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APPROACH TO ACID BASE PROBLEMS

Acid base status in a patient is regulated by and affected by pathology in two systems- 1) the metabolic system [HCO3] & 2) the respiratory system [PCO2]. Abnormal "processes" in these systems cause acid base disorders. To diagnose & understand a patient's acid base disorders the clinician must interpret a complete database, which includes data from the history & physical examination as well as laboratory data, mainly a blood gas, blood chemistries and often urine chemistries. The clinician should suspect acid bases disorders in certain clinical situations & seek to document them, determine their severity & determine the need for treatment. Laboratory data must always be related to the patient's clinical situation and cannot be interpreted in a vacuum.

Laboratory evaluation of Acid base disorders.

A] First determine if the patient is ACIDEMIC or ALKALEMIC

These terms only refer to the net **pH** of blood, and do not describe the process that led to the alteration of the pH. An ABG or free flowing venous blood gas is required for this determination.

Acidemic: patient's pH < 7.35

Alkalemic: patient's pH >7.45

If the patient is acidemic or alkalemic there is at least one major abnormal acid base process present which must be explained by further analysis of data from the history, physical & lab. Acid base processes like metabolic acidosis or respiratory acidosis refers to specific pathophysiologic states which, if they are unopposed, would make the patient acidemic or alkalemic respectively. Remember that patients with a normal pH could have severe, counterbalancing, acid base processes. For example an ESRD patient with vomiting could have a metabolic acidosis & metabolic alkalosis with a normal pH.

B] Next try to **explain the abnormal pH** by a simple acid base disorder i.e. one abnormal acid base process in one system with appropriate compensation in the other system. Examine the directional change of PCO2 and HCO3 from normal. If they are abnormal in the same direction there is a mixed disorder. If they are abnormal in opposite directions only one can explain the change in pH. Assume that that is the primary process & that the other system is trying to compensate. For example if the pH is low & the PCO2 and the HCO3 are low, only the low HCO3 can explain the low pH. Therefore an initial guess as to what is wrong with the patient would be that the patient has a simple metabolic acidosis with respiratory compensation.

C] Next **determine if the compensation is appropriate**- see table below for appropriate compensation expected in various primary simple acid base disorders. If the changes in the other system fall outside the expected changes in this table then the acid base disorder is complex ie there are disorders in both the respiratory & metabolic acid base systems. Compensation never returns the pH to normal or over corrects. One easy rule on compensation is Winter's rule which states that the last 2 digits of pH greater than 7 predicts the CO2 in a patient with a primary metabolic

acidosis & appropriate respiratory compensation. So if a patient has a metabolic acidosis with a pH 7.25 one should expect a CO2 of 25. If the CO2 is higher, than the patient is not having an appropriate compensation, suggesting respiratory dysfunction, if it is lower then there is a coexisting respiratory alkalosis.

Primary Disorder	Expected Compensatory Response	Limits of Compensation
Metabolic Acidosis	ΔPCO2 = 1-1.3 x ΔHCO3	PCO2 not < 10 mmHg
Metabolic Alkalosis	ΔPCO2 = 0.5-0.6 x ΔHCO3	PCO2 not > 55 mmHg
Respiratory Acidosis		
Acute Respiratory Acidosis	ΔHCO3 = 0.1 x ΔPCO2	HCO3 not > 30 mEq/L
Chronic Respiratory Acidosis (3-5 days)	ΔHCO3 = 0.4 x ΔPCO2	HCO3 not > 45 mEq/L
Respiratory Alkalosis		
Acute Respiratory Alkalosis	ΔHCO3 = 0.2 x ΔPCO2	HCO3 not < 17-18 mEq/L
Chronic Respiratory Alkalosis (2-4 days)	ΔHCO3 = 0.5 x ΔPCO2	HCO3 not < 12-15 mEq/L

D] Next **determine the serum anion gap** [Na- (Cl+HCO3), normal 12 +/- 2] especially if a potential metabolic acidosis exists (low HCO3-). Metabolic Acidosis is commonly divided into anion gap and non-anion gap acidosis.

If the anion gap is greater than 17, it suggests the patient has an anionic gap acidosis. Anion Gap acidosis differential is remembered by stating this acronym: CAT MUDPILES. **C** for cyanide or carbon monoxide, **A** for alcohol, **T** for toluene, **M** for methanol, **U** for uremia, **D** for DKA, **P** for paradehyde, **I** for iron and isoniazid, **L** for lactic acidosis, **E** for ethylene glycol, and **S** for salicylates and strycnine. In simple AG acidosis, the decrease in serum bicarbonate should equal the increase in the AG (.ie 1 mmol of bicarbonate titrates 1 mmol of acid which forms Na Acid. The Acid anion is an unmeasured anion that increases the anion gap by 1. **Calculate the excess anion gap**. The excess anion gap = total anion gap minus the normal anion gap (12 mmol per liter). Add the excess anion gap to the measured bicarbonate concentration. If the sum is greater than a normal serum bicarbonate (> 24-28 mmol per liter) there is an underlying metabolic alkalosis (e.g. vomiting in a renal failure patient). If the sum is less than normal bicarbonate (< 23) there is an underlying non-anion gap metabolic acidosis process (e.g. shock & diarrhea). If the value is not less than 23 or greater than 28 then no additional metabolic process is going on.

If there is no anion gap but the bicarbonate is low, the patient has a non anion gap acidosis. This usually means loss of HCO3 from the gut (diarrhea, fistula) or the renal system (RTA, carbonic anhydrase inhibitors). Other causes include dilution of HCO3 by large infusions of normal saline or addition of a Cl acid or a GI/urinary diversion or augmentation. A **urinary anion gap** can help differentiate renal vs. GI loss of bicarbonate. Urine AG =(Na + K)- Cl and correlates with urinary ammonium excretion. As ammonium excretion increases the urinary gap narrows. With GI losses of HCO3 ammonium excretion is unimpaired and increases with acidosis & the urinary AG becomes

negative. With RTA the gap remains positive since the kidneys have lost the ability to absorb HCO3 and form ammonium.

E] Put together the clinical laboratory information. Acid-base disorders are merely laboratory signs of an underlying disease. After determining the pathophysiologic nature of the acid-base disturbance, the underlying pathologic cause(s) is(are) often obvious. Additional laboratory data including urine electrolytes, pH and creatinine; renin, aldosterone and toxicology screens may be indicated.

F] Determine appropriate therapy. If possible, it is better to identify & reverse the abnormal process rather than non-specifically trying to normalize the pH by giving the patient acid or base. Attention should be paid to restoration of extacellular volume, correction of K or Cl deficiency, removal of toxic substances and improvement in ventilation. In short, it is better to treat the metabolic acidosis of shock by reversing the shock than giving HCO3 to normalize the pH.

If metabolic acidosis is severe and respiratory compensation is maximal, temporizing therapy with NaHCO3 may be desirable to improve pH to less dangerous level although this is controversial. Some would argue that blood pH less than 7.1 should be treated back to a level of 7.2 & HCO3 of 10 with HCO3 as long as ventilation is assured. This especially makes sense in a HCO3 losing acidosis process. Do not over correct increased anion gap acidosis since the unmeasured anions will be converted to HCO3 when the patient's acidosis process is reversed and could result in overshoot alkalosis. Giving HCO3 in severe lactic acidosis may actually worsen intracellular acidosis & cellular function & thus should be used with caution & not be used unless pH is less than 7.1. Dose of HCO3 can be estimated by (wt in kg/2) X (10- patients HCO3). Before giving HCO3 make sure Ca & K levels are not dangerously low since they may decrease with HCO3 administration.

Most metabolic alkalosis in pediatrics responds to treatment of Cl or K deficiency. With severe alkalosis (pH>7.55) & emergency symptoms such as seizures or arrhythmia the fastest treatment is to intubate & control respiration. With severe but asymptomatic metabolic alkalosis unresponsive to routine treatment other options are Diamox, H2 blockers, anti emetics, & K sparing diuretics in appropriate cases. If these fail, acidifying agents can be considered. There is no ideal acidifying agent but dilute HCL in concentration of 150 meq/L can be given in a central vein. Dose should be calculated to lower HCO3 to 35-40 assuming volume of distribution of 200 cc/kg.

ANAPHYLAXIS

I. Definition/Pathophysiology

A systemic reaction (usually life-threatening) that occurs secondary to an IgE mediated antigen induced reaction (allergen) or exposure to mast cell degranulating agents (anaphylactoid). Both reactions cause mediator release (histamine, leukotrienes, PAF, etc.) which produce the symptoms. While there is often a history of prior exposure to a given antigen, in the non-IgE mediated (anaphylactoid) reactions, symptoms may occur during the first exposure.

II. Clinical Course

A. Symptoms usually occur within seconds to 60 min. of Ag exposure.

B. Variable: Initial symptoms may be mild or life threatening. Generally, the earlier the onset, the more severe the reaction.

C. Symptoms - cutaneous (urticaria/angioedema, pruritus), respiratory (bronchospasm, stridor, pulmonary edema, laryngeal edema), rhinitis, cardiovascular (hypotension, arrhythmias, myocardial ischemia, vaso-dilation, flushing), gastrointestinal (nausea, emesis, diarrhea, pain), asymmetric swelling of a limb or perioral area.

III. Most Common Etiologic Agents

A. Antibiotics (for instance penicillin, although any could be involved)

B. Insect (hymenoptera) stings

C. Foods (nuts, eggs, seafood)

D. Immunotherapy

E. Non-IgE (Anaphylactoid) mediated mast cell degranulation:

1. Morphine

2. Codeine

3. Polymyxins

4. Radiocontrast dye

IV. Risk Factors:

A. Personal history of previous allergic reaction.

B. Positive skin test.

C. Sick patient on multiple medications.

V. Therapy

A. ABC's

1. Establish airway if significant compromise.

2. May need intubation or trach. if no relief with epi.

3. Oxygen if respiratory distress or hypotension.

B. Stop antigen administration - if insect bite or allergy shot, isolate antigen site with tourniquets and inject 0.01 cc/kg epi. (1:1000) SQ into site after tourniquet applied. **Flick off (do not squeeze) any stinger present.**

C. Epinephrine:

1. Mainstay of treatment

2. SQ or IM 0.01 cc/kg of 1:1000 sol'n, max 0.3 cc, may repeat

3. Rarely IV 1:10,000 by drip and titrate to achieve response, begin at drip of 0.1 mcg/kg/min (only in refractory hypotension).

D. Immediate IV placement with IVF (LR/NS, bolus 20 cc/kg as needed for shock).

E. Continue to observe for 24 hrs, as symptoms may recur.

1. Subjective: SOB, anxiety.

2. Objective: stridor, retractions, wheezing, cyanosis, pallor.

3. BP: q 5-10 min initially, then q 1 hr.

4. Continuous EKG monitor or A-line as needed.

F. Other drugs as needed (**NOT** a substitute for epi.).

1. H1 Antihistamine - Benadryl 0.5-1.0 mg/kg po or slow IV push.

2. Steroids - 1-2 mg/kg methylprednisolone to prevent late phase response.

3. Cimetidine IV 5-10 mg/kg given over 5 min or Ranitidine 1mg/kg - given in association with H1 antihistamines may reverse profound hypotension unresponsive to fluids/pressors and lessen severity of anaphylactic reaction.

4. Glucagon may be effective in reversing hypotension in rare cases, especially if beta-blockade is present. (Dose: < 10 kg: 0.1mg/kg IM, > 10 kg: 1 mg/dose IM).

G. For cardiorespiratory arrest, continue with BCLS/ACLS algorithms.

VI. Differential diagnosis includes:

A. Insulin reaction

B. Vasovagal syncope

C. Arrhythmias

D. Hereditary angioedema

BITES AND STINGS

I. Mechanisms of Injury

A. Children may be at increased risk for severe reactions to stings and envenomations due to an increased dose of venom per kg.

B. There are several mechanisms for the toxic effects of bites and stings:

1. Immunologic, including IgE mediated anaphylaxis and serum sickness (Ab-Ag complex).

2. Hemotoxic

3. Neurotoxic

C. Most venoms are toxic due to a combination of the above factors

II. Purveyors of Venom

A. Snakes

Several different types of snakes must be differentiated due to the varying effects of their venoms.

1. Pit Vipers (Crotalidae)

a. These account for the majority of significant envenomations in the United States. Included are

(1). Rattlesnakes (60%): Eastern and Western Diamondback Rattlesnake are most dangerous, accounting for 95% of fatalities, but only 10% of bites.

(2). Water moccasins:

a. Copperheads (30%)

b. Cottonmouths (< 10%)

b. Epidemiology:
   a. Of all bites in US – only about 18% are venomous
   b. Top 5 States for venomous bites (descending order) are North Carolina, Texas, Arkansas, Mississippi and Lousinianna.
   c. Location of bites: Most common is LE, however many rattlesnake bites are provoked and thus involve the upper extremities (more common in older children and adolescents), torso and head bites are seen rarely in handlers.

c. Pit viper venom is voluntarily injected by venom gland contraction. It generally contains digestive enzymes. Depending on the species there may be other components. The Mojave rattlesnake makes Mojave "toxin", a neurotoxin which may lead to paralysis and respiratory arrest. There may be varying

hemotoxins which profoundly decrease platelet and clotting factors.

d. Treatment

(1). First Aid Management

- Initiate BLS as necessary (ABCs)

- Move the patient to a health care facility rapidly

- Minimize movement of an affected extremity and keep the extremity below the level of the heart

- Avoid ice, aspirin, alcohol or sedatives

- Do not try to capture snake

- Tourniquets, constriction bands, incision and suction are NOT recommended.

(2). Hospital Management

- History of evenomation
- Was it a poisonous snake? Species? Size? Circumstances of bite? Time of bite? Rapidity of symptom progression.
- PMHx, previous snakebites and treatment

- Exam:

Local Symptoms: teeth marks, discoloration, size of erythema and swelling (mark immediately), circumferential measurements should be performed serially at the level of the lesion and about 5-10cm above the lesion.

Systemic Symptoms: VITAL signs!! Nausea/vomiting? Bleeding? diarrhea? shock?

Laboratory abnormalities: Hemoconcentration? Hypoproteinemia? DIC-like picture?

- Labs

(a). PT, PTT, Fibrinogen, Fibrin Split Products

(b). CBC, Platelets, blood for type and cross

(c). Lytes, BUN, Cr, CPK, glucose

(d). UA

(e). Skin testing for hypersensitivity to horse serum should be done only if it is known that antivenin will be administered

e. Staging

In approximately 10-20% of known rattlesnake strikes, no venom is released and only a fang mark will be present.

A staging system helps to provide a general scheme for intervention. Remember though, that what appears to be a minimal envenomation may develop severe manifestations.

(1) **No envenomation**: "dry bite" – punctures/abrasion w/pain and tenderness at bite.

(2) **Mild Envenomation**: A fang mark is surrounded by edema and tissue necrosis, but these are confined to the immediate segment of the extremity involved. May have perioral paresthesias. No laboratory abnormalities.

(3) **Moderate Envenomation**: A fang mark is present and surrounded by tissue breakdown including edema, bullae, and/or hemorrhagic blebs extending beyond the immediate area of the bite but not involving the entire extremity. Can have perioral or peripheral paresthesias, gustatory changes, nausea, vomiting, diarrhea, weakness, light-headedness, chills. Lab: elevated PT, PTT and Hgb, decreased fibrinogen and platelets.

(4) **Severe Envenomation**: A fang mark is present with obvious tissue breakdown, including edema, bullae, and/or hemorrhagic blebs. Tissue ecchymoses involving an entire extremity or systemic effects such as tachycardia, hypotension, shock, bleeding, ventilatory insufficiency, altered mental status, fasciculations or seizures. Lab abnormalities consistent w/coagulopathy or muscle.
breakdown.

(5) **Bites on the thorax or head/neck are all assumed to be severe. Early intubation should be considered for these patients as respiratory compromise is frequent.**

f. Basic Therapy

(1) Clean the wound area and administer tetanus prophylaxis

(2) Do q 15 minute measurements (circumferentials) of the involved extremity

(3) Use acetaminophen or mild opiates (codeine) for relief of pain

(4) All children, severity of bite aside, will be observed for 24 hours

(5) Establish rapid IV access and support shock as necessary with fluid and pressors

(6) Consider antivenin for moderate to severe

envenomations (antivenin is most effective within the first 12 hours after the bite, antivenin is not indicated after 24 hours). Prior to initiation of antivenin therapy, volume expand with a 20 cc/kg fluid bolus, unless contraindicated by preexisting medical condition

(7) Antibiotics are controversial but may be appropriate esp. in dirty wounds.

g. Use of Antivenin

(1) For North American pit vipers (Crotalidae), the only approved antivenin is the polyvalent Crotalidae antivenin (Wyeth). It is active against all pit vipers, as well as the Bushmaster, Fer de Lance and Mamushi.

(2) This is a horse-derived product and has significant risk for anaphylaxis and serum sickness. Obtain consent prior to use. The anaphylactic reactions are not all IgE mediated and may occur on first exposure. Administer antivenin slowly.

(3) Prior to use attempt to ensure cardiovascular stability by correcting hypovolemia and using pressors as needed. During administration, continually monitor for changes in CV status. **Do not shake the vials** when mixed with fluid; stir them only by rocking in your hands - gently back and forth.

(4) After the decision is made to use antivenin, skin test, using an intradermal injection of antivenin. This is done by injecting 0.02 cc of a 1:10 saline diluted horse serum intradermally with observation for at least 20 - 30 minutes for the development of erythema, hives, pruritis or other adverse effects. If positive, the patient should be pretreated with benadryl and steroids prior to administration. A negative skin test does not eliminate risk for anaphylaxis. Never skin test mild or non-venomous bites "just in case we need to use antivenin." You may sensitize the patient to horse proteins.

(5) Administration of antivenin is done in five vial aliquot increments. Moderate bites require an average of 10 vials of antivenin. In severe envenomations, as many as thirty vials of antivenin have been administered to halt symptom progression. For children, many experts recommend that the dose of antivenin be increased by 50 % because of a higher ratio of venom to body mass.

(6) Reconstituted antivenin is diluted with NS or D5W in a 1:5 to 1:10 dilution. If pt can tolerate volume, recommend maximally diluting (5 vials in 500 cc NS) or to create volume equal to 20cc/kg. Infuse antivenin slowly (start at no more than 60 cc/hr) and increase every 3 minutes to max of 1L/hr with goal of 1-5 vials/hr. Goal is to give entire antivenin dose within the first 4-6 hours to bind the venom and prevent further toxicity.

(7) Infusion of one to two vials per hour is appropriate

to minimize the side effects seen at higher infusion rates. Mild reactions (pruritus, urticaria etc.) can be treated with benadryl. With serious reactions consider D/Cing antivenin and treat with epinephrine SQ (0.01 cc/kg 1:1000 max 0.3-0.5 cc)

(8) After each five vial aliquot delivered, assess for changes in swelling, necrosis or systemic signs. If unimproved or worsening administer five more vials.

(9) Serum sickness is almost universal in children and may occur up to 10 days post infusion. Parents should be informed of this likely occurrence.

h. Other Therapy

(1). If required use FFP for volume replacement

(2). It is unusual for active bleeding to occur

(3). Have a low threshold for intubation of a patient with a symptomatic neck bite

i. Controversies

(1) Wide fasciotomies of swollen extremities are not beneficial. Compartmental pressures may be measured in concerning situations, but it is rare that an increase occurs which requires fasciotomy. Consult orthopedics.

(2) Steroids are useful only in managing anaphylaxis or hypersensitivity to antivenin.

2. Coral Snakes (Elapidae)

a. Significant species are the Arizona, Texas and Eastern coral snakes. They are very shy of humans and most bites are the result of provocation or molestation by humans. They are brightly colored and non-venomous snakes mimic their pattern. The mnemonic "red on yellow, kill a fellow, red on black, venom lack" helps identify the venomous species. Unlike crotalids, their fangs are fixed and grooved, so for effective envenomation to occur, they must gnaw or hang onto its victim for at least several seconds.

b. Symptomatic bites are largely neurologic with relatively little local tissue toxicity. In fact no bite marks may be evident. Also symptoms may be delayed up to 13 hours. Local hypesthesia may occur with changes in consciousness, muscle weakness, fasciculations and paralysis. Respiratory failure may ensue.

c. No significant lab abnormalities occur other than hypercarbia or hypoxia in those w/ respiratory failure.

d. Antivenin (micrurus fulvius – equine origin, Wyeth-Ayerst Labs) is available for Eastern and Texas coral snakes, but none is available for the Arizona coral snake. If history of coral snake bite is reliable or signs / symptoms exist, early treatment with antivenin is recommended.

Before treatment a skin test can be performed, risks are similar to that or crotalid antivenin. Recommended initial dose is at least 5 vials, 10 for bites by large snakes, particularly long exposure time or in very small children. A subsequent dose of 5 vials is indicated for continued worsening after first dose. Once signs of neurotoxicity are present, progression may not be halted by antivenin. Supportive care w/ early intubation is paramount.

e. Tetnus prophylaxis should be given. Antibiotics are not indicated.

3. Nonvenomous Snakes

a. May cause local reaction due to digestive enzymes.

4. Non-indigenous Snakes

a. A wide variety of exotic snakes are illegally imported, many poisonous.

b. The Arizona Poison Center (602-626-6016) keeps general inventory of antivenins maintained in zoos and hospitals throughout the country. The San Diego Zoo also has many antivenins available (619-231-1515). The San Antonio Zoo stocks some exotic snake antivenins (734-7183). **WHMC IV pharmacy** carries coral snake and pit viper antivenins and BAMC carries others (916-6638)

B. Scorpions

1. In general only the southwestern desert scorpion (Centruoides) produces mortality. The venom is a neurotoxin and primarily affects the autonomic and skeletal neuromuscular system. Classically envenomation leaves no significant local effect, but produces a tingling sensation which may progress up the extremity. Young children may develop fasciculations, agitation, opisthotonus or seizures.

2. Therapy

a. Mild envenomations may be treated with cool compresses and mild analgesics.

b. Severe Envenomation

(1). Basic supportive care: Increased parasympathetic tone may give increased secretions and loss of bulbar tone. Follow for airway compromise. Severe tachyarrhythmias may occur. These are best treated with propranolol slow IV 0.01 - 0.1 mg/kg over 5-10 minutes. Intubation may become necessary.

(2). Establish a firm diagnosis and consider sepsis/meningitis prior to a primary diagnosis of scorpion sting, especially with an unverifiable story.

(3). If symptoms are severe, an unlicensed antivenin is available in Arizona for the Centruoides species. Use the Arizona poison control number.

C. Hymenoptera Stings

The toxicity of ant, bee, and wasp stings is related primarily to their ability to produce anaphylactic and hypersensitivity reactions. Up to 80% of fatalities occur in individuals with no prior history of sensitivity. See anaphylaxis chapter. Fire ants deserve special consideration as its venom differs from venom of other hymenoptera. Fire ant venom has a direct toxic effect on most all membranes. The fire ant bites with its jaws then inflicts multiple stings which leave an immediate wheal and flare which may develop into the classic white-cloudy pustule, surrounded by painful erythema. Systemic reactions can occur as with other hymenoptera.

1. Therapy

a. Local - Cool compresses and soap and water cleansing
The pustule of the fire ant sting is usually sterile, so there is no need for antibiotic creams or ointments.

b. Systemic - Benadryl 5 mg/kg/day divided q 6 hours prn itching or swelling.

c. Treat anaphylaxis as outlined in anaphylaxis chapter.

D. Spiders

All spiders possess venom. Highly toxic venom is limited to a few species. In North American two major patterns of bites occur, one associated with the black widow, the other with necrotizing spider bites (primarily associated with the brown recluse). Both live in Texas

1. Black Widow Spider

a. The female of the species delivers venom. It is a mixture of polypeptides that includes a neurotoxin that stimulates myoneural junctions, nerves and nerve endings.

b. Favorite locations are moist, dark areas away from sunlight

c. Signs and Symptoms

- Local pain with progression up an extremity.

- Increased motor tone with muscle spasm that may generalize. This may be very prominent over the abdomen and mimic an acute abdomen. Nausea and vomiting are often reported in children. Usually normal bowel sounds and x-rays.

- Diaphoresis, tachycardia, and periorbital edema.

- 4-5% mortality rate with death resulting from cardiovascular collapse. The mortality rate in young children may be as high as 50 %.

- Labs may show an increased CPK, also leukocytosis and hyperglycemia due to increased sympathetic tone.

d. Therapy

- Majority of cases are mild and resolve over 24 hours with mild analgesia.

- Young children are more seriously affected. Thus use of antivenin should be instituted in any child presenting with severe pain and muscle rigidity after a spider bite.

- Assess vitals (ABCs)

- Establish IV access

- Rule out other infectious and surgical conditions

- Severe muscle spasm may be treated, in an ICU setting, with diazepam (0.1 mg/kg IV). Calcium gluconate 10% soln. (0.1 cc/kg/dose IV slowly) can also be given for control of leg and abdominal cramps. Both of these agents are variably effective and short-lived.

- Impaired diaphragmatic excursion due to muscle spasm may necessitate intubation and ventilation.

- For severe envenomations a horse serum antivenin is available (from Merck, Sharp and Dome). Method of preparation, administration and cautions are similar to those for pit viper antivenin. The only difference is use of <u>one</u> vial in preparing the initial antivenin drip with additional vials added in <u>one</u> vial increments. One vial for children < 40 kg. The use of antivenin is controversial.

- The venom produces smooth muscle contraction, and the uterus is very sensitive. The result of a bite in a pregnant women may be spontaneous abortion. Antivenin should be administered early in the pregnant patient.

2. Necrotizing Spiders

a. The brown recluse (Loxosceles reclusa) is most common in the Southeast and Midwest U.S. There are several species of Loxosceles in the Southwest.

b. The venom of reclusa is extremely potent on a mg/kg basis. It contains multiple proteolytic enzymes and is cytotoxic.

c. Classically patients present with a target like skin lesion with a blackened necrotic center. Typically the patient is unaware an envenomation has occurred until an indurated area with a small vesiculated center develops. This ruptures and becomes a dark, necrotic area. This area may increase in size with continued necrosis for periods up to weeks. Then contraction of the wound with involution

occurs.

- Systemic reactions are more common in young children and are usually seen 24-48 hours after the bite and include fever, chills, malaise, nausea, vomiting, weakness or pain, rash, and renal failure.

d. There are case reports of hemolysis and DIC like syndromes associated with these bites. It is prudent to screen for these (CBC, PT/PTT, fibrinogen, and urine for hemoglobin).

e. Therapy

- Good local wound care and debridement

- Tetanus prophylaxis

- Consider treating intravascular hemolysis with steroids (controversial!)

- There are many suggested therapies of unproven and questionable value, these include local injection of phentolamine, dapsone and steroids. Wide excision seems unnecessary in view of the regression of these bites naturally into a smaller, final cosmetic lesion. **However**, excision and debridement of necrotic areas > 2 cm in diameter with antibiotic coverage is appropriate if the wound is being seen in the first 48 hours. For necrotic areas > 2.5 cm in diameter skin grafting may be necessary. Early involvement of our plastic surgery and pediatric surgery consultants is advised.

- Work is presently being done on the development of an antivenin.

CARDIOLOGY PROBLEMS

I. General approach to dysrhythmias:

A. First, rule out artifacts:

1. Flat line can be due to a loose or detached lead. If you are using the defibrillator monitor the "paddles" lead will be flat and may be the default lead when the defibrillator is turned on. Check the defibrillator set-up.

2. Tall T-waves may be perceived by the monitor as extra R-waves and be double counted. Run a strip and count for yourself.

3. Leads perpendicular to the P-wave axis may make P-waves appear absent. Check more than one lead to be certain.

4. Rhythmic movement artifacts (seizures, hiccoughs in neonates) may mimic dysrhythmias.

B. If hemodynamically stable obtain 12-lead ECG with rhythm strip prior to intervention.

C. Record rhythm strip during intervention.

D. As soon as feasible, ***repeat*** 12-lead ECG with rhythm strip after successful intervention.

II. Abnormal Rhythms: (**Cardiology should be consulted.**)

A. Principles of therapy:
- treat emergently only if cardiac output compromised (an unstable patient)or if rhythm has the potential to degenerate into a lethal (collapse) rhythm such as with V. fib.
- normal heart rates (HR) are given below.

Heart Rates in Normal Children

Age	Awake rate	Mean	Sleeping rate
Newborn to 3 mos.	85 - 205	140	80 - 160
3 mos. to 2 yr.	100 - 190	130	75 - 160
2 - 10 yr.	60 - 140	80	60 - 90
> 10 yr.	60 - 100	75	50 - 90

from : Gillette PC et al. Dysrhythmias. In Adams FH, Emmanouilides GC, Riemenschneider TA, eds. Moss' Heart Disease in Infants, Children and Adolescents. 4th ed. Baltimore, Md: Williams & Wilkins; 1989: 725-741

B. Tachyarrhythmias:

1. Sinus tachycardia (ST): - therapy is directed to underlying cause: anxiety, fever, volume depletion, pain, stimulant medications, anemia, CHF, thyrotoxicosis.

a. Beat-to-Beat heart rate variability is common.

b. Acceleration and deceleration of heart rate is typical.

2. Supraventricular Tachycardia (SVT):

a. HR depends on patient age, usually 220 or greater (up to 300 bpm). Etiologies: idiopathic in approximately 50%, Wolff-Parkinson-White syndrome (WPW), congenital heart defects (Ebstein's anomaly, single ventricle, L-TGA), associated with hydrops fetalis, sepsis, trauma, central lines.

b. HR very regular, rarely associated with A-V block.

c. P-waves may not be visible at high rates.

d. QRS duration is normal in 90% of cases. Wide QRS may be indistinguishable from V-Tach.

e. May see ischemic ST-T changes in SVT of long duration.

f. Long-lasting SVT may cause a cardiomyopathy and/or congestive heart failure which may then lead to cardiomegaly; a CXR may be useful.

g. ECG criteria: ST vs. SVT.

(1). ST usually < 220 bpm, SVT > 220 bpm.

(2). In ST there is beat to beat variation in rate. No HR variation in SVT.

(3). Both onset and cessation of SVT are abrupt.

h. Therapy: ***depends on cardiac stability***. If the patient has a good BP, and cap. refill, is responsive and has no signs of CHF then he/she is probably stable. If the patient has weak or absent pulses, poor cap. refill and BP, is lethargic or unresponsive, has HSM, edema or rales then he/she is probably unstable.

(1). **Synchronized cardioversion** (0.5-1.0 joules/kg) for cardiovascular instability; may use adenosine if IV present and adenosine readily available (see below).

(2). If persists, repeat synchronized cardioversion at 2.0 joules/kg; SVT normally converts easily with synchronized cardioversion.

(3). If no success with cardioversion, consider sinus tachycardia, atrial fibrillation or atrial flutter. Review the ECG strips performed while you were attempting to cardiovert.

(4). In non-emergent cases attempt vagal maneuvers (stimulate gag reflex, ice bag to face (forehead to chin, ear to ear) Valsalva, carotid massage in **older** children. **Never press on the eyeballs.**

(5). Adenosine 0.1 mg/kg rapid IV push followed immediately with rapid fluid flush. Expect transient asystole at conversion (adenosine T 1/2 is seconds). May need higher dose if patient on theophylline. If first dose of 0.1 mg/kg has no effect, double the adenosine dose (maximum single dose is 12 mg).

(6). Consider digitalization. (see section at end of this chapter for dig. doses, side effects etc.) If WPW present, consult cardiology first. (dig + WPW deaths reported). Diagnose WPW when isoelectric PR segment is absent (i.e. short PR interval) and QRS is wide. May also see delta wave.

(7). Verapamil 0.1 mg/kg IV over 3-5 min. **only if patient stable and > 1 year old.** Contraindications : CHF present, age < 1 year, concomitant Beta-blocker therapy, myocardial depression, or if patient has a bypass tract. Always have calcium chloride available as antidote!

(8). Procainamide 2 - 6 mg/kg/dose IV over 5 minutes. Maintenance is 20 - 80 **mcg**/kg/min IV drip.

3. Ventricular Tachycardia (V-Tach):

a. Rate may vary from normal to 400 bpm (usually 150-250).

b. Majority of cases have underlying structural heart disease or a prolonged QT interval.

c. May be caused by hypoxia, acidosis, electrolyte imbalance, drugs (esp. methylxanthines, amphetamines, tricyclics, digitalis/ digoxin), myocarditis, poisons, long QT syndrome, or post surgery.

d. ECG criteria:

(1). Rate at least 120 BPM and regular.

(2). Wide QRS (> 0.08 sec).

(3). P-waves not seen, or dissociated

(4). T-waves opposite in polarity to QRS

(5). May resemble SVT with aberrant conduction; however, wide QRS tachycardia in children is V-Tach until proven otherwise!

e. Therapy:

(1). **Synchronized cardioversion** with cardiovascular instability 0.5 - 1.0 J/kg. This is done for unstable patients **with** a pulse. If patient has V-tach. with**out** a pulse then treatment is similar to V-fib. and uses defibrillation instead - **see algorithms !!**

(2). Lidocaine bolus (1.0 mg/kg) results in higher success rates of cardioversion.

(3). Lidocaine infusion (20 - 50 mcg/kg/min) will help maintain sinus rhythm after conversion.

(4). If cardioversion needs to be repeated use 2.0 J/kg

(5). If lidocaine is unsuccessful, use bretylium 5 mg/kg slow IV push and repeat cardioversion.

4. Atrial Fibrillation/ Flutter - mortality as high as 25% in infants

a. Flutter is defined by the morphology

(1). Flutter waves (sawtooth pattern) are seen in the inferior and right precordial leads. Rates of 300 or so are common but may be as high as 500 BPM.

(2). AV conduction is variable - it usually is 1:1 in infants

(3). Causes: In infants the heart is usually structurally normal. Flutter is also associated with congenital heart disease though, with 75% of episodes occurring post-op cardiothoracic surgery, especially after Fontans, Mustards, or Sennings. Also occurs from digitalis toxicity, myocarditis, and hypokalemia.

b. Fibrillation is characterized by an irregularly irregular rate and rhythm with variable "p" wave morphology. Ventricular rates are often > 200 BPM and atrial rates > 400 BPM.

(1). Causes: idiopathic, stimulants may precipitate episodes, congenital heart disease (Ebstein's anomaly, mitral stenosis, tricuspid atresia etc.), rheumatic heart disease, hyperthyroidism, cardiomyopathies, myocarditis

c. Treatment of Atrial Fibrillation or Flutter:

(1). Synchronized cardioversion 0.5 - 1.0 J/kg.

(2). Transesophageal overdrive pacing at 125% of flutter rate if available.

(3). If the above maneuvers fail: **Make sure you do not have SVT.** Digitalize with 1/2 the digitalizing dose (see digoxin section at end of this chapter). 8 hours later give 1/4 the digitalizing dose, and 8 hours after that give the final 1/4 digitalizing dose. Digitalis slows the ventricular rate. Do not perform if patient is already on dig.

(4). If you have given the first dose of dig. and the patient has not converted in 30 minutes then load with procainamide: If the patient is < 1 year old: give 7 mg/kg

IV followed by 3.5 mg/kg IV q 4 hours. If the patient is > 1 year old: give 15 mg/kg IV followed by 7 mg/kg IV q 4 hours.

(5). If the above steps fail repeat the cardioversion.

(6). If still not converted use IV amiodarone, 1 mg/kg/dose q 10 min. X 10. May repeat q 12 hours. Monitor the QTc on the ECG. If the QTc is > 0.53 seconds decrease the dose.

(7). Continue all drugs used for cardioversion, monitor procainamide and NAPA (n-acetyl-procainamide) levels, use continuous ECG monitoring.

C. Bradyarrhythmias:

1. ECG:

a. Slow rate is all that matters.

b. P-waves may be present or absent.

c. QRS is narrow or wide.

d. In context of CPR, the exact rhythm is not important.

e. Etiologies: normal athletes, vagal stimulation, increased ICP, hypothyroidism, hypothermia, hypoxia, hyperkalemia, digitalis, beta-blockers, acidosis, heart block, seizures, rapid calcium infusions, tricyclics.

2. Heart block:

a. Congenital, complete AV block:

(1). Patients are usually asymptomatic.

(2). QRS is usually narrow.

(3). Treatment is not urgent and often not necessary.

b. Acquired heart block:

(1). Notify the cardiologist.

(2). Most commonly occurs postoperatively.

(3). QRS is usually wide.

(4). May cause significant compromise of cardiac output.

(5). If patient is unstable, refer to bradycardia algorithm as isoproterenol infusions and cardiac pacing may be necessary.

(6). In older patients, transthoracic external pacemakers are available for temporary use in an ICU setting.

3. Therapy:

a. Ensure adequate ventilation.

b. Chest compressions.

c. Epi and other meds as per algorithms. Atropine.

d. Atropine.

D. Absent or disorganized rhythms:

1. Asystole:

a. Diagnosed by absence of auscultated or palpated pulse, straight line ECG, absent spontaneous respirations, and poor perfusion.

b. Therapy: appropriate ACLS steps as per algorithm.

2. Ventricular Fibrillation (V-fib):

a. Uncommon terminal event in pediatrics, very rare in infants. Etiologies: postoperative, hypoxia, hyperkalemia, digitalis or quinidine toxicity, myocarditis, infarctions, catecholamines, anesthetics.

b. No identifiable P, QRS, or T-waves.

c. Therapy: **Defibrillation** and treatment per ACLS algorithm.

3. Electromechanical Dissociation: (pulseless electrical activity)

a. Organized electrical activity on ECG, but ineffective or absent cardiac contraction, absent peripheral pulses.

b. Causes include severe acidosis, pneumothorax, pulmonary embolism, pneumopericardium, hypovolemia, hypoxemia, cardiac tamponade, hyperkalemia, tricyclic antidepressants, Beta-blockers, Calcium channel blockers, and hypothermia.

c. Therapy: see algorithm

III. Defibrillation and Cardioversion:

A. Paddle size:

1. 4.5 cm for infants (usually < 1 yr, or < 10 kg)

2. 8 or 13 cm for older children (usually > 1 yr, or > 10 kg)

3. Largest paddle size possible is good rule of thumb.

B. Electrode interface: use electrode gel or redux cream, **NOT** ultrasound gel. Saline pads drip and cause short circuits.

C. Position: one on upper right chest below clavicle, other to left of the nipple in anterior axillary line. Try to "cup" the heart with the paddles. Reverse this position in cases of dextrocardia, i.e.. upper left chest and right anterior axillary line.

IV. Hypercyanotic or "Tet Spells"

"Tet Spells" most often occur in patients with uncorrected Tetrology of Fallot between the ages of 2 to 4 months of age

These spells occur when either systemic vascular resistance (SVR) decreases or pulmonary vascular resistance (PVR) increases. Common triggers are dehydration, a warm bath, fever, exercise, excessive crying or respiratory illness.

These spells are life threatening. In addition to cyanosis, the patient may present with hyperpnea, restlessness and agitation. During a spell the pulmonary stenosis murmur decreased or disappears secondary to decrease flow across the pulmonary valve.

Treatment: Should be done in a stepwise fashion and not undertaken unless previous step unsuccessful. Ancillary staff should page the on-call peds cardiologist

1. If patient is conscious have parents hold infant in knee-chest position and attempt to calm child.

2. Provide supplemental O_2 by route that causes least amount of agitation

3. Bolus IV fluid-NS @ 10-20cc/kg

4. MSO_4 0.1 mg/kg SQ or IM. Observe closely for respiratory depression.

5. If patient still having spell, the cardiologist may advise you to give one or more of the following:

a. Propranolol 0.10-0.25 mg/kg IV (max 10 mg) over 2-5 minutes. May repeat once after 15 minutes.

b. Phenylephrine (neosynephrine) 0.1 mg/kg SC or IM, 0.01 mg/kg IV or as a drip 0.1-0.5 mg/kg/min

c. Intubation and ventilation

d. Sodium Bicarb 1 meq/kg IV if acidosis present

6. Avoid dopamine, dobutamine and digoxin

7. Correct anemia if present

V. Cardiac Tamponade

Cause: Occurs when there is sufficient fluid within the pericardial sac to cause significant impairment of ventricular diastolic filling which may lead to inadequate cardiac output and eventually myocardial ischemia. Often associated with pericarditis, infection, or post-op heart surgery.

Clinical findings: (**Beck's triad:** hypotension, increased CVP, quiet pericardium)

Symptoms: Dyspnea, fatigue, cold extremities
Vitals: Tachycardia, pulsus paradoxus, tachypnea, hypotension, desaturation
Exam: Muffled heart sounds, rub, crackles, hepatomegaly, poor perfusion, JVD, peripheral edema
CXR: Cardiomegaly, pulmonary congestion
ECG: Sinus tach., low voltage QRS complexes with T-wave and S-T segment abnormalities
CVP: High
ECHO: RV collapse in early diastole, RA/LA collapse in early systole

Initial Treatment:

1. ABCs!!! Secure the airway, get vascular access
2. Urgent decompression of pericardial space by pericardiocentesis

Pericardiocentesis:

Drainage of the pericardium is safest in a controlled environment, ICU with ECHO guidance or Cath Lab with fluoro guidance

1. Monitor patient with ECG, BP, Pulse Ox; sedate as appropriate
2. Place patient in reverse Trendelenberg (approx 30 degrees)
3. Sterilize, prep and drape patient
4. Anesthetize site with 1% lidocaine
5. Insert 18 or 20 gauge needle attached to large syringe with stopcock, just left of xiphoid process, 1cm below rib at 45 degree angle to skin
6. Advance needle towards patients left shoulder while gently aspirating
7. Stabilize needle at skin once fluid return is noted
8. Slowly remove fluid and send for appropriate studies (Culture and cell count)

Potential complications: Puncture of cardiac chamber, pnemopericardium/pneumopericardium, dysrhythmias, pneumothorax

See illustration in Harriet Lane 16th ed. Fig. 3.13, page 68.

VI. Cardiogenic Shock

Cause:

Myocardial dysfunction/ischemia is the most likely cause and may be secondary to a myriad of factors and events:

1. Congential heart disease with low cardiac output
2. Sepsis and/or myocarditis
3. Dyshythmias-SVT, VT, CAVB, long QT
4. Metabolic conditions - severe hypoglycemia, severe hypocalcemia, adrenal insufficiency, rare metabolic disorders
5. Myocardial ischemia/infarction - Kawasaki disease, anomalous LCA

Pathophysiology:

Cardiac: decreased ventricular performance leads to arterial hypotension or vice versa, which leads to further dysfunction and ischemia

Skeletal muscle: a resultant lactic acidosis form hypoperfusion, which worsens myocardial performance

Renal: oliguria/anuria secondary to hypoperfusion

Heme: DIC

Clinical Findings:

Vitals: Tachycardia, tachypnea, hypotension, desturation
Exam: Gallop rhythm, crackles, hepatomegaly, poor perfusion
CXR: Cardiomegaly pulmonary congestion
ECG: Low voltage QRS complexes with T-wave abnormalties
CVP: High: heart failure Low: Sepsis, hypovolemia

Differential Dx:

1. ABCs!!! - secure the airway
2. ECG to R/O dysrrhythmia
3. Vascular access-need a central line
4. Send blood ABG, CBC, chem, Bld Cx, type and cross
5. May need volume, inotropes or both. Start with a bolus while you are still evaluating

Medications:

Inotropic support of cardiac output:

First line:

Dopamine 5-20 ug/kg/min
Doputamine 5-20 ug/kg/min
(synergistic when used together e.g., Dopa 2; Dobut 3)

Second line:

Consider Epinephrine if systemic vascular resistance is low (good agent in the face of sepsis)

Epinephrine 0.1-10 ug/kg/min

Manage ischemic pain (if present) - Morphine 0.1 mg/kg/dose, titrate

Tx dysrhythmias -

Ventricular dysrythmias

Amidarone: Load 5 mg/kg over 30 minutes > 5ucg/kg/min
Lidocaine; 1 mg/kg bolus may repeat q 10-15 minutes

Bradycardias

Atropine: 0.02 mg/kg bolus q 5 minutes min. dose 0.1 mg. Max dose 0.5 mg in children, 1mg in adolescents. Total max dose 1 mg in children, 2 mg in adolescents.

CHEMOTHERAPY DRUGS

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PEDIATRIC CHEMOTHERAPY

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CHEMOTHERAPEUTIC AGENT		PHARMACOLOGY		CLINICAL USE		TOXICITY
		ADM MODE	CSF BRAIN	EXCRETION LIVER	BILE	
VINCA ALKALOIDS						
Vincristine (Oncovin)	N	Poor	Minor	Predominant, Rapid	ALL ANLL, Hodgkin's, NHL, soft	Neurotoxcity, peripheral neuropathy with foot drop, loss of deep tendon reflexes, paresthesia
Vinblastine (Velban)	N	Minimal	Minor	Predominant, Rapid	Hodgkin's, NHL, Histiocytosis	Nausea/vomiting, myleosupression, mild neural toxicity, alopecia, vesicant
Nitrosureas						
BCNU (Carmustine)	N	Good/ Rapid	Rapid	Probably Nil	Hodgkin's NHL, soft tissue sarcoma, primary CNS tumor. High doses in BMT preparative therapy	Nausea, vomiting, myleosupression, liver/renal toxicity, pulmonary fibrosis, vesicant, alopecia.
CCNU (Lomustine)	P.P.	Good/ Rapid	Predomi- Nant Slow	Probably Nil	As above	Similar to BCNU
Epipodophyclotoxins						
VM26	IV	Poor	Slow	Predominant Rapid	Leukemias/lymp- homas, Ewing's neuroblastoma, Wilms' germ cell tumors	Hypotension, vomiting, nausea, bone marrow depression, alopecia, hepatic dysfunction, peripheral neuropathy
VP-16	IV	Poor	Slow	Predominant, Rapid	As above	Blood pressure, changes, nausea, vomiting, decreased WBC and platelet counts, alopecia secondary leukemia
Alkylating Agents						
Mechlorethamine (Nitrogen Mustard)	IV	Poor	<1%	Probably Nil	Hodgkin's NHL, brain tumors	Nausea, vomiting, myelosupression, fever, vesicant, alopecia, phlebitis
Cyclophosphamide (Cytoxan)	IV or P.O.	Poor	Predomi- Nant slow	Nil	Soft tissue sarcomas, neuroblastoma, Hodgkin's, MHL, Ewing's ALL	Nausea, vomiting, myelosupression, hemorrhagic cystitis, bladder fibrosis, alopecia, sterility, amenorrhea, second malignancy.
Ifosfamide	IV	Poor	Predomi- nant slow		Undergoing clinical trials for use in solid tumors	Similar to Cytoxan

PEDIATRIC CHEMOTHERAPY						
CHEMOTHERAPEUTIC AGENT	**PHARMOCOLOGY**				**CLINICAL USE**	**TOXICITY**
	Adm Mode	**C S F /Brain**	**Excretion Urine**	**Bile**		
Alkylating Agents - Continued						
Busulfan	**P.O.**	**Poor**	**Minority**	**Probably Nil**	**CML, also used in BMT setting for myeloablation**	**No acute toxicity, but with prolonged use: myelosupression, pulmonary fibrosis, hyperpigmentation, cataracts, gynecomastia**
Melphalan	**IV or PO**	**Poor**	**10-65%**		**Used primarily in BMT setting for myeloablation**	**Similar to Mechlorethamine**
Cisplatinum	**IV**	**Poor**	**Predominant slow**	**Probably Nil**	**Osteogenic sarcoma, brain tumors, soft tissue sarcoma, neuroblastoma**	**Renal toxicity with azotemia and electrolyte disturbances, specifically hypomagnesemia, high frequency hearing loss, myelosupression, nausea/vomiting, peripheral neuropathy**
Carboplatin	**IV**	**Good**	**Mostly**	**Nil**	**Same as Cisplatinum**	**Myelosupression, nausea/vomiting, renal toxicity, ototoxicity, peripheral neuropathy (all less severe than with Cisplatinum, except for myelosupression, which is more severe)**
Antibiotics						
Actinomycin-D (Dactinomycin)	**IV**	**Poor**	**Excreted unchgd.**	**Excreted unchgd.**	**Soft tissue sarcomas, Ewing's sarcoma, Wilm's germ cell tumors**	**Vesicant myelosupression, severe nausea/vomiting, mucositis, radiation recall, hyperpigmentation, diarrhea, alopecia**
Doxorubicin (Adriamycin)	**IV**	**Poor**	**Minority (Red urine)**	**Rapid**	**Wilm's neuroblastoma, soft tissue sarcomas, Ewing's and osteogenic sarcoma, ALL, lymphomas**	**Cardinal toxicity both acute and chronic. Have chronic cardiomyopathy with cumulative dose >450 mg., phlebitis, urticania nausea/vomiting, mucositis, myelosupression, alopecia, vesicant, nail bed hyperpigmentation.**
Daunorubicin	**IV**	**Probably minimal**	**Minority**	**Predominate, but slow**	**More commonly used in acute leukemias**	**Similar toxicity to adriamycin**
Bleomycin	**IV, IM, SQ, Intraarterial**	**Poor**	**Predominant Rapid**	**Nil**	**Hodgkin's, NHL, Germ cell tumor**	**Not myelosupressive, dose limiting factor as pulmonary fibrosis. May also see pneumonitis, anaphylasix, mucositis, alopecia, nausea./vomiting, rash with hyperpigmentation and pruitus, nail changes**

CHEMOTHERAPEUTIC AGENT	PHARMACOLOGY				CLINICAL USE	TOXICITY
	Adm Mode	CSF/ Brain	Excretion			
			Urine	Bile		
Antimetabolites						
Methotrexate (Folate Analog)	IV or POC an also give intra-theral	Minimal at low dose	Predomina nt rapid	Rapid	ALL, CNS metastasis, osteogenic sarcoma, lymphomas, intrathecal prophylaxis for ALL	Myelosupression, nausea/vomiting, mucositis, hepatic toxicity, rash/fever, leukoencephalopathy, osteoporosis
Mercaptopurine (6-MP) (Purine analog)	P.O.N.	Fair	Rapid, small fractions excreted	Probably Nil	ALL, AML, lymphoma	Myelosupression, hepatic toxicity, myositis nausea/vomiting, megaloblastic anemia
Thioguanine (6-TG) (Purine Analog)	P.O.N.	Fair	Rapid, small fractions excreted	Probably Nil	ALL, AML	Similar to 6-MP, but with less than severe G2 toxicity
Cytosine Arabinoside (ARA-C)	N or SQ	Good	Rapid	Probably Nil	AML, ALL, NHL, intrathecal therapy and prophylaxis for acute leukemia	myelosupression, mucositis, nausea, vomiting, fever, hepatoblastic changes, hepatotoxity, alopecia, CNS toxicity with high doses
5FU (F-Fluorouracil)	N	Yes	Minimal	Predomina nt	Hepato-Blastoma	Myelosupression, mucositis, nausea/vomiting, diarrhea, skin rash, neurotoxicity, ocular
Miscellaneous						
L-asparaginase	IV	Poor	Minimal	Unknown	ALL NHL	Anaphylaxis, pancreatitis, fever, hyperglycemia, liver toxicity, CNS depression, nausea, vomiting, myelosupression, decreased protein synthesis, decreased fibrinogen levels (Get coagulopathies)
Prednisone/Dex	P.O. IV	Good	Undefined	Probably Predomi-nant	ALL, NHL, Hodgkin's	Obesity, fluid retention, hyperglycemia, hypertension, osteoporosis, hirsutism, cataracts, psychosis, GI irritation
Procarbazine	P. O. IV	Good /Rapid	Predomi-Nant Rapid	Minimal	Hodgkin's, NHL, Lymphoma, CNS tumors	Myelosupression, nausea/vomiting, dermatitis, alopecia, postural hypotension, CNS effects
Hydroxyures	P.O. IV	Poor	Predomin ant Rapid	Probably Nil	CML, NHL	Nausea/Vomiting, depressed blood counts, skin rash
DTIC (acarbazine)	P. O. IV	Poor	Unknown	Unknown	Soft tissue sarcomas, neuro-Blastoma	Nausea/vomiting, myelosupression, flu-like symptoms

MECHANISMS OF ACTION (in general terms)

Vinca Alkaloids	**Bind to tubulin and act as mitotic inhibitors**
Nitrosureas	**Alkylation with cross linking of DNA**
Epipodophyllotoxins:	**Interact with DNA and TYPE II topoisomerase leading to single and double strand DNA breaks**
Alkylating agents	**Covalently binds alkyl group to DNA template, inhibiting DNA synthesis** **Cisplatinum/Carboplatinum, however, platinate rather aklylate**
Antitumor antibiotics	**Avidly bind the DNA by intercalation causing protein associated DNA breaks**
Antimetabolites	**Most directly incorporated into DNA during the synthesis or () phase. Methotrexate, however, is a folate analog and interferes with folate metabolism.**
Miscellaneous	**L-Asparaginase: Catalyzes conversion of L-Asparaginase to aspartic acid and NH3, depleting leukemic, cells of L-Asp.** **Steroids: Receptor mediated lympholysis** **Procarbazine: Alkylation and free radial formation** **DTIC: Alkylation**

Other Drugs Used in Hematology-Oncology

Drug Name	Therapeutic Category	Toxicity	Use
ATG (Antithymocyte Globulin)	**Immunosuppressant Agent**	**Hypersensitivity-anaphylaxis CNS-Seizures, nausea, diarrhea, arthralgia**	**Prevention and treatment of acute allograft rejection; prevention treatment of GVHD following BMT, aplastic anemia.**
Cyclosporin	**Immunosuppressant Agent**	**Cardiovascular: Hyper/hypotension, CNS: seizures, GI discomfort, hepato and renal toxicity tremors, rash**	**Immunosuppressant used with adrenal corticosteroids to prevent graft vs host disease in patients with kidney, liver, heart, bone marrow, transplants.**
FK506	**Immunosuppressant**	**Same as CSA**	**Same as Cyclosporine**
Interferon Alpha 2A	**Antineoplastic agents**	**Flu-like symptoms, pancytopenia, elevated liver transaminases**	**Hairy cell leukemia, aids-related kaposi's sarcoma, multiple unlabeled uses.**
Gamma-1B (gammaglobulin)	**Biological response modulator**	**Same as above**	**Reduce frequency and severity of serious infections associated with chronic granulomatous disease.**
Mesna	**Antidote, Cyclophosphamide, and Ifosfamide induced hemorrhagic cystitis**	**Hypotension, malaise, headache, GI symptoms, nausea, diarrhea, vomiting, ketonuria**	**Detoxifying agent used as a protectant against hemorrhagic cystitis.**
Leucovorin	**Antidote, Methotrexate folic acid derivative**	**Dermatologic -rash, pruritus, erythema**	**Antidote for folic acid antagonists: treatment of folate deficient megaloblastic anemias of infancy, sprue, pregnancy.**
Neupogen (G-CSF)	**Colony stimulating factor**	**Fever, medullary bone pain, splenomegaly, thrombocytopenia**	**To reduce the duration of neutropenia and the associated risk of infection in patients with nonmyeloid malignancies.**
GMCSF	**Colony stimulating factor**	**High fever, hypotension, tachycardia bone**	**As G-CSF**

		pain, GI hemorrhage	
Epogen (Epoetin Alfa)	**Recombinant Human Erythropoietin**	**Hypertension, fatigue, dizziness, rash, nausea, arthralgias, hypersensitivity**	**Anemia associated with end stage renal disease, anemia related to therapy with azt-treated HIV infected patients.**
Ondansetron (Zofm)	**Antimetic**	**Tahycardia/Bradycardia, angina syncope, headache, rash, GI symptoms, transient elevation in liver enzymes.**	**Prevention of nausea, vomiting associated with initial and repeat courses of chemotherapy.**

CHILD ABUSE

I. Physical Signs of Abuse

A. Bruises

1. < 12 mo. old unlikely to have multiple bruises except by non-accidental means

2. Sites suggestive of abuse:

a. Buttocks, thighs, lower back (paddling)

b. Genitalia, inner thighs (sexual abuse)

c. Cheek (slap)

d. Ear lobes (pinch)

e. Upper lip/frenulum, lingular frenulum (forced feeding or attempt to stop crying)

f. neck (choking)

3. Human hand marks

a. Oval grab marks (finger tips)

b. Trunk encirclement bruises (if present, also R/O frx ribs, pneumothorax, subdural hemorrhage, retinal hemorrhage from violent shaking)

c. Linear marks (fingers)

d. Hand print

e. Pinch marks

4. Human bite marks

a. Doughnut or double horseshoe shaped

b. 2-12 teeth impressions

c. Fade rapidly so especially important to get photo early

d. Salivary swabbings

e. May need forensic orthodontist to identify mouth size (adult vs. child)

5. Strap marks

a. Linear bruises (belts or whips)

b. Belt buckle (C, U, or [] shaped)

c. Loop marks (doubled over cord)

6. Bizarre marks

a. Blunt instruments

b. Tattoos

c. Fork mark punctures

d. Circumferential marks (wrists, ankles)

e. Gag marks

7. Multiple bruises at different stages of healing, dating of bruises by appearance (estimates):

Age of bruise	Appearance
< 6 hrs	Red, swollen, tender
6-12 hrs	Blue, swollen, tender
4-10 days	Yellow to green
10-14 days	Brown
2-4 wks	Clearing

**These are estimates and are not enough evidence in court.

8. Normal bruises and external injuries

a. Facial scratches in infants with long fingernails

b. Knee, shin, forehead bruises (and bruises over other bony prominences) in ambulatory child

c. Excoriations in a child with Atopic Dermatitis

B. Burns

1. Inflicted:

a. Cigarette (7 - 10 mm - should all be the same size)

b. Match tip/incense

c. Iron/curling iron

2. Forced contact with:

a. Heating grate/radiator

b. Hot plate

3. Scalding from forced immersion:

a. Buttocks/perineum (look for doughnut of sparing)

b. glove/stocking burns

C. Head injuries

1. Scalp swelling/bruises

2. Traumatic alopecia

3. Subgaleal hematoma

4. Skull frx

5. Subdural hematoma: from direct blow or shaking, never spontaneous

6. "Shaken baby syndrome"

a. Retinal hemorrhages - if present make sure Staff ophthalmologist signs consult.

b. Subdural hematoma.

c. Circumferential thoracic bruises, rib fractures- especially posterior.

d. Assoc. long bone frx in 25% - do skeletal survey!

D. Abdominal injuries- may cause shock from acute blood loss

1. Compression of viscus against vertebral column

2. Pummeling blows by blunt objects, may see abodominal bruises in periumbilical region, or over liver or spleen.

3. Rarely discolored

4. Injured sites:

a. Ruptured liver or spleen

b. Intestinal perforation

c. Intramural hematoma of duodenum (most common)

d. Ruptured blood vessel (rare)

e. Pancreatic injury (pseudocyst, traumatic pancreatitis)

f. Kidney injury (rare)

E. Bone injuries

1. Spiral fracture (fx.) or transverse fx. Spiral fx. more common in accidental as well as NAT. Consistent with described method of injury being a twisting injury.

2. Any fx. in a non-ambulatory child

3. Hx and mech of injury incompatible

4. Chip or cornier fx. of metaphysis (pathognomonic, especially if multiple), bilateral long bone fxs.

5. Subperiosteal bleeding, subperiosteal new bone formation, or bone bruise

6. Fx. in different stages of healing

7. Repeated fx. to same site

8. Rib fx. - highly suggestive in child < 2 yrs (post. > lat. > ant.)

F. Failure to thrive due to underfeeding

1. Underweight

2. Failure to gain weight at home

3. Rapid weight gain out of home

4. Ravenous appetite

5. Deprivation behaviors

G. Additional signs of physical abuse

1. Delay in seeking medical attention

2. History incompatible with injury or the history changes!! Or you receive different histories from different people and they don't make sense.

3. Injuries on the back

4. Injuries on the back of the arms (defensive)

5. Excessive clothing (attempt to hide wounds)

6. Child reports abuse: **do not ignore or minimize**

7. Repeated poorly explained trauma.

II. **Reporting**

A. Whom to call:

1. Child protective services 1-800-252-5400. For **Air Force** cases, consult with senior pediatric resident or staff, notify Dr. Davis, WHMC pager 513-7806, and call family advocacy (FA)@ ext. 2-5967, after hours WHMC pager #0932. If an active duty USAF member is involved, also call Office of Special Investigations (OSI)@ ext. 3-1852, after hours beeper number available by contacting the ER. If an on-base occurrence call Security Police 2-7135. For **Army** cases: contact LTC. Reginold Moore at pager 1-877-906-4441, home phone 651-6680, FA @ WHMC as above if pt at WH or Social Work at BAMC if pt. at BAMC, and if and active duty member is

involved the Criminal Investigations Division (CID) at 221-1763/4. If occurrence on-post call For Sam Military Police 221-1221.

2. If the case is determined to be suspicious of abuse or is documented abuse:

a. Admit to Peds service if unable to determine if child has a safe place to go.

b. If patient is a dependent of retired Air Force, then family advocacy will not be involved and Child Protective Services (CPS) 532-2873, will need to be notified. If retired Army, both CPS and FA should be notified.

c. Remember, it is the job of FA or CPS to determine if the home is safe in questionable cases. They need to talk with guardians and make that determination - not pediatrics.

B. The individual who discloses that abuse may have occurred is required BY LAW to report

C. Explain to the parents in a non-judgmental manner that you're required by law to report any injury that may have been non-accidental regardless of your personal opinion about the injury or the parents.

III. Documentation

A. Carefully document in medical record:

1. Quotes from parent and child regarding circumstances of injury.

2. All injuries (use diagrams).

3. In all Army cases, complete a PCAN form (located in Ward work room.

B. Additional studies:

1. PT/PTT & CBC if indicated in cases of bruising

2. Skeletal survey is indicated in all children when there is concern of physical abuse. A repeat skeletal survey should be performed a week later if the initial survey is concerning for subtle findings.

3. Head CT/MRI, other radiologic procedures, ophthalmology exam as indicated.

C. Photos

1. Call med photo; someone can be called in 24 hours a day.

2. Do not delay as evidence may fade

3. Get photos of all injuries, as well as a whole child picture

4. Serial photos of evolving injuries

IV. Disposition

A. CPS will place a legal hold prohibiting the parents from taking the child home if necessary. Again CPS will make that determination, not Pediatrics.

B. Hospitalize if medically indicated and Rx as appropriate (document injuries before Rx if possible)

C. If no medical indication for admission, but cannot send home, will need to be admitted until a proper placement can be made.

D. If no suspicion that child is in further danger (eg convincing story that perpetrator is not in home), consider sending child home with F/U. If in doubt, hospitalize. Clear the decision through CPS, attending staff, and child abuse staff (Dr. Davis-USAF/ Dr. Moore-USA).

E. If hospitalized and legal hold placed, DO NOT discharge until CPS has cleared child for discharge. A note to that effect must be placed on chart, containing name of CPS worker contacted and time. Discharge order must be specific in regards who is allowed to take child (eg: parents, name of foster parent, etc.) Foster parents must show identification.

V. Child Sexual Abuse

A. Acute - if said to have taken place in last 48-72 hours.

1. If female $\geq$ 12 years old - then should be evaluated by OB-GYN.

2. If female < 12 years old - then should be evaluated by Peds.

a. If there is a possibility of transmission of STD (i.e. penetration or oral sex) then rape kit should be completed.

b. Rape kits are in ER and self explanatory.

c. If no chance of STD (i.e. fondling breasts), then full exam with careful documentation needs to be done, but no need for cultures.

d. If offender is Active Duty, then FA, CPS, Military Police, and Office of Special Investigations (USAF) or CID (USArmy) need to be notified. (see #s sect II,A,1.)

e. As above, hospitalize if patient does not have a safe place to return.

B. Chronic or Distant - if abuse took place in the distant past.

1. If female $\geq$ 12 years - OB-GYN to evaluate. Defer to better setting than ED. If teenager, obtain informed consent from teen.

2. If female < 12 years or male - full evaluation (for subtle signs of old trauma) may be scheduled with child abuse staff. Defer exam to better setting than ED.

3. Again FA, CPS and possibly OSI or Military Police should be notified.

C. Sedation may be considered in a child unable to cooperate with an exam.

COAGULOPATHIES

I. DDX
   A. Hemophilia A
   B. Hemophilia B
   C. von Willebrand's disease
   D. Other rare hereditary disorders:
      1. Factor I: Afibrinogenemia, hypofibrinogenemia, and dysfibrinogenemia.
      2. Factor II: Hypoprothrombinemia & dysprothrombinemia.
      3. Factor V: Parahemophilia. Autosomal (1q) recessive.
      4. Factor VII: Very rare autosomal (13q) recessive.
      5. Factor X: Autosomal (13) recessive.
      6. Factor XI: Hemophilia C Autosomal (4) recessive.
      7. Factor XII: Autosomal (6) recessive.
      8. Factor XIII: Very rare autosomal (subunit A on 6p, subunit B on 1q) recessive.

   E. Acquired bleeding disorders:
      1. Liver disease:
         a. Site of synthesis of most coagulation factors, predisposing to clinical bleeding.
         b. Prolonged PT, aPTT, TT. FVIII nl or increased.
         c. Presents with hemorrhage, HSM and jaundice.
      2. Vitamin K deficiency:
         a. Cofactor for γ-carboxylation for C-terminus of protein, required for function. Factors II (prothrombin), VII, IX and X, and Proteins C and S.
         b. Requires normal bacterial flora for intestinal absorption.
         c. Hemorrhagic disease of the newborn, cystic fibrosis, biliary atresia, obstructive jaundice, small intestine dysfunction, rarely with antibiotic therapy.
      3. Cyanotic congenital heart disease: Polycythemia associated with poor coagulation function.
      4. Renal failure:
         a. Platelet function is abnormal in uremia.
         b. DIC in acute renal failure, allograft rejection, and chronic renal insufficiency.
         c. Protein loss in nephrotic syndrome may associate with hemorrhage or thrombotic complications.
      5. Anticoagulants:
         a. Acquired hemophilia-in adults with autoimmune antibodies to factor VIII. Presents with severe life threatening hemorrhage, prolonged PTT which does not correct on mixing study.
         b. Lupus anticoagulant in patients with SLE. Predisposes to DVT but not bleeding.
      6. Disseminated intravascular coagulation (DIC):
         a. In the newborn: intrauterine infections, maternal toxemia, abruptio placentae, severe respiratory distress syndrome, and necrotizing enterocolitis.
         b. Most common causes in childhood: fulminant bacterial sepsis, disseminated viral diseases, and massive head injuries.
         c. Usually associated with:

1) fragmented RBCs,
2) low or decreasing platelet count,
3) prolonged PT and APTT, and low or decreasing fibrinogen. Confirm by measuring fibrin split products (FSP's), or D-dimers
4) Factors V and VIII (decreased).
5) Clinical manifestations: bleeding and/or thrombosis. Minimal until consumption of platelets and coagulation factors has occurred.

7. Thrombocytopenia:
   a. Platelet production failure: Generalized bone marrow failure due to leukemia, myelodysplasia, aplastic anemia, megaloblastic anemia, uremia or marrow infiltration.
   b. Selective megakaryocyte depression due to drugs, alcohol, chemicals or viral infections.
   c. Abnormal distribution of platelets: Splenomegaly.
   d. Increased destruction of platelets:
      1) Immune: neonatal alloimmune thrombocytopenia, post transfusion, ITP, SLE, post-infection, AIDS, post-BMT.
      2) Drug induced.
      3) DIC, including hemolytic uremic syndrome, and Kasselbach-Merrit syndrome.
   e. Dilutional loss: Massive transfusion of stored blood.

8. Qualitative platelet disorders (disorders of platelet function):
   a. Characterized by a prolonged bleeding time out of proportion to the platelet count.
   b. Hereditary forms include: Bernard-Soulier syndrome, Wiskott-Aldrich syndrome, Chediak-Higashi syndrome, gray platelet syndrome, von Willebrand's disease, and others
   c. Most common acquired form is secondary to drug use (e.g. aspirin, NSAIDs).

II. Diagnosis

A. History:
1. Trauma
2. Headache (consider intracranial bleed).
3. Prior bleeding (type, extent, and duration).
4. Careful family history
5. Medication use (particularly aspirin).

B. Pattern of bleeding: (see table 3)
1. Mucocutaneous bleeding (petechiae, ecchymoses, epistaxis, and GI & GU bleeding) suggestive of platelet disorder.
2. Palpable purpura think factor def or vasculitis with other systemic illnesses, not associated with thrombocytopenia.
3. Bleeding into potential spaces such as joints, between facial planes and into the retroperitoneum is characteristic of factor deficiencies or warfarin toxicity.
4. Bleeding from multiple sites to include both mucocutaneous and potential space bleeding may be seen in DIC.
5. Prolonged menstrual bleeding only think von Willi.

C. Physical Examination:
1. Evaluate hemodynamic status.

2. Identify source of bleeding. Early hemarthrosis will show only pain with ROM, or bearing wt. All acute musculoskeletal pain is assumed secondary to occult bleed when factor level is low in a hemophiliac.
3. Look for other sites of blood loss (e.g. bruising, petechiae). Assess wound sites for oozing (IV sites, umbilical cord stump).

D. Screening assays:
1. CBC: check plt count, assess for microangiopathic anemia.
2. Platelet count usu adequate if> 50,000. Platelet counts < 10,000 may lead to spontaneous hemorrhage.
3. Prothrombin Time (PT): identifies coagulation abnormalities of the extrinsic & common pathways; requires VII, X, V, II, and I.
4. Activated Partial Thromboplastin Time (aPTT): identifies coagulation abnormalities of the contact phase and the intrinsic and common pathways; requires XII, XI, IX, VIII, V, II, and I
5. Mixing studies: Pt's blood and nl blood mixed, if PT and PTT correct then it is a factor def, if not it is an inhibitor.
6. Bleeding Time: Unreliable test in children < 4yrs. In expert hands, a bleeding time > 15 minutes is frankly abnormal and indicates:
   a. Severe impairment of platelet function.
   b. Very low blood levels of vWF.
   c. Afibrinogenemia or severe Factor V deficiency, or
   d. Functional platelet problems.
   e. Bleeding times between 8 and 15 minutes are usually associated with moderately low plasma vWF. Antiplatelet drugs, lupus-like anticoagulant, Factor XI deficiency.
7. Fibrinogen level, FSP's, D-dimers.
8. Thrombin Clotting Time/Thrombin Time Assay (TCT/TT): Isolates the common pathway. Requires fibrinogen especially. Heparin will inhibit this test.
9. vonWilli screen: ristocentin cofactor, factor 8 activity, and either factor 8 or vonWilli antigen

E. Confirmatory tests:
1. Factor Assays are reported as % activity compared to controls.
2. Quantitative assays measuring factor levels.
3. Gene analysis only available for known genetic abnormalities. Usually requires a proband have a defined abnormality, then the test can be applied to other family members as a screen.

III Treatment
A. General Principles:
1. Stabilize patient.
2. Utilize mechanical methods of hemostasis (e.g.: topical thrombin, cauterize bleeding vessels, oral surgery, etc.)
3. Give directed therapy for factor or platelet correction.
4. Pain control.
5. Avoid aspirin containing products.

B. Mucosal bleeds:
1. Local applications of GELFOAM®. Afrin for epistaxis, repeat every 20 min for bleeding as BP tolerates.
2. AMICAR® (epsilon aminocaproic acid) prevents clot dissolution in mouth bleeds. Contraindicated in hematuria or DIC. Dose = 100 mg/kg IV or PO q 6 hr (up to 24 gm/day).

C. Blood component therapy:

1. Fresh frozen plasma (FFP).
   a. Contains all blood coagulation factors (by definition, 1mL = 1 unit of factor activity). Useful when diagnosis is unknown.
   b. Indications. (WHMC 7/99)
      1) Prophylaxis prior to procedures PT > 17, aPTT > 66
      2) Bleeding with acquired coagulopathy due to a deficiency of coagulation factors.
      3) Massive blood transfusion > 1 blood volume with evidence of a coagulation deficiency and bleeding.
      4) Reversal of warfarin effect.
      5) Congenital deficiency of Factor II, V, X, XI, or XIII.
   c. Dose: 10-ml/kg-body weight. Monitor with PT and aPTT.
   d. Remember: 6 units of platelets or 1 platelet pheresis unit delivers 1 unit of FFP.
   e. Contraindicated as a volume expander (JAMA, March 9, 1994, p.778).

2. Cryoprecipitate:
   a. 1 unit (9 to 16 mL) contains 80-120U Factor VIII and vWF, 200-300 mg fibrinogen, and 40-60U Factor XIII. Insignificant amounts of other factors.
   b. Indications:
      1) Hypofibrinogenemia. Most cases DIC so FFP also needed.
      2) VonWillebrand disease if DDAVP not effective.
      3) Hemophilia A when treated commercial factor VIII concentrates are not available.
   c. Dose:
      1) Congenital hypofibrinogenemia: 1 bag/5 kg body weight qod.
      2) Consumptive hypofibrinogenemia: 1 bag/5 kg body weight. Monitor fibrinogen level to guide frequency.
      3) vonWillebrand disease: 1 bag/10 kg body weight.
      4) Hemophilia A: Number of Bags of Cryo = [(Plasma/Volume in mL x % Increase in Factor VIII Needed)/100]/80.
      5) See Factor VIII below for guidelines.

3. Platelets:
   a. Indications (WHMC 7/99)
      1) Decreased platelet production and/or increased platelet.
      2) Bleeding prophylaxis for counts below 5000 ($5X10^9$).
      3) Between 5000 and 20,000 give on the basis of significant bleeding risk.
      4) Congenital platelet dysfunction: weigh risk of alloimmunization vs. bleeding Consider pharmacological methods of enhancing platelet functions (e.g., DDAVP).
      5) Acquired platelet dysfunction (e.g., drug-related etc.).

   b. Dose: 1 unit platelets/M^2 body surface area incrementally raises platelet count by $10x10^9$/L.

D. Blood Derivative Therapy:
   1. Human Factor VIII concentrate:
      a. One unit/kg body weight of Factor VIII will raise plasma activity by 2%.
      b. Biological half-life: 8 to 12 hours.
      c. Prepared from as many as 22,000 donors.
      d. Indications:
         1) Severe Factor VIII deficiency, or mild to moderate Factor VIII deficiency with inadequate response to DDAVP.

2) Only one product, HUMATE-P®, (Armour, Kankakee, Illinois), contains adequate amounts of vWF for treatment of vonWillebrand disease, and is preferred over cryoprecipitate.
3) Dosage depends on type and severity of bleeding (Table 1).
4) Available products: (Table 2).

2. Porcine Factor VIII concentrates: for patients with Factor VIII deficiency and inhibitors. Dose the same as human factor VIII.
3. Factor VIIA: FDA approved for use in patients with VIII inhibitors. Heme consult to set up and give (has very short half life and requires continuous infusion)
4. Prothrombin complex concentrate (Factor IX complex):
   a. One unit/kg body weight of Factor IX will raise plasma level by 0.5% to 1.0%.
   b. Biological half-life: 10.5 to 13.5 hours
   c. Indications:
      1) Factor IX deficiency.
      2) Factor VIII deficiency with inhibitors (would be first choice of treatment)
      3) Cautions:
         a) Never administer simultaneously with AMICAR® (results in hypercoagulable state with risk of thrombosis).
         b) Risk of thrombosis and DIC is high in patients with liver disease.
         c) Dosage usually 75-80 units/kg every 12-24 hours.
         d) Available products: (Table 2).
5. Activated prothrombin complex concentrates (AUTOPLEX®, FEIBA®):
   a. For use only in patients with inhibitors.
   b. Dose: 50 to 100 U/kg q12hours.
   c. May cause DIC.
6. Purified and recombinant Factor IX concentrates.
   a. Indications: first line therapy for factor IX deficiency
   b. Recombinant Factor IX (Benefix®) requires 20% dose increase.

E. Desmopressin (DDAVP, STIMATE®)
1. Transiently increases in all components of the FVIII, increases plasminogen activator.
2. Indications:
   a. Mild to moderate hemophilia A
   b. VonWillebrand disease with known previous response to DDAVP.
      1) Use in type IIb vonWillebrand disease will result in severe drop in platelets.
      2) Dose: 0.3 micrograms/kg diluted in 50cc normal saline, IV over 30 minutes.
      3) Also approved for intranasal administration 3 microgram/kg.
      4) Can be repeated at 12 hour intervals, BUT decreasing response is noted with each successive dose.
      5) Causes a rise in plasminogen activator.
      6) For oral bleeding use AMICAR®. 100 mg/kg q 6hr x 4-7 days.

Table 1: RECOMMENDED DOSAGES OF FACTOR VIII* and IX

Indications	Initial Dose (Factor VIII, U/kg)	Initial Dose (Factor IX, U/kg)	Other Treatment
Routine dose			
E.g.: sutures, joint, muscle, mouth	20-25	30-40	Amicar with mouth bleeds
Major Dose			
E.g.: Head, GI, prior to invasive procedure (ex LP), and large joint bleeds (hip, knee)	40-50 Repeat (q12-24)	40-50 (Add 20% if using Benefix®) Repeat (q 24-48)	Ice packs, Non-weight bearing, light weight splint, Complete bed rest for iliopsoas hemorrhage

****In individuals who have mild hemophilia A, DDAVP (Desmopressin®) is the treatment of choice rather than factor VIII concentrates.**

Adapted from Lusher JM, Warrier I: Hemophilia. Pediatrics in Review 12:275, 1991. And Emergency Care for Patients with Hemophila, by Nursing Group of Hemophilia RegionVI, 1999

Table 2. PRODUCTS AVAILABLE FOR TREATMENT OF HEMOPHILIA A, HEMOPHILIA B, VON WILLEBRAND'S DISEASE.

Product	Manufacturer	Method of Viral Inactivation
	FACTOR VIII	
Intermediate Purity		
Koate Hp®	Alpha	Solvent/detergent
Humate-P®	Armour	Pasteurized (10 hr, 60°C)
Monoclonal Purified		
Monoclate-P®	Amour	Monoclonal antibody-purified plus pasteurization (10hr, 60°C)
Hemofil-M®	Hyland	Monoclonal antibody-purified plus solvent/detergent
Method-M®	American Red Cross	Monoclonal antibody-purified plus solvent/detergent
Porcine VIII		
Hyate C®	Porton	Porcine factor VIII
Recombinant VIII		
Recombinate®	Baxter-Hyland	None/ Synthetic (uses pasteurized human albumin in prep)
Bioclate®	Centeon	Same
Kogenate®	Bayer	Same
Fresh blood product		
Cryoprecipitate	Local blood blank	None (donor screening tests only)
DDAVP	Rorer	None/Synthetic preparation
	FACTOR IX	
Prothrombin Complex		
Konyne®	Cutter	Dry Heat (80 hr, 68°C)
Proplex T®	Baxter Hyland	Dry Heat (150 hr, 60°C)
Activated Prothrombin Complex		
Autoplex T®	Baxter Hyland	Dry Heat
FEIBA®		
Profilnine HT®	Alpha	Heated in an organic solvent [N-Heptane] (20 hr, 60°C)
Monoclonal IX		
Mononine®		
Alphanine ®	Alpha	Monoclonal antibody-purified plus heated in organic solvent
Recombinant IX		
Benefix®	Genetics Institute	None/ synthetic (No human albumin in prep or storage)
Fresh blood product		
FFP	Local blood bank	None (donor screening tests only)
	FACTOR VII A	
Recombinant VII A		
NovoSeven®	NovoNordisk	None/ synthetic (No human albumin in prep or storage)
	PRODUCTS FOR VON WILLEBRAND'S DISEASE	
DDAVP	Rorer	None/Synthetic preparation
Humate-P®	Armour	Pasteurized (10 hr, 60°C)
Cryoprecipitate	Local blood bank	None (donor screening tests only)

Adapted from Julius C, Westphal RG: The Safety of Blood Components and Derivations, Hematology/Oncology Clinics of North America 6:1071, 1992.

Table 3. DIFFERENTIATION OF PLATELET-VASCULAR ABNORMALITY FROM COAGULATION PROTEIN DEFICIENCY BY HISTORY AND PHYSICAL EXAMINATION

	Platelet or Vascular Abnormality	Coagulation Factor Deficiency

Ecchymoses	Small and superficial	Large and deep (often palpable)
Petechiae	Frequent	Never
Mucosal hemorrhage	Frequent	Uncommon in hemophilia: frequent in acquired disorders
Muscle, joint, or internal hemorrhage	Uncommon	Frequent
Prolonged bleeding from cuts and scratches	Frequent	Rare
Bleeding with trauma or surgery	Immediate; stops with pressure	Delayed (1-2 days later); does not stop with pressure

CROUP (LARYNGOTRACHEITIS)

I. Introduction

A. Viral infection causing subglottic and tracheal swelling.

B. Most common cause of stridor in children.

C. Parainfluenza virus (I) recovered in 50%. Additional causes: Parainfluenza (II & III), influenza, RSV, adenovirus, measles, EBV.

D. More common in fall and winter.

E. Usual age 3 mos - 5 years (mean = 18 months), male>female

II. Pathophysiology

A. Virus invades epithelium of the nasopharynx with local spread to larynx and trachea.

B. Epithelial damage causes mucous production and loss of ciliary function.

C. Edema of the subglottic larynx. A small amount of edema within the ring of the cricoid cartilage leads to a large decrease in air flow.

D. Fibrinous exudate partially occludes the lumen of the trachea.

III. Clinical Manifestations

A. Insidious onset of fever, coryza, cough and sore throat.

D. Stridor and barking cough develop on day 2-3.

E. Sxs usually last 4 days after seeking medical attention, but may last total of 7-14 days

F. May be unable to maintain PO intake.

G. Majority appear mildly to moderately ill.

F. Fever is quite variable (100 to 105 F).

G. Minimal to severe respiratory distress with varying amounts of tachypnea, dyspnea, stridor, flaring and retractions, symptoms usually worse at night.

H. Lungs are clear with transmitted upper airway sounds; wheezes occur if there is concomitant lower airway involvement.

I. Rarely cyanotic.

IV. Lab/X-ray - rarely abnormal or of diagnostic value.

A. WBC mildly elevated with predominance of PMN's.
B. The "steeple sign", a manifestation of subglottic narrowing, seen on PA X-ray of the neck, is neither sensitive nor specific.

V. Differential diagnosis includes:

A. Epiglottitis, foreign body, retropharyngeal or peritonsillar abscesses, bacterial tracheitis, congenital or acquired subglottic stenosis, hemangioma, laryngeal papillomatosis, paraquat poisoning and laryngeal diphtheria.

B. The history is extremely important. It may be the only source suggestive of another process such as a foreign body.

C. Recurrent croup or prolonged (>10-14 days) stridor should raise suspicion of airway anomalies.

D. Spasmodic croup: similar findings, but recurrent episodes with acute onset and more rapid resolution, often without other viral sxs, usually found in atopic patients.

E. Secondary bacterial tracheitis should be suspected in patients whose clinical course does not improve within several days.

VI. Management

A. Make the patient comfortable. Avoid unnecessary procedures that will increase anxiety and worsen respiratory status.

B. Contact isolation. Pulse oximetry.

C. Rehydration. Account for ongoing losses such as tachypnea and fever.

D. Medical management.

1. Mist therapy:

a. Water droplets moisten mucosa and decrease viscosity of secretions.

b. Temperature not important (although cold mist may provoke bronchospasm in patient with RAD).

c. Administer with O_2 in hypoxic patient.

2. Racemic Epinephrine

a. Vasoconstrictive effects decrease mucosal edema.

b. 2.25% sol'n 0.05 cc/kg (0.5 cc max dose) in 3 cc NS.

c. Hold for HR > 180 (unless tachy from respiratory failure).

d. Potential rebound phenomenon: initial improvement followed by deterioration over the next 1-2 hours can occur and should be anticipated. The deterioration is usually not to a worse state than the child’s pre-racemic epinephrine baseline.

e. Contraindications: subvalvular aortic stenosis, pulmonary stenosis, Tetralogy of Fallot

3. Corticosteroids

a. Edema decreased by suppressing local inflammatory reaction, decreasing lymphoid swelling and decreasing capillary permeability.

b. Dexamethasone (Decadron) 0.6 mg/kg IV/IM/PO. 1-4 doses given q6hr.

c. Budesonide (Pulmicort) 0.5mg nebulized BID (alternative to Decadron)

4. Antibiotics not indicated.

5. Sedation contraindicated.

E. Intubation in respiratory failure (< 5% of hospitalized patients).

1. Call ENT and anesthesia for help in intubation.

2. Preferably done in OR under controlled conditions.

3. Endotracheal tube (ETT) should be 1-2 sizes smaller than normally used.

4. ENT should be prepared for emergent bronchoscopy or tracheostomy.

5. Once safely intubated orally, may switch to more secure nasotracheal tube if desired.

6. CXR to verify tube position.

7. If needed may sedate or paralyze and use mechanical ventilation.

8. Extubation best done when significant air leak develops (2-6 days after intubation).

9. Decadron has been used to help decrease edema; 0.25 - 0.5 mg/kg IV q 6-12 hours prior to the extubation attempt and may be given again at extubation then prn.

F. Indications for admission (> 85% can be managed as outpatients).

1. Significant respiratory compromise.

2. Dehydration.

3. Recurrent Emergency Department or clinic visits in 24 hours.

4. Other situations, which <u>may</u> require admission:

a. Patient < 1 year old.

b. Patient lives a long distance from the hospital or has inadequate transportation.

c. Inadequate observation or follow-up is likely.

d. Significant parental anxiety exists.

G. Criteria for discharge from the clinic or Emergency Department:

1. The episode must be the first visit to the hospital for croup.

2. If the patient has received a racemic epi. neb., steroids, and is in no respiratory distress 2.5 hours after the drugs were administered, then they may be considered for discharge home.

3. Phone follow-up must be assured a few hours later. Documentation of the phone call should be performed.

4. If any doubt exists for the fulfillment of any of these criteria the patient should be admitted.

DIABETIC KETOACIDOSIS

Definition: A metabolic state in an insulin dependent diabetic caused by insufficient insulin and excess of glucagon. It is characterized by hyperglycemia with blood glucose concentrations usually exceeding 300 mg/dl, ketonemia with total ketones positive at a 1:2 dilution in the serum or a positive sodium nitroprusside reaction with undiluted urine (Acetone, ketostix, etc.), acidosis with a pH of less than 7.30, and serum bicarbonate level of less than 15 mEq/l. The insulin lack allows unchecked ketogenesis and gluconeogenesis to occur with additional glucose released through unimpeded glycogenolysis. The elevated glucagon/insulin ratio promotes ketone body formation, glycogenolysis and gluconeogenesis.

Treatment Regimen for DKA in Children

I. Admit to PICU if: under 3 years of age, hemodynamically unstable, alteration in mental status, pH < 7.2, abberation in vital sign other than mild tachycardia from IVVD.

A. History

1. Known diabetic? Missed insulin dose? Insulin Pump?

2. Emotional or physical trauma?

3. Infection? ASA or other ingestion? Known weight loss? Pregnancy? Appendicitis?

B. Physical Examination

1. Vital Signs, Level of consciousness

2. Respiratory status: depressed or Kussmaul? (fast and deep)

3. Extent of dehydration: BP, skin turgor, mucous membranes. (Most patients with DKA will be at least 10% dehydrated.) Patients are total body H_2O depleted as extracellular glucose causes an osmotic diuresis.

4. Flushed face? Acetone (fruity) breath?

5. Source of infection?

6. Abdominal pain

a. Commonly seen as a non-specific symptom accompanying metabolic acidosis

b. If persistent, consider diff. dx. of "acute abdomen": i.e. appy, pyelonephritis, PID, etc.

c. Severe abdominal pain may be associated with a transient elevation of pancreatic (? salivary) enzymes in the absence of documented pancreatitis.

C. Laboratory Data

1. Blood

   a. Dextrostix--every 30 minutes until dextrose is added to IV fluids, then may go to every one hour until stabilized. Glucose often drops significantly with initial fluid given in ED. **Watch rate of fall**--average rate is 75 mg/dl/hr, but may be as high as 300 mg/dl/hr. **We desire a fall of 50 - 100 mg/dl/hr**, add D5 as needed to maintain desired rate of fall.

   b. Serum glucose--on admission and then every 4 hours

   c. Serum ketones--on admission

   d. Urine ketones--on admission and every void; may actually increase even as acidosis is improving due to a shift of Beta-hydroxybutyrate to acetoacetate and acetone.

   e. pH--venous blood gas sufficient to follow level; follow every 2 hours. Occasionally ABG (A-line) is needed.

   f. Serum electrolytes--follow every 4 hours.

   g. BUN/Creatinine--BUN every 4 hours; creatinine on admission.

   h. Serum calcium/phosphate--follow every 4 hours.

   i. Serum magnesium--on admission and every 8 hours.

   j. Serum osmolarity--follow every 4 hours by lab; and every 1-2 hours initially by calculation: 2Na + [glucose/18] + [BUN/3]; normal is < 300. Don't let serum osmolarity fall too fast, ie, too rapid a fall in glucose (see a. Dextrostix above).

   k. Vital signs including mental status exam every 30 min - 1 hour initially. Cerebral edema most often occurs within first 12 hours.

   l. B-HCG if pregnancy is possible.

2. EKG - on admission and monitor throughout ICU stay. Screen for hyperkalemia (peaked T waves) and hypokalemia (flattened T waves).

3. Look for source of infection and consider:

   a. Blood cultures

   b. Chest X-ray

   c. Urinalysis/Urine C&S

   d. Lumbar Puncture

   e. Other cultures as history and physical exam suggest

4. **If NEW diabetic, draw the following :**

   a. Anti-insulin antibodies

b. Anti-islet cell antibodies

c. C-peptide

d. HbAlc

e. TFT's, anti-thyroid antibodies.

5. Record all lab values on a flow sheet (flow sheet at end of chapter may be enlarged on a copy machine and used).

II. Treatment

A. Insulin

1. No initial bolus.

2. Start drip (0.5 units Regular insulin / cc NS) at 0.1 units/kg/hr (piggybacked into main IV line)

3. Continue drip until serum $HCO3^-$ is > 15 mEq/L, pH > 7.30.

4. Record all changes on a flow sheet.

5. If glucose is dropping too quickly, titrate up glucose delivery and follow the glucose more closely. Try NOT to stop or decrease the insulin drip.

6. Aim to keep B.G. 150-250 until acidosis resolved, pH> 7.30, HCO_3 15.

B. Fluids and Electrolytes

1. Initial Bolus

a. No fluid bolus is necessary in a warm, well-perfused pt with normal LOC. If the patient is slightly cool, give 10 cc/kg NS or 20 cc/kg of NS if the patient in shock, repeat as necessary to restore circulation.

****If the patient is unstable remember your ABC's and intubate / oxygenate !!**

b. Further fluid boluses should be guided by the CVP, BP; not given empirically.

2. Maintenance and deficit replacement

a. After initial rehydration, start 3/4 NS with 30 Meq/L KAc and 30 Meq/L Kphos (don't add K until after first void and K < 5.5) at 2.5 x maintenance x 24 hours or until acidosis resolves (whichever comes first), then decrease to 1 to 1.5 x maintenance.
b. Glucose should be added to the fluid regimen once patient's glucose approaches 250-300 mg/dl to prevent hypoglycemia and hypoosmolality. This is done by hanging second bag w/10%Dextrose with identical solute solution to that above and titrate the rates of each to deliver

appropriate glucose concentration to continue slow decrease in serum glucose and then stabilazation in 150 – 200 range without any manipulation of insulin drip. **Try to avoid manipulation or stopping of insulin drip.** This 2-bag system, one w/glucose (10%) + solute, and other with just identical solute allows titration between D_0 and D_{10} without getting new bags from pharmacy. It save $$ and time.

(1). If patient is hypoglycemic but alert you may give orange juice.

(2). If patient is hypoglycemic and unconscious may give glucagon (< 10 kg use 0.1 mg/kg, > 10 kg use 1 mg/dose IV, IM or SQ) and glucose, (0.5 g/kg of D25W) and increase glucose concentration in IV. Stop the insulin infusion temporarily, resuming it when soon as the hypoglycemia has resolved. (Insulin is needed to clear the acidosis, even with a normal glucose).

c. Goal is replacement of deficit over 48 hours.

d. Most patients will resume enteral diet within 24 hours and complete correction on own enterally.

e. Frequently reassess the patient's neurologic, fluid, and laboratory status. Gradual improvement in neurologic status, resolution of metabolic acidosis, and avoidance of iatrogenic hypoglycemia and electrolyte abnormalities are the main goals of monitoring and therapy.

C. Flow sheet: A flow sheet of all labs and interventions, such as changes in IVF or insulin rates is an invaluble tool in following the patient's progress and should always be at the bedside.

Recommendations for frequency of lab tests, checks of vital signs, etc. are only guidelines - There may be situations where more frequent testing and documentation is required.

D. Bicarbonate Therapy

1. Sodium bicarbonate is **NOT indicated** in DKA and has been associated with an increase risk for cerebral edema.

a. HCO3 is produced endogenously with appropriate insulin therapy by oxidation of ketoacids.

b. Alkalosis shifts the O2-dissociation curve to the left decreasing oxygen release to the tissues thus increasing lactic acidosis.

c. Increases potassium needs by accelerating the entry of potassium intracellularly.

d. Worsens cerebral acidosis.

e. Causes CNS hypoxia in laboratory animals w/DKA

f. Alkalosis decreases ionized Calcium.

2. Complications with pH at 7.0 or less

(1). Diminishes respiratory minute volume

(2). May produce hypotension with peripheral vasodilatation

(3). Impairs myocardial function and increases the risk of arrhythmias.

(4). May be a factor in insulin resistance

3. Consider using bicarbonate for cardiac arrest, life-threatning hyperkalemia or arrythmias at pH of 7.0 or below

Interpretation of Laboratory Tests

A. Ketones

1. Acetest measures acetoacetate (and acetone) only, whereas B-hydroxybutyrate is the major (80%) ketone body in early DKA.

2. In the severely hypoxic patient almost all ketone bodies may be B-OHB and Acetest negative

3. Urine ketones may paradoxically increase even in the face of improving serum acidosis as B-OHB is converted to acetoacetate.

B. Sodium

1. Hyperglycemia falsely lowers the serum Na: for each 100 mg/dl increase in serum glucose over 100 mg/dl, there is a decrease in serum sodium of 1.6 mEq/L.

2. Significant hyperlipidemia also falsely lowers the serum sodium. The Na decreases 2 mEq/L for each 1.0 gm/dL increase in triglycerides.

3. True Na = measured Na + 1.6 X [(glucose - 100)/100]. Failure of the “true” or “corrected” Na to increase with treatment may suggest that excess free water is present and may increase the risk of cerebral edema. Be especially concerned if hyponatremia was present at the start of treatment as the risk of cerebral edema may be increased further.

C. Potassium

1. Acidosis causes increase in serum potassium secondary to the intracellular to extracellular shifts. This scenario may not be a mechanism of relative importance in DKA. With a lack of insulin, potassium moves from the ICF to the ECF. With the osmotic diuresis, potassium can be lost in great quantities.

2. Normal plasma concentrations may be present which do not reflect the intracellular deficits

3. As the acidosis resolves, potassium shifts intracellularly, so potassium needs lessen. Frequent assessment is needed to avoid hypo or hyperkalemia.

D. Chloride

1. Falsely lowered with hyperglycemia and hyperlipidemia

2. Deficits are about 2/3 that of sodium, but since replaced as NaCl, a mild hyperchloremia (110-115 mEq/1) is frequently seen during the treatment of DKA

3. Hyperchloremia may decrease bicarbonate reabsorption that can delay recovery from the acidosis.

E. Amylase

1. Often elevated in DKA, does not always indicate pancreatitis as it is usually of salivary origin and plasma lipase is usually normal.

F. Phosphate

1. Acidosis causes intracellular to extracellular shifts that may cause elevated level initially. In addition, osmotic diuresis is responsible for phosphate losses.

2. Level frequently falls during the course of therapy

3. With replacement, can see a decrease in Mg and Ca. Rare to see tetany.

4. A low level of serum phosphate (< 1.0) may produce a tendency to prolong tissue hypoxia.

G. Creatinine

1. May be falsely elevated

2. Presence of acetoacetate in the blood interferes with the usual lab method of determining creatinine

3. If abnormal, recheck prior to discharge after acidosis and ketosis have resolved

H. Magnesium

1. May be low in DKA but treatment is rarely needed unless the patient is symptomatic

I. Leukocytosis

1. Often seen, should have healthy suspicion for infection, although often attributable to increase intrinsic catecholamines associated with DKA.

IV. Transitioning from IV to SQ insulin

A. Preferable to do this at the morning or evening meal, once the acidosis has resoved (serum $HCO3^-$ > 15 mEq/L.

B. Assure that meal tray is at bedside. Give SQ insulin dose (do not stop IV insulin infusion):

1. Give usual dose if known diabetic

2. If new diabetic, calculate approximate insulin needs:

a. Start with 0.5-0.75 units/kg/day

b. Divide 2/3 of total dose as AM dose, and 1/3 as PM dose

c. AM dose is divided 2/3 NPH and 1/3 regular

d. PM dose is divided 1/2 NPH and 1/2 regular

e. Adjust dosing as necessary during hospital stay, but do not try to "fine tune"

C. Allow patient to eat.

D. Stop IVF and insulin 30 min after SQ insulin dose.

E. Monitor QAC and QHS dextrosticks (or more frequently if indicated)

V. Diabetic Coma

10% of patients with DKA will present in a comatose state. Diabetic Coma appears to correlate better with serum osmolality better than other laboratory values. A head CT Scan is indicated in patients presenting in coma to assess for evidence of CNS infarction secondary to hyperviscosity. The depressed mental status tends to improve with treatment. In an infant in DKA who presents with fever and a clouded sensorium, sepsis or meningoencephalitis should be considered. Spinal tap should probably be deferred until after a head CT is obtained to assess for ICP and the potential for herniation.

If the patient's Glasgow coma score is $\leq$ 8, intubation is indicated and consultation for ICP monitoring should be sought. If, as the hyperglycemia is corrected, there is no improvement or a worsening of mental status, an ICP monitor is indicated.

Intubation of these patients should be performed with rapid sequence technique including the use of appropriate sedation and neuroprotective agents. Etomidate 0.3 mg/kg, lidocaine 1 mg/kg, vecuronium 0.2 mg/kg is one appropriate regimen. Atropine is added in children less that 1-2 years of age. Fentanyl and Versed is an acceptable alternative to Etomidate. Ketamine is **contraindicated.**

VI. Cerebral Edema

Clinically apparent cerebral edema occurs in 1% of episodes of DKA and is associated with a mortality rate of 40 – 90%. It is responsible for 50 – 60% of diabetic related deaths in children. In contrast to a diabetic coma, the patient's mental status declines once treatment begins. It occurs more frequently in new onset diabetics.

A. Signs/symptoms

1. Severe Headache

2. Changes in arousal or behavior, lethargy, loss of consciousness

3. Incontinence

4. Fixed/dilated/sluggish pupils

5. Blood pressure changes, bradycardia, temperature instability.

6. Seizures

B. Can occurs any time between presentation and 48 hours after starting therapy. Most commonly seen within first 12 hours.

C. Etiology still unclear – has been associated with severe hypocapnia and higher serum urea nitrogen on admission, rates on fluid, sodium and insulin administration as well as the use of Bicarbonate.

D. Emergency management for sudden decreased mental status (increased ICP) includes mannitol (0.25 – 1.0 gm/kg IV), rapid sequence intubation, and mild hyperventilation (pCO_2 30-35).

E. Very important complication of DKA to anticipate, diagnose promptly, and treat immediately. Once CNS findings occur, CT may show diffuse cerebral edema at base of the brain, subarachnoid hemorrhage, or infarction.

F. Prevention of life threatening cerebral edema is thought to include:

1. Avoid over aggressive fluid administration.

2. Avoid Bicarbonate

3. Extend fluid replacement for deficit over 48 hours especially if hyperosmolar.

4. Avoid rapid declines in Na or glucose. Patients with hypernatremia on presentation may be placed on 0.9 NS for maintenance fluids.

5. Treat for symptoms of increased ICP early.

VII. Shock

An ETT, central venous line, arterial line, and foley are indicated for patients in shock.

VIII. Pulmonary Edema

Pulmonary Edema is rare but occurs. The etiology is poorly understood. Some have suggested it could be from neurogenic edema in those with CNS manifestations.

IX. Acidosis

Delayed clearing of acidosis may be related to increased requirements for insulin, hyperchloremic acidosis, or further needs for fluid resuscitation.

EPIGLOTTITIS

I. Introduction

A. Definition: A life threatening bacterial infection of the epiglottis and aryepiglottic folds.

B. Etiology

1. Before the era of the HIB vaccine, Hemophilus influenza type B was the etiologic agent in > 75% of cases.

2. Group A Strep, Pneumococcus, S. aureus, H. parainfluenza - other etiologies.

C. Epidemiology

1. No seasonal predominance.

2. Most common between 2-6 y/o (mean = 40 months).

II. Pathophysiology

A. Pharynx often colonized with potentially pathogenic organisms.

B. Bacteria penetrate the mucosal barrier and invade the bloodstream.

C. Focal infection may occur at the epiglottis and surrounding structures causing inflammation and edema.

D. Edema leads to reduction in the caliber of the airway, which leads to turbulent air flow on inspiration and stridor.

III. Clinical Manifestations

A. Signs and symptoms

1. Abrupt onset - usual duration of illness before hospitalization < 24 hours, 50% with URI sxs.

2. Stridor and labored respirations.

3. Febrile - often > 103°F.

4. Sore throat.

5. Aphonia, hoarseness, muffled voice

6. Anxious appearance.

7. Prefer sitting position, with jaw thrust forward.

8. Cyanosis in later stages.

9. Drooling.

10. Tachycardia.

11. Tachypnea (but rarely > 40 b/min).

12. Retractions.

B. Visualization of the epiglottis is hazardous and should not be done in the child with suspected epiglottitis!! Agitating the child may precipitate complete airway obstruction!! Do **NOT** use a tongue depressor on these patients !!

C. Labs/X-ray - may be obtained only after airway is secured!

1. CBC - elevated WBC with bandemia.

2. Blood cultures - positive 70 - 90%.

3. Culture of epiglottis - positive in about 50%. Caution – make sure the lab does not set this up as a routine throat CX.

4. Lateral neck X-rays, usually time consuming, are often non-diagnostic and place the child in an area of the hospital where emergency airway care is suboptimal. If epiglottitis is suspected, radiographs are absolutely contraindicated until airway stable.

(1) Swollen epiglottis - assumes a configuration that is convex on both sides, commonly called the "thumb sign".

(2) Thickened aryepiglottic folds.

(3) Obliteration of the vallecula.

5. Meningitis occurs uncommonly (2-3% of cases). Consider LP in the OR in children with signs and symptoms of meningitis.

D. Complications

1. Sudden respiratory obstruction - most serious and potentially fatal.

2. Extraepiglottic spread of infection - eg. lungs, pericardium, soft tissues, synovium, and meninges.

3. Spread to susceptible contacts.

IV. Management Protocol - should be followed in ANY situation where the airway is acutely at risk or suspicion exists for impending airway compromise.

A. True Emergency - STAT anesthesia (Beepers #1023, #1085), ENT (Beeper #2822; Ext 5623/5605) and Pediatrics (Beeper #1030, ext 7715/7835) consults. Arrange for O.R. (ext 7467/5655). If O.R. is not immediately available, patient will be taken to the PICU, or the recovery room if PICU bedspace is not available.

B. Anesthesia and ENT attending physicians to remain with patient at all times - be prepared to provide an emergency airway and resuscitate at any time.

C. Physical exam WILL NOT include attempts at visualization of pharynx by depressing the tongue!!

D. Keep child calm and avoid agitation. Parents should be allowed to stay with the child until just before intubation. Don't attempt to lay the patient down. The child may determine the position he/she is most comfortable in.

E. Oxygen may be given by mask, but not at expense of agitating patient. Usually child will allow parents to give O2.

F. May see improvement with racemic epinephrine, therefore, an improvement with racemic DOES NOT always imply croup.

G. Prepare the child for transport.

1. Use gurney if possible.

2. Oxygen tank full and open.

3. Ambubag with appropriate size mask.

4. Laryngoscope.

5. Appropriate size ETT and smaller sizes.

6. Trach set.

7. Portable suction.

8. Atropine 0.02 mg/kg (min = 0.1 mg, max = 1.0 mg).

9. Succinylcholine (2 mg/kg) for use by anesthesia.

10. Culture swabs, blood culture bottles, IV equipment, LP tray (if needed), and antibiotics.

H. Transport the child and parents only when a physician experienced in intubation is present with proper equipment.

I. Controlled intubation should occur by anesthesia in the O.R. with ENT in attendance in case of need for emergency bronchoscopy or tracheostomy.

J. Initial intubation should be orally, using an ET tube 1-2 sizes smaller than usual. Only after intubation should IV be started and blood drawn for lab studies and cultures, LP etc.

K. Recommended antibiotic - Cefuroxime 150 mg/kg/day IV divided q 8 hours, Cefotaxime 200 mg/kg/day IV divided q 8 hours, or Ceftriaxone 100 mg/kg/day IV divided every 12-24 hours. First dose STAT in OR. If bacterial tracheitis is suspected add better gram ⊕ coverage - eg. Nafcillin, 150 mg/kg/day, IV, divided q 6 hours . Respiratory isolation for 24 hours after initiation of antibiotics should be ordered.

L. After stabilization, consider changing ETT to a more secure nasotracheal tube. Document position with CXR!

M. Humidified air, with or without supplemental 02 as required. ABG's as needed. Usually an A-line is required to adequately assess course.

N. CPAP if evidence of atelectasis. Suctioning Q1-2 hours and PRN.

O. Sedation - to prevent accidental extubation - Versed (0.1 mg/kg) or Morphine (0.1 mg/kg). Remember Morphine causes histamine release. Versed is relatively short acting. Sedation may be given as boluses or continuous infusion.

P. Soft restraints to prevent extubation.

Q. Sometimes necessary to sedate, paralyze and mechanically ventilate to maintain airway. Versed 0.01 mg/kg PRN or 0.1 mg/kg/hr and Vecuronium 0.1 mg/kg Q 1-3 hours prn or 0.1 mg/kg/hr is one acceptable regimen.

R. Extubate after objective evidence of improvement, i.e. development of an air leak. Usually 24-36 hours after intubation. Best done in O.R. with ENT present.

S. Observe in ICU for 12-24 hours post extubation. Should receive 7-10 day course of antibiotics (not necessarily all IV).

T. Robinul to decreased secretions as needed. Antisecretory dose is 0.004-0.010 mg/kg/dose IV q 4-8 hrs.

U. Prophylaxis of contacts of patient with H.influ. type epiglottitis.

1. Individuals residing with the index case or individuals who spent 4 or more hours with the index case for at least 5 of the 7 days prior to admission need prophylaxis, irrespective of age, if household contains:

   a. One incompletely vaccinated child < 48 months.

   b. Child < 12 months.

   c. Immunocompromised child of any age.

2. In families receiving prophylaxis, the index case also requires prophylaxis.

3. Use Rifampin 20 mg/kg (max = 600 mg) q d x 4 days.

FEBRILE SEIZURES

I. Introduction:

A. Definition: A seizure associated with fever in a child age 6 mos - 6 years without evidence of other cause (no evidence of trauma, CNS infection or metabolic cause, and no history of epilepsy *or other neurologic abnormality.*

B. Incidence:

1. 3 -5% of all children

2. 30% of children of a parent who had febrile seizure(s)

C. Recurrence risk (after first event):

1. 30% have a second seizure (50% if <1 year old)

2. 15% have a third seizure

3. 9% have more than three seizures

4. 70% recur within one year, 90% within two years.

D. **Simple Febrile Seizure, Definition**:

1. Single event

2. Generalized, without focal onset.

3. Duration less than 15 minutes

4. No history of epilepsy or other neurologic abnormality.

5. Patient ages 6 mos - 6 years

E. Risk factors for future epilepsy:

1. lasting greater than 15 min.

2. focal at onset

3. recurrence within 24 hours.

a. 1-3 constitute features of a "complex" febrile sz

b. complex febrile sz are NOT more likely to recur than simple febrile sz

4. Family history of an afebrile seizure.

5. Neurologically abnormal before seizure.

6. With zero or one risk factor, risk of epilepsy is 1.5-4%
with two or more risk factors, risk of epilepsy is 6%

II. Work Up:

A. History (as per status epilepticus).

B. Careful general exam, neuro exam - identify source of fever.

C. Lab

1. No routine labs. Consider based on history and PE:

a. Lytes, BUN, creatinine, glucose, Ca, Mg if dehydration suspected or at risk for electrolyte imbalance

b. CBC with diff if indicated for evaluation of fever

c. Blood cultures if indicated for evaluation of fever

2. Lumbar Puncture (per AAP recommendations)

a. Under 12 months and first seizure

b. 12-18 mos: consider LP, especially if pretreated with oral antibiotics

c. Over 18 mos: LP if meningitis suspected clinically, consider strongly if pretreated

d. No guidelines exist for workup of recurrent febrile seizures Young age, ill appearance, pretreatment and meningeal signs argue for strong consideration of LP

3. EEG as an outpatient if "complex" febrile seizure

4. Neuroimaging is not indicated unless exam shows focal deficit

III. Hospitalize if:

A. Abnormal Exam

B. Abnormal Labs

C. Parental Concerns - it is not unusual to seize again in the first 24 hours

D. Pediatrician concerns - observation if you are not comfortable with patient.

IV. Treatment:

A. Education:

1. Anti-pyretics during illness dosed around the clock even if afebrile.

2. Seizure first aid and reassurance of low risk

B. Rectal Diazepam for home use:

1. recurrent or prolonged febrile seizures

2. 0.5 mg/kg/dose given when seizure lasts >10 minutes; Available 2.5 mg or 5 mg pre-filled syringes

C. **DAILY SEIZURE MEDICATION IS NOT INDICATED FOR THE VAST MAJORITY OF FEBRILE SEIZURES**

1. Decreases the risk of recurrent febrile seizures. Side effects of meds outweigh risk for almost everyone.

2. Does not reduce the risk of epilepsy.

3. Only for young children with multiple recurrences

4. Phenobarbital 4-5 mg/kg/day PO divided b.i.d.

a. may cause behavior changes (50% - hyperactivity).

b. taper medication after 1-2 years if no further seizures.

5. Valproate in usual doses also effective for prevention

E. Phenytoin and Carbamazepine are ineffective for febrile seizures.

F. Benzodiazepine prophylaxis during febrile illness

1. Lorazepam 1 - 2 mg PO or PR q 8 hours for 3 days or until without fever for 24 hours, whichever is less.

2. **YOU MUST STRESS THAT SEIZURE PREVENTION MEDICATION IN NO WAY SUBSTITUTES FOR THE NECESSARY MEDICAL EVALUATION FOR FEVER !!**

ELECTROLYTE AND FLUID ABNORMALITIES

I. Introduction

A. Understanding and treating fluid & electrolyte problems requires that the clinician understand body fluid spaces and know how to quantitatively estimate deficits/excesses in these spaces (often misleading lumped under the term "dehydration")

B. Treatment of deficits/excesses

C. Estimation of fluid and electrolyte losses over the next 24 hours so they can be accurately replaced

1. Routine maintenance requirements (insensible losses from skin & lungs & normal urinary losses)

2. Unusual losses (diarrhea, NG drainage etc)

II. Body Fluid Compartments

A. Roughly, we are comprised of two compartments, extracellular fluids (ECF) and intracellular fluids (ICF)

1. ECF space
   a) 1/3 of the total body water (TBW)
   b) Na containing fluids outside of cells which may be
      (1) Interstitial (¾ of the ECF)
      (2) Plasma (1/4 of the ECF)
   c) ECF compartment's size variables
      (1) Na balance
      (2) External losses (sweating, bleeding, GI losses
      (3) "Third spacing" of fluids

2. ICF space
   a) 2/3 of the TBW
   b) Na free fluids (free H2O) inside the cells
   c) ICF size variables (Intake – Output)
      (1) H2O intake partially regulated by CNS thirst center
      (2) Free H2O losses are unregulated (insensible, sweat) or tightly regulated (kidney- ADH system)

3. Fluid compartment calculations
   a) TBW = 0.6 X weight (kg), for children/adults (0.78 X weight (kg), for neonates)
   b) 2/3 or 40% of body wt is ICF
   c) 1/3 or 20% of body wt is ECF (35% in neonates)
      (1) 3/4 of ECF is interstitial fluid or 15% of body wt
      (2) 1/4 of ECF is plasma or 5% of body wt

B. Abnormalities in the Body Fluid Spaces (See end of chapter for management examples)

1. ECF space deficits ("**Dehydration**")
   a) ECF deficits can be classified as mild, moderate, or severe on the basis of physical exam findings

(1) Mild - 3% deficit (5% infant), slight thirst, flat fontanel, good tears, moist mucous membranes, good skin turgor, normal urine output
(2) Moderate - 6% deficit (10% infant), irritable, moderate thirst, dry mucous membranes, +/- tears, +/- fontanel, decreased skin turgor, oliguria, tachycardia, weak distal pulses, skin pale
(3) Severe - 9% deficit (15%infant), lethargic, hyperirritable, intense thirst, dry mucous membranes, no tears, sunken fontanel, poor turgor, pale cold skin, oliguria or anuria, thready pulses, prolonged cap refill

b) Deficit replacement
(1) ECF deficit (%) x Body Wt (Kg) = fluid loss from ECF space and is the amount of fluid to be replaced
(2) Fluid deficits affect CV function & should in general be replaced aggressively with isotonic crystalloids
(3) Replace 50% of the deficit in 8 hours & the entire deficit in 24 hours

2. ECF space excess
a) Edema or wt gain unexplained by tissue wt gain (anabolic state) or gain of free water (hyponatremia)
b) Therapy
(1) Na diet restrictions
(2) Diuretics
(3) Dialysis

3. ICF space deficits
a) Increase body fluid tonicity ("**Hypernatremia**")
b) Free H2O deficit is estimated by multiplying to % increase in Na above 150 times the Total body water (60% of the body wt)
c) Free H2O deficits are corrected slowly over 2-3 days to avoid cerebral edema

4. ICF space excess
a) Decrease in body fluid tonicity ("**Hyponatremia**")
b) Volume of deficit is estimated by multiplying the % decrease in Na below 130 times the TBW (60% of patient's wt)

C. Calculations for Maintenance Fluid/Electrolyte Requirement

1. Caloric expenditure

Body Weight (kg)	**Caloric Expenditure (Est)**
0 - 10	100 Cal/kg/day
11 - 20	1000 Cal + 50 Cal/kg each kilo > 10
> 20	1500 Cal + 20 Cal/kg each kilo > 20

Estimated H2O needs are 100 cc for every 100 Cal

2. Body weight (General Rule)
a) 100 ml/kg for the first 10 kg of weight
b) 50 ml/kg for the next 10 kg of weight
c) 20 ml/kg for each Kg above 20 kg

d) Divide total by 24 to determine hourly rate

3. Maintenance electrolyte requirements
   a) Na+ 3 mEq/kg/day
   b) K+ 2 mEq/kg/day
   c) Cl 5 mEq/kg/day

D. Modification to Maintenance Requirements

1. Fever
   a) Intermittent temperature elevations usually do not significantly increase metabolic rate
   b) Prolonged fever does increase the metabolic rate, maintenance fluid requirement is increased by 12% for each 1-degree above 37 degrees Centigrade

2. High osmolar load diet
   a) Routine calculations assume a diet with an osmolar load of 15 mosm/100Cal
   b) High protein or electrolyte diets will require an increase in urine H2O to dissolve waste products

3. Acute renal failure
   a) Patients with acute renal failure require meticulous management of their fluids and electrolytes
   b) Management includes twice-daily weights, strict I/O's, and close laboratory monitoring
   c) **Basic management principles**
      (1) Restore intravascular volume regardless of the degree of renal impairment. Use isotonic crystalloid fluids acutely (NS, LR)
      (2) Use D10W at 400 cc/M^2 or 30cc/100Cal/day for insensible losses
      (3) Give as many non-protein calories as possible to limit catabolism
      (4) Limit protein intake to RDA & use high quality protein
      (5) For urine, GI, and other fluid losses, replace the fluid loss cc for cc with IV fluids chosen to contain electrolytes with a similar composition to the lost fluids
      (6) Replace any lost Na with NaAcetate or NaHCO3 rather than NaCl to treat the acidosis of renal failure
      (7) Avoid administration of K+ containing fluids
      (8) CALL A NEPHROLOGIST

4. Other conditions that alter maintenance requirements
   a) SIADH (Syndrome of Inappropriate AntiDiuretic Hormone) [Lymphoma, Ewing's Sarcoma, Asthma, CF, Pneumothorax, Encephalitis, Meningitis, Head Trauma, Brain Tumors, Cavernous Sinus Thrombosis, CVA)
   b) DI (Diabetes Insipidus) Central or Nephrogenic
   c) Cerebral Salt Wasting Syndrome
   d) Diuretic use - H2O & electrolytes must be increased for loop, thiazide or osmotic (glucose, manitol) diuretics

E. Electrolyte composition of body fluid

1. Fluid losses should be replaced cc per cc with a fluid that contains proper electrolytes

2. Body fluid electrolyte estimation table (Na, K, Cl in mEq/L, protein in mg%)

FLUID	Na	K	Cl	Protein
Gastric	20-80	5-20	100-150	-
Pancreatic	120-140	5-15	90-120	-
Small Intestine	100-140	5-15	90-130	-
Bile	120-140	5-15	80-120	-
Ileostomy	45-135	3-15	20-115	-
Diarrheal	10-90	10-80	10-110	-
Sweat:				
Normal	10-30	3-10	10-35	-
Cystic Fibrosis	50-130	5-25	50-110	-
Burns	140	5	110	3-5

F. Composition of commonly used IV fluids (in mEq/Liter)

FLUID	Na	K	Cl	HCO3	Ca	CHO
NS (0.9%)	154	-	154	-	-	-
½ NS (0.45%)	77	-	77	-	-	-
¼ NS (0.2%)	34	-	34	-	-	-
3% saline	513	-	513	-	-	-
LR (Lactated Ringers	130	4	109	28	3	-
Plasmanate (5% Alb)	110	2	50	29	-	-
25% Albumin	100-160	<1	120	-	-	-
D5W	-	-	-	-	-	5
D10W	-	-	-	-	-	10

III. Sodium and Potassium Abnormalities

A. HYPOTONICITY/HYPONATREMIA (Na^+ < 135 mEq/L)

1. True hypotonic/hyponatremic states (ICF space), characterized by the status of the ECF space
   a) Hypovolemic, hypotonic states
      (1) Renal losses, (urine [Na+] > 20 mEq/L): diuretic excess, osmotic diuresis, obstructive uropathy, adrenal insufficiency, Fanconi syndrome, pseudohypoaldosteronism, Bartter's syndrome, interstitial nephritis, RTA (bicarb. loss)
      (2) GI losses, (urine [Na+] < 20 mEq/L): vomiting, diarrhea, fistula, post-op tubes, gastrocystoplasty
      (3) Sweat, (urine [Na+] < 20 mEq/L): CF (hyponatremic, hypochloremic, metabolic alkalosis), heat stroke
      (4) Third space, (urine [Na+] < 20 mEq/L): effusions, ascites, burns, muscle trauma, pancreatitis, peritonitis
   b) Euvolemic, hypotonic (+ free H2O balance with no gain or loss of Na, Urine Na>20)

(1) Water intoxication: IVF's, tap water enema, psychogenic water drinking, diluted formula feedings (WIC Syndrome)
(2) ADH excess: SIADH, pain, drugs (MSO_4, cytoxan, vincristine, TCA's, ASA, indomethacin, etc.)
(3) Glucocorticoid deficiency
(4) Hypothyroidism
(5) Reset osmostat: CVA, infection (TB), malnutrition

c) Hypervolemic, hypotonic (net positive H_2O & Na balance)
(1) Edematous states, (urine [Na+] < 20 mEq/L): CHF, cirrhosis, nephrotic syndrome
(2) Renal failure, (urine [Na+] > 20 mEq/L: acute, chronic

d) Exceptions (conditions that mimic hyponatremia)
(1) Hypertonic hyponatremia, plasma Osm (POsm)* > 295
(a) Hyperglycemia (for every 100 mg/dl glucose is > 100 mg/dl, "true" [Na] is 1.6 mEq/L higher) eg. DKA
(b) Mannitol, glycerol
(2) Isotonic pseudohyponatremia, POsm 280-295
(a) Hyperproteinemia
(b) Hyperlipidemia
(3) **Calculated POsm = 2Na + (Glucose/18) + (BUN/2.8);** will be similar to measured osmo

2. Clinical Manifestations of Hypotonic States
a) Symptoms depend on degree of hypotonicity, whether it developed rapidly or slowly & the age of the patient
b) Symptoms: Apathy, agitation, anorexia, nausea, vomiting, diarrhea, weakness, hypothermia, altered mental status, coma, hypotension, seizures
c) Hypothermic infant with seizures most likely has acute hyponatremia

3. Treatment of Hypotonic States
a) Therapy depends on etiology, acute vs. chronic hyponatremia, symptomatic vs. asymptomatic, ECF space status (i.e. hypovolemic shock)
b) Hypovolemic states are treated with the correction of shock/ECF deficit with aggressive isotonic crystalloid replacement
c) Euvolemic states are treated with water restriction
d) Hypervolemic states are corrected with water restriction and may require Na restriction as well

4. Monitor electrolytes every 4 hours during treatment

5. **Symptomatic Hyponatremia**
a) Acute decrease in Na^+ to < 120 mEq/L
b) Clinical CNS symptoms → seizures, coma & often hypothermia
c) Symptoms usually resolve when Na^+ increased by 3-5 mEq/L
d) **Calculation of 3% saline dose**
(1) mEq Na needed = [(125 – measured Na^+)][wt. (kg)] x 0.6
(2) 3% saline has 0.513 mEq/ml (approximately 0.5 mEq/cc)
(3) So mEq needed/0.513 mEq/ml = ml 3% saline needed

(4) Roughly, to increase Na by 3-5 mEq, give 3-4 cc/kg of 3% saline over 30-90 minutes
(5) Repeat dose if symptoms persist

6. Chronic/Asymptomatic Hyponatremia
a) Correct hyponatremia slowly, no faster than 0.6-1 mEq/L/hr
b) Rapid correction may cause osmotic demyelination syndrome may occur
c) Correct deficit over 24-48 hours, Do **not over correct**
d) Follow electrolytes every 4 hours to monitor for overly rapid correction

7. SIADH – Syndrome of Inappropriate ADH Secretion
a) Diagnostic criteria
(1) Hypotonicity (hyponatremia, hypoosmolality)
(2) Inappropriately concentrated urine (Urine Osm>100)
(3) Euvolemia, nonedematous with a low urine output and high urine specific gravity
(4) Elevated urine Na while on normal Na diet
(5) Absence hypothyroidism, adrenal insufficiency
b) Etiologies
(1) CNS disorders: infection (meningitis, encephalitis, abscess), hypoxia-ischemia, trauma, CVA, tumors, psychosis, Guillain-Barre syndrome, vasculitis, shunt obstructions, cavernous sinus thrombosis, MS
(2) Pulmonary disorders: infections (bacterial, tubercular, viral, mycoplasma, fungal), decreased left atrial pressure (pneumothorax, atelectasis, asthma, bronchiolitis, CF)
(3) Tumors: bronchogenic carcinoma, Ewing's sarcoma, lymphoma, ALL, thymoma, adenoma of the pancreas or duodenum, ureter or prostate carcinoma, lymphosarcoma, mesothelioma
(4) Drugs: vasopressin, desmopressin, oxytocin, nicotine, barbiturates, narcotics, carbamazepine, colchicine, isoproterenol, vincristine, vinblastine, amitriptyline, ASA, acetaminophen, NSAID's, chlorpropramide, cyclophosphamide
c) Treatment
(1) Fluid restriction (1/2 - 3/4 maintenance)
(2) Chronic SIADH that does not respond to fluid restriction may respond to therapy with lithium or demeclocycline which inhibit ADH action

B. HYPERTONICITY/HYPERNATREMIA (Na^+ > 150 mEq/L)

1. General Information
a) Hypertonicity = free H2O/intracellular deficit, deficit stimulates thirst mechanism. Populations at risk for developing a water deficit are those patients who can not respond to their thirst center & obtain water ie the very old, the very young & the infirm
b) Hypernatremia usually accompanies hypertonicity, unless high amounts of glucose or other tonically active particles (Mannitol) are present. If these particles are

present, the patient may have a normal or even a low serum [Na]

2. Hypertonic/Hypernatremic Categories and Etiologies
   a) Euvolemic hypernatremia (decrease in ICF space with normal ECF space)
      (1) Exchange transfusion (infants < 1500 gms), dialysis
      (2) Iatrogenic, intravenous fluids or medications
      (3) Increased insensible losses (skin, respiratory)
      (4) Decreased H2O intake
   b) Hypovolemic hypernatremia (decreased in ECF & ICF spaces)
      (1) Increased extra-renal losses (urine [Na+] < 20 mEq/L)
         (a) Skin: phototherapy, burns, sweating
         (b) GI: AGE, diarrhea, hypertonic enemas, or poor intake
      (2) Increased renal losses (urine [Na+] > 20 mEq/L)
         (a) Central or Nephrogenic DI
         (b) Diabetes mellitus, osmotic diuresis
         (c) Renal dysplasia, obstructive uropathy
   c) Hypervolemic hypernatremia (decreased ICF & increased ECF space)
      (1) "Salt poisoning" urine [Na+] > 20 mEq/L
      (2) Hypertonic salt solutions (mixing errors of formula or oral rehydration solutions, steroid excess, IV hypertonic NaHCO3, primary hyperaldosteronism

3. Clinical Symptoms of Hypertonicity/Hypernatremia
   a) CNS: Apathy, irritability, tremors, altered mental status, seizures
   b) GI: Anorexia, thirst, vomiting, diarrhea
   c) SKIN: Doughy skin

4. Treatment of Hypertonicity/Hypernatremia
   a) Identify etiology and stop the excessive free water loss
   b) Degree of hypovolemia may be underestimated based only on physical exam findings, the doughy skin turgor does not demonstrate the "tenting" of advanced dehydration
   c) Correct hypernatremia to 150 mEq/L over 48-72 hrs
      (1) Rate of decrease should not exceed 0.5-1 mEq/L/hr
      (2) Rapid correction may result in rebound cerebral edema
      (3) If Na > 175-180 mEq/L, consider rapidly correcting to 165-170 mEq/L (Remember 0.9% NS has 154 mEq/L of Na which will decrease the serum Na if > 154)
      (4) CNS bleeding or venous thrombosis can occur with POsm >350 & death from resp failure occurs when POsm approaches 430
   d) If shock is present, rapidly infuse 20 cc/kg of NS
   e) Calculate free water deficit
      (1) **Deficit (L) = 0.6 x wt (kg) x [(current Na –150)/150]**
      (2) Roughly, 4 cc/kg for every mEq/L the Na+ is over 150 mEq/L
      (3) Free H2O deficit is given over 2-3 days in addition to maintenance fluids
      (4) Additional replacement fluids for unusual on going losses & fluids required to replace saline deficits also need to be calculated

f) Fluid more hypotonic than D2.5 1/4 NS should be avoided as it may lyse cells and lead to cerebral edema
g) Monitor patient clinically & serum sodium q 4 hrs until stable trend
   (1) If Na falling too rapidly or if patient shows initial neurologic improvement but later deteriorates, suspect cerebral edema
   (2) In either case add more sodium to IVF's &/or slow infusion rate & prepare to treat cerebral edema
h) Monitor glucose (patients often are hyperglycemic at presentation- do not Rx with insulin) & Ca levels (patients often develop hypercalcemia during correction of hypernatremia & may require Ca Rx if symptomatic

5. **In general, the more dilute the replacement fluid that is being used to correct the free water deficit, the SLOWER it should be infused. The *majority* of pediatric intensivists will rehydrate hypernatremic patients with a crystalloid solution no more hypotonic than 0.45% NS (1/2 NS)!!!!**

6. Diabetes Insipidus (DI)
   a) Definition
      (1) Hypernatremia due to an excessive flow of dilute urine due to lack of ADH secretion (central DI) or failure of the kidney to respond to ADH (nephrogenic DI)
      (2) A water deprivation test diagnoses the condition & differentiates between central & nephrogenic DI
   b) Etiologies – Central DI
      (1) Primary: familial and non-familial forms, syndromes involving midbrain (septo-optic dysplasia, cleft lip/palate)
      (2) Secondary: head trauma, CNS tumors, granulomas (sarcoid, TB, Wegener's, syphilis), meningitis, encephalitis, histiocytosis, vascular anomalies; Drugs that inhibit ADH release [alpha-agonists, ethanol, naloxone, diphenylhydantoin, clonidine, carbon monoxide poisoning
   c) Etiologies – Nephrogenic
      (1) Primary: X-linked or autosomal recessive
      (2) Secondary: renal disease (obstructive uropathy, reflux, RTA, Fanconi's syndrome); electrolyte imbalance (hypokalemia, hypercalcemia), sickle-cell, amyloidosis, sarcoidosis, cystinosis; Drugs which inhibit peripheral ADH effects: lithium, amphoB, cisplatin, cyclophosphamide, angiographic dyes, osmotic diuretics (mannitol)
   d) Treatment
      (1) Usually a hypovolemic, hypernatremic situation
      (2) Give saline fluids if shock or poor circulation is present
      (3) Maintenance fluids regime is: D5W at 400 cc/M^2/day for insensible losses & replace urine output cc for cc with D2.5 1/4 NS q 4 hours (Using D5 1/4 NS would cause hyperglycemia at the high infusion rates)

(4) Add KCl to the urine replacement fluids by measuring the amount of K+ in the urine and adding this amount to the fluid used for urine replacement
(5) Monitor I/O's every few hours!

C. HYPOKALEMIA (K < 3.5 mEq/L)

1. Etiologies
a) Redistribution - Normal total body K (50-60 mEq/kg) but K shifted intracellularly
(1) Metabolic alkalosis - 0.1 increase in pH = 0.4 mEq/L K decrease
(2) Respiratory alkalosis - minimal shift
(3) Insulin
(4) ß2 agonists (esp. albuterol, theophylline)
(5) Hypothermia
b) Decreased total body K
(1) Decreased intake: starvation, malnutrition, kwashiorkor, anorexia nervosa, alcoholic diet
(2) GI losses: chronic diarrhea (10-80 mEq/L), fistula, laxative abuse, colostomy, nasogastric drainage, ureterosigmoidostomy
(3) Renal losses: tubular diseases, Cushing's syndrome, □ mg, meds (aminoglycosides, amphoB, NSAID's, diuretics), nephritis, licorice ingestion, Fanconi's syndrome, distal RTA, Bartter's syndrome
(4) Skin losses: cystic fibrosis, burns

2. Clinical Manifestations
a) CNS: Weakness, paralysis, hyporeflexia
b) GI: Ileus
c) CV: PAC, PVC, ST depression, flattened T wave, presence of U wave, prolonged Q-U interval, enhanced digitalis toxicity
d) Renal: Polyuria & polydipsia, increased NH3 production in kidney
e) Other: Glucose intolerance, rhabdomyolysis

3. Treatment
a) Oral route preferred 1-3 mEq/kg/d
b) Severe/symptomatic hypokalemia ($K^+ < 2.5$) will need intravenous replacement
(1) Dose: 0.5-1 mEq/kg
(2) Max "safe" dose is 1 mEq/kg/hr. Needs to be done a continuously monitored area
(3) Treat to reverse symptoms or to get K to 3 mEq/L, then switch to slower rates or preferably oral K supplementation
(4) IVF concentration of $\leq$ 40 mEq/L is safe for peripheral vein, 80 mEq/L can be given in central vein

D. HYPERKALEMIA ($K^+ > 6.5$ mEq/L)

1. Etiologies
a) Psuedohyperkalemia ("normal" ECF level)

(1) Hemolyzed specimen, prolonged tourniquet time
(2) Thrombocytosis (> 1 million, measure plasma K on anticoagulated specimen)
(3) Leukocytosis (> 100,000, avoid by separating plasma from cellular elements)

b) Intracellular to extracellular shift (Normal total body K)
(1) Acidosis (Inorganic metabolic acidosis > respiratory acidosis > organic acidosis)
(2) Insulin deficiency – DKA
(3) Beta blockade
(4) Succinylcholine especially in renal failure, trauma or burns
(5) Digitalis poisoning
(6) Familial hyperkalemic periodic paralysis

c) Increased total body K
(1) Impaired renal excretion (renal failure, adrenal insufficiency, psuedohypoaldosteronism type II)
(2) Renal tubular dysfunction (obstructive uropathies, type IV RTA, SLE, Transplant rejection, SS disease)
(3) Drugs that inhibit K excretion (ACE inhibitors, NSAIDS, K sparing diuretics, trimethoprim, Cyclosporin A)
(4) Stored PRBC or platelet transfusions
(5) Rhabdomyolysis (trauma, heat stroke), burns, tumor lysis syndrome, hemolysis, HUS, catabolic state

2. Clinical Manifestations
a) CNS: Weakness, paralysis, paresthesia
b) CV/EKG changes
(1) K ≈ 7.5 - Tenting & peaking of T wave
(2) K ≈ 8 - Flattening of the P wave & increased PR interval, widened QRS
(3) K ≈ 9 - ST segment depression, further widening of QRS
(4) K ≈ 10 - Deep S wave, sign wave, first degree AV block, Vent dysrhythmias, asystole

3. Treatment
a) In general
(1) Treat the underlying etiology for hyperkalemia
(2) Remove K from IVF's or diet
(3) Obtain an EKG immediately
(4) An acute rise in K to a level > 6.5 mEq/L needs immediate treatment
(5) Correct hypocalcemia & hyponatremic states, both of which make hyperkalemia more toxic

b) Remove K from the body (start when K 6.0-7.0)
(1) Loop diuretics if appropriate clinically (Lasix 0.5-1 mg/kg)
(2) Kayexalate (sodium polystyrene)
(a) Removes potassium from body and substitutes with Na+, follow lytes/ECF volume closely
(b) 1-2 gm/kg (max 30 gms) in 4 cc/kg 30 % sorbitol po, ng; 1 gm/kg (max 30 gms) in 3 cc/kg 10% sorbitol pr (30 min retention enema)
(c) Rectal works faster, PO removes more K

(d) 1 gm/kg removes approx. 1 mEq/L of K if given po, & 0.5 mEq/L of K if given pr
(e) Onset of action in 1 hr, may repeat q 2-6 hrs

c) Shift K intracellularly (for K> 7.0 or EKG changes)
(1) Insulin and glucose
(a) Insulin (0.1-0.2 units/kg) IV push + glucose (.5-1 gm/kg) over 30 min
(b) Repeat in 30-60 minute or start infusion of D25 at 1-2cc/kg/hr & insulin at 0.5-1U/kg/hr
(c) Never give glucose without insulin (hyperglycemia can worsen hyperkalemia transiently)
(d) Onset < 30 min; duration several hours
(2) Sodium bicarbonate
(a) 1-2 mEq/kg IV over 5-30 minutes
(b) Has little effect if used alone especially in absence of acidosis
(c) Onset 3-4 hrs
(3) Albuterol nebulization
(a) Dosage
(i) Children: < 10 kg use 2.5-5 mg
(ii) 10 - 40 kg use 5-10 mg
(iii) > 40 mg use 10-20 mg/dose
(b) Not effective in all patients
(c) Onset 30 minutes, duration 2 hours

d) Stabilize cardiac membrane (reverse EKG changes)
(1) Calcium gluconate (10%)
(2) Dosage: 0.5-1 cc/kg IV over 3-5 mins. May repeat dose once in 10 minutes if EKG changes persist
(3) Antagonizes cardiac/neuromuscular effects
(4) Onset within minutes; duration 30-60 min
(5) Incompatible with NaHCO3- must clear line between these meds

e) Dialysis

IV. Calcium Emergencies

A. In general

1. Serum calcium is comprised of ionized or unbound calcium (40%), protein bound calcium - principally to albumin (50%), and 10% is complexed

2. A change in serum albumin of 1 gm/100 ml changes the serum calcium, in the same direction, by 0.8 mg/100 ml

3. In hypoproteinemic states lower **total** serum calcium is tolerated as long as the ionized calcium is normal

4. Alkalosis = ↓ ionized calcium, acidosis = ↑ ionized calcium

5. Ionized portion carries out the metabolic functions

B. HYPOCALCEMIA (Ca < 8 mg/dl or iCa < 1.13 mmol/L children, Ca < 7 mg/dl or iCa < 1.0 mmol/L neonates)

1. Etiologies of hypocalcemia

a) Parathyroid deficiency: hypoparathyroidism, post-neck surgery, DiGeorge Syndrome, hypomagnesemia, pseudo hypoparathyroidism, burns
b) Vit D deficiency: nutritional, malabsorption, liver disease, renal disease, nephrotic syndrome, phenobarbital, phenytoin
c) Tissue deposition of ionized Ca from ECF: hyperphosphatemia (renal insuff, enemas, tumor lysis), pancreatitis, rhabdomyolysis, osteoblastic metastases
d) Chelation of ionized Ca: massive blood transfusion, (citrate), lactic acidosis, respiratory alkalosis, bicarb, Foscarnet, NaEDTA
e) Miscellaneous: drugs (aminoglycosides, furosemide glucocorticoids, glucagon, calcitonin, mithramycin, chemotherapy), sepsis & critical illness

2. Laboratory/Radiographic evaluation
a) iCa, ABG, Lytes, Cr, BUN, PO4, Mg, PTH, Vit D levels, LFTs, AlkPhos;
b) Urine Ca, PO4, Cr
c) Chest & wrist X-ray

3. Clinical Manifestations
a) Muscle twitching, circumoral & acral paresthesias, stiffness, spasms, laryngospasm, tetany, confusion, seizures
b) Chvostek's sign – twitching of facial muscles after tapping the facial nerve just in front of the ear
c) Trousseau's sign - carpal spasm after 3 min of arterial occlusion with BP cuff
d) Prolongation of QT interval, T wave inversion, heart block, V fib

4. Treatment
a) Correct underlying disorder (i.e. correct hypomagnesemia if present)
b) Emergent, symptomatic calcium replacement therapy
(1) Single dose for cardiac arrest or severe hypocalcemia (iCa < 0.8 mmol/L)
(2) Give over 2-10 minutes while monitoring for bradycardia, hypotension from too rapid infusion:
(3) Calcium chloride (10% soln, 27% Ca) 10-20 mg/kg or 0.1-0.2 cc/kg IV (acts immediately, requires no metabolism, very irritating to tissues, make sure IV is in large secure vein)
(4) Calcium gluconate (10% soln, 9% Ca) 50-100 mg/kg or 0.5-1 cc/kg IV (slower onset, requires liver metabolism, less irritating to tissues than Cl)
(5) Calcium gluceptate (22% soln, 8% Ca) 55-110 mg/kg or 0.25-0.5 cc/kg IV (slower onset, requires liver metabolism, less irritating to tissues than Cl)
c) Maintenance therapy: calcium gluconate (10%) 200-500 mg/kg/d given continuously or divided into 6 doses
d) If hypocalcemia refractory consider Mg depletion even if Mg level normal

C. HYPERCALCEMIA (Calcium > 10.5 mg/dl)

1. Etiologies of hypercalcemia
   a) Rarely seen in children
   b) High PTH or PTHRP
      (1) Malignancy producing PTH, hyperparathyroidism (multiple endocrine neoplasias, adenoma)
      (2) Chronic renal failure, familial hypocalciuric hypercalcemia
   c) Normal or low PTH
      (1) Malignancy (breast, lung, renal, head & neck, myeloma)
      (2) Granulomatous disorders (sarcoidosis, TB, histo, coccidio)
      (3) Immobilization, milk alkali syndrome, parenteral nutrition, vitamin D or A intoxication, hyperthyroidism, William's syndrome, thiazide diuretics, subcutaneous fat necrosis, hypophosphatasia, Jansen syndrome, Addison's dx, Paget's Dx

2. Laboratory evaluation
   a) Intact PTH, iCa, P04, 25 & 1,25 VitD, lytes, BUN, Creatinine, Mg, VBG, TP, Albumin, Alk Phos
   b) Chest & Abd Xray, renal US
   c) UA & urine Ca, Cr, PO4
   d) EKG

3. Clinical Manifestations
   a) Central & peripheral nervous system - Weakness, hypotonia, Decreased DTR, depression, confusion, memory loss, personality change, psychosis, stupor, seizures, coma
   b) Renal - Hypertension, polyuria, polydipsia, nephrolithiasis, nephrocalcinosis, reduced GFR, metastatic calcifications
   c) GI - Anorexia, nausea, vomiting, constipation, pancreatitis, peptic ulcer disease
   d) Cardiovascular - Shortened QT interval, rarely serious arrhythmia
   e) Musculoskeletal - Proximal muscle weakness, bone pain

4. Treatment - Total calcium of > 13.5 mg/dl or symptomatic hypercalcemia is an emergency
   a) Increase renal excretion
      (1) Saline hydration - 20-40 ml/kg over 1 hour then 2-5 cc/kg/hour + maintenance fluids
      (2) Furosemide: 1-2 mg/kg/dose every 4-8 hrs
      (3) Fluid overload, hypokalemia and hypomagnesemia may result from aggressive use of IVF's and furosemide, follow lytes I&Os closely
      (4) Ionized calcium begins to decline within 4 hrs of therapy
   b) Decrease GI absorption or bone resorption
      (1) Steroids
         (a) For mild hypercalcemia in certain malignancies (lymphoma, leukemia, multiple myeloma), granulomatous disease & Vit D toxicity
         (b) Dose - 5-10 mg/kg hydrocortisone/day

(c) Effect seen in 1-2 days

(2) Calcitonin

(a) Rapidly effective, used with severe symptomatic hypercalcemia

(b) Decrease in ionized calcium in 2-4 hours but only by 1-2mg/dL

(c) Effect not sustained & subsequent doses less effective

(d) Dose - 4 units/kg s.c. q 12-24 hrs

(e) Mechanism of action - Inhibits osteoclastic bone reabsorption & increases renal excretion

(3) Bisphosphanates (Pamidronate)

(a) Agents of choice to inhibit bone resorption but have slow onset of action

(b) Dose - 0.5-1 mg/kg diluted in 5cc/kg & given over 4-24 hrs

(c) Effect starts in 1-2 days, max effect 7 days

(4) Mithramycin (not used much with advent of bisphosphonates)

(a) Most effective in hyperparathyroidism or malignancy

(b) Decreases bone resorption

(c) Dose - 15-25 mcg/kg IV over 4 hrs q.d. for 3-4 days

(d) Caution, fairly toxic (nausea, thrombocytopenia, liver toxicity, proteinuria); don't use in liver, renal or bone marrow dx

(e) Effect begins within 12-24 hrs and peaks at 2 days & lasts 3-4 days.

(5) Oral Phosphate

(a) Action – Binds Ca in GI tract and inhibits absorption

(b) Dose - 250 mg qid

(c) Cautions - Do not use in renal failure or if PO4 is elevated. Minimally effective, causes diarrhea

c) Hemodialysis or peritoneal dialysis with calcium free dialysate is effective & may be necessary if there is renal failure or intolerance to fluid loads

V. Phosphate Emergencies

A. In general

1. 80% of body PO4 is in bones, 19% is in cells & only 1% is in ECF
2. Intracellular PO4 is critical for cellular functions as part of ATP, 2,3-DPG & other energy containing compounds essential for energy supply & O2 delivery

B. HYPOPHOSPHATEMIA (Phosphorus < 2.5 mg/dl in adults, < 3.5 in children but usually only severe (<1.0 mg/dl) causes symptoms & require urgent treatment)

1. Etiologies

a) Renal losses

(1) Diuretics (acetazolamide) & osmotic diuresis (Diabetes)

(2) X-linked hypophosphatemic rickets, Fanconi's, hyperparathyroidism, vit. D deficiency
(3) Gentamicin

b) Redistribution
(1) Respiratory alkalosis
(2) Drugs - Insulin, Beta-agonists, Glucagon, Androgens

c) Inadequate intake: TPN, breast-fed premies, alcoholics

d) GI losses: malabsorption, NG suctioning, phosphate binding agents, enteric fistulas, vit. D deficiency

e) Increased utilization
(1) Refeeding syndrome after severe protein-calorie malnutrition
(2) Hungry bone syndrome after surgery for HyperPTH

f) Other: hypothermia, Cushing's disease, burns, thyrotoxicosis

2. Clinical Manifestations

a) Cardiomyopathy

b) Respiratory muscle weakness

c) Red blood cell dysfunction (hemolysis, decreased 2,3 DPG leading to tissue hypoxia), leukocyte dysfunction, thrombocytopenia

d) Rhabdomyolysis

e) Altered mental status

3. Treatment

a) Severe (P < 1 mg/dl) or symptomatic hypophosphatemia
(1) 0.15-0.33 mmol P/kg/dose over 6 hrs
(2) Potassium phosphate: 4.4 mEq K/ml and 3.0 mmol P/ml
(3) Sodium phosphate: 4.0 mEq Na/ml and 3.0 mmol P/ml

b) Maintenance requirements are 0.1-0.2 mmol P/kg/d

c) Adverse effects of administration
(1) Hypocalcemia (especially if infused faster than over 6 hrs)
(2) Metastatic calcification
(3) Hypotension
(4) Hyperkalemia or hypernatremia

C. HYPERPHOSPHATEMIA (>9 mg/dl neonates, > 6 mg/dl children, >4.5 mg/dl adults)

1. Etiologies

a) Decreased renal excretion

b) Increased phospate load
(1) Internal: tumor lysis, rhabdomyolysis, severe hemolysis
(2) External: phosphate enemas, IV boluses, Vit D toxicity

c) Intracellular to extracellular shift
(1) Acidosis
(2) Hyperglycemia, insulin deficiency (DKA)

2. Clinical Manifestations

a) Symptoms arise from the secondary decrease hypocalcemia &/or ectopic calcification of tissues & blood vessels

b) Hypocalcemia: paresthesias, tetany, seizures

c) Calcium phosphate soft tissue deposits in skin (pruritis), cornea (keratitis), blood vessels, myocardium (cardiomyopathy), heart valves when CaxP product exceeds 70
d) Calciphylaxis is rapid occlusion of small & medium size arteries that results in gangrene of digits & extremities

3. Treatment
a) Decrease ECF phosphate load
(1) Convert to anabolic state, stop cellular death
(2) Oral phosphate binding agents with meals, CaCarbonate or CaAcetate or AlOH (not in renal failure)
b) Increase renal P excretion
(1) ECF expansion (crystalloid infusion)
(2) Diuretics - Proximal acting (diamox or osmotic)
c) Intracellular shift
(1) Correct respiratory or metabolic acidosis
(2) Treat hyperglycemia & insulin deficiency
d) Dialysis

VI. Magnesium Emergencies

A. In general

1. Serum Mg level is reported in different units-1.7-2.3 mg/dl or 1.4-1.9 mEq/L or 0.7-0.95 mmol/L

2. 60% of serum Mg is ionized & filterable, 30% protein bound & 10% complexed

B. HYPOMAGNESEMIA (Mg <1.4 mEq/L or <1.7 mg/dl)

1. Etiologies
a) Nutritional deficiencies: starvation, TPN, prematurity, IUGR
b) GI losses: malabsorption (intestinal bypass, bowel resection), chronic diarrhea, NG suctioning, emesis
c) Renal losses: volume expansion, diuretics (loop & osmotic), drug induced tubular dysfunction (aminoglycosides, ticarcillin, amphoB, cisplatin, cyclosporin, carboplatin, ifosphamide, alcohol, foscarnet, pentamidine), hyperaldosteronism, Fanconi syndrome, Bartter's syndrome, Gitelman's syndrome, ATN, post transplant & pyelo induced tubular damage, hypercalcemia
d) Endocrine and metabolic: DKA, hyperparathyroidism, hyperthyroidism, hypophosphatemia
e) Other: sepsis, burns, lipolysis, hypothermia, hepatobiliary disease, pancreatitis

2. Clinical Manifestations (Similar to hypocalcemia)
a) CNS - Apathy, delirium, coma, tremors, tetany, seizures, weakness
b) CV - Prolonged PR, QRS intervals; T wave inversion, ventricular & supraventricular arrhythmias & increased risk of Dig toxicity

c) Often associated with hypokalemia, hypocalcemia & metabolic alkalosis which don't correct without correction of Mg deficiency

3. Treatment
   a) Serum level > 1.2 mEq/L (1.4 mg/dl)
      (1) Supplement diet 0.5-1 mmole Mg/kg/day in 4 doses
      (2) Stop loop or thiazide diuretics & consider K sparing diuretic
   b) Serum level <1.0 mEq/L (1.2 mg/dl) or symptoms
      (1) Magnesium sulfate 25-50 mg/kg/dose [0.1-0.2 mmole Mg/kg q 4-6 hour IV or IM (painful)
      (2) Can go up to 100-200 mg/kg/dose (0.4-0.8mmole/kg/dose) for seizures
      (3) Give over 2-4 hours, unless emergency & then never more rapidly than 0.5 mmole/kg/hr
      (4) Rapid administration may cause hypermagnesemia, CNS depression (3 mg/dl); loss of DTRs, flushing (5 mg/dl); hypotension, respiratory depression/arrest, and heart block (12 mg/dl).
      (5) Ca Gluconate is antidote for hypermagnesemia

C. HYPERMAGNESEMIA (Mg > 2.0 mEq/L or 2.4 mg/dl)

1. Rarely seen in children except those in renal failure, the normal kidney is capable of dumping large amounts of Mg

2. Etiologies
   a) Renal failure
   b) Excess Mg loads (often in association with decreased renal function)
      (1) Exogenous - maternal magnesium therapy, magnesium laxatives, antacids or enemas, lithium
      (2) Endogenous - rhabdomyolysis, acidosis, catecholamine release
   c) Other: lithium, Addison's, hyperparathyroid

3. Clinical Manifestations
   a) Directly related to Mg level
   b) Symptoms usually mild until level above 5mg/dl
   c) CNS - Somnolence, lethargy, weakness, Hyporeflexia, respiratory depression/apnea, coma, hypotension
   d) CV - Prolonged PR, QRS, and QT intervals, bradycardia, Ht block & arrest

4. Treatment
   a) Discontinue supplemental magnesium
   b) Stop tissue breakdown if possible
   c) Normal saline and furosemide diuresis (see hypercalcemia treatment section)
   d) IV calcium to reverse the neuromuscular and cardiovascular effects of magnesium (see hyperkalemia treatment section)
   e) Glucose & Insulin (see hyperkalemia treatment section)
   f) Hemodialysis if renal failure

VII. **Fluid & Electrolyte Examples**: (refer to maintenance fluid and electrolyte requirements at beginning of this chapter). This is one approach, others exist as well. A nephrology consult should be considered.

Calculations for combined deficits/excesses
FIRST CALCULATE FREE H2O STATUS
% change in tonicity [osmolality, Na] = % change in TBW
Na of 117 represents a 10% decrease from 130 or a 10% increase in TBW.
Na of 165 represents a 10% increase from 150 or a 10% decrease in TBW.
Remember free H2O is distributed 2/3 ICF & 1/3 ECF whether is added to or removed from the TBW

NEXT ASSESS CHANGES IN ECF VOLUME
Clinical assessment: Deficit is estimated as percentage of Weight 10% Deficit means the ECF has decreased by [0.1 X Body Weight]

RECONCILE THE TWO ASSESSMENTS TO "RECREATE" THE PATIENT
Determine how much saline must be lost or gained by the ECF space which, when combined with the H2O induced changes in the ECF space, will result in the clinically assessed deficits or excesses of the ECF space.

A FLUID PLAN for 34 hours is then devised using the following principles:

A. Maintenance fluids are given throughout the 24-hour period
B. Ongoing or unusual losses are replaced as they occur
C. Saline deficits are corrected rapidly with pushes of 10-20c/kg as needed to normalize circulation and overall goal of correcting 1/2 of the deficit in the first 8 hours of treatment.
D. Free water deficits (hypernatremia) are corrected slowly over 48-72 hours to avoid cerebral edema.
E. Free water excesses (hyponatremia) are corrected slowly over 24-48 hours unless there are severe symptoms.

Example 1 Normonatremic dehydration

18 month old 15 kg healthy contracts viral GE and shows signs of mild (5%) ECV depletion & serum Na 140.
What is a F& E plan for next 24 hours ?

	24 hr H2O requirements	24 hr Na requirements	24 hr K requirements
Maintenance Requirements Insensible losses Urine losses	1250	36	30
Deficit/Excess correction ECF/Saline ICF/Free H2O	750 0	112 0	0 0
Ongoing or unusual losses	0	0	0
Total for 24 hours	2000	148	30

Bolus with 20cc/kg of isotonic NaCl solution (200cc with 30 mEq of Na) then give 900 cc of 1/2 normal saline in first 8 hours and 900 cc of 1/2 normal

saline in last 16 hours. Note this plan assumes vomiting & diarrhea are going to stop when patient is put NPO & on IVs & that the patient has normal kidneys, no fever etc.

Example 2 Hyponatremic dehydration

10 kg child with moderate ECF depletion by clinical exam, Na of 117
TBW increased by 0.1x6l=600cc 2/3 in ICF, 1/3 [200cc] in ECF
ECF vol is down 0.1x10kg=1000cc ie 1200cc of saline has been lost
net: patient has gained 600cc of H2O & lost 1200cc of saline. Treatment is to induce a negative 600 cc H2O balance & a 1200 cc positive saline balance.

	24 hr H2O requirements	24 hr Na requirements	24 hr K requirements
Maintenance Requirements Insensible losses Urine losses	1000	30	20
Deficit/Excess correction ECF/Saline ICF/Free H2O	1200 -300 (½ of excess)	180 0	0 0
Ongoing or unusual losses	0	0	0
Total for 24 hours	1900	210	20

Bolus with 20 cc/Kg (200cc) of isotonic NaCl solution (30 mEq Na) then give 1700 cc 2/3 Normal saline over 24 hours- 1/2 in first 8 hrs & 1/2 in last 16 hrs. Note you could argue to correct the free H2O excess over 2 days & to give the maintenance fluid & H2O restriction at a constant rate while correcting the saline deficit aggressively.

Example 3 Hypernatremic dehydration

10kg child who has moderate ECF deficit & a Na of 165
H2O deficit = 10%x6l=600cc, 2/3 from ICF, 1/3 [200cc] from ECF
ECF deficit=10%x10kg =1000cc eg 800cc of saline+200cc H2O
Overall patient has lost 600cc H2O & 800cc saline

PLAN FOR 1st 24 HOURS

	24 hr H2O requirements	24 hr Na requirements	24 hr K requirements
Maintenance Requirements Insensible losses Urine losses	500 250	30	20
Deficit/Excess correction ECF/Saline ICF/Free H2O	800 300 (½ of deficit)	120 0	0 0
Ongoing or unusual losses	0	0	0

Total for 24 hours	1850	150	20

Note only 1/2 the free water deficit is replaced the first day, but all the saline deficit is replaced.
Note that reduced maintenance (750 vs 1000 cc) is given because ADH will force the kidney to put out concentrated urine.
The first day's fluid plan:
Bolus with 20 cc/kg (200cc with 30 of Na) of isotonic NaCl solution to restore circulation.
First 8 hours give 1/3 of the maintenance fluid (250 cc & 10meq Na), 1/3 of the water deficit (100 cc) & 1/2 of remaining saline deficit (300 cc & 45 mEq Na)- 80cc/hr of 2/3 normal saline.
In the last 16 hours give the remaining 2/3 of maintenance fluid (500 cc & 20 mEq of Na) and 2/3 of water deficit (200 cc of water) and 1/2 of saline deficit (300 cc of water & 45 mEq Na)- 65cc/hr of 1/3 normal saline

The second days fluids will consist of restricted maintenance (ADH will still be present since the patient is still hypertonic & thus urine will still be concentrated) plus the remaining 1/2 of the water deficit

PLAN FOR 2nd 24 HOURS

	24 hr H2O requirements	24 hr Na requirements	24 hr K requirements
Maintenance Requirements	500		
Insensible losses	250	30	20
Urine losses			
Deficit/Excess correction	800	120	0
ECF/Saline	300 (½ of deficit)	0	0
ICF/Free H2O			
Ongoing or unusual losses	0	0	0
Total for 24 hours	1050	30	20

This can be spaced out evenly over 24 hours- 65cc/hr of 1/5 normal saline.

GI BLEEDS

Assessment and data gathering needs to be coordinated with stabilization and initial management. The most important determination is whether hypovolemic shock is present or is likely to occur.

I. Clinical Status Assessment: Infants and children compensate well until they become critical. Indications of the hemorrhage extent may be subtle. Vital signs are an essential part of the evaluation

A. Pulse rate - in a child this is the most sensitive indicator of acute, severe blood loss. Increase in pulse of > 20 beats/minute from supine to sitting or standing suggests significant volume loss.

B. Blood Pressure **(**lying, sitting, and standing) - not reliable indicator of shock. A decrease in diastolic BP > 10 from supine to sitting or standing suggests significant volume loss

C. Capillary refill – when is prolonged the intravascular volume deficits exceeds 25%

D. Mental status

If the patient is homodynamic stable, proceed with a more complete evaluation, if not start immediate resuscitation as described further.

Bleeding Episode Evaluation

I. Is it really blood and is it coming from the gastrointestinal tract?
II. How much has the child bled, and what is the color and character of the blood?
III. Is the child acutely or chronically bleeding?
IV. Is the patient still bleeding, and from what site?

I. Is it GI blood?

a. Nasopharyngeal: History antecedent epistaxis
b. Pulmonary: Significant coughing
c. Genitourinary symptoms
d. Menses
e. Serratia Marsescens
    1. Pink color in diapers left out awhile before discarding

II. Confirm the presence of blood

a. Hemoccult - stool specimen
    1. False negative in acid environment
b. Gastrocult - vomited material or gastric aspirate
c. Apt test in neonates - swallowed maternal blood

III. Localizing the bleeding site

a. Hematemesis: Vomiting either bright red blood or coffee ground material
   1. Suggests source above Ligament of Treitz
   2. Red coloring food: Popsicles, strawberry, medications

b. Melena: Dark, black tarry stools
   1. Suggests source above ileocecal valve
   2. Results from the action of bacteria on hemoglobin to form hematin
   3. Mimicked by iron, bismuth containing compounds, blueberries

c. Hematochezia: Bright red blood per rectum
   1. Suggests colonic etiology or massive UGI bleeding
   2. If associated with normal stools - implies bleeding from anal or rectal lesions
   3. Mixed with mucus and diarrheal stools - diffuse colitis

History

I. History Present Illness

a. Associated gastrointestinal symptoms
   1. Forceful vomiting/ diarrhea
   2. Abdominal distention/abdominal pain
b. Associated systemic symptoms
   1. Febrile illness / dizziness/ shortness of breath/ rash/ joint pains
c. Circumstances surrounding bleeding
d. Recent or concurrent use of medications: aspirin, steroids, NSAIDS, tetracycline

II. Past Medical History

a. Underlying medical disorders: GERD, chronic liver disease, IBD, coagulopathy
b. Previous GI bleeding episode
c. Previous abdominal surgery
d. Hospitalizations
e. Umbilical vein catheterization

III. Family History

a. Gastrointestinal disorders (peptic ulcer disease, IBD, polyps)
b. Liver disease,
c. Bleeding diathesis

Physical Exam

I. Oropharyngeal: examine mouth, nose, throat for evidence of epistaxis, ulcerations, bleeding from tonsils, dental bleeding

II. Skin: any cutaneous hemangiomas, palmar erythema, telangiectasias, icterus, petechiae, purpura

III. Cardiovascular: heart rate (lying and sitting), blood pressure (lying and sitting), capillary filling

IV. Abdomen: Caput medusa, ascites, hepatosplenomegaly, liver consistency and contour

V. Perineum /rectum: per anal skin tags, anorectal hemorrhoids, fissures, and polyps

Diagnostic Tools

I. Laboratory Tests

a. CBC/retic count – anemia with normal RBC volume is suggestive of acute blood
loss vs. anemia with reduced RBC volume is suggestive of chronic loss
b. PT/PTT; Type and screen/cross
c. Serum electrolytes/Ca/BUN/liver enzymes

II. Endoscopy: EGD and/or Colonoscopy

a. Procedure of choice - UGI bleeding
b. Establishes the diagnosis > 85% cases
c. Emergency EGD fourfold greater complication rate than during elective EGD
d. Stabilize before EGD if possible
Hct > 20-25%, Plts > 50K, NL PT/PTT

III. Meckel's Scan - 99 m Tc pertechnetate

a. Identify the presence of ectopic gastric mucosa
b. More than 90% of bleeding Meckel's diverticulum contains gastric mucosa

IV. Technetium Bleeding Scan

a. Used to evaluate for unknown site of bleeding
b. Technetium labeled patient RBC's
c. Can detect 0.1 ml/min or greater
d. Can't pinpoint exact gut location

V. Arteriography

a. Used to pinpoint exact site of bleeding-usually following a technetium scan
b. Can detect 0.5 ml/min or more
c. Can attempt coil embolization
d. Can also mark site for surgery with methylene blue

Management of GI bleeding

I. Stabilization and Resuscitation

A. Establish adequate IV access: for a significant bleed, should have 2 IV's

B. Fluid resuscitation

1. Initially with most readily available isotonic solution
   a) 10 - 20-cc/kg/10 min until vital signs normalized.

2. Blood if significant loss
   a) Transfuse if Hct < 25% with active bleeding, < 30% in patients with high oxygen requirement
   b) If needed urgently - O neg. blood
   c) Estimate 5 cc/kg of packed red blood cells will increase Hgb by 1, & HCT by 3

3. Transfuse platelets if < 50 K

4. FFP if > 40 cc/kg of blood required

C. Nasogastric lavage

1. Largest possible size tube (can do OG)
2. Use room temp saline/water
   a) Iced saline: Prolongs bleeding time and can cause hypothermia
   b) Irrigation amount
      1. 30-50 cc for infants
      2. 100-200cc for older children
3. Leave in place temporarily if active bleeding is found so you can monitor status
4. No blood only means there is not active bleeding from the stomach. There can still be active bleeding from the duodenum

II. Medical Therapy

A. Acid suppression
1. Ranitidine (H_2 receptor antagonist): IV 4mg/kg/day divided q 6 hrs, oral 6 mg/kg/day divided in 2 or 3 doses (maintenance dose 4 – 6 mg/kg/day)
2. Omeprazole (proton pump inhibitor): Oral 0.8 – 3.0 mg/kg/d divided QD or BID
3. Pantoprezole (proton pump inhibitor): Only IV PPI available. Dose in children not established.

B. Cytoprotection
Sucralfate (it binds to damage mucosal surfaces): oral 1 – 4 gm/day in four divided doses

C. Vasoactive agents

1. Vasopressin (decrease blood flow through the celiac and mesenteric vessels)
   a) Children: Start at 0.002 – 0.005 U/kg/min, increase the dose as needed to 0.01 U/kg/min
   b) Adults: Start at 0.2 – 0.4 U/min, increase the dose as needed to a max dose of 1U/min
   c) Side effects: fluid retention, hyponatremia, hypertension, arrhythmias and myocardial and peripheral ischemia.

2. Octreotide (a synthetic somatostatin analog) It has become the agent of choice because of its minimal side effects and equal efficacy when compared with Vasopressin

a) Dose: Children: 1 mcg/kg (IV bolus) followed by 1 mcg/kg/hr
Adult: 50 mcg (IV bolus) followed by 50 mcg/hr
b) Side effects: Hyperglycemia (dose related), headache

III. Endoscopic Therapy

A. Indications: active bleeding from an ulcer, non-bleeding ulcer with a visible vessel and varices, polyp removal

B. Modalities
a. Coagulation: cautery, heater probe, and laser photocoagulation
c. Variceal ligation (banding) or injection (epinephrine or saline)
d. Polypectomy

IV. Interventional Radiology
A. Angiographic embolization- used when endoscopy therapy fails
B Transjugular intrahepatic portosystemic shunt (TIPS) – alleviate intrahepatic portal hypertension

V. Surgery
Patients requiring multiple transfusions (greater than 1 ½ times their blood volume) should be considered for surgical exploration

Differential Diagnosis

These are the more common diagnoses in each category but are not an exhaustive list. Other less common diagnoses are possible.

I. UGI Bleeding: Hematemesis, Melena

A. Neonates (0-30 days)
1. Swallowed maternal blood: Apt-Downey test
2. Hemorrhagic gastritis
3. Duodenitis

B. Infants (30 days - 1 year)
1. Gastritis and gastric ulcer
2. Esophagitis
3. Duodenitis

C. Children (1-12 years)
1. Esophagitis
2. Gastritis and gastric ulcer
3. Duodenal Ulcer
4. Mallory-Weiss tear
5. Nasopharyngeal bleeding
6. Esophageal varices

D. Adolescents
1. Duodenal ulcer - most common cause
2. Esophagitis
3. Esophageal varices
4. Gastritis
5. Mallory - Weiss tear

II. Lower GI Bleeding: Hematochezia

A. Neonates (0-30 days)
 1. Anorectal lesions
 2. Swallowed maternal blood
 3. Milk allergy
 4. Necrotizing enterocolitis
 5. Midgut volvulus

B. Infants (30 days - 1 year)
 1. Anorectal lesions
 2. Midgut volvulus
 3. Intussuseption (<3 years)
 4. Meckel's diverticulum
 5. Infectious diarrhea
 6. Milk allergy

C. Children (1 - 12 years)
 1. Juvenile polyps
 2. Meckel's diverticulum
 3. Intussusception (<3 years)
 4. Infectious diarrhea
 5. Anal fissure
 6. Nodular lymphoid hyperplasia

D. Adolescents
 1. Infectious diarrhea
 2. Inflammatory bowel disease
 3. Polyps
 4. Hemorrhoids
 5. Anal fissure

HYPERTENSIVE CRISIS

I. Introduction

Hypertensive crisis exists when the patient's blood pressure becomes an immediate threat to the patient's well being especially the function of certain target organs including the brain, heart, kidneys & eyes. Extreme acute blood pressure elevations can overwhelm the autoregulatory mechanisms for organ blood flow resulting in damage to the arteriolar and capillary beds. This process produces organ hemorrhages and edema from the leakage of blood and fluid. How much threat a given BP level is to a patient depends on several factors including the degree of HTN, the patient's baseline BP, the acuity with which the HTN developed & the clinical setting in which the HTN occurs. A major factor determining the outcome of children with hypertensive emergencies is the speed of initiating a plan to safely lower BP to non-threatening levels. It must be remembered that acutely lowering a patient's blood pressure may cause more harm than good in certain circumstances. Thus the management of hypertensive crisis requires careful, meticulous clinical management.

The objective of emergency treatment is prevention or reversal of hypertension-related adverse events (e.g., stroke, cardiac failure, encephalopathy, post op bleeding) without causing damage from to rapid lowering of BP. This usually requires only a modest reduction in BP. Attempts to rapidly achieve "normal" BP are contraindicated. In patients with chronic hypertension, a rapid lowering BP to "normal" can decrease perfusion to the heart and brain resulting in ischemia. For this reason, in individuals with longstanding hypertension or hypertension of unknown duration, an initial BP reduction (10-20%) followed by gradual normalization of BP is recommended. In known acute hypertension, the therapy can be directed towards bringing the BP to normal values. Hypertensive emergencies usually require PICU admissions where BP & side effects can be closely monitored.

B. Terminology in this area of medicine is confusing. Terms such as hypertensive crisis, severe hypertension, hypertensive emergency, hypertensive urgency, malignant hypertension & accelerated hypertension are all used in the literature and are often poorly defined &/or used interchangeably. Some definitions include a specific diastolic or systolic blood pressure reading others emphasize an acute change in the blood pressure or the presence target organ damage or severe HTN coexistent with a specific clinical syndrome. Currently accepted definitions are as follows:
Hypertension is defined as a diastolic or systolic blood pressure above the 95%ile BP for the patient's age, sex and height. Tables (section V) have been developed for children, however 95%ile BP levels can be quickly approximated by the following equations: 95%ile systolic BP = 100 + (age x 2); 95%ile diastolic BP = 60 + (age x 1.5). Mild HTN is 0-10% above these levels, moderate HTN is 10-20% above these levels & **severe HTN is defined as > 20% above these levels (115 mm Hg diastolic for adult)**. Patients with severe hypertension may or may not be having a hypertensive crisis. Conversely patients can have a hypertensive crisis with BPs lower than these levels.
Hypertensive Crisis are divided into 2 categories
Hypertensive Urgency is defined as diastolic BP > 30% above the patient's baseline BP or 95%ile BP for the patient's age, sex and height (120 for an adult) in the absence of any evidence of acute end organ damage. At this

level BP may cause target organ damage in a matter of months. Traditionally aggressive oral therapy has been used in the ER or observation unit to lower the BP by 10-20% over a few hours & complete correction over a matter of a few days. There is no proof in adults that this approach is better than simply trying to control the BP as an outpatient over a period of weeks to months. In fact in certain adult populations aggressive oral treatment of elevated BP levels can be dangerous. The correct approach in children is unknown but in general child have less chronic & more acute HTN and have healthier hearts & vasculature. It may therefore still be appropriate to urgently treat acute severely elevated BPs in asymptotic children.
Hypertensive Emergency occurs when an acute elevation of blood pressure causes rapid and progressive target organ damage, particularly in the cardiac, renal, ocular and central nervous systems. Severe HTN in certain clinical settings may be considered a hypertensive emergency even in the absence of evidence of acute end organ dysfunction. Examples of the later would be severe HTN in the post surgical (especially neurosurgery, coronary artery surgery, trauma surgery, transplant surgery or post op patient with bleeding) or severe HTN in the patient with acute aortic dissection.
One rare but very serious subtype of HTN emergency is **accelerated/malignant hypertension**. In this syndrome, the end organ damage includes hypertensive neuroretinopathy (soft exudates, flame shaped hemorrhages +/- papilledema) indicating the presence of a hypertensive vasculopathy.

II. Causes of Pediatric Hypertensive Crisis

A. IN NEONATES & INFANTS

Group	Cause
Vascular	Renal artery thrombosis/stenosis, Renal vein thrombosis, Aortic thrombosis, Coarctation of the aorta
Renal	Acute renal failure, Renal parenchymal anomalies, Obstructive uropathy, Renal ischemic events, polycystic kidneys
Drug-related	Corticosteroids, Sympathomimetics, Infants of narcotic-addicted mothers/cocaine, Theophylline
Endocrine	Thyrotoxicosis, Congenital adrenal hyperplasia, Hyperaldosteronism
Other	Pain, Fluid overload, Increased intracranial pressure, Bronchopulmonary dysplasia, Hypercalcemia, Neuroblastoma, Repair of abdominal wall defects; ECMO

B. IN CHILDREN AND ADOLESCENTS

Group	Cause
Essential hypertension	Unknown (genetic?, environmental?)
Renal	Acute glomerulonephritis (APSGN, HSP, RPGN) chronic glomerulonephritis, hemolytic uremic syndrome, polycystic kidney disease, hypoplastic kidneys, obstructive uropathy, congenital glomerulonephritis, collagen vascular disorders, chronic renal failure, acute renal failure, post-renal transplantation, pyelonephritis/reflux nephropathy, chronic interstitial nephritis, Wilm's or other renal tumor, renin secreting tumor

Renovascular	Renal artery disease, intraluminal (thrombosis), intrinsic (fibromuscular dysplasia, Takayasu's, neurofibromatosis), extrinsic (compression)
Cardiac	Coarctation of the aorta, other (anemia, polycythemia, arteriovenous fistula, PDA, SBE, pseudoxanthoma elasticum)
Endocrine	Pheochromocytoma, neuroblastoma, congenital adrenal hyperplasia, Cushing's syndrome, hyperthyroidism, primary aldosteronism (Conn's), Liddle's syndrome, neuroblastoma, hyperparathyroidism, ovarian tumor
Metabolic	Hypercalcemia, porphyria, diabetes with renal involvement
Neurologic	Dysautonomia, neurofibromatosis, increased intracranial pressure, Guillain-Barre syndrome, poliomyelitis, anxiety
Drug-related	Steroids, heavy metals, amphetamines, sympathomimetics, licorice, oral contraceptives, cocaine, decongestants, diet drugs, NSAIDs, pancuronium, withdrawal of HTN meds*
Miscellaneous	Post trauma and surgery, burns, Stevens-Johnson syndrome, iatrogenic fluid overload, bronchopulmonary dysplasia, traction-related, eclampsia or pre eclampsia, increased intracranial pressure, ECMO
PDA = patent ductus arteriosus; SBE = subacute bacterial endocarditis. *"Rebound hypertension" -occurs with abrupt withdrawal of clonidine, angiotensin converting enzyme inhibitors or beta-blockers	

Diagnosis & Evaluation of patient with severe HTN

A. Signs & Symptoms of a Hypertensive crisis

1] Hypertension well documented with proper technique
Blood pressure - measured with an appropriately sized cuff (width of bladder = 40% of arm circumference)& with patient as non stressed as possible. Two or more readings should be averaged before the BP is accepted as elevated. 4 extremity BP should be done in neonates & children. Supine & standing BP should be done in older children & adolescents. Sphygmomanometer is recommended to check machine accuracy.

2] CNS signs & symptoms
- Headache
- Seizure
- Focal neurologic deficits
- Stupor, coma
- Nausea, vomiting
- Retinopathy
- Visual disturbances

3] Cardiac signs & symptoms
- Chest pain
- Shortness of breath, dyspnea, orthopnea
- Pulmonary edema

Gallop rhythm, distended neck veins, hepatomegaly, elevated CVP

4] Renal signs & symptoms
Acute renal failure

5] Other signs & symptoms
Post op Hemorrhage
Thrombosis
Embolus
Abdominal pain

B. Immediate actions on the patient with hypertensive crisis.

1] Admit, preferably to ICU-the need for an ICU is based on the severity of the HTN and if signs and symptoms are present.

2] Obtain a concise medical history, stressing renal, endocrine, cardiac and neurological systems, current medications or ingestions and hydration status.

Historical Information to Elicit

Information	Relevance
Family history of hypertension, preeclampsia, toxemia, renal disease, tumors	Important in essential hypertension, inherited renal disease, and some endocrine diseases (e.g. familial pheo. with multiple endocrine adenopathy II)
Family history of early complications of hypertension and/ or atherosclerosis	Suggests likely course of hypertension and/ or presence of other coronary artery disease risk factors
Neonatal history	Use of umbilical artery catheter suggests need to evaluate renal vasculature and kidneys
Headaches, dizziness, epistaxis, visual problems	Nonspecific symptomatology, usually not etiologically helpful
Abdominal pain, dysuria, frequency, nocturia, enuresis	May suggest underlying renal disease
Joint pains/ swelling, facial or peripheral edema	Suggests connective tissue disease and/ or other forms of nephritis
Weight loss, failure to gain weight with good appetite, sweating, flushing, fevers, palpitations	In combination, symptoms suggest pheochromocytoma
Muscle cramps, weakness, constipation	May suggest hypokalemia and hyperaldosteronism
Age of onset of menarche, sexual development	May be helpful in suggesting hydroxylase deficiencies
Ingestion of prescription and over-the-counter drugs, contraceptives, illicit drugs	Drug-induced hypertension

3] Perform physical examination: Insure that blood pressure measurement in all extremities is correctly performed with correct sized cuff and that pain and anxiety are minimized. Rest of PE concentrates on the cardiovascular, genitourinary, dermatologic and neurologic systems & has 2 purposes: identify possible treatable etiology of the HTN & determine if there is evidence of target organ damage.

Findings to Look for on Physical Examination

Physical Findings	Relevance
General:	
Pale mucous membranes, facial or pretibial edema	Renal disease
Pallor, evanescent flushing, increased sweating at rest	Pheochromocytoma vs. hyperdynamic Essential hypertension
Cafe au lait spots, neurofibromas	Von Recklinghausen disease
Moon face, hirsutism, buffalo hump, truncal obesity, striae	Cushing syndrome
Webbing of the neck, low hairline, wide-spaced nipples, wide carrying angle	Turner syndrome
Elfin facies, poor growth, retardation	Williams syndrome
Thyroid enlargement	Hyperthyroidism
Virilization	CAH
Cardiovascular:	
Absent or delayed femoral pulses, low leg BP relative to arm BP; Murmur	Aortic coarctation
Heart size, rate, rhythm, murmurs, tachycardia and/ or arrhythmia respiratory difficulty, large heart, gallop, hepatomegaly	Pheochromocytoma; possible target organ damage
Bruits over great vessels	Arteritis, arteriopathy
Abdomen:	
Epigastric bruit	Renovascular diseases isolated or Associated with Williams or Von Reck-Linghausen syndromes, or arteritis
Unilateral or bilateral masses	Wilms tumor, neuroblastoma, pheochromocytoma, polycystic kidneys, other tumors
Neurologic:	
Fundascopic changes	Malignant HTN or chronic HTN
CNS dysfunction	
Bell palsy	Chronic hypertension (HTN) &/or acute target organ dysfunction &/or stroke
Neurologic deficits (e.g. hemiparesis)	
Encephalopathic	

4] Gain vascular access for therapy.

5] Obtain baseline studies including: CBC and diff, BUN, creatinine, serum electrolytes, calcium, glucose, phosphorus, triglycerides, cholesterol, lipoprotein analysis (HDL, LDL), ESR, catecholamines, plasma renin activity (PRA), aldosterone, urinalysis and urine culture & urine drug screen (when indicated).

Note: Catecholamines and PRA should be placed immediately on ice. These levels should be obtained before pharmacologic therapy is administered when possible.

6] Correct obvious causes (e.g. umbilical catheter, increased ICP, pain, anxiety)

Note: If rebound hypertension is suspected, reinstitution of the discontinued antihypertensive medication may rapidly and effectively control the hypertension.

7] Institute appropriate therapy based on initial assessment (see below).

8] Obtain EKG with rhythm strip and CXR request renal ultrasound, cardiac echocardiogram. Depending on neurological status obtain head CT. Major differential in someone with HTN & CNS dysfunction is primary CNS pathology and/or increased ICP causing the HTN vs. HTN causing CNS dysfunction (hypertensive encephalopathy, stroke). Always RO primary CNS disorders &/or increased ICP before lowering the BP in such a patient.

IV. Treatment of the patient with hypertensive crisis

A. General Principles

Hypertensive Emergencies: If ongoing end-organ damage is thought to be secondary to the hypertensive state or the elevated BP is occurring in certain clinical situations (post op, aortic dissection) prompt treatment with aggressive oral or usually intravenous medication is indicated. Monitor patient closely preferably with continuous intrarterial monitoring in an ICU so that a rapid fall in blood pressure can be avoided. General goal is to lower the mean arterial pressure (one-third of the sum of twice the diastolic pressure plus the systolic pressure) by 1/3 of desired correction (usually to within 10% of the 95th percentile BP levels) over 6 hours, another 1/3 by 24 hours & complete the planned correction by 48 hours. Normalization of BP is not the immediate goals this is done as an outpatient over weeks to months. If signs of hypoperfusion develop the rate of decline in BP should be slowed. When BP is under control with parenteral medications, gradually switch to oral antihypertensives

Hypertensive Urgencies (severely elevated BP without evidence of acute target organ damage or a risky clinical situation)- correct treatment strategy is not known. Children can be treated with oral agents with the goal of lowering mean BP by 10-20% over an hour followed by close observation & institution of oral maintenance therapy with the goal of normalizing the BP over days to weeks.

B. ANTIHYPERTENSIVE DRUG THERAPY

1] Parenteral therapy for Emergencies

Medication	Dose	Onset of Action	Duration of Action	Adverse Effects	Special Indications	Drug Mechanism
Nicardipine	1-5 mug/kg/min IV	Immediate	30-60 min	Tachycardia, headache, flushing, local phlebitis	Most hypertensive emergencies except acute heart failure or ht block; caution with coronary ischemia	Calcium-channel blocker
Fenoldopam (Corlopam)	0.1-1.5 mug/kg/min IV as infusion Little data in children	<5 min	1-4 h	Tachycardia, headache, nausea, flushing, hyperkalemia, increased intraocular pressure	Most hypertensive emergencies especially with renal failure; caution with glaucoma	Dopamine-1 receptor agonist
Enalaprilat	5-10mug/kg q 6-	15-30 min	6 h	Precipitous fall in	Acute left	ACE

(Vasotec I.V.)	12 h IV			pressure in high-renin states; response variable	ventricular failure; avoid in acute myocardial infarction, caution in patients with renal failure	inhibitor
Hydralazine	0.1-0.2 mg/kg IV/IM maximum 25 mg; q 4-6 h	<30 min	4-12 h	Tachycardia, flushing, headache, vomiting, aggravation of angina	Eclampsia, CHF, avoid in aortic dissection	Direct arterial vasodilator
Diazoxide	1-2 mg/kg/dose IV rapid push every 10-15 min (0.25-5 mg/kg/min); maximum 300 mg/20 min	Within minutes	24 h	Nausea, flushing, tachycardia, chest pain, fluid retention hyperglycemia	None, rarely used, avoid in coronary insufficiency or stroke	Direct arterial vasodilator
Furosemide	1-4 mg/kg IV	5 min	2-3 h	Over diuresis, hypokalemia	Na retaining states	Loop diuretic
Phentolamine	0.1-0.2 mg/kg IV	Immediate	30-60 min	Tachycardia, flushing, headache, angina	Catecholamine excess	alpha-blocker
Esmolol	100-500 mug/kg IV load; infusion of 25-500mug/kg/min	1-2 min	8 min	Hypotension, nausea, bradycardia, asthma exacerbation	Aortic dissection, perioperative HTN	Selective $beta_1$ - blocker
Propranolol	0.01-0.05 mg/kg IV over 1 h; maximum 10 mg	Immediate decrease in HR, BP up to 24 h	8 h	Hypotension, nausea, bradycardia, ht block asthma exacerbation	Syndromes of coronary insufficiency	beta-receptor blocker
Labetalol	0.2-1 mg/kg IV; 1-3 mg/kg/h IV	Immediate	During infusion or 3-6 h	Vomiting, scalp tingling, burning in throat, dizziness, nausea, heart block, asthma exac, orthostatic hypotension	Most hypertensive emergencies except with acute heart failure, ht block, asthma	alpha/beta receptor blocker
Nitroglycerin	0.5-10 mug//kg/min IV as infusion	2-5 min	3-5 min	Headache, vomiting, methemoglobine	Coronary ischemia CHF; avoid in CVA	Direct arterial & venous

				mia, tolerance with prolonged use		vasodilator
Sodium nitroprusside	Continuous infusion 0.3-0.5 mug/kg/min up to 4 mug/kg/min (maximum 10 mug/kg/min)	Immediate	Minutes	Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication, increased ICP	Most hypertensive emergencies, aortic dissection, catecholamine excess; caution with high intracranial pressure, azotemia or liver failure	Direct arterial vasodilator

2] Oral agents for hypertensive crisis

Medication	Dose	Onset of Action	Duration of Action	Adverse Effects	Special Indications	Drug Mechanism
Nifedipine	0.25-0.5 mg/kg PO or SL; maximum 20 mg	20-30 min	6 h	Hypotension		Calcium-channel blocker
Labetolol	4-40mg/kg/day divided q 12	10-90 min	8-24 h	Burning in throat, dizziness, nausea, heart block, asthma exac, orthostatic hypotension	Catecholamine excess, coronary insufficiency & most hypertensive emergencies except with acute heart failure or Ht block	alpha/beta receptor blocker
Clonidine	5-50mug/kg/day divided q 6-8 h	30-60 min	6-10 h	Hypotension, bradycardia, sedation		Adrenergic agonist
Minoxidil	0.1-0.2 mg/kg per dose	30 min	days	Hypotension, tachycardia, angina, fluid retention, pulmonary HTN, pericardial effusion	Severe unresponsive HTN	Direct vasodilator
Captopril	0.05-2 mg/kg/day q 6-12 h in neonates; 0.5-6 mg/kg/day q 6-12 h	15-30 min	6-24 h; increased in renal failure	Precipitous fall in pressure in high-renin states & neonates; response variable	Acute left ventricular failure with HTN	ACE inhibitor

3] Details on selected agents

A. Nifedipine - Most commonly used medication for HTN urgencies/emergencies in children. Used to be used in HTN urgencies in adults but is no longer recommended since risks of aggressive control of asymptomatic HTN in adults may outweigh benefits. Calcium channel blocker that decreases BP by arteriolar vasodilatation. Nifedipine lowers both systolic and diastolic BP in children by 30-40 mm Hg within 30 minutes (which may be dangerous). Comes in a gelatin capsule with 10 mg in 0.34 cc of solution. In older children the capsule should be chewed and swallowed to obtain optimal results. In small children the solution should be aspirated from the capsule and administered orally. Sublingual administration is actually less effective.

1. Trade name: Procardia
2. Formulation: 10 or 20 mg capsule
3. Dose and route: 0.25 - 0.5 mg/kg, PO
4. Interval: q 30 min. X 1, then q 3 - 4 hours
5. Onset of action: 30 min.
6. Duration of action: 1 - 4 hours
7. Major acute problems: hypotension, dysrhythmias

B. Hydralazine-Vasodilator, less potent than other vasodilatory drugs but it can be effective, has long track record in pediatrics & can be given IV, IM or PO.

1. Trade name: Apresoline
2. Formulation: 20 mg/ml
3. Dose and route: 0.1 - 0.5 mg/kg/dose; max. dose: 20 mg, IV or IM
4. Interval: repeat q 30 min. if no response, usual interval q 3 - 6 hours
5. Onset of action: 5 - 20 min.
6. Duration of action: 4 - 6 hours
7. Major acute problems: tachycardia, headaches, flushing, nasal congestion, palpitations, vomiting, diarrhea, hypotension, myocardial ischemia , sodium and fluid retention

C. Diazoxide-Vasodilator, very effective and rapid onset of action. Must be given by rapid iv push. Considered dangerous in adults. Be prepared to treat hypertension

1. Trade name: Hyperstat
2. Formulation: 300 mg/ 20 ml
3. Dose and route: 1-3mg/kg (mini boluses rather than old 5mg/kg bolus may be safer), **rapid IV push:**
4. Interval: **For rapid IV push:** may repeat in 15-30 min. if no response, or use prn
5. Onset of action: 1 - 3 min.
6. Duration of action: 30 min. to 24 hours
7. Major acute problems: hyperglycemia, hyperuricemia, hypotension, nausea, vomiting, flushing, dysrhythmias, tachycardia, cardiac ischemia, sodium and fluid retention

D. Nitroglycerin-Vasodilator, immediate onset of action, must be given as continuous infusion. Preferred over nitroprusside in patients with renal impairment. Requires continuous A-line monitoring. Low dose is

mainly venous dilator decreasing preload, above 3-5 mug/kg/min becomes arteriolar dilator & decrease systemic resistance.

1. Trade name: NitroBid
2. Formulation: 5 mg/ml
3. Dose and route: 0.5 - 10.0 mug/kg/min IV; use polypropylene infusion sets & glass bottles (drug absorbed to plastic tubing)
4. Interval: continuous infusion
5. Onset of action: immediate
6. Duration of action: only effective during infusion
7. Major acute problems: hypotension, abdominal pain, dizziness, headache, increased ocular & intracranial pressure, methemoglobinemia, can antagonize heparin; withdrawal reaction if stopped to fast after prolonged use

E. Sodium Nitroprusside-Vasodilator. The gold standard for hypertensive emergencies- immediate onset of action, reliable, short t1/2 so overcorrection can be reversed rapidly. Requires continuous A-line monitoring. Reduces pre-load and after-load. Photosensitive.

1. Trade name: Nipride
2. Formulation: 50 mg; dilute in D5W only, protect bottle form light (don't need to wrap tubing); discard highly discolored solutions
3. Dose and route: 0.5 - 10 mug/kg/min., IV
4. Interval: continuous infusion
5. Onset of action: immediate
6. Duration of action: only effective during infusion
7. Major acute problems:
Thiocyanate intoxication (confusion, weakness, psychosis, seizures) with chronic use, high dose or renal failure (can occur within 12 hours in patients with renal failure)- maintain thiocyanate levels < 5 mg/dl.
Cyanide toxicity (metabolic acidosis, methemoglobinemia, tachycardia, decreased pulses, pink skin, CNS depression, loss of reflexes, almond smell) occurs in setting of liver failure or high dose (> 4 mug/kg/min)/chronic usage (> 72 hrs). Toxic at levels > 2 mcg/ml potentially lethal at levels of 3 mcg/ml
Other: chest pain, abdominal pain, headaches, rigidity, GI upset

F. Labetalol-alpha and beta blocker which can be given as IV bolus or continuous drip. Use with caution in patients with asthma or other lung disease, or cardiac disease. May mask hypoglycemic symptoms or paradoxically increase BP in pheochromocytoma (or other catecholamine excess states) or clonidine withdrawal. May have less cerebral vasodilating effects than diazoxide or Hydralazine so may be better in cases of increased ICP

1. Trade name: Normodyne
2. Formulation: 100 mg/ 20 ml
3. Dose and route: 0.2 - 3 mg/kg/hour, IV
4. Interval: continuous infusion
5. Onset of action: 5 min.
6. Duration of action: only effective during infusion
7. Major acute problems: orthostatic hypotension, nausea, PVC's, bradycardia, rhinorrhea, CHF, bronchospasim, myopathy in infants, CNS depression

G. Esmolol-beta blocker. More rapid onset of effect and more rapidclearance than Labetalol, use with caution in patients with asthma or other lung disease.

1. Trade name: Brevibloc
2. Formulation: 100 mg/10 ml
3. Dose and route: 100 - 300 **micrograms**/kg/min., IV
4. Interval: continuous infusion
5. Onset of action: immediate
6. Duration of action: only effective during infusion
7. Major acute problems: nausea, dizziness, somnolence, bronchospasm (less than Propranolol, hypotension, bradycardia, withdrawal syndrome

H. Nicardipine- only parenteral Ca channel blocker.

1. Trade name: Cardene
2. Formulation: 2.5 mg/ml; 20 & 30 mg immediate release & 30, 45, & 60 mg sustained release tab
3. Dose and route: 0.5 - 3 mug/kg/min., IV; 1-2 mg/kg/day PO
4. Interval: IV continuous infusion; BID to TID PO
5. Onset of action: immediate IV; 20 min PO
6. Duration of action: 3 hours following PO dose or single IV dose
1. Major acute problems: Accumulates in liver & renal failure, hypotension, Headache, edema, GI upset

I. Fenoldopam- selective Dopamine-1 receptor agonist, causes peripheral vasodilation, increased renal blood flow & GFR. May be drug of choice for HTN emergency with renal insufficiency

1. Trade name: Corlopam
2. Formulation:
3. Dose and route: 0.1-1 **micrograms**/kg/min., IV
4. Interval: continuous infusion
5. Onset of action: 5-15 min
6. Duration of action: 1-4 hours
7. Major acute problems: headache, dizziness, flushing, increased intraoccular pressure (contraindicated in glaucoma), hyperkalemia

V Normal Blood pressures for children & neonates

BLOOD PRESSURE LEVELS FOR THE 90TH AND 95TH PERCENTILES OF BLOOD PRESSURE FOR BOYS AGED 1 TO 17 YEARS BY PERCENTILES OF HEIGHT

Age (y)	Blood Pressure Percentile	Systolic Blood Pressure by Percentile of Height (mm Hg)							Diastolic Blood Pressure by Percentile of Height (mm Hg)						
		5%	*10 %*	*25 %*	*50 %*	*75 %*	*90 %*	*95%*	*5%*	*10 %*	*25%*	*50 %*	*75%*	*90 %*	*95%*
1	90th	94	95	97	98	100	102	102	50	51	52	53	54	54	55
	95th	98	99	101	102	104	106	106	55	55	56	57	58	59	59
2	90th	98	99	100	102	104	105	106	55	55	56	57	58	59	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
3	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	111	112	113	63	63	64	65	66	67	67
4	90th	102	103	105	107	109	110	111	62	62	63	64	65	66	66
	95th	106	107	109	111	113	114	115	66	67	67	68	69	70	71
5	90th	104	105	106	108	110	112	112	65	65	66	67	68	69	69
	95th	108	109	110	112	114	115	116	69	70	70	71	72	73	74
6	90th	105	106	108	110	111	113	114	67	68	69	70	70	71	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
7	90th	106	107	109	111	113	114	115	69	70	71	72	72	73	74
	95th	110	111	113	115	116	118	119	74	74	75	76	77	78	78
8	90th	107	108	110	112	114	115	116	71	71	72	73	74	75	75
	95th	111	112	114	116	118	119	120	75	76	76	77	78	79	80
9	90th	109	110	112	113	115	117	117	72	73	73	74	75	76	77
	95th	113	114	116	117	119	121	121	76	77	78	79	80	80	81
10	90th	110	112	113	115	117	118	119	73	74	74	75	76	77	78
	95th	114	115	117	119	121	122	123	77	78	79	80	80	81	82
11	90th	112	113	115	117	119	120	121	74	74	75	76	77	78	78
	95th	116	117	119	121	123	124	125	78	79	79	80	81	82	83
12	90th	115	116	117	119	121	123	123	75	75	76	77	78	78	79
	95th	119	120	121	123	125	126	127	79	79	80	81	82	83	83
13	90th	117	118	120	122	124	125	126	75	76	76	77	78	79	80
	95th	121	122	124	126	128	129	130	79	80	81	82	83	83	84
14	90th	120	121	123	125	126	128	128	76	76	77	78	79	80	80
	95th	124	125	127	128	130	132	132	80	81	81	82	83	84	85
15	90th	123	124	125	127	129	131	131	77	77	78	79	80	81	81
	95th	127	128	129	131	133	134	135	81	82	83	83	84	85	86
16	90th	125	126	128	130	132	133	134	79	79	80	81	82	82	83
	95th	129	130	132	134	136	137	138	83	83	84	85	86	87	87
17	90th	128	129	131	133	134	136	136	81	81	82	83	84	85	85
	95th	132	133	135	136	138	140	140	85	85	86	87	88	89	89

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BLOOD PRESSURE LEVELS FOR THE 90TH AND 95TH PERCENTILES OF BLOOD PRESSURE FOR GIRLS AGED 1 TO 17 YEARS BY PERCENTILES OF HEIGHT

Age (y)	BP %ile *	Systolic Blood Pressure by Percentile of Height (mm Hg)							Diastolic Blood Pressure by Percentile of Height (mm Hg)						
		5%	*10%*	*25%*	*50%*	*75%*	*90%*	*95%*	*5%*	*10%*	*25%*	*50%*	*75%*	*90%*	*95%*
1	90th	97	98	99	100	102	103	104	53	53	53	54	55	56	56
	95th	101	102	103	104	105	107	107	57	57	57	58	59	60	60
2	90th	99	99	100	102	103	104	105	57	57	58	58	59	60	61
	95th	102	103	104	105	107	108	109	61	61	62	62	63	64	65
3	90th	100	100	102	103	104	105	106	61	61	61	62	63	63	64
	95th	104	104	105	107	108	109	110	65	65	65	66	67	67	68
4	90th	101	102	103	104	106	107	108	63	63	64	65	65	66	67
	95th	105	106	107	108	109	111	111	67	67	68	69	69	70	71
5	90th	103	103	104	106	107	108	109	65	66	66	67	68	68	69
	95th	107	107	108	110	111	112	113	69	70	70	71	72	72	73
6	90th	104	105	106	107	109	110	111	67	67	68	69	69	70	71
	95th	108	109	110	111	112	114	114	71	71	72	73	73	74	75
7	90th	106	107	108	109	110	112	112	69	69	69	70	71	72	72
	95th	110	110	112	113	114	115	116	73	73	73	74	75	76	76
8	90th	108	109	110	111	112	113	114	70	70	71	71	72	73	74
	95th	112	112	113	115	116	117	118	74	74	75	75	76	77	78
9	90th	110	110	112	113	114	115	116	71	72	72	73	74	74	75
	95th	114	114	115	117	118	119	120	75	76	76	77	78	78	79
10	90th	112	112	114	115	116	117	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
11	90th	114	114	116	117	118	119	120	74	74	75	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	79	79	80	81	81
12	90th	116	116	118	119	120	121	122	75	75	76	76	77	78	78
	95th	120	120	121	123	124	125	126	79	79	80	80	81	82	82
13	90th	118	118	119	121	122	123	124	76	76	77	78	78	79	80
	95th	121	122	123	125	126	127	128	80	80	81	82	82	83	84
14	90th	119	120	121	122	124	125	126	77	77	78	79	79	80	81
	95th	123	124	125	126	128	129	130	81	81	82	83	83	84	85
15	90th	121	121	122	124	125	126	127	78	78	79	79	80	81	82
	95th	124	125	126	128	129	130	131	82	82	83	83	84	85	86
16	90th	122	122	123	125	126	127	128	79	79	79	80	81	82	82
	95th	125	126	127	128	130	131	132	83	83	83	84	85	86	86
17	90th	122	123	124	125	126	128	128	79	79	79	80	81	82	82
	95th	126	126	127	129	130	131	132	83	83	83	84	85	86	86

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Neonatal Systemic Hypertension:

The following 2 tables provide further information for neonates.

1. Systolic (S) and Diastolic (D) Blood Pressures in Low Birthweight Infants

Birthweight 600 - 999 g			**Birthweight 1000 - 1249 g**		
Day	**S (± 2 SD)**	**D (± 2 SD)**	**Day**	**S (± 2 SD)**	**D (± 2 SD)**
1	37.9 (17.4)	23.2 (10.3)	1	44 (22.8)	22.5 (13.5)
3	44.9 (15.7)	30.6 (12.3)	3	48 (15.4)	36.5 (9.6)
7	50 (14.8)	30.4 (12.4)	7	57 (14.0)	42.5 (16.5)
14	50.2 (14.8)	37.4 (12.0)	14	53 (30.0)	-
28	61.0 (23.5)	45.8 (27.4)	28	57 (30.0)	-
Birthweight 1250 - 1499 g			**Birthweight 1500 - 1750 g**		
Day	**S (± 2 SD)**	**D (± 2 SD)**	**Day**	**S (± 2 SD)**	**D (± 2 SD)**
1	48 (18.0)	27 (12.4)	1	47 (15.8)	26 (15.6)
3	59 (21.1)	40 (13.7)	3	51 (18.2)	35 (10.0)
7	68 (14.8)	40 (11.3)	7	66 (23.0)	41 (24.0)
14	64 (21.2)	36 (24.2)	14	76 (34.8)	42 (20.3)
28	69 (31.4)	44 (25.2)	28	73 (5.6)	50 (9.9)

from: Ingelfinger JR, Powers L, Epstein MF: Blood Pressure Norms in Low-birth-weight Infants: Birth through 4 Weeks, Pediatr Res 17: 319A, 1983

2. Mean Arterial BP (MAP) in mmHg (± SD) in Preterm and Term Ill Neonates

Birthweight (kg)	< 1.0 kg	1.0 - 1.5 kg	1.5 - 2.5 kg	> 2.5 kg
Birth	32.9 ± 15.4	39.1 ± 18.2	42.4 ± 19.6	48.8 ± 19.4
7 days	41.4 ± 15.4	47.2 ± 18.2	50.4 ± 19.6	60.2 ± 19.4
14 days	44.6 ± 15.4	50.1 ± 18.2	53.2 ± 19.6	64.2 ± 19.4
28 days	47.6 ± 15.4	53.0 ± 18.2	56.1 ± 19.6	68.3 ± 19.4

from: Stork EK, Carlo WA, Kliegman RM, et al: Hypertension redefined for critically ill neonates. Pediatr Res 18: 321A, 1984

INCREASED INTRACRANIAL PRESSURE

I. Introduction

The Monro-Kellie doctrine, based on the concept of a fixed intracranial volume, states that an increase in the volume of one intracranial compartment (blood, brain, CSF) must be accompanied by a decrease in one of more of the other compartments if intracranial pressure is to remain unchanged. The CSF and cerebral blood volume are the two compartments best able to be manipulated to buffer changes in increased intracranial volume. When compensatory mechanisms become overwhelmed, life threatening intracranial hypertension can result from relatively small increases in volume. A pathologic increase in intracranial volume should be anticipated in predisposing conditions such as trauma, meningitis, diabetic ketoacidosis, and Reye's syndrome. Additionally, seemingly trivial physiologic abnormalities in atrial and venous pressure, PCO2, Na, and osmolality can result in catastrophic consequences in patients with severe compromise of intracranial pressure (ICP) homeostatic mechanisms.

II. Etiology

A. Diffuse brain swelling from:

1. Impaired autoregulation of cerebral blood flow (head injury, Reye's syndrome, encephalitis, asphyxia)

2. Cytotoxic edema (head injury, toxins, asphyxia)

B. Mass Lesion

1. Tumor

2. Bleeding (subdural, parenchymal, epidural, AVM)

3. Abscess

C. CSF obstruction (hydrocephalus, mass lesion, meningitis, Subarachnoid hemorrhage)

D. Hyperosmolar states (DKA, hypernatremia, non-ketotic hyperglycemic coma)

III. Presentation

A. Headache

B. Vomiting

C. Cushings Triad: Increased ICP associated with Hypertension, Irregular respiratory pattern, and Bradycardia
(tachycardia may be seen early). Bradycardia is usually a late sign and may herald an arrest.

D. Papilledema (very sensitive finding, but seen in < 50 % of patients early on in the course)

E. Depressed level of consciousness

F. Pupils dilated, unequal, unresponsive

G. Difficult to control seizure activity or prolonged seizures are especially associated with mass lesions, infections or hemorrhage.

H. Cranial Nerve findings (especially VI)

I. Obtundation, confusion, restlessness, agitation and progressive unresponsiveness to environmental stimuli are early manifestations of increased ICP. Glasgow Coma Scale of <8 suggests severe injury. (see neurologic assessment chapter for GCS's)

J. Decerebrate or decorticate posturing.

K. Bulging fontanelle.

IV. Emergency Management

A. As nothing can be done about the primary injury or neuronal damage already suffered, the goal centers on preventing secondary injury. In the immediate post-injury period, secondary insults will most likely occur as a result of **hypoxia**, ischemia from frank or relative **hypotension**, or the detrimental effects of intracranial hemorrhage.

B. Airway (the "A" in ABC's)

1. Must establish quickly to avoid hypoxia. The threshold for intubation should be very low in a head injured child.

2. Any child unable to open his or her eyes or verbalize should be considered for intubation.

3. Patients with abnormal respiratory rate and rhythm, upper airway obstruction (loss of pharyngeal muscle activity, inability to clear secretions, foreign body, direct trauma, seizures), loss of protective airway reflexes, sign of ICP hypertension, or significant pulmonary or cardiovascular disease should be intubated.

4. C-spine precautions are paramount. The neck should not be extended and intubation medications should include a combination of sedation (for blunting of cardiovascular reflexes, and blunting of intracranial responses), lidocaine (for blunting of increased ICP response to laryngeal stimulation) and paralysis for ease of intubation). The intubation should be done via rapid sequence protocol which includes the Sellick's maneuver cricoid pressure) and pre-oxygenation with 100% FIO2 without bag ventilatiion (when possible). (See Rapid Sequence Induction chapter).

C. Breathing (B = breathing)

1. In the head injured patient, hypercapnia must be avoided. Carbon dioxide is a very potent cerebral dilator, which could increase cerebral blood volume and accordingly increase ICP. However, aggressive hyperventilation may lead to cerebral ischemia, and should similarly be avoided.

D. Shock (C = circulation)

1. Once the airway and ventilation have been assured, the adequacy of circulation and perfusion must be assessed and restored as needed to prevent secondary injury.

E. Physical Assessment

1. A detailed history is needed to understand the mechanism of injury. If the patient looks uninjured but the mechanism of injury was significant, look carefully for occult injury.

2. Mechanism details: pt ejected?, amount of damage to the vehicles?, estimated speed?, distance of fall?, seatbelt/car seat?, surface on which the pt. fell?

3. It also is important to ask how the patient responded at the scene: Was the patient conscious at the scene and did the patient have a seizure at the scene?

4. Past medical history; important for previous health problems, allergies, tetanus history, and current medications.

F. Complete physical exam - look for signs of occult trauma: blood behind TMs, CSF from ears/nose, retinal hemorrhages, broken ribs, unequal breath sounds, muffled heart sounds, chest/abd contusions, extremity swelling.

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G. Labs:

1. ABG

2. dextrostix

3. CBC, type and cross (if significant blood loss suspected)

4. Chem 10, glucose, osmo

5. LFT's, amylase, lipase

6. Ammonia (if Reye's sydrome or metabolic disease suspected)

7. Toxicology screen if an ingestion is suspected

8. UA (for evidence of hematuia and renal injury)

9. Blood cultures, urine culture (if infection suspected)

H. Medical treatment of increased ICP (see below)

I. Consult Neurosurgery

J. CT Scan, continue aggressive brain resuscitation during scan. Perform emergently if hx of LOC, seizure, coma, focal neuro exam, blood behind TM's, CSF rhinorrhea or otorrhea.

V. Medical Management

A. Intracranial Pressure Monitoring

1. The two major purposes for monitoring ICP are prevention of herniation and preservation of cerebral perfusion. Though ICP monitoring has not been proven to improve outcome, it is used extenisively to guide therapy and likely partially accounts for the general improvement in outcome from traumatic brain injury that has occurred over the last 2 decades.

2. ICP monitoring is indicated in the following children:

   a) Those with a GCS of < 8

   b) Those with significant trauma requiring non-neurosurgical procedures

   c) Those who require continued deep sedation or neuromuscular blockade for ventilatory management (or other in whom sequential neurologic exams cannot be adequately performed)

3. The two most common methods of ICP monitoring are the ventriculostomy and the intraparenchymal (Camino) catheter.

   a) The ventriculostomy is silastic catheter that is placed through the frontal lobe into the anterior horn of the lateral ventricle. Advantages of this device include accurate measurement of ICP, ability to recalibrate the device, and ability to drain CSF in an attempt to lower ICP. Disadvantages include difficult placement in a patient with small ventricles, higher potential for ventriculitis (and worse outcome)in the case of catheter infection.

   b) The intraparenchymal catheter contains a membrane, distortion of which deflects a mirror and attenuates a fiberoptically transmitted beam of light. This attenuation, detected by a sensor, provides a measure of the pressure on the transducer membrane. The device can be placed into the parenchyma, ventricle or subdural space. Advantages include easy placement and less risk of ventriculitis. Disadvantages include drift in readings over time and inabilibty to recallibrate the device as well as inability to drain CSF throught the catheter. Intraparenchymal monitors are ~5X more expensive ($4,000-6,000) than ventriculostomies.

4. All monitors have a risk of infection. Infectious risk increases with duration of monitoring, particularly after the 5th day. The site of monitoring is typically changed every 5-7 days. Prophylactic antibiotics (Ancef) are indicated for the duration of ICP monitoring.

5. Intracranial waveforms resemble arterial waveforms. Plateau waves are sustained ICP elevations up to 40-50 mm H2O lasting 5-20minutes, falling quickly back to baseline. These appear to represent a “tight” brain and sudden increase in ICP, usually secondary to a fall in CPP and reflex increase in MAP until CPP is restored. (see below)

6. An arterial line is indicated in all patients with an ICP monitor.

B. Cerebral Perfusion Pressure (CPP)is the difference between the pressure of blood going to the brain (the mean arterial pressure or MAP) and the back pressure to this flow (the ICP). Thus:

CPP = MAP - ICP

A normal **ICP** is **10-15 mm Hg** or less. ICP will increase with agitation, coughing, etc., but should rapidly return to baseline. Patients with sustained increases in ICP should be treated in a stepwise fashion to try to decrease their ICP with the least invasive means possible being employed first. **Maintaining an adequate CPP is probably more important than keeping the ICP value normal.** Our goal should be to maintain cerebral perfusion pressure at **50-70mm Hg.**

F. Fluid Management

1. A central line is indicated to guide fluid management.

2. Patients with increased ICP need an adequate CVP and MAP to perfuse their brains. They should **not** be routinely fluid restricted. They should receive appropriate fluid resuscitation and be started on maintenance fluids with further management guided by clinical status, vital signs, CVP, and perfusion.

VI. Medical Manipulation of ICP

A. The art of ICP/CPP management is really related to the appropriate selection and timing of these therapeutic maneuvers and understanding their limitations. Though specific management varies somewhat between trauma centers, a stepwise approach to various interventions similar to the one below is attempted for patients with elevated ICP/low CPP:

1. Appropriate ABC's and fluid resuscitation and frequent monitoring of VS, exam, ICP, electolytes, osm.

2. Intubation using rapid sequence induction. Prophylactic hyperventilation is no longer routinely employed, however moderate hyperventilation (PCO2 ~ 30-35) may be used for suspected increase ICP in the field or prior to CT scanning.

3. Sedation using Versed or Ativan 0.1 mg/kg IV or 0.1 mg/kg/hour continuous infusion. Additional sedation and/or analgesia should be considered before suctioning, patient transfer, procedures, etc. In addition Lidocaine 1 mg/kg iv before suctioning may blunt the increased ICP associated with this intervention.

4. Elevation of the head of the bed 15-30 degrees and keeping the head midline may enhance cerebral venous drainage.

5. Removal of CSF if a ventriculostomy is in place.

6. Osmole Therapy

a) Decreases blood viscosity resulting in lower cerebrovascular resistance, reflex cerebral vasoconstriction and reduction in cerebral blood volume.

b) May act as an osmotic agent to decrease brain water with subsequent osmotic diuresis.

c) Dose: Mannitol 0.25-0.5 gm/kg rapid IVP over ~ 5 min.
-OR-
3% NaCl 5 cc/kg rapid IVP

d) Goal: reduction in ICP, improvement in CPP or maximum osmolality of 310-320. If multiple doses are administered, the patient can be placed on scheduled mannitol Q4-6 hours. Serum osm and Na are followed at a similar interval and mannitol is withheld if the osm are >310. Na typically are in the 150s.

e) Foley catheter is indicated

f) Lasix in addition to osmotic therapy has been shown to decrease CSF production and to lead to preferential excretion of water over solute.

7. Hyperventilation

a) Hyperventilation causes cerebral arterial constriction with subsequent decreased cerebral blood flow and decreased ICP. It is a potentially harmful method of decreasing ICP as CPP may concomitantly be compromised. Moderate HV to a **PCO2 of 30-35** is typically well tolerated. More extreme hyperventilation is no longer practiced at most trauma centers.

b) The beneficial effects of HV diminish after 24-48 hours, due to buffering, however rapid reversal of HV results in rebound increased ICP. Thus it is important that HV is weaned slowly (i.e. over hours to days).

7. Neuromuscular blockade can be considered to decrease any muscle movement (coughing, shivering, etc.) that might contribute to increased ICP. Increased sedation alone can often accomplish this. If NMB is instituted a high level of suspicion for seizure activity must be maintained as tonic-clonic activity will not be apparent.

8. Barbiturate coma

a) Employed for increased ICP unresponsive to less invasive therapies.

b) Dose is 5 mg/kg bolus every hour X 3 and an infusion of 1-5 mg/kg/hour titrated up or down to achieve control of intracranial hypertension or to achieve burst suppression (2-9 bursts/minute on EEG), whichever comes first. Continuous EEG monitoring is necessary until burst suppression is achieved, intermittent monitoring may be appropriate once the patient has stabilized.

c) Hypotension due to cardiac depression is common and patients frequently require vasopressor support with epinephrine or norepinephrine. It is prudent to have vasopressor medications at the bedside before loading with pentobarb. A pulmonary artery catheter should be considered to guide management.

d) Due to discontinuation of production of some barbiturates, it may be necessary to use another agent. Propfol (Diprivan) and midazolam (Versed) are acceptable alternatives.

9. Other issues of monitoring and management.

a) Hyperthermia and seizures cause elevations in ICP and should be anticipated, prevented if possible, and treated aggressively. Patients with significant brain injury or mechanism of injury are routinely treated with Dilantin prophylactically for 5-10 days.

b) Hyperglycemia has been associated with worse outcome in stroke victims. This may or may not be relevant to trauma, but avoidance of hyperglycemia is probably prudent.

c) Patients with traumatic brain injury are at risk for DI and SIADH which can be identified by monitoring UOP and electrolytes.

d) Patients with traumatic brain injury are at risk for gastric ulcers. Prophylaxis with H2-blockers is recommended.

e) Patients with TBI are relatively immunosuppressed. A high index of suspicion for infection (especially pneumonia) should be maintained and infections aggressively treated.

f) Steroids are not indicated in the management of traumatic brain injury. They may have a role in the management of edema surrounding a brain tumor (Decadron 1.0 mg/kg/day IV divided q 6 hours). Steroids are of benefit in spinal cord injury (Solumedrol 30 mg/kg iv ASAP after injury, followed by 5.4 mg/kg/hour continuous infusion for 23 hours)

VI. Surgical Management

A. Mass lesions (hematomas, tumors) may require immediate surgical evacuation. With the initial surgical intervention, a bone flap can also be removed, especially if it is anticipated that the patient will have tremendous difficulty with intracranial hypertension. Subsequent craniotomy or frontal/temporal lobectomies are occasionally employed to treat refractory ICP.

B. An acute rise in ICP or change in neuro exam (i.e. blown pupils, posturing, decreased responsiveness) warrants consideration of a **stat CT scan** to rule out any surgically correctable lesions.

VII. Weaning of Interventions

Once a patient has stabilized (hours, days, or sometimes weeks into therapy), interventions are typically weaned in the reverse order that they were instituted. A significant number of children that require pentobarb coma will recover and be

neurologically intact. Survival is best predicted by the patient's GCS and cardiovascular status upon arrival to the ED.

VIII. Summary

Children with severe increased ICP requiring ICP monitoring should be managed by an intensivist, neurosurgeon, and ICU nurses experienced in the care of critically ill children. Important points to remember include: ABC's, cervical spine protection, consideration of increased ICP at all times, close attention to changes in VS and PE, prevention of secondary injury (hypoxia and hypotension), stepwise increase in interventions, knowledge of potential etiologies of deterioration and/or side effects of therapies.

NEUROLOGIC ASSESSMENT, ALTERED MENTAL STATUS, GLASGOW COMA SCALES

I. Neurologic assessment:

A. The signs of brain hypoperfusion depend on the severity and duration of the insult. In cases of sudden onset brain ischemia, few signs of neurologic compromise may precede loss of consciousness. Convulsions and pupillary dilation may occur with loss of muscular tone.

B. With shock, symptoms may be insidious. Confusion and lethargy may appear. Agitation alternating with lethargy is common. Failure to recognize parents is an early, ominous sign of cortical hypoperfusion.

C. In later stages of hypoperfusion deep tendon reflexes may be depressed, pupils may be small but reactive and a crescendo-decrescendo breathing pattern (Cheyne-stokes) may be present.

D. Hypotonia and intermittent flexor or extensor posturing may occur with prolonged cerebral hypoperfusion or extreme hypoxemia.

E. Always check electrolytes **and** a dextrostix on any neurologically impaired patient. (the dextrostix result returns faster than a lab glucose)

F: The Goals of the neurologic assessment

1. To determine the patient's level of consciousness.

2. To determine the presence of localizing (abnormal) findings.

3. It also serves as a baseline for comparison later in the hospital course.

4. The exam needs to be tailored to the situation. For instance, in comatose patients the Glasgow Coma Scale may give you all the information you need. In other patients a more detailed exam will be both possible and necessary.

G. The neurologic assessment should follow a simple and rational plan:

1. Begin with the level of consciousness (the mental status equivalent).

2. Next, assess the cranial nerves from the top of the brainstem (pupils) to the bottom (respirations, BP, HR, gag reflex)

3. Perform a motor exam looking for weakness, asymmetry, or tone abnormalities.

4. DTR's, including the Babinski reflex assessment, may help determine a level of asymmetry.

A positive Babinski response (extension of the great toe and abduction of the other toes instead of the normal flexion to plantar stimulation) is abnormal after the age of 12 months, and always abnormal if asymmetric. It is an "Upper Motor Neuron" finding that implies central (supranuclear) dysfunction.

5. Perform a sensory examination. This may be difficult in young children and comatose patients but their response to stimulation can be assessed.

6. **Neonates** should be assessed carefully for level of consciousness, cranial nerve and motor function. In addition, neonatal reflexes should be elicited.

Reflex	Appearance age	Disappearance age
Adductor spread of knee jerk	Birth	7 - 8 mos.
Babinski reflex (positive)	Birth	12 mos.(see above)
Landau reflex	10 mos.	24 mos.
Moro	Birth	5 - 6 mos.
Palmar grasp	Birth	6 mos.
Parachute	8 - 9 mos.	Persists
Plantar grasp	Birth	9 - 10 mos.
Rooting	Birth	3 mos.
Tonic neck response	Birth	5 - 6 mos.
Truncal incurvation	Birth	1 - 2 mos.

II. **Glasgow Coma Scale (GCS) (best for patients > 1 year old)**

Activity	Best Response Points
1. Eye opening	
No response	1
Response to pain	2
Response to voice	3
Spontaneously	4
2. Verbal Response	
No response	1
Incomprehensible Sounds	2
Inappropriate Words	3
Disoriented conversation	4
Oriented and appropriate	5
3. Motor Response	
No response	1
Decerebrate posturing	2
Decorticate posturing	3
Flexion withdrawal	4
Localizes pain	5
Obeys Commands	6
Maximum Score	15

Scores < 9 indicate severe injury, airway support usually required.

III. **Modified Glasgow Coma Scale (especially helpful for ages ≤ 1 year).**

Activity	Best Response
1. Eye Opening	
None	1
To pain	2
To speech	3
Spontaneous	4
2. Verbal Response	
None	1
Moans to pain	2
Cries to pain	3
Irritable cries	4
Coos, babbles	5
3. Motor Response	Points
None	1
Extensor Response	2
Abnormal Flexion	3
Withdraws to pain	4
Withdraws to touch	5
Normal Spontaneous Movements	6
Maximum Score	15

Scores < 9 indicate severe injury, airway support usually required.

III. **Brief Neuro Exam: Follows assessment for "ABC's", general exam, and GCS.**

A. Cranial Nerves: pupils (size, symmetry), fundi, response to visual threat, extraocular muscles (use doll's eyes maneuver in comatose patient **with a stable neck**, cold calorics in those in whom the cervical spine has not been cleared), corneal reflex, facial grimace to pain, gag/swallow reflex.

1. Doll's eyes (oculocephalic response) **ONLY PERFORM IN PATIENTS WITH A STABLE, CLEARED C-SPINE !** : Grasp the head firmly and hold the eyelids open. Quickly turn the head to one side. Repeat by turning the head in the other direction.

   a. If the eyes continue to gaze straight ahead the response is positive (the eyes actively deviated in the opposite direction of the turn). A positive response indicates an intact brainstem.

   b. The lack of this response in **both** eyes is part of the picture of brain death. A low brainstem lesion will show a negative response. This means that the eyes will move in the direction of the head turn, as if they were fixed in the orbits and were not mobile.

2. Cold calorics (oculovestibular reflex) may be performed in patients with C-spine injuries: First, examine the external auditory canal to make sure no obstruction or foreign matter is

occupying the canal. Next, make sure there is no tympanic membrane perforation. Elevate the head of the bed 30 degrees. Gently instill 30 - 50 cc of ice water in the ear canal while holding the patients eyes open (may use an assistant). Observe both eyes for the response. Wait 5 min. to restabilize the vestibulo-ocular system and repeat in the other ear. This test is usually **NOT** performed in non-comatose patients as it is uncomfortable.

a. If the brainstem is intact the eyes should move towards the irrigated side. If done in an alert patient nystagmus occurs.

b. In the presence of severe brainstem damage the reflex is abolished and no deviation of the eyes occurs.

B. Motor - note posture at rest, spontaneous movements.
- tone assessment (resistance to passive movements).
- motor response to stimulation (posturing).

C. DTR's - including Babinski

D. Sensory - response to stimuli (localizes pain, withdraws, postures), other testing possible in more alert patient.

E. Coordination - rapid alternating movements
- finger-nose-finger
- heel-shin

F. Gait - width of base, stability, Romberg, heel/toe/tandem for more alert, cooperative patient.

IV. Altered states of consciousness (altered mental status)

A. Pathologic alterations in consciousness are caused by a variety of disease processes. These processes may lead to decreased responsiveness to visual, auditory, and tactile stimulation. They are **NOT** all or none phenomena. Altered levels of consciousness may be divided into four categories.

1. **Lethargy**: This is a state of minimally decreased wakefulness where the primary deficit is attention. The patient is easily distracted and has faulty memory, but retains the ability to communicate by verbal or nonverbal means. Drowsiness is prominent.

2. **Obtundation**: This is a mild or moderate blunting of alertness accompanied by a lessened interest in or response to the environment. Communication is partially preserved.

3. **Stupor**: Stupor is clinically equivalent to deep physiologic sleep from which the patient can be partially or only temporarily aroused, and only by vigorous and repeated stimulation. Communication is minimal or nonexistent.

4. **Coma**: Coma can be defined as a reduction in neuronal function resulting from disruption of cerebral cortical or brain stem integrity. This is a state of unarouseable unresponsiveness in

which the patient lies without spontaneous movement with the eyes closed. There is no intelligent speech. The patient may withdraw from noxious stimuli, but cannot localize pain with discrete, defensive movements.

B. These states are not to be confused with **delirium** which is an abnormal mental state characterized by disorientation, instability, delusions, or hallucinations. Delirium is prominent when toxic or metabolic disorders affect the cerebral hemispheres, either primarily or exclusively.

C. Distinguishing metabolic etiologies from structural damage provides the basis for developing and investigating the differential diagnosis of an altered state of consciousness.

D. Differential features:

1. Supratentorial destruction or mass lesions

   a. Initial signs are focal

   b. There is a rostral to caudal progression

   c. Hemispheric dysfunction (i.e. right or left hemisphere) occurs depending on handedness and site of injury

2. Infratentorial destructive or mass lesions

   a. You usually see a preceding brain stem dysfunction

   b. Onset of coma is sudden

   c. Cranial nerve palsies occur

   d. Respiratory disturbances may be seen early

3. Toxic, metabolic or infectious diseases

   a. Confusion or stupor precedes the motor signs

   b. Motor signs are symmetric

   c. pupillary reactions are preserved

   d. Asterixis, myoclonus, tremor, or seizures may be seen

   e. May see hyper or hypoventilation

E. Etiologic spectrum of diseases producing an altered state of consciousness:

1. Supratentorial lesions of the brain

   a. Extracerebral

      (1). Neoplasm

(2). Epidural or subdural hematoma

(3). Subdural empyema or effusion

b. Intracerebral

(1). Hemorrhage (parenchymal, intraventricular, or subarachnoid)

(2). Infarction

(3). Expanding mass lesions (Neoplasm, abscesses, granulomas)

(4). Edema

2. Infratentorial lesions of the brain

a. Infarction

b. Hemorrhage (brain stem or cerebellar)

c. Expanding mass lesions

d. Edema

3. Hydrocephalus

4. Toxic, metabolic, or infectious disorders

a. Deprivation of oxygen, substrate or metabolic cofactors

(1). Hypoxia

(2). Ischemia

(3). Seizure or postictal states

(4). Cofactor deficiency (thiamine, niacin, pyridoxine)

(5). Inborn error of metabolism

5. Other organ failure

a. Liver (hepatic coma, or hyperammonemia)

b. Kidney (uremic coma)

c. Lung (CO_2 narcosis)

d. Endocrine (thyroid, parathyroid, or adrenals)

6. Exogenous poisons

a. Sedatives

b. Acid poisons

c. Heavy metals

d. Cyanide

e. Others (see poisoning chapter)

7. Abnormal ionic and acid-base balance

a. Water

b. Sodium

c. Potassium

d. Magnesium

e. Calcium

8. Infectious and parainfectious diseases

a. Meningitis

b. Encephalitis

c. Acute disseminated encephalomyelitis

d. Toxic encephalopathy

9. Trauma

F. Important points of the history:

1. Duration and development of the coma

a. Sudden onset: vascular catastrophe or seizure

b. Acute onset after period of normalcy: ingestion of drug, toxin, or poison

c. Coma developing over a period of hours to days: expanding intracranial mass, metabolic derangement, or infectious process

2. Recent illness or fever? Think of infectious process or Reyes

3. Trauma

a. Recent head injury? epidural? subdural?

b. Child abuse?

4. Recent travel?

a. Fungal, rickettsial, rabies, viral, plague, parasitic, Salmonella or Shigella infections

5. History of headache?

   a. Chronic headache: brain tumors, vascular malformations, congenital anomalies, hydrocephalus, and other mass lesions

   b. Headache of sinus origin: venous thrombosis, subdural empyema

   c. Migraine can produce a reversible confusional state

6. History of other diseases?

   a. Malignancy: think brain met.

   b. Blood dyscrasia: think hemorrhage

   c. Congenital heart disease: think infarct, embolization, or brain abscess

   d. Renal disease: think uremia, or dialysis encephalopathy

   e. Liver disease: think hyperammonemia

   f. Diabetics: think hypo or hyperglycemia

G. Physical examination

1. ABC's first !! Then assure vital signs are stable or being addressed.

2. A careful evaluation for trauma, exanthems of the skin, and skin findings of the neurocutaneous syndromes or other systemic diseases should be performed.

3. Listen for cranial bruits. Check the character of the anterior fontanelle.

4. The retina of every child with an altered state of consciousness should be examined.

5. Examine the ears and nose for the presence of blood or leaking CSF.

H. Laboratory evaluation

1. **The following is indicated for ALL patients with an altered state of consciousness:** glucose *and* dextrostix, BUN, creatinine, lytes, osm, calcium, phosphorus, magnesium, ammonia, CBC and diff, UA and ABG. (also, see number 5 below)

2. **The following MAY ALSO be indicated for patients with a suspected metabolic derangement:** urine metabolic screen, blood and urine amino and organic acids, thyroid screen, plasma cortisol, LFT's, urine porphyrins, plasma free fatty acids, ketones, and carnitine level.

3. **The following is MAY ALSO be indicated for patients with a suspected toxic ingestion:** blood and urine drug screens, lead level, blood salicylate level, blood alcohol level

4. **The following MAY ALSO be indicated for patients with a suspected infection:** blood and other bodily fluid bacterial cultures, viral and/or fungal cultures or titers, ophthalmology exam if indicated for chorioretinitis etc., exams for parasites

   a. Lumbar puncture: An LP should be considered if a CNS infection is suspected. Meningitis and encephalitis are probably the only absolute indication for an LP. ***REMEMBER***: an LP may be hazardous in patients with increased intracranial pressure. A head CT should be performed before the LP. LP should also be deferred in patients with significant cardiovascular compromise or shock.

5. **EVERY** comatose patient should have a head CT unless the etiology has clearly been established.

I. General principles of management:

1. Maintain optimal HR, BP and respiratory status

2. Correct any systemic glucose, acid-base, or fluid and electrolyte imbalance

3. Manage hypo or hyperthermia

4. Treat increased intracranial pressure

5. Administer anticonvulsants for non-metabolic induced seizures

6. Perform frequent examinations and follow the patient's clinical status closely

NEWBORN RESUSCITATION

I. Introduction

A. General

1. 3.7 million infants are born in 5,000 hospitals in the U.S. each year. Only 5% have NICU's (Level III).

2. 6% will need life support in the Delivery Room. If under 1500 grams 80% will need resuscitation.

B. Basic Approach to CPR same as adult

1. Airway

2. Breathing

3. Circulation

a. Cardiac arrest is extremely uncommon in children or infants and when it does occur it is usually secondary to respiratory arrest. This makes airway and breathing even more important in infants and children.

Anticipation and Preparedness

1. If you are asked to attend a delivery and you feel it's worth your time to go, then it's worth going prepared and anticipating a disaster.

2. Know the equipment and know that it is functioning **BEFORE** the infant arrives.

3. NRP requires that at least 2 people with resuscitation skills be present at all deliveries, one must have intubation skills. The second person is absolutely necessary to evaluate the effectiveness of ventilation and to monitor the heart rate and if necessary to give chest compressions. If the delivery is considered high risk, two people must be dedicated only to the infant. If the resuscitation is prolonged, a third person will be required to insert lines and administer medications. **DO NOT GO BACK BY YOURSELF!!** Take a partner with you.

4. If you are alone and not with an established Resuscitation Team, the tasks should be divided among the available help **BEFORE** the infant arrives.

5. **Equipment List:**
   Radiant warmer (on and warm)
   Suction with manometer
   Resuscitation bag (250-500cc)
   Premature, and term face masks
   Laryngoscope
   Laryngoscope blades (straight 0 and 1)
   Stethoscope
   Towels

3-way stopcock(s)
Oral airways (newborn and premmie)
Bulb syringe
Meconium suction device
2.5, 3.0, 3.5 ETT's
Suction catheters (5,8,10 French)
ETT stylet
Syringes (10, 20 cc's)
Feeding tubes (5, 8 French)
Cord cutting scissors, clamp, gloves
3.5 and 5 Fr. umbilical catheter, sterile water
Medications: Epinephrine (1:10,000)
Sodium Bicarbonate 4.2%
Volume Expander – NS
D10W
Narcan

II. Basic Physiology

A. Fetal Circulation	B. Neonatal Circulation
1. Low flow (placenta)	1. Increased flow
2. High PVR	2. Decreased PVR
3. In parallel	3. In series

C. The pulmonary pressure is controlled in part by perivascular pH,PaO2, PaCO2. If ventilation and oxygenation are not established soon after birth, there is persistent pulmonary hypertension or persistent fetal circulation which will cause right to left shunting across the ductus arteriosus and the foramen ovale.

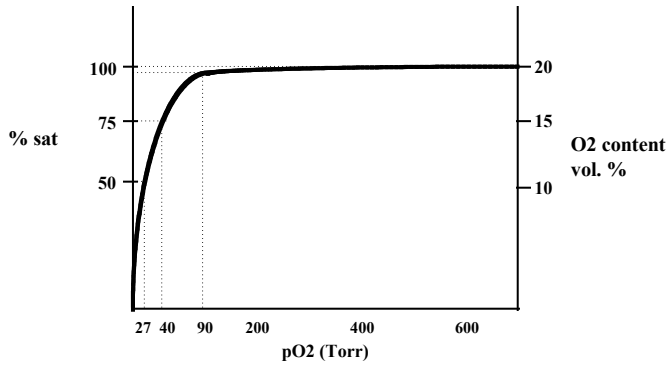
D. If ventilation and oxygenation are not soon established glycogen stores are used up, tissue hypoxia develops and anaerobic metabolism begins to produce large amounts of lactic acid. Cardiac output falls causing decreased perfusion to the organ systems and eventually the brain, heart, and adrenals.

The following graph depicts the ***adult*** oxyhemoglobin dissociation curve.

Neonates have fetal hemoglobin which shifts the curve to the left.

Shifts of this curve to the **left** are caused by: alkalosis, hypocarbia, decreased temperature, decreased 2,3-DPG, increased cardiac output, or fetal hemoglobin. These cause an increased oxygen affinity but a decreased oxygen release. Thus, the oxygen tension must drop lower than normal for the hemoglobin to release an equivalent amount of oxygen to the tissues compared to adult hemoglobin. However, fetal hemoglobin has a greater affinity for oxygen at lower PaO2's (such as occurs with placental blood perfusing the fetus) so more oxygen is bound in utero.

Shifts of this curve to the **right** are caused by: acidosis, hypercarbia, temperature elevations, increased 2,3-diphosphoglycerate (DPG), or decreased cardiac output. These cause a decreased oxygen affinity but increased oxygen release.



pO2, Saturation, and O2 Content

Oxygen content is the amount of oxygen contained in our blood. This oxygen may be in solution in the liquid portion of blood, or bound to hemoglobin inside the red cells.

1. Factors involved in calculating "oxygen content" include how much hemoglobin there is in the blood, how much oxygen a gram of hemoglobin can hold, the degree to which the hemoglobin is saturated, and finally how much oxygen is contained in the liquid portion of the blood. The equation which expresses the oxygen content of blood is:

0_2con = [Hgb] x (% sat) x 1.36 + ($p0_2$ x 0.0031)

"0_2con" is oxygen content

"[Hgb]" is the hemoglobin concentration in grams per 100 ml of blood,

"(% sat)" is the percent saturation of hemoglobin,

1.36 ml of oxygen per gram of hemoglobin is the oxygen carrying capacity of adult hemoglobin

"$p0_2$" is the partial pressure of oxygen in the plasma in mmHg, and

0.0031 ml of oxygen per 100 ml per mmHg is the solubility of oxygen in plasma.

It is impressive to note from this equation that the magnitude of the contribution of dissolved oxygen in plasma, the only element affected directly by the $p0_2$, to total oxygen content of the blood is quite minimal. Yet, pO_2 is the parameter most commonly followed clinically!

2. A moment's diversion on this point may be helpful. You may ask, "If the $p0_2$ is in fact such an unimportant parameter, why do we follow it so closely?" Historically, the $p0_2$ could be easily measured clinically. The hemoglobin saturation was either measured with a separate and specialized apparatus or was derived from the $p0_2$ and the pH. It also has to do with a fortuitous relationship between the $p0_2$ and hemoglobin saturation in the usual physiologic range as shown by the preceding diagram.

3. Between $p0_2$ values of approximately 40 and 90 torr, the relationship between the $p0_2$ and the hemoglobin saturation is fairly linear. Thus, a given increase in the $p0_2$ is accompanied by a roughly proportional increase in the hemoglobin saturation and thus in the oxygen content of the blood. However, it may also be clearly seen from the figure that below 40 torr and above 90 torr this is not the case. Below 40 torr, a small change in $p0_2$ is associated with a rather larger change in hemoglobin saturation. Thus, when the $p0_2$ decreases from 40 only to 27 torr the saturation falls from 75% to 50%. (Meaning that small changes in the $p0_2$ in this range can make a large difference in the well being of the patient's tissues!) The opposite is true above 90-100 torr where, even with dramatic increases in the $p0_2$, the saturation rises only very little. Thus, when the $p0_2$ rises from 90 to 600 torr the saturation goes only from about 99% to 100%. (Hemoglobin saturation cannot go any higher than 100%).

4. The relationship between changes in oxygen saturation and in changes in oxygen content are also depicted in the figure. It is important to note that these two parameters are related in a consistently linear fashion. That is to say that changes in one are accompanied by similar and proportional changes in the other. Because of this, hemoglobin saturation is a good indicator of oxygen content and is therefore a very useful clinical parameter to follow.

III. Infants at Risk

A. All infants are actually at risk for asphyxia during labor and delivery. Contractions decrease flow to the placenta and therefore gas exchange. A normal term infant without complications tolerates this without problems. There are four main mechanisms that can cause asphyxia to the fetus/neonate:

1. Interruption of umbilical blood flow i.e. cord compression.

2. Failure of exchange across the placenta because of separation (i.e. abruption.)

3. Inadequate perfusion on the maternal side of the placenta (i.e. maternal hypotension, toxemia.)

4. Neonatal asphyxia from failure to inflate the lungs from a variety of reasons:

   a. Upper/lower airway obstruction i.e. meconium.

   b. Inability to expand the lungs i.e. drugs,

RDS/prematurity.

c. Inability to expand the lungs secondary to fetal asphyxia.

B. Maternal, perinatal, and postnatal complications and presentation identify the infants at risk.

1. Most asphyxia occurs prenatally when it is much more difficult to monitor. The best measure of in utero asphyxia is the cord blood gas pH. The arterial side is the side that reflects the fetus while the venous side reflects the placental well being. Obviously, we are more interested in the arterial or fetus side. The CO_2 is very helpful in determining the cause of the asphyxia. A high CO_2 on the arterial side out of proportion to the venous side is probably a cord compression causing CO_2 build up in the fetus. If utero-placental insufficiency is the problem, both gases would be abnormal.

Normals

VENOUS CORD GAS		ARTERIAL CORD GAS
7.29 (7.20 low normal)	pH	7.26 (7.15 low normal)
40	pCO_2	45-55
35	pO_2	20

2. Once the fetus/neonate has an abnormal gas, the neonate/fetus must be evaluated by a physician. A repeat blood gas from the newborn may be indicated.

3. It is very rare we are not forewarned of fetal distress and/or prematurity before the actual delivery. There is no excuse not to BE PREPARED BEFORE THE DELIVERY. CHECK THAT EQUIPMENT IS PRESENT, THE CORRECT SIZE AND PROPERLY FUNCTIONING!

4. A high risk delivery should be anticipated if any of the following are present:

Antepartum Factors

Maternal diabetes	Post-term gestation
Pregnancy induced hypertension (PIH)	
Multiple gestation	Oligohydramnios
Chronic hypertension	Size-dates discrepancy
Preeclampsia	Previous stillbirth
Eclampsia	Maternal infection
Previous Rh sensitization	Hydramnios
Bleeding in 2nd or 3rd trimester	Maternal drug abuse
Premature rupture of membranes	No prenatal care

Drug therapy:
- Reserpine
- Lithium
- Magnesium
- Adrenergic blockers

Decreased fetal movement	Fetal abnormality

Intrapartum Factors

Elective or emergency cesarean section	
Non-reassuring fetal HR	
Abnormal presentation	General anesthesia use
Premature labor	Uterine tetany
Rupture of membranes > 24 hrs	
Maternal narcotic w/in 4 hrs	Precipitous labor
Foul smelling amniotic fluid	Meconium stained fluid
Prolonged labor (> 24 hrs)	
Prolonged 2nd stage of labor (>2 hrs)	
Prolapsed cord	
Abruptio placenta	Placenta previa

IV. Assessment

A. APGAR SCORE SHOULD **NOT** BE USED TO DETERMINE THE NEED FOR RESUSCITATION

1. If the 5 minute score is less than 7 a score should be assigned every additional 5 minutes until greater than 7 or for a total of 20 minutes to assist in evaluating transition. The 15 and 20 minute scores are of more prognostic value than the 1 and 5 minute scores.

V. Steps in Neonatal Resuscitation

A. Temperature Regulation/Drying

1. Asphyxiated infants have an unstable thermoregulatory system and hypothermia delays recovery from acidosis.

2. Place the infant under a preheated radiant warmer.

3. Dry off amniotic fluid. Remove the wet towel.

4. The warmest place for a normal infant when a radiant warmer is not available is skin to skin against the mother.

B. Positioning

1. On back with neck in neutral or slightly extended position. If there are copious secretions, the head should be turned to the side.

2. A 1" blanket or towel may be place under the shoulders for maintaining the proper head and neck positions, esp. in babies with large occiputs from molding, edema etc.

3. Take care to prevent hyperextension or underextension of the neck.

C. Suctioning

1. First the mouth and then the nose. (The mouth is suctioned first to prevent aspiration should the infant gasp when the nose is

suctioned). If secretions are copious turn the head so that secretions will pool in the mouth and not the posterior pharynx.

2. Use bulb syringe, or wall suction {**use no more than -100 mm Hg**,(80-100 mmHg) or -136 cm H_2O}. Use 8 or 10 F. catheter.

3. Dangers:

Vagal bradycardia
Trauma
Hypoxia (suction no more than 5 sec.)
Vomiting and aspiration

D. Suctioning Meconium

1. Meconium staining of amniotic fluid occurs in up to 11% of all deliveries. The percentage may be as high as 44% in post dates pregnancies. It may be a sign of fetal distress as well as a cause of pneumonitis.

2. Infants may aspirate this fluid before, during or after delivery. Approximately 4-6% of all infants with aspirated meconium stained amniotic fluid will develop respiratory distress, pneumonitis, PPHN, air leaks.

3. To prevent aspiration of this fluid during or after delivery, the head should be delivered and the mouth, oropharynx, and hypopharynx thoroughly suctioned before delivery of the thorax and the first breath.

4. If the infant does not make any respiratory effort and will need positive pressure ventilation, the trachea should be intubated and suctioned before positive pressure ventilation is given. This is done by connecting a wall suction meconium device to the endotracheal tube and suction while withdrawing the tube.

5. When meconium-stained fluid is present and the infant has repiratory depression, tracheal suctioning should be completed as soon after delivery as possible. The vigorous baby with meconium-stained fluid does not require tracheal suctioning.

E. Stimulation

1. 2 flicks or slaps on the soles or 2 back rubs only. If no response proceed to ventilation. Further stimulation will only cause more hypoxia, and waste valuable time.

2. May rub head, body if baby is breathing and has a good HR.

VI. Assessment

A. The need for resuscitation should be determined by evaluating the:

Respiratory Activity
Heart Rate ($\frac{\text{HR for 6 sec}}{\text{X 10}}$)
Color

VII. Ventilation/Oxygenation

A. If breathing:

1. Evaluate heart rate and then color.

2. If heart rate is above 100 and baby is centrally cyanotic give 100% blow by oxygen. Once baby is pink withdraw in increments, reassessing HR and breathing. (1/2" = 80%, 1" = 60%, 2" = 40%, then off.) Oxygen is not needed for peripheral cyanosis (acrocyanosis).

3. If HR > 100 and there is no central cyanosis, O_2 is not needed.

B. Indications for positive pressure ventilation. (4)

1. Apnea

2. Heart rate < 100

3. Persistent central cyanosis on 100% O_2

4. Gasping respirations

C. Maintain position of infant

D. Face masks are labeled preterm, and term infant. Should have no more than 5ml of dead space. Establishing an airtight seal is the most critical step. Mask should be on bridge of the nose and cleft of the chin. The most common place to leak is between cheek and bridge of the nose. Do not put pressure on the trachea.

E. The person ventilating should be at the head of the bed and should have a clear view of the chest.

F. Remember the bag is 500-750 cc's and the infant's T.V. is only 20-30cc's. Do not empty the bag with each squeeze. Use 5-8 liters/min of 100% O_2.

G. Give 40 to 60 breaths per minute. Count: squeeze, two, three, squeeze. Give enough to see chest rise a "normal easy breath".

LISTEN over the upper chest or axilla and over the stomach.

H. If BVM applied for longer than 2 minutes insert an orogastric tube and leave in place during ventilation to prevent stomach distention. (Length = Bridge of nose to earlobe to xiphoid) Use 8 Fr. feeding tube and 20cc syringe. Tape to cheek. Consider intubation.

I. **IF NOT VENTILATING** check in order:

1. Reapply mask to obtain adequate seal

2. Reposition the head to correct a blocked airway

3. Check for secretions and suction if present to correct a blocked airway

4. Ventilate with infant's mouth open to correct for blocked airway.

a. An oral airway or laryngeal mask airway may be used in this situation with choanal atresia or Pierre Robin Syndrome. Insert over tongue but don't force the tongue back as you insert it! It is not necessary to first reverse the position for insertion as in adults. These airways may cause gagging or vomiting so are usually not used in conscious patients. Often lying the baby on the stomach is sufficient to maintain airway patency.

5. Increase pressure delivered to correct for decreased compliance and inadequate tidal volume.

J. **Pressure**: May require 30-40 or even as high as 60 cm H_2O for initial inflation. How much pressure is 'enough'? 'Enough' means you observe the following:

1. Chest rising up and down

2. Bilateral breath sounds

3. Heart rate improving

4. Color improving. This may be 15-20 cm H_2O pressure or may be 20-40 cm H_2O or higher in lung disease with decreased compliance.

K. Bags

1. Self inflating i.e. Hope, Ambu, Laerdal

a. Many have pop off valve at 30-35 cm H_2O

b. Delivers only about 40% oxygen and 90-100% even with a reservoir because of intake of room air which is mechanism of self inflation.

c. Can't give O_2 passively and usually no manometer in line for measuring PIP or PEEP.

d. Good to have for transports if out of gas.

2. Anesthesia Bags

a. Delivers 100% O2

b. Compliance detected

c. Pressure measured

Disadvantages: needs gas source, rebreathing of CO_2 if low flow and used for long periods.

L. After adequate ventilations established for 15-30 seconds, check the heart rate. Check the heart rate by listening with a stethoscope or feeling the umbilical or brachial pulse. The next step depends on the heart rate.

>100 and spontaneous respirations = O_2

<60 = continue ventilation, RECHECK VENTILATIONS and start chest compressions

When HR > 60 discontinue chest compressions, continue positive pressure ventilations until HR > 100

M. Signs of improvement:

1. Increasing heart rate

2. Spontaneous respirations

3. Improving color

VIII. Chest Compressions (External Cardiac Massage)

A. Recommendations by AHA/NRP

1. Never give a thump even with monitored fibrillation

2. Asphyxia leads to:

a. peripheral vasoconstriction

b. tissue hypoxia

c. acidosis

d. poor myocardial contractility

e. bradycardia

f. eventual cardiac arrest

3. Perform CC if

HR < 60, or
despite adequate ventilation for 15 -30 seconds

4. Position: Prefered method is hands encircling chest with thumbs over the sternum at the level of the nipples. Alternative is ring and middle fingers one finger's breadth (index finger) below the line between the nipples.

5. Rate: 120 times per minute, do not remove your thumbs/fingers from the chest between compressions

6. Compressions: 1/2 to 3/4 inch or 1/3 the chest AP diameter. If connected to blood pressure transducer, attempt to generate 75% of the systolic pressure present before the arrest.

7. Continue compressions until HR is 60 or greater. Continue ventilating until the HR is > 100.

8. Recheck Heart Rate every 30 seconds for 6 seconds (multiply X 10)

9. ALWAYS GIVE POSITIVE PRESSURE VENTILATION WITH 100% OXYGEN WHILE GIVING CHEST COMPRESSIONS!

10. Compressions should be coordinated with ventilations in a 3:1 ratio so as not to compromise breaths. 120 "events" should occur each minute: 90 compresions and 30 breaths.

IX. Intubation

A. Indicated when bag and mask ineffective, for suctioning meconium, for prolonged ventilation or for known prenatal dx. of congenital diaphragmatic hernia.

B. Infant should be on a flat surface and in the sniffing position. May use a 1" towel roll under shoulders. DO NOT HYPEREXTEND because the cartilage of the trachea is collapsible.

C. The larynx is more cephalad, anterior, the epiglottis shorter and more U shaped, and the angle of the epiglottis with the cords more acute than in the adult.

D. Establish ventilation with bag and mask BEFORE ATTEMPTING INTUBATION. Most of the time intubation will be an elective procedure. Ventilation should not be interrupted for more than 20 sec. for intubation. Stop if the HR < 60 and bag. DON'T PANIC, an infant can almost always be ventilated with a bag and mask. Exceptions:

1. ELBW <1200 grams with RDS

2. Diaphragmatic Hernia

3. Upper airway obstruction

ET Tubes

1. 2.5: <1000 grams, extremely premature, <28 weeks gestation
2. 3.0: 1000-2000 grams, premature, 28-34 weeks gestation
3. 3.5: 2000-3000 grams, term, 34-38 weeks gestation
4. 3.5 - 4.0: >3000 grams, large term, >38 weeks gestation
5. Use 0 laryngoscope blade for preterm and 1 for term infants

F. Technique

1. Laryngoscope is a left handed delicate instrument not a tire iron. A straight blade or Miller is preferred in infants. Check that the light functions ("white, bright and tight")!

2. Get down in the same plane as the infant's glottis.

3. Insert blade of laryngoscope and sweep tongue from right to left. Usually it is placed too deep into the esophagus. Pull back slowly, until the epiglottis comes in view, then lift epiglottis up. The cords will be posterior to or under the epiglottis. If they are not visible, apply cricoid pressure with your little finger or ask an assistant to apply it. While holding the blade in the direction of the handle, insert E.T. tube from the right side (2 to 3 o'clock position). An assistant may pull down the corner of the mouth for easier insertion. DO NOT SQUEEZE THE TUBE OR LET IT TOUCH THE GUMS!! This only directs the tube away from where you want it.

4. A stylet is not usually necessary. Those who think they need one should check and secure it so the tip does not go beyond the Murphy's eye. Remove the stylet once the ETT is in place.

5. If the cords are in spasm do not touch them. Ask someone to give the infant a gentle Heimlich maneuver and they will open. Never force the tube.

6. Monitor HR if it drops STOP, bag and try again.

7. If you don't see the cords, revisualize or have someone else do so. Attempting to intubate without adequate visualization rarely results in success and may lead to complications.

8. Distance from glottis to carina in term infant is 5 cm so place tube 2.5 cm below cords. Check breath sounds; **Lip to Tip measurement (cm = 6 + WT in kg), and CXR.**

9. Supervisors: <u>if the baby is not responding to ventilation after intubation by a junior resident, he/she is not intubated until proven otherwise.</u> **Look** to make sure the ET tube is between the cords.

10. Flexion of the baby's head causes tube to go down and extension causes it to move up.(the ETT goes the way the baby's nose moves)

11. Once in, note cm mark at upper lip and tape. Cut off tube so that no more than 4 cm of dead space exists.

12. ETT is correctly placed if: you hear bilateral breath sounds, see the chest rising with each ventilation, no air is heard entering the stomach, no gastric distention occurs.

13. An intubated patient who desaturates should have the ETT carefully evaluated. Six problems occur in this situation:

1. Patient is extubated with ETT in the esophagus.
2. ETT is in the right mainstem bronchus.
3. ETT is plugged.
4. Patient has a pneumothorax.
5. Patient has decreased compliance so requires more pressure.

6. Ventilator, gas supply, or equipment is malfunctioning. Check that ETT is not kinked !

X. Medication/Volume

A. Myocardial dysfunction and shock in the neonatal period are usually the result of profound hypoxia, acidosis, and/or hypovolemia.

B. Shock may also be secondary to hypovolemia.

1. Place UVC and measure CVP. If low consider hypovolemia. If normal or high, no help.

2. Usually there will be a history of blood loss, abruption, placenta previa, cord compression (especially if venous occlusion occurred only-cord gases will be helpful), fetal distress with fetal to placental transfusion.

3. Signs of hypovolemia:

a. Decreased B.P. - may not be present. BLOOD PRESSURE DOES NOT EQUAL PERFUSION. Shock can be present with normal or even high blood pressure.

b. Poor response to resuscitative efforts

c. Rapid heart rate with weak pulses, cap. refill (on chest) > 2sec.

d. Pallor persisting despite oxygenation

e. Decreased CVP - but may not be decreased secondary to increased RV and pulmonary pressures.

4. Give volume over 5-10 minutes

a. 10 cc/kg 0 neg. blood crossmatched with mother if indicated.

b. 10 cc/kg N.S. or L.R.

5. Check Dextrostix and give 2 cc/kg of $D_{10}W$ if glucose < 40.

C. Medication should be administered if, after adequate ventilation with 100% oxygen and chest compressions, the heart rate remains < 60.

1. AHA/ACLS "There is no current evidence that two previously recommended drugs atropine and calcium, are useful in the acute phase of neonatal resuscitation. Sodium bicarbonate may be useful in the acute phase of neonatal resuscitation to help correct a documented metabolic acidosis but its' use is discouraged in brief arrests or episodes of bradycardia.

2. Epinephrine

a. An endogenous catecholamine with potent B adrenergic stimulating properties; in a cardiac arrest setting, the Alpha adrenergic mediated vasoconstriction may be the more important action.

b. Vasoconstriction elevates the perfusion pressure during chest compression, enhancing the delivery of oxygen to the heart.

c. It also enhances the contractile state of the heart, stimulates spontaneous contractions, and increases HR.

d. Indications

(1) Asystole, or hypotension unrelated to hypovolemia.

(2) HR <60-despite adequate ventilation for a minimum of 30 sec's with 100% oxygen and chest compressions.

e. Dose

(1) 0.01-0.03 mg/kg (0.1-0.3 cc/kg) 1:10,000

(2) May repeat q. 5 min

(3) I.V. or E.T. (May dilute 1:1 with NS if given via ETT)

3. Sodium bicarbonate will not improve blood pH in the absence of adequate ventilation, therefore the initial approach to resuscitation concentrates on oxygenation and ventilation to correct hypoxemia and acidosis. If needed, based on documented metabolic acidosis:

a. 2 mEq/kg over at least 2 minutes. (1 mEq/kg/min)

b. Remember that hypovolemia causing a metabolic acidosis should be treated with volume initially.

4. Naloxone

a. Indications

(1) For reversal of respiratory depression induced by narcotics given to the mother within 4 hours of delivery.

b. Ventilate and oxygenate first

c. Consider admission to NICU on a monitor if mother or baby given naloxone, as the duration of action of naloxone is 1-4 hours and narcotics have a longer duration of effect.

d. **May induce withdrawal symptoms in baby if mother addicted**

e. Dose: 0.1 mg/kg of 0.4 mg/ml solution of Narcan rapidly

f. Route: I.V., E.T., if good perfusion I.M.,

S.Q.

XI. Vascular Access

A. UMBILICAL VEIN IS THE PREFERRED VASCULAR ACCESS

B. Place a 3.5-5.0 F. inserted so the tip is just below the skin level but has free flow (2-4 cm). Avoid placing the line higher in the acute phases of a resuscitation to avoid infusing hypertonic solutions into the liver.

C. Peripheral veins may be used

D. E.T. tube may be used for:
Narcan
Atropine
Valium > NAVEL
Epi
Lidocaine

E. Same dose but may dilute it with 1 cc of N.S. to aid in delivery. Place via feeding tube down E.T. and stop compressions during bagging.

XII. Countershock and Cardioversion

A. Defibrillation

1. Asystole and bradyarrhythmias are responsible for 90% of the arrhythmias in Pediatric cardiac arrest. Ventricular arrhythmias make up the remaining 10%.

2. If fibrillation present, DO NOT THUMP, oxygenation and ventilation with chest compressions usually is all that is necessary.

3. Paddle size: Infants 4.5 cm (< 10 kg, < 1 yr)
Children 8.0 cm (> 10 kg, > 1 yr)

4. Dose: 2-4 Joules/kg (follow algorithm)

B. Cardioversion

1. 0.5-1.0 Joules/kg (follow algorithm)
2.

References: JAMA 255:2961-2973,1986, American Heart Association Newborn

ONCOLOGIC EMERGENCIES

ACUTE TUMOR LYSIS SYNDROME

I. CLINICAL FEATURES

A. Definition: Acute tumor lysis syndrome is a phenomenon of cellular death causing electrolyte abnormalities and renal dysfunction which occurs after malignant cell degradation.

B. Onset: may occur before therapy or 1 to 5 days after start of cytotoxic therapy (induction).

C. Most commonly seen in Burkitt's lymphoma and T-cell leukemia/ lymphoma. Also associated with bulky abdominal disease.

D. Associated with elevated pretreatment serum uric acid (see below), LDH (an indirect marker of tumor burden), and serum creatinine. Uric acid levels > 7.0, LDH > 250 and creatinine > normal for age place the patient at risk for tumor lysis syndrome.

E. Poor urine output.

II. PATHOPHYSIOLOGY

A. Degradation of malignant cells causes the release of phosphates and potassium during tumor lysis.
1. PO_4^{2-} concentration is 4-fold higher in lymphoblasts.
2. Calcium phosphate crystals precipitate in the microvasculature and renal tubules when $[PO_4^{2-}]x[Ca2^{++}]$ > 60 mg/dL.

B. Development of hyperuricemia occurs.
1. Purines are released by fragmented tumor nuclei. This causes increased substrate for uric acid production.
2. Xanthine oxidase is responsible for the enzymatic conversion of hypoxanthine to xanthine and xanthine to uric acid:

purine → hypoxanthine → xanthine → uric acid

C. Patients become symptomatic at uric acid levels > 10 mg/dL. Symptoms include lethargy, nausea and vomiting, uric acid calculi, oliguria, anuria, and hematuria. A neurologic syndrome with lethargy, seizures and paresthesias may be observed in severe cases. (It also is associated with gouty arthritis in patients with solid tumors or chronic leukemia.)

D. The excretory capacity of the kidneys is exceeded resulting in inadequate renal function. Oliguric renal failure may ensue, resulting in hyperkalemia and hyperphosphatemia.

III. EVALUATION/MONITORING

A. Monitor electrolytes (especially K^+, PO_4^{2-}, Ca^{2+}, uric acid) and renal function (BUN, creatinine) every 4 to 6 hours.

B. Obtain an ECG if the K^+ is elevated. Widened QRS complexes and peaked T waves will precede malignant arrhythmias or asystole.

C. Strict volume status monitoring is essential. Evaluate I/Os q 6 hours.

D. Patients with tumor lysis syndrome are admitted to the PICU for constant monitoring of cardiac rhythm and BP.

E. Placement of central venous/ pulmonary artery catheters and arterial lines to facilitate hemodynamic monitoring is usually required.

IV. THERAPY (see Figure 1 which follows)

A. Establish metabolic stability before treatment.

B. Management of hyperkalemia, hyperphosphatemia and hypocalcemia are discussed in the chapter on electrolyte and fluid abnormalities. Avoid severe alkalosis which potentiates precipitation of calcium phosphate crystals in the microvasculature and renal tubules.

C. Hyperuricemia
1. Decrease uric acid production with allopurinol, a xanthine oxidase inhibitor.
2. Promote uric acid excretion, keeping urine pH alkaline ($\geq$6.5 and $\leq$ 7.5). Start with $NaHCO_3$ 40-60 mEq/L added to IVF.
3. Decrease the uric acid concentration in the urine. Hydrate at 1½ to 2 times maintenance (2400 to 3000 cc/M^2/day - see body surface area formula below). IVF should be age appropriate, most typically D51/2NS with 40 meq/l $NaHCO_3$

4. Treat renal insufficiency. Early insufficiency can be managed with lasix 1 mg/kg or mannitol 0.5 to 1.0 g/kg. MANNITOL IS CONTRAINDICATED IN CASES OF OLIGURIA (urine output < 0.5 cc/kg/hr). Acute or severe oliguric renal failure is managed by Pediatric Nephrology with hemoperfusion, hemodialysis or peritoneal dialysis.

D. Body surface area in $M^2 = \sqrt{\frac{\text{height (cm) X weight (kg)}}{3600}}$

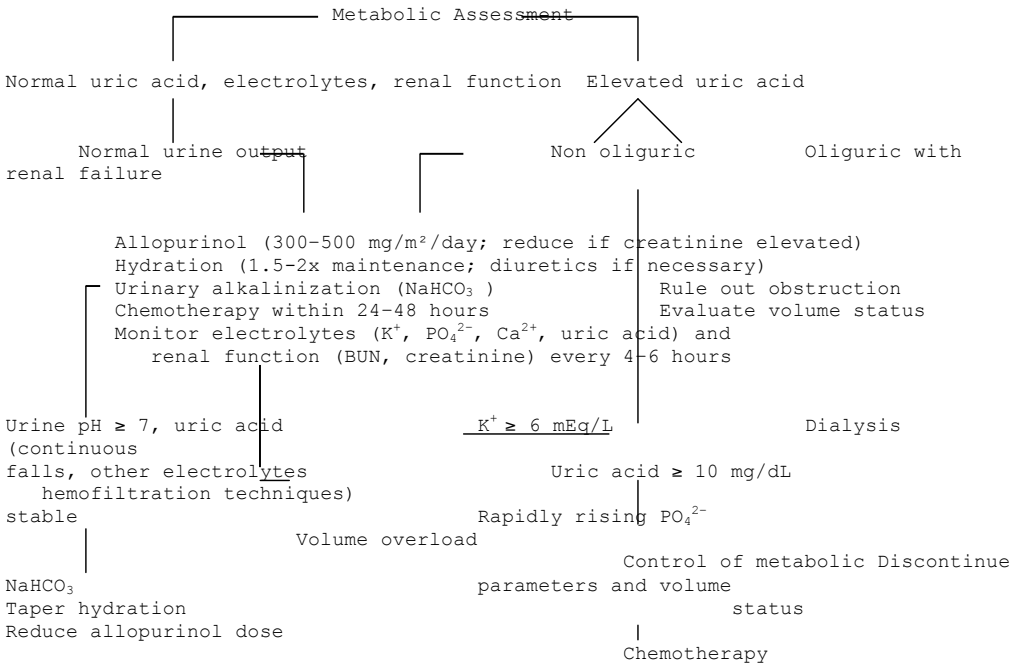


Figure 1. Management of patients with tumor lysis syndrome (Burkitt lymphoma or lymphoblastic leukemia). Adapted from Ognibene, F. P. and Pizzo P. A., "Oncologic Issues" in Holbrook, P. R., ed., Textbook of Pediatric Critical Care, W. B. Saunders Company, Philadelphia, 1993, p. 809.

LEUKEMIA

I. Introduction

A. Leukemia occurs when a single progenitor cell undergoes malignant transformation giving rise to poorly differentiated blasts which do not differentiate further but replace the normal marrow cells. Acute Lymphoblastic Leukemia (ALL) accounts for 80% of childhood leukemias with approximately 2,500 new cases being diagnosed per year in the United States. Acute Nonlymphocytic Leukemia (ANLL), previously referred to as Acute Myelogenous Leukemia (AML), accounts for the other 20%. ALL is of lymphoid origin while ANLL is of myeloid origin.

II. Clinical presentation

A. Signs and symptoms

1. Fever

2. Pallor - the mean Hgb at diagnosis is 7.0

3. Bruising/ Petechiae - the mean platelet count at diagnosis is 50,000

4. Neutropenia - leukocytosis may be seen secondary to the increased numbers of blasts but this causes a functional neutropenia

5. Hepatosplenomegaly

6. Bone pain

7. Lymphadenopathy

8. Mediastinal mass

B. The most common signs and symptoms are secondary to the marked pancytopenia.

C. The ANC at diagnosis is usually < 1,000.

D. ANLL may present with skin findings.

1. Chloromas are solid collections of myeloblasts. They may occur anywhere but are most common in the epidural space, retroorbital areas, and the skin. When they occur in the skin they are called leukemia cutis or granulocytic sarcoma.

III. Laboratory evaluation

A. Screening labs and tests

1. CBC with differential. **If the patient is neutropenic and has fever he/she needs broad spectrum IV antibiotics (see neutropenia and fever chapter).**

2. Chem 20

a. Creatinine: this serves as a screen for tumor lysis (see that chapter) and renal involvement.

b. LDH as an indirect marker of tumor burden and lysis.

c. Uric acid as a marker of tumor lysis.

d. LFT's as a screen for hepatic involvement.

e. PT, PTT, fibrinogen: M3 subtype of ANLL associated with DIC.

f. Type and cross for PRBCs and platelets if needed (**ALWAYS** give CMV negative, irradiated and leukofiltered blood products as the patient may be a bone marrow transplant candidate in the future)

g. CXR: T-cell ALL is associated with mediastinal masses.

IV. Complications

A. The most common complications after diagnosis are:

1. Bleeding: treat the patient if the platelet count is < 20,000. Treat DIC if present.

2. Infection: if fever and neutropenia are present treat with the appropriate antimicrobials.

3. Tumor lysis syndrome

4. Leukostasis: this is rare unless the WBC count is > 200,000. Organs at risk are the brain and lungs. CNS symptoms vary from somnolence to stroke. The first pulmonary sign is usually tachypnea, often accompanied by a decreased oxygen saturation. CXR changes are late findings. The treatment is the rapid initiation of chemotherapy. Leukapheresis or exchange transfusion will quickly lower the WBC count. The effect is transient though, and chemotherapy should be started as soon as possible. Prophylactic use of leukapheresis or exchange transfusion should be considered in patients with very high WBC counts.

5. Mediastinal mass: if signs of airway compromise occur the patient may need emergent radiation therapy prior to diagnosis.

NEUTROPENIA AND FEVER

I. PHYSIOLOGICAL ALTERATIONS IN CHILDREN WITH CANCER

A. Altered cellular immunity predisposes patients to infections with intracellular bacteria, fungi, herpes virus group, and protozoa.

B. Altered humoral immunity predisposes patients to encapsulated bacteria.

C. Neutropenia predisposes patients to gram-negative bacilli and *Staphylococcus* species.

D. Mass effect of tumors, tumor invasion, mucositis, medical devices and medical interventions violate physical barriers which normally protect against infection.

II. EVALUATION OF A CHILD WITH FEVER AND NEUTROPENIA

A. History
1. Cough, dyspnea, tachypnea, chest pain.
2. Diarrhea, pain with defecation.
3. Skin sores.
4. Pain with swallowing, sore throat.
5. Exposure to persons with infections (particularly varicella and other herpes viruses).
6. Date of last chemotherapy.
7. Expected interval until the granulocyte count returns to normal.

B. Complete Physical Examination

C. Laboratory Evaluation
1. CBC with differential and platelets.
2. BUN and creatinine.
3. Liver function tests.
4. Cultures all ports of catherters and obtain one peripheral cx.
5. Urinalysis and urine culture. Do not catheterize patient.
6. If patient has meningeal signs discuss LP with heme-onc staff ***prior*** to performance.

D. Radiographic Evaluation
1. Posterior and lateral chest X-rays, if pulmonary symptoms present.
2. Other radiographic studies as clinically appropriate.

III. PRINCIPLES OF ANTIBIOTIC THERAPY

A. Initial therapy must have a broad spectrum of coverage. Among many options include:

1. **β-lactam with or without n aminoglycoside. Cefipime only or with an aminoglycoside. Cefipime as single agent therapy may be used if patient is very stable. If patient has tachycardia, abdominal pain, low blood pressure or any other concerning sign or symptom, double coverage for gram negative infections (i.e Cefipime and Gent/Tobra/Amikacin should**

be used). Cefipime and Gentamicin: *This is the most commonly used regimen.*

2. **Zosyn alone or with an aminoglycoside. Same indications as in #1 apply.**

3. **Vancomycin, aminoglycoside, and a β-lactam**. Expands coverage for gram-positive organisms. **Vancomycin as as a front line therapy should not be done due to emergence of vancomycin-resistant organisms such as *Enterococcus*.** Delaying the addition of Vancomycin until confirmation of a gram-positive infection doesn't appear to influence the outcome of therapy. If gram + coverage is desired, Nafcillin/Oxacillin should be used

4. If psuedomonas is documented or likely, double gram negative coverage is indicated.

B. Bacterial isolates and antibiotic susceptibility vary greatly. Familiarize yourself with antibiotic susceptibilities in your institution.

C. Therapy should be safe, with minimal toxic effects.

D. The rate of superinfection or development of resistant organisms should be minimized.

IV. RE-EVALUATION OF INITIAL EMPIRIC THERAPY

A. 24 to 72 hours:
1. Evaluate response to therapy.
2. Optimize treatment based on results of pre-treatment cultures.
3. Modify therapy if persistent bacteremia or development of new symptoms or signs occurs.
4. Continue broad antimicrobial therapy until neutropenia resolves.

B. 5 to 7 days:
1. **Fever and neutropenia resolving**: If infection is documented, give 10 to 14 days of antibiotics. If no infection demonstrated, discontinue antibiotics.
2. **Neutropenia persists**: Continue antibiotics until neutropenia resolves. Because this is associated with an increased risk of bacterial or fungal superinfection, an alternative is to continue antimicrobial therapy for a week, or for 5 days after the fever subsides, whichever is longer, and reinstitute therapy at the first sign of any deterioration in clinical status.
3. **Fever and neutropenia persist**: A diligent search for the source of infection is important. Add amphotericin B and continue throughout the period of neutropenia.

C. Breakthrough bacteremia.
1. Gram-positive isolate: add vancomycin.
2. Gram-negative isolate: assume resistant organism. Switch to a new regimen.

D. Catheter-associated infections.
1. **No evidence of local infection**: Use vancomycin as well as coverage for gram-negative organisms such as an aminoglycoside. Remove catheter if

cultures remain positive after 48 hours of appropriate antibiotic coverage. If cultures become negative, do not remove catheter, complete 10 to 14 day antimicrobial course.

2. **Exit site infection without fever or bacteremia:** Culture all ports, peripheral blood and the local catheter site. Treat with vancomycin, an aminoglycoside and a β-lactam. If parenteral therapy fails, remove catheter.

3. **Exit site with fever or bacteremia:** Culture all ports, peripheral blood and local site. If normal ANC, administer vancomycin and aminoglycoside. If neutropenic, administer vancomycin, aminoglycoside and β-lactam. Reassess at 48 to 72 hours. Remove catheter if cultures still positive.

4. **Tunnel infection:** Remove catheter.

E. Severe oral mucositis or necrotizing gingivitis.

1. Cover anaerobic organisms with clindamycin or metronidazole.
2. Perform viral cultures and consider Acyclovir therapy for herpes.

F. Esophagitis.

1. Institute a trial of oral clotrimazole, ketoconazole, fluconazole or IV amphotericin B.
2. Perform viral cultures and start acyclovir.

G. Pulmonary infiltrates.

1. **Patchy or localized:** Continue antibiotics expectantly if ANC rising. If neutropenia persists, perform broncho-alveolar lavage (BAL) or open biopsy and treat according to findings. If a diagnostic procedure cannot be tolerated, begin empiric Amphotericin B.

2. **Diffuse or interstitial:** In patients with neutropenia, perform a BAL or open biopsy, or begin empiric therapy with trimethoprim-sulfamethoxazole, erythromycin and amphotericin B. If normal ANC, institute a trial of TMP-SMZ and erythromycin and do diagnostic procedure only if patient does not improve.

H. Perianal tenderness. In addition to broad spectrum antibiotics, add anaerobic coverage with clindamycin or metronidazole.

SPINAL CORD COMPRESSION

I. ETIOLOGY

A. Compression caused either by local tumor extension or by tumor metastasis.

B. Tumors: lymphoma, neuroblastoma or soft tissue sarcoma most common.

II. PRESENTATION

A. Radicular back pain and motor weakness.

B. Sensory deficits are seen less frequently.

C. Bladder and bowel dysfunction. Incontinence is typical of lesions below L2.

III. DIAGNOSIS

A. Diagnosis is based on demonstration of vertebral lesion with dural compression.

B. Imaging techniques: spinal MRI, contrast myelography if MRI not available.

C. Tissue diagnosis via biopsy.

IV. THERAPY

A. Once compression is documented, urgent therapy aimed at nerve decompression should be initiated.

B. High-dose dexamethasone: 50 mg/M^2 bolus followed by 10 mg/M^2 every 6 hours.

C. Emergency radiation therapy consult. Lymphomas and neuroblastomas are particularly radiosensitive.

D. A neurology consult should be considered to carefully assess the pre-treatment neurologic function. Therefore, any post-treatment improvement will be apparent.

E. Laminectomy is indicated if the etiology is hemorrhage, the tumor is not radiosensitive, or if radiation therapy fails to produce neurologic improvement. Consult neurosurgery.

SUPERIOR VENA CAVA SYNDROME / SUPERIOR MEDIASTINUM SYNDROME

I. FEATURES

A. Extrinsic compression of the superior vena cava usually caused by the mass effect of an anterior mediastinal tumor. Often associated with tracheal compression.

B. Hodgkin's disease, non-Hodgkin lymphoma, and T-cell leukemia are the most common etiologies. Also associated with rhabdomyosarcoma and neuroblastoma when mediastinal involvement occurs.

C. Presentation:
1. Plethora or facial cyanosis.
2. Cyanosis of neck and upper chest.
3. Upper extremity edema.
4. Distended neck veins.
5. Stridor, dyspnea and anxiety if there is associated airway obstruction.
6. Neurologic symptoms due to increased ICP: headache, stupor, coma, or seizures.
7. Cardiac compromise with shock due to decreased venous return and/or decreased ventricular volume.

II. EVALUATION

A. History and physical exam.

B. Radiographic evaluation:
1. Chest X-ray – reveals clinically significant mediastinal mass.
2. Chest CT – determines the extent of the mass. Must be performed without sedation.
3. Echocardiogram - to evaluate for thrombi from stasis of flow

C. Tissue diagnosis is necessary to implement specific therapy.
1. Non-sedated bone marrow biopsy and/or superficial lymph node biopsy.

2. High risk of death during intubation, especially if greater than 50% reduction in trachea size documented on CT scan. **A skilled bronchoscopist must be on hand if intubation is attempted. Call pediatric pulmonology, pediatric surgery, or ENT.**

3. Establish diagnosis with least invasive measures. Be aware of potential for curculatory and respiratory failure associated with anesthesia or sedation.

4. Empiric therapy is initiated if no tissue is available and the risk of intubation is too great. It may include radiation, steroids, and/or chemotheray.

RESUSCITATION OF PEDIATRIC SHOCK

I. Shock: a clinical state characterized by inadequate tissue perfusion, i.e. the delivery of oxygen and metabolic substrates fails to meet the metabolic demands of tissues. May occur with normal, increased or decreased blood pressure.

A. *Compensated Shock:* Clinical state of tissue perfusion that is inadequate to meet metabolic demand in the presence of blood pressure within the normal age-defined range.
B. *Decompensated Shock:* Inadequate tissue perfusion with **hypotension**, ie, systolic blood pressure less than the 5th percentile for age.

Etiologies

A. Hypovolemic Shock (#1 cause of shock in PEDS)

1. Definition: Diminished circulating blood volume which results in decreased preload and thus decreased stroke volume and cardiac output.

2. Common types

i. Fluid and electrolyte losses (vomiting/diarrhea, DKA, DI)

ii. Hemorrhage (internal or external)

iii. "Third spacing" (Capillary leak syndromes, ie. Sepsis, burns, peritonitis, hypoproteinemia)

iv. Pathologic renal diuresis (post-obstructive diuresis, high-output renal failure)

3. Clinical features: Tachycardia, hypotension, poor perfusion without signs of CHF or sepsis

B. Cardiogenic Shock

1. Definition: Depressed cardiac function due to depressed contractility. CHF usually occurs prior to the onset of shock as the LV begins to fail after compensatory mechanisms have been overcome.

2. Common types:

i. Congenital Heart Disease (HLHS, AS, PS, Aortic Coarctation

ii. Primary dysrhythmias (SVT)

iii. Cardiomyopathy

iv. Infectious (Myocarditis, Endocarditis)

v. Drug intoxication (TCA, Ca-channel/ß-blockers)

vi. Hypoxic-ischemic injury (Asphyxiations, near drowning, aberrant left coronary artery, Kawasaki's)

3. Clinical features: Gallop rhythm, jugular venous distention, hepatomegaly, pulmonary edema

C. Distributive Shock

1. Definition: Widespread abnormalities in vasomotor tone can result in a general **maldistribution of blood flow**. Such abnormalities in distribution may result in profound inadequacies in tissue perfusion even in the face of normal or high cardiac output.

2. Common types

i. Septic shock

ii. Anaphylaxis

iii. Central nervous system injury/spinal cord injury (vasodilation and flaccid paralysis)

iv. Drug intoxication

3. Clinical features: Vasodilation

D. Obstructive Shock

1. Definition: Mechanical obstruction of ventricular outflow

2. Common types

i. Cardiac tamponade/effusion

ii. Tension pneumothorax

iii. Pulmonary embolus

3. Clinical features: Low voltage EKG, narrow pulse pressure, profound hypoxemia, PEA/EMD

E. Dissociative Shock

1. Definition: Oxygen utilization by cells is impaired despite normal perfusion.

2. Common types

i. Carbon monoxide poisoning

ii. Methemoglobinemia

3. Clinical features: Hypoxia with normal PaO_2, elevated carboxyhemoglobin/methemoglobulin levels, chocolate-colored blood

III. Evaluation

A. Identification of patients at risk of shock (ie patients who need monitoring).

1. Respiratory distress (See below)

2. Trauma/Burns

i. Loss of consciousness

ii. Hemorrhage

iii. Blunt abdominal trauma (liver/splenic lacs)

iv. Chest trauma (pulmonary contusion, seat belt bruising, unbelted driver)

v. Burn > 15% BSA

3. Surgical

i. Post-operative cardiac repair (post-cardiopulmonary bypass dysfunction, tamponade)

ii. Open-chest procedures (lobectomy, pneumonectomy)

iii. Post-operative craniotomy

iv. Excessive intraoperative blood loss

4. Medical

i. Immunodeficient patients with fever

ii. > 10% dehydration with oliguria/lethargy

iii. Oncologic patients at risk of Tumor Lysis Syndrome

iv. Myocarditis/Endocarditis/Cardiomyopathy

v. Drug ingestions

vi. Fever with petechial rash

B. Evaluation of Respiratory Performance

1. **Remember ABC's**

2. Signs/Symptoms of potential respiratory failure

i. Tachypnea, Increased work of breathing

ii. Use of accessory muscles, retractions

iii. Cyanosis

iv. Upper airway obstruction

v. Grunting, "head-bobbing", tripod position

vi. Diminished level of consciousness, poor pain response, failure to recognize parents

vii. Poor chest excursion, diminished air entry

viii. ***Tachypnea without distress*** may be a compensatory mechanism in:
   a. Septic shock
   b. DKA
   c. Inborn errors of metabolism
   d. Severe diarrhea
   e. Salicylate overdose
   f. Chronic renal failure

ix. Hypoventilation in an ill patient is ominous and may indicate:
   a. Hypothermia
   b. Fatigue
   c. CNS depression

3. In circulatory failure, taking control of the airway (intubation) will decrease total body metabolic workload. Early intervention is the key to prevent the development of respiratory failure and associated mortality.

C. Evaluation of Cardiovascular Response

1. General principles

i. Organ perfusion is based on cardiac output and perfusion pressure (**CO = HR x SV)**.

ii. HR and BP are easily determined, while stroke volume and peripheral vasculature resistance must be assessed by examining pulses and tissue perfusion (**CO = MAP/SVR** so **MAP = SVR x SV**).

iii. Remember septic and anaphylactic shock may be associated with increased cardiac output and normal BP. **NORMAL BP DOES NOT EXCLUDE SHOCK!** When vascular resistance is low, perfusion will appear normal with bounding pulses and wide pulse pressure.

iv. ***Vital signs are vital!!*** HR and perfusion assessment are the mainstays in your determination of shock.

2. Heart rate

i. Tachycardia - may be a response to hypoxia, hypercapnia, hypovolemia or fever.

ii. Bradycardia is an ominous sign of arrest.

3. Skin color and temperature (perfusion)

i. Skin color and temperature should be consistent over the trunk and extremities if well oxygenated in a warm environment.

ii. As perfusion deteriorates, the hands and feet tend to be affected first (prolonged capillary refill, > 2-3 sec). The skin over the trunk and extremities becomes mottled as hypoxemia and perfusion worsen.

iii. Central cyanosis is a late sign.
   a. Cyanosis requires that 5 gm/dL of reduced hemoglobin be present in skin capillaries.
   b. Cyanosis may not be present in anemic children.
   c. Most likely to be seen with combination of low arterial blood saturation and low cardiac output.

4. Blood pressure

i. Maintained by vasoconstriction (□SVR) and increased cardiac contractility.

ii. Hypotension ensues when compensatory mechanisms fail. It is a late sign of cardiovascular decompensation.
   a. A formula to estimate the 50th percentile of systolic BP in children (>5 yo) is 90 + (2 X age in years)
   b. SBP lower limit is 70 + (2 X age in years)
   c. If systolic BP falls 10 mg Hg then begin prompt, frequent evaluations for shock.

5. End Organ Perfusion - skin, brain, kidneys.
i. Skin: decreased perfusion is an early sign of shock (see above)

ii. Brain: Signs of decreased perfusion
   a. Failure to recognize/consoled by parents
   b. Hypotonia
   c. Seizures
   d. Pupillary dilatation

iii. Kidney: History of □ output is useful
   a. Adequate output is 1cc/kg/hr (infants)
   b. Adequate output is 300 cc/m2/24 hrs in older children.

IV. Laboratory Evaluation

A. Initial evaluation is clinical; treatment is initiated BEFORE lab results are available. Initial studies on shocky patients should include:

1. Blood gas analysis

i. ABG – "gold standard"
ii. CBG – take into account perfusion, poor perfusion to cap bed will give "worse" values
iii. VBG – comparison of arterial saturation to mixed venous saturation (aSO2 – MVO2 = 25 [norm]) can estimate cardiac output (ie. an increased difference indicates poor CO)

2. Lytes, BUN, Cr, Ca, Glucose

3. Immediate dextrostix - only takes a drop of blood, you get results faster than a lab draw

4. PT/PTT/fibrinogen if sepsis/bleeding are considered

5. Other labs (LFT's, ammonia, drug levels, etc) as dictated by situation (altered mental status, prolonged resuscitation, suspected hypoxic-ischemic injury)

B. If metabolic acidosis is present, determine Anion Gap: A.G. = Na^+ - (Cl^- + HCO_3^-) = unmeasured cations minus unmeasured anions, normal = 12 $\pm$ 2 mEq/Liter.

1. Increased A.G acidosis

i. Electrolyte disturbance: ↓ K, ↓ Ca, ↓ Mg
ii. Organic acid accumulation: lactate, ketones (DKA), phosphates, sulfates, formates, nitrates
iii. Toxic ingestions: ethanol, methanol, ethylene glycol, penicillins, paraldehyde, salicylates, toluene, carbon monoxide, iron, isoniazid, strychnine, cyanide
iv. Inborn errors of metabolism: glycogen storage, urea cycle defects, MSUD, etc…
v. Renal failure/Uremia
vi. Hyperosmolar hyperglycemic nonketotic coma

2. Decreased A.G. acidosis

i. Electrolyte disturbance: ↑ K, ↑ Ca, ↑ Mg
ii. Medications: IgG, THAM, lithium (increased cation),
iii. Hypoalbuminemia (decreased unmeasured anion)

3. Normal A.G. acidosis (loss of HCO_3^-)

i. Renal tubular acidosis
ii. Diarrhea
iii. Hyperchloremic metabolic acidosis
iv. Medications: Aldactone, Diamox
v. Others: pancreatic fistula, enterostomies

V. Therapy

A. Airway

1. Provide maximal 02

2. Airway protection - intubate early if any concerns for compromise (seizures, coma, etc). Place an OG/NG tube if BVM > 2 minutes

3. High PEEP may be needed to oxygenate some patients, especially in septic shock with capillary leak

4. In the awake patient, intubation is most successful using rapid sequence intubation

5. In the hypovolemic patient, most sedatives are vasodilators and negative inotropes, profound hypotension may occur during administration. A nonsedated intubation may be necessary.

B. Airway support

1. Nasal cannula - only used if modest O_2 requirement is present. Flows > 6 liters/min are irritating to nasopharynx.

2. Oxygen Hood - usually used in children $\leq$ 1 year. Humidification is possible.

3. Oxygen mask - delivers 35-60% O_2 at flow rates of 6-10 liters/min. Nonrebreather system with an oxygen reservoir can provided *nearly* 100%

4. Face Tent - often better tolerated than a facemask. Not reliable for FiO_2 > 0.40.

5. Oral airway - holds tongue away from posterior pharynx. Only used in unconscious patients (occasionally used for Pierre-Robin or choanal atresia in conscious neonates but may induce gagging).

6. Nasopharyngeal airway - soft rubber or plastic tube. Well tolerated and may be used in responsive patients. Outside diameter should not be so large that it causes sustained blanching of ala nasae. Length: measure distance from tip of nose to tragus of ear. Lubricate when insert. May damage adenoidal tissue resulting in a nose bleed that may compromise airway.

7. Esophageal Obturator Airway - not recommended for pediatric patients.

C. Fluid resuscitation for circulatory shock

1. Objectives

   i. Rapidly restore circulating blood volume
   ii. Restore oxygen-caring capacity
   iii. Correct metabolic imbalances

2. Isotonic crystalloid solutions (LR, NS)

   i. Rapidly infuse 20 cc/kg bolus (over 5-10 min)
   ii. Repeat as needed, children with septic shock may require > 100 cc/kg for resuscitation
   iii. If severe myocardial dysfunction is present, infuse 5-10 cc/kg boluses (over 10-20 min)
   iv. Monitor electrolytes, large infusions of normal saline may cause a hypernatremic, hyperchloremic metabolic acidosis
   v. Large infusions of lactated ringers in patients with liver disease will increase serum lactate levels and cause a metabolic acidosis
   vi. Avoid dextrose containing fluids during resuscitation (unless hypoglycemic) since hyperglycemia may induce an osmotic diuresis
   vii. Only ¼ of crystalloid infusion remains in the intravascular space, thus 4-**5x the calculated deficit must be given for adequate resuscitation**

3. Colloidal solutions

i. Blood, 5% albumin, FFP, synthetic colloids (hetastarch, dextran)
ii. Remain in intravascular space longer, may be more effective volume expander
iii. Risk of hypersensitivity reactions, infectious risk to human blood products
iv. Blood and blood products are indicated for replacement of blood loss (trauma) or for correction of coagulopathies
v. Rapid infusion of blood products may cause hypothermia. Monitor ionized calcium due to citrate use in stored blood

D. Fluid resuscitation for burn patients

1. Indications for intravenous resuscitation

i. Infants with > 10% BSA burn
ii. Children with > 15% BSA burn
iii. Evidence of smoke inhalation

2. Initial bolus of 20 cc/kg of LR/NS plus maintenance fluids. Goal of urine output of 0.5-2 cc/kg/hr

3. PIV placement in a nonburned area. Consider central venous access if > 30% BSA burn

4. Galveston formula

i. DAY #1: Give 5000 ml/m2 of BSA (burn losses) plus maintenance (2000 ml/m2) over 24 hours
ii. Calculation of fluid needs begins at the time of the burn, NOT the time of evaluation
iii. Infusion ½ of burn loss fluid over the first 8 hours, the second half over 16 hours
iv. Deduct any fluid given from calculated total fluid to determine rate of infusion
v. DAY #2: Give 3750 ml/m2 of BSA and maintenance fluids (1500 ml/m2) over 24 hours

5. Parkland formula (Use either formula, at Wilford we refer burns to Galveston and preferentially use the Galveston formula)

i. First 24 hours, give 4 ml/kg/%BSA over 24 hours, with ½ of total given over the first 8 hours
ii. Second 24 hours, fluid requirements average 50-75% of the first days requirement
iii. **NOTE:** This equation provides for losses and replacement, not maintenance fluids. Maintenance fluids need to be added.

E. Vascular access

1. During an active resuscitation, the preferred site access site is the one that is most readily available (PIV vs. Central vs. IO)

2. Peripheral

i. “Gold standard” is two, large-bore IVs

ii. The larger the bore of the catheter, the more rapidly fluid can be administered
iii. All medications and fluids can be administered peripherally during emergent resuscitations
iv. **NOTE:** blood flow in peripheral vascular beds maybe poor during CPR, all medications administered should be followed with a rapid flush of isotonic crystalloid (5-10 ml)

3. Central

i. Theoretically, infusion of medications centrally during CPR results in more rapid onset of action and higher peak levels than peripheral, but this does not appear to be significantly different in children
ii. Accessible veins: Femoral, jugular, subclavian
iii. Benefits
    a. Administration of hypertonic saline, vasopressors, calcium that may cause tissue damage if infiltration occurs
    b. Femoral vein is easiest and safest to access without needing to stop CPR
iv. Central venous pressure (CVP) monitoring
    a. Tip of catheter in SVC/RA junction for "true" CVP
    b. Can be used as guidance for continued fluid resuscitation vs. need to begin inotropic support
    c. Low CVP with poor perfusion and hypotension, give more fluid
    d. High CVP with poor perfusion and hypotension, suspect RV dysfunction and begin inotropic support, an echo can be helpful to assess cardiac function.
v. Risks: Infection, bleeding, thrombosis, embolism, pneumothorax, hemothorax, chylothorax, cardiac arrhythmia, air embolus

4. Intraosseus

i. If unable to achieve ***rapid*** venous access, IO access should be obtained
ii. Advantage
    a. Marrow cavity venous plexus serves as a safe, rapid, and reliable access point for crystalloids, colloids, and medications
    b. Access can be achieved in < 30-60 secs
    c. Onset of action and drugs levels are comparable to venous administration
    d. May obtain mixed-venous samples for laboratory evaluation
iii. Risks
    a. Complication rate reported: < 1%
    b. Tibial fracture, compartment syndrome
    c. Severe extravasations of drugs
    d. Osteomyelitis
iv. Technique
    a. Use sterile technique, identify the tibial tuberosity
    b. Cannulation site is 1 - 3 cm below (distal) to the tuberosity on the medial tibial side
    c. Support leg on firm surface, do not allow your hand to rest *behind* the insertion site.

d. Use a gentle but firm twisting motion to direct the needle perpendicular to the long axis of the bone or slightly caudal (toward the toes) to avoid the epiphysial plate
e. Stop advancing the needle when you feel a sudden decrease in resistance as the needle enters the marrow cavity.
f. The needle is in the marrow cavity if: the needle can remain upright without support, marrow can be aspirated [(looks red and grainy) - not always achievable], free flowing fluid without subcutaneous infiltration.
g. **Do NOT use an IO in a fractured bone.**

VI. Vasoactive Medications **for doses see algorithms and code drug sections inside front and back covers**).

A. Inotropes/Vasopressor

1. General principles

i. Therapy directed at improving myocardial contractility and decreasing LV afterload
ii. Indicated in patients with hypotension or poor perfusion despite "adequate" volume resuscitation.
iii. Most agents are sympathomimetic and work via alpha (□) or beta (□) receptors.
a. □-1: found mostly in cardiac myocytes, stimulation □ □HR and □contractility.
b. □-2: found primarily in blood vessels and bronchi, stimulation □ vaso/bronchdilation.
c. □-1: found primarily in blood vessels, stimulation □ vasoconstriction

2. Specific Agents
i. **Dopamine**
a. Action at □-1, □-1, and dopaminergic receptors, effects are dosage dependent
a. dopaminergic: 1-3 mcg/kg/min, increased renal perfusion and splanchnic blood flow
b. □-1: 4-10 mcg/kg/min, increased HR and contractility (*inotropic*)
c. □-1: 10-20 mcg/kg/min, vasoconstriction (*pressor*)
b. Indication
a. Low cardiac output state with hypotension
b. Usually first-line vasoactive infusion started
c. Precautions
a. Adverse effects: tachycardia, dysrhythmias, hypertension, extravasation necrosis
b. ≥ 50% of dopamine's action is indirect via postsynaptic norepi release. Critically ill children may lack adequate intrinsic catecholamine stores. Thus dopamine may be ineffective, epinephrine may be a better drug

ii. **Dobutamine**
a. Action primarily □-1 effect
a. Dose: 5-20 mcg/kg/min
b. Effect: □HR, + inotropy, vasodilatation

b. Indication
    a. Low output state without hypotension
    b. Hypoperfusion associated with high vascular tone
c. Contraindicated in patients with hypotension (vasodilatation may worsen hypotension)

iii. **Epinephrine**
a. The drug of choice in post arrest situations and in most pediatric patients with severe shock
b. Action
    a. □-1: 0.05-0.3 mcg/kg/min, □HR and □inotropy
    b. □-1: 0.3-5 mcg/kg/min, vasoconstriction
c. Indications
    a. Similar to dopamine. Acts directly on myocardium and vasculature, may be effective when dopamine has failed
    b. Symptomatic bradycardia unresponsive to ventilation and oxygen administration
d. Precautions
    a. Adverse effects: tachycardia, dysrhythmias, hypertension, extravasation necrosis
    b. Causes increased myocardial oxygen consumption.
    c. May cause decreased splanchnic perfusion.

iv. Norepinephrine
a. Action
    a. □-1: potent vasoconstrictor of all vascular beds
    b. □-1: + inotrope
b. Dose: 0.1-5 mcg/kg/min
c. Indication
    a. "Warm" shock, shock states with low systemic vascular resistance, "spinal shock", anaphylaxis
    b. Shock states where myocardial perfusion pressure must be acutely maintained
d. Precautions
    a. Enhances cardiac contractility but cardiac output may not be increased due to increased afterload
    b. Increased myocardial oxygen consumption, may cause myocardial ischemia
    c. Vasoconstriction of all vascular beds, including renal (oliguria) and splanchnic (gut ischemia)
    d. Adverse effects similar to dopamine and epinephrine

v. Milrinone
a. Action
    a. Phosphodiesterase type III inhibitor
    b. Both positive inotropy and vasodilatory effects by increases in myocyte and vascular smooth muscle cAMP
    c. □ CO □ afterload
b. Dose
    a. 50 mcg/kg load (may cause significant hypotension)
    b. Infusion 0.5-1 mcg/kg/min
c. Indication
    a. CHF
    b. Cardiac dysfunction and afterload reduction s/p cardiac surgery

c. Shock with cardiac dysfunction and elevated vascular tone
d. Precautions
a. Rarely causes thrombocytopenia
b. Potential for hypotension

B. Other agents

1. Atropine

i. Action
a. Accelerates sinus/atrial pacemakers
b. Increases AV conduction
ii. Indications
a. Symptomatic bradycardia
b. Vagally mediated bradycardia (ie, from intubation)
iii. Dose: 0.02 mg/kg, 1 mg max
iv. Precautions
a. Smaller than vagolytic dose may cause paradoxical bradycardia (minimum dose 0.1 mg)
b. May mask hypoxia induced bradycardia

2. Calcium

i. Action
a. Intracellular cation, signal transduction
b. Positive inotrope in face of hypocalcemia
ii. Indication
a. Documented hypocalcemia (i.e. transfusion of large volume of citrated blood products)
b. Cardioprotection in hyperkalemia or hypermagnesium
c. Ca-channel blocker overdose
iii. Dose: CaCl 10-20 mg/kg
iv. **GIVE SLOWLY to avoid bradycardia**

3. NaHCO3

i. Action
a. Correction of metabolic acidosis
b. Improves cellular function and myocardial performance
c. Decreases systemic and pulmonary vascular resistance
ii. Indication
a. Severe metabolic acidosis in shock states not responsive to fluid resuscitation
b. Metabolic acidosis related to renal tubular acidosis or other renal etiology
c. Hyperkalemia - □ pH □ □ intracellular potassium movement
iii. Dose
a. [0.3 (body weight in Kg) X (Base deficit) = the mEq's of HCO3
b. 1-2 mEq/kg (rough estimate)
iv. Precautions
a. Results in intracellular and CSF acidosis – potential for worse CNS outcome since acidosis is CNS protective
b. Adequate ventilation must be assured or it will aggravate respiratory acidosis

c. Shifts oxyHgb curve to the left with impaired tissue oxygen delivery
d. Precipitation formation when mixed with Ca or catecholamine infusions

4. Antimicrobials

i. In suspected septic shock give antibiotics immediately. PUSH the antibiotics and initially give half the full daily meningitic dose. **The following are <u>first</u> doses** in septic patients, to be followed by maintenance doses

ii. Neonate
a. Ampicillin 100 mg/kg and
b. Gentamicin 1.25 to 2.5 mg/kg depending on weight or Cefotaxime 100mg/kg.
c. Meningitic doses of ampicillin and Cefotaxime are 200 mg/kg/day
d. Consider Vancomycin and Amikacin if already on antibiotics or has indwelling lines
e. If seizures or high-risk HSV, consider Acyclovir 25-50 mg/kg/day q 8 hrs

Neonatal Dosages (mg/kg) and Intervals

Antibiotic	Rou	Wt < 1200 g	Weight 1200 – 2000 g		Weight > 2000 g	
		Age 0-4 wks	Age 0-7 days	> 7 days	Age 0-7 days	> 7 days
Amikacin	IV, IM	7.5 q 18-24 hr	7.5 q 12-18 hr	7.5 q 8-12 hr	10 q 12 h	10 q 8 h
Vancomycin	IV	15 q 24 h	15 q 12-18 hr	15 q 8-12 hr	15 q 12 h	15 q 8 h
Ampicillin	IV, IM	50 q 12 h	50 q 12 h	50 q 8 h	50 q 8 h	50 q 6 h
Cefotaxime	IV, IM	50 q 12 h	50 q 12 h	50 q 8 h	50 q 12 h	50 q 8 h

iii. Infants 1-2 mos:
a. Ampicillin 100 mg/kg and Cefotaxime 100 mg/kg
b. If already on antibiotics or has lines in, consider Vancomycin and Amikacin

iv. Children > 2 mos:
a. Ampicillin 100 mg/kg/d and
b. Cefotaxime or Ceftriaxone 100 mg/kg/d
c. If already on antibiotics or has lines in consider Vancomycin and Amikacin

Dosages (mg/kg) and Intervals for Children and Older Infants

Antibiotic	Route	Dosage	Interval
Amikacin	IV, IM	15 - 22.5 mg/kg/d	q 8 hrs
Vancomycin	IV	40 mg/kg/day (mening 60mg/kg/day)	q 6 hrs
Ampicillin	IV, IM	100 – 200 mg/kg/d (meningitis 200 – mg/kg/day)	q 6 hrs
Cefotaxime	IV, IM	100 – 150 mg/kg/d (meningitis 200	q 6 - 8 hrs

		mg/kg/day)	
Ceftriaxone	IV, IM	50 – 100 mg/kg/da (meningitis 100 mg/kg/day)	q 12 - 24 hrs (q 12 hrs for meningitis)

POISONING - GENERAL MANAGEMENT

The clinician should maintain a high index of suspicion to be able to arrive at the often difficult diagnosis of poisoning. **Strongly consider an ingestion in any patient with an unexplained loss of consciousness. For any questions or for a discussion with a toxicologist call the Poison Control Center at 1 - 800 - POISON - 1**

I. Seven Phases of Poisoning Management. **Emergency stabilization of the patient comes first.**

A. First, treat the patient, not the poison!!

B. ABC's of resuscitation then add "D" for:

C. Disability;

1. Perform a brief neurologic exam, establish the level of consciousness (Glasgow Coma Scale), and determine pupillary size and reactivity.

2. Institute drug therapy: oxygen, dextrose, and naloxone as indicated.

3. Consider decontamination: ocular, dermal, GI, etc.

II. Clinical evaluation (see specific chapters in this manual as well)

A. Symptom complexes (toxidromes) may give clues to an unknown poisoning. **(also see tables at end of chapter). Not all findings may be present! Mixed ingestations may present with confusing findings.**

Drug Class	Level of Consciousness	Pupils	Vital Signs	Miscellaneous
1. Anticholinergics (atropine, cyclic antidepressants, antihistamines)	Delirium, psychosis, seizures, coma	Mydriasis (dilated)	↑HR, ↑T, ↑BP, Arrhythmias - cyclic anti-depressants	Flushing, hot skin, dry skin, hyperreflexia, urinary retention
2. Sympathomimetics - (amphetamines, cocaine)	Agitated, tremors, psychosis, hyper-active, seizures	Dilated	↑HR, ↑BP, ↑T	Sweaty, delirium
3. Opiates (narcotics, clonidine)	Euphoria, coma	Pinpoint	↓RR, ↓HR, ↓BP, ↓T	Shallow respirations, hyporeflexia
4. Organophosphates	Sedated, coma	Miosis (pupill-lary constric-tion)	↑↓HR, ↑↓BP	"S.L.U.D." - salivation, lacrimation, urination, defecation, also fasciculation, bronchorrhea
Drug Class	**Level of Consciousness**	**Pupils**	**Vital Signs**	**Miscellaneous**

5. Barbiturates, sedatives-hypnotics, ethanol	Confusion, coma, slurred speech	Miosis or Mydriasis	↓RR, ↓BP, ↓T	Ataxia, nystagmus, hyporeflexia
6. Phenothiazines-Haloperidol	Sedated, coma, tremor, seizures	Miosis	↓BP, ↓T, ↑HR	Dystonic rxns, ataxia, back arching, trismus, torticollis
7. Salicylates	Lethargy, seizures, coma	-	↑RR, ↑T	Vomiting, tinnitis, met. acidosis
8. Theophylline	Agitation, tremor, seizures	-	↑RR, ↑HR, ↓BP	Nausea, vomiting, hypokalemia, met. acidosis
9. Methanol, ethylene glycol	sedated, visual disturbances	-	↑ RR	oxalate crystals in urine (ethylene glycol), osmolal gap

Signs or symptoms may also provide valuable clues to identifying the agent.

Sign or Symptom	**Associated Drugs**
Bradycardia	β-blockers, cyclic antidepressants, calcium channel blockers, clonidine, digoxin, thioridizines, mesoridizine, nicotine, carbamates, organophosphates, opiates
Tachycardia and myocardial irritants	amphetamines, sympathomimetics, cocaine, cyclic antidepressants, caffeine, theophylline, propoxyphen, beta agonists, digoxin, thioridizines, mesoridizine, anticholinergics, procainamide, carbon monoxide, cyanide, freon solvents, organophosphates, phenothiazines
Hypotension	diuretics, β-blockers, ACE inhibitors, calcium channel blockers, clonidine, imidazoles, serotonin reuptake blocking antidepressants, cyclic antidepressants, thioridizines, mesoridizine, caffeine, theophylline, propoxyphen, beta agonists, quinine, quinidine, NSAIDS, isuprel, nicotine, carbamates, organophosphates, carbon monoxide, cyanide, nitrites, opiates, barbiturates, ethanol, phenothiazines
Hypertension	amphetamines, sympathomimetics, cocaine, MOI, phencyclidine, clonidine, imidazoles, nicotine, anticholinergics, carbamates, organophosphates
Hypoglycemia	insulin, alcohol, oral hypoglycemic agents, aspirin, β-blockers
CNS depression	opiates, sedative – hypnotics, anticonvulsants, antipsychotics, antidepressants, anticholinergics, iron, phencyclidine, lithium, carbamates, organophosphates, freon, carbon monoxide, cyanide, salicylates, ethanol, methanol, ethylene glycol
Seizures	NSAIDS, amphetamines, sympathomimetics, cocaine, tegretol, antidepressants, anticholinergics, iron, theophylline, lithium, phencyclidine, organophosphates, isoniazid, phenothiazines, carbon monoxide, cyanide, camphor, strychnine, salicylates
CNS agitation	anticholinergics, amphetamines, sympathomimetics, caffeine, theophylline, salicylates, cocaine, phencyclidine, carbon monoxide

B. History - focused and complete.

1. Substance or substances - including ingredients. Meds in house.

2. Maximum possible amount (number in bottle originally – number left)

3. Estimate ingestion - usually grossly underestimated.

4. Estimated time of ingestion.

5. Symptoms.

6. Home treatment.

7. Significant PMH: hobbies (glue exposure?), recurrent episodes etc.

8. Parents vocation.

C. PE - Vitals, level of consciousness (GCS), motor function, eyes (pupils, EOM, fundi), mouth (lesions, odors) heart (rate, rhythm), lungs (rate, pattern), skin, odors (breath, clothing), **can the patient maintain the airway, does the patient have a gag?**

D. Major modes of presentation - COMA, cardiac arrhythmias, metabolic acidosis, GI disturbances, seizures.

E. Lab exam (individualize) CBC, lytes, BUN, creat, glucose, calcium, dextrostix, LFT's serum osmolality, ABG, EKG, CXR, KUB, urine and blood for TOX screen, drug levels if intoxicant known.

F. Calculate anion gap:

1. $[Na^+] - ([HCO3^-] + [C1^-]) = A.G.$

2. Normally 12 - 14 mEq/Liter

3. Causes of increased anion gap (see Peds. Resus. chapter), **Mnemonic: "CAT MUD PILES"**

C - Cyanide, carbon monoxide
A - Alcohol
T - Toluene
M - Methanol
U - Uremia
D - DKA
P - Paraldehyde
I - Iron, Isoniazid, Inborn errors of metabolism
L - Lactic Acidosis
E - Ethylene glycol
S - Salicylates, Strychnine

G. Calculate osmolality:

1. $2[Na^+] + [glucose/18] + [BUN/2.8] = Osm.$

2. **Osmolal gap** = lab osmolality - calculated osmolality

3. Normally < 10 mOsm

4. **Osmolal gap** is increased with acetone, ethanol, ethylene glycol, isopropyl alcohol, mannitol, methanol, and propylene glycol

III. Elimination of the poison from the GI tract, skin and eyes

A. Gastric emptying

1. Syrup of Ipecac - usually used at home, rarely used after presenting to medical facility.

a. **Dose - < 1 year = 1 cc/kg**
1 to 12 years = 15 ml
> 12 years = 30 ml

b. Follow with water or juice (induction of emesis will be delayed if given with milk) - may repeat once if no emesis in 30 minutes. Keep emesis for analysis.

c. Contraindications:

- lost gag reflex, decreased level of consciousness, seizures

- ingestion of agent that rapidly depresses mental status (cyclic antidepressants, hypnotics, strychnine)

- ingestion of caustic agent

- petroleum distillate/hydrocarbon ingestion

- Nissen fundoplication

- < 6 months of age

2. Gastric Lavage - usually used for extremely toxic substances, in cases of unknown ingestions or when loss of consciousness is present

a. Intubation required prior to lavage in patients unable to protect their own airway.

b. Place large bore OG/NG tube (16 - 36 Fr)

c. Confirm placement by auscultation. Place patient in left lateral decubitus position (left side down) with head lowered (delays gastric emptying). Consider the use of a bite block in older patients.

d. Warm saline is instilled in aliquots until stomach contents are clear. **In children, aliquots of 50-100 cc with total lavage of 500-1000 cc. In adolescents and adults, aliquots of 150-200 cc with total lavage of 1-2 L.**

*******Check lavage fluid for pill fragments.*******

e. ***Contraindications*** - alkalis, sharp objects, pills larger than lavage hose, drug packets/vials, nontoxic ingestions.

B. Activated Charcoal

1. Almost irreversibly absorbs drugs and chemicals, preventing absorption.

2. Consider for all significant toxic ingestions; poorly binds Fe and Lithium, not to be used in caustic ingestions (mineral acids or bases, solvents, hydrocarbons) because of poor binding. Makes endoscopy difficult.

3. **Dose = 1 gm/kg or 30-60 gm for children and 60-100 gm in adults.** Prepared as a slurry with a ratio 1:4 charcoal to water. Goal is to have a charcoal to toxin ratio > 10:1

4. Repetitive doses of charcoal (1 gm/kg q 4-6°) will help clear enterohepatic circulation of some drugs (carbamazepine, digoxin, phenobarb, salicylates, theophylline).

5. Cathartics such as sorbitol (5 ml/kg) can be used with first dose of charcoal to prevent constipation.

6. Cathartics should not be used repetitively as it will cause fluid and electrolytes disturbances.

7. Ideally, the dose of charcoal is given within 1-2 hours of the ingestion. However, it may be given up to 12-24 hours after the ingestion in the case of anticholinergic, narcotic, or sustained release/enteric coated preparations ingestions.

8. **ADVERSE EFFECTS:** Nausea, vomiting and constipation are the most common. Pulmonary aspiration of charcoal is the most serious complication (usually seen with hydrocarbon ingestions).
REMEMBER: Airway protection before administration!!!!!

B. Whole Bowel Irrigation

1. Use of isotonic polyethylene glycol electrolyte solution (**GoLytely**) to flush the GI tract without causing fluid/electrolyte shifts.

2. Theoretical advantage of decreasing drug bioavailability by decreasing drug absorption.

3. Can be used with Lithium, Fe, Pb chips, sustained release preparations (Theophylline, Calcium channel blockers), and drug packets/vials.

4. **DOSE: 1-2 L/hour in adolescents and adults, 0.5 L/hour in children.** Continue for 4-6 hours or until the stool is clear.

IV. Antidotes **(see table at end of chapter)**

A. Use of specific antidotes is invaluable; unfortunately few poisons have antidotes

B. Contact poison control for specific antidotes and doses

V. Elimination of the Absorbed Substance

When indicated, the following 5 modalities can be used:

A. Supportive therapy (while the patient metabolizes the particular poison). Intubation, ventilation, even ECMO!

B. Forced diuresis (falling out of favor)

1. When used with pH modification, patient needs close monitoring for toxicity.

2. 1 1/2 - 2 X maintenance (3000 cc/M^2/day) (see DKA or Acute Tumor Lysis chapters for M^2 nomogram or calculation)

3. U.O. should approach 3-6cc/kg/hr

C. Alkalinization

1. Ingestions of phenobarbital, salicylate.

2. 0.5-2 mEg/kg/hour IV NaHCO3 - titrate to keep urine pH 7.5-8.0.

3. Monitor for hypokalemia. Unable to alkalinize a hypokalemic patient.

D. Acidification

1. Used for ingestions of amphetamine, chloroquine, lidocaine, quinidine

2. Ammonium chloride 75 mg/kg/day ÷ q 4-6° p.o. (contraindication - hepatic insufficiency).

3. Keep urine pH 5.5 -6.0

E. Adsorbent hemoperfusion and dialysis (consult nephrology)

1. Dialysis has been used for many substances, **some** of which include: ammonia, amphetamines, anilines, antibiotics, barbiturates, boric acid, bromides, calcium, chloral hydrate, ethylene glycol, fluorides, iodides, isoniazid, meprobamate, methanol, paraldehyde, potassium, quinidine, quinine, salicylates, strychnine, thiocyanates.

2. Substances that are dialyzable usually are large (MW > 500), poorly protein bound, highly water soluble, and have a low volume of distribution.

VI. Supportive Therapy and Observation

The support of respiration, circulation, and other vital functions takes priority over all other aspects of therapy.

VII. Disposition

A. May involve medical and/or psychiatric follow-up (if inpatient psychiatric treatment is necessary the psych. residents will arrange)

B. Consider social service involvement

C. "Preach" preventive medicine

TOXIC SYNDROMES

SYNDROME	MANIFESTATIONS	TYPES
Anticholinergic	**"mad as a hatter, red as a beet, blind as a bat, hot as a hare, dry as a bone"** **Parasympatholytic:** dry skin/ mucous membranes, thirst, dysphagia, blurred vision (near objects), fixed, dilated pupils, tachycardia, hypertension, flushing, scarletiniform rash, hyperthermia, abdominal distention, urinary urgency and retention **Central:** lethargy, confusion, delirium, hallucinations, delusions, ataxia, respiratory failure, cardiovascular collapse, extrapyramidal movements	Belladonna alkaloids, atropine, scopolamine, plants (jimson weed, nightshade, mushrooms, Jerusalem cherries), phenothiazines Synthetic:Glycopyrrolate Others: Antihistamines, cyclic antidepressants
Anticholinesterase	**Muscarinic:** sweating, constricted pupils, lacrimation, wheezing, cramps, vomiting, diarrhea, tenesmus, bradycardia, hypotension, blurred vision, urinary incontinence, excessive salivation **Nicotinic:** Striated muscle: fasciculations, cramps, weakness, twitching, paralysis, respiratory compromise, cyanosis, cardiac arrest **Sympathetic ganglia:** tachycardia, hypertension **Central:** anxiety, restlessness, ataxia, convulsions, insomnia, coma, absent reflexes, Cheyne-Stokes breathing, respiratory/ circulatory depression	Organophosphates, carbamate insecticides

SYNDROME	MANIFESTATIONS	TYPES
Extrapyramidal	**Parkinsonian:** dysphonia, dysphagia, oculogyric crisis, rigidity, tremor, torticollis, opisthotonos, shrieking, trismus	Chlorpromazine, haloperidol, perphenazine, promazine, thioridazine, trifluoperazine
Hemoglobinopathy	disorientation, headache, coma, dyspnea, cyanosis, cutaneous bullae, gastroenteritis	Carboxyhemoglobin (carbon monoxide), methemoglobin, sulfhemoglobin
Salicylism	Fever, hyperpnea, respiratory alkalosis or mixed acid-base disturbance, hypokalemia, tinnitus	Aspirin
Narcotics	CNS depression, pinpoint pupils, slowed respirations, hypotension Response to naloxone: pupils may dilate and excitement may predominate	Codeine diphenoxylate (Lomitil), fentanyl, heroin, morphine, opium, oxycodone
Withdrawal Syndromes	diarrhea, mydriasis, goose bumps (piloerection), hypertension, tachycardia, insomnia, lacrimation, muscle cramps, restlessness, yawning, hallucinosis	Cessation of: alcohol, barbiturates, benzodiazepines, chloral hydrate, glutethimide, meprobamate, methaqualone, narcotics, opioids, paraldehyde
Sympathomimetic	CNS excitation, convulsions, hypertension, tachycardia	Aminophylline, amphetamines, caffeine, cocaine, dopamine, ephedrine, epinephrine, fenfluramine, levarterenol, methylphenidate, pemoline, phencyclidine

Ref: Adapted from Goodenberger, Daniel: Medical Emergencies, in The Washington Manual of Medical Therapeutics, 29th Edition, Carey, CF et al. eds. Lippincott-Raven, 1998

ACETAMINOPHEN POISONING

I. Metabolism

A. Sulfation, glucuronidation, CP-450 pathway

1. Only CP-450 pathway produces toxic metabolites (especially as glutathione stores are depleted in toxic ingestions).

2. Main toxicity is to the liver; children (< 6 y/o) are less susceptible to liver damage than adults.

B. Most common toxic ingestion in U.S.A.

C. Readily absorbed.

D. Potentially toxic dose- > 150 mg/kg children, 7.5 gm adult. The clinical manifestations and course are different in infants and young children; they are strikingly resistant to the toxic effects of acetaminophen when compared to adults. Fulminant liver failure is rarely seen.

II. Clinical Course

A. Stage 1 (0-24 hrs post-ingestion).

1. Nausea, vomiting, diaphoresis, anorexia.

2. CNS depression is rare unless a coingestion exists.

B. Stage 2 (24-48 hrs) initial manifestation of liver injury.

1. Clinically improved.

2. SGOT, SGPT, bili, PT begin to rise.

C. Stage 3 (48-96 hrs), maximal hepatotoxicity

1. Asymptomatic to fulminant hepatic failure.

2. AST values > 20,000 not unusual.

3. Fatalities occur between 3 and 5 days; survivors reach stage IV.

D. Stage 4 (4 days - 2 weeks)

1. Resolution of hepatic dysfunction usually complete by one week.

E. Patients who are treated late or who are untreated and eventually die, maintain high levels of liver enzymes beyond 72-96 hrs.

F. Miscellaneous (unusual)

1. Hematologic - coagulopathy secondary to liver dysfunction (anemia, thrombocytopenia, agranulocytosis, methemoglobinemia with phenacetin)

2. Hypersensitivity (maculopapular rash, laryngeal edema, urticaria, angioedema, anaphylaxis)

3. Renal (ATN, ADH effect, acute renal failure) occurs in 25% of cases with documented hepatotoxicity

4. Cardiomyopathy/myocarditis

5. Metabolic (hypoglycemia, metabolic acidosis, hyperammonemia)

6. Dermatitis

7. Neurologic (cerebral edema, herniation)

III. Management

A. Assessment of toxicity of ingestion

1. History

a. Toxicity unlikely for dose < 150 mg/kg in children or 7.5 grams in adults.

b. History often unreliable (lack of knowledge, faulty recollection, active deception).

2. Acetaminophen level.

a. Draw at least 4 hrs post ingestion.

b. If you can get level back quickly, then await results and plot on nomogram, treat for level above lower line. (see R.M. nomogram at end of section). The nonogram is not useful with chronic ingestions.

c. If level not available quickly, then begin therapy and continue or discontinue **depending on result of 4 hour level.**

d. Only initial (4 hour) blood level is used.

e. Subsequent blood levels that may fall below the line are NOT an indication to terminate treatment.

B. Specific therapy

1. Empty stomach via Ipecac or lavage as indicated.

2. Treat any other coingestant with the standard approach.

3. Draw baseline LFT's, PT, lytes, BUN, Cr, Glucose, tox. screen.

4. Activated charcoal should be used if less than 4 hours have elapsed since ingestion or if a mixed ingestion is suspected.

a. Activated charcoal will bind N-acetylcysteine (NAC, mucomyst) but with the large doses of NAC administered, there's only a small decrease in bioavailability. Gastric lavage of the charcoal **IS NOT** necessary prior to administration of NAC.

b. NAC is rapidly absorbed in stomach and proximal small bowel so most efficacious if given a short time after charcoal.

c. NAC (N-Acetylcysteine, , Mucomyst) promotes glucuronyl system hopefully preventing CP-450 toxin accumulation.

5. Prepare NAC as 5% solution in water, grapefruit juice or a cola beverage (it will taste and smell terrible).

6. NAC dose - 140 mg/kg loading followed by 70 mg/kg q 4 hrs x 17 doses (18 doses total).

a. No difference exists in the incidence of hepatotoxicity if NAC is given anytime within 8° after ingestion.

b. Standard of care has been to treat as late as 24 hours after ingestion.

c. May be beneficial to treat later than 24 hours especially if acetaminophen is still detectable.

7. If any dose is vomited within one hour of administration, repeat the dose.

8. If emesis becomes a constant problem, the NAC may be administered by DUODENAL intubation or may give antiemetics (eg. **Metoclopramide 1 - 2 mg/kg/dose q 2 - 6 hours IV**, metoclopramide may cause extrapyramidal sx. so premedicate with diphenhydramine 5 mg/kg/day divided q 6 hours PO, NG, or use another antiemetic such as **phenergan 0.25 - 0.5 mg/kg/dose PO, NG, or PR q 4 - 6 hours** prn, adult dose is 12.5 - 25 mg q 4 - 6 hours).

9. SGOT, SGPT, Bili, PT should be followed daily until values normalize. Repeat 8 days post-ingestion.

ASPIRIN POISONING

I. Pharmacokinetics

A. Absorption

1. Therapeutic doses are rapidly absorbed in stomach; gastric emptying is **delayed** in overdoses. In large ingestions the tablets may form concretions that can remain in the stomach for many hours. They may slowly release salicylates and prolong the toxicity. Gastric lavage with epigastric or even endoscopic manipulation may be necessary to break up and remove such masses.

2. Enteric-coated preps delay absorption even longer; peak serum salicylate levels can occur up to 60 hours after an excessive ingestion.

B. Metabolism and Excretion

1. 80 % of a normal dose is conjugated with glycine and glucuronic acid in liver.

2. These pathways are rapidly saturated, even at therapeutic plasma salicylate concentrations.

3. After their saturation, renal excretion becomes increasingly important.

C. Distribution

1. Unbound, nonionized fraction of salicylate crosses membranes including the blood - brain barrier. The ionized form does **not** cross the BBB.

2. As pH decreases, nonionized salicylate increases (fall in pH from 7.4 to 7.2 doubles the nonionized form).

3. This is an important consideration during treatment with alkalinization.

II. Clinical Features

A. Pathophysiologic Effects

1. Direct CNS respiratory center stimulation --> hyperpnea and respiratory alkalosis.

2. Uncoupling of oxidative phosphorylation causes:

a. Increased heat production ---> hyperpyrexia

b. Failure of high energy phosphate (e.g. ATP) production

c. Increased oxygen utilization and CO_2 production due to increased skeletal muscle metabolism

d. Increased tissue glycolysis

e. CNS hypoglycemia; may have decreased glucose in CNS even in the face of normal blood glucose levels!!

3. Stimulation of lipid metabolism --> ketone body formation

4. SIADH --> oliguria, fluid overload

5. Hemostatic effects

a. Decreased prothrombin and factor VIII formation

b. Decreased platelet aggregation

c. Actual hemorrhagic manifestations are in practice very uncommon

6. Electrolyte abnormalities

a. Hypernatremia common

b. Assume total body K+ depletion, even if [K+] normal

B. Signs/Symptoms

1. Asymptomatic - No objective signs

2. Mild

a. **CLASSIC TRIAD:** Vomiting, Hyperpnea, Hyperpyrexia. ALWAYS consider the possibility of a salicylate ingestion when these coincide in a patient.

b. Tinnitus

c. Hypocapnia without frank acidosis

3. Moderate

a. Severe hyperpnea and marked lethargy and/or excitability

b. Usually no coma or convulsions

c. Compensated metabolic acidosis in child

4. Severe

a. Coma, possibly convulsions

b. Uncompensated metabolic acidosis in child after 12 hours

5. Children under 4 y.o. almost invariably have Acidosis. Acidosis may alter the estimation of the severity of the intoxication.

III. Management

A. Assessment of severity of poisoning

1. Altered consciousness is the most important indicator of severe salicylate intoxication.

2. By history: (although clinical condition is usually the best guide)

   a. < 150 mg/kg is usually non-toxic

   b. 150 - 300 mg/kg: mild to moderate toxicity

   c. 300 - 500 mg/kg: severe toxicity

   d. > 500 mg/kg: potentially lethal

3. "DONE" nomogram (see at end of section)

   a. Only useful in single dose, acute ingestion

   b. Nomogram not useful
      i. Chronic ingestions (hours or days)
      ii. Enteric coated or sustained release
      iii. Oil of Wintergreen
      iv. Underlying renal insufficiency
      v. Severe metabolic acidosis

   c. An initial "nontoxic" level may evolve into severe ASA poisoning due to delayed gastric emptying. **GET MORE THAN ONE LEVEL !!** In large overdoses salicylate levels should be obtained q 4 - 6 hours to determine that no further absorption is occurring.

B. Specific Measures

1. Induce emesis or lavage (airway protected??)- significant amounts may be present in stomach up to 12 - 24 hours (longer with time released products). Enteric coated pills are larger and may not be removed with lavage. X-rays may help as *some* preps are radiopaque - however, if X-rays are negative it does not rule out an ingestion.

2. Activated charcoal - multiple doses may be superior to a single dose

   a. Dose: 1 - 2 grams/kg followed by 20 - 60 grams q 3 - 4 hours until passage of charcoal stool.

3. Saline cathartic

4. Laboratory analysis - salicylate level (6 hrs after ingestion), lytes, glucose, ABG, PT/PTT, ionized Ca++

   a. Monitor labs frequently (q 4 - 6 hours), consider arterial line.

   b. Repeat salicylate levels until downward trend established, draw q 1 - 2 hours until levels are declining and the patient's clinical condition stabilizes.

5. Treat shock if present, use fluid resuscitation as needed.

6. Forced alkaline diuresis (urine output of 3 - 6 cc/kg/hour) to increase ASA excretion.

   a. Use D5 1/2 NS + 15 mEq NaHCO3/L at 3000 cc/M^2 /day (see DKA chapter or Acute Tumor Lysis chapters for nomogram and calculation of body surface area)

   b. Add 30 mEq KCL/L after good urine output obtained.

   c. HCO3 must be used with caution, especially in children >4 y.o. who will often have respiratory alkalosis and blood pH > 7.40, even in the face of low HCO3 levels.

   d. Aim of HCO3 therapy is to maintain blood pH 7.45 - 7.50 and urine pH > 7.5.

   e. **Adverse effects**: Metabolic alkalosis, Hypernatremia, Hypokalemia, Hypocalcemia with tetany, Hypoglycemia.

7. Hemorrhagic tendency

   a. Vit K, 5-10 mg IM

   b. Guaiac all stool/emesis

   c. FFP for severe bleeding

8. Hyperthermia - sponging, cooling blanket

9. Severe intoxications may require exchange transfusions or hemodialysis. Obtain a nephrology consult early on in the course. This is especially true in cases where the salicylate level is rising, or if evidence of end-organ damage has developed such as pulmonary edema, CNS deterioration, persistent acidemia, or coagulopathy.

CAUSTIC INGESTIONS

I. Epidemiology

A. Most commonly seen between 1 - 3 years (peak 18 - 24 mos.)

B. May be accidental in children and the mentally retarded - volume is generally small because of immediate and severe pain with the ingestion.

C. Deliberate in adults as suicide attempt with large ingested volumes.

D. Rarely a cause of child abuse.

E. Most common exposure is to household bleaches - relatively neutral pH makes them less irritating than other alkalis or acids.

F. Other frequent exposures include automatic dishwasher agents, laundry detergents, swimming pool products, toilet bowl and oven cleaners. (see table at end of chapter)

II. Pathogenesis

A. Esophageal burns account for the most serious injuries and complications - liquid Drano™, lye, and ammonia are the most caustic

B. Injuries to lips, oropharynx and upper airway occur.

C. Solids adhere to mucosa producing deep burns of the oral cavity and esophagus - less likely, however, to reach stomach

D. Powders tend to injure upper airway causing stridor and epiglottitis

E. **Alkaline agents - (pH > 7)**

1. Liquefaction necrosis and early disintegration of the mucosa cause deep penetration leading to perforation

2. Depth of injury is related to concentration of the agent and duration of contact with the mucosa

3. Small amounts of alkaline substances with pH > 11 may cause severe burns

4. Agents with pH's of 9 - 11 rarely cause serious injury unless large amounts are ingested

5. In the first week inflammation and vascular thrombosis cause additional destruction

6. In the second week granulation tissue forms with weakening of the esophageal wall making it susceptible to perforation

7. Beyond the third week fibrogenesis and stricture formation occurs which makes perforation less likely

F. **Acidic agents, also called corrosives - (pH < 7)**

1. Coagulation necrosis forms a coagulum on the mucosa limiting deeper penetration

2. Alkaline pH of the squamous epithelium of the esophagus is protective of esophageal damage but not totally in all cases

3. Greater amounts reach the stomach causing gastric injury and perforation

4. Pooling in the antrum with antral spasm causes injury in the "prepyloric" area

5. Up to 20 % of acid ingestions also cause esophageal burns

G. Batteries - small button type

1. Most measure 7.9 - 11.6 mm and pass spontaneously

2. Larger ones ($\geq$ 15.6 mm) may lodge in the esophagus and leak their caustic contents

3. They contain silver or mercuric oxide, manganese dioxide, zinc, or lithium

III. Clinical presentation

A. **The presence or absence of oral lesions or symptoms does NOT predict the presence or severity of esophageal or gastric burns.**

B. Dysphagia is the most common symptom. It results from alterations in peristalsis secondary to esophageal irritation.

C. Drooling

D. Retrosternal or abdominal pain

E. Stridor, hoarseness, nasal flaring and retractions

F. Epiglottitis may be severe (especially in children < 2 y.o.) and may require intubation !!

G. Vomiting and hematemesis

IV. Initial management - (see flow sheet at end of chapter also)

A/B. AIRWAY and BREATHING

1. Respiratory distress requires oral intubation

2. Cricothyroidotomy or tracheotomy may be necessary if tracheal visualization is impossible

C. Circulation

1. Hypotension and shock (? perforation) require fluid resuscitation

2. GI hemorrhage may require blood products

D. Gastric decontamination is **CONTRAINDICATED**

1. Induction of vomiting (ipecac) will reexpose the esophageal mucosa to the caustic agent

2. Blind placement of a nasogastric tube for purposes of lavage may cause additional injury or even perforation of the injured mucosa

E. Neutralizing substances are **discouraged**

1. Neutralization may cause heat production and further injury

F. Dilution with milk or water is **not** recommended

1. The volume needed to dilute the caustic agent is too great

2. Additional vomiting may occur with large amounts of a diluting agent

3. **CONTRAINDICATED** in the presence of respiratory distress

4. Not beneficial if $\geq$ 1 hour after ingestion

G. Labs: ABG, CBC with diff, electrolytes, Ca++, BUN, creat, T&C

H. X - rays - of chest and abdomen

1. Perforation - see subdiaphragmatic free air, mediastinal emphysema

2. Impending perforation - gastric dilatation, intramural air

3. Pulmonary aspiration

I. Early consultation with Peds GI or Peds surgery is **MANDATORY**

V. Endoscopy

A. Usually performed in any suspected ingestion although observation may be considered if the ingestion was questionable or if agent was household bleach

B. Done within first 24 - 48 hours after the ingestion

C. If done < 12 hours, may not see full extent of injury but does not change treatment

D. Done under general anesthesia with severe burns, respiratory distress, or if rigid scope used

E. Flexible scope may be placed past damaged esophageal mucosa into stomach

F. Rigid scope is not advanced beyond first significant burn to avoid risk of causing perforation

G. Allows grading of esophageal burns

1. *First degree*: limited to edema and erythema

2. *Second degree*: linear ulceration and necrotic tissue with white plaques

3. *Third degree*: circumferential injury with sloughing of the mucosa

VI. Treatment

A. Nasogastric tube

1. **<u>ONLY</u> to be placed under direct visualization at time of endoscopy**

2. Used with extensive circumferential burns or in possibilities of perforation

3. Provides route for nutritional support

4. Maintains lumen during stricture formation

5. Serves as guide for esophageal dilatation after stricture forms

B. Corticosteroids are controversial (used to prevent strictures)

1. May be beneficial in first or second degree burns

2. Dose used is equivalent to prednisone 1 - 2 mg/kg/day (max. 60 mg/day) for 3 - 4 weeks; given IV until patient taking medication orally

3. NOT indicated in third degree burns since strictures are inevitable; any mediastinitis or infection secondary to perforation would be masked as well

4. NOT indicated in acid ingestions since gastric injury is more common; would mask gastric necrosis and perforation

5. Prophylactic antibiotics are generally used with steroids in second degree burns because of an increased risk of infection, especially bacterial spread to the mediastinum

C. Antibiotics

1. Used in second or third degree burns even if steroids are not used

2. Recommendation: Unasyn 50 mg/kg/day divided q 6 hours

3. Gentamicin use is +/-, 5 mg/kg/day divided q 8 hours

D. UGI is done 3 - 4 weeks after the injury, earlier if obstruction or dysphagia are present

E. Batteries

1. Evaluation by X-ray (AP and lateral neck, CXR, Abdominal)

2. Prompt removal if in esophagus

3. If battery is past the esophagus F/U X-ray after 3 - 4 days

VII. Early complications

A. Systemic

1. Airway obstruction, ARDS

2. Shock

3. Nutritional failure

4. Infection

B. Gastrointestinal

1. Perforation

2. Pyloric obstruction from edema

3. Hemorrhage

VIII. Delayed complications

A. Strictures

1. Primary complication

2. Occur in most third degree burns, less likely in second degree burns

3. 80 % will have obstructive symptoms by 2 months

4. Repeated dilatation is required

5. < 50 % will have success with dilatation and will require colonic interposition

B. Pyloric stenosis

1. Occurs with both acids and alkalis

2. Sx’s develop over 3 to 10 weeks

3. Treatment is surgical bypass or balloon dilatation

C. Esophageal carcinoma

1. Incidence approximately 5 %

2. Detection of cancer has occurred as late as 16 - 42 years after the ingestion

CYCLIC ANTIDEPRESSANT OVERDOSE

I. Introduction:

A. Cyclic antidepressants include bicyclics, tricyclics and tetracyclic forms. While showing undeniable clinical efficacy, their narrow therapeutic and toxic range creates a dilemma for physicians. Cyclic antidepressants include the tricyclics **amitriptyline, doxepin, imipramine, trimipramine, amoxapine, desipramine, nortriptyline** and **protriptyline,** the tetracyclic **maprotiline,** the monocyclic **bupropion,** the triazolopyridine **trazodone** and the serotonin reuptake inhibitors (SSRI) **fluoxetine, sertraline,** and **paroxetine.** The development of the SSRI classification (including **trazodone**) has resulted in the reduction of significant cardiac and central nervous system toxicity.

B. Death rate from overdose 2.2%.

C. Accounts for 25% of all drug overdose hospital admissions.

D. Most common cause of death from prescription drug overdose.

II. Pharmacology - 3 ring aromatic nucleus with aliphatic aminoprophyl side chain.

A. Absorption

1. Rapidly absorbed in alkaline small intestine with rapid distribution.

2. Absorption delayed in overdose because of delayed gastric emptying and decreased GI motility from the anticholinergic drug effect.

3. Significant enterohepatic circulation leading to decreased excretion.

4. Up to 95% of the drug is protein bound at physiologic pH and is inactive. Hypoalbuminemia and acidemia increase free drug.

B. Metabolism

1. Almost entirely metabolized in liver.

2. Half-life variable - 10 to 81 hrs. This long half-life is due to an extremely large vol. of distribution from extensive tissue distribution of the drug and its' active metabolites. This is why neither dialysis, nor hemoperfusion, are effective in removing significant quantities.

C. Mechanism of action

1. Peripheral and central anticholinergic effect. Block muscarinic - cholinergic and alpha-adrenergic receptors.

2. Block reuptake of released norepinephrine and serotonin at presynaptic adrenergic nerve endings. Leads to biphasic effect with initial excess of catecholamines followed by depletion.

a. Initial accumulation of norepi --> tachycardia and hypertension (alpha effects). This may precipitate dysrhythmias.

b. Later norepi depletion --> bradycardia and hypotension (alpha blockade) or depletion. May see decreased contractility and/or decreased vasomotor tone.

3. Inhibits fast Na^+ channel resulting in slowing of depolarization.

4. Direct effect on myocardium which causes disturbances in excitability and conduction defects --> almost any arrhythmia! Often see a quinidine - like conduction delay (wide QRS tachycardia, indistinguishable from V. Tach). Bradydysrhythmias are ominous. AV block may also occur.

5. Earliest toxic sign is a QRS > 0.10 sec.

6. Death is usually due to cardiac complications.

III. Clinical Presentation

A. Anticholinergic effects (less pronounced with doxepin, desipramine, amoxapine and maprotiline. Trazodone has little or none).

1. Tachycardia, mild HTN, blurry vision, mydriasis (often poorly reactive), urinary retention, pulmonary edema, hypoventilation. Priapism is common with trazodone.

2. Dry mouth, fever, hallucinations, agitation, ataxia, absent bowel sounds (ileus).

3. Myoclonic twitching, seizures (especially with amoxapine or maprotiline), coma, flaccid paralysis, hyperreflexia. Seizures more common if QRS > 0.16 sec. in one study.

4. Diff. Dx. of these effects includes many other antihistamines, antispasmodics, plants, etc.

5. Earliest signs usually tachycardia, dry mouth, ileus, mydriasis, and altered mental status.

B. Cardiotoxic effects (see above) - include cardiac arrhythmias, hypotension, and pulmonary edema. More common if QRS > 0.16 sec.

IV. Management

A. Assessment of Severity of Ingestion

1. Toxic effects are not necessarily dose dependent. Any ingestion should be considered life threatening!!

2. Ingestion of $\geq$ 1000 mg generally assoc. with severe toxicity.

3. Toxic symptoms may be seen with a dose of 10 mg/kg but are the rule when ingestion >20 mg/kg.

4. As mentioned, QRS > 100 msec (0.10 sec.) => severe toxicity.

5. SSRI's have a much higher toxicity threshold. The reported toxicities have been limited to CNS depression (lethargy), sinus tachycardia, and GI symptoms.

B. Specific Measures

1. ICU, "ABC's"!! BEWARE of RAPID onset of s/s! A decrease in level of consciousness and loss of airway control may produce a respiratory acidosis leading to increased free drug concentrations!

2. Continuous cardiac monitoring, pulse oximetry. Make sure you have secure IV access. EKG interpretation is essential.

a. At least 24-48 hrs of monitoring.

b. Continue until dysrhythmia free for at least 24 hrs.

3. Labs: Stat lytes, BUN, creat, glucose, ABG, drug screen for coingestants, and EKG. Drug levels not helpful, no correlation exists between plasma levels and symptoms of serious poisoning.

4. Consider foley

5. Gastric decontamination (**Remember: Airway protection!**)

a. Gastric lavage - can be helpful even 24 hrs after ingestion. Ipecac not recommended as patients are frequently lethargic and may rapidly deteriorate to coma, seizures or dysrhythmia.

b. Charcoal - Delayed gastric emptying and enterohepatic recirculation make GI decontamination very important. Dose 1 gram/kg initially then 1 gram/kg every 4-6 hours for 24-48 hours if GI motility is present and patient is symptomatic.

c. Cathartic - sorbitol.

d. Left lat. decub. position may decrease gastric emptying.

e. Again, because of marked protein binding and large volume of distribution, forced diuresis, dialysis, exchange transfusion and hemoperfusion are not indicated.

6. Drug reversal

a. **Physostigmine** - acetylcholinesterase inhibitor, previously touted to reverse cholinergic symptoms, **NOT RECOMMENDED** due to potential side effects including seizures, heart block, hypotension, bradycardia/asystole, respiratory distress, excess salivation, sweating, diarrhea

7. Management of BP

a. Hypertension rarely necessitates treatment

b. For hypotension, correct acidosis, vasopressors (phenylephrine, norepinephrine) for refractory hypotension.

8. Correction of arrhythmias

a. **NaHCO3** is the treatment of choice. A bicarb drip 1-2 meq/kg/hour is initiated and titrated to keep the serum pH 7.45-7.55 in comatose pts, pts with QRS > 100 msec or arrhytmias. Alkalization should also be considered in pts with a suspected large ingestion. The drip is continued until the pt is stable and has a normal EKG for at least 24 hrs.

9. Ventricular arrhythmias

a. First try **NaHCO3** bolus (1 mEq/kg).

b. **Lidocaine** if NaHCO3 fails (1 mg/kg then drip 20-50 micrograms/kg/min). No documented efficacy in controlled studies.

c. **Propranolol**, dose 0.1 mg/kg, slow IV - may lead to hypotension, bradycardia or asystole in cyclic antidepressant overdoses so only use for life-threatening tachycardias after other measures have failed.

d. **Phenytoin (Dilantin)** use controversial. Has been used successfully for vent. dysrhythmias and conduction delay. Dose is 15 mg/kg over 15-20 min. (max. 50 mg/min).

e. Type Ia (quinidine, procainamide, disopyramide) and Type 1c (flecainide, encainide, propafenone) antiarrhythmics are contraindicated

10. Bradycardia

a. **Atropine** ineffective due to muscarinic receptor blockade and has been associated with onset of asystole.

b. Complete heart block, Mobitz II heart block, and refractory bradycardia are indications for insertion of a temporary pacemaker. However, the patient may be resistant to pacemaker capture.

11. Other:

a. If all these measures fail consider ECMO to support the patient until detoxification occurs. WHMC was the first ECMO center to report this successful application.

b. Resuscitation efforts should continue for a minimum of one hour. Full recovery of cyclic antidepressant induced cardiac arrest after five hours is documented.

12. Contraindicated - (cyclic antidepressants cause conduction delays which these drugs may worsen).

a. Quinidine

b. Procainamide

c. Disopyramide

d. Flecanide

e. Encainide

f. Propafenone

13. Correction of seizures - may be intractable especially with amoxapine.

a. Benzodiazepines (valium, lorazepam, midazolam) are the drug of choice. Flumazenil contraindicated (associated with increased incidence of seizures).

b. Phenobarbital is second line therapy. Continuous infusions of midazolam and/or propofol have been used successfully for refractory seizure control. Use of phenytoin is unclear.

c. Use of naloxone, thiamine, dextrose in patients with coma or altered mental status in ED is considered standard of practice prior to antiepileptic treatment.

14. Scheme for monitoring.

a. Asymptomatic patient who has had stomach emptied and charcoal - monitor 24 hrs in ICU.

b. Non-cardiac S/Sx.s - monitor till Sx. free.

c. EKG changes - monitor for at least 24-48 hrs after normal EKG.

DIGOXIN TOXICITY

- Digoxin has a very narrow therapeutic window. Toxicity can occur with a dosage error; with drug interactions; or as an accidental/intentional ingestion

- Toxicity is more likely to occur with hypokalemia; hypercalcemia; or hypo or hypermagnesemia; or renal failure

- Common drug interactions: indomethacin, quinidine, verapamil, and amioderone

- Therapeutic levels are 1-2 ng/ml. Levels are generally not followed unless toxicity is suspected, secondary to possible inaccuracies caused by "dig like" substances

Note: Spironolactone and Digibind® interfere with digoxin imnmuno assay

-. Adverse effects and precautions:

1. GI manifestations: nausea, feeding intolerance, vomiting, and diarrhea

2. CNS effects: lethargy confusion, blurred vision with yellow halos

3. Cardiac effects: some of these are partially due to hyperkalemia, which is seen with digoxin/digitalis toxicity

Nontoxic Cardiac Effects	Toxic Cardiac Effects
Shortening of Qtc interval	Prolongation of PR interval
Sagging ST segment	Sinus bradycardia or SA block
Diminished T-wave amplitude	Atrial or nodal ectopic beats
Slowng of heart rate	Ventricular arrhythmias

Management of Digoxin Toxicity

1. Stop the digoxin

2. Obtain EKG, electrolytes and blood gas

3. Correct any electrolyte and acid-base abnormalities

4. Use digoxin-immune "Fab" antibody (Digibind®)

5. Charcoal

Treatment for symptomatic bradycardia is atropine and temporary pacing

Treatment for ventricular ectopy is lidocaine and phenytoin

a. For **acute** ingestions of **unknown amounts** 20 vials is adequate to treat both adults and children. If the child is small and volume is a

concern, 10 vials may be given to the child first and then they may be monitored for their response and an additional 10 vials be given as needed.

b. For **acute** ingestions of **known** amounts each vial of Digibind® contains 38 mg of the Fab fragments which will bind approximately 0.5 mg of digoxin or digitoxin. The dose of Digibind® may be based on the number of tablets or capsules ingested or the digoxin level in ng/ml (see following tables for adults and children).

Digibind® Dose for Adults and Children Based on
Number of Tablets or Capsules Ingested in a Single Large Digoxin Overdose

Number of digoxin tablets or capsules Ingested (0.25 mg tablets or 0.2 mg Lanoxicaps® capsules	Digibind® dose (number of vials)
25	10
50	20
75	30
100	40
150	60
200	80

Digibind® Dose (mg) for Infants and Small Children
Based on Steady State serum Digoxin Concentration and the Patient's Weight

Serum digoxin concentration (ng/ml)							
Weight (kg)	1	2	4	8	12	16	20
1	0.4 mg*	1 mg*	1.5 mg*	3 mg*	5 mg	6 mg	8 mg
3	1 mg*	2 mg*	5 mg	9 mg	14 mg	18 mg	23 mg
5	2 mg*	4 mg	8 mg	15 mg	23 mg	30 mg	38 mg
10	4 mg	8 mg	15 mg	30 mg	46 mg	61 mg	76 mg
20	8 mg	15 mg	30 mg	61 mg	91 mg	122 mg	152 mg

* dilution of reconstituted vial by adding 34 cc of sterile isotonic saline to achieve a final concentration of 1 mg/ml may be desirable

Digibind® Dose (vials) for Adults and Large Children
Based on Steady State Serum Digoxin Concentration and the Patient's Weight

Serum digoxin concentration (ng/ml)							
Weight (kg)	1	2	4	8	12	16	20
40	0.5 v	1 v	2 v	3 v	5 v	7 v	8 v
60	0.5 v	1 v	3 v	5 v	7 v	10 v	12 v
70	1 v	2 v	3 v	6 v	9 v	11 v	14 v
80	1 v	2 v	3 v	7 v	10 v	13 v	16 v
100	1 v	2 v	4 v	8 v	12 v	16 v	20 v

V = number of vials
Tables are from Digibind® package insert 2003

HYDROCARBON INGESTIONS

I. Introduction

A. Petroleum distillates are comprised of aliphatic and aromatic hydrocarbons. Contamination with heavy metals or toxic chemicals is common. Most hydrocarbons are petroleum distillates, however, some such as turpentine are derived from pine oil. The large number of hydrocarbon containing products, bright labels and 'fruity' fragrances all increase children's exposure to these products.

II. Pathogenesis:

A. Incidence of pulmonary complications differs depending on hydrocarbon derivative. High volatility, (volatility means the tendency of a liquid to form a gas) decreased viscosity and low surface tension distillates are more likely to be aspirated leading to respiratory injury. Lower viscosity enhances distal airway penetration. Lower surface tension facilitates spread.

B. Pulmonary injury usually occurs either from aspiration or direct installation into the lung **NOT** from GI absorption. (Some GI absorption occurs but is usually minimal.)

C. Small ingestions may result in aspirations with significant pathology.

D. The intentional abuse by inhalation of gasoline or paint thinners is usually not associated with significant pulmonary toxicity.

III. Pathology

A. Pulmonary injury is of principle importance.

B. Lungs show interstitial inflammation, atelectasis, hyperemia, vascular thrombosis, bronchial and bronchiolar necrosis, intra-alveolar hemorrhage, edema, bronchospasm and emphysema.

C. Hydrocarbons directly injure pulmonary tissue and capillaries and inhibit surfactant activity.

D. Lipoid pneumonias are usually more localized, may occur with higher viscosity agents.

E. Bacterial pneumonias may supervene but are less frequent than once thought. (probably result from aspiration of oral microorganisms).

F. Local mouth or pharynx irritation, nausea and emesis occur most frequently with fuel or furniture polish ingestions.

G. Intravascular hemolysis and hemoglobinuria have been reported with gasoline ingestions.

IV. Clinical Effects:

A. Respiratory signs/symptoms predominate.

1. Choking, coughing, hemoptysis, SOB, dyspnea, cyanosis, tachycardia, tachypnea, nasal flaring, grunting, retractions, rhonchi, wheezes, rales all may be present.

2. Cyanosis may occur rapidly as alveolar gas is displaced by hydrocarbon vapors. Hypoxia, hypercarbia may occur.

3. Prolonged, persistent cough is suggestive of aspiration and requires evaluation.

B. CNS

1. Somnolence is the chief neurologic manifestation. Coma and convulsions may occur.

2. Lethargy, dizziness, stupor, coma or seizures may indicate the presence of toxic additives (insecticides or aromatic hydrocarbons), a large ingestion or serious aspiration.

C. Gastrointestinal

1. Spontaneous vomiting is common (up to 40% of cases) and is associated with aspiration.

2. Local irritation to mouth etc. is common. Melena is rare.

3. Bloating, flatus, abdominal pain, liquid feces, all may occur.

4. Minimal, if any, absorption by the GI tract occurs and the agent is usually eliminated in the stools.

5. Oral antacids or H2 - receptor antagonists may precipitate vomiting and are usually not given in the unintubated patient.

D. Fever

1. High fever is common. It is usually due to chemical pneumonitis, but may be due to occur with secondary infection (pneumonia).

E. Other

1. Hepatosplenomegaly is rare. Etiology unclear. May be due to a toxic additive effect.

2. Cardiac dysrhythmias are rare.

V. Evaluation and Treatment

A. ABC's FIRST!! Perform complete history and physical exam next.

B. **PICU admissions: S**pontaneous emesis after the exposure, respiratory distress or whose parents cannot observe the patient. TOTALLY asymptomatic children with a normal CXR after 6 hours may be followed as an outpatient only if frequent telephone calls (every 2 hours x 6) are possible, the parents are reliable and will return immediately if symptoms occur and if okayed by ED or pediatric staff. ***Twenty-four hour observation in the PICU is preferred in the vast majority of cases***.

C. Patients with respiratory distress should receive oxygen and an ABG. Serial CXR's (every 6 hours), IV access and continuous cardiorespiratory monitoring should all be obtained. An arterial line should be placed if frequent ABG's are needed.

D. Labs: CBC with differential, liver function tests and electrolyte panels should be drawn. If the ingestion was deliberate consider tox screens. If the patient is intubated, serial tracheal aspirates for gram stain and culture should be considered if a bacterial pneumonia is suspected.

E. CXR: Positive findings in > 65% in the first 6 hours after ingestion. Abnormalities may occur as early as 30 minutes after exposure or as late as 12 hours. Resolution of radiographic findings usually lags behind improving clinical status.

1. Most common findings: bilateral basilar infiltrates (65%), right basilar infiltrates (30%), fine, punctuate perihilar densities (5%).

2. Patchy densities that may coalesce to form larger areas of consolidation, atelectasis, emphysema, pleural effusions, pneumatoceles, pneumothoraces, pneumomediastinum and sub Q emphysema are all reported.

3. CXR may be markedly abnormal even in the presence of a normal exam!

F. Intubation: Consider if:

1. Moderate to severe respiratory distress.

2. ABG abnormalities; paO2 <60 on 6 liters O_2 or paCO2 >50mmHg.

3. Deteriorating mental status

4. Absent breath sounds

5. Cyanosis on 40% FiO2

6. Exhausted patient leading to decreased respiratory effort.

G. Most authorities usually **recommend AGAINST gastrointestinal decontamination** in hydrocarbon ingestions to reduce the chances of lavage induced emesis and subsequent aspiration. Activated charcoal

does not bind most petroleum distillate products or other hydrocarbons so is of little benefit.

1. Ipecac induction of emesis is likewise usually not indicated to avoid aspiration.

2. ***Exception:*** Products contaminated with pesticides, heavy metals or toxins such as anilene or nitrobenzene should be evacuated. In the alert child who can guard his airway some people use syrup of Ipecac, but an elective intubation and lavage may be safer. In the unconscious or stuporous patient, protect the airway first with a cuffed endotracheal tube then perform gastric lavage.

H. Bronchodilators as needed.

I. Steroids have repeatedly been shown to be ineffective.

J. Prophylactic antibiotics are not routinely prescribed.

1. Antibiotics may be necessary later in the course in the face of persistent fever (> 36 hours), leukocytosis (> 36 hours), clinical deterioration or a positive tracheal gram stain or culture.

2. Antibiotics should cover for mouth and GI flora: H. influenza, *Staph aureus*, *Strep pneumoniae* etc. Usual choices are Cefuroxime, Ceftriaxone, Clindamycin or Penicillin G.

3. HFOV or ECMO have both been used successfully in severe cases. The longest ECMO air transport in history was performed by WHMC for a hydrocarbon ingestion/aspiration.

VI. Prognosis

A. Majority recover fully.

B. May predispose to increased risk of future respiratory infections.

C. 75% may have PFT abnormalities.

IRON POISONING

I. Pathophysiology

A. Local effects:

1. Direct corrosive mucosal lesions of stomach and proximal small bowel (early events).

2. Mucosal irritation, ulceration, bleeding, ischemia, infarction and perforation may occur. Perforations are usually late events.

3. Produces profound fluid losses and hypotension.

B. Systemic effects:

1. Venodilation

a. Results from elevated serum and tissue iron levels

b. Causes secondary hypotension with low CVP

2. Increased capillary membrane permeability leads to edema

3. Inhibition of serum proteases

a. Iron directly inhibits thrombin thereby prolonging PT unrelated to liver dysfunction

b. The coagulopathy in later stages is secondary to hepatic dysfunction

4. Metabolic acidosis

a. Results from poor perfusion with increased anaerobic metabolism secondary to hypotension, anemia from GI bleeds, and hypovolemia.

b. Liberation of H+ from conversion of iron from ferrous to ferric state.

c. Poisoning disrupts oxidative phosphorylation with resulting anaerobic glycolysis and lactic acidosis.

5. Cellular damage

a. Liver - greatest risk for injury because of first pass effect. Mitochondria are the primary intracellular target. This leads to disturbances in the electron transport chain, Kreb's cycle, and ATP production.

b. Renal failure

c. Coma / seizures

C. Liver effects:

1. Cloudy swelling, portal damage, fatty degeneration, Kupffer/parenchymal deposition of iron

2. Once iron accumulates in the hepatic mitochondria it cannot be removed nor can the pathology be reversed

D. Other (much less frequent) effects:

1. Pancreatic injury

2. Bleeding in lungs/kidney

3. Fatty degeneration of heart and renal tubules

II. Clinical Presentation

A. Three stages of acute phase (in severe ingestions)

1. Early (< 6 hrs)

a. Abdominal cramps, vomiting, diarrhea, and GI hemorrhage due to direct effects of Fe on the gut mucosa.

b. Hypotension, pallor, lethargy

c. Leukocytosis, metabolic acidosis, hyperglycemia

2. Intermediate (6 to 48 hrs)

a. Transition between resolution of GI symptoms and overt systemic toxicity

b. May continue to recover or progress to stage three

3. Late (2 to 3 days) - multiple organ failure

a. Cerebral dysfunction and coma

b. Myocardial dysfunction with vascular collapse or shock

c. Massive hepatic failure with jaundice, increased transaminases, coagulopathy, and hypoglycemia

d. Renal failure

e. Ischemic bowel

f. Pulmonary edema

4. Sequelae

a. Intestinal scarring, gastric outlet and small bowel obstruction

b. Hepatic cirrhosis, rare in children

III. Management

A. Assess severity of ingestion

1. Assess amount of **elemental iron**

a. Ferrous fumarate = 33%

b. Ferrous sulfate = 30%

c. Ferrous gluconate = 11.6%

d. Ferrous chloride = 28%

2. Average lethal dose = 180 mg elemental Fe/kg

a. Minimum lethal dose as little as 600 mg

b. Total doses of 200-400 mg have caused severe symptoms in young children

c. **Toxic dose generally > 20 mg/kg**

3. Plasma level peaks at 2-6 hrs post-ingestion (mean = 4 hrs). The serum level correlates with the severity of ingestions. After 6 hours the iron has been rapidly cleared from the serum, primarily by the liver, and the serum level may be normal.

- Level peaks later with enteric coated preparations.

4. Iron levels - if readily available. Vomiting, diarrhea, hyperglycemia (> 150 mg/dl), and leukocytosis (> 15,000) that develop in the 6 hours after ingestion and an abdominal radiograph that demonstrates the presence of radiopaque material are highly predictive of and specific for a serum iron level $\geq$ 300 mcg/dl. Vomiting is considered to have the highest sensitivity and predictive value, so it is unlikely that after an asymptomatic period of more than 6 hours after the ingestion that serious toxicity will occur.

a. < 300 mcg/dl --> no specific treatment

b. 300-500 mcg/dl --> chelation therapy

c. 500-1000 mcg/dl --> chelation therapy and aggressive support

d. > 1000 mcg/dl --> vigorous support and prolonged chelation therapy, significant increase in mortality

5. Deferoxamine Challenge

a. Chelates with Fe to form soluble/excretable complex

b. In the past this challenge was performed to determine the need for chelation therapy. After the deferoxamine injection one would observe the urine for a "vin rose wine" color as an indication for continuation of therapy. **This is NO Longer recommended** as some patients will have a toxic ingestion without production of the urine color changes.

B. Specific Therapy

1. Observation alone with ingestions < 20 mg/kg and a negative KUB. Not all preps radiopaque, however.

2. If asymptomatic for 6 hours following the ingestion they do not require admission.

3. Ipecac - is not contraindicated in the awake, alert child but may mask the vomiting produced by the iron ingestion resulting in an underestimation of the toxicity

4. Gastric lavage

a. Abd x-ray will help determine if lavage successful (again, not all preps radiopaque)

b. Use large bore OG, 1/2NS (not Fleet's) for lavage

c. Sodium bicarb. or deferoxamine are **NO LONGER** recommended as part of the lavage.

d. Examine for Fe tablets

5. Activated charcoal is not indicated as it does not prevent iron absorption and is not used UNLESS a coingestion exists.

6. Chelation therapy **(Deferoxamine)**

a. Indications

(1). All symptomatic patients exhibiting more than transient minor symptoms

(2). Patients with lethargy, coma, seizures, significant abdominal pain, hypovolemia, or acidosis

(3). Patients with a positive radiograph showing multiple radiopacities (retained pill fragments will lead to further absorption and toxicity)

(4). Patients with serum iron levels $\geq$ 300 mcg/dl, ingestion > 100 mg/kg Fe.

b. Route

(1). Given IV, IM or SQ. **IV preferable, and is most appropriate route.**

(2). IM contraindicated if patient is hypotensive, poor absorption. IM route is painful, especially as repeated injections required. It has erratic absorption, obtains higher peak deferoxamine levels and shows a higher incidence of side effects.

c. Dose

(1). 15 mg/kg/hour IV, no maximum dose although package insert states 6 grams/day

d. Side Effects (rare if given at above rate)

(1). Hypotension / shock seen at rates > 45 mg/kg/hr.

(2). **NOT to be given with compazine as coma can result!**

e. Cautions

(1). The iron-deferoxamine complex is excreted in the urine so the patient must be making adequate urine for this to work.

(2). If oliguric/anuric then use chelation and dialysis, (hemodialysis, continuous arteriovenous hemofiltration, or peritoneal dialysis)

f. Most patients require no more than 24 hours of therapy

g. Treatment is continued until all the following criteria are satisfied:

(1). Patient is free of s/s of iron toxicity

(2). Serum iron level is normal or low (< 100 mcg/dl)

(3). KUB shows no radiopacities

(4). If patient developed "vin rose" colored urine, the urine color has normalized

7. Supportive therapy

(1). ICU, CVP, A-line, etc. as indicated

(2). Adequate fluid resuscitation can not be over emphasized

8. Other considerations

a. Severe coagulopathies - draw **baseline** PT, PTT, fibrinogen levels.

b. Hepatic failure

c. Intestinal infarction

- Due to retained pill fragment or hypotensive episode

9. Other therapies: whole bowel irrigation, gastrotomy, especially if iron containing aggregates occur in the stomach or intestines on X-ray.

C. Lab Evaluation

1. Serial serum Fe's and TIBC's

a. Run Fe levels **STAT** with first level drawn 2-4 hrs after ingestion if possible

b. Follow until within safe range

c. Some labs are unable to measure serum Fe accurately in the presence of deferoxamine.

2. Electrolytes, BUN, creat, glucose. Follow serum glucoses carefully as sudden hypoglycemia may develop after a period of hyperglycemia.

3. CBC with diff (leukocytosis, anemia)

4. ABG to assess respiratory status and metabolic acidosis

5. Type and Cross

6. Clotting Studies, (PT, PTT, fibrinogen)

7. LFT's - baseline and serially

8. Assess urine output

9. Guaiac stools and emesis

LEAD POISONING

I. Introduction

A. Lead is absorbed through the GI tract (ingestion) and the lungs (inhalation). Increased intake results in deposition in the soft tissues, especially kidney, liver and brain.

B. Poisoning is usually from prolonged, excessive exposure; 1/2 life is approximately 20 years.

C. Sources

1. Lead pigmented paints (greatest hazard)

2. Contamination of food and beverages by lead glazed ceramic pitchers and lead soldered cans

3. Ingestion and retention in the stomach of fishing weights, shot, jewelry painted with lead paint, pencil coatings

4. Sniffing fumes of leaded gasoline containers

5. Mexican and oriental folk medicine (azarcon, greta, paylooah)

II. History of High Risk Children

A. High risk environment

1. Dilapidated housing

2. Exposures as above

B. Pica

C. Sibs with lead intoxication

III. Lab / X-ray

A. Venous lead level - fingerstick levels are inaccurate

B. CBC with peripheral smear (microcytic anemia, basophilic stippling)

C. UA (glycosuria, proteinuria), BUN, creat to evaluate for renal damage.

D. KUB (flecks of lead in GI tract)

E. X-rays of long bones (lead lines in children age 2-5 yrs) - lines of increased density in metaphyseal plates represent growth arrest

F. FEP, (free erythrocyte protoporphyrin) - until recently was used to screen children for lead poisoning; it has a poor sensitivity for Pb levels < 25 micrograms/dl and is not specific as it is increased in iron deficiency anemia, levels > 190 almost exclusively lead poisoning

IV. Clinical Picture and Management

A. Acute Lead Encephalopathy

1. Onset may be sudden

2. Coma, seizures, bizarre behavior, ataxia

3. Any of these sx. with an elevated blood lead level constitutes a medical emergency

4. Almost always assoc. with levels > 100, although reported at lower levels.

5. Diagnosis can usually be made without LP that is dangerous because of increased ICP, which may be present in the absence of any of the usual sx. If LP necessary for differential, consider pre LP CT scan!

6. Treatment

a. Supportive

- NPO until significant improvement

- Fluid restrict to maintenance plus losses

b. Chelation (see below)

c. Seizures

- Treat initially with lorazepam 0.1 mg/kg IV q 2 min. to total initial dose of 1 mg/kg.

- If resistant use phenobarbital 15 - 20 mg/kg IV.

- Further therapy with either valium 0.1mg/kg IV, or phenytoin 10 mg/kg slow IV.

7. Cerebral Edema: Mannitol 0.25 - 0.5 grams/kg slow IVP.

8. Renal and hepatic function, lytes, blood lead monitored daily

B. Symptomatic without encephalopathy

1. Lethargy, anorexia, vomiting, abdominal pain, constipation

2. Usually assoc. with lead levels > 70 (if level < 50, consider other cause).

3. All symptomatic children potentially have lead encephalopathy, therefore treat immediately.

a. Supportive as above

b. Chelation (see below)

C. Asymptomatic with increased lead level

1. Although asymptomatic, have metabolic effects and subclinical neurobehavioral effects

2. Essential to have diagnosis based on lead level

3. If blood lead level 25-44 micrograms/dl, perform the CaNa2-EDTA provocation test; this is expensive and usually done only at centers where large numbers of lead poisoned children are treated. To perform:

a. Obtain a baseline lead level

b. Patient empties bladder

c. CaNa2-EDTA 500 mg/M^2 IV in 250 cc/M^2 D5W over one hour (see DKA chapter or Acute Tumor Lysis chapters for nomogram and calculation of body surface area)

d. Collect all urine over 8 hrs in lead free equipment

e. Results: $\frac{\text{urine lead excreted (mcg/cc)X total volume(cc)}}{\text{CaNa2-EDTA given (mg)}}$

Test is positive if > 0.6

V. Prevention

A. Do not return children to lead environment (consult social services for assistance in obtaining safe housing)

B. Screen all family members

C. Report all cases to public health for investigation and abatement of lead hazards

D. Extended follow up to at least age 6 yrs

VI. Chelation Therapy for Lead Poisoning

A. Symptomatic

1. Acute Encephalopathy, (usually for Pb > 100 micrograms/dl)

a. BAL (dimercaprol) 450 mg/M^2/day and CaNa2-EDTA 1500 mg/M^2/day

1. Start with BAL 75 mg/M^2 IM q 4 hrs

2. After 4 hrs, start continuous infusion of EDTA 1500 mg/M^2/day

3. Continue BAL and EDTA for 5 days

4. Interrupt therapy for 2 days

5. Treat for 5 additional days with EDTA and BAL, if Pb level remains high (> 70 micrograms/dl)

6. Measure rebound venous Pb level 7 - 10 days after therapy.

a. Other cycles will be needed if Pb rebounds > 50 micrograms/dl.

2. If symptomatic at **any** level without acute encephalopathy **OR** Pb level > 70 micrograms/dl

a. BAL 300 mg/M^2/day and CaNa2-EDTA 1000 mg/M^2/day

1. Start with BAL 50 mg/M^2/day IM Q 4 hrs

2. After 4 hrs, start continuous infusion of EDTA 1000 mg/M^2/day

3. Continue EDTA for 5 days

4. BAL may be DC'd after 3 days if Pb level < 50 micrograms/dl

5. Interrupt therapy for 2 days

6. Treat for 5 additional days with EDTA and BAL if Pb level remains high (> 70 micrograms/dl)

7. Other cycles may be needed depending on Pb rebound for levels > 50 micrograms/dl as above.

3. Asymptomatic - Before treatment measure blood Pb level:

a. Level of 45 - 69 micrograms/dl:

1. CaNa2-EDTA 1000 mg/M^2 /day by continuous infusion for 5 days

2. FDA recently approved (1991) DMSA (succimer) for asymptomatic children with Pb levels of 45 - 69 micrograms/dl. Dose is 350 mg/M^2 (or 10 mg/kg) q 8 hours X 5 days PO, then 350 mg/M^2 (or 10 mg/kg) q 12 hours X 14 days PO. Its' use has been limited.

b. Level of 25 - 44 micrograms/dl: CaNa2-EDTA provocation test as above then:

1. If ratio > 0.6 : CaNa2-EDTA 1000 mg/M^2/day IV for 5 days

SUMMARY OF ANTIDOTES

POISON	ANTIDOTE	DOSAGE
Acetaminophen	N-Acetylcysteine (Mucomyst)	Initial: 140 mg/kg PO Subsequent: 70 mg/kg q4hr for 17 doses Begin within 24 hours of ingestion
Anticholinergics	Physostigmine	Adult: 2 mg IV/IM/SQ Child: 0.5 mg IV/IM/SQ q5min, max 2 mg NOT WITH TCA INTOXICATIONS Monitor: Seizures, Cholinergic crisis, bradyarrhythmias, asystole
Anticholinesterase Organophosphate insecticides	Atropine Pralidoxine (2-PAM)	Adult: 2-5 mg IV Child: 0.05 mg/kg IV Repeat q 5-10 min until atropinization **Consider infusion 0.02-0.08 mg/kg/hr** Adult: 1 gm IV over 30 min Child: 20-40 mg/kg IV Repeat dose in 1 hr if symptoms persist Consider infusion 0.5 g/hr (adult)
Benzodiazepine	Flumanzenil	0.1 mg/kg IV max dose 3 mg
□-Blocker	Glucagon Vasoactive infusions (Dopamine, Epinephrine)	Adult: 3 mg IV then drip 1 mg/hr **Child: 0.05 mg/kg IV then 0.07 mg/kg/hr** Titrate to effect
CaChannel Blocker	Calcium chloride 10% Calcium gluconate Glucagon Vasoactive infusions	Adult: 10 ml **Child: 0.2 ml/kg** Adult: 30 ml **Child: 0.6 ml/kg** Adult: 3 mg IV then drip 1 mg/hr **Child: 0.05 mg/kg IV then 0.07 mg/kg/hr** **Titrate to effect**
Carbon monoxide	100% oxygen Hyperbaric oxygen	Minimum of 90 minutes, until CO < 5% Severe cases
Cyanide	Amyl nitrite NaNitrite/NaThiosulfate	**Adult: Inhalation therapy** Adult: NaNitrite 300mg IV then NaThiosulfate 12.5 g IV Child: < 25 kg dose depends on [Hgb] Hgb Na nitrite Na thiosulfate 8 g 0.22 ml (6.6 mg)/kg 1.10 ml/kg 10 g 0.27 ml (8.7 mg)/kg 1.35 ml/kg 12 g 0.33 ml (10 mg)/kg 1.65 ml/kg 14 g 0.39 ml (11.6 mg)/kg 1.95 ml/kg
Fluoride	Calcium gluconate	0.6 ml/kg IV until sx abate, repeat prn
Ethylene glycol	Ethanol Dialysis	Load—Adult 0.6 g/kg IV, Child 0.7 g/kg IV Maintenance-125 mg/kg/hr adult/child Titrate infusion to keep level 100 mg/dL
Methanol	Ethanol Dialysis	See above
Isoniazid	Pyridoxine	1 g per 1 g INH ingested IV over 30-60 min
Methemoglobinemia	Methylene blue 1%	1-2 mg/kg (0.1-0.2 mL/kg) over 5-10 min
Narcotics	Naloxone	Child 0.1 mg/kg IV/ETT

POISON	ANTIDOTE	DOSAGE
Iron	Deferoxamine	15 mg/kg/hr until Fe level < 100 mcg/dL
Lead	British Antilewisite (BAL)	3-5 mg/kg/dose deep IM q 4 hours for 2 days, every 4-6 hours for an additional 2 days, then every 4-12 hours for up to 7 additional days
	EDTA	50-75 mg/kg/24 hours deep IM or slow IV infusion given in 3-6 divided doses for up to 5 days; may be repeated for a second course after a minimum of 2 days; each course should not exceed a total of 500 mg/kg body weight
	Penicillamine	100 mg/kg/day (max. 1 gram) PO in divided doses for up to 5 days; for long term therapy do not exceed 40 mg/kg/day
	DMSA (Succimer)	350 mg/M^2 (10 mg/kg) PO every 8 hours for 5 days, followed by 350 mg/M^2 (10 mg/kg) PO every 12 hours for 14 days
Phenothiazines	Diphenhydramine (Benadryl)	0.5-1 mg/kg IV/IM
Warfarin	Vitamin K	Adult: 10 mg IM/SQ/PO Child: 1-5 mg IM/SQ/PO

Adapted from Woolf et al Poisoning and the Critically Ill Child in Textbook of Pediatric Intensive Care (3rd Edition), Rogers MC ed.,Willians and Wilkens, 1996, p1315-1391.

RAPID CARDIO-PULMONARY ASSESSMENT

I. Introduction

A. Selected Conditions Requiring a Rapid Cardiopulmonary Assessment (partially from PALS, Chapter 2.)

B. The purpose of this assessment is to determine in < 30 seconds which patient has cardiac or pulmonary failure that may lead to an arrest. **Any of the following selected conditions require a rapid cardio-pulmonary assessment**

i. Respiratory rate > 60
ii. Heart rate > 180 or < 80 (under 5 years)
- 160 or < 60 (over 5 years)

iii. Respiratory Distress - increased work of breathing (retractions, nasal flaring, grunting)
iv. Trauma
v. Burns totaling > 10 % of surface area
vi. Cyanosis
vii. Failure to recognize parents
viii. Diminished level of consciousness - unusual irritability, or lethargy
ix. Seizures
x. Fever with petechiae
xi. Admission to an ICU

II. Airway

A. Is the airway patent?

B. Is the airway maintainable with head positioning, suctioning, or adjuncts?

i. Nasopharyngeal airway
ii. Oral airway (unconscious patient)
iii. Bag-mask ventilation

C. Unmaintainable?

i. Removal of foreign body
ii. Intubation
iii. Needle cricothyrotomy

III. Breathing

A. Respiratory Rate (<u>also see Status Asthmaticus chapter</u>)

Normal Newborn	Normal 1 year	Normal 18 years	
< 40 - 60	24	18	> 60 <u>always</u> abnormal

A slow or irregular RR in an acutely ill child or infant is ***<u>OMINOUS</u>***! This may indicate the patient is deteriorating rather than improving secondary to hypothermia, fatigue or CNS depression.

B. Air Entry

i. Chest rise?
ii. Bilateral breath sounds?
iii. Stridor?
1. Upper (extrathoracic) airway obstruction
2. Examples
a. Tongue
b. Laryngomalacia
c. Vocal cord paralysis
d. Hemangioma, tumor, cysts
e. Infection
f. Foreign body aspiration
iv. Wheezing?
1. Intrathoracic obstruction
2. Examples
a. Bronchiolitis
b. Asthma
c. Pulmonary edema
d. Intrathoracic foreign body

C. Mechanics

i. Retractions - intercostal, subcostal, suprasternal
ii. Grunting - to preserve functional residual capacity (FRC)
iii. Nasal flaring
iv. Gasping - often a sign that bag-valve mask is needed esp. in neonates.
v. Head bobbing - indicates increased respiratory effort

D. Baseline Color

IV. Circulation

A. Heart Rate (<u>also see Cardiac Dysrhythmia chapter</u>)

	Newborn - 3 mos.	3 mos. - 2 yr.	2 - 10 yr.	> 10 yr.
Normal:	140	130	80	75

Abnormal: < 5 yr.: > 180 or < 80, > 220 consider SVT, 5 yr.: > 160

B. Blood Pressure (BP)
i. Hypotension is a LATE and often sudden sign of cardiovascular decompensation

Normal	Newborn	1 yr.	> 1 yr
Systolic	> 60	>70	> 70 + (2 x yr.) - lower limit (5th percentile) of normal 90 + (2 x yr.)- 50th percentile

C. Blood <u>volume</u>: Neonate 85 cc/kg, infants 80 cc/kg, children 75 cc/kg

D. Peripheral/Central Pulses

i. Present/absent

ii. Volume/strength
iii. Pulse pressure [PP] (systolic - diastolic BP)
1. Narrow pulse pressure: As Cardiac Output decreases, PP narrows and the pulse becomes thready
2. Wide pulse pressure: As Cardiac Output increases (septic or anaphylactic shock), PP widens and pulses are bounding.
3. A wide PP does ***not*** mean that perfusion is adequate!

E. Skin Perfusion

i. Capillary refill time: Normal is < 2 sec.
ii. Temperature
iii. Color - cyanosis, pallor?
iv. Mottling

F. CNS Perfusion

i. Quick assessment of responsiveness
1. Awake
2. Responds to voice
3. Responds to pain
4. Unresponsive
ii. Recognition of parents
iii. Response to painful stimuli
iv. Muscle tone
v. Pupil size
vi. Posturing

V. PRIMARY Confirmation of Endotracheal Tube Placement

A. Direct visualization (Direct Laryngoscopy)

i. Provider should visualize the tube passing through the vocal cords
ii. Vocal cord mark should be at the level of the vocal cords

B. Symmetric chest rise

C. Listen for breath sounds over peripheral lung fields

i. Symmetry and equality of breath sounds are dependent upon the patients underlying disease process
ii. If the breath sounds are asymmetric prior to intubation, they may still be asymmetric after intubation

D. Listen for breath sounds over epigastric area

E. Look for water vapor in the ETT during exhalation

i. Presence of water vapor is *encouraging*
ii. The presence of water vapor ***does not definitively*** confirm ETT placement

VI. SECONDARY Confirmation of Endotracheal Tube Placement
A. Continuous capnography (i.e. the continuous ET-CO2 monitor used in the ICU on ventilated patients)

B. Colorimetric device

i. PURPLE = Little or no CO2 detected
ii. TAN = Minimal CO2 detected
iii. YELLOW = CO2 detected (Confirmation of ETT placement)

C. These devices are very sensitive and specific for confirming ETT placement, ***provided that the patient has a perfusing cardiac rhythm***

D. After placement, 6 ventilation breaths are given

i. 6 "breaths" will wash-out CO2 that may be present in the esophagus or stomach
ii. Detected CO2 then indicates tracheal positioning, but it does not indicate exact position since a right mainstem intubation will also yield CO2

E. Utilization during a resuscitation

i. If the child has a nonperfusing rhythm or cardiac arrest, the cardiac output is so low that CO2 is not delivered to the lungs to be exhaled, so there will be no CO2 sensed
ii. The **absence** of detectable CO2 **does not confirm esophageal placement**
iii. If placement is unsure, confirm with clinical examination and/or direct laryngeal examination

F. Reasons for a low exhaled CO2

i. Severe airway obstruction, bronchospasm, pulmonary edema
ii. Contamination of colorimetric detector with gastric secretions or acidic drugs (i.e. epinephrine)
iii. Suspect contamination if the detector remains YELLOW through the entire respiratory cycle
iv. IV bolus of epinephrine may transiently decrease pulmonary blood flow and thus exhaled CO2

VII. Pulmonary Assessment of the Deteriorated Intubated Patient

A. Mnemonic **DOPE**

i. Displacement of endotracheal tube
ii. Obstruction of the endotracheal tube
iii. Pneumothorax
iv. Equipment failure

B. Assessment steps

i. Remove patient from ventilator and manually ventilate
ii. Examine the next for tracheal deviation and possible tension pneumothorax (trachea deviated AWAY from the side of the pneumothorax), emergently decompress the affected lung
iii. Evaluate the endotracheal tube, a "kinked" tube will cause inadequate ventilation to occur
iv. Auscultate the lung fields; if no chest movement, breath sounds, or expired CO2 □ tube is dislodged, remove the tube and reintubate
v. Suction endotracheal tube

1. Resume manual ventilation
2. Remember, not all “sticky” secretion can be suctioned from endotracheal tubes, this may require replacement of the tube

vi. If no pneumothorax, endotracheal tube position confirmed, and not obstructed with secretions, consider equipment failure of the ventilator and maintain manual ventilation

vii. Reassess the ventilator settings
1. Check your inspiratory pressures with a mamometer
2. Match the ventilator settings to your manual ventilation

RAPID SEQUENCE INDUCTION

I. Rapid sequence induction (RSI) for intubation implies the use of sedation and neuromuscular blockade, avoidance of positive pressure BVM ventilation prior to intubation, and use of cricoid pressure. These measures are an attempt to decrease the cardiovascular and CNS responses to intubation and decrease the risk of aspiration.

II. Use of paralysis may be contraindicated if intubation is anticipated to be difficult due to anatomic abnormality or pathology. If airway problems anticipated, Anesthesia should be consulted.

III. RSI is performed in any patient with a potential for a full stomach or possible increased intracranial pressure.

V. Rapid sequence induction:

A. Preparation, preoxygenation, premedication, sedation, cricoid pressure, paralysis, intubation, verify.

B. Preoxygenation involves 2-5 minutes of 100% O2 via nonrebreather in spontaneously breathing patients or 1-2 minutes in apneic patients via BVM.

C. Standard Medication Regimen

1. Atropine 0.02 mg/kg with a minimum of 0.1 mg IV, if less than 2 years of age

2. Versed (midazolam) 0.1- 0.2 mg/kg IV +/- Fentanyl 1-2 mcg/kg

3. Paralysis if able to Bag Mask Ventilate and no anatomic abnormalities or other contraindications to paralysis:

a. Vecuronium 0.2-0.3 mg/kg IV or Rocuronium 1 mg/kg:

b. Succinylcholine 1 - 2 mg/kg IV. Succ. has many side effects (see below) and probably is not as safe in inexperienced hands as vecuronium. Infants tend to need a larger dose of succinylcholine (2-3 mg/kg).

c. Preoxygenation is continued until the pt. is fully relaxed.

d. **In children older than 4 years of age,** if succinylcholine is used, a defasciculating dose of a nondepolarizing muscle relaxant (vecuronium 0.01 mg/kg) may precede the depolarizing agent to prevent muscle fasciculations and elevation of intragastric pressure, which may be associated with regurgitation.

e. If continued paralysis is required after patient intubated, a non-depolarizing NMB (vecuronium) is used.

VI. There are patients in which sedation and paralysis is contraindicated (unstable airway - epiglottitis, mediastinal mass, anatomic abnormalities making it difficult or impossible to use the usual methods of intubation).

VII. Each patient should be evaluated on a case by case basis, especially since there may be contraindications to using certain medications for intubation. IN GENERAL:

A. **For sepsis/ shock/ asthma:**

1. Consider using ketamine for sedation rather than versed (maintains BP, bronchodilator). Dose is 2.0 mg/kg IV. Ketamine increases secretions so atropine 0.02 mg/kg (min 0.1 mg) IV or Robinul 5 mcg/kg is given as well. Ketamine can also cause nightmares/emergence reactions. Versed 0.1 mg/kg given with Ketamine should prevent this.

2. May consider Fentanyl 1-2 mcg/kg for sedation rather than Ketamine if shock is severe.

3. Paralyze fast with Vecuronium 0.3 mg/kg IV, **or** Rocuronium 1 mg/kg.

B. **For head trauma or other diseases with increased ICP:**

1. Use lidocaine (1.0 mg/kg IV) 1 minute prior to intubation to buffer the ICP spike in response to laryngeal stimulation.

2. Etomidate 0.3 mg/kg is the drug of choice as it is cerebral protective and has minimal hemodynamic effects. Thiopental (2-4 mg/kg IV) is an alternative, but may result in hypotension.

3. Use atropine for children younger than 2 years of age 0.02 mg/kg.

4. Use vecuronium (0.3 mg/kg IV) or Rocuronium 1 mg/kg.

5. Ketamine causes a rise in ICP - should **not** be use for sedation in this situation.

VIII. Unwanted Effects of Succinylcholine

A. Cardiovascular - bradycardia, hypertension or hypotension. Atropine prior to administration may prevent bradycardia.

B. Hyperkalemia – life threatening hyperkalemia is most likely to occur following: burns (24-48 hours post burn), spinal cord injury, tetanus, severe intraabdominal infections, encephalopathy, polyneuropathy including Guillain-Barre syndrome, and chronically ill children.

C. Increased intraocular pressure- avoid in globe injury.

D. Hypersensitivity reactions - anaphylactic reactions

E. Muscle pains - ameliorated with pancuronium

F. Rhabdomyolysis and myoglobinuria

G. Malignant hyperthermia

H. Pulmonary edema and pulmonary hemorrhage; several infants in whom pulmonary edema (increased SVR, decreased PVR, leaky capillaries) formed only minutes after 4 mg/kg of IM succinylcholine were given are reported.

I. Increased ICP - can be attenuated with prior administration of nondepolarizing agent and thiopental or lidocaine. Increased cerebral blood flow.

J. Increased gastric pressure and increased risk of regurgitation.

K. Not effective in patients with Myasthenia Gravis.

IX. Why use drugs.

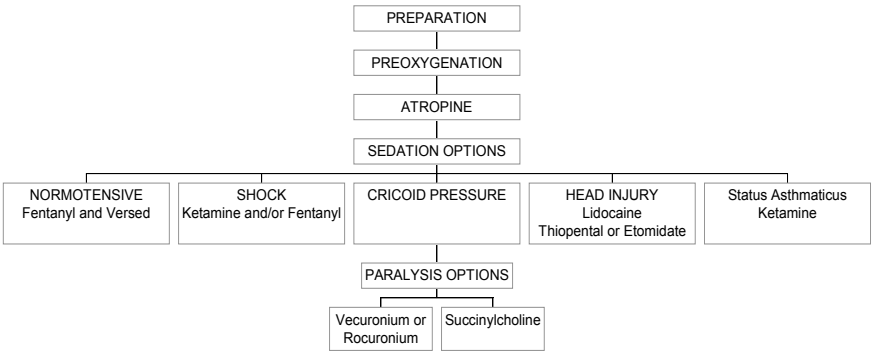
A. AVOID STRUGGLING & TRAUMA

B. AVOID HYPOXEMIA

C. AVOID UNDESIRABLE PHYSIOLOGICAL RESPONSES -Hypertension, tachycardia, increased ICP, etc

D. PAIN CONTROL & AMNESIA

E. TO FACILITATE INTUBATION



CONTINUOUS RENAL REPLACEMENT THERAPY IN THE PEDIATRIC INTENSIVE CARE UNIT

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The development of acute intrinsic renal failure is a relatively common complication of the critically ill pediatric patients in the intensive care unit. Most often it is not an isolated event but may be associated with respiratory failure, hepatic insufficiency, or may be part of the multiorgan dysfunction syndrome (MODS) secondary to trauma or sepsis. While isolated acute renal failure can be treated adequately by conventional forms of intermittent dialysis's, volume overload and hemodynamic instability are complications that can be advantageously treated by continuous renal replacement therapy.

Modalities of Continuous Renal Replacement Therapies:

Mode	Principles Involved	Access	Pump Assisted	Fluid Removal	Solute Clearance	Correction of Electrolyte Imbalance	FRF	Systemic Anticoagulation
HD	Convection + Diffusion	AV	Yes	++	++++	++++	No	Yes
PD	Convection + Diffusion + Osmosis	IP	No	+++	++	++	No	No
SCUF	Convection	AV	No	++	No	No	No	Yes
	Convection	VV	Yes	++	No	No	No	Yes
CAVH	Convection	AV	No	++	±	+++	Yes	Yes
CVVH	Convection	VV	Yes	+++	±	+++	Yes	Yes
CAVHD	Convection + Diffusion	AV	No	+	++++	++++	Yes	Yes
CVVHD	Convection + Diffusion	VV	Yes	+++	++++	++++	Yes	Yes

AV = Arteriovenous; VV = Venovenous; IP = Intraperitoneal; FRF = Filter Replacement Fluid

Advantages:

- Fluid removal is gradual and continuous
- It is ideal for use in hemodinamically unstable patients.
- It allows for precise volume control
- Can adapt immediately to changing circumstances
- Gives unlimited ability to administer all types and volumes of fluid
- Allows for aggressive nutritional support
- Continuous clearance of urea provides more stable blood levels without peaks and troughs
- Provides excellent clearance of solutes over 24 hours
- Requires less technical support than hemodialysis
- Removal of Cytokines (?)

Disadvantages:

- Need for a continuous vascular access
- Need for continuous anticoagulation management
- Need for a specially educated nursing staff.
- Needs constant vigilance
- Immobilization of patient
- Removal of therapeutic drugs
- Slow K removal
- Creates scheduling problems (X-rays, CT scan, MRI, etc.)
- More expensive than peritoneal or hemodialysis

Considerations in Selection of Modality:

Patient Factors	Modality Factors	Physician Factors
Patient size	Solid removal	Training
Hemodynamic stability	Fluid removal	Expertise of the clinician
Mean arterial pressure	Solute and fluid removal	Personal preference
Pulmonary status	Rate of correction electrolyte abnormality	Aggressiveness
Vascular access	Removal of inflammatory mediators	
Peritoneal integrity	Availability	
Abdominal distention	Labor intensiveness	
Recent abdominal surgery	Complications	
Mobility and location	Cost	
Multiorgan failure	Nursing support	
Catabolic status		

Indications for CRRT:

- Massive fluid overload
- Congestive heart failure with diuretic unresponsive oliguria despite inotropic support
- Acute renal failure in patients with multiple organ failure
- Respiratory compromise in patients with acute renal failure
- Cardiogenic shock with pulmonary edema
- Massive tumor lysis syndrome
- Fluid-restricted patients on hyperalimentation
- Patients with electrolyte and acid-base derangements
- When PD is contraindicated due to poor perfusion of the peritoneal membrane
- Drug removal in patients with intoxication
- Patients with sepsis for removal of cytokines (?)

Contraindications:

- Active bleeding is a relative contraindication to CRRT especially if peritoneal dialysis can be performed.
- A recent cerebral hemorrhage that might be extended with heparinization is also a relative contraindication to CRRT, unless regional anticoagulation or no anticoagulation is used.
- Life threatening hyperkalemia as potassium is not significantly removed by CRRT

Filter Replacement Fluid (FRF):

- In CRRT large ultrafiltrate volumes are generated thus making it crucial to replace large quantities of ultrafiltrate with near-equal amounts of sterile and pyrogen-free electrolyte solution.

- Crystalloid solutions that have an electrolyte composition comparable to normal plasma water composition are used.
- FRF may be injected either before the blood has passed the hemofilter in the extracorporeal circulation [pre-dilution mode] or after the filter [post-dilution form. FRF is not routinely warmed
- The most commonly used FRF are either bicarbonate-based or lactate-based.

Site of Replacement Fluid	**Indications**	**Advantages**	*Disadvantages*
Pre-Dilution	- UFR > 10 mL/min - Hematocrit > 40% ***- No/low anticoagulation*** - Increased clotting	- ↓ Heparin requirements - ↓ Risk of clotting - ↑ Lifespan of filter - Faster UFR	- Requires ↑volume of FRF - Urea clearance = 80-90% of UFR
Post-Dilution	- No specific indications	***- ↓ Volume of FRF*** - No hemodilution - Urea clearance = UFR	- Limited UFR - Heparin requirements - May ↑ risk of clotting - ↓ Lifespan of filter

Vascular Access:

- The vascular access catheter is the Achilles Heel of CRRT in infants and children.
- The ideal catheter should be easy to insert, allow maximum blood flow rate for the patient's size without occluding the vessel, have low recirculation rates, not be prone to kinking, and have a low risk of causing vascular injury.
- The arteriovenous modalities of CRRT, CAVH and CAVHD, require both arterial and venous cannulation.
- A large variety of catheters for CRRT has been used in pediatric patients, however the use of double lumen hemodialysis catheters has simplified vascular access for CVVH.
- A subclavian or internal jugular access is usually preferred.

Suggested Correlation of Patient to Acute Access Site		
Patient Size	**Catheter Size**	**Access location**
Neonate	UVC: 5.0, 8.5 Fr UAC: 3.5, 5.0 Fr	Umbilicus
3 – 15 kg	7.0 Fr Dual Lumen	Femoral vein/Subclavian
16 – 30 kg	9.0 Fr Dual Lumen	Femoral vein/Subclavian
31 – 50 kg	10.0 Fr Dual Lumen	Femoral vein/Subclavian
> 50 kg	10.0 Fr Dual	Femoral

	Lumen	vein/Subclavian

Anticoagulation:

Modality	Advantages	Disadvantages
Heparin	* Good anticoagulation	* Thrombocytopenia * Bleeding
Low MW Heparin	* Decreased thrombocytopenia	* Increased bleeding * Monitor by anti-Factor X * More expensive than heparin
Citrate	* Lowest risk of bleeding	* Very labor intensive * Hypocalcemia * Hypertonic
Prostacycline (PGI_2)	* Decreased bleeding risk	* Hypotension * Limited experience * Poor efficacy
Nafamostat mesilate	* Low risk of bleeding	* Short half-life * Lack of availability
NO Anticoagulation	* No risk of bleeding	* Poor efficacy

- Clotting of the extracorporeal system is the most common factor that contributes to ineffective treatment during hemofiltration.
- The objectives for anticoagulation include
  - 24-48 hour filter patency
  - Minimum systemic anticoagulation to reduce the risk of bleeding
  - An anticoagulant with minimum side effects and a short half-life, which can be reversed easily if necessary
- Simple and inexpensive monitoring of the level of anticoagulation.
  - Heparin is the most commonly utilized anticoagulant in patients on CRRT.
    - Loading dose: 20 units/kg given 3 to 5 minutes before the circuit is connected
    - Maintenance: 5 to 10 units/kg/hour given pre-filter
    - Goal: Keep the post-filter ACT at 170-200 sec.

Fluid Balance:

- Precise fluid balance is one of the most attractive features of CVVH.
- Strict hourly intake and output must be recorded, and calculations made carefully each hour.

Intake = Output in CRRT	
Intake	**Output**
Intravenous fluids	Ultrafiltrate
Replacement fluid	Drains
Oral and NG intake	Nasogastric suction
Hyperalimentation	Gastrointestinal losses
Medications	Insensible water loss
Blood products	Urine
Drips	Stools
Filter flushes	Emesis

Drug removal During CRRT:

- A substantial amount of most non-protein bound pharmacologic agents is lost into the ultrafiltrate during CRRT.
- Therapy-related factors (ultrafiltration rate, dialysate flow rate, membrane electrical charge, membrane binding) and drug-related factors (volume of distribution, molecular weight of agent, endogenous clearance, protein binding) are known to influence drug removal.
- Other factors to be taken into consideration are: drug-drug interactions, drug-membrane interactions, pharmacokinetics of specific drugs.
- Ideally, drug therapy should be closely monitored by frequent drug level determinations and the dose of the drug being delivered adjusted accordingly.

Complications of CRRT:

Complications of CRRT in Acute Renal Failure			
Vascular Access	**F. Treatment**	**Anticoagulation**	**Patient**
Infection	Volume depletion	GI bleeding	Hypotension
Thrombosis	Hypothermia	Intraperitoneal bleeding	Hemodynamic instability
Dissection	Air embolism	Thrombosis of circuit	Rhythm disorders
Aneurysm	Electrolyte disturbances	Clotting of hemofilter	Hemorrhagic syndrome
Fistula	Disequilibrium syndrome		Neurological disorders
Distal arterial ischemia	Lactic acidosis		Cerebrovascular accidents
Loss of limb	Excessive drug clearance		Ischemic accidents
	Hemofilter rupture		

SICKLE CELL ANEMIA

I. DEFINITION AND PATHOPHYSIOLOGY - sickle cell anemia comprises several distinct disorders caused by abnormal hemoglobin (Hgb) which results in polymerization and formation of long hemoglobin chains. These chains distort the shape of red cells causing changes in blood viscosity and in the red cell membrane.

A. The mutation in sickle cell disease occurs when the sixth amino acid in the beta chain (usually glutamic acid) is replaced by valine. This causes the hemoglobin to form polymers when deoxygenated.

B. Pathophysiologic mechanisms:

1. Oxygen saturation: deoxygenated hemoglobin S polymerizes to form long rods (tactoids) that distort the shape of the red cell. Sickling is reversed by oxygenation but repeated sickling and unsickling damages the cell membrane.

2. Hemoglobin concentration: the polymerization rate changes in proportion to the thirtieth power of the hemoglobin concentration.

3. Temperature: polymerization of sickle hemoglobin is potentiated by fever or hypothermia.

4. Blood pH: acidosis increases polymerization. Reperfusion of the tissue results in lactic acidosis. Renal tubular defects seen in patients with sickle cell disease reduce the capacity of the kidneys to excrete acid. Oversedation may result in respiratory acidosis.

II. GENERAL MANAGEMENT

A. IDENTIFICATION

1. Hemoglobinopathy screening of newborn infants.

a. Nearly 100% Hgb S, some Hgb F, no Hgb A:
i. Sickle cell anemia — homozygous (Hgb SS)
ii. Sickle β^{o}-thalassemia

b. Hgb A, Hgb S, ± Hgb F:
i. Sickle trait – heterozygous
ii. Sickle β^{+}-thalassemia

c. Hgb S, Hgb C: Sickle hemoglobin C disease

2. Consultation with a pediatric hematologist is advised.

B. ROUTINE AND PREVENTIVE HEALTH CARE MEASURES

1. Treat as normal children. Provide all routine immunizations, good nutrition, and other preventive health care measures.

2. Must have a primary health care provider with whom there is a mechanism for prompt emergency care when the need arises.

3. Infection prevention:

a. By 3 to 4 months of age (when the fetal hemoglobin declines to below 50% of the total), clinically significant hemolytic anemia and impairment of splenic function develops.

b. Children with sickle cell anemia are at risk of overwhelming septicemia, often without a primary focus, due to the encapsulated organisms *Streptococcus pneumoniae and H. influenzae* type b. Without preventive measures, 15-20% of infants and young children with sickle cell anemia die before 5 years of age.

c. Penicillin. Either tablets or suspension can be utilized. Since the suspension necessitates a prescription refill every 2 weeks, tablets, which can be crushed and given in a spoonful of formula or food, are preferred.
i. Prior to 2 years of age: Pen-VK 125 mg BID po.
ii. After age 2: Pen-VK 250 mg BID
iii. Continue until at least 5 years of age.

d. Vaccinations.
i. As per normal infants.
ii. The 23-valent pneumococcal vaccine at 24 months of age. A "booster" dose of pneumococcal vaccine should be given every 5 years after the first dose.

III. FEVER

A. ETIOLOGY

1. Fever is usually the initial manifestation of sepsis. Prompt antibiotic therapy can be life-saving.

2. Septicemia due to *Streptococcus pneumoniae* or *Hemophilus influenzae* type b is the most common cause of death in young children with sickle cell anemia

B. EVALUATION

1. **Whenever a child with sickle cell anemia has a temperature > 101.5 °F, he or she should be evaluated <u>at once</u>.**

2. Rapid but complete history and physical examination.

3. Immediately place an intravenous catheter or needle. Obtain a CBC (including differential, WBC count and reticulocyte count) and blood culture.

4. Immediately administer intravenous (or intramuscular if the intravenous route is impractical) ceftriaxone (Rocephin) 50-75 mg/ kg, maximum 2 grams. If ceftriaxone is unavailable, give cefuroxime (Zinacef, Kefurox) 50 mg/kg.

5. Parenteral antibiotics should be given even if there is an obvious focus of infection (otitis, URI, etc.).

6. A chest X-ray should be considered when the child has a fever, cough, tachypnea, chest pain, O2 sat <95% or other physical findings suggesting pneumonia or other pulmonary process.

7. Other laboratory tests may be indicated (e.g., type and cross match for possible red blood cell transfusion, CSF analysis and culture, urine culture, etc.) depending upon the clinical findings.

8. Prompt and careful physical assessment and administration of IV antibiotics should have high priority. Do **not** wait until after the chest X-ray or blood count results return.

C. CRITERIA FOR HOSPITALIZATION

1. IF THE CHILD IS **"TOXIC"** OR IF THEY HAVE AN **ALTERED MENTAL STATE**, THE CHILD SHOULD BE ADMITTED FOR OBSERVATION AND ADDITIONAL PARENTERAL ANTIBIOTIC THERAPY. **IF IN DOUBT**, ADMIT THE PATIENT TO THE HOSPITAL.

2. Significant pain.

3. Temperature greater than or equal to 103°F.

4. Recent doses of prophylactic penicillin missed.

5. Child under 12 months of age.

6. Infiltrate on chest X-ray, O2 stats < 94%, or any signs of respiratory distress.

7. WBC count > 30,000 per mm^3 <5,000 or shifted to the left and/or other hematologic parameters greatly altered from baseline values (e.g., hemoglobin < 6 gm/dl, platelets < 150,000 per mm^3).

8. Admit if follow-up (telephone contact, return visit, etc.) is uncertain or unlikely because of distance, inconvenience, or poor compliance.

D. INPATIENT MANAGEMENT

1. Administer intravenous Ceftriaxone (preferably) 100 mg/kg/day in 2 divided doses x 48 hr until cultures are sterile and clinical status improves.

2. Observe closely for deterioration in clinical status that may indicate septicemia or development of acute chest syndrome.

3. Mycoplasma coverage.

E. OUTPATIENT MANAGEMENT

1. If the evaluation suggests that outpatient management is possible, a period of observation 4-6 hours, is advised with multiple reevaluations prior to releasing the patient. Reevaluation should include assessment of vital signs, O2 sats, level of consciousness, and ability to take oral fluids and medications.

2. Normal CBC & retic, (for the child), blood cx, CXR if indicated, Rocephin 100 mg/kg X1 dose.

3. **Follow-up by a repeat outpatient visit within 24 hours is necessary in all cases.**

4. **Blood culture & CBC with retic must be checked daily x 2 days at least. The blood cultures must be followed and patient recalled at once if positive.**

IV. VASO-OCCLUSIVE EPISODE/PAIN CRISIS (see drug doses below)

A. DEFINITION/ ETIOLOGY

1. Vaso-occlusive crisis is the most common complication of sickle cell disease. It is characterized by episodic attacks of ischemic pain and infarcts of various organs.

2. Precipitating factors include infection, fatigue, fever, dehydration, or exposure to cold.

B. MILD PAIN

1. The Child with MILD pain may not appear to be uncomfortable but complains of pain.

2. Treatment:

a. Ibuprofen every 4 hours.

b. Hydration with maintenance fluids.

c. Send home with prescription for at least 20 doses of acetaminophen with codeine (1 mg/kg/codeine/dose) for more severe pain. Ibuprofen may be alternated with the acetaminophen with codeine; so that some medication is given every two hours.

C. MODERATE PAIN

1. The child with a MODERATE episode evidences discomfort by facial grimacing, unhappiness, irritability, a poor appetite, and has not responded to home treatment.

2. If the child has not received codeine, give an appropriate dose of acetaminophen with codeine (1 mg/kg/codeine/dose).

3. If pain does not improve, give IV fluids at maintenance and a bolus injection of morphine (0.1 - 0.15 mg/kg to a maximum of 8 mg). Fluid bolus as appropriate if evidence of dehydration.

4. If the child has received codeine in an appropriate dose at home, treat as severe crisis (see below).

D. SEVERE PAIN

1. The child with severe pain is extremely uncomfortable, may be agitated, crying, screaming and cannot be consoled.

2. If the patient has been taking codeine at home in appropriate doses then immediately start IV fluids at maintenance, give an IV bolus injection of morphine (0.15 mg/kg/dose to a maximum of 8 mg per dose) and observe for pain relief.

3. If the patient is comfortable for more than two hours after an IV morphine bolus, then give a dose of oral medication such as acetaminophen with codeine and observe the child for at least one more hour. Send home with a prescription for 20 doses of acetaminophen with codeine. The patient should continue Ibuprofen. Have parent call the hematology/oncology clinic the next day. Reassure family that pain is not dangerous and will resolve in a few days.

4. If pain returns 1 or 2 hours after an IV morphine bolus, repeat the dose (0.15 mg/kg/dose to a maximum of 8 mg per dose) and observe for another hour. If a child receives 2 IV boluses with continued discomfort, then admit to hospital. Decrease IV fluids to maintenance rate if admitted to hospital.

5. In a child with poor venous access consider SQ or IM injection of pain medication.

E. INPATIENT MANAGEMENT OF ACUTE PAIN EPISODE

1. Exclude a precipitating complication or other cause of pain.

2. Bed rest and oral or intravenous hydration at maintinance.

3. Tailor the analgesic used, dosage, route and frequency of administration to the severity of pain and the patient's reported response. Use of a pain scale may be beneficial.

4. Always provide the pain medication on a fixed schedule of administration, **NOT PRN**, based on the duration of drug action. Periodic adjustments should be based on pain control and level of sedation. Intermittent administration is not recommended because of high acute blood levels, excessive euphoria, respiratory depression, and short duration of action. As pain improves, reduce the amount of medication per dose, not the frequency of administration. A **PCA** pump should be considered.

5. If treatment is required for more than 5 days, physical withdrawal may occur so the medication should be tapered over several days.

F. DRUG DOSES

1. Severe Pain:

a. Morphine: 0.1 to 0.15 mg/kg/dose; IV (preferred; repeat q 1-3 hours. Maximum 8 mg per dose. If using PCA: basal rate of 0.03 mg/kg/hour with PCA doses of 0.015 mg/kg Q 10 min with 4 hour lockout 0.3mg/kg is a reasonable regimen to start with.

b. Hydromorphone (Dilaudid): 0.02 mg/kg/dose (IM, IV) q 3-4 hr. or 0.04 mg/kg/dose po q 4 hr.

c. Oxycodone: 5-10 mg/dose po q 4 hr.

d. Toradol is a NSAID that can be given IV and may be beneficial in mild-moderate pain as well as an adjuct to narcotics in severve pain (it may decrease the dose of narcotics needed to control pain).

2. Moderate Pain:

a. Codeine: 1 mg/kg po q 4 hr with Ibuprofen: 10 mg/kg po q 4 to 6 hr.

3. Mild Pain:

a. Acetaminophen: 8 mg/kg/dose po q 4 hr.

b. Ibuprofen: 10 mg/kg po q 4 to 6 hr.

V. ACUTE CHEST SYNDROME

A. DEFINITION/ETIOLOGY.

1. An acute respiratory illness characterized by cough, fever, pleuritic chest pain, respiratory distress, leukocytosis and pulmonary infiltrate on chest x-ray.

2. Etiology is uncertain, but in most cases it probably represents a combination of infection and intrapulmonary sickling (infarction).

3. Less common etiologies of chest pain include myocardial ischemia, chest wall pain from bone infarction, part of the diffuse pain of a pain crisis, esophageal disease, peptic ulcer disease, and gallbladder disease.

B. CRITERIA FOR HOSPITAL ADMISSION:

1. Moderate or severe chest pain.

2. Fever greater than 39°C or 102°F.

3. Oxygen saturation more than 3% below baseline or <92% in room air.

4. Respiratory distress (tachypnea, dyspnea, retractions, flaring, prominent cough, etc.)

C. INPATIENT MANAGEMENT

1. Blood culture initially: repeat after q 24 hours for persistent temperature over 38.5°C.

2. Intravenous fluids at maintenance rate; watch for volume overload.

3. Daily weight, strict I & 0s, frequent vital signs.

4. Supplemental oxygen by mask should may be given; the level of oxygenation should be continuously monitored by pulse oximetry, and maintained at or above baseline value (see data base) or if no baseline available > 92%.

5. Chest X-ray initially and then every day, or as clinically indicated.

6. CBC with differential and reticulocyte count initially, then daily Hgb/HCT/Retic. The hemoglobin often falls by 2-3 gm/dl during severe acute chest syndrome.

7. Antibiotic coverage for *S. Pneumoniae*, *H. influenzae* type b and concomitant mycoplasma infection. Current recommendations: Ceftriaxone, 100 mg/kg/day IV plus Erythromycin 40 mg/kg/day po divided TID.

8. Cautious use of narcotics for chest wall pain due to the risk of hypoventilation, however pain may lead to splinting and hypoventilation as well. Toradol may be a good option for control of mild-moderated pain.

9. Chest physiotherepy to involved area of lung when consolidation, atelectasis,or abundant secretions are present.

10. Bronchodilators by inhalation.

11. Steroids may be of use as well.

D. MANAGEMENT OF SPECIFIC COMPLICATIONS

1. Monitor arterial blood gases for increasing respiratory distress and falling O_2 saturation. Cyanosis may not be obvious in such patients, and if pO_2 is less than 60 mm Hg, generalized sickling may occur.

2. Give packed red blood cell transfusion of 7-10 ml/kg each for declining hemoglobin and worsening clinical condition (to increase oxygen carrying capacity). Post transfusion hemoglobin should not exceed 11 gm/dl. Do not routinely transfuse stable patients as there is no evidence that correction of the anemia hastens recovery. Adjust IV rate during transfusion to avoid volume overload.

3. Transfer to ICU for a 1 to 2 blood volume exchange transfusion (see below) using whole blood (to remove sickled cells} in patients with a pO_2 less than 60 mm Hg despite maximal oxygen therapy and/or clinical deterioration. If the patient is over 20 to 25 kg consider use of automated pheresis with packed red blood cells (see below).

4. Intubation and mechanical ventilation as indicated for hypoxemic respiratory failure or respiratory failure due to fatigue.

VI. APLASTIC CRISIS

A. DEFINITION AND PATHOPHYSIOLOGY

1. A rapid decline in hemoglobin concentration resulting from transient cessation of erythropoiesis.

2. Etiology: direct cytotoxic effect of a virus (commonly parvovirus B19 on erythroid precursors) on the bone marrow. Erythroid precursors disappear from the bone marrow for about 10 days following parvovirus infection, resulting in a reticulocyte count usually less than 0.1% and a reduction in hemoglobin values, often by 3-5 gm/dl.

3. Patients with aplastic crisis do not usually exhibit the other manifestations of parvovirus B19 infection (such as the "slapped cheeks rash of erythema infectiosum or arthralgia/arthritis).

4. Approximately one week following the onset of erythroid aplasia, patients develop an antibody response (initially IgM and then IgG), which results in viral neutralization, resumption of marrow erythroid activity, and a rapid rise in the reticulocyte count and hemoglobin that is often heralded by a large number of of nucleated red blood cells on the peripheral blood smear.

B. CLINICAL MANIFESTATIONS/ LABORATORY FEATURES:

1. Occurs between 2 and 15 years of age.

2. Patients usually present with fever, malaise, lethargy, and possibly syncope.

3. Physical examination shows pallor and tachycardia. Patients with severe anemia may exhibit congestive heart failure. The spleen is <u>not</u> larger than usual.

4. Laboratory abnormalities include severe anemia (hemoglobin usually 2 to 6 gm/dl) and reticulocyte count < 1.5 % (usually < 0.1 % unless the patient is already in the recovery phase). The WBC count is usually normal or slightly elevated. Platelet count is generally normal.

C. MANAGEMENT AND OUTCOME

1. Type and crossmatch for a total of 15-20 ml/kg of packed RBCs. For very young patients ask the blood bank to divide a unit of blood into aliquots.

2. Transfuse patient with 5-7 ml/kg of packed RBCs over 3 to 4 hours. After assuring that the patient is stable (i.e., not in heart failure), repeat the transfusion until a total of 15-20 ml/kg is administered. Patients with profound anemia who are in heart failure may require an exchange transfusion (see below). Do not over transfuse (Hb~11).

3. Patients with parvovirus should be placed in <u>contact isolation</u> since parvovirus Bl9 is highly contagious. They should have no contact with

pregnant care-givers or ward personnel. Patients must wear a mask when out of their rooms.

4. Serum parvovirus antibody and antigen studies are usually not required.

5. Many patients with acute parvovirus infection have high fever and require blood cultures and intravenous antibiotics. Fever during an aplastic crisis is usually due to parvovirus B19 infection but bacteremia and the risk of sepsis cannot be initially excluded.

6. Following transfusion the patient may be promptly discharged from the hospital. Hemodynamically stable patients with less severe anemia (i.e., over 4.0 gm/dl) may be managed in the outpatient setting.

7. Hemoglobin levels should be followed every 2-3 days in the outpatient unit until reticulocytosis resumes and hemoglobin increases. When seen in clinic, patients should wear a mask to avoid the spread of the virus.

8. Siblings with sickle cell anemia (or other patients with sickle cell anemia with whom the patient has come in dose contact) should have a hemoglobin, hematocrit, and reticulocyte count immediately and again 10-14 days later to be sure that they, too, are not infected.

9. Recurrent aplastic events are rare since life-long humoral immunity against parvovirus B19 follows an aplastic crisis.

VII. ACUTE SPLENIC SEQUESTRATION CRISIS (ASSC)

A. DEFINITION AND PATHOPHYSIOLOGY:

1. Characterized by sudden enlargement of the spleen and decline in the hemoglobin concentration. Large quantities of sickled erythrocytes are pooled (sequestered) in the splenic red pulp.

2. A large percentage of the patient's blood volume accumulates in the spleen.

3. At one time, ASSC was one of the most common causes of death in infants with sickle cell anemia.

B. CLINICAL FEATURES:

1. Most common in infants and young children with sickle cell anemia between 6 months and 5 years of age.

2. Also seen in patients with preexisting chronic splenomegaly.

3. May affect teenagers and young adults with sickle C disease.

4. Usually no obvious triggering event is known.

5. Signs and symptoms are nonspecific, including lethargy or irritability, pallor, tachycardia, and sometimes pain in the left upper quadrant (especially in older patients). Occasionally, only an increase in spleen size is appreciated.

6. Patients with severe ASSC may present in frank cardiovascular collapse.

7. Physical examination:

a. Signs of anemia and/or hypovolemia.

b. The spleen is larger than the baseline, sometimes massively so.

C. LABORATORY FEATURES:

1. The hemoglobin is at least 2 gm/dl below the baseline steady state value. In some severe cases, the hemoglobin declines to life threatening levels.

2. Reticulocyte counts are elevated (usually 10 to 30%), and nucleated RBCs are almost always present on the blood smear.

3. The WBC count usually remains normal or slightly elevated.

4. The platelet count often declines to 50,000 to 150,000/mm3.

D. MANAGEMENT AND OUTCOME:

1. Identify that ASSC is occurring. Parents of most patients with sickle cell anemia have been taught to palpate the spleen & may present with the chief complaint of the spleen being larger than usual. Consulting the pt's database or hospital chart will confirm the patient's usual hemoglobin value & spleen size.

2. In mild cases of ASSC (i.e., spleen only slightly larger than usual, hemoglobin 2-3 gm/dl below baseline, patient hemodynamically stable), the child may be followed as an outpatient with daily physical examinations and blood counts. Consult peds heme-onc.

3. Patients with moderate or severe ASSC should be hospitalized and require the following:

a. Careful and repeated physical assessments for spleen size and vital signs.

b. Type and crossmatch for PRBCs.

c. Serial hemoglobin determinations.

d. If hemoglobin decline is substantial (i.e. to below 4.5-5.5 gm/dl),transfuse with 10 ml/kg packed RBCs (repeated as necessary) to raise the hemoglobin and maintain cardiovascular stability.

4. ASSC usually resolves within 2-5 days. Often, especially following blood transfusion, hemoglobin values rise to above steady state levels since the blood that had been pooled in the spleen is redistributed in the circulation. When the hospitalized patient shows stable or rising hemoglobin values and smaller spleen size, he or she should be discharged, with close outpatient follow-up.

5. Following an episode of ASSC, some patients have persistent splenomegaly and hypersplenism, with lower than usual hemoglobin and platelet values lasting weeks or months. All children who experience an episode of ASSC are at risk of repeat events.

6. Recurrent episodes of ASSC that require transfusion should be treated with splenectomy. Many patients, however, will not require splenectomy but exhibit gradual diminution in spleen size, with eventual autoinfarction.

VIII. TRANSFUSION THERAPY

A. INDICATIONS FOR TRANSFUSION

1. Definite indications

a. Acute neurologic event, stroke or TIAs.

b. Splenic sequestration with substantial decline in hemoglobin (i.e. to below 4.5-5.5 gm/dl), or hemodynamic instability.

c. Pneumonia or pulmonary infarction with declining hemoglobin or worsening clinical condition. Exchange transfusion indicated if pO_2 less than 60 mm Hg despite maximal oxygen therapy.

e. Severe anemia with cardiac decompensation.

f. Aplastic crisis with severe anemia.

g. Acute arterial hypoxia ($S_aO_2 < 90\%$).

h. Hyperhemolytic crisis with enlarging liver/spleen.

i. Ophthalmological surgery.

2. Relative indications:

a. Symptomatic anemia.

b. Hepatic sequestration.

c. Leg ulcers refractory to conservative management.

d. Priapism, recurrent, or resistant to acute treatment.

e. Severe or prolonged pain episodes.

f. Frequent pain episodes.

g. Chronic respiratory insufficiency.

h. High dose intravascular contrast studies.

i. Surgery with general anesthesia.

j. Pregnancy.

B. SIMPLE TRANSFUSION

1. Indicated for severe anemia, aplastic crisis, hyperhemolytic crisis, & in chronic transfusion programs. Also used in patients with a relative indication & a HCT < 20%.

2. **ALWAYS USE SICKLE-CELL (SICKLE DEX) NEGATIVE BLOOD.** All patients with a history of previous transfusions should be carefully screened for the presence of autoantibodies. Use washed or reconstituted frozen blood in patients with a history of allergic transfusion reactions.

3. Chronic transfusion:

a. Give PRBCs to raise the hematocrit to 30%.

b. Then transfuse q week until the % Hgb S is < 50%.

c. After the % Hgb S is < 50%, the hematocrit can be raised to 35%.

d. Transfuse every 3 to 4 weeks to maintain hematocrit > 30%, % Hgb S < 30% and the reticulocyte count < 4%.

4. Acute transfusion:

a. Give PRBCs to raise the hematocrit to 28 - 33%.

b. Further transfusions are administered based on symptoms.

5. Useful approximations:

a. Total Blood Volume (TBV) = 70 cc X weight in kg. Total Blood Volume (in chronic anemia) = 75 cc X weight in kg.

b. Red Cell Volume of Patient = TBV X Hematocrit.

c. To raise Hgb by 1 gm/dl: give 3 cc/kg of PRBCs.
To raise Hematocrit by 10%: give 10 cc/kg of PRBCs.

d. **Transfusion volume =** TBV X (HCT desired - HCT current)/HCT of donor unit

e. Average values in transfused units
i. Whole Blood: Hematocrit = 35%.
ii. PRBCs: Hematocrit = 65%.

C. EXCHANGE TRANSFUSION: (THIS DESCRIPTION ONLY APPLIES TO PATIENTS WITH SICKLE CELL ANEMIA)

1. Indicated in patients with acute neurologic events, severe pneumonia or pulmonary infarction, acute arterial hypoxia, ophthalmological surgery, high dose intravascular contrast studies, surgery with general anesthesia, and pregnancy.

2. Preparation

a. Insert venous and arterial catheter OR two large-bore venous catheters OR a double-lumen hemodialysis catheter.

b. Send blood to laboratory for:
i. Complete blood count.
ii. Quantitative sickle cell preparation (correlates well with the quantity of Hb SS noted at electrophoresis).
iii. Electrolytes and calcium determination.
iv. Cross-match with PRBC (**sickle negative**).

c. Calculate and prepare volume to be transfused (see below).
i. PRBCs are assumed to have a hematocrit of 65%.
ii. The whole blood equivalent is whole blood with a hematocrit of 40% or PRBCs reconstituted to a hematocrit of 40% with saline or FFP.

3. Procedure

a. If the patient's hematocrit is $\leq$ 19% (Hgb < 6.5 g/dL). Give PRBCs equal to 30 cc/kg of body weight while removing an equal volume of the patient's blood. Then give donor whole blood equivalents cc for cc while removing an additional 40 cc/kg of patient blood.

b. If the patient's hematocrit is between 20 and 30% (Hgb 6.6 to 10 g/dL). Give PRBCs equal to 10 cc/kg of body weight while removing an equal volume of patient blood. Then give donor whole blood equivalents cc for cc while removing an additional 70 cc/kg of patient blood.

c. If the patient's hematocrit is > 30% (Hgb > 10 g/dL). Remove 10 cc/kg of patient blood and exchange with 10 cc/kg of normal saline. Then give donor whole blood equivalents cc for cc while removing an additional 80 cc/kg of patient blood.

d. Rate of exchange transfusion and aliquots:

i. Adjust the intravenous rate so the exchange transfusion occurs over 4 to 6 hours (increase the exchange transfusion time to 8 - 10 hours if over 1000 ml are to be exchanged).

iii. Withdraw blood at 10 to 15 minute intervals from the arterial line or a large-bore venous catheter. The aliquot for each draw will be determined by dividing the exchange transfusion volume by the total exchange transfusion time.

iii. If only a single catheter is available, exchange 2.5 cc/kg every 10 minutes. Attempts to establish a second line should continue after the exchange transfusion begins.

4. Monitoring

a. Heart rate and blood pressure (continuously).

b. Hematocrit and/or hemoglobin every 2 hours and at the last hour. Hemoglobin levels of greater than 12 g/dL (hematocrit > 36%) during the exchange may be associated with increased blood viscosity and complications.

c. Electrolytes, calcium every 2 hours.

5. Endpoint. This protocol should give a Hgb S level of about 30% and a final hemoglobin level between 10 and 12 g/dL.

STATUS ASTHMATICUS

I. Definition: Status asthmaticus (SA) is a life threatening form of asthma that is defined as a condition in which a progressively worsening attack is unresponsive to the usual appropriate therapy that leads to pulmonary insufficiency. The primary mechanical event in status asthmaticus is a progressive increase in airflow resistance. Mucous plugging, mucosal edema and inflammation are the major causes for the delayed recovery in status asthmaticus. The combination of hypoxia, hypercapnia, and acidosis may result in cardiovascular depression and cardiopulmonary arrest.

II. History:

A. Known asthmatic?

B. Asthma meds? Compliance? Time of last dose/nebulizer Tx?

C. Previous clinic/ED visits?

D. Previous hospitalizations, intubations, steroid courses?

E. When did current wheezing/resp distress begin?

F. Precipitating factors.

III. Physical Exam:

A. Vital Signs:

1. T: Fever may indicate URI, atelectasis or pneumonia

2. P: Usually elevated, especially if treated w/epi

3. R: Often tachypneic {see tables below for normal respiratory rates (RR)}

Respiratory Rates (breaths/min) of Normal Children Age 6 mos. to 8 years

	SLEEPING		AWAKE	
Age	**Mean**	**Range**	**Mean**	**Range**
6 - 12 mos.	27	22 – 31	64	58 - 75
1 - 2 yrs.	19	17 – 23	35	30 - 40
2 - 4 yrs.	19	16 – 25	31	23 - 42
4 - 6 yrs	18	14 – 23	26	19 - 36
6 - 8 yrs	17	13 – 23	23	15 - 30

Respiratory Rates (breaths/min) of Normal Children Age 8 - 18 years

	Mean	Range
8 - 10 yrs.	19.5	17 - 22
10 - 12 yrs.	19.5	17 - 22
12 - 14 yrs.	19	16 - 22
14 - 16 yrs.	18	15 - 21
16 - 18 yrs.	17	14 - 20

4. BP: Pulsus paradoxus (a decrease in systolic BP during inspiration of > 10 mmHg in children or > 15mmHg in adolescents) correlates well with moderate to severe disease. It can be measured with sphygnomanometer and a stethoscope: Inflate the cuff, deflate it slowly. At a certain pressure, you will hear pulse sounds during expiration, but not inspiration. As the cuff is deflated further, you will be able to hear sounds during inspiration and expiration. The difference in systolic BP between these two phenomina is the pulsus paradoxus. Pulsus paradoxus is

readily apparent in patients with arterial lines where it is observed as a dampening of the arterial wave form during inspiration.

5. The use of accessory respiratory muscles correlates with the severity of airway obstruction (abdominal paradoxic breathing, sternocleidomastoid use, nasal flaring, intercostal retractions). Wheezing is the least sensitive indicator of obstruction. Crepitus indicates air leak in subcutaneous tissues.

B. **Asthma score:**

	0	1	2
1. PaO2	70-100 in air	$\leq$ 70 in air	$\leq$ 70 in 40%
2. Cyanosis	none	in air	in 40%
3. Inspir. BS	none	unequal	Dec. to absent
4. Access. mus. use	none	moderate	maximal
5. Exp. wheeze	none	moderate	marked
6. Cerebral function	normal	depressed or agitated	Coma

1. Clinical asthma score > 5 signifies impending respiratory failure, > 7 plus PCO2 > 65 signifies existing respiratory failure. **May substitute saturations for PaO2: > 95, 90-95, < 90.**

2. Be aware of the possibility of sudden deterioration in patients condition (mucous plugging, pneumothorax, worsening bronchoconstriction).

C. Must have air movement in order to wheeze, so lack of wheezing does **NOT** necessarily mean everything is fine!!

D. I:E ratio normally 5:2; may be 1:2 with severe attack

E. Symmetry of breath sounds:

1. Some asymmetry may be heard with asthma alone

2. Increased wheezing unilaterally may indicate foreign body

3. Decreased breath sounds unilaterally may indicate pneumonia or pneumothorax.

F. Mental Status: severe attack causes hypoxia and hypercarbia, causing confusion and decreased consciousness.

IV. Lab/X-ray

A. Pulmonary function tests: Obtain peak flow with Wright's Peak flow Meter on children old and well enough to cooperate.

B. CXR:

1. A CXR should be obtained on every child admitted to the hospital with SA to define the extent of the associated parenchymal disease; any complications, and to differentiate other disease entities.

a. The EKG may show acute RAD “p” pulmonale and a right ventricular strain pattern. During a severe attack hypoxemia and hyperinflation may lead to increased pulmonary vascular

resistance. Also, negative pleural pressures become even more negative which, with lung hyperinflation, may lead to increased LV afterload.

2. Usually shows hyperinflation (diaphragm flat or everted)

3. May see pneumomediastinum, pneumothoraces, pneumoperitoneum, and/or subcutaneous emphysema

4. R/O pneumonia

5. Consider bilateral decub. films or insp./exp. films to R/O foreign body (unilateral hyperinflation, tracheal shift, radio-opaque foreign body).

C. ABG:

1. Usually not necessary in children who have responded partially to initial treatment and continue to improve.

2. An ABG should be obtained on patients:

a. With moderate - severe respiratory distress

b. Not responding to therapy

c. Serial ABG's may be necessary to evaluate progress/ deterioration

3. Because of air trapping, oxygenation is impaired and PaO2 decreases. Initially, hyperventilation leads to a decreased PaCO2. However, with further air trapping, work of breathing increases and lung compliance decreases leading to hypoventilation and increased PaCO2. Thus, a "normal" PaCO2 of 40 is abnormally high in the face of the increased respiratory rate and indicates a moderately severe attack. Similarly, the initial hyperventilation causes a respiratory alkalosis and increased pH. However, as hypoventilation ensues, a respiratory acidosis occurs as well as a metabolic acidosis from work of breathing and poor tissue oxygenation.

4. Blood Gases: Acidemia in excess of that predicted from measured PaCO2, accompanied by an abnormally large serum anion gap and high plasma lactate level, has been shown to occur in those severe asthmatic patients who require intubation. PaO2's less than 60 mmHg are an additional danger signal. Hypoxemia during severe asthma exacerbations occurs because of mismatching of ventilation and perfusion and can persist for days. If PEFR < 25%, you may see alveolar hypoventilation and a rise in PCO2.

5. Blood Gases:

		pO2	pCO2	pH	Severity
Example on RA pH/pCO2/pO2					
7.4/39/89	Stage I	↓	normal	normal	mild
7.45/35/78	Stage II	↓	↓	alkalotic	mild but worsening
7.4/38/68	Stage III	↓↓	normal	normal	moderate
7.3/48/55	Stage IV	↓↓	↑	acidotic	severe

V. Differential Diagnosis of Wheezing:

A. Wheezing in a known asthmatic is almost always an asthma attack.

B. First time wheezing in an infant may be bronchiolitis, or pneumonia (the last two may also occur in asthmatics).

C. Congenital Malformations

D. Laryngotracheomalacia, vocal cord paralysis, tracheal or bronchial stenosis, GER, vascular ring

E. Enlarged lymph nodes from infection or tumor.

F. Foreign bodies in trachea, bronchus, or esophagus.

G. Infections

H. Acute bronchiolitis

I. Bronchitis and asthmatic bronchitis

J. Vocal cord paralysis

K. Cystic Fibrosis

L. Aspergillus

M. Anaphylaxis (hx. of insect sting or drug?)

N. Toxic fume induced bronchospasm

VI. Treatments in Clinic or Emergency Department:

A. Acute:

1. Beta-agonist nebulizer treatment, may give 5-10 mg nebs back-to-back if minimal initial response.

a. Albuterol 0.15 mg/kg (max 10 mg/dose)

2. Atropine 250mcg (<2 y.o.), 500 mcg (>2 y.o.), add to 2nd or 3rd beta-agonist neb

3. Subcutaneous injection - subcutaneous epi. rarely done today as nebulizers are so commonplace. Terbutaline also may be used.

a. Epinephrine: 1:1000 0.01 cc/kg/dose (0.3 cc max)

b. Terbutaline 0.05% solution, 0.01 mg/kg/dose with a max. of 0.25 mg q 20 - 30 minutes.

4. Steroids: Solumedrol 2 mg/kg IV, then 1-2 mg/kg IV Q 6 hours. If mild exacerbation or quick response to above, may consider oral prednisone 2 mg/kg.

5. Oxygen

a. In younger patients, the distress caused by fighting the mask may only make the wheezing worse.

b. Humidified 02 should be placed on all patients who show evidence of hypoxia (O2 sat <90% on sat monitor/pulse oximeter) or respiratory distress. Remember the sat monitor gives no information regarding ventilation and pCO2.

6. A child who goes home after a clinic/ED visit needs additional therapy usually. If not on meds, begin albuterol orally or via inhaler. If on theo and subtherapeutic but yet claim good compliance, increase theo dose

and add Albuterol. If therapeutic on theo, add another med (Albuterol - orally, or inhaler, or steroids). Arrange f/u to assess interventions.

VII. Treatments in the PICU

A child with a low paO2, high paCO2, decreased breath sounds, severe wheezing, retractions or altered mental status is in danger of respiratory failure and should be considered for admission to the PICU. A-line monitoring should be considered and is indicated in most intubated patients. Patients requiring neb more frequently than Q1 hour for a prolonged period should probably be admitted to the PICU. Once in the PICU, patients must continue to be followed closely - (VS, mental status). Use continuous cardio-respiratory monitors. Beware of sudden deteriorations in the patient's condition.

A. Beta-agonists

1. Epinephrine - Has both B1 and B2 adrenergic agonist effects. Dose 1:1000, 0.01 ml/kg/dose SC, max 0.5 ml every 15-20 min. Generally not used over the selective B2 agonists.

2. Selective B2 agents

a. Albuterol

(1). If a patient is not optimally responding to standard doses of albuterol (0.15 mg/kg), one can increase the hourly dose and/or increase the frequency. Intermittent doses of 0.3 mg/kg (to max of 10 mg) every 20 min for 1-2 hours is acceptable. Tachycardia is generally mild with its greatest degree occurring during the first 60-80 minutes. Gradual improvement in the tachycardia despite continuation of therapy usually occurs.

(2). Continuous nebulized dose is 0.6 mg/kg/hour to a maximum of 20 mg/hr. **Administer the neb as close to the patient as possible if administering into the ventilator circuit.** Doses higher than 20 mg/hr may be needed if the drug is adhering into the ventilator tubing. Make sure that at least 6 liters of gas flow administer the nebulized dose.

(3). One will want to use a nebulizer with at least 8 liter/min of O2 flow if patient is not intubated. A Maxiheart nebulizer delivers 20 ml/hour of mist at 8 liters of flow. It delivers 30 and 50 ml/hour of mist at 10 and 15 liters of flow.The miniheart nebulizer is only used on the ventilator circuit. It uses 2 liters of flow to deliver 8 ml/hour of mist.

(4). Side effects - tremor, hypokalemia, headache, arrhythmias, anaerobic metabolism leading to met. acidosis with overdoses, chest pain.

b. Terbutaline

(1). Nebulized terbutaline has safely been administered to children with severe asthma (up to 0.4 mg/kg/dose) as well as by continuous nebulization (0.4 mg/kg/hr) with good results. Usual nebulizer dose: 0.03 mg/kg (up to 1 mg) in 1 cc NS.

(2). Terbutaline SC dose - 0.05% solution 0.01 mg/kg/dose (max 0.25 mg) every 20-30 min.

(3). May consider using continuous IV infusion if patient does not improve with inhaled beta-agonists. The recommended dose: 10 **mcg**/kg bolus over 10 minutes *immediately* followed by 0.4 **mcg**/kg/min infusion. This can be increased by 0.2 **mcg**/kg/min at a time to a maximum of 6 **mcg**/kg/min. Limit dose for extreme tachycardia (180 in and infant or child; 160 in an adolescent or adult) Monitor EKG q8 – q12 while on an infusion. Watch for evidence of strain / infarct.

(4). There is a recommendation of reducing the maintenance dose of terbutaline by 50% in patients who are already receiving theophylline.

(5). Side effects: tremor, nervousness, headache, nausea.

B. Aminophylline

1. Studies of the emergency department management of asthma indicate that methylxanthines do not significantly enhance the bronchodilator response to B2 agonists when the latter are repetitively given at short intervals. However, when the dose and frequency of inhaled B2 agonists are reduced, methylxanthines and B2 agonists may maintain bronchodilation better than B2 agonists alone. **Metabolism varies - if you think you are subtherapeutic or toxic, check a level!**

Suggested mixing of IV Aminophylline: mix 1000 mg in 100 cc of **total** volume (10 mg/cc) or 500 mg in 500 cc of **total** volume (1 mg/cc) depending on the patients size and fluid requirements.

Suggested dosing of IV Aminophylline for continuous infusion:

0-1 month	0.15 mg/kg/hr
1-6 month	0.5 mg/kg/hr
6 month-1 year	1.0 mg/kg/hr
1-9 years	1.0-1.5 mg/kg/hr
10-16 years	0.8-1.2 mg/kg/hr
> 16 years	0.5-0.7 mg/kg/hr

2. The therapeutic level is 10-20 mg/liter and the desired level is 8-12 mg/liter. It is **not** necessary to keep levels as close as possible to the upper limit (20 mg/liter). Levels > 20 mg/liter are toxic. If the patient is not on theophylline one may begin the infusion by loading with 6 - 7 mg/kg over 20 minutes and then starting the appropriate infusion rate (see the above table). One then checks a post-loading dose at one hour after the bolus, and at 4 hours after the bolus. If the post bolus level is low one may reload with the appropriate amount **(1 mg/kg increases the level by 2 mg/liter)**. If the 4 hour level is lower then the post-bolus level, that suggests the infusion rate is too low and the patient should get rebolused, have the infusion increased by 10%, and have another 1 hour post-bolus level and 4 hour post-bolus level checked. If the 4 hour level is higher then the post-bolus level, that suggests the infusion rate is too high and the patient should have the infusion decreased by 10%, and another level should be checked in a few hours. A 12 - 16 hour level indicates steady state. If the patient is on theo. already, check a level and give an appropriate amount to reach a level of 12-14. So: the 1 hour post-bolus level indicates how the bolus did, the 4 hour post-bolus level indicates how well the drip is maintaining the bolus, and the 12-16 hour level indicates steady state.

3. Meds that alter theo clearance:

1. Increased theo metabolism:

   a. Barbiturates

   b. Phenytoin

   c. Isoproterenol

2. Decreased theo metabolism:

   a. Allopurinol

   b. Cimetidine

   c. Erythromycin

   d. Propranolol

   e. Oral Contraceptives

C. Isoproterenol

1. Nonselective B-adrenergic agonist once used for asthma unresponsive to Aminophylline is **NO LONGER INDICATED** in asthma as it causes a increased myocardial oxygen consumption and may put patients as risk for myocardial ischemia. There are more selective beta-2 agonists that provide all of the advantages of Isoproteranol with less risk.

D. Anticholinergic Agents - The anticholinergic agents are believed to act by blocking the irritant receptors and inhibiting cGMP metabolism which results in bronchodilation. The higher the parasympathetic tone in the patient, the more responsive to anticholinergics they will be.

1. Ipratropium Bromide (Atrovent)

   a. Synthetic quaternary ammonium derivative of atropine.

   b. When given by inhalation, its' peak effect appears in 30 minutes, and lasts 4-6 hours.

   c. Dose - 250 **mcg** for children less than 2 years of age, and 500 **mcg** for older children. The side effects seem fewer than atropine; there is no CNS effect. There is no significant effect on the tracheal mucous transport rate.

   d. An Ipratropium Bromide dose of 250 mcg via neb. given along with repeat doses of nebulized Albuterol at 0.15 mg/kg q 20 minutes may reduce hospitalizations from the ER.

E. Corticosteroids (Solumedrol, methylprednisolone)

1. Anti-inflamatory

2. Initial improvement occurs within 6 hours, but a longer time is needed for full affect.

3. Helps speed the resolution of severe asthma refractory to bronchodilator therapy.

4. Optimal dose is not known - 2 mg/kg IV for the initial dose than 1 mg/kg IV every 6 hours thereafter is one recommendation, 2 mg/kg IV every 6 hours x 4 then 1 mg/kg IV every 6 hours thereafter is another. Observe for hyperglycemia and hypertension.

F. Magnesium

1. Theoretical reasons explaining $MgSO_4$'s bronchodilatory effect include its' calcium channel blocker capabilities, sedative action, and its' effect in decreasing acetylcholine release from nerve terminals. $MgSO_4$ levels greater than 10 have been associated with cardiac arrest and respiratory insufficiency. Levels must be followed.

2. Suggested dose 25 mg/kg of $MgSO_4$ to a maximum of 2 grams delivered over 20 minutes in children to obtain levels of 4-7 mg/dl. Consider using in patients who are in moderate to severe distress despite usual therapy.

G. Ketamine

1. A dissociative anesthetic which causes amnesia with potent bronchodilator properties.

2. May be administered as a bolus dose of 0.5-1.0 mg/kg followed by a continuous infusion of 0.25 - 1.0 mg/kg/hr. Excersise extreme caution in non-intubated patients due to risk of respiratory depression.

3. Caution is recommended when using ketamine in patients suspected of having increased PVR, especially during spontaneous ventilation without a protected airway. Ketamine increases ICP and should be avoided after head trauma and in other patients at risk for elevated ICP. Also increases secretions.

4. The emergence phenomenon in older patients can be decreased with the concurrent administration of benzodiazepines.

H. Heli-ox

1. Helium is an inert gas with lower density than ambient air. The addition of helium to inhaled gases enhances the diffusibility of the gases by decreasing resistance in areas of turbulent flow.

2. 60-80% helium, 40-20% O_2 (Heliox) has been reported to decrease airway pressures and CO_2 retention in intubated patients. A trial of Helium-oxygen mixtures should be considered for patients in moderate to severe distress or those mechanically ventilated asthmatics with a respiratory acidosis who fail conventional therapy and who may tolerate 20-40% FiO_2.

I. Antibiotic Therapy

1. Respiratory infections are usually caused by viruses so antibiotics have no role in treatment.

2. Think about RSV and mycoplasma. Erythromycin increases theo levels (decreases clearance) - follow theo levels carefully.

J. Hydration and Correction of Acidosis

1. If dehydration is present, it should be corrected. High insensible losses occur due to decreased po intake and increased respiratory losses.

2. Overhydration must be prevented. Monitor for hyponatremia, SIADH and evidence of water intoxication. The more negative intrapleural pressure during severe asthma favors fluid accumulation in the interstitial space around the bronchiole.

3. Patients should be kept NPO to avoid aspiration / full stomach intubation.

4. IV fluids of 1 X maintenance are usually adequate. Tachycardia may occur from asthma drugs. UOP and cap. refill are better indicators of hydration status.

5. Monitor for hypkalemia secondary to beta agonists.

6. If you wish to correct a metabolic acidosis, Tham is the agent of choice, as it will not further compromise ventilation. (Administration of HCO3 will result in conversion to CO2 and may further compromise ventilation)

7. Respiratory Acidosis does not require correction unless very severe – pH < 7.1 or other complicating factors such as hypotension, cardiac depression, unresponsiveness to catecholamines or hyperkalemia.

K. Chest Physical Therapy

1. In selected patients who manifest severe mucous hypersecretion, postural drainage, chest vibration and percussion may be beneficial.

L. Oxygen

1. Administer humidified O2 to keep saturations at $\geq$ 90%.

2. Hypoxemia is associated with air hunger, anxiety, bronchoconstriction and increased bronchial reactivity.

M. Mechanical Ventilation

1. Due to high airways resistance, patients with severe asthma are difficult to manage on mechanical ventilation. Complications occur at nearly 3 times the usual rate. Endotracheal intubation may intensify the degree of bronchospasm.

2. Indications for mechanical ventilation

a. The presence of apnea or near apnea, diminished level of consciousness with inability to protect the airway and/or progressive exhaustion.

b. Hypercarbia--although initial hypercapnia in an acute asthmatic is worrisome, these patients should be evaluated individually and most will **not** require intubation. Elevated CO2 may respond to aggressive treatment. If the patient is oxygenating and his/her level of consciousness is reasonable, there is not a specific CO2 level that mandates intubation.

c. Clinical deterioration despite aggressive therapy as evidenced by paradoxical abdominal movement, cyanosis on 40% FiO2, paO2 < 60 on 6 liters O2, exhaustion, absence of breath sounds, increasing WOB.

3. Rapid sequence induction with Ketamine (bronchdilating properties) and neuromuscular blockade is recommended for intubation. Maintenance of sedation with Ketamine or benzodiazepines during mechanical ventilation

is usually adequate, though some patients will benefit from NMB. Continuous NMB in the face of steroids places the patient at risk for stroid myopathy, a state of prolonged muscular weakness that may result in the need for prolonged ventilator support and rehabilitation.

4. The approach to mechanical ventilation generally employs use of low rates to allow for long inspiratory and expiratory time with an I:E ration of 1:2-1:4 to allow pts time to exhale and prevent air trapping; tidal volumes of 8-10 cc/kg in an attempt to limit pead inspiratory pressures, and PEEPs of 2-4. Another strategy in the unparalyzed patient is pure pressure support ventilation. This allows the patient to actively exhale – something we cannot do with conventional ventilation. Permissive hypercapnea and hypoxia are used to limit barotrauma, volutrauma, and oxygen toxicity. A typical goal is to achieve a pH > 7.20, allowing elevated pCO2's and correcting acidosis with Tham. However, if the patient has a poorly functioning heart or suffered an anoxic cerebral injury, this strategy may be contraindicated.

N. Anesthetics - call Anesthesia. Most of of your anesthetics have moderate bronchodilator qualities.

1. Halothane

a. Concentrations of 0.5-2%.

b. The duration of treatment depends on the clinical response and PaCO2. Once PaCO2 is stabilized and clinical airway obstruction is diminished, as indicated by decreased PIP or decreased wheezing, halothane inhalation can be discontinued.

(1). Side effects

(a). Myocardial depression

(b). Arrhythmias

2. Isoflurane

a. Has fewer side effects than halothane.

b. Isoflurane causes systemic vasodilation secondary to arterial smooth muscle relaxation.

STATUS EPILEPTICUS

I. Initial Management: position on side, protect from injury, loosen clothing.

A. **Airway**

1. Jaw lift

2. Bite block or oral airway if able (no tongue blade or fingers in mouth)

3. Suction secretions or emesis

4. Roll on side.

B. **Breathing**

1. O2 by mask

2. Intubate if needed

a. Address seizures first - will be difficult to intubate and ventilate if patient is seizing (unless you paralyze them); AND respiratory status generally improves when seizures stop.

b. May need to intubate for respirator depression from medications.

c. all patients with generalized status will have some degree of respiratory and/or metabolic acidosis; this is not an absolute indication for intubation.

C. **Circulation** - start IV, monitor BP, O_2 SAT.

II. Medication protocol

A. General principles

1. Order of medications is designed to balance rapid efficacy and minimal respiratory depression:
Benzo→ phenytoin -> phenobarb

2. Use step-wise doses and allow time for medication to act between doses (3-5 minutes)

B. If hypoglycemic, D50 IV 0.5-1.0 gm/kg=1-2 cc/kg.

C. Lorazepam (Ativan)

1. 0.1 mg/kg IV, over 1-2 min, up to 2 mg
repeat after 5-10 min if seizures continue. May give IV liquid by rectal route.

2. Alternative: Diazepam (Valium) - 0.5 mg/kg IV

over 1-2 mins., q 10 - 30 minutes, up to 10 mg.
May give PR or via ETT.

3. Major problems:

a. Short half life – risks recurrence of seizures may need longer acting medications even if seizures have stopped.

b. Respiratory depression, esp. in combination with phenobarb (be prepared to intubate).

E. Fosphenytoin (Cerebryx)/Phenytoin (Dilantin)

1. Fosphenytoin ALWAYS preferable:

a. more rapid infusion (avg:13 vs 44 min)
b. less risk of hypotension (can still occur)
c. neutral pH—no skin sloughing/purple hand
d. can give IM if no IV available

2. Dose:

a. fosphenytoin: 20 PE/kg (max 1000 PE) IV, max rate 3 PE/kg/min (150 PE/min adult)
b. phenytoin: 20 mg/kg (max 1 g) IV max rate 1 mg/kg/min (50 mg/min adult)
b. adjust dose for renal failure or hypoalbuminemia.

3. C/V and BP monitor during infusion for hypotension and arrhythmia; hold infusion if they occur. May cause sedation or ataxia.

F. Phenobarbital

1. Dose: 20 mg/kg IV over 20 mins.
2. Can be given IM if no IV established
3. Requires several minutes to work
4. Major side effects are sedation and respiratory depression.
5. If PB not available, give add'l fosphenytoin 10 PE/kg.

G. If patient is on chronic phenobarb or phenytoin: use small boluses of same drug (5mg/kg) until levels are available.

H. Pyridoxine

1. Dose: 100 mg IV
2. should be given if standard anticonvulsants are ineffective in a child under 1 year with unexplained status.
3. May cause respiratory depression if given too rapidly.

I. If above measures are ineffective, proceed to pentobarbital coma or benzodiazepine drip.

a. call neurology, EEG,
b. admit to ICU
c. have dopamine and fluids ready, and intubate the patient (if not already done).

III. Quick assessment, pertinent history - ask yourself: Why is this patient seizing now? Trauma? Toxin? History of past seizure? Infection? Has the seizure pattern changed?

A. Seizure History

1. Description: precipitating event, onset: focal/generalized, duration, post-ictal state?

2. Fever? S/S illness?

3. Previous seizures? (degree, control, etc.)

4. Chronic seizure meds? (dose, compliance, prior levels)

5. Hx. trauma? (Accidental or non-accidental)

6. Toxin ingestion?

7. Chronic medical problems? Hx. of syncope?

8. Behavior changes?

9. Vomiting? / diarrhea? - Consider inborn error of metabolism in infants.

B. Physical Exam

1. Vital Signs

a. **Evidence of increased ICP / herniation** {increased BP, tachycardia (early), bradycardia (late, ominous sign), dilated pupils, papilledema}

b. Decreased BP from sepsis, toxins

4. Fever from meningitis

2. Mental Status / Level of Consciousness, Glasgow Coma Scale (see Neurologic Assessment chapter)

3. Respiratory Pattern

a. Assure good air exchange

b. Abnormal patterns with worsening level of consciousness

4. HEENT

a. Pupils (size, reactivity)

b. Fundi (papilledema, hemorrhage)

c. Signs of head trauma

d. meningismus

5. Neuro. Exam – asymmetry of tone or of spontaneous movement (Todd's paralysis or due to structural lesion/injury/infection), eye deviation (gaze preference or tonic deviation or nystagmus) all constitute focal signs = indication for imaging

IV. Diagnostic evaluation

A. Labs

1.STAT dextrostix – 1 drop of blood, quick result

2. STAT anticonvulsant levels (newer meds are send-out labs, results not available for days)

3. STAT lytes, BUN, creatinine, glucose, Ca++, Mg++, calculate anion gap (see Pediatric Resus. chapter)

4. CBC with diff (sepsis) and blood cultures as indicated.

5. Serum Tox screen ("coma/dangerous drug panel")

6. Other studies (if indicated):
   a. LFT's/ammonia (Reyes),
   b. Lactate/ inborn error w/u (esp. in infants)
   c. consider long QT syndrome especially if the a history of recurrent syncope, syncope with exercise, is an athlete or has a positive family history for sudden death, syncope, or cardiomyopathy.

B. Lumbar puncture (LP)

1. This is to evaluate for meningitis - antibiotics should **not** be held if you think the patient has a CNS infection!! You have about 4 hours to tap the patient after antibiotics before cultures would be affected, so consider early treatment.

2. Needed on some patients, but not emergently. R/O increased ICP with a head CT before LP!! **Focal exam findings or focal seizures are especially important indications of possible CNS mass lesions.**

3. An LP is needed for febrile patients with S/S infection, and for comatose patients **(after CT).** If septic or unstable, push antibiotics STAT, and LP later. Consider Acyclovir (10 mg/kg/dose) IV every eight hours if encephalitis is suspected,(send viral and herpes cultures on the CSF, and do nasopharyngeal, rectal, eye, and urine viral cultures)

4. Obtain CSF opening and closing pressures.

C. Neuroimaging

1. CT scan (noncontrast):

a. Indications

1. increased ICP, head trauma, or comatose.
2. first AFEBRILE seizure
3. suspicious circumstances
4. focal findings on exam, or focal seizure.

b. rapidly obtained; sensitive for acute blood

2. MRI scan: eventually required in most cases

D. EEG

1. Once stable or at Peds neurology discretion

2. Arrange immediately if seizures do not respond to standard anticonvulsants

3. Nonconvulsive status:

a. Subtle signs of ongoing seizures (nystagmus, focal clonic activity)

b. Decreased mental status after accounting for sedating meds and postictal state

1. Do not expect rapid recovery of alertness

2. reliable responsiveness (nonlocalizing movement) to stimulation in postictal period in absence of signs suggesting seizures r/o nonconvulsive status in almost all cases

c. Diagnosed only by emergent EEG

d. Absence and complex partial status may present with isolated persistent disorientation

TRANSFUSION REACTIONS AND BLOOD COMPONENT THERAPY

I Transfusion Complications

A. Hemolytic transfusion reactions

1. Signal Symptoms:

a. Anxiety
b. Red or black urine, flank pain
c. Nausea, vomiting, pain, chest tightness, headache
d. Chills, shaking
e. Fever
f. Shock with subsequent renal and other end organ failure
g. Disseminated Intravascular Coagulation

2. Hemolytic reaction may be delayed one to several days:

a. Most common in previously transfused patients (alloimmunization).
b. Common signs include fever, declining hemoglobin, mild jaundice, and renal failure (rare).

D. Non-Hemolytic transfusion reactions

1. Allergic: urticaria, pruritus, flushing, rash, rarely angioedema or anaphylaxis (consider IgA deficiency or transfusion related acute lung injury/TRALI).
2. Isolated Fever/ Infection- fever, headache, hypotension, flushing, emesis, diarrhea???
3. Circulatory overload: hypertension, signs/sx of CHF.
4. Air Embolus: shortness of breath, cough, chest pain, anxiety, shock.
5. Hypothermia: chills, low temperature, irregular heart rhythm, possible cardiac arrest.
6. Hyperkalemia: nausea, diarrhea, muscular weakness, paralysis, extremity paresthesias, bradycardia, apprehension, arrest.
7. Acidosis.
8. Depletion of clotting factors: bleeding signs/symptoms.
9. Hypocalcemia: myoclonus, tetany, EKG changes.
10. Sepsis (contaminated unit): fever, rigors, circulatory collapse (some experience milder symptoms).

II. Treatment

A. STOP TRANSFUSION IMMEDIATELY:

1. Assess and treat from evidence of shock, observe urine for color change.
2. Give 0.9% NaCL through IV at rapid rate (1-2X maint)for 1-2 hr. 3. Consider oxygen.
4. Treat symptoms (Tylenol, Benadryl, epinephrine).
5. Verify correct product was given.
6. Laboratory evaluation (suspected hemolytic reaction, or if transfusion is discontinued).

B. Hemolytic Reaction: assume if hemoglobinuria, shock, or clerical error identified, treat ASAP.

1. Give mannitol 0.25 grams/kg IV to force diuresis, Desired UOP after mannitol:
   a. Infant: 10 cc/hr
   b. Child < 20 kg: 40 cc/hr
   c. Child > 20 kg: 60 to 100 cc/hr
2. Give $NaHCO_3$ 3 meq/kg/12 hours, to urine to pH > 7.
3. Begin treatment for acute renal failure. IV rate should match urine output and insensible losses.

C. Febrile Reactions:
1. Defined as 2 degrees Fahrenheit increase during transfusion.
2. Administer tylenol (not aspirin or NSAID's to patients with thrombocytopenia).
3. Discontinue transfusion, then lab evaluation with cultures.
4. Start antibiotics in neutropenic patients, and other patients at risk.

D. Allergic reactions:
1. Treat mild urticaria or pruritis with benadryl 1 mg/kg IV or po.
2. Can restart after 15-20 min if mild symptoms, alleviated with meds.
3. Anaphylaxis: Administer epinephrine, discontinue transfusion, lab evaluation.

E. Rigors
1. Especially problematic, most common reaction in patients repeatedly transfused with platelets.
2. Assume this could be a hemolytic reaction or infected blood component.
3. Treat as above for fever.

F. Circulatory overload:
1. Place child upright with feet in dependent position. Lasix 1 mg/kg IV.
2. Start O_2.
3. Consider PEEP, pressors, etc.

III Laboratory evaluation

A. Required by blood bank: (new products will not be released until the transfusion w/u is completed).
1. Red top: 5 to 10 cc of patient blood.
2. Return the blood bag, unused donor blood and transfusion set up. (a repeat crossmatch is performed).
3. Urine: A UA is done to assess for hemoglobin
4. Purple top: post transfusion CBC and possibly a DAT performed.

B. Consider doing:
1. PT/PTT, fibrinogen.
2. Serum and urine hemoglobin.
3. Bilirubin (total/direct). If the reaction is hemolytic, the indirect bilirubin often rises in the first few hours and is usually normal by 24 hours.
4. If sepsis is suspected, get blood cultures from both the patient and the donor units.
5. Haptoglobin and LDH if considering acute hemolysis

6. Test serum for IgA if anaphylaxis
7. Test for anti HLA and/or neutrophil antigen if suspect TRALI.
8. Test serum for alloantibodies if considering a delayed hemolytic transfusion reaction.

IV Prevention of Transfusion Reactions

A. Blood products must be completed before expiration (4 hours-PRBC's, 1 hr- Platelets).

B. Most lethal transfusion errors occur because of human clerical error.
1. Verify patient identification.
2. Verify correct blood product.
3. Identifying donor and recipient blood types before transfusion is begun.

C. Transfuse blood slowly for the first 15 to 20 minutes. Someone should remain with the patient during this time to monitor for acute transfusion reaction.

D. Allergic Reactions:
1. Premed future transfusions: Benadryl (0.5-1mg/kg), consider Solumedrol (1mg/kg)

E. Febrile Reactions
1. May give acetaminophen for prophylaxis.
2. Leukocyte-poor (leuko-depleted) platelets are less likely to cause reaction.

F. Rigors
1. For patients with repeated history: plasma removal ('washed' cells) and/or premed with Solumedrol (1mg/kg).

G. Circulatory Overload
1. Transfuse blood slowly (max 5cc/kg/hr for routine transfusion, max 1cc/kg/hr for chronic Hb <5).
2. Consider ordering a "split pack", which is a half unit and giving over 2 four hour aliquots.
3. Platelets are given rapidly, be cognizant of volumes.
4. Platelet volumes ea. random unit = 50 cc("6-Pack"= 300cc), (pheresis unit = 300-400 cc).

H. Air Emboli:
1. May occur when blood is transfused under pressure.
2. Normalize pressure before container is empty when infusing with pressure cuff.
2. Clear tubing of air by aspirating air with syringe at nearest Y connector. If air is observed in tubing, disconnect tubing and allow blood to flow until air has escaped.

I. Hypothermia:
1. From rapid infusion of refrigerated blood.
2. Must use blood warmer (PICU and NICU only) if anticipated > 20cc/kg PRBC over 12 hours.
3. Never use microwave oven.

J. Hyperkalemia:
   1. Use washed PRBCs or fresh blood if patient is at risk.
   2. Observed with massive transfusions, exchange transfusions, patients with renal insufficiency, and poorly perfused patients.

V. Selection of Therapeutic Blood Components

A. Whole blood
   1. Fresh whole blood is unavailable.
   2. Blood can be reconstituted to a desired Hct using FFP or saline by the blood bank only, on request. (i.e. priming pheresis or ECMO circuit).
   3. Blood reconstituted in FFP can be used in treating symptomatic large volume deficits.
   4. Practical use in trauma: PRBCs are run cc/cc with NS. Remember to give FFP if approaching one blood volume transfusion.

C. Packed red blood cells (PRBCs)
   1. Most commonly used form of RBCs.
   2. Indications: symptomatic anemia.
   3. Criteria for transfusion varies (preprinted orders have institutional recommendations.)
      a. A hemoglobin level of 8 g/dL is not a hard and fast indication for transfusion.
      b. Dose is usually 10 ml/kg. Round to the nearest unit (approx 380cc) or consider ordering a split pack.
      c. If patient has long-standing severe anemia it is safer to give only lmL/(Hgb in g/dL)/kg.
         For example: if a patient with iron deficiency anemia has a hemoglobin of only 5 g/dL and weighs 20kg, give: lmL X 5 X 20 = 100cc.

D. Leukopoor RBC's (leukocyte filter)
   1. This is not the same as the particulate filter that is within the infusion tubing.
   2. Generally recommended in patients who will receive repeated transfusions.
   3. Will reduce chances of CMV infection if donor is CMV positive.
   4. Almost all peds patients (transplants, chronic illnesses, infants, cancer, sickle cell anemia).

E. CMV negative RBC's
   1. Used in CMV negative patients who are transplant candidates.
   2. Also used in neonates and ECMO candidates.
   3. Leukofilter may come to substitute for CMV testing in the near future.
   4. No proof that CMV- blood is necessary in a patient who is + for CMV.

F. Irradiated Blood products
   1. Inactives T-cells to block a GVH response.
   2. All immunocompromised patients (including all neonates)
   3. All "fresh" products, (ie not FFP).

G. Granulocytes /WBCs
   1. Rarely used due to severe transfusion reactions due to leukocyte antigens.

2. Used only for severe infections in patients with prolonged neutropenia.

H. Fresh frozen plasma FFP)—See chapter on coagulopathies.

I. Cryoprecipitate— See chapter on coagulopathies.

J. Random donor platelets— See chapter on coagulopathies.

1. Pheresis platelets-Indicated if multiple units of platelets are expected to be given or if alloimmunization has occurred.
2. One pheresis unit equals approximately 6 random donor units.

K. Factor VIII concentrate (anti-hemophilic factor) and Porcine factor VIII concentrate— See chapter on coagulopathies.

L. Prothrombin complex concentrate (factor IX complex) and Activated prothrombin complex concentrate— See chapter on coagulopathies.

M. Donor Directed Blood donation:

1. This service is available to patients on request (Autologous and allogeneic).
2. Requires minimum of 3 business days to arrange
3. There are very few autologous indications in pediatrics
4. Be advised that infectious risks are dramatically increased
   a. Potential donors are not usually as educated as the random volunteer donor pool regarding infectious risks.
   b. potential donors are relatively coerced on the behalf of the ill patient.
   C. potential donors may not be frank especially with family members about behavioral risks.

TRAUMA

I. Introduction:

A. **Trauma is the leading cause of death and disability in the pediatric age group.** While principles of resuscitation for trauma are the same as for nontraumatic pediatric patients, some aspects of the stabilization phase are unique to the trauma setting. This chapter does **NOT** take the place of the Advanced Trauma Life Support class (ATLS). Its' purpose is to expose the pediatric resident to fundamental concepts of trauma care. The information in this chapter is taken primarily from the ATLS and PALS courses.

B. A trimodal distribution of death from injuries occurs. The first peak of death is within minutes of the injury. Deaths during this time are usually due to lacerations of the brain, brain stem, higher spinal cord, heart or great vessels. The second peak occurs within minutes to several hours of the injury. This is the period that ATLS focuses upon. Deaths here occur secondary to subdural or epidural hematomas,hemopneumothoraces, a ruptured spleen, liver lacerations, pelvic fractures and/ or multiple injuries with significant blood loss. The third death peak occurs several days to weeks after the initial injury. These deaths are usually secondary to sepsis, multiple system organ failure (MSOF), or unrecoverable pulmonary injury.

C. The child with multisystem trauma may have **both** cardiorespiratory failure and shock. A rapid cardiopulmonary system evaluation must be performed as well as a rapid thoracoabdominal examination to detect life threatening chest or abdominal injuries which may interfere with a successful resuscitation. For instance, ventilation, oxygen and perfusion therapies may be ineffective until a tension pneumothorax is treated.

D. Basic ATLS concepts include:

1. Treat the greatest threat to life first.

2. The lack of a definitive diagnosis should never impede the application of an indicated treatment.

3. A detailed history is not an essential prerequisite to begin evaluating an acutely injured patient.

E. Improper resuscitation has been identified as a major cause of preventable pediatric death. Common errors in resuscitation include failure to:

1. Open and maintain the airway.

2. Provide appropriate and adequate fluid resuscitation to head injured children.

3. Recognize and treat internal hemorrhage.

F. A qualified surgeon should be involved ASAP in the resuscitation.

G. A child with a pediatric trauma score of 8 or less **or**

a child with a revised trauma score of 11 or less should be transported to a pediatric trauma center. (***see following tables***)

PEDIATRIC TRAUMA SCORE

	Coded value		
Patient characteristics	**+ 2**	**+ 1**	**- 1**
Weight (kg)	> 20	10 - 20	< 10
Airway	Normal	Maintained	Unmaintained
Systolic BP (mm Hg)	> 90	50 - 90	< 50
Central nervous system	Awake	Obtunded	Coma
Open wound	None	Minor	Major
Skeletal trauma	None	Closed	Open, multiple

REVISED TRAUMA SCORE

Glasgow Coma Scale Score *	Systolic Blood Pressure (mm Hg)	Respiratory Rate (breaths/ min)	Coded Value
13 - 15	> 89	10 - 29	4
9 - 12	76 - 89	> 29	3
6 - 8	50 - 75	6 - 9	2
4 - 5	1 - 49	1 - 5	1
3	0	0	0

***** ***Glasgow Coma Scales (GCS) are in the Neurologic Assessment, ... chapter.***

H. At WHMC, pediatric trauma patients are primarily managed by a trauma team. Usually our pediatric surgeons head these teams. We assist in the initial stabilization of the patient but remain under the primary guidance of the trauma team. The pediatric dept. PICU team **consults** on all of these patients and facilitates fluid, electrolyte, and ventilation management. We also offer **suggestions** concerning other problems or organ system management.

II. General approach to the trauma patient

A. Trauma patients should be taken to the closest appropriate facility. Once triaged, the patient is assessed and assigned a treatment priority which is based on their injuries, stability, and the injury mechanism.

B. The **Primary Survey** is performed next to identify and **simultaneously** manage life threatening conditions. (ABC's plus D and E)

A = Airway maintenance **with cervical spine control**
B = Breathing and ventilation
C = Circulation with hemorrhage control
D = Disability: neurologic status
E = Exposure/ Environmental control: **completely** undress the patient, but prevent hypothermia

1. Airway - assess for signs of airway obstruction such as foreign bodies or facial, mandibular, or tracheal/ laryngeal fractures. Cervical spine protection must be insured (use chin lift/ jaw thrust). Do not hyperextend, hyperflex, or rotate the cervical spine. Cervical immobilization should be achieved.

2. Breathing - auscultation, percussion, inspection, and palpation should be performed to assess for tension

pneumothoraces, flail chest, pulmonary contusions, open pneumothoraces, fractured ribs etc.

3. Circulation with hemorrhage control - hypotension after trauma should be considered as hypovolemic in origin until proven otherwise. Level of consciousness if reduced, may be from cerebral hypoperfusion. Skin color especially if ashen gray or white are signs of hypovolemia. Rapid, thready pulses are early signs of hypovolemia. Rapid external blood loss should be managed initially by direct manual pressure on the wound. Pneumatic splints may also lessen hemorrhage. Tourniquets should **not** be used as they crush tissue and cause distal ischemia.

4. Disability - (Neurologic evaluation) - the "**AVPU**" method is used to assess the level of consciousness, and pupillary size and reactiveness. The Glasgow Coma Scale (GCS) may be performed in lieu of the AVPU. The GCS is always performed in the Secondary Survey.

A = Alert
V = responds to Verbal stimuli
P = responds only to Painful stimuli
U = Unresponsive

a. An altered level of consciousness should prompt an immediate reevaluation of oxygenation, ventilation, and perfusion. If these are adequate assume trauma is the etiology for the decreased level of consciousness. Alcohol or drugs may also do this but are a diagnosis of exclusion in the trauma patient.

5. Exposure/ Environmental control - completely undress the patient but protect them from hypothermia. **Warm blankets, warmed IV fluids, conchas for ventilators and a warm environment must be provided.**

C. Resuscitation:

1. The airway must be protected and maintained at all times. Nasopharyngeal airways may be used in conscious patients.

2. Patients with compromised airways, those with ventilatory problems or who are unconscious should be endotracheally intubated. If oral or nasal intubation is contraindicated a surgeon should place a surgical airway. (decision tree follows)

3. Oxygen should be given to all trauma patients. ABG's should be freely used.

4. A minimum of 2 large bore IV's should be placed. Remember if an IV cannot be placed promptly, place an intraosseous (IO) catheter, especially in patients < 6 years old (described in pediatric resuscitation chapter). If patient is in severe shock go directly to an IO. **Do NOT use an IO in a fractured bone.**

5. All patients should receive a Type and crossmatch, CBC, UA, baseline electrolytes and an amylase. Females of child bearing age should receive a pregnancy test.

6. If colloid is needed, and Type specific blood is not immediately available, then O neg. blood may be used. Shock should be assumed to be hypovolemic in origin and should be treated aggressively with fluids rather than pressors, steroids or bicarb.

7. Continuous ECG monitoring must be used.

a. Dysrhythmias, tachycardia, A-fib, PVC's, and ST segment changes may all indicate cardiac contusion.

b. EMD may indicate cardiac tamponade, tension pneumothorax, profound hypovolemia, severe acidosis, pulmonary embolism, pneumopericardium, hypoxemia, hyperkalemia, tricyclic antidepressants, Beta-blockers, Calcium channel blockers, and hypothermia.

c. Bradycardia, premature beats or aberrant conduction patterns may indicate hypoxia, hypothermia, or hypoperfusion

8. Urinary catheters should be placed unless urethral transection or injury is suspected. Contraindications to placing a foley are: 1) blood at the urethral meatus, 2) blood is in the scrotum, or 3) the prostate is high riding or cannot be palpated. Therefore, an exam of the genitalia and rectum is required prior to urinary catheter insertion.

9. Gastric tubes should be placed to reduce stomach distention and decrease the risk of aspiration. If the cribiform plate is fractured or suspected to be fractured, the gastric tube should be placed orally or through a properly placed nasopharyngeal airway to prevent intracranial passage. Such a fracture may be suspected in patients with otorrhea, rhinorrhea, Battle's sign, hemotypanum, or raccoon eyes. However, sometimes these findings do not appear until hours after the injury.

10. The following X-rays are always obtained: 1) lateral C-spine, 2) AP chest, and 3) AP pelvis films. Later, complete radiographs of the neck and other areas, CT's etc. should be obtained.

E. The Secondary Survey:

1. The secondary survey begins once the primary survey (ABC's) is completed, resuscitation has commenced and the patient's ABC's have been reassessed. The secondary survey is a head-to-toe evaluation including a full set of vital signs, and complete history and physical examination. A complete neurologic evaluation and the GCS, X-rays, labs and peritoneal lavage (if indicated) are performed here.

2. The history should be complete especially for the mechanisms of the injury, and whether it was blunt or penetrating. The **"AMPLE"** mnemonic is useful.

A = Allergies
M = Medications
P = Past illnesses
L = Last meal time

E = Events/ Environment related to the injury

a. A history in blunt trauma such as from automobile collisions, falls, etc. should include questions concerning seat belt use, infant car seat use, steering wheel deformations, the direction of the impact, damage to the vehicle, speed of the vehicle, mortalities associated with the accident, loss of consciousness, and whether the patient was ejected or not.

b. A history in penetrating trauma such as from firearms, stabbings, or from impaling objects should address the region of the body injured, the velocity of the missile, caliber of the bullet, trajectory, and the distance from weapon to wounded.

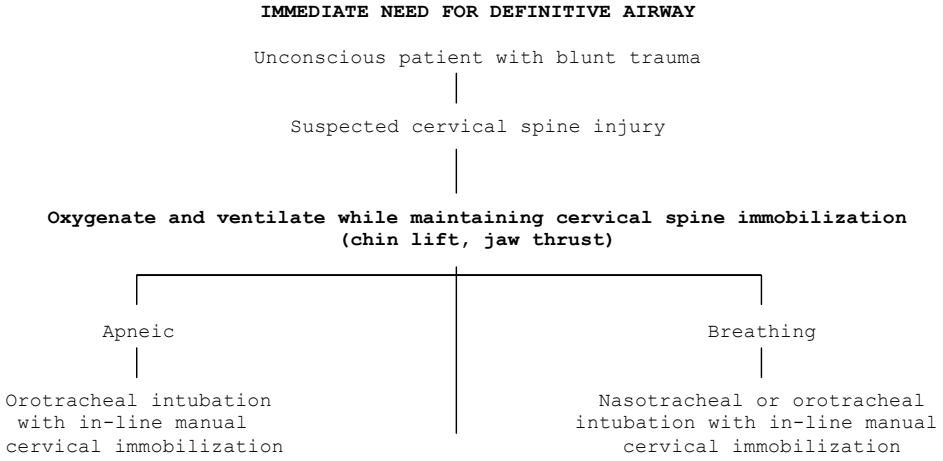
c. Histories should include exposure to burns, cold injuries, toxin exposure, chemical exposure, radiation exposure, duration of any such exposure, and extraction time from the vehicle.

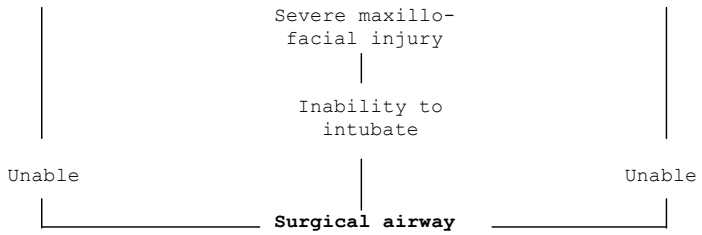
III. Specific considerations:

A. Airway - the airway must frequently be assessed for patency and adequacy of ventilation. Failure to heed this advice is one of the most common reasons for failure in trauma evaluation and resuscitation ! Oxygen should be freely used.

1. **A definitive airway is necessary for: apnea, inability to protect the airway with other means, to protect the lower airway from aspiration of blood or vomitus, when potential or impending compromise of the airway may occur such as with facial fractures, inhalational injuries, or sustained seizures, for patients with closed head trauma requiring hyperventilation, for failure to maintain adequate oxygenation by other means, and for GCS's < 9.**

2. The following decision tree helps determine airway appropriateness for apneic patients in whom a cervical spine injury is suspected. **A surgeon will perform a cricothyroidotomy if needed**.





B. Shock - this is covered in the GI bleed, newborn and pediatric resuscitation chapters so will only be touched on here. **Remember**, shock should be assumed to be hypovolemic in origin and should be treated aggressively with fluids rather than pressors, steroids or bicarb. This is because almost all shock from trauma is hypovolemic in origin. Neurogenic shock and cardiogenic shock are rare in pediatric trauma patients. Specifics concerning trauma are:

1. Pneumatic Antishock Garment (PASG) - this raises systolic pressure by increasing peripheral vascular resistance and myocardial afterload. **Not used in pediatric trauma patients unless an unstable pelvic fracture is present.**

a. Indications:

(1). Splinting and control of pelvis fractures **with** continuing hemorrhage and hypotension.

(2). Intra-abdominal trauma with severe hypovolemia **only** in patients en route to the OR or another facility.

b. Contraindications:

(1). Pulmonary edema

(2). Known diaphragmatic rupture

(3). Uncontrolled hemorrhage outside the confines of the garment

(4). If inflation of the garment causes an increase in respiratory rate or increased respiratory distress it must be deflated regardless of BP. Assume a diaphragmatic rupture.

C. Abdominal trauma

1. At WHMC abdominal trauma patients always get a CT scan unless going immediately to the OR for a celiotomy.

a. CT scan indications include:

(1). Abdominal distention

(2). Abdominal findings such as: tenderness, masses, or inability to assess the abdomen such as in a unconscious patient

b. Pediatric CT scans are done with enteral, IV and rectal contrast. The dose for pediatric patients follows.

(1). ***Oral*** contrast is dilute gastrograffin (4 cc's in 8 oz. of water). The oral dose of this mixture is 10 cc/**kg**.

(2). ***IV*** contrast is 1 cc/**pound** of weight of non-ionic contrast. This is usually given as a bolus in < 1 minute.

(3). ***Rectal*** contrast is dilute gastrograffin (4 cc's in 8 oz. of water). This is given via a pediatric rectal tube and is delivered via gravity by hanging a bag above the CT table. The exact dose is per the radiologist

2. Diagnostic Peritoneal Lavage (DPL), **rarely used in pediatric patients** because most intra-abdominal injuries, even if they cause bleeding, are monitored expectantly without surgical intervention. Additionally, CT scans can be obtained relatively quickly. Howver, if a pt is being taken to the OR for another indication and a CT is not practical, DPL may have a role in pediatric trauma.

a. May be 98 % sensitive for intraperitoneal bleeding.

b. The abdomen may sequester large amounts of blood without appearing abnormal.

c. The only **absolute** contraindication for a DPL is an already existing indication for celiotomy (exploration).

d. **Relative** contraindications include: previous abdominal operations, morbid obesity, advanced cirrhosis, or pre-existing coagulopathy. Use in pregnancy is controversial.

e. A positive DPL, and therefore, need for surgical intervention is indicated by:

(1). $\geq$ 100,000 RBC's/mm^3 (controversial in children)

(2). > 500 WBC's/mm^3

(3). Bacteria on gram stain

(4). Fecal material

3. Indications for celiotomy

a. Hypotension with evidence of abdominal injury (i.e. gunshot or stab wounds, blunt trauma with gross blood on DPL)

b. Peritonitis - early or subsequent

c. Recurrent hypotension despite adequate resuscitation.

d. Extraluminal air

e. Injured diaphragm

f. Intraperitoneal perforation of the urinary bladder on cystography.

g. A positive contrast study of the upper or lower GI tracts.

h. Persistent amylase elevation with abdominal findings.

D. Head trauma

1. Approximately 50% of all trauma deaths are associated with head injury.

2. Anatomy - 5 tissue layers cover the skull bone. “SCALP”

a. Skin

b. subCutaneous tissue

c. galea Aponeurotica

d. Loose areolar tissue

e. Periosteum

- the loose areolar tissue is subject to subgaleal hematomas, scalping injuries, and large flaps from injury

- due to the generous blood supply, a laceration may result in a major blood loss, especially in children

3. Skull - comprised of the cranial vault (calvarium) and the base. The base is irregular and rough therefore allowing injury to occur as the brain moves within the skull during acceleration and deceleration.

4. Meninges - the tough dura adheres to the internal surface of the skull. A potential space under it (the subdural space) exists before you encounter the arachnoid. Hemorrhage can occur into this space, usually from trauma to veins (bridging veins) that traverse the space and cause a subdural hematoma. Meningeal arteries lie between the dura and the internal surface of the skull (epidural space). Laceration of these arteries causes an epidural hematoma. Under the arachnoid is the pia which firmly attaches to the brain cortex. Between the arachnoid and the pia

is the subarachnoid space where CSF circulates. Hemorrhage into this space causes a subarachnoid hemorrhage.

5. The brain is comprised of the right and left cerebral hemispheres with the left usually dominant and controlling language, frontal lobe (emotions, motor function), occipetal lobe (vision), parietal lobe (sensory function), temporal lobe (memory, may be relatively silent on the right side), cerebellum and brain stem.

6. **An alteration of consciousness is the hallmark of brain injury.**

7. Examination is based on the "AVPU" mnemonic and a mini-neurologic exam (GCS, assessment of pupillary function and assessment for any lateralized extremity weakness).

a. GCS - if $\leq$ 8 the patient is considered comatose
- if > 8 patient is not in coma
- if $\leq$ 8 the patient has a severe head injury
- if 9 - 12 the patient has a moderate head injury
- if > 12 the patient has a minor head injury

b. A difference in pupil diameters of $\geq$ 1 mm is abnormal.

c. A delay in onset of movement to a painful stimuli, less movement than expected, or need for more stimulus on one side is significant. A lateralized weakness suggests an intracranial mass lesion.

d. A patient has a severe head injury **irrespective of the GCS** if any of the following conditions are present:

(1). Unequal pupils

(2). Unequal motor examination

(3). An open head injury with leaking CSF or exposed brain tissue

(4). Neurologic deterioration (a decrease in the GCS by $\geq$ 2 points)

(5). Depressed skull fracture

e. If headache increases, pupil size increases, or weakness develops on one side then the neurologic status may be deteriorating !! The initial neurologic evaluation is only the beginning. Exams must be repeated !

f. Patients with significant loss of consciousness or the above findings get an immediate head CT without contrast. Depending on the neurologic evaluation these patients may be admitted to the PICU for observation and frequent neuro checks. The treatment of increased intracranial pressure is discussed in its chapter.

8. Types of head injury

a. Skull fracture - common, may not be associated with severe injury, higher likelihood the patient will have intracranial hematoma exists with skull frx., therefore all patients require a neurosurgical consult

(1). Linear, nondepressed frx. - if lies across vascular arterial grooves or suture lines it should raise the suspicion of epidural hemorrhage

(2). Depressed skull frx. - requires elevation

(3). Open skull frx. - dura is torn, requires early surgical intervention

(4). Basal skull frx. - otorrhea, rhinorrhea, eccymosis in mastoid region (Battle's sign), hemotypanum, raccoon eyes (periorbital eccymoses) are all associated with cribiform plate frx's.

b. Diffuse brain injuries - associated with acceleration/ deceleration injuries

(1). Concussion - brief loss of neurologic function, confusion, amnesia, or a temporary loss of consciousness may be present. Observation is required in the PICU.

(2). Diffuse axonal injury - prolonged coma (days - weeks), mortality is up to 33%, results in microscopic damage scattered widely throughout the brain, does not require surgery

c. Focal injuries - contusions, hemorrhages, hematomas

(1). Contusion - may be single or multiple, small or large, associated with severe concussions, coup/ contrecoup forms, commonly in frontal or temporal lobes, edema may result

(2). Intracranial hemorrhages

(a). Meningeal hemorrhage

((1)). Acute epidural hemorrhage - usually from a tear in the dural arteries especially the middle meningeal artery, rapidly fatal, associated with a loss of consciousness, intervening lucid period, then a secondary depression of consciousness, and development of a hemiparesis on the opposite side, and sometimes a fixed and dilated pupil on the same side (Hallmark sign)

((2)). Acute subdural hemorrhage - also life threatening and more common than epidurals, usually due to a rupture of bridging veins between the cortex and the dura

((3)). Subarachnoid hemorrhage - bloody CSF associated with photophobia, headache

b. Brain hemorrhages and lacerations

((1)). Intracerebral hematomas

((2)). Impalement injuries - leave the object in place until a neurosurgeon arrives

((3)). Bullet wounds

E. Spine and spinal cord trauma **(BEWARE OF spinal cord injury with*out* radiographic abnormality (SCIWORA). See below under pediatric nuances.**

1. A vertebral column injury should be presumed and **total** spinal immobilization of the entire patient should be maintained until screening X-rays are obtained and fractures or fracture-dislocations are excluded for any patient:

a. With an injury above the clavicle or

b. With a head injury resulting in an unconscious state

c. This is especially true if the injury resulted from high speed vehicles

2. Conscious patients can usually identify pain at the injury site and will have a loss of sensation below this level.

3. Unconscious patients may have the following clinical signs suggesting a cervical cord injury:

a. Flaccid areflexia - especially with a flaccid rectal sphincter

b. Diaphragmatic breathing

c. Ability to flex but not extend the elbow

d. Grimaces to pain above, but not below the clavicle

e. Hypotension with bradycardia especially without hypovolemia

f. Priapism

4. Neurologic assessment - 3 spinal cord tracts may be assessed clinically (all are paired tracts which may be singly or dually injured)

a. Corticospinal tract (posterolateral aspect of cord) - controls motor power on the same side of the body. Tested by voluntary muscle contraction or involuntary responses to painful stimuli.

b. Spinothalamic tract (anterolateral aspect of cord) - transmits pain and temperature from opposite side of body. Test by pinch or pin-prick.

c. Posterior columns - carry proprioceptive impulses from the same side of the body. Tested by position sense of fingers and toes or tuning fork vibration.

5. Neurogenic shock results from impairment of the descending sympathetic pathways in the spinal cord. This leads to loss of vasomotor tone and loss of sympathetic innervation of the heart. The patient is vasodilated and hypotensive without hypovolemia but may not become tachycardic and may even be bradycardic. Pressors usually help maintain the BP. Once again, neurogenic shock is rare so trauma patients in shock are treated as hypovolemic initially.

6. Spinal shock occurs soon after the spinal cord injury. Function may not be apparent although all areas are not permanently destroyed and only time will demonstrate return of function. You see flaccidity and loss of reflexes.

IV. Pediatric Trauma Nuances

A. Nearly 22,000,000 children are injured in the U.S.A. each year.

B. Encounters with motor vehicles (as an occupant, pedestrian, or cyclist) account for the largest fatally injured group followed by drownings, house fires, and homicide.

C. Multisystem injury is the rule rather than the exception.

D. The order and priorities of pediatric trauma management are the same for injured children as adults, however, their unique anatomic characteristics deserve special consideration:

1. Because of smaller body mass, energy from linear forces (fenders, bumpers, falls) results in greater force applied per unit body area. Children have less fat, less elastic connective tissue, and close proximity of organs which leads to more multisystem organ injuries.

2. The skeleton is incompletely calcified and is more pliable. Internal organs may be damaged without evidence of overlying bone fractures. If bones are broken assume a massive amount of energy must have been applied.

3. The body surface area to volume ratio is highest at birth so hypothermia may develop quickly.

4. The child's ability to interact and cooperate with care-givers is limited making history and physical examinations difficult.

5. Shock resuscitation fluids are LR or NS, with 20 cc/kg boluses.

6. Solid abdominal organ injuries (spleen, liver) in a pediatric patient may be observed in the PICU with bedrest and frequent HCT checks rather than taken directly to the OR as with adults.

E. Airway:

1. The smaller the child, the greater is the disproportion between the size of the cranium and midface. This produces a greater propensity for the posterior pharyngeal area to buckle as the relatively large occiput forces passive flexion of the c-spine. To prevent this assume a "sniffing" position, while maintaining c-spine control.

2. Visualization of the larynx may be difficult as the soft tissues (tongue, tonsils) are large compared to the oral cavity.

3. The larynx is more antero-caudal and is naturally shorter so right mainstem intubations occur more easily.

4. **Orotracheal** intubation under direct visualization while maintaining c-spine immobilization is the preferred method of establishing airway control, especially in children 8 years of age or younger.

F. Chest trauma:

1. The child's chest wall is very compliant which allows for the transfer of energy to intrathoracic soft tissues, frequently without any evidence of external chest wall injury. Consequently, pulmonary contusions and intrapulmonary hemorrhages are commonly seen.

2. Mobility of mediastinal structures makes the child more sensitive to tension pneumothoraces and flail segments.

G. Head trauma:

1. Children are particularly susceptible to the secondary effects of brain injury which are produced by hypoxia, hypotension, seizures and hyperthermia. Shock resuscitation and avoidance of hypoxia is critically important to a good outcome.

2. Young children with open fontanelles and mobile cranial suture lines are more tolerant of expanding intracranial mass lesions. They may not decompensate until the mass lesion has become large. A bulging fontanelle or suture diastases should prompt neurosurgical evaluation.

H. Spinal cord injury:

1. Children may sustain spinal cord injury without radiographic abnormality (**SCIWORA**). **Normal spine X-rays do not exclude significant spinal cord injury !!** This is due to the pediatric spine being so much more elastic and mobile than the adult spine. The interspinous ligaments and joint capsules are more flexible, the facet joints are flatter, and the relatively large head allows for more angular momentum to be generated during flexion and extension, resulting in greater energy transfer. Spinal precautions must be maintained (Philadelphia c-spine collar and logrolling for examinations).

2. **Neurosurgical evaluation should be obtained if there is any doubt that a spinal cord injury exists.**

I. Abdominal trauma: Doses of contrast for pediatric abdominal CT's are listed in the previous abdominal trauma section.

J. Shock:

1. Hemorrhagic shock may be classified based on systemic signs as listed in the following table:

Hemorrhagic Shock Classification

	Class I	Class II	Class III	Class IV
Degree of hemorrhage	very mild	mild	moderate	severe
Blood volume loss	< 15 %	15 - 25 %	26 - 39 %	≥ 40 %
Cardiovascular	HR normal or mildly ↑'d, normal pulses, normal BP	Tachycardia, peripheral pulses may be ↓'d, normal BP	significant tachycardia, thready peripheral pulses, ↓'d BP	severe tachycardia, thready CENTRAL pulses, significantly ↓'d BP
pH	normal	normal	metabolic acidosis	significant acidosis
Respiratory	RR normal	tachypnea	moderate tachypnea	severe tachypnea
CNS	slightly anxious	irritable, confused, or combative	irritable, lethargic, or diminished pain response	lethargic, coma
Skin	warm, pink, capillary refill brisk	cool extremities, mottled, delayed cap. refill	cool extremities, mottled or pallor, prolonged cap. refill	cold extremities, pallor or cyanosis
Kidneys	normal urine output	oliguria, increased specific gravity	oliguria, increased BUN	anuria

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