Management of Pediatric Hematologic Emergencies

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- None

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Objectives

- Diagnosis
- Management

  Hem-Onc emergencies
- Bleeding (thrombocytopenia)
- Anemia

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Hematology - Oncologic Emergencies

- Metabolic/endocrine as a result malignancy or therapy
- Lesions press/obstruct vital organs
- Pancytopenia secondary to malignancy or chemotherapy-hemorrhage/anemia/infection
- Organ dysfunction/failure

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Other Hematologic Emergencies

- Thrombosis (previous lecture)
- Bleeding

  Thrombocytopenia
- Anemia

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Oncologic emergencies

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Hyperleukocytosis

- WBC > 100,000/mm^3
- Increased blood viscosity/tumor emboli microcirculation
- Intracranial hemorrhage, thrombosis, pulmonary hemorrhage, leukostasis
- Tumor lysis
- 23% mortality ANLL and 5% ALL

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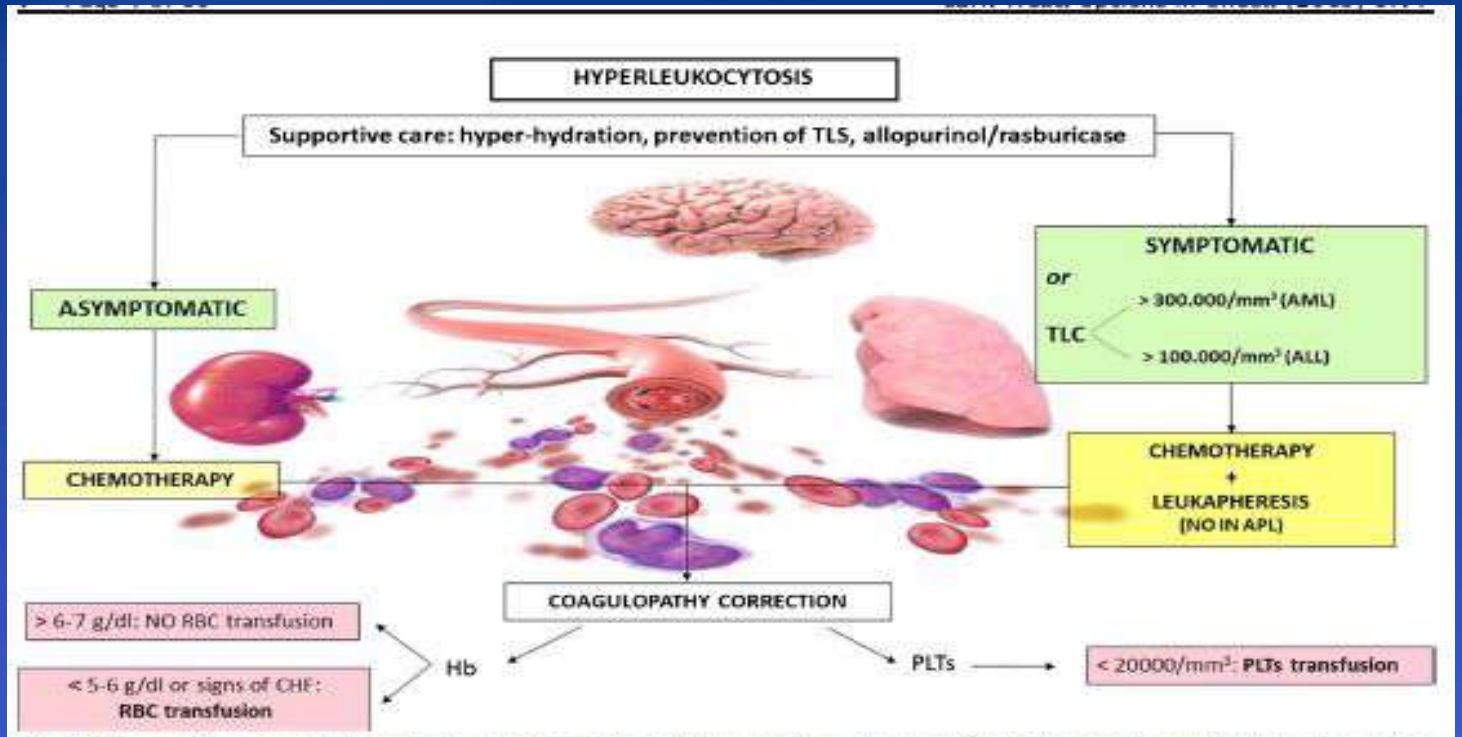

Fig. 1. Therapeutic approach to acute hyperleukocytosis. *TLS* tumor lysis syndrome, *TLC* total leukocyte count, *AML* acute myeloid leukemia, *ALL* acute lymphoblastic leukemia, *APL* acute promyelocitic leukemia, *RBC* red blood cell, *Hb* hemoglobin, *PLTs* platelets, *CHF* congestive heart failure.

Curr. Treat. Options in Oncol. (2016) 17: 7

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Tumor lysis

- Occurs bulky B cell or T cell leukemias or lymphomas
- Rapid lysis or cell death leading to hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia
- If not treated: cardiac arrythmias, renal failure, seizures, coma, DIC, death

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TLS: Risk stratification and treatment

- **Low risk**

  -Uric acid <7.5

  -Indolent NHL

Hydration/close monitoring

- **Intermediate**

  -Uric <7.5

  - LDH

  - Bulky disease (>10 cm)

Aggressive hydration/rasbicurase if uric acid rises despite allopurinol

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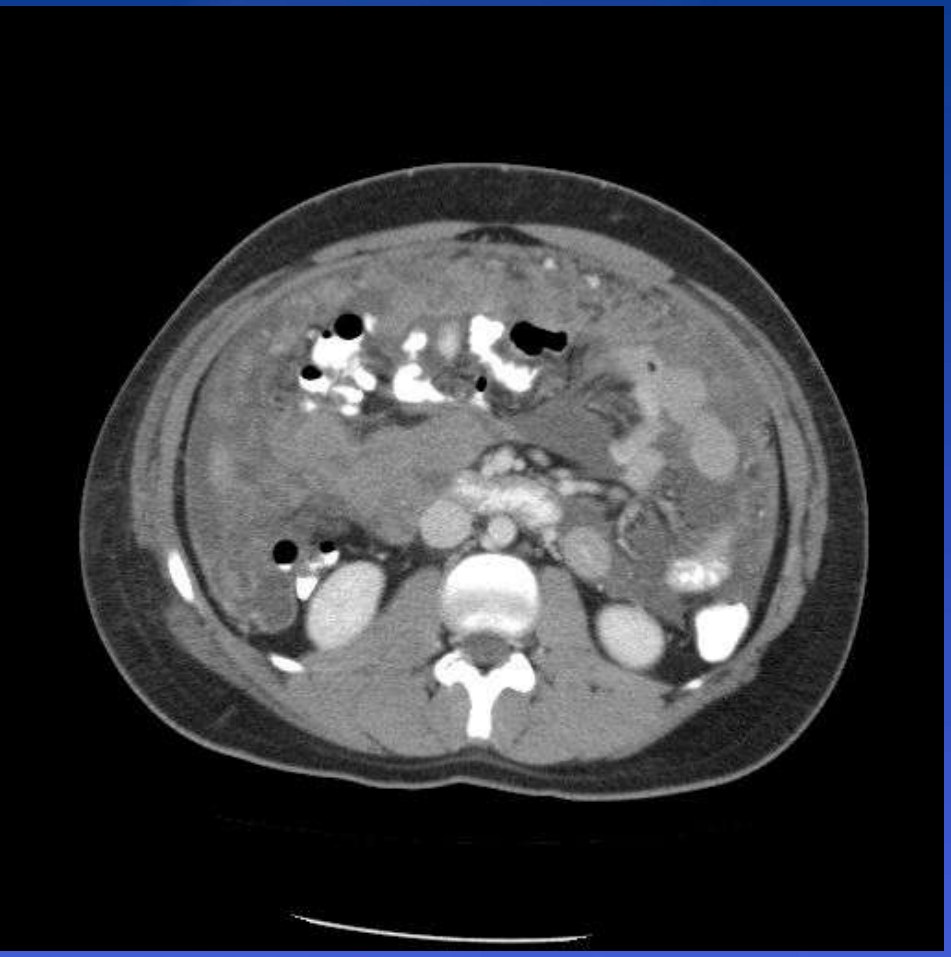
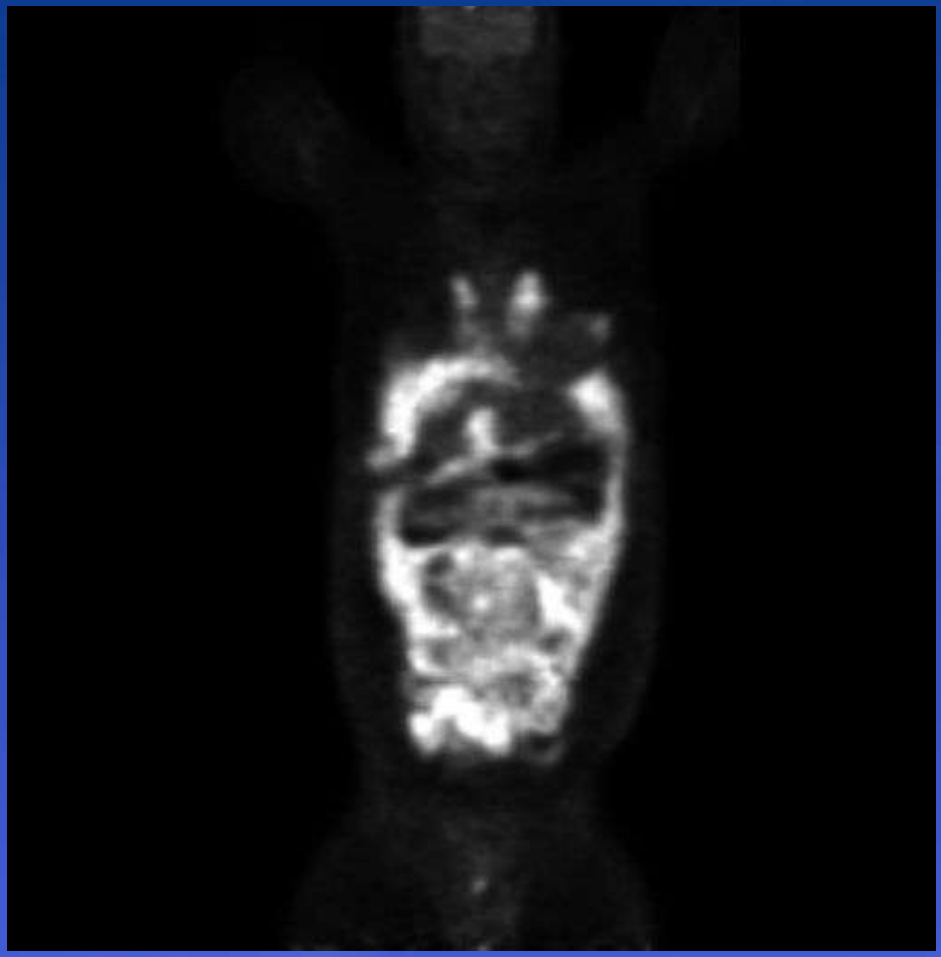
Burkitt's Lymphoma





