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Hematologic Disorders

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Overview

- Splenic
- Peripheral Blood
- Bone marrow
- Genetic Disorder
- Myeloproliferative

True or False ???

Therapeutic procedures cures the
underlying disease disorder



Goals of Splenectomy

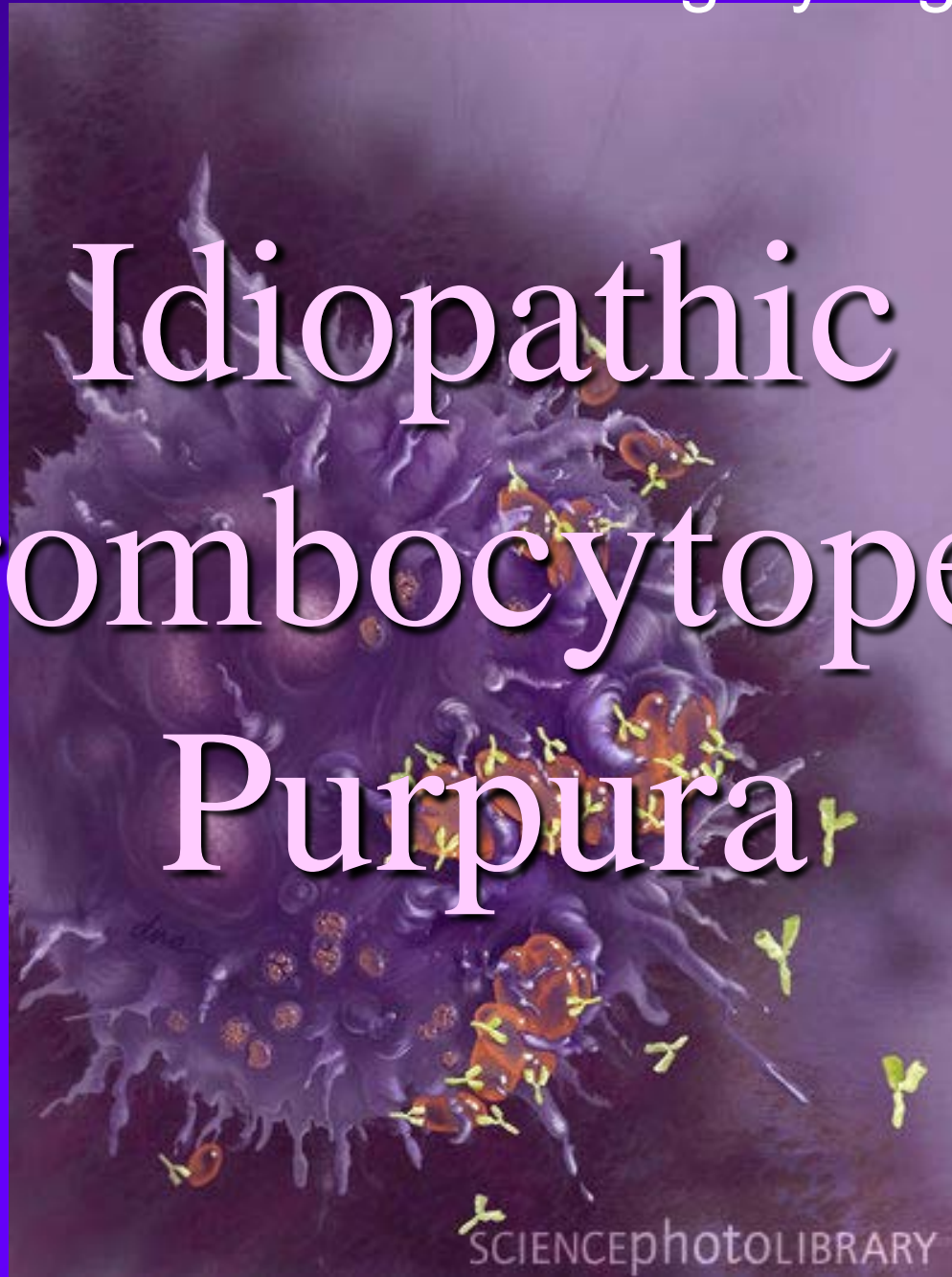
- Ameliorate the pathologic effects of splenic sequestration and symptomatic splenomegaly
- Correct the hematologic abnormality
- Aid in diagnosis and staging
 - Rare

Autoimmune/Idiopathic Disorders

What is the most common indication for splenectomy in the US?

- A) Felty Syndrome
- B) Thrombotic Thrombocytopenic Purpura
- C) Autoimmune Hemolytic Anemia
- D) Idiopathic Thrombocytopenic Purpura
- E) Sarcoidosis

Idiopathic Thrombocytopenic Purpura



A 43-year-old man has thrombocytopenia, ecchymoses, and a history of melena. His primary doctor suspects that he might have idiopathic thrombocytopenia purpura (ITP). Which of the following is true about this condition?

- **A** It is characterized by a low platelet count, mucosal hemorrhage, normal bone marrow, and an enlarged spleen.
- **B** It is caused by splenic overproduction of IgM, which attacks the platelet membrane and causes platelet destruction.
- **C** The bone marrow often hypertrophies to counteract the increased platelet destruction.
- **D** It affects young men more commonly than women.
- **E** Diagnosis requires exclusion of other causes of thrombocytopenia.

The patient previously described undergoes a complete work-up and ITP is diagnosed. Which of the following about the treatment of ITP is true?

- **A** Platelet transfusions are best given before ligation of the splenic artery.
- **B** Initial medical therapy includes steroid therapy with the possible addition of intravenous IgG.
- **C** Initial response rates to medical therapy in adults are as high as 75%, with permanent cure from medical therapy being achieved in greater than 50%.
- **D** Spontaneous resolution is rare in children.
- **E** Splenectomy is indicated if ITP does not improve after 1 year of steroid therapy or if thrombocytopenia recurs following steroid taper.

Mechanism of ITP



Clinical Presentation of ITP



Diagnosis of Exclusion

- Spleen is of normal size
- Megakaryocytes



Illnesses

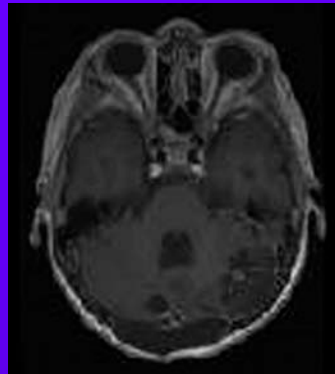
- HIV
- SLE
- Antiphospholipid Ab Syndrome
- Hepatitis C
- Lymphoproliferative Disorders

Medication

- Cocaine & gold
- Antibiotics & antiinflammatories
- Heparin, quinidine, abciximab

ITP in Children

- Young age (<5 yo)
- Sudden onset of petechiae or purpura
- May follow infectious illness: days to weeks
- Self-limiting
 - >70% will resolve
- Intracranial hemorrhage
 - Plt <20,000/mm³



Management of ITP in Children

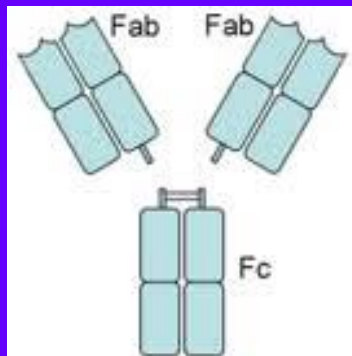
➤ Medical

➤ Observation

➤ IV IG

➤ Prednisone

➤ 4 mg/kg x 4 days



➤ Splenectomy

➤ Thrombocytopenia

➤ >1 year

➤ Failures of medical therapy

➤ Severe thrombocytopenia

➤ Severe or life-threatening
bleeding

➤ Rare!

