OVERDOSES 4/3/2010

Acetominophen: Toxicity at > 7.5 gm. But toxicity occurs at < 4gm if malnutrition!

Serum peaks 4 hours after ingestion, or 8 hours for XR.

Obtain level at 4 hours or at 8 hours if extended release.

½ life = 3 hours, but is delayed with XR and liver toxicity.

5% is metabolized to a toxic benzoquinoneimine, which is conjugated by hepatic glutathione to non-toxic cysteine. OD saturates this mechanism.

NAPQI binds with hepatic macromolecules and produces oxidative injury and centrilobular necrosis.

Risk can be enhanced (via CP450 and others) by:

Chronic alcoholism: NADPQI is increased, which reduces the amount of glutathione. Acute alcoholism does not raise the risk. Malnutrition reduces the amount of glutathione.

Malnutrition

Certain drugs cause toxicity at lower acetominophen doses: INH, rifampin, carbamazepine, dilantin, phenobarbitol, TMP/SMX, zidovudine,

CM's:

< 24 hours: non-specific sx's of vomiting, malaise.

At 24 hours, AST can elevate.

At 36 hours, all patients who are going to develop hepatic toxicity will have elevated AST.

3 to 4 days: liver enzymes peak, jaundice, confusion, bleeding diathesis.

4 Days: Absent death, recovery begins.

Approach:

Acetominophen level 4 hours (8 hours if extended release) and at 24 hours post ingestion.

>200 mcg/ml at 4 hours or > 5 mcg/ml at 24 hours indicates toxicity. (Nomogram)

Management:

Charcoal in 1st 4 hours. N Acetyl cysteine (NAC) dose NOT need to be increased in presence of Charcoal.

NAC increases glutathione stores. NAC indications are:

Ingestion over the hepatooxicity nomogram.

>7.5 gm ingestion.

Unknown time of ingestion and > 10 mcg/ml acetominophen level.

Lab evidence of hepatotoxicity.

Patients with repeated ingestion, risk factors, and > 10 mcg/ml acetominophen level.

Administer NAC within 10 hours of ingestion; however, NAC may be effective up to 24 hours after ingestion.

Oral may be more effective than IV due to ability to achieve higher dose orally.

Factors for transplantation are hepatic encephalopathy, PT > 100, ph < 7.3, creatinine > 3.3

CAUSES OF INCREASED CREATININE WITHOUT LOSS OF GFR:

True increase in creatinine: ^ loss of muscle mass, cimetidine, TMP/SMX

Pseudo increase in creatinine (interferes with Jaffe reaction: cephalosporins, ketone bodies, methanol, isopropyl alcohol

ASA, Acute:
Initially respiratory alkalosis with K wasting (H+ is conserved) and v Kser followed by metabolic acidosis due to salicylate uncoupling mitochondrial oxidative phsphorylation.
Sx:
N, V, UGI bleed, tinnitus, hearing loss, diaphoresis, ^ T, coma.
Lab: ^ Anion Gap, but Normal osmolar Gap
Rx:
Saline (unless cerebral or pumlonary edema), IV dextrose, NaHCO3, Kcl.. Hemodialysis if pre-coma, pulmonary edema, or renal insufficiency.

ASA, Chronic.
Common in elderly
Sx's: Tinnitus, hearing loss, dementia, nausea, vomiting, dyspnea with normal lung exam, hyperthermia (due to resetting of temperature point)
Lab: acidosis, hypoglycemia, elevated ASA levels.
In chronic salicylate toxicity there can be a combined metabolic acidosis and respiratory alkalosis which leads to a normal pH !! The clues are an anion gap acidosis and a very low PCO2 … overcompensation for the metabolic acidosis. E.g: Na, K, Cl, HCO3 = 140, 3.9, 85, 16. Ph=7.40. PCO2 = 20. (The latter should be 30 if it were to be appropriately compensated.)
Unique features are fever, UGI bleeding, and hypokalemia.

Rx: As with acute posioning.

Tricyclic Antidepressants (amitriptyline, doxepin, imipramine; lesser anticholinergic effects from nortriptyline and desipramine)
pathogenesis: 1) reuptake blockade of norepi and serotonin, 2, anticholinergic effect, 3 quinidine like membrane stabilizing effect, and 4) alpha blockade.
^HR, QRS wide, Ventricular arrhythmias, hypotension, seizures, obtundation, acidosis, and fever.
Rx:
Intubate
Hyperventilate to counter the acidosis and produce a ph of 7.47.
NaHC03
Epinephrine.

Hypothermia causes:
Endocrine: hpothyroidism, DKA, Adrenal Insufficiency.
Hypothalamic disorders
Skin: Psoriasis, burns
Cervical spine injuries
Hepatic failure
Substance abuse: etoh, opioids, lithium, phenothiazines
Malnutrition
Sepsis

COMMON TOXIDROMES (NEJM 2006;355:606.)

agent	physical findings	antidote
cocaine-like	^ HR, excessive speech and motor activity, tremor	benzodiazepines
sedative-hypnotic(etoh)	sedation, confusion, delirium, hallucinations, coma, slurred speech, saliva	supportive
opiate (heroin)	miosis, unresponsiveness, v Respiratory rate, v Temperature	naloxone
anticholinergic (diphenhydramine)	Fever, ileus, flushing, ^ HR, urinary retention, dry skin, blurred vision, mydriasis, psychosis.	
cholinergic (sarin gas, organophosphate pesticide)	"Sludge": Salivation, lacrimation, urination, defecation, diarrhea, emesis and bronchorrhea.	Atropine, pralidoxime

LITHIUM POISONING

Sx's:
Change in MS
Tremor
^ reflexes
Rx: ^ volume, hemodialysis.

CO poisoning:

Sx: Winter time with indoor heating.
HA, "FLU", coma. Mild symptoms at 20% of carboxyhemoglobin, moderate sxs at 30%, severe sxs at 45%, Fatal at > 60%.
CO prevents binding of O2 to Hgb because CO binds 240 x more tightly to Hgb than O2, it shifts Hgb dissociation to left which retards release of O2 into tissues, and interferes with the mitochondrial respiratory chain.
Rx: 100% O2, hyperbaric O2.
The ½ life of carboxyhemoglobin is 4 hours without Rx, 1 hour with 100% O2, and 20 minutes with hyperbaric O2.

BETA BLOCKERS & CALCIUM CHANNEL BLOCKERS

Sx: Bradycardia, Heart block, hypotension, pulmonary edema, drowsiness & seizures, hypoglycemia.
EKG: Heart block
Ddx= hypothyroidism
RX: Airway, Normal Saline, Glucagon, for Calcium Channel Blockers give calcium IV.
Epi if needed.

DIGOXIN TOXICITY

Sx's: Nausea, malaise, weakness.
Lab: **Hyperkalemia** if there is acute poisoning; otherwise normokalemic (Dig blocks the sodium-K pump and depletes K intracellularly.)

3 classic dig arrhythmias:

*PAT with block
*Junctional tachycardia
*Bidirectional V tach.

RX:
If ^ K, give $NaHCO_3$, insulin & glucose.
Give Immune Fab fragments (dig Abs)
Magnesium for V tach.
Avoid calcium.

SEROTININ, NEUROLEPTIC MALIGNANT SYNDROME, ANTI-CHOLINERGIC CRISIS, MALIGNANT HYPERTHERMIA, COCAINE

Name	Drugs	latency	Vital	pupils	mucosa	bowel snds	neuro-muscular tone	reflexes	mental status	RX
Serotonin syndrome	SSRI OD. SSRI+MAOI SSRI+Tricyc Also lithium, amphetamines, cocaine, and l dopa	<12hrs	^BP, HR, R, >41.1c	Mydr-iasis	sialo-rrhea	^^	Increased	^^ clonus	agitation coma	Cooling Benzos cypro-heptadine
Anti-cholinergic syndrome	Scopalamine (1) ipratropium diphenydramine	<12 hrs	^BP, HR, R, 38.8c	Mydr-iasis	dry	V or absent	Normal	Normal	agitated delirium	
Neuroleptic malignant syndrome (2)	chlropramine (thorazine) prochlorperazine (compazine)	1-3 days	^BP, HR, R, >41.1c	Normal	sialo-rrhea	normal or V	Lead pipe rigidity	brady-reflexia	stupor alert mutism coma	Cooling Bromocriptin e, Dantrolene
Malignant hyperthermia	general anesthesia	½ hr to 24 hrs post anesthesia	^BP, HR, R, up to 46c	Normal	normal	V	rigor mortis like	hypo-reflexia	agitation	Dantrolene cooling hydration
Cocaine Abuse (3)	Cocaine Amphetamines Ecstasy	Minutes		Mydr-iasis	dry	V	^	^ or nl	agitation	Benzo's Labetolol (or phentolamine + propanol) ASA.
Thyroid storm	radio-iodine Rx acute illness surgery		T to 105 arrhythmias ^ Respirations			Diarrhea Emesis	tremor		Delerium seizures coma	PTU(hi dose) KI Steroids Propanolol

1. Several anti-cholinergics are used for urge incontinence; these are: oxybutynin, dicyclomine, imipramine, flavoxate, tolterodine. Tricyclics are used for depression.
2. Patients with Parkinson's disease can develop neuroleptic malignant syndrome if their medication is withdrawn, e.g., due to vomiting. In NMS and Parkinson's disease not the lack of mydriasis and the presence of brady-reflexia rather than, as in serotonin syndrome, the presence of mydriasis, hyper-reflexia and clonus.
3. Also occuring are: CVA, CV ischemia, renal ischemia, rhabdomyolysis; Pathogenesis of vascular ischemia and infarction: a) vasospasm and b) platelet activation, aggregation, and thromboxane activation. EKG: J point elevation.
For a review see NEJM 2005;352: 1118.

OPIATES, METHADONE
Sx: Narcosis, miosis, etc.
Lab: Because synthetic opiates are extremely potent, small quantities are potent and toxicology screens can be NEGATIVE.
Rx: Naloxone, repeatedly if methadone.

GAMMA-HYDROXYBUTYRATE AND GAMMA-BUTYROLACTONE.
Sx'S: Used in date rape.
Coma, bradycardia.
Lab: Toxicology screen NEGATIVE..
Rx: Supportive.

HYPERKALEMIA
Symptoms & Signs: Weakness; peaked T waves on EKG.
RX of hyperkalemia
If very severe and life threatening:
*10% Calcium gluconate, 10 cc, infused over 3 minutes with cardiac monitoring and repeat in five minutes. This is the fastest approach to correction.
THIS IS RELATIVELY CONTRAINDICATED IN PRESENCE OF DIGOXIN OR DIGOXIN-INDUCED HYPERKALEMIA.

*10 units of rapid acting insulin with 50 cc of 50% glucose (or 50 cc of 50% glucose alone without the insulin) following by a glucose infusion to prevent hypoglycemia. Begins in 15 minutes, peaks in 60 minutes and lasts several hours.

*45 meq of NaHCO3 infused over 5 minutes. Acts in ½ hour, lasts several hours.

*Beta agonist: Albuterol 0.5 mg i.v.. Peaks within 30 minutes. (??? Might be contraindicated if ventricle is irritable.)

ANALGESIA (Q93, MKSAP 12)
*Conversion of PO morphine to IV morphine is at a ratio of 3:1.
*PCA is 1/3 to one times the hourly rate, given Q 10 to 15 minutes.
For example:
Patient is receiving 240 mg PO QD. So I.V. maintenance does is about 80 mg or 3mg/hour.
The PCA is then between: minimally 1 mg with a 15 minute lockout or maximally 3 mg with a 10 minute lockout .

I.V. NSAID is ketorolac (Toradol), given 15 - 30 mg Q 6h R. PO 10 mg Q6HR (max) Limit to 5 days.

Symptoms	Agent	Response
(1) Skin lesions (intense itching then vesicular then eschar & non-pitting edema) OR Flu followed by Pneumonia with shock and **wide mediastinum** (in 1/2)& **pl. effusion(2/3)**	Anthrax. Sporulating, Gram+Rod. Box cars. PCR. (Wool Sorters Disease... exposure to yarn and animal hide processing.)	Use bleach. No p-p transmission Rx"crave" cipro+rifampin+vancomycin Post exposure Cipro or Doxy x 60ds. (Ann Int Med 2006;144:270)
(1) (2) Bubonic: Fever, painful nodes. Septicemic: Fever, no nodes. Pneumonia: Severe & **hemoptysis**. & pleural effusion.	Plague. Y. Pestis.Gm-Rod. Fleas Transmission in So West via cats, rabbits, squirrel. Ag test 100%S&S.	Droplet precautions; contact for buboes Streptomycin, Doxycycline OR TMP/SMX
(1) Tick-borne: Ulceroglandular Glandular Typhoidal (i.e., sepsis) Flu & pharyngitis then **pleuropneumonitis**. And hilar adenopathy.	Tularemia. Grm - Cocco baccilus Dx: via serology So West: Rabbit Hunting. Ticks in landscaping.	Streptomycin. No person to person trasmission. (Tetracycline is less effective)
Cough, dyspnea, nausea, myalgias, then pulmonary edema. (Looks like pneumonia.)	Ricin, inhaled. Ddx: bacterial pneumonia.	None
Dyspnea, SOB, ARDS. Skin burns. Latency 2-48 hrs. Necrosis of resp. mucosa. Bone marrow suppression occurs 7-21 days post exposure.	Mustard Gas, chlorine, phosgene	Leave area, decontaminate.
(1) *Descending flacid paralysis, pupillary dilation, palsies of Cr N 3,4 & 6, ptosis, diploplia, dysarthria, dysphonia, dysphagia. (3) *respiratory failure *Urinary retention & constipation *Latency: 12-36 hours (up to 1 week)	Clostridium botulinum, anaerobic gram + rod, Foodborne, or bio-aerosol. Mouse Bioassay. Ddx: Guillain Barre (acute inflammatory demyelinating poly N), which causes ascending paralysis.	Anti-toxin. Enemas or cathartics if no ileus. Supportive.
Cholinergic crisis: DUMBBBEL: Defecation, Urination, miosis, bronchorrehea, bradycardia, bronchospasm, emesis, lcrmtn. Nicotinic block: Convulsions, apnea, flaccid paralysis. Skin contact gives localized sweating and nausea. (4)	Sarin & VX, vapor or skin contact. Acteyl cholinesterase inhibitors leading to excess acetyl choline and cholinergic crisis.	IV Atropine (the muscarinic problem.) IV Pralidoxime (for the nicotinic diaphragm weakness) Treat surfaces with bleach and water. Benzodiazepines for Seizures.
*Bitter almond odor; *Metabolic acidosis *ENT irritation. *Increased HR, Decreased BP, *Bradycardia, coma, respiratory failure. *Neurologic symptoms	Cyanide. Prevents intracellular O2 use by blocking electron transport in mitochondria.	IV sodium nitrite, followed by sodium thiosulfate.
*Bleeding, liver & kidney failure (localized tissue necrosis if injected).	Ricin, ingested or injected. ? Water supply.	None
(1) (2) Incubation period 7-10 days, flu like symptoms, then diarrhea, vomiting, abdominal pain, diarrhea, cough, and chest pain. Maculopapular rash with purpura on day 6. Leukopenia and thrombocytopenia.	Viral hemorrhagic fevers: Ebola and Marburg. Diagnosis: ELISA and PCR.	Aerosol, fluid, and fomite precautions. Supportive
(1)(2). LP 7-10 days. **Cold then** rash, then pustules of face, arms, palms & soles. **Crops simultaneous** in any 1 area. Scabs in 12 days vs chicken pox in 5 days.	Small Pox. DNA pox virus Serology positive 8 days post inf'n.	Aerosol precautions Vaccine if <3 days post exposure.
Hrs to ds post exposure: N,V,D. Latent phase 2-6 weeks. if 1 Gy, sx's mild; if 1-4 Gy: bone marrow x 3 weeks. 4-8Gy: GI sx's, diarrhea, hemorrhage & sepsis. > 9Gy: death.	Radiation. Gamma and X-rays.	Wipe test to determine internal and external contamination. Remove clothing & decontaminate. Health care workers not at risk from clothing..

(1) Category A Bioterror Agent: 2 viral and 4 bacterial (2) Person to person aerosol or droplet transmission. Aerosol prophylaxis involves N95 respirators and negative pressure rooms. Droplet precautions use standard masks. (3) Ocular complaints may be minimal or the sole manifestation of Botulism. Black tar heroin. (4) Following the cholinergic crisis there can be a) the "Intermediate Syndrome" in 25% with a latency of 1-4 days, characterized by weakness of proximal limbs, neck flexors, cranial nerves and respiratory muscles, and b) Delayed Neurotoxicity (e.g., with malathion) with a latency of 1-3 weeks, characterized by painful symmetric polyneuropathy and an ascending symmetric motor weakness (Like GBS!)

Effects of specific drugs on specific adrenergic receptors. January 31, 2004

Drug	Effect	ADRENERGIC RECEPTOR Alhpa1: vaso-const; heart: inc duration of contr'n.(2)	Beta-1: Increase Inotropy & chronotropy	Beta-2. Vascular walls cause vasodilation.	Other	Adverse effects
Phenylephrine (neosynephrine)	^ BP *	YYY				
Norepinephrine (levophed)	^ BP ^ HR	YYY	YYY			
Fenoldopam (Corlopam)	v BP				post-synaptic (D1) dopamine agonist(3)	tachycardia
Dopamine, 5 - 15 mcg/kg/min (Intropin)	^ CO some vasodil some vasocons	Y	YYY		YY	
Dopamine, 15+ mcg/kg/min	^ BP	YY				
Dobutamine (Dobutrex)	^ CO Slight v BP		YYY	YYY		
nitroprusside (nipride)	vasodilates venous & arterial					cyanide formed; look for neuro changes and metabolic acidosis.
Nitroglycerin	v BP					
Isoproteronel	^ HR v BP		YY	Y		
Epinephrine <1 mcg/min	^ CO	Y	YYY	Y		
Epinephrine > 1 mcg/min	^ CO ^ BP	YYY	YYY			
nessiritide (natrecor)	venous & art vasodilation; diuresis, naturesis.				Inhibits r-a-a system,	
milrinone (primarcor)	vasodilates venous & arterial sm muscle; ^ cardiac cntrlty				phosphodiesterase inhibitor. Decreased C Amp degradation.	ventricular arrhythmias; renal excretion
vasopression	volume retains.				inc CAMP; v urine vol.	
fenoldipam						

(1) Dopamnie at 5-15 mcg/kg/min does not enhance renal perfusion.

(2) This is associated with a reflexive decrease in heart rate and cardiac output.

(3) Fenoldopam: renal artery vasodilation, natriuresis, diuresis. It is 6 times more potent than dopamine in promoting renovasodilation. It reduces acute kidney injury and death in critical illness. For all cause mortality NNT=17. (ACP Journal Club 2007;146(3):58.)

OTHER AGENTS USED IN CRITICAL CARE:
Lorazepam (ATIVAN): ANA, Glaucoma, CNS depression, CV collapse, respiratory depression, sedation, ataxia.
PROPOFOL.
METOPROLOL
LOPRESSOR
LACTOBACILLUS (ACIDOFILUS): Creates an environment unfavorable to pathogenic bowel flora by creating an acid environment; helps re-establish normal GI flora.
Clonazepam (KLONOPIN):
CLONIDINE
ARGATROBAN: Thrombin inhibitor; cleared by liver. Used in HIT. Monitor the PTT.
NEUPROGEN (Filgastrin): Colony stimulating factor. Causes fever, rash, splenomegaly, bone pain in the posterior iliac crest, sternum, epistaxis in 10% and MI in 3%. Monitor CBC 2x/week.

From Harrison's Accessmedicine:
Systemic Inflammatory Response Syndrome requires
RR > 24,
HR > 90,
Temp > 38 or below 36,
WBC > 12K or < 4K.
Severe sepsis: 1 or more organ systems is malfunctioning distant from the site of infection.
Septic shock: BP < 90 or drop from patient's normal BPs of > 40.

Use thrombolytic therapy in PE when the patient is not hemodynamically stable.

Some Criteria for extubation:

RR/Tidal Volume (liters) [e.g., 30/.25 = 120] < 105.
Inspiratory pressure > -30 cm H2O
VC > 10 ml/kg
PH 7.35 – 7.40
Minute ventilation < 20 L/min
PO2 > 60, O2 Sat > 90%.
Peep < 5 CM H20
FiO2 < 0.5.
On breathing trial, an increase in heart rate of no more than 20/min or BPs no more than 20 mmHg

Ventilator response to hypotension in intubated patient:

Decrease Peep
Decrease TV
Increase the inspiratory flow rate to decrease the ratio of inspiratory time/expiratory time.
Change from AC to IMV.
Decrease the respiratory rate.

Relative adrenal insufficiency
>This occurs in the critically ill patient population, **even in the absence of other risk factors or causes such as prior use of prednisone**.
>Treatment with hydrocortisone and fludrocortisone lowers mortality.
>Assess adrenal function in critically ill patients with 250g cosyntropin and replete with hydrocortisone and fludrocortisone in patients whose serum cortisol levels rise 9g/dL or less.

Falling albumin levels in the elderly lead to increased free (active) levels of some medications, including warfarin.

Prealbumin and retinol-binding protein complex have the same half-life of 2 days.
Fibronectin has the shortest half-life: 1 day.

Vitamin A intoxication: A 74-year-old female is brought to your office by her son for evaluation of weight loss and alopecia. The female reports that she has been taking ultrahigh doses of nutritional supplements to prevent cancer for the last 9 months. She has noted that her skin has become dryer and that she frequently gets sores at the corners of the mouth. Over the last month the patient has begun to lose her hair and has diffuse bone pains. The physical examination is notable for red, scaly lips and a red, friable tongue. The patient's joints have

no inflammation, effusion, or synovitis. The long bones are diffusely tender to touch. Her skin is dry, but there are no rashes, petechiae, or echymoses

These patients often have a flulike syndrome before the development of the erythema. Most cases of TEN are caused by drugs started 1 to 3 weeks before the presentation. The most common among these drugs are phenytoin, barbiturates, sulfonamides, penicillins, and nonsteroidal anti-inflammatory drugs.

Disulfuram, an aldehyde dehydrogenase (ALDH) inhibitor, produces an unpleasant reaction to alcohol as a result of rapidly rising levels of acetaldehyde. This drug has many side effects and should be used with caution in patients with heart disease, hypertension, stroke, and diabetes mellitus. Furthermore, it has not been consistently shown to be superior to placebo in clinical trials.

The opioid antagonist naltrexone has been used in this population, and several small studies have suggested a decreased probability of relapse and shortened periods of relapse. Larger trials have questioned this finding, and definitive data are lacking.

Acamprosate has been tested in Europe and has been found to have efficacy similar to that of naltrexone.

Fudala et al, Buprenorphine/Neloxone Collaborative Study Group, N Engl J Med 349:949 958, 2003. Oral or sublingual buprenorphine maintenance therapy has recently been proposed as a new office-based therapy for opiate dependence. Buprenorphine is a drug with mixed properties, acting as an agonist at the receptor and an antagonist at the receptor. It is usually administered at a dose of 8 to 32 mg daily for 3 to 7 days a week. The advantages of buprenorphine over other maintenance options include a low potential for overdose, easier detoxification, and a ceiling threshold that limits its ability to cause a feeling of euphoria. In a recent placebo-controlled trial, buprenorphine with or without naloxone was shown to lead to a significant decrease in the proportion of urine samples positive for opiates and a decrease in opiate cravings. In contrast to methadone, buprenorphine is the first drug approved for the office- based treatment of opiate addiction. Primary care physicians in the community can prescribe buprenorphine if they are designated as addiction specialists by completing training programs through the American Society for Addiction Medicine, the American Psychiatric Association, and the American Osteopathic Association, among others

Heroin has a shorter half-life compared with other narcotics, and symptoms of withdrawal appear within 8 to 16 h of the last dose. The symptoms are in general opposite to those of opiate intoxication and include nausea, diarrhea, sweating, piloerection, mydriasis, and muscle fasciculations. In addition, mild elevations in heart rate, temperature, respiratory rate, and blood pressure may be seen. Symptoms peak within 36 to 72 h and persist for up to 5 days. Mood disturbance and changes in pain threshold and sleep pattern may persist for up to 6 months.

Pregnancy complicated by hypertension is associated with intrauterine growth restriction, increased perinatal mortality, and an increased risk of preeclampsia and placental abruption. It is important to note that certain blood pressure medications are contraindicated by pregnancy, notably, the angiotensin-converting enzme (ACE) inhibitors and angiotensin receptor blockers, which increase the risk of oligohydramnios and have adverse effects on fetal renal function. Most practitioners use methyldopa and labetalol during pregnancy. Baseline renal function should be measured so that abnormal function noted later in pregnancy will be appropriately interpreted. Pregnancies in females with a creatinine less than 1.5 mg/dL are associated with a favorable prognosis.

The lesion shown is hairy leukoplakia. These lesions usually arise on the lateral tongue and rarely involve other sites of the oral mucosa. They appear as white areas ranging from small and flat to extensive accentuation of the vertical folds. The lesions are due to Epstein-Barr virus infection and respond to high-dose acyclovir, but they may recur. Patients with HIV infection or risk factors are at increased risk. Painful lesions should raise the suspicion of candidal secondary infection. Other white lesions (Table 28-3, Harrison's) in the mouth include smoker's leukoplakia, erythroplakia (squamous cell carcinoma), candidal infection, and warts.

Alopecia:
>Non-Scarring: hair follicles not damaged but hair shafts missing. Reversible.

Causes: telogen effluvium, androgenetic alopecia, alopecia areata, tinea capitis, and traumatic alopecia (see 1. Table 48-5 in Harrison's). Many drugs may cause nonscarring alopecia, included those listed in the question plus heparin, propylthiouracil, vitamin A, colchicines, and amphetamines.
>Scarring: the damage to the follicle results in a smooth scalp with a decreased number of follicular openings. Microscopically, there is fibrosis and inflammation.

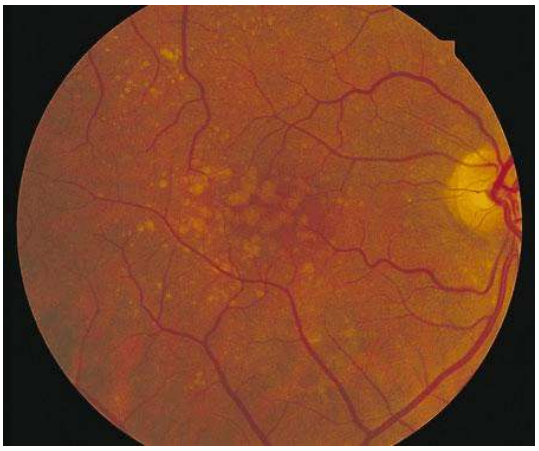
Causes: lichen planus, cutaneous lupus, and linear scleroderma. Antimitotic agents such as daunorubicin

International Perinatal HIV Group, N Engl J Med 325:1371, 2003. Recent studies have shown that zidovudine treatment of both the mother during the prenatal and intrapartum periods and the neonate at birth can reduce the risk of vertical transmission to 7.3%. When such therapy is combined with elective cesarean section, the risk of vertical transmission drops to 2%. The benefit of multiple drug therapy has not been established. Risk factors for the transmission of HIV infection in the perinatal period include vaginal delivery, preterm delivery, trauma to the fetal skin, and maternal bleeding.

These are drusen which eventually coalesce.

Patients with cancer cachexia probably get no net benefit from nutritional support except for those about to undergo cancer surgery who have severe protein-calorie malnutrition.

The classic presentation for methemoglobinemia is dyspnea, headache, gray-brown discoloration of the skin and mucous membranes, and abnormal oxygen saturation.



Certain medications, including isoniazid used for tuberculosis, L-dopa used for Parkinson's disease, and penicillamine used for scleroderma, promote vitamin B6 (pyridoxine) deficiency by reacting with a carbonyl group on 5-pyridoxal phosphate, which is a cofactor for a host of enzymes involved in amino acid metabolism. Foods that contain vitamin B6 include legumes, nuts, wheat bran, and meat. Vitamin B6 deficiency produces seborrheic dermatitis, glossitis, stomatitis, and cheliosis (also seen in other vitamin B deficiencies). A microcytic, hypochromic anemia may result from the fact that the first enzyme in heme synthesis (aminolevulonic synthetase) requires pyridoxal phosphate as a cofactor. However, vitamin B6 is also necessary for the conversion of homocysteine to cystathionine. Consequently, a deficiency of this vitamin could produce an increased risk of cardiovascular disease caused by the resultant hyperhomocystinemia.

Metabolic causes of coma:

Pancreas V or ^ glucose
Kidneys: ^ B/C
Liver ^ NH4+
Lung: hypoxemia.
Carbon monoxide poisoning
Thyroid Thyroid storm or myxedema coma
Lytes: ^ or V Na and change in Na.
Drugs:-- recreational alcohol, opioids
Drugs med analgesics, opioids, anxiolytics, barbiturates
Thiamine deficiency

Timing of alcohol withdrawal:
6 hrs to 1.5 days: tremulous, anxious, GI upset, diaphoresis, palpitations
6 hrs to 2 days: seizures rarely status
12 hrs to 2 days: hallucinosis
2 days to 4 days: DTs: delirium, tremor, agitation, fever to 104, tachycardia
Rule of 5's: 5% of alcoholics in withdrawal get DTs, and 5% of DTs die. (Previously, 30% fatality)

Blood alcohol levels: 100 mg/dL = 0.1 Gm/dL = 0.1Gm/100ml = 0.1%

<30 mg/dL	<0.03%	mild sedation((0.02+ for under age 21 is illegal in CT)
30 - 50	0.03 - 0.05	euphoria, decreased inhibition
60-100	0.06 - 0.10	Decreased memory, reaction time and coordination
80+	0.08% +	illegal when driving
200 - 300	0.2 - 0.3	Disorientation & ataxia
400 - 500	0.4 - 0.5	Stupor, incontinence, inability to stand
500+	0.5+	Coma & death

Case
40 y.o. alcoholic. H/O vomiting. Chest pain. Or, on NSAIDs. Or, HIV patient with CMV esophagitis
CXR: Pneumomediastinum. Suggestion of free peritoneal air.
Treated with observation and to r/o MI and pancreatitis.
Preliminary diagnosis was Pneumomediastinum.
Patient failed to improve.

Shock due to sepsis and multiorgan failure >> Death.
Ddx: Rupture of esophagus
Definitive studies:
CT of chest: peri-esophogeal air and fluid.
Gastrograffin with water soluble contrast esophogram.
Distal esophageal rupture has high mortality, and is more common.
Cervical rupture can be treated medically.
If negative, do a barium study which is more sensitive.
Rx: Surgery

Diabetes management in hospital:
Type 1 DM:
TDDI 0.5 u/kg

Type 2 DM
On oral agents: TDDI = 0.3 U/kg
Known insulin TDDI, for in hospital use 20% of TDDI.

Correcting the glucose:
Calculating how much blood sugar will decrease for each unit of rapid acting insulin:
For aspart or lispro: Rule of 1800: 1800/TDDI.
So for a TDDI = 60 units, each unit will decrease glucose by 1800/60 = 30 mg/dL.
For regular insulin: Rule of 1500. 1500/60 units = 25 mg/dL.

It is best to use an insulin drip when the patient is not eating.
Determine yesterday's total insulin dose administered and review yesterday's glycemic control:
For some glucose < 90, use 80% of yesterday's total.
For 90 - 179, use 100%.
For $\geq$ 180 and no glucose < 90, use 110% of yesterday's total.

Case
A 56-year-old man admitted to the ICU with a hypertensive crisis after cocaine use. Initial blood pressure is 245/132.
PE: Dense left hemiparesis. When presented with painful stimuli, the patient responds with flexure posturing on the right side.
Lab: Computed tomography (CT): large intracranial bleed in the right frontoparietal area.
Course: He deteriorates in several hours. BP is 189/100. Right sided mydriasis.
He has corneal reflexes.
Dx: Increasing intracranial pressure related to the intracranial bleed.
Management:
Hyperventilation causing vasoconstriction, reducing cerebral blood volume and decreasing intracranial pressure.
Mannitol to diurese.
*Hypertonic to elevate sodium levels and prevent worsening of edema.
*a ventriculostomy to drain the cerebrospinal fluid (CSF).
*Do NOT decrease the arterial BP. In cases of increased intracranial pressure, nitroprusside is not a recommended intravenous antihypertensive agent because it causes arterial vasodilation and may decrease cerebral perfusion pressure and worsen neurologic function.

ANION GAP ACIDOSIS: "MUD PILES": Methanol/ Uremia/ DKA/ Paraldehyde/ INH or IRON/ Lactic Acidosis/ Ethanol OR Ethylene Glycol/ Salicylates.

NON-ANION GAP ACIDOSIS: "USED CARP": Uereterostomy/ Small bowel fistula/ Extra chloride/ Diarrhea/ Carbonic anhydrase inhibitors/ RTA/ Pancreatic fistual.

FAT EMBOLISM: Classic sx's: Reddish brown petechiae of axilla, CNS dysfunction, hypoxemia. Causes: Blunt Trauma, Joint reconstruction, pancreatitis, burns, diabetes, SSA.

Beta hydroxy butyrate is converted into aceto-acetate and acetone. Nitroprusside reacts with aceto-acetate and acetone but not beta hydroxybutyrate. Beta hydroxy butyrate makes up 75% of ketones in DKA, but this can reach 90% in alcoholic keto-acidosis or concurrent lactic acidosis. Hence keto-acids may not be measured. One way to follow the improvement is to look at the correction of the anion gap. Another way is to add hydrogen peroxide to the urine to convert the Beta hydroxybutyrate to acetoacetate and then measure the aceto-acetate.

Competency: 4 criteria:
1. Able to communicate a choice.
2. Factual understanding
3. Appreciates the situation and its consequences.
4. Rational manipulation of information (examine the process of reasoning).

OSMOLAL GAP = The difference between the measured and calculated plasma osmolality (measured - calculated < 10).
The calculated osmolality = 2 x Na + glucose/18 + BUN/2.18 + alcohol/4.6.

CONDITIONS WITH AN ELEVATED OSMOLAL GAP:
A. With an anion gap metabolic acidosis:
*Alcohol toxicity.
*DKA
*Lactic acidosis
*Ethylene glycol (anti-freeze)
*Methanol (Wood alcohol)

B. Without a metabolic acidosis
*Isopropanol (rubbing alcohol)
*Diethyl ether
*Mannitol
*Severe hyperproteinemia
*Severe hyperlipidemia.

Abnormal Right Atrial wave form

Hemodynamic tracing	Clinical condition
Cannon A Wave	Tricuspid stenosis or AV dissociation
Cannon V WAve	tricuspid regurgitation
Steep Y descent	constricutive pericarditis, right ventricular infarct, restrictive cardiomyopathy
Loss of Y descent	cardiac tamponade

ABNORMAL RIGHT VENTRICULAR AND LEFT ATRIAL WAFEFORMS

Hemodynamic tracing	Clinical condition
Dip and plateau (square root sign)	constrictive pericarditis, right ventricular infarction
Cannon A Wave (left atrium)	mitral stenosis and AV dissociation (CHB, V tach)
Cannon V wave (left atrium)	mitral regurg, ventricular septal defect, poor left ventricular function, aortic valve disease
Steep Y descent	constrictive pericarditis, restrictive cardiomyopathy
Loss of Y descent	Cardiac tamponade

Normal Mean arterial pressure = 70 - 105 mm Hg
Cardiac Output 5+ L/min
PCWP 3 - 12 mm Hg

SELECTED NORMAL HEMODYNAMIC VARIABLES

Systemic vascular resistance	(MAP-RAP)x80/Cardiac Output	800 - 1200 dyne-sec-cm-5
Pulmonary vascular resistance	(MPAP-PCWP)x80/Cardiac Output	150 - 250 dyne-sec-cm-5
Stoke volume	Cardiac output/heart rate	> 50 ml
Coronary perfusion	DBP - PCWP	>50 mm Hg
Pulmonary artery diastolic pressure to pulmonary wedge pressure gradient	PAD - PCWP	< 5 mm Hg

SHOCK PROFILES

SHOCK STATE	BLOOD PRESSURE	CARDIAC OUTPUT	PCWP	SVR
Hypovolemic	Lo	Lo	Lo	Hi
Cardiogenic	Lo	Lo	Hi	Hi
Cardiac tamponade	Lo or Normal	Lo or Normal	Hi or normal	Hi or normal
Massive PE	Lo	Lo	Normal or Lo	Hi
Distributive	Lo	Hi	Lo	Lo

Encephalopathy:
v PO2
^ PCO2
v glucose
Alcohol withdrawal
CNS infection
Sepsis
Visceral pain

Opioid withdrawal: cholinergic crisis, muscle twitching and mydriasis.

Withdrawal from cocaine or amphetamines can cause severe respiratory and CNS depression.