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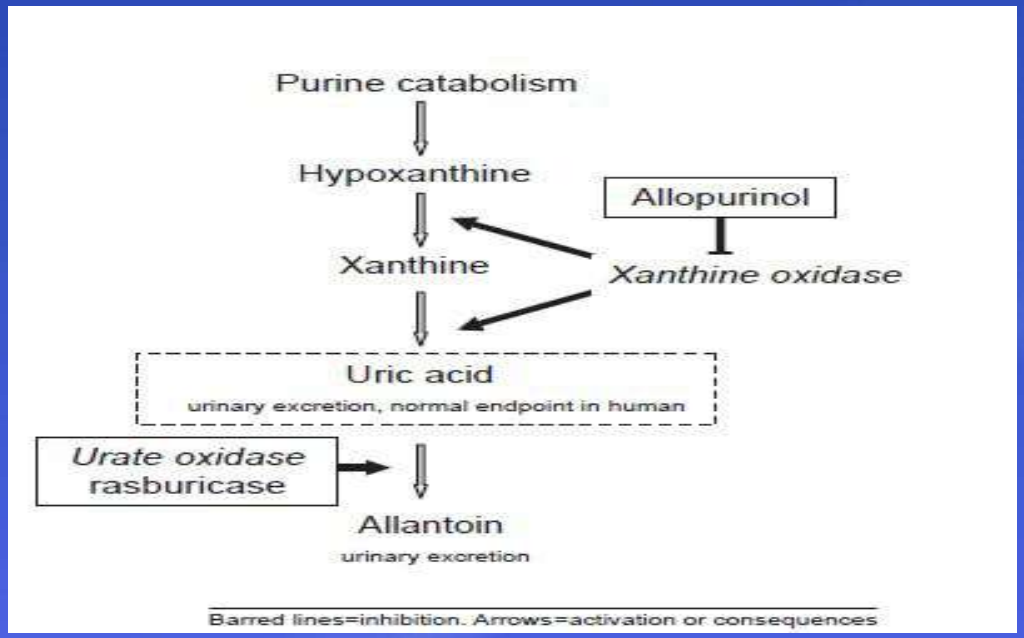
Management tumor lysis

- Monitor I/O, sp gravity, pH
- Monitor lytes, Ca, PO4, uric acid q 6 hrs
- Cardiac monitoring if hyperkalemia or hypocalcemia
- Hydration, allopurinol, rasbicurase



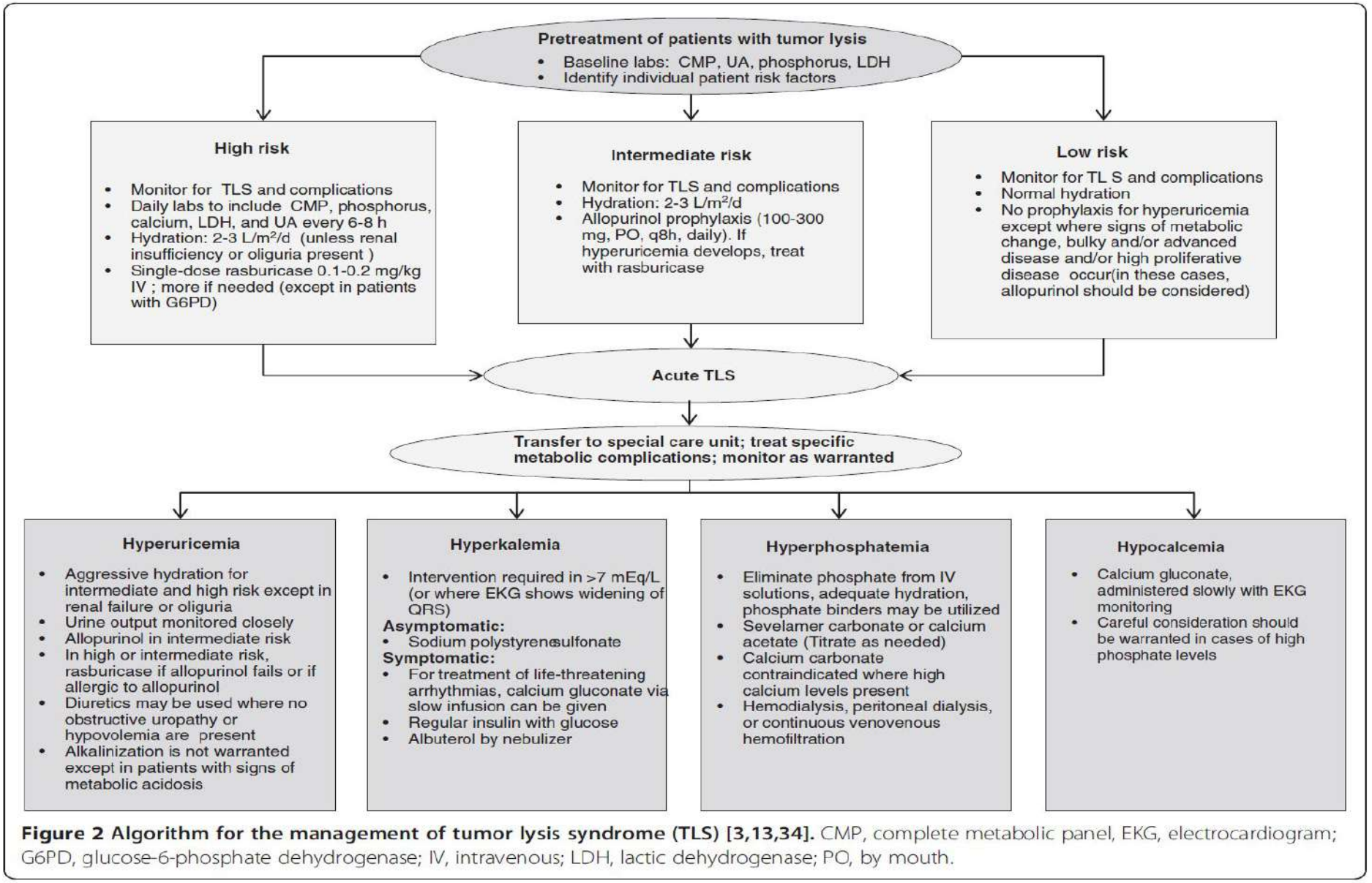


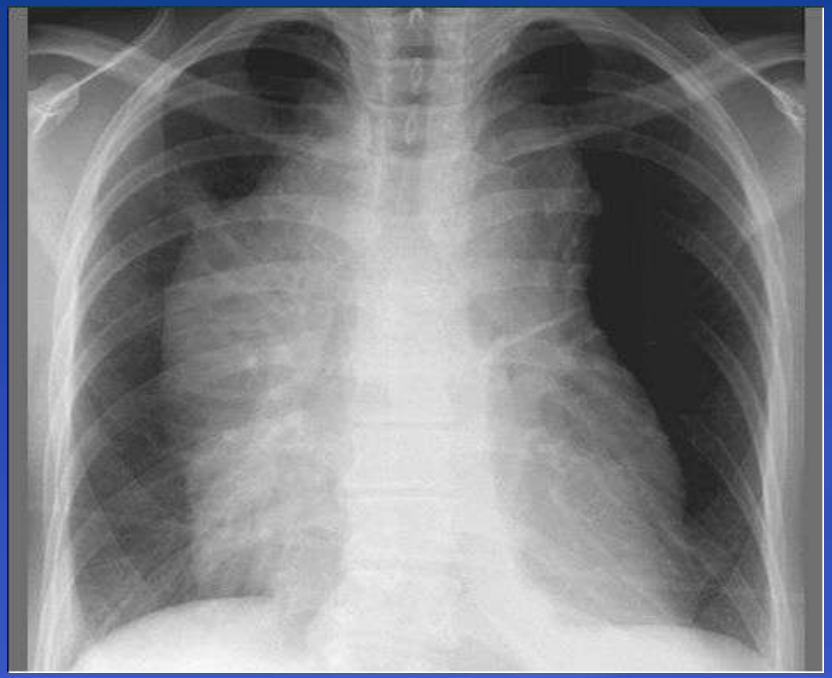
Figure 2 Algorithm for the management of tumor lysis syndrome (TLS) [3,13,34]. CMP, complete metabolic panel, EKG, electrocardiogram; G6PD, glucose-6-phosphate dehydrogenase; IV, intravenous; LDH, lactic dehydrogenase; PO, by mouth.

Thoracic Emergencies

- **SVC syndrome**
- Etiology: thrombosis, malignant anterior mediastinal masses (Hodgkin's, NHL, teratoma or other germ cell tumors)
- Signs and symptoms: swelling, plethora, cyanosis face, neck and upper ext
- **SMS**

  cough, hoarseness, dyspnea,

  orthopnea, chest pain



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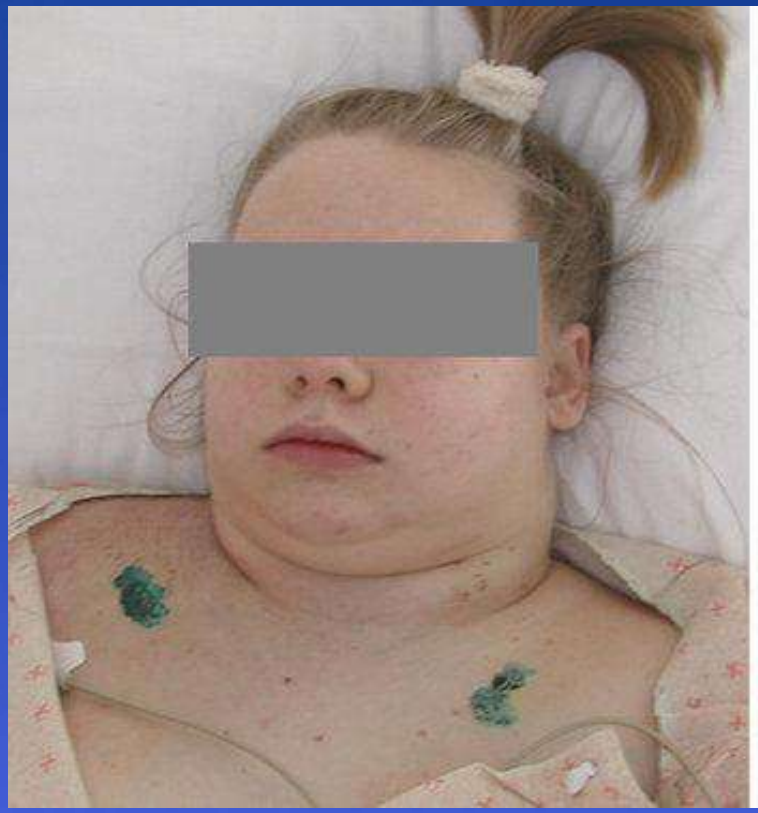
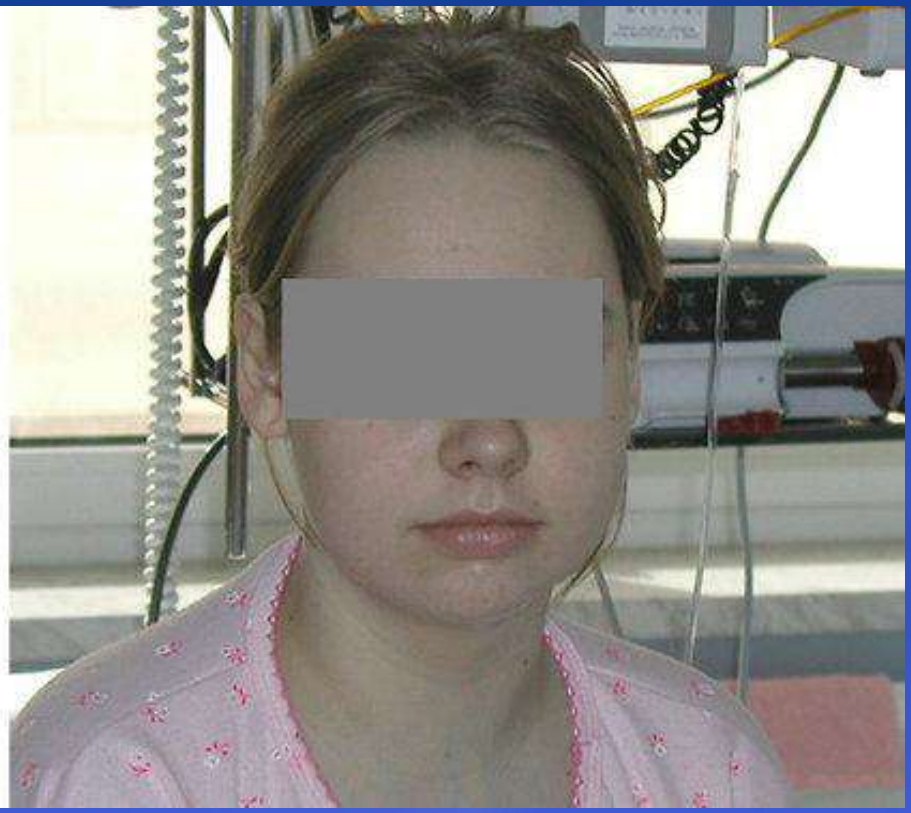
SVC syndrome





http://telemedicina.med.muni.cz/pediatric-oncology/index.php?pg=emergencies-in-pediatric-oncology--superior-vena-cava-syndrome

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Management

- Prevent: supine position, stress, sedation
- Might need intubation (extubation until decrease size mass)
- ECMO
- Dx: CXR or CT, needle biopsy, serum markers
- Tx: thrombosis-thrombolytics if clot, malignancy (rad tx, steroids -pred 40 mg/m2, chemotherapy)

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Infection

- Comprehensive evaluation of the patient (vital signs, complete exam including perfusion)
- Gram positive and gram negative coverage
- Consider anaerobic coverage [if abdominal pain, perirectal findings (fissure, redness, pain)].
- Fluid resuscitation/blood transfusion if needed
- Continue antibiotics until count recovery (rising absolute neutrophil count, neg blood cx, no fever)
- Antifungal therapy

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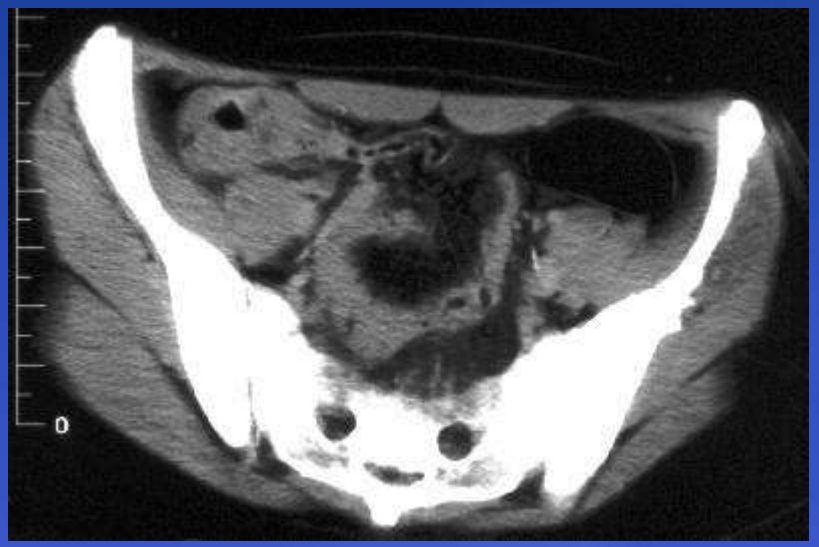
Typhylitis

- Necrotizing colitis localized cecum
- Severe neutropenia
- Right lower quadrant pain
- Clostridium and Pseudomonas
- Mortality 50-100%
- Dx: clinical and CT
- Management: antibiotics, bowel rest if severe



www.emedicine.com/ardio/images

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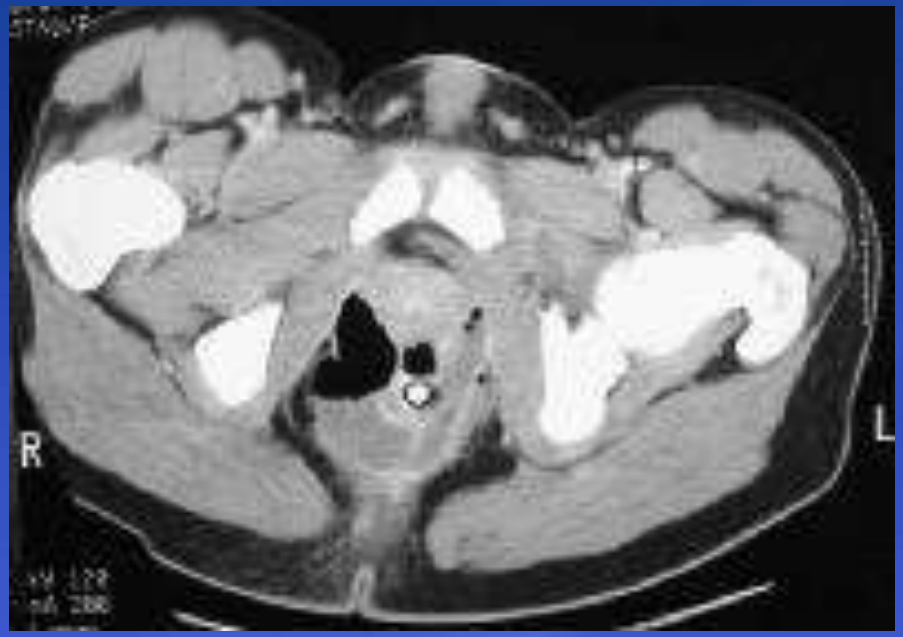
Perirectal abscess

- Perirectal pain, tenderness, painful bowel movements
- Antibiotics to cover gram neg and anaerobes
- GCSF/granulocyte transfusions
- Surgical (debridement, colostomy)



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Neurologic Complications

- Spinal cord compression: 3-5% children with cancer
  - ✓ Sarcomas account ½ (remainder lymphoma, neuroblastoma, leukemia)
  - ✓ Metastases (brain tumors)
- Back pain
- Incontinence, urinary retention
- Loss strength and sensory deficits

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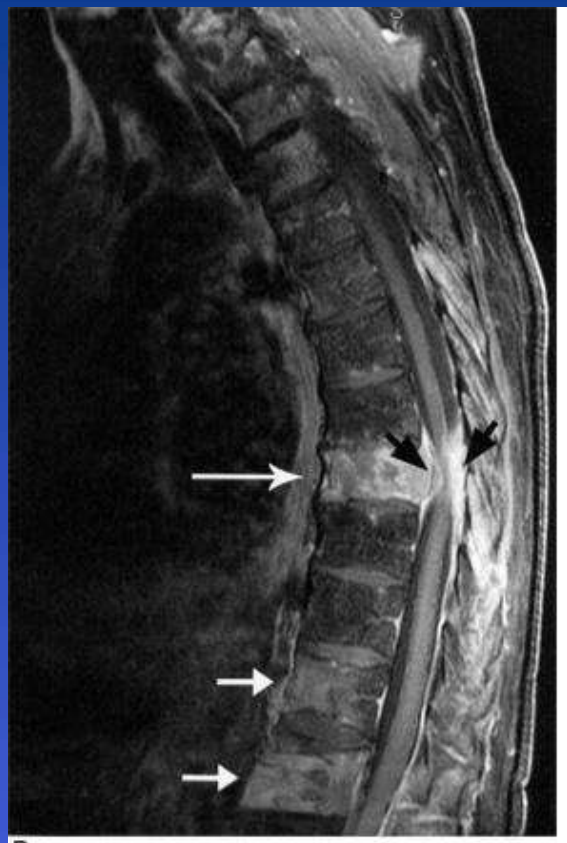
Spinal cord compression

- Dexamethasone 1-2 mg/kg loading dose (max 10 mg) followed by 1.5 mg/kg/day (max 4 mg/dose)
- Mild deficits (0.25-1 mg/kg q 6 hrs)
- Epidural mass (decompression-surgical, chemotherapy, radiation)



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Source: Kantarjian HM, Wolff RA, Koller CA: *MD Anderson Manual of Medical Oncology*: http://www.accessmedicine.com

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Seizures

- Stabilize patient
- Evaluate CT/MRI
- Etiologies (brain tumor, sinus-venous CNS thrombosis, bleeding, PRES)
- Tx: treat underlying disorder

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Evaluation Bleeding Disorders

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Bleeding assessment

Bleeding history

Age/gender

Location:

Skin/mucous membranes: plt and blood vessels

Soft tissue/muscles/joints: coagulation factor

Medications

Other abnormal bleeding: circumcision, dental extraction, menses, surgery?

Complete family history: (consanguinity? Neonatal death? Bleeding post-surgery? Menorrhagia? Post-partum hemorrhage?)

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Abnormal bruising or bleeding

- Frenulum bleeding (more severe if hemostatic disorder)
- Retinal (uncommon), Fractures (uncommon) non-accidental trauma?
- ICH (outside neonatal period)
- Umbilical cord bleeding or delayed separation?
- Prolonged bleeding heelprick?
- Hematoma formation (vit K, immunizations?)

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Clinical Evaluation

Bleeding Characteristics		
	Platelet Disorders	Plasma coagulation disorders
Location	Superficial, Mucosal	Deep
Types	Petechiae, Purpura	Hematomas/ecchymoses
Size	Smaller	Larger
Timing	Immediate, mild	Delayed, severe
Example	Menorrhagia, Epistaxis, palatal petechiae	Hemarthroses, soft tissue hematomas

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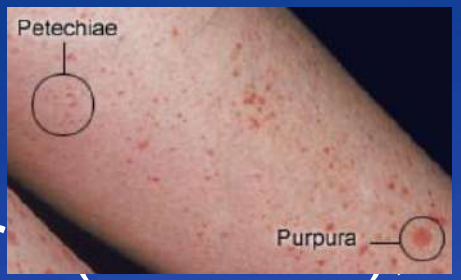
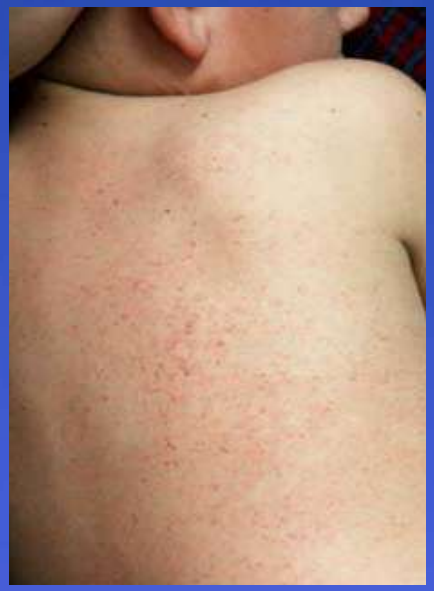
Clinical Evaluation

PHYSICAL EXAMINATION

- Skin and Mucosa
  - Petechiae (1-2mm), Purpur
    Ecchymoses (>10mm)
    -red/purple, non-blanching
    subcutaneous hemorrhage





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Clinical Evaluation

PHYSICAL EXAMINATION

- Skin and Mucosa
  - Telangiectasias
    - permanent dilation of superficial blood vessels
  - Hemangioma
    - typically benign tumor of blood vessels

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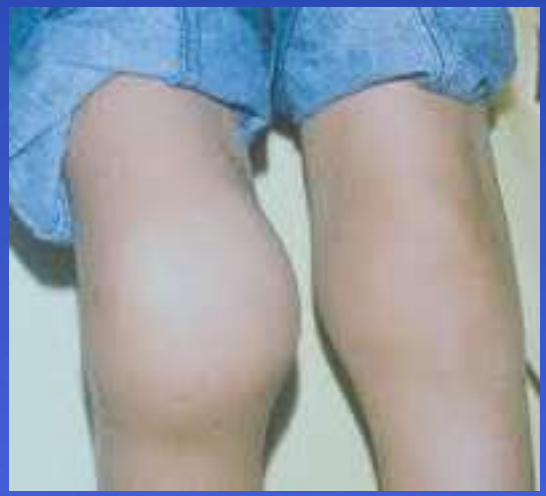
Clinical Evaluation

PHYSICAL EXAMINATION

- Musculoskeletal system
  - Hemarthroses, Hypermobility, skin hyperextensibility



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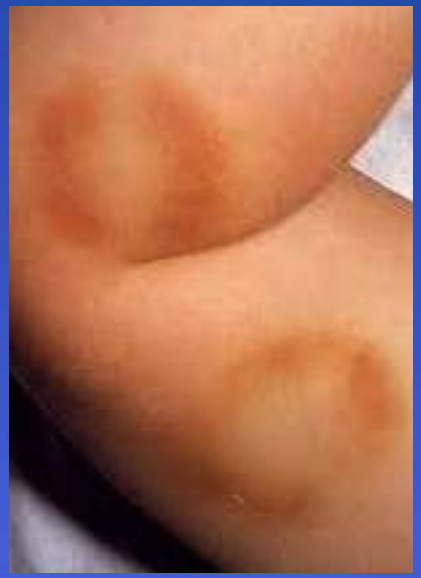
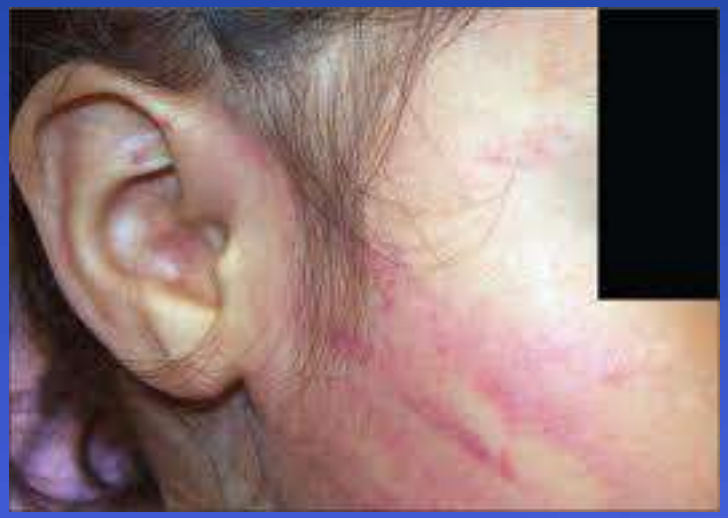
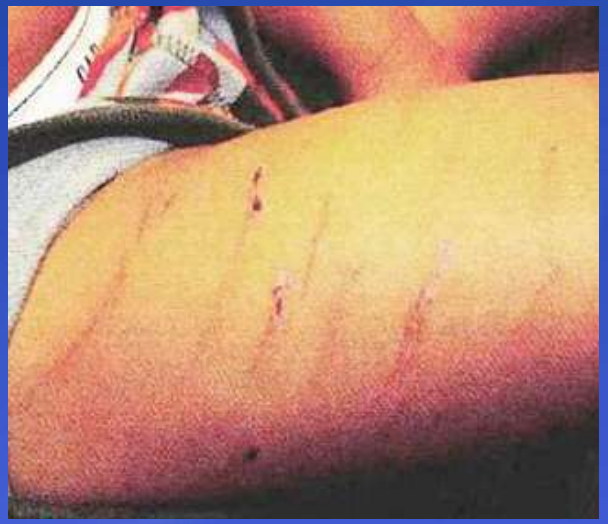
Clinical Evaluation

PHYSICAL EXAMINATION

- Skin and Mucosa
  - Bruising patterns







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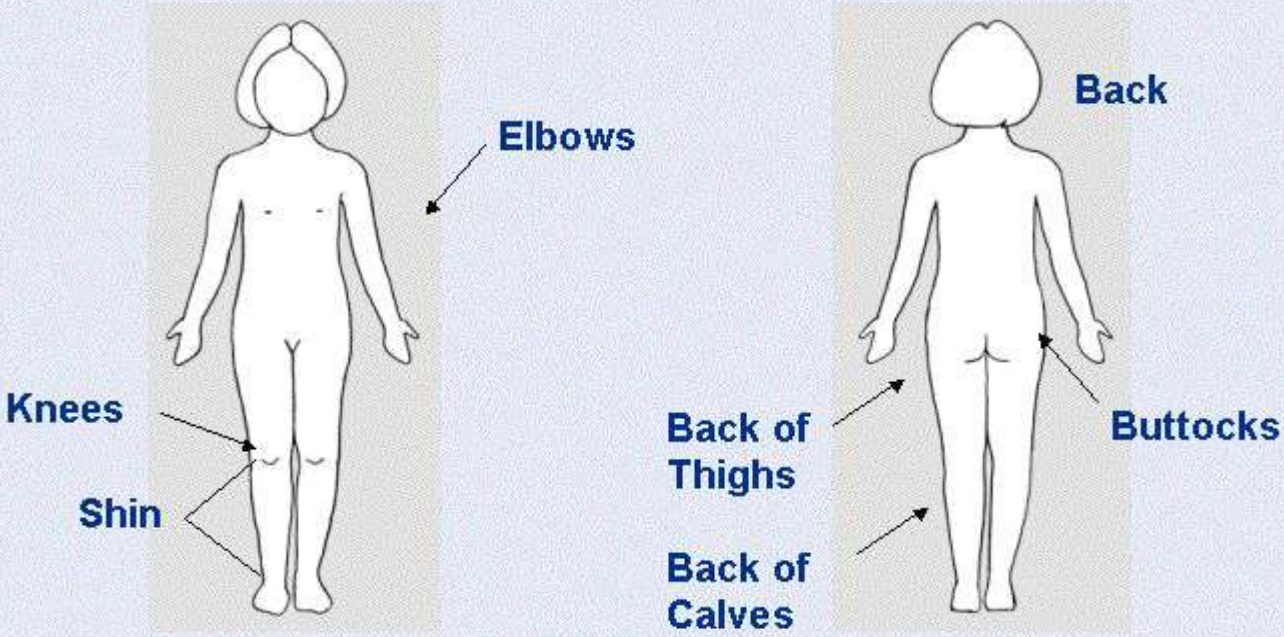
Bruising Areas



https://www.abusewatch.net/child_medimage.php

Clinical Evaluation

- **Red flag abuse**
  - unusual location
  - inconsistent with the injury
  - no explanation offered for the injury
  - inconsistent with the child's developmental level
  - blamed on another child or sibling
  - multiple bruises at various stages of healing
- **Documentation is key**
  - Objective, complete
    - Location, size, color, description
    - Document with medical pictures – Extremely important

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Investigation hemostatic system in children with bruising or bleeding

- CBC and peripheral smear
- PT, aPTT
- Fibrinogen
- TT
- Factor XIII screen
- vWD (factor VIII, von Willebrand antigen, RCo activity)
- Platelet function

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Classification

Inherited	Acquired
Hemophilia A and B	Vitamin K deficiency
von Willebrand Disease	Liver disease
Deficiency factors II, V, VII, X, XI, or XIII	DIC
Dys-, hypo- or afibrinogenemia	Massive transfusion
alpha-2 antiplasmin	Malignancy
PAI-1 deficiency	Coagulation inhibitors
	Platelet (dysfunction, production)
	Munchausen
	Spurious lab tests

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Treatment

- Factor replacement (Factor VIII/IX deficiency)
- Antifibrinolytics (Tranexamic acid, Aminocaproic acid)
- DDAVP
- Cryoprecipitate, Fibrinogen concentrate (RiasTap)
- Recombinant Factor VII
- Hormonal therapy (menorrhagia)
- FFP
- Platelets

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Disseminated Intravascular Coagulation

- DIC: systemic activation of blood coagulation, generation intravascular thrombin and fibrin.

- Three types:
  1. Bleeding: hyperfibrinolysis predominant (e.g. leukemias)
  2. Organ failure type: hypercoagulation (e.g. sepsis)
  3. Major bleeding: hypercoagulation and hyperfibrinolysis (e.g. surgery)

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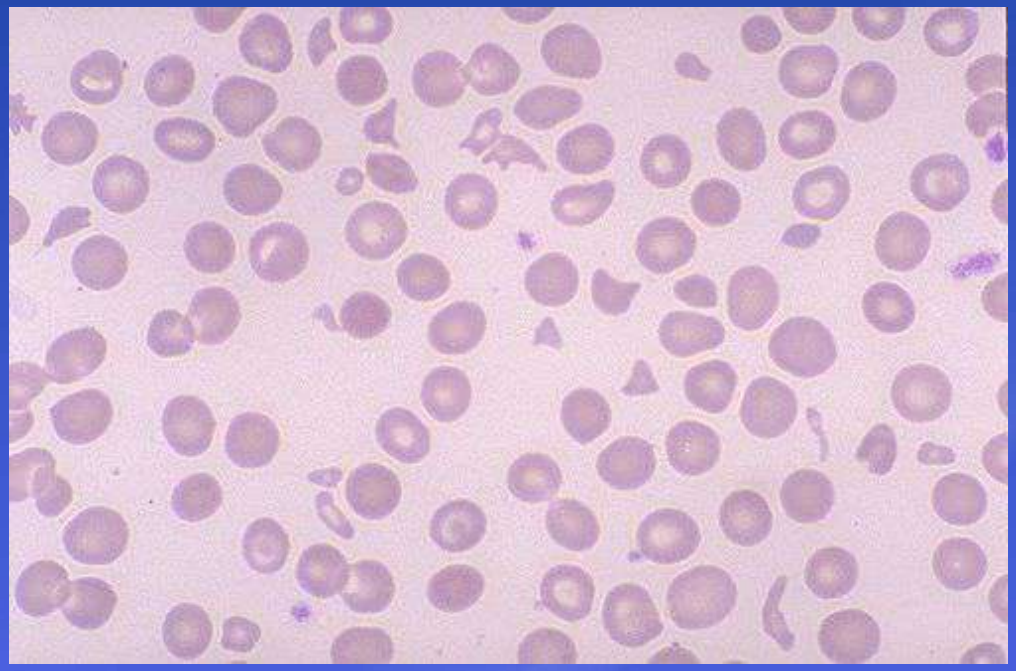
DIC

- Infection
- Malignancy
- Vascular malformation (e.g. hemangioma)



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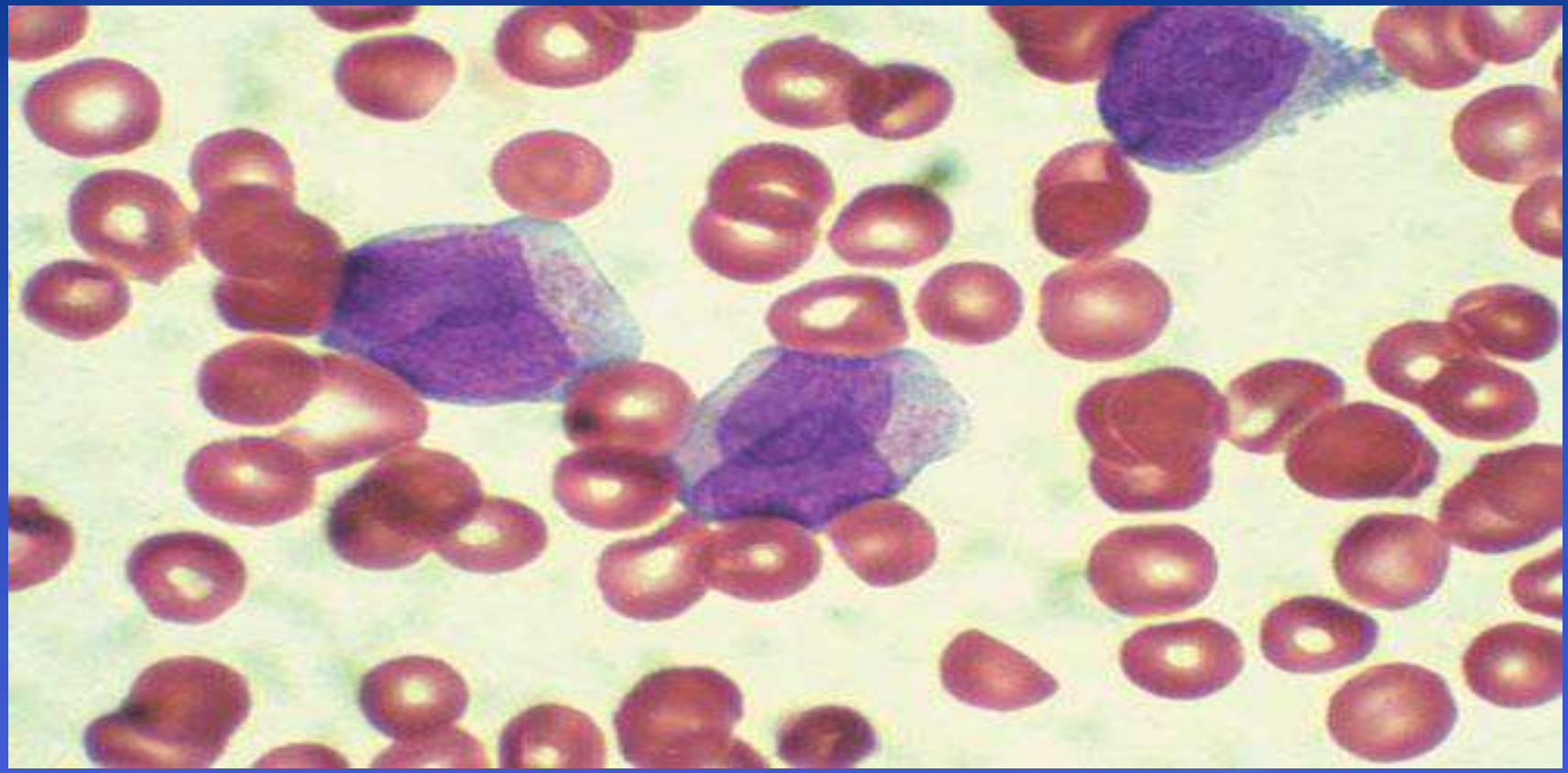
Acute Promyelocytic Leukemia



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http://www.merck.com/mmpe/sf/multimedia/Photo3sec11ch142/t/sec11-ch142-ch142b.html

General guidelines

- Administration red blood cells and platelets patients bleeding or at risk bleeding
- FFP 15 ml/kg (if concerns fluid overload, consider prothrombin concentrates)
- Low fibrinogen: cryoprecipitate or fibrinogen concentrates
- Heparin: only thrombosis predominant DIC

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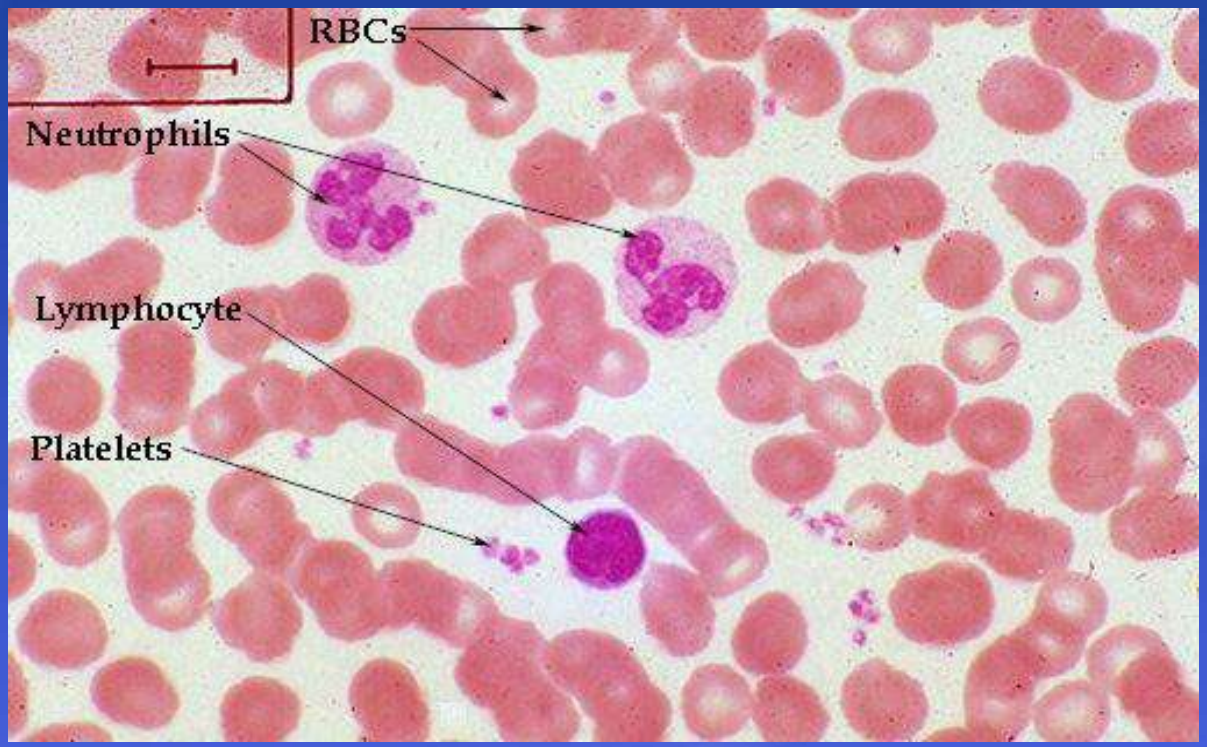
Platelet Disorders

- Thrombocytopenia
  - Platelet count of less than 150,000/microL



Causes of thrombocytopenia

Table 1. Causes of Thrombocytopenia

Increased Platelet Destruction

- Immune-mediated
  - –Immune thrombocytopenic purpura
  - –Neonatal alloimmune thrombocytopenia
  - –Neonatal autoimmune thrombocytopenia
  - –Autoimmune diseases
  - –Drug-induced
- Platelet activation/consumption
  - –Disseminated intravascular coagulation
  - –Hemolytic-uremic syndrome
  - –Thrombotic thrombocytopenic purpura
  - –Kasabach-Merritt syndrome
  - –Necrotizing enterocolitis
  - –Thrombosis
- Mechanical platelet destruction
- Platelet sequestration
  - –Chronic liver disease
  - –Type 2B and platelet-type von Willebrand disease
  - –Malaria

Decreased Platelet Production

- Infection
- Cyanotic congenital heart disease
- Bone marrow failure or infiltrate
  - –Acute lymphoblastic leukemia and other malignancies
  - –Acquired aplastic anemia
  - –Fanconi pancytopenia
- Nutritional deficiencies
- Genetically impaired thrombopoiesis
  - –Thrombocytopenia with absent radii syndrome
  - –Congenital amegakaryocytic thrombocytopenia
  - –Wiskott-Aldrich syndrome
  - –X-linked thrombocytopenia with thalassemia
  - –Giant platelet disorders
  - –Bernard-Soulier syndrome
  - –May-Hegglin/Fechtner/Epstein and Sebastian syndromes

Thrombocytopenia in Infants and Children
Deborah M. Consolini
Pediatrics in Review 2011;32;135
DOI: 10.1542/pir.32-4-135

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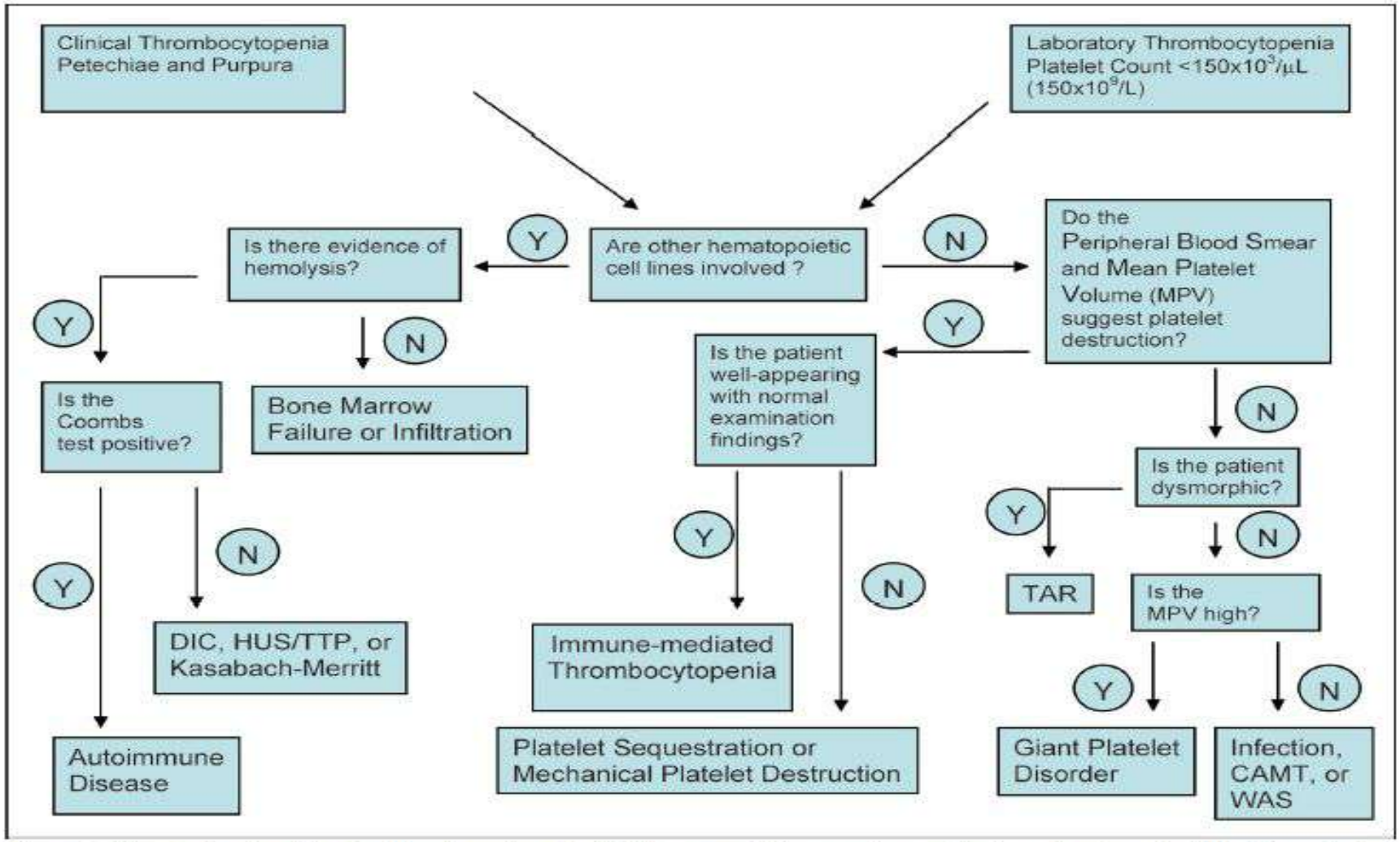

Figure 2. Diagnostic algorithm for thrombocytopenia. CAMT=congenital amegakaryocytic thrombocytopenia, DIC=disseminated intravascular coagulation, HUS=hemolytic-uremic syndrome, TAR=thrombocytopenia with absent radii syndrome, TTP=thrombotic

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Physical findings

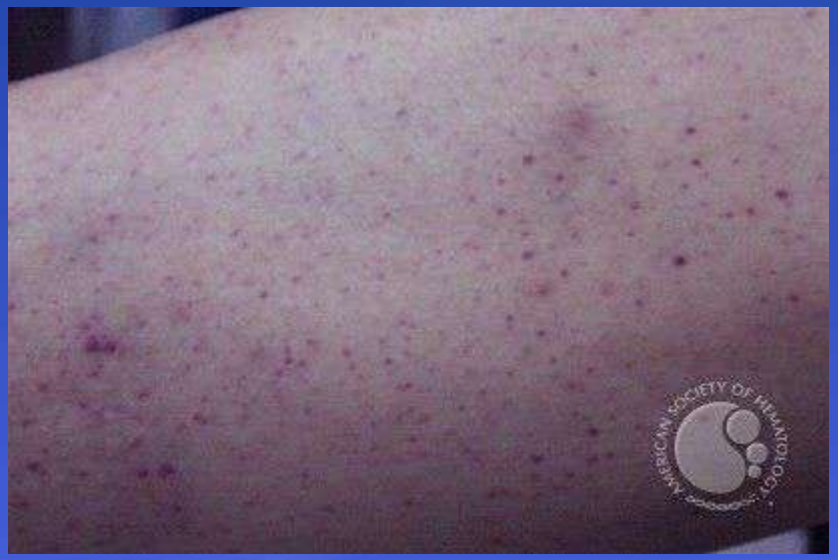

Table 4. Red Flags Suggesting a Diagnosis Other Than Immune Thrombocytopenic Purpura

History

- Fever
- Bone pain
- Weight loss
- Fatigue
- Recent history of infections or vaccinations
- Past medical history of diseases associated with thrombocytopenia (eg, autoimmune disorders, cirrhosis)
- Dietary history suggestive of iron, vitamin B12, or folate deficiency
- Exposure to medications known to be associated with thrombocytopenia
- Travel history to an endemic area for malaria

Physical Examination

- Lymphadenopathy
- Splenomegaly
- Joint swelling
- Short stature
- Limb defects, including radial agenesis and thumb abnormalities
- Cataracts
- Sensorineural hearing loss
- Oral leukoplakia
- Dystrophic nails
- Eczema in male patient
- Frequent infections
- Superficial hemangiomas

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Summary

- ✓ History and physical exam are the best screening tests for bleeding disorders
- ✓ The absence of a family history of bleeding disorders does not exclude the diagnosis of a genetic disorder
- ✓ Thorough evaluation and documentation of bleeding symptoms are essential for identifying cases of non-accidental trauma
- ✓ Use pediatric reference values to assess laboratory findings based on a patient's age
- ✓ Refer to a specialist if concerned about bleeding disorder

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Anemia

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Anemia

- Morphologic classification
  - RBC indices (MCV)
  - Hemoglobin content (MCH)
- Physiologic classification
  - Decreased Production
    - Increased Destruction
  - Blood loss

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History

- Age
  - Newborn
    - Congenital RBC disorder, perinatal loss, immune
  - Age 3-6 months
    - Congenital, RBC aplasia
  - Age >6 months
    - More often acquired (e.g. nutrition, TEC)
- Gender
  - X linked disorders (G6PD)
- Race/Ethnic origin
  - Thalassemia, sickle, Hgb E, G6PD etc.
- Neonatal history
  - Neonatal jaundice? HS, G6PD, ABO incompatibility

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Diet

- Pica
  - Suggestive of iron deficiency.
- What kind of Milk
  - Whole milk (Fe def. if too early)
  - Goat's milk (deficient in Folate)
- Vegan
  - Can be B12 deficient

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Drugs

- Oxidant induced hemolytic anemia e.g. G6PD
- Drug induced megaloblastic anemia e.g. purine and pyrimidine analogs (6 MP, 5 FU)
- Drug and chemical induced aplastic anemia e.g. Chloramphenicol, insecticides, etc

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History of Blood Loss

- GI blood loss
- Menstrual blood loss in teenage girls
- CNS bleeding does not cause anemia outside the newborn period

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Evaluation of Anemia

- Detailed history and physical examination
- Complete blood count
- Determination of the morphologic characteristics based on blood smear, MCV and RDW
- Bone marrow aspiration
- Additional tests for specific type of anemia

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Blood Film

- Exam for red cell morphology
- Exam for basophilic stippling and red cell inclusions
- Exam of other cell lines

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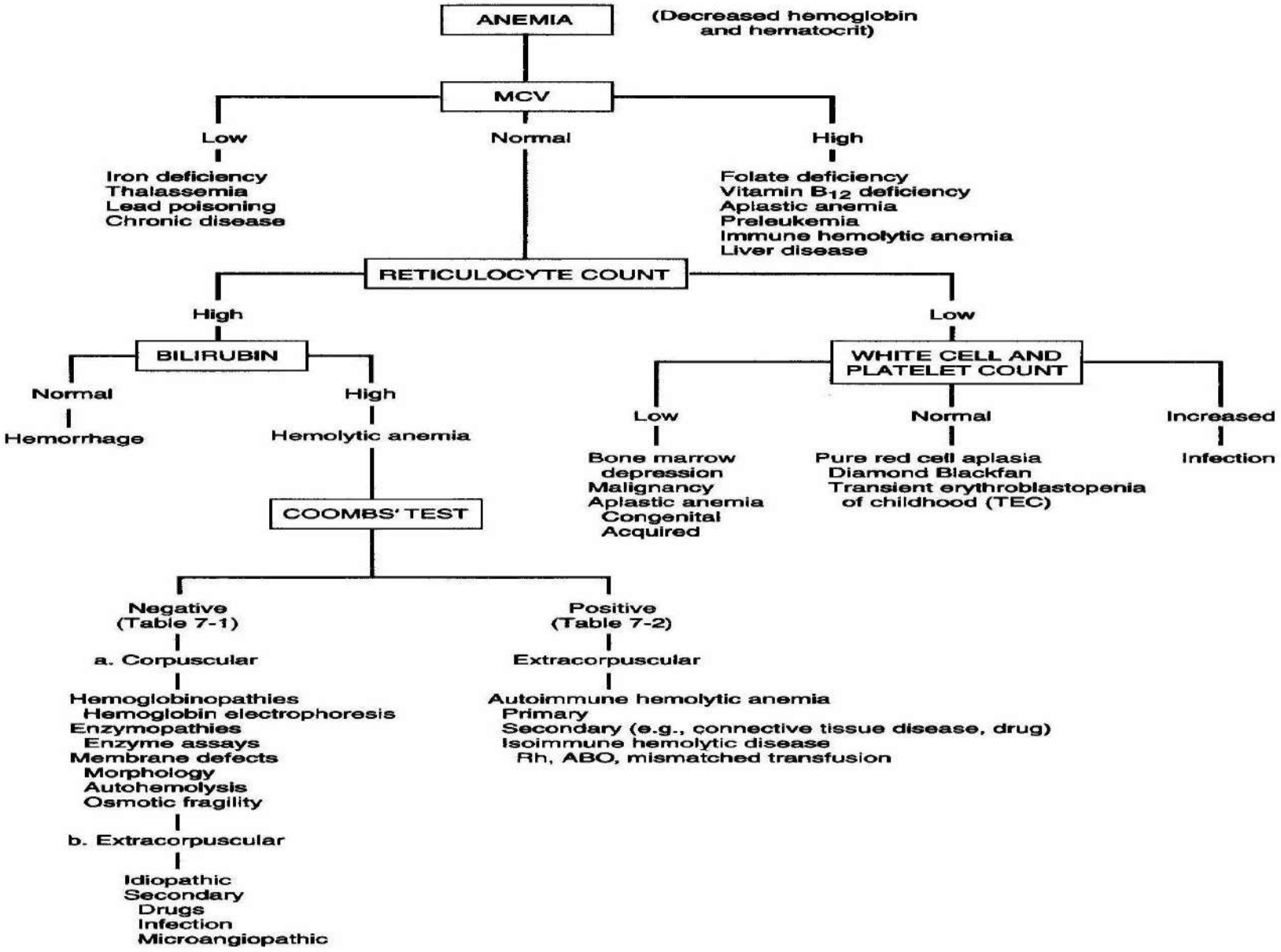

Normal Values of Hemoglobin

TABLE 10–1. Values (Normal Mean and Lower Limits of Normal) for Hemoglobin, Hematocrit, and Mean Corpuscular Volume (MCV) Determinations

	Hemoglobin (g/dL)		Hematocrit (%)		MCV (μ^3)	
Age (yrs)	Mean	Lower Limit	Mean	Lower Limit	Mean	Lower Limit
0.5–1.9	12.5	11.0	37	33	77	70
2–4	12.5	11.0	38	34	79	73
5–7	13.0	11.5	39	35	81	75
8–11	13.5	12.0	40	36	83	76
12–14:						
Female	13.5	12.0	41	36	85	78
Male	14.0	12.5	43	37	84	77
15–17:						
Female	14.0	12.0	41	36	87	79
Male	15.0	13.0	46	38	86	78
18–49:						
Female	14.0	12.0	42	37	90	80
Male	16.0	14.0	47	40	90	80

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Other tests…

- Mentzer index: MCV/RBC mass
- >13 iron deficiency
- <13 Beta thalassemia
- Hemoglobin electrophoresis: rule out hemoglobinopathy (alpha Thal trait needs gene sequencing)
- Coombs, creatinine, bilirubin, LDH, haptoglobin, osmotic fragility, TSH

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Management

- Transfusion: if severe and symptomatic
- Consider diagnostic evaluations prior to transfusion
- If anemia not symptomatic, treat underlying problem (e.g. iron in iron def anemia; prednisone: autoimmune hemolytic anemia).

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