ITP in Adults

- Insidious onset
- Treatment begins:
 - Plt 20,000 – 30,000/mm³
 - 50,000/mm³ w/significant mucosal bleeding



Medical Management of ITP in Adults

➤ Steroid

➤ 1 to 1.5 mg/kg/day

➤ 3 qwwka

➤ Taper when response

➤ 50-75% response rate

➤ 15-20% long-term
response

➤ IV IG

➤ Internal bleeding w/plt

<10,000/mm³

➤ Adjunct to steroid therapy

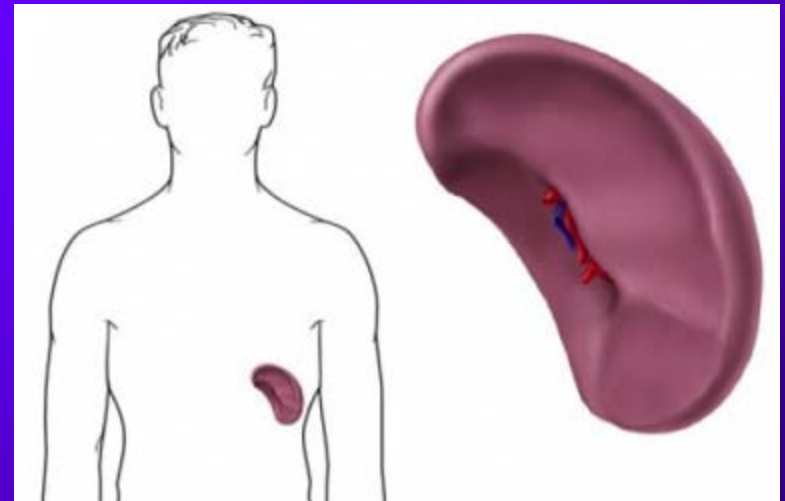
➤ Extensive purpura

➤ High risk for bleeding

w/continued low plt despite
steroid therapy

Splenectomy in ITP in Adults

- Plt counts remain low after 6-8 wks of steroid therapy
- Failure of medical therapy
- Relapse
- Unwanted side effects from prolonged steroid use
- 75-85% permanent response
- **Platelet transfusion**
 - Peri-op bleeding
 - Plts $<10,000/\text{mm}^3$
 - Held until after splenic artery ligation!!!



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- **D** It affects young men more commonly than women.
- **E** Diagnosis requires exclusion of other causes of thrombocytopenia.

Idiopathic thrombocytopenia purpura is a disorder of increased platelet destruction caused by autoantibodies to platelet membrane components. This results in platelet phagocytosis in the spleen, and the bone marrow does not adequately compensate for this increased destruction. Although ITP is characterized by a low platelet count, mucosal hemorrhage, and relatively normal bone marrow (not hyperactive), the spleen is not enlarged. The autoantibodies are IgG antibodies, not IgM, directed against the platelet fibrinogen receptor. The mechanism underlying the use of intravenous IgG for the treatment of ITP is that IgG saturates the fibrinogen receptors so that they will not bind and thus destroy platelets. This autoimmune disorder affects women more commonly than men. A diagnosis of ITP requires exclusion of other potential causes of thrombocytopenia such as drugs, myelodysplasia, thrombotic thrombocytopenia purpura (TTP), systemic lupus erythematosus, lymphoma, and chronic disseminated intravascular coagulation.

The patient previously described undergoes a complete work-up and ITP is diagnosed. Which of the following about the treatment of ITP is true?

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- **D** Spontaneous resolution is rare in children.
- **E** Splenectomy is indicated if ITP does not improve after 1 year of steroid therapy or if thrombocytopenia recurs following steroid taper.

Initial therapy for **idiopathic thrombocytopenia purpura** is medical and consists of **high-dose corticosteroids, usually prednisone, 1 mg/kg/day**. The goal of therapy is to induce remission and achieve platelet counts higher than $100,000/\text{mm}^3$. This is effective initially in approximately **75% of patients**, usually within **1 week, but up to 3 weeks** of therapy may be required. Treatment is generally initiated when platelet counts fall to less than $20,000$ to $30,000/\text{mm}^3$ or for individuals with platelet counts of less than $50,000/\text{mm}^3$ and mucous membrane bleeding or significant risk factors for bleeding. Although the initial response to treatment is good, only **15% to 25% of patients achieve a lasting response**. If platelet counts remain low despite steroid therapy, intravenous IgG is indicated at doses of 1 g/kg for 2 days. In most cases, this increases platelet counts within 3 days. In contrast to adults, **70% to 80% of children will experience spontaneous permanent remission**. **Splenectomy is considered if platelet counts remain below $10,000/\text{mm}^3$ after 8 weeks of therapy**, regardless of whether bleeding is present. Splenectomy is also recommended for those who experience a relapse after initial success with glucocorticoid treatment or who have significant morbidity from continued high-dose steroids. Intracranial bleeding in patients with ITP is usually managed by prompt administration of intravenous IgG followed by splenectomy. Finally, women in their second trimester of pregnancy are offered splenectomy if they have platelet counts of less than $10,000/\text{mm}^3$ or bleeding with counts of less than $30,000/\text{mm}^3$ despite appropriate medical therapy. Platelet transfusion during splenectomy should be withheld until **after ligation of the splenic artery**, if possible, to prevent platelet consumption.



What is the likely diagnosis of a 17 yo female w/fever, purpura, hemolytic anemia, and hematuria w/renal insufficiency?

- A) Viral illness
- B) Thrombotic Thrombocytopenic Purpura
- C) Autoimmune Hemolytic Anemia
- D) Idiopathic Thrombocytopenic Purpura
- E) Henoch Schonlein Purpura

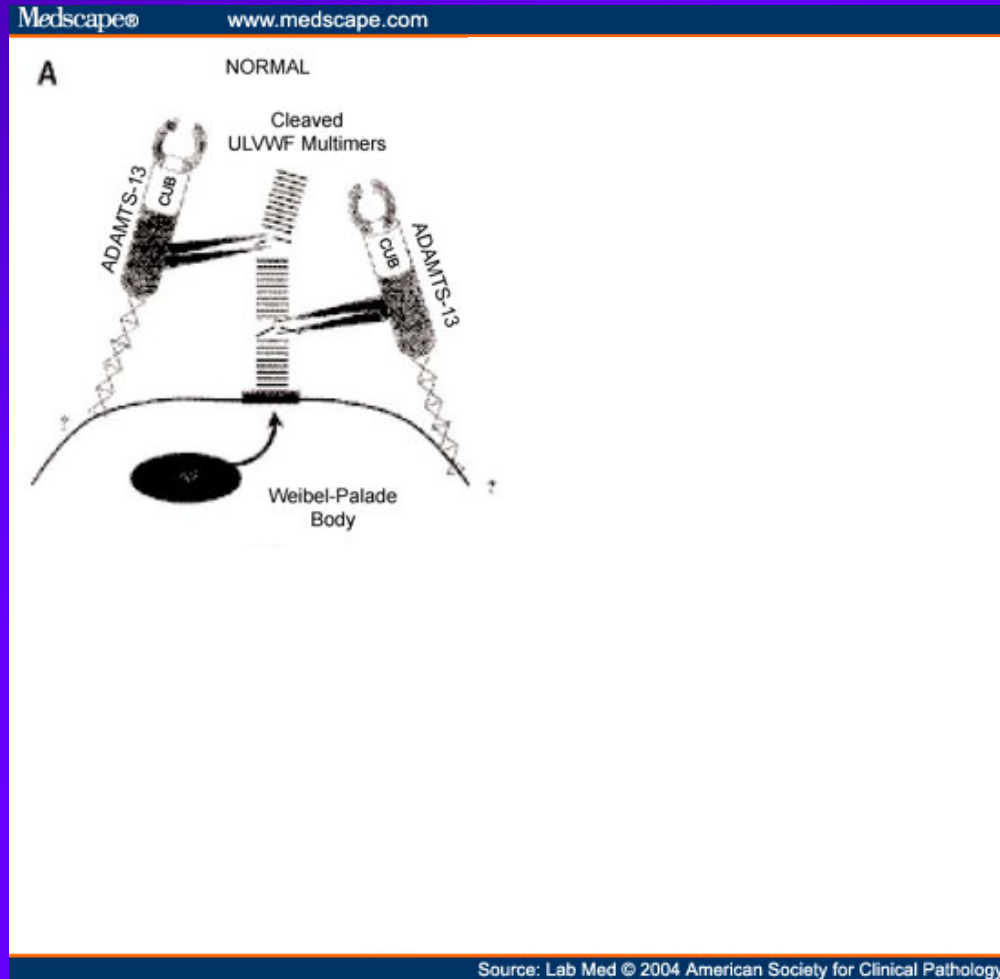


Thrombotic Thrombocytopenic Purpura

A 17-year-old girl is evaluated for fever, purpura, hemolytic anemia, and hematuria with renal insufficiency. Focal neurologic defects soon develop, and head computed tomography (CT) demonstrates an intracranial hemorrhage. Which of the following is true regarding this condition?

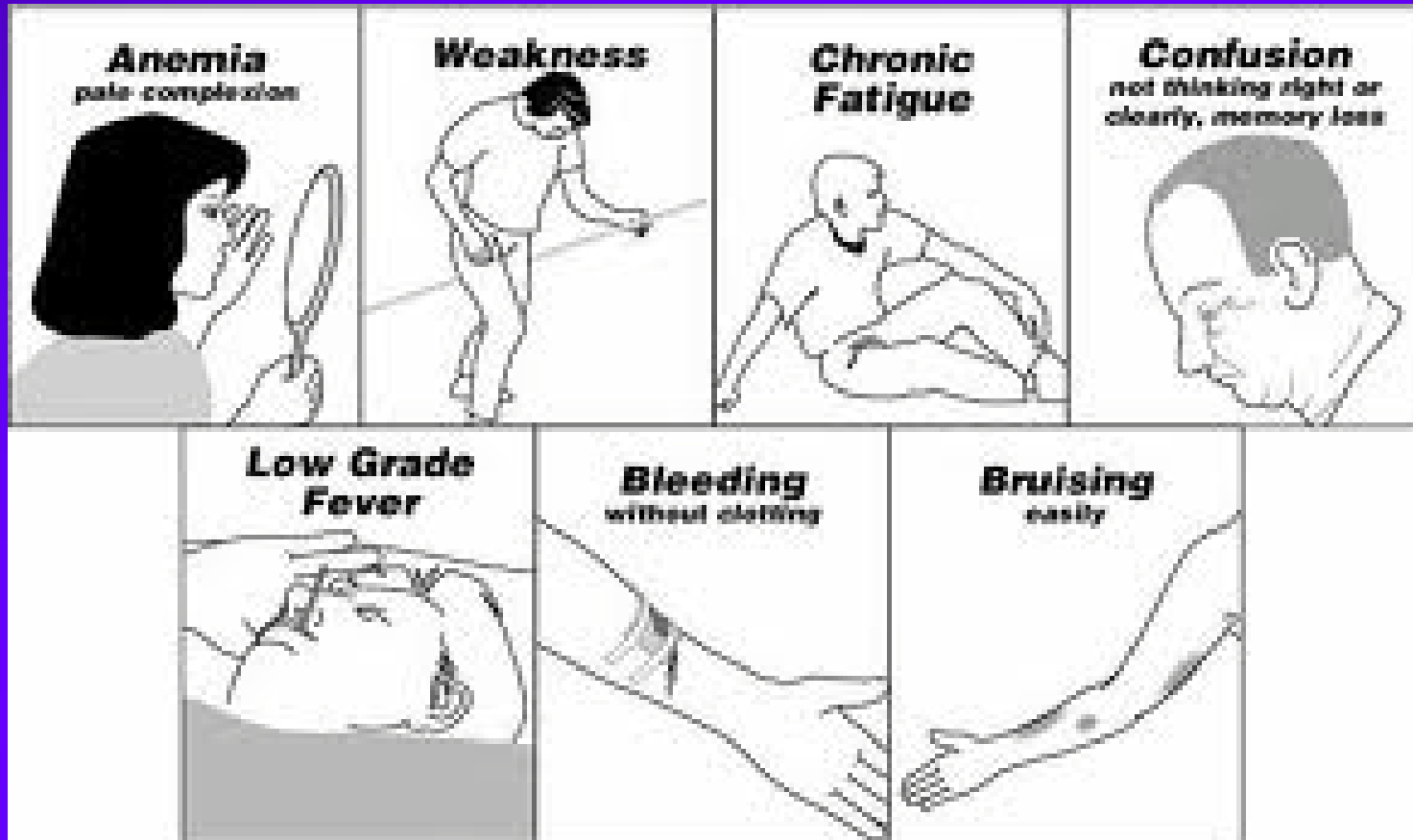
- **A** Splenectomy is curative in most patients and should be considered after a trial of steroids.
- **B** It is caused by hyaline membranes that form within arterioles and capillaries and resultant platelet aggregation.
- **C** Plasmapheresis is considered as a last resort when other therapy fails.
- **D** Administration of platelets can result in clinical improvement, thereby allowing splenectomy to be delayed.
- **E** Even with rapid progression, the prognosis is generally good because of the high success of medical therapy with splenectomy for salvage.

Mechanism of TTP



Clinical Presentation of TTP

- Damage to the endothelium triggers platelet deposition in small arterioles and capillaries
- Microvascular thrombotic episodes



Symptomatology of TTP

➤ Petechiae

➤ lower extremities

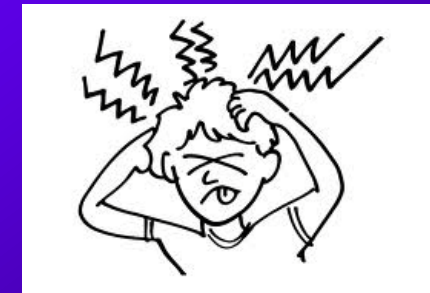
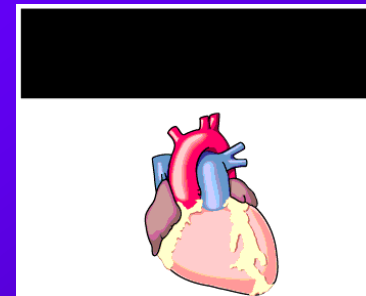
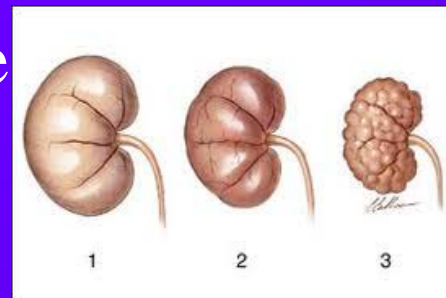
➤ Fever, myalgia, & fatigue

➤ Neurological Symptoms

➤ Headache, mental status changes, seizures, coma

➤ CHF or cardiac arrhythmias

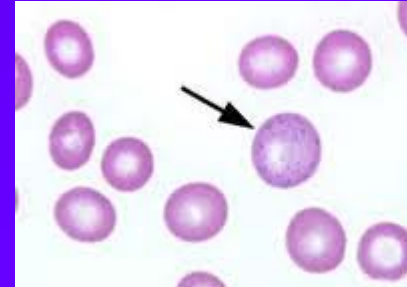
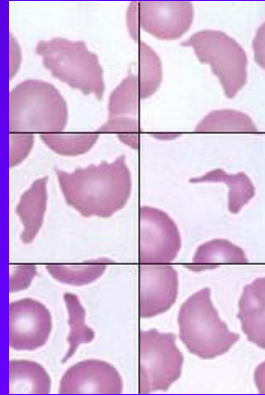
➤ Renal failure



Diagnosis & Etiology of TTP

➤ Peripheral Blood Smear

- Schistocytes
- Nucleophilic red blood cells
- Basophilic stippling



Illnesses

- Pregnancy
- Postpartum

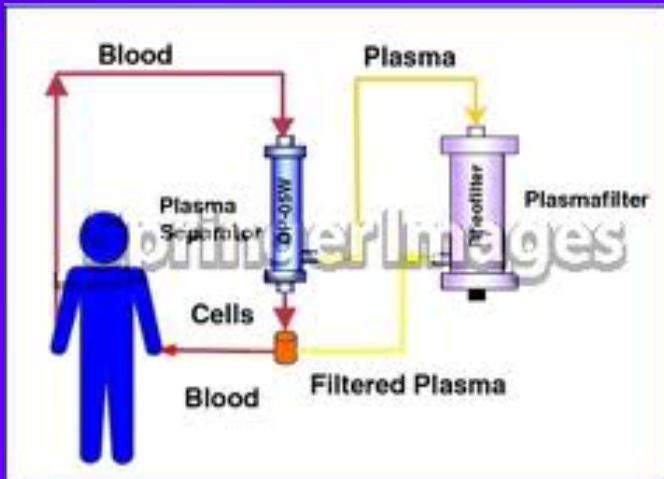
Medication

- Ticlopidine
- Clopidogrel

Management of TTP

➤ Medical

- Daily plasmapheresis
- Daily FFP



➤ Splenectomy

- Frequent relapses
- Prolongs relapse-free interval when in combo w/high-dose steroid therapy
- Response rate: 40%

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- **D** Administration of platelets can result in clinical improvement, thereby allowing splenectomy to be delayed.
- **E** Even with rapid progression, the prognosis is generally good because of the high success of medical therapy with splenectomy for salvage.

This patient has **thrombotic thrombocytopenic purpura**. The disease is characterized by **occlusion of arterioles and capillaries by hyaline deposits of aggregated platelets and fibrin**. **First-line therapy is plasmapheresis**. Fresh frozen plasma and high-dose corticosteroids may be used to control bleeding. **Splenectomy is not curative** and is considered only for salvage therapy. **Mortality rates in patients with TTP can approach 50%**, mostly from intracranial hemorrhage or renal failure. The disease can have a rapidly fulminant course. Most long-term survivors of TTP have undergone splenectomy. **Platelet transfusion does not control the bleeding**; therapy should be focused on high-volume plasmapheresis.

Summary of TTP

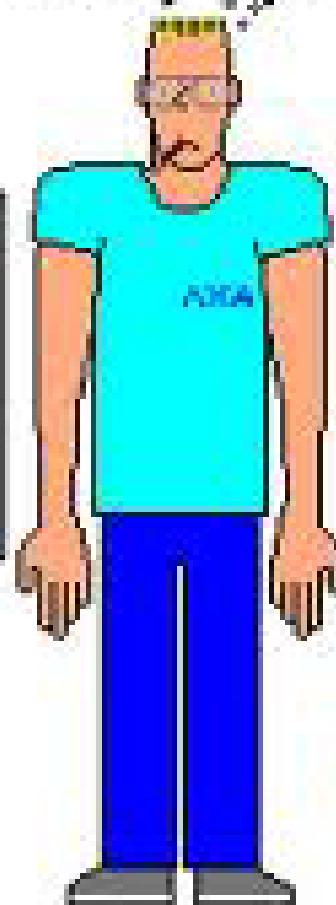
Thrombotic Thrombocytopenic Purpura

Easy to diagnose and treat -- if you think of it.

The 5 Clinical Features

thrombocytopenia
red cell fragmentation
fever
transient neurologic deficits
kidney failure

Untreated, TTP is deadly.
Treatment usually involves replacing the plasma repeatedly until the patient recovers.

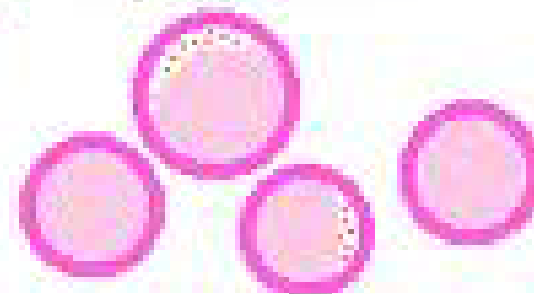


The usual problem, loss of a protein that removes activated VIII-R, is just now being figured out.

RBC fragments...



Essential anatomic lesion: Widespread thrombi made mostly of platelets & vWF



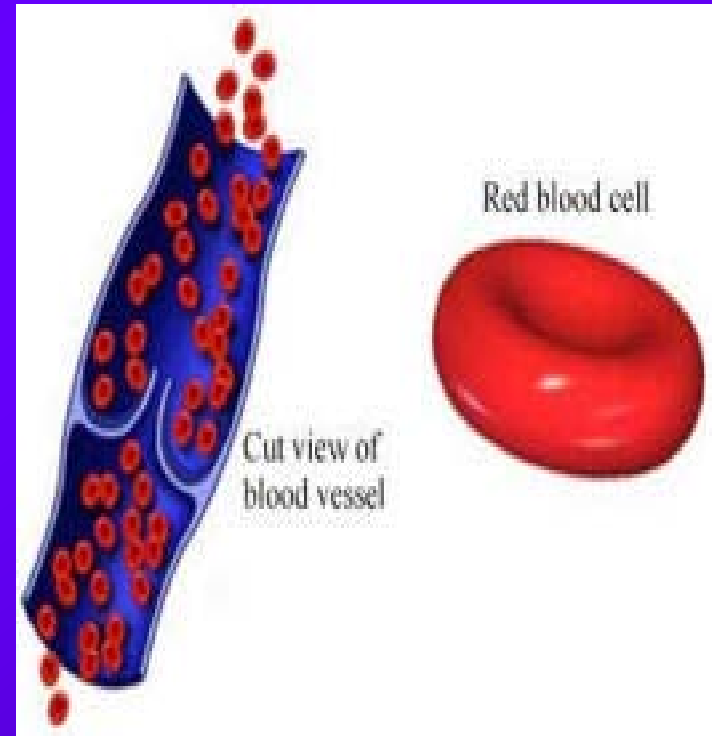


A microscopic image showing a dense field of red blood cells. The cells are spherical and have a reddish-brown color. Some cells are in focus, showing their characteristic biconcave shape. The background is dark and slightly blurred, emphasizing the individual cells.

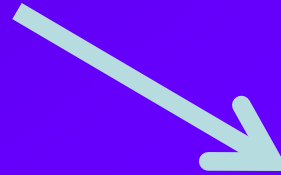
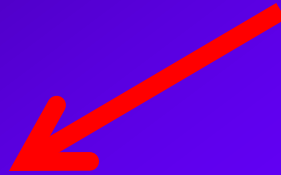
Autoimmune Hemolytic Anemia (AIHA)

Presentation of AIHA

- Autoantibodies are formed & directed against red blood cell antigens
- Signs & Symptoms of anemia
- Physiology of red blood cells
 - Sequestered by macrophages
 - Destroyed in periphery
- Etiology
 - Idiopathic
 - Infectious
 - SLE
 - Leukemia



Types of AIHA



➤ Warm Autoimmune
Hemolytic Anemia

➤ Cold autoantibody
syndromes

➤ Cold agglutinin
syndrome

Warm AIHA

- IgG autoantibodies react optimally at 37°C
- Peak incidence at 40-70 yo
- Children
 - Self-limited: 2-3 mo
 - S/p viral illness
- Diagnosis on clinical findings
 - + peripheral blood smear
 - Direct antiglobulin test



Management of Warm AIHA

➤ Medical

- High-dose steroids
- Taper to lowest dose to control hemolysis
- Children respond better than adults

➤ Splenectomy

- Failed remission in 3 wks
- Hb can't be maintained by low dose steroids
- Response rate: 60-80% w/i 2 wks of splenectomy
- 50% will require low-dose steroids (15mg/day)

Cold Agglutinin Syndrome

- IgM autoantibodies react optimally at 0-5°C
- 15-20% of AIHA
- Etiology
 - Infectious process: EBV
 - Lymphoproliferative disorder
- Raynaud phenomenon



Management of Cold agglutinin

➤ Medical

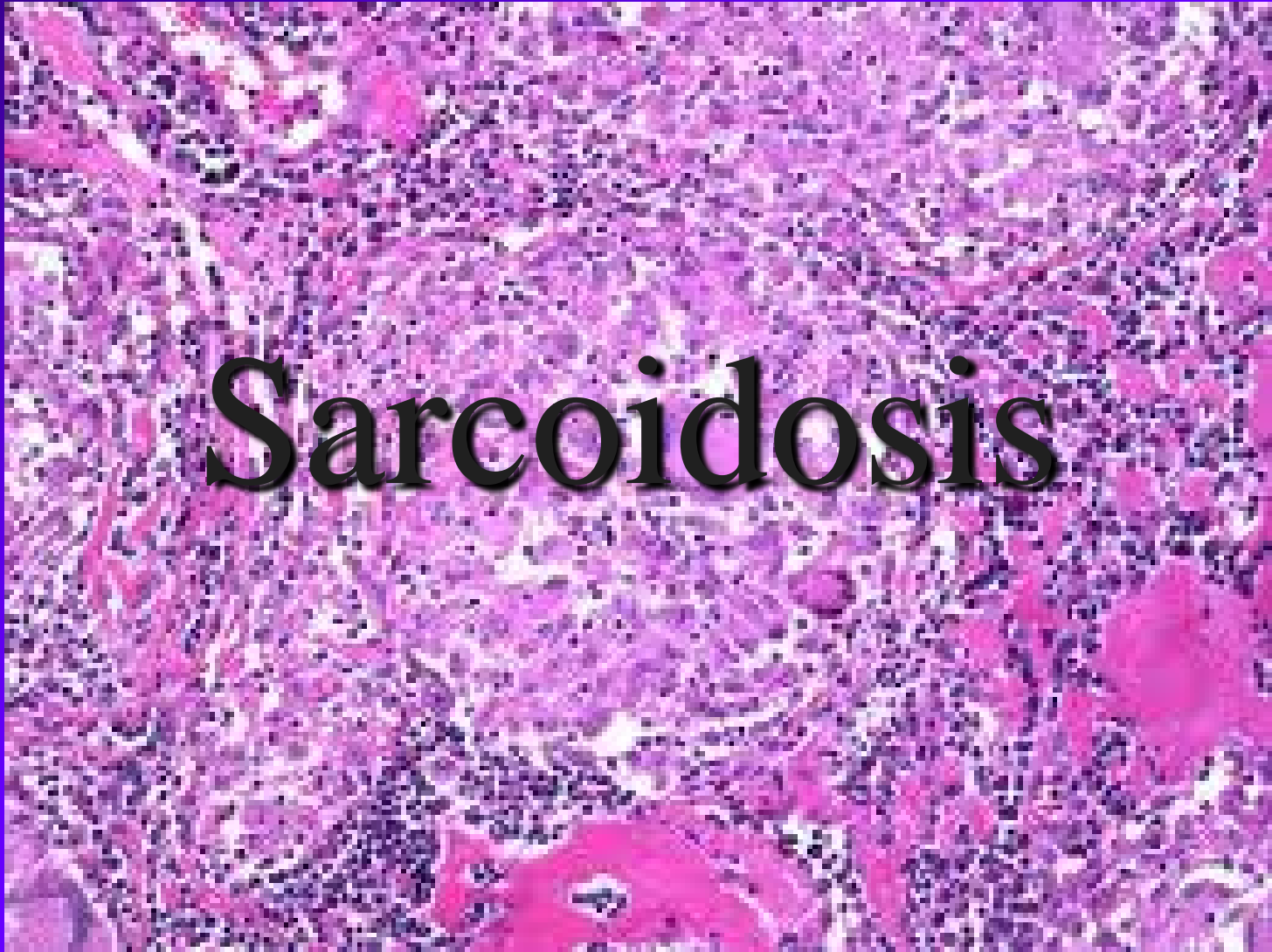
- Avoid cold
 - Stay indoors
 - Wear warm clothing
- Alkylating agents
 - Chlorambucil
 - Cyclophosphamide
- Plasmapheresis

➤ Splenectomy

- Not indicated!!!
- Erythrocytes are destroyed in the liver & not spleen



Sarcoidosis



A 56-year-old African-American man with a history of lung disease is referred to your office for evaluation of an abnormality seen in his spleen on abdominal CT. He also has a history of sarcoidosis. Which of the following is not true about splenic involvement in his case?

- **A** One fourth of patients have splenomegaly from granulomatous involvement of the spleen.
- **B** Not all patients who have splenomegaly experience thrombocytopenia.
- **C** Splenic rupture can occur as a result of granulomatous involvement of the spleen.
- **D** Caseating granulomas are the hallmark of sarcoidosis.
- **E** Patients with active sarcoidosis may have elevated levels of angiotensin-converting enzyme, which may be secreted by cells within the granuloma.

Splenic Sarcoidosis

- Non-caseating granulomatous disease
- 90% have primary lung involvement
- Splenic involvement usually part of multi-organ sarcoidosis
 - Splenomegaly: 40%
 - Massive splenomegaly: 3%
- Treatment:
 - Corticosteroids or methotrexate
- Splenectomy
 - Splenomegaly, intractable pain, hematologic sequestration



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- **D** Caseating granulomas are the hallmark of sarcoidosis.
- **E** Patients with active sarcoidosis may have elevated levels of angiotensin-converting enzyme, which may be secreted by cells within the granuloma.

Sarcoidosis is a disease that is characterized by **noncaseating granulomas**. One quarter of patients will have **granulomatous involvement of the spleen**, although bilateral lung involvement is even more common. Granulomas may also be found in the liver. **Splenic involvement can lead to splenomegaly, but of those affected, only 20% have hypersplenism** (increased hemolytic function of the spleen resulting in a deficiency of one or more peripheral blood elements, hypercellularity of the bone marrow, and splenomegaly). Thrombocytopenia usually resolves following splenectomy. **Complications of granulomatous involvement of the spleen include splenic rupture, anemia, and neutropenia.** **Epithelial cells within the sarcoid granulomas may produce angiotensin-converting enzyme**, thereby resulting in elevated serum levels of this enzyme.

Felty's Syndrome



A 49-year-old woman with Felty's syndrome undergoes successful splenectomy. Several years after surgery, examination of her peripheral blood smear would reveal which one of the following to be true?

- **A** Howell-Jolly bodies, which are suggestive of the presence of an accessory spleen
- **B** Stippling, spur cells, and target cells because of the lack of filtration
- **C** High levels of properdin and tuftsin
- **D** No change in the level of antibodies needed to clear organisms as in the presplenectomy state
- **E** Red blood cells undergoing maturation more quickly.

Felty's Syndrome

- Rheumatoid arthritis
- Unexplained neutropenia
- Splenomegaly
- HLA DR4 antigen: 85%
- Treatment
 - Low-dose methotrexate
 - Disease-modifying antirheumatic drugs
- Splenectomy
 - Medical treatment failure w/recurrent infections or severe neutropenia



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Howell-Jolly bodies are abnormal cytoplasmic inclusions within red blood cells. They are seen in individuals who have undergone **splenectomy** because normally they are removed by a functioning spleen, and thus their absence would suggest the presence of an **accessory spleen**. **Stippling, spur cells, and target cells are all functionally altered erythrocytes that are normally cleared from the circulation by the spleen and thus are commonly seen following splenectomy.** Properdin and tuftsin are important opsonins **manufactured in the spleen**. Properdin helps initiate the alternative pathway of complement activation, which is particularly useful for fighting encapsulated organisms. Tuftsin enhances the phagocytic activity of granulocytes. Asplenic individuals lack the ability to produce these substances. The spleen is the initial site of IgM synthesis in response to bacteria. Without this primary defense mechanism, asplenic individuals **require increased levels of antibodies to clear organisms relative to the presplenectomy state.** **Erythrocytes do not undergo maturation more quickly** after splenectomy. As part of its “pitting” function, the spleen removes cytoplasmic inclusions (particles such as nuclear remnants [Howell-Jolly bodies], insoluble globin precipitates [Heinz bodies], and endocytic vacuoles) from within circulating red blood cells. **Felty's syndrome** is an uncommon disorder marked by splenomegaly, neutropenia, and rheumatoid arthritis. Patients may have thrombocytopenia and anemia, with a predisposition to infections. Splenectomy in patients with Felty syndrome is beneficial in correcting the anemia and neutropenia associated with this syndrome.

Red Blood Cell Disorders



What is the most common red blood cell disorder in Europe and North America?

- A) Hereditary Elliptocytosis
- B) Hereditary Pyropoikilocytosis
- C) Hereditary Spherocytosis
- D) Hereditary Stomatocytosis
- E) Hereditary Xerocytosis
- F) What's a Red Blood Cell Disorder?

Hereditary Spherocytosis (HS)

A microscopic image of red blood cells, showing several spherocytes (smaller, spherical cells) and some normal biconcave disc-shaped cells. The background is a reddish, slightly blurred field of cells.

HEREDITARY SPHEROCYTOSIS

A 10-year-old boy is found to have an abnormal complete blood count notable for an elevated mean cell hemoglobin concentration, an elevated red cell distribution width, and reticulocytosis. On examination of his peripheral smear, the red blood cells exhibit a lack of central pallor and loss of the usual biconcave shape, and the cells are fairly uniform in size and shape. Which of the following is true regarding this condition?

- **A** It is usually transmitted as an autosomal recessive disorder and causes a membrane abnormality that results in decreased osmotic fragility.
- **B** Splenectomy can decrease the incidence of secondary complications such as jaundice, pigmented gallstones, and anemia.
- **C** Surgery should be delayed until after the age of 10 because of the risk for overwhelming post-splenectomy sepsis in younger patients.
- **D** It is less severe than other heredity membrane disorders, including pyruvate kinase deficiency, sickle cell anemia, thalassemia, and elliptocytosis, and less likely to require splenectomy than these conditions.
- **E** It is associated with a small spleen.

Partial vs total splenectomy in children with hereditary spherocytosis...

- **A** is associated with persistent anemia
- **B** is associated with a higher future risk of cholelithiasis
- **C** is associated with splenic regrowth that predicts failure
- **D** is associated with a shorter postoperative length of stay
- **E** will later require completion splenectomy

Physiology of HS

- Deficiency of cytoskeletal protein spectrin & ankyrin
 - Loss of cell membrane surface area
 - Sphering of RBCs
 - Increased osmotic fragility & decreased deformability
 - Impairs passage of RBC through splenic pulp
 - Premature destruction of spherocytes
- Autosomal Dominant
 - 75% will have family member
- Autosomal recessive variant (rare)
 - More severe hemolytic anemia



➤ Mild cases:

- Asymptomatic or mild jaundice

➤ Severe cases:

- Anemia
- Jaundice
- Splenomegaly
- Cholelithiasis w/pigmented stones
 - 50% & after age 5 years

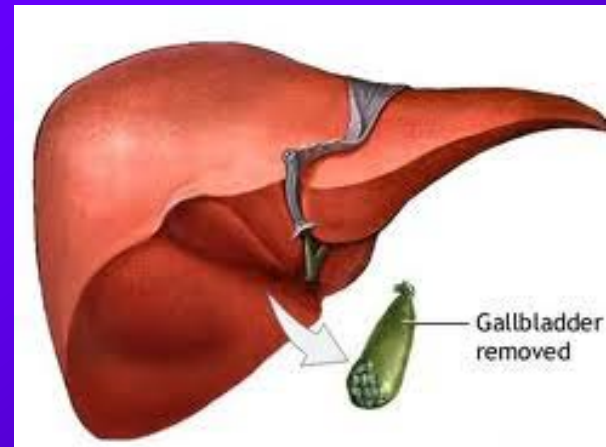


➤ Diagnosis by family Hx, blood smear & splenomegaly

- Spherocytes & reticulocytosis

Treatment of HS

- Splenectomy is curative!!!
 - Indicated in common forms of HS
 - Delay until age 5 to prevent OPSI
- Cholecystectomy concomittant if gallstones are present
- Milder forms
 - Controversial
 - Partial splenectomy in children younger than 5 yo



Other Cell Membrane Disorders

➤ Hereditary Elliptocytosis

- Mutation of RBC cell membrane skeleton proteins
- AD
- Chronic hemolysis:
 - Blood transfusion
- Severe hemolysis:
 - Splenectomy is curative

➤ Hereditary Poikilocytosis

- Thermal instability of RBC
- Micropoikilocytosis
- Subtype of common HE
- AR
- Newborns & infants present w/anemia & jaundice
- Severe anemia:
 - Splenectomy is curative

More Cell Membrane Disorders

- Hereditary Stomatocytosis
 - Mouth-shaped area of central pallor
 - AD
 - Severe hemolysis:
 - Splenectomy should be carefully considered
 - May develop hypercoagulability w/catastrophic thrombotic episodes
- Hereditary Xerocytosis
 - Target cells
 - Membrane cation permeability & cell volume decreased
 - AD
 - Severe hemolysis:
 - Splenectomy improves anemia

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- **D** It is less severe than other heredity membrane disorders, including pyruvate kinase deficiency, sickle cell anemia, thalassemia, and elliptocytosis, and less likely to require splenectomy than these conditions.
- **E** It is associated with a small spleen.

Hereditary spherocytosis (HS) is generally inherited as an **autosomal dominant disease**, although up to 25% of cases in the United States are inherited in an autosomal recessive manner. It is the most common hereditary hemolytic disorder in persons of northern European descent, with an incidence of approximately 1 in 5000 or less. HS results from deficiency of an erythrocyte cytoskeletal membrane protein, most commonly spectrin. Lack of spectrin produces spherical erythrocytes that are small and rigid with **increased osmotic fragility and results in increased destruction of erythrocytes as they pass through the trabeculae of the spleen**. The clinical manifestations are variable. Anemia may develop, as well as **jaundice, splenomegaly, and pigmented gallstones from hemolysis. Splenectomy can decrease these secondary complications** but should be **delayed until after 6 years of age**, if possible, to preserve immunologic function in young children (who are at greatest risk for **overwhelming post-splenectomy infection**). Cholecystectomy may be required in patients with symptomatic cholelithiasis but otherwise mild HS. Splenectomy is clearly indicated for patients with severe anemia. **The hereditary disorders listed in choice D are often less severe than those in HS** and much less likely to require splenectomy. **Splenomegaly** is a prominent feature of HS.

Partial vs total splenectomy in children with hereditary spherocytosis...

- **A** is associated with persistent anemia
- **B** is associated with a higher future risk of cholelithiasis
- **C** is associated with splenic regrowth that predicts failure
- **D** is associated with a shorter postoperative length of stay
- **E** will later require completion splenectomy

In studies comparing partial versus total splenectomy in children with hemolytic anemias, partial splenectomy for children with hereditary spherocytosis is associated with increased hemoglobin values, decreased reticulocyte and bilirubin levels, and preserved splenic function. Over time, variable rates of splenic regrowth are noted, although regrowth did not necessarily correlate with recurrent hemolysis. However, at least one group has reported gallstone formation, presumed to be the result of persistent mild hemolysis, in children in whom cholecystectomy was not performed. In a Toronto study, length of stay after partial versus total splenectomy was actually longer and was associated with more postoperative pain and a longer time to oral intake.



What is the most common primary splenic neoplasm w/splenic involvement?

- A) Hairy Cell Leukemia
- B) Chronic Myelogenous Leukemia
- C) Chronic Lymphocytic Leukemia
- D) Hodgkin's Lymphoma
- E) Non-Hodgkin's Lymphoma
- F) Darned if I know!

A microscopic image showing a cluster of cells, likely lymphoma cells, with prominent nuclei and some cytoplasmic detail. The image is overlaid with text.

Hodgkin's
&
Non-Hodgkin's
Lymphoma

A 23-year-old woman is seen with left supraclavicular adenopathy. She has no history of fever, chills, night sweats, or weight loss. CT of the chest and abdomen shows no other findings. Bone marrow biopsy is negative. Biopsy of the lymph node discloses nodular sclerosing Hodgkin's disease. Which of the following statements regarding further surgical intervention for this patient is not true?

- **A** Staging laparotomy (or laparoscopy) for Hodgkin's disease, when indicated, includes thorough abdominal exploration, splenectomy with splenic hilar lymphadenectomy, bilateral wedge and core needle liver biopsies, bilateral retroperitoneal lymph node sampling, bone marrow biopsy, and oophoropexy for female patients.
- **B** Staging laparotomy (or laparoscopy) has largely been supplanted by CT and positron emission tomography (PET) for assessing the extent of disease.
- **C** Eighty percent of patients undergoing splenectomy will have evidence of Hodgkin's involvement of the spleen.
- **D** The spleen is the only site of intra-abdominal disease in approximately one half of patients with Hodgkin's disease found to have splenic involvement.
- **E** Except for patients with early-stage Hodgkin disease, who may be treated with radiation therapy alone, most patients receive systemic chemotherapy.

Which of the following descriptions of the extent of Hodgkin's disease is paired with the correct clinical stage?

- **A** Bilateral involvement of the axillary lymph nodes with no subdiaphragmatic disease is considered stage I.
- **B** Epigastric lymph node and liver hilar lymph node involvement is stage III if there is no disease above the diaphragm.
- **C** The presence of positive left cervical and right mediastinal nodes denotes stage IV disease because of involvement of the contralateral side.
- **D** Splenic involvement in the presence of mediastinal lymph node involvement represents stage III disease.
- **E** Bone marrow involvement represents stage II disease but carries a poor prognosis.

Lymphoma

➤ Hodgkin's

- Malignant neoplasm
- Lymphoreticular cell origin
- Young adults 2nd-3rd decade
- Treatment
 - Chemotherapy & radiation
- Splenectomy
 - Thrombocytopenia
 - Symptomatic splenomegaly

➤ Non-Hodgkin's

- Most common primary splenic neoplasm w/splenic involvement
- Splenectomy
 - Anemia
 - Massive splenomegaly
 - Thrombocytopenia
 - Neutropenia

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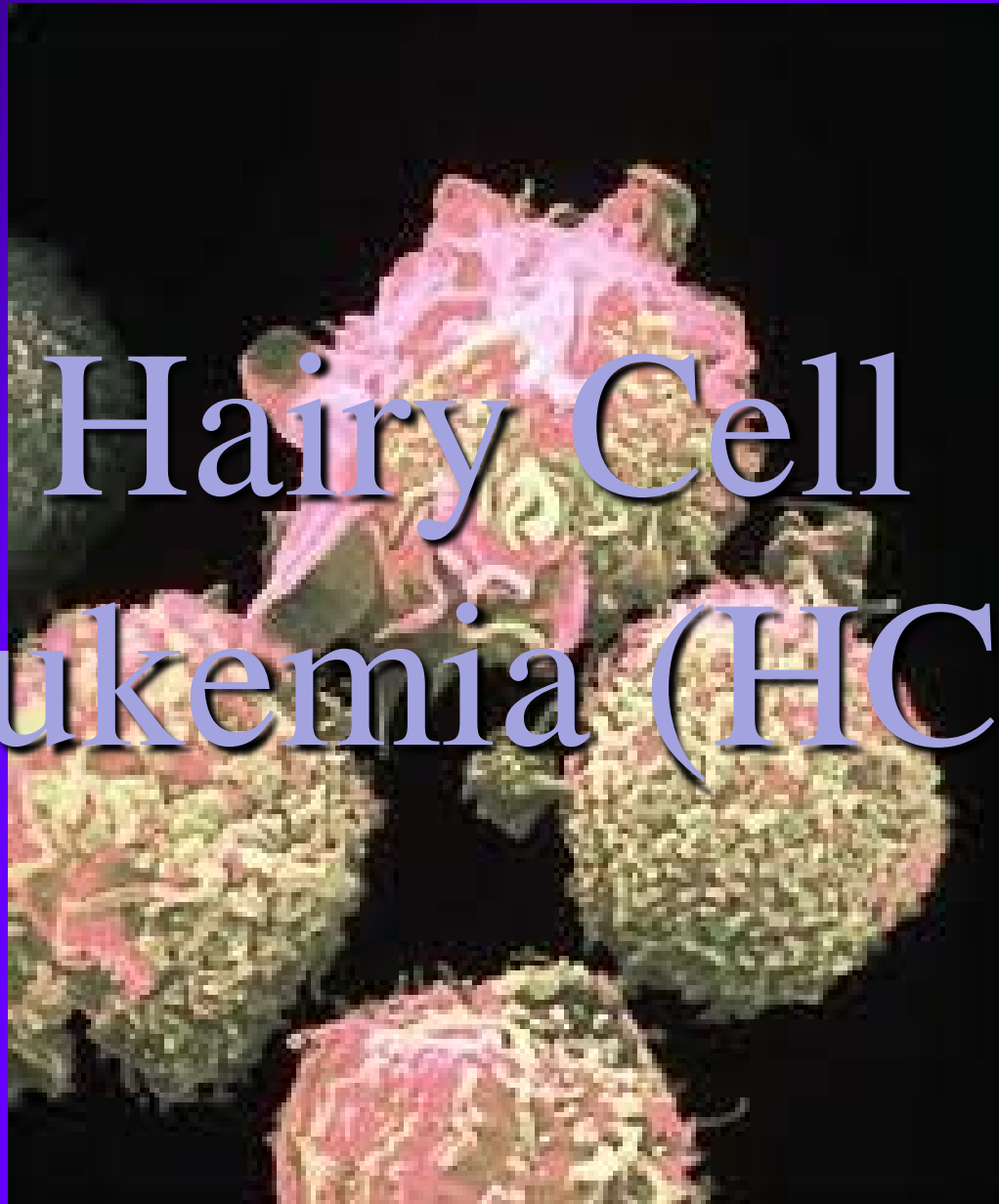
Staging laparotomy (or laparoscopy) for Hodgkin lymphoma is now largely of **historical** interest because **PET and CT have all but replaced the need for operative staging**. The components of a staging laparotomy (laparoscopy) are listed in choice A. When splenectomy is performed, approximately **40% of patients will be found to have splenic involvement**. **In one half of these patients with splenic involvement, there will be no other site of disease in the abdominal cavity or pelvis.**

Which of the following descriptions of the extent of Hodgkin's disease is paired with the correct clinical stage?

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According to the **Ann Arbor classification**, **Hodgkin's disease** is staged as follows: stage I—one or two contiguous areas of lymph node involvement on the same side of the diaphragm; stage II—two noncontiguous areas on the same side of the diaphragm; **stage III—involvement of lymph node groups on both sides of the diaphragm** (the spleen is considered a lymph node for this classification); and stage IV—involvement of the liver, bone marrow, lungs, or any other non-lymph node tissue, exclusive of the spleen. A superscript E signifies extranodal involvement adjacent to the involved lymph nodes. In addition, patients are subcategorized as being asymptomatic (A) or having constitutional symptoms (B) if they have had fever ($>38^{\circ}\text{C}$), night sweats, or 10% weight loss within 6 months.

Hairy Cell Leukemia (HCL)

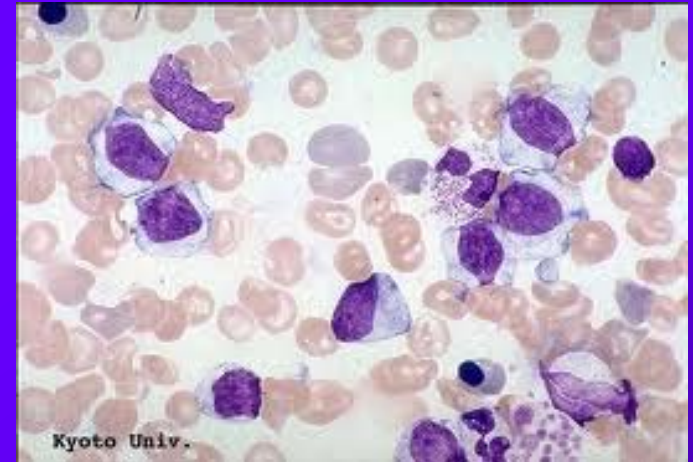


Hairy cell leukemia is diagnosed in a 58-year-old man with pancytopenia and palpable splenomegaly. He is referred to your office for a second opinion after another surgeon did not offer him a splenectomy. Which of the following is true regarding his condition?

- **A** It is a B-cell lymphoma characterized by cytoplasmic protrusions that first invade the thymus and then the spleen secondarily.
- **B** The mainstay of treatment is methotrexate chemotherapy.
- **C** It is associated with a two- to threefold risk for the development of a second malignancy, including prostate, skin, and lung cancers.
- **D** Splenectomy may be palliative but is infrequently done because of the lack of sustained response.
- **E** The 5-year survival rate is less than 20%.

Physiology & Presentation of HCL

- B-lymphocytes w/cytoplasmic projections from cell membrane
- 5th decade of life
- Symptoms
 - Splenomegaly
 - Pancytopenia
 - 2ry hypersplenism & replacement of bone marrow by leukemic cells
 - Neoplastic mononuclear cells in periphery & bone marrow



Management of HCL

➤ Medical

- Pentostatin
- Cladribine
- 92% response rate
- Complete remission
 - 80%
- 10 yr survival
 - >90%

➤ Splenectomy

- Rarely indicated
- Indications:
 - Pancytopenia refractory to medical therapy
 - Splenic rupture
 - Severe bleeding from thrombocytopenia

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Hairy cell leukemia is a clonal disorder of B lymphocytes that involve the blood and bone marrow (not the thymus). It usually affects elderly men and is characterized by **filamentous cytoplasmic projections on lymphocytes and splenomegaly**. Pancytopenia is common because of bone marrow replacement by leukemic cells. It is associated with a **two- to threefold risk for a second solid tumor, most commonly prostate, skin, lung, or gastrointestinal tract adenocarcinoma**. As many as 10% of affected patients have an indolent course requiring no specific therapy. Survival after medical treatment with purine analogues (**cladribine**) is generally good (**80% at 5 years**). **Splenectomy** is now reserved for patients who fail medical management or have **bleeding complications from thrombocytopenia**. Splenectomy results in improvement of the pancytopenia in 40% or more of patients and may be sustained for many years.

Other White Blood Cell Disorders

➤ Chronic Lymphocytic

Leukemia

- B-cell leukemia
- Progressive accumulation of functionally incompetent lymphocytes
- Splenectomy:
 - Sx of Massive splenomegaly
 - Severe thrombocytopenia & anemia

➤ Chronic Myelogenous

Leukemia

- Abnormal proliferation & accumulation of granulocytes
- Philadelphia chromosome
- Treatment: Imatinib
- Bone marrow transplant
- Splenectomy for palliation



Genetic Deficiencies



Thalassemia

- Defect in synthesis of hemoglobin chains: AD
- Inadequate hemoglobin production
 - Minor – microcytosis & mild anemia
 - Major – severe
- Symptoms
 - Abdominal swelling & pallor
 - Growth retardation & skeletal abnormalities
 - Irritability
 - Jaundice & pigmented gallstones
 - Splenomegaly



Management of Thalassemia

➤ Medical

- Lifelong blood transfusion
- Iron chelation therapy

Bone Marrow Transplant
is only cure

➤ Splenectomy

- Severe splenomegaly
- Transfusion requirement >180-200 mL/kg/yr
- Reduces transfusion by 25-60%
- May develop thrombocytosis

Sickle Cell Anemia



Characteristics of Sickle Cell

- Amino acid substitution on β chain of hemoglobin
- HgS deforms & sickle in low-oxygen tension
- Stasis & vasoocclusion in microvasculature
 - Tissue ischemia, severe pain, & chronic organ tissue damage
- Autosplenectomy from multiple infarcts
- Indications for Splenectomy
 - Splenic abscess & sequestration



Gaucher Disease

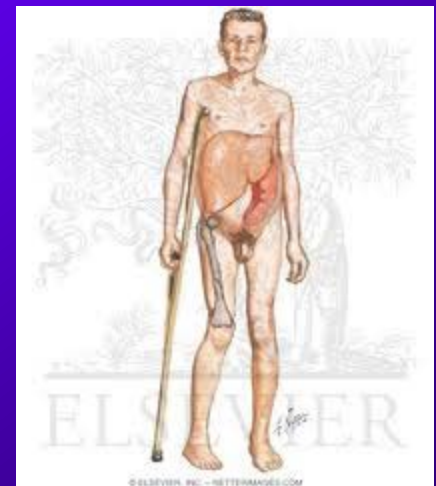


Presentation of Gaucher Disease

- Deficiency of glucocerebrosidase: AR
- Deposition in reticuloendothelia system
 - Organomegaly, pulmonary infiltrates, bone marrow infiltrates

- Symptoms:

- Bone pain
- anemia & thrombocytopenia
- Osteopenia
- Osteonecrosis
- Massive hepatosplenomegaly



Treatment of Gaucher

- Partial splenectomy
 - Preserve splenic function
 - Thrombocytopenia improves

- Side Effects:
 - Severe bone disease
 - Osteonecrosis
 - Worsening lung or kidney function

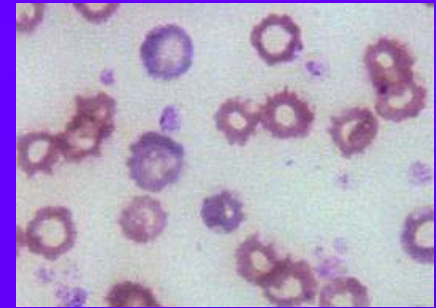
Pyruvate Kinase



Deficiency (PKD)

Presentation of PKD

- Most common genetic defect causing congenital enzymopathic hemolytic anemia
 - Defect in glycolytic pathway
 - Deficiency of ATP
 - RBC's less deformable & destroyed by spleen
- Splenomegaly
- Splenectomy in severe hemolytic anemia or frequent transfusions



Other Genetic Deficiencies

➤ G6PD Deficiency

➤ Most common enzyme defect in hereditary hemolytic anemia

➤ X-linked

➤ Damage of RBC by toxic O₂ products

➤ Acute infections, oxidant drugs (sulfa & antimalarials), fava beans

➤ Amyloidosis

➤ Extracellular deposition of insoluble fibrillar proteins in tissues & organs

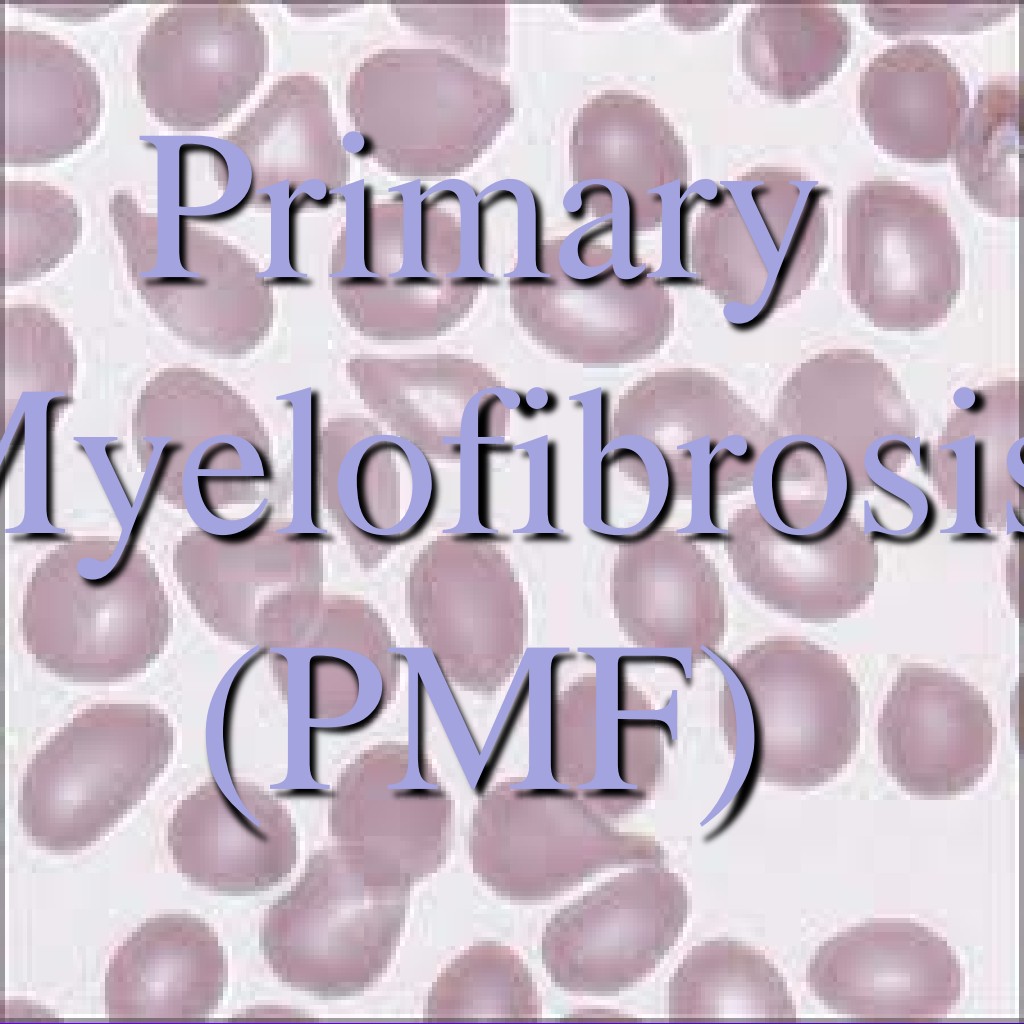
➤ Hepatosplenomegaly 25%

➤ Severe splenomegaly 10%

➤ Functional hyposplenism & splenectomy

A 3D white figure stands next to a large, vibrant red question mark. The figure is positioned to the right of the question mark, looking towards it. The scene is set against a plain white background.

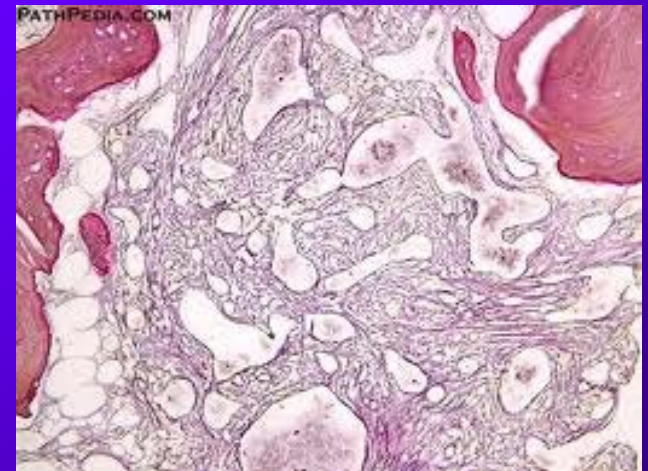
Myeloproliferative Disorders

A microscopic view of bone marrow cells, showing numerous large, dark-staining cells with prominent nuclei and some cytoplasmic granules, characteristic of myeloid cells.

Primary
Myelofibrosis
(PMF)

Presentation of PMF

- Chronic, malignant hematologic disorder
- Hyperplasia of abnormal myeloid precursor cells
 - Marrow fibrosis
 - Extramedullary hematopoiesis in liver & spleen
- Symptoms
 - Splenomegaly
 - Cytopenias – splenic sequestration
 - Portal hypertension – venous thrombosis
- Men > Women
- 65 yo



Indications for Splenectomy in PMF

- Thrombocytopenia
- Hemolysis requiring significant transfusions
- Pain from massive splenomegaly
- Recurrent splenic infarctions
- Portal hypertension w/refractory ascites & variceal hemorrhage
- Morbidity (15-30%) & mortality (10%)
 - Hemorrhage, infection, leukocytosis, severe thrombocytosis, progressive hepatomegaly, fatal hepatic failure, & leukemic transformