites found in the left over soup

No Nitrites found in the unopened cans

 High concentration of nitrite found in the heating system







EM pathway



Hexose monophosphate shunt

Case #6

- A 50 year-old woman with a dental abscess presents to the ED with severe tinnitus.
- HR 108 bpm, BP 161/73 mmHg, RR 20 bpm, T 96.7°F

Salicylate Kinetics

- Pharmacokinetics
 - $pK_a of 3.5$
 - Peak serum levels in 30 minutes
 - Absorbed well in stomach and intestine

- Toxicokinetics
 - Above 30 mg/dL
 - Delayed absorption from pylorospasm, bezoar formation
 - Peak serum levels 4 –
 6 or more hours
 - At toxic levels, elimination routes are saturated

Toxicity

- Primary respiratory stimulant
- Tinnitus
- Gastrointestinal upset and pylorospasm
- Diaphoresis
- Mental status changes
- Acute Lung Injury
- Increased brain utilization of glucose
- Metabolic acidosis





Management

- Decontamination
- Blood work
 - -ABG
 - ASA level mg/dL
 - Electrolytes K⁺, BUN/Cr
- An appropriate cry for help?

Urinary Alkalinization

- Acidemia facilitates transfer of ASA into tissue
- Acetazolamide creates alkyluria AND metabolic acidosis – so not useful here
- NaBicarbonate increases urinary elimination 10-20 times
 - Target Urine pH 7.5-8.0
 - Serum pH not to exceed 7.55

Effects of Urinary Alkalinization

After Alkalinization



Temple AR. Acute and chronic effects of aspirin toxicity and their treatment. Arch Intern Med 1981;141:367

Case 7

Case 7

- 3 yo black male seen twice by his PMD for loss of appetite and occasional vomiting.
- He is taken to an ED for vomiting and a throat culture is taken which grows beta hemolytic streptococcus

What is significance of strep in 3 yo

- What is natural course
- Why do we treat
- What else could be going on?
- What would you like to know about the case?

Case 7

• 2 weeks later taken to ED actively seizing

What would you like to know now?

PICA Old house Low Hgb

Lead level 175 mcg/dl


Health Effects of Lead

- Blunted intellect
- School failure
- Societal pathologies
- Reduced earning potential

A Multifaceted Problem Requiring Multiple Strategies

- Nutrition
- Housing
- Education of the public
- Medical care

Chelation is NOT the treatment

Follow-up Incredibly Important!

- Eliminate source
- Diet
- "Rebound"

Decline in Lead levels Without Chelation



Roberts, James et al Journal of Toxicology -- Clinical Toxicology, 2001, vol. 39(2)153-160

Case 8

Case

2 ½ year old boy was shopping with his father in a hardware store. The father lost sight of the boy for less than 5 minutes and the boy returned with a plastic bottle saying it tasted yuk. The father felt the boy took very little. There was liquid on his shirt. They went to the doctor's office.

Case (continued)

On arrival at doctor's office he was asymptomatic and was given milk to drink, thinking the child may have tasted paint.

- He became irritable, then listless, had excessive drooling and couldn't hold his head up. He had no vomiting or diarrhea.
- An ambulance was called and while being taken to the ambulance he developed a seizure.

Someone went to the store and retrieved the bottle:





Chlorpyrifos 11.2%

Normal Nerve Function





neuro-transmitter=Acetylcholine

Normal Nerve Function



Acetyl choline

Normal Nerve Function Termination of Action



Acetylcholine esterase

Acetylcholine

How Carbamates/OP Insecticides Work



Acetyl choline esterase

Organo phosphate/Carbamate

Acetyl choline

Effects of OP/C Agents Muscarinic Sites

- DUMBELS
 - Diarrhea
 - Urination
 - Miosis
 - Bronchorrhea/Bronchospasm/Bradycardia
 - Emesis
 - Lacrimation
 - Salivation/Sweating

Effects of OP/Cs Nicotinic Sites

- Skeletal muscles
 - Fasciculations
 - Twitching
 - Weakness
 - Flaccid paralysis
- Other (ganglionic)
 - Tachycardia
 - Hypertension



OP/C Toxicity: Atropine

- Antagonizes muscarinic effects
- Dries secretions; relaxes smooth muscles
- Given IV, IM, ET
 - No effect on pupils
 - No effect on skeletal muscles
 - IV in hypoxic patient

OP/C Toxicity: Treatment Pralidoxime Chloride (2-PAM)

- Remove nerve agent from AChE in absence of aging
- 1 gram slowly (20-30) in IV infusion
 - Hypertension with rapid infusion
- No effects at muscarinic sites
- Helps at nicotinic sites



Case (continued)

He was treated with appropriate antidotes and did well.

Case #9

 A 1 month-old child presents with a history of constipation, poor feeding, and poor muscle tone. The mother has been medicating the child for colic with a tea of chamomile flowers and anise seeds.

Physical Examination

- Temp. 36.6 °C, P 147, R 34, O₂ sat. 99%, BP 126/73
- Increased Drooling
- "Droopy Eyelids"
- Difficulty latching onto breast
- Poor suckle

Differential Diagnosis

- Dehydration
- Failure to thrive
- Hypotonia of unknown etiology
- Sepsis
- Viral syndrome
- Other rarer sources of weakness

Other Rarer Sources

- Aminoglycoside poisoning
- Anticholinergic
- Buckthorn
- CO
- CVA
- Diphtheria
- Eaton-Lambert
- Elapid envenomation
- Encephalitis

- Food poisoing
- Guillain Barre
- Myelopathy
- Multiple sclerosis
- Myasthenia gravis
- Cholinergic poisoning
- Paralytic shellfish
- Poiliomyelitis
- Polymyositis
- Tick paralysis

Botulism

- Clostridium botulinum
 - Produces toxins type A through G
 - Type A (West of Mississippi river)
 - Type B (East of Mississippi river)
 - Type E (Pacific northwest)
 - Spore-forming bacteria
 - Ubiquitous spores are very resistant to damage
 - Spores produce toxin
 - Toxin is heat labile
 - Toxins ultimately prevent release of Acetylcholine



Types of Botulism

- Foodborne ingestion of toxin
- Infant intetstinal colonization
- Wound
- Adult infectious abnormal gut function
- Inadvertant

Testing

- Tensilon test
 - Myasthenia gravis
- Electromyography
 - Post-tetanic facilitation
- Laboratory
 - Mouse studies

Treatment

- Supportive care
- Gastrointestinal decontamination
- Botulinum antitoxin
 - Does not reverse effects
 - Type-specific vs. trivalent (A/B/E)

Case #10

 A 42 year-old male is transported to the ED in respiratory arrest. A rapid physical examination reveals pinpoint pupils.

Toxidromes

- Opioid
 - CNS depression, respiratory depression, miosis
- Sympathomimetic
 - Mydriasis, hypertension, tachycardia, diaphoresis, agitation
- Anticholinergic
 - Dry, hot, flushed, urine retention, decreased bowel sounds
- Cholinergic
 - SLUDGE
- Benzodiazepines po
 - Coma with normal vital signs

Poppy Fields



HEROIN





Smack, Brown sugar, Horse Mud, H, Skag, Junk Black Tar

Opioid Effects

- Analgesia
 - Mu brain/articular surfaces
 - Delta/Kappa spine
- Respiratory depression
 - Mediated via diminishing sensitivity of medullary receptors to hypercapnea and hypoxia
 - May manifest as either depression in respiratory rate or in tidal volume

Common Modes of Use for Heroin

- Insufflation
- Subcutaneous
- Intravenous

"Chasing the Dragon"



Who needs Naloxone?

- Identify patients by toxidrome, context
- Respiratory rate < 12 *Hoffman, Ann Emerg Med 1991
- Small doses to reverse toxicity (0.1-0.4mg)
 - Titrate to effect
 - Reinstitution of adequate ventilation
- Naloxone infusion

- 2/3 initial dose per hour, titrate to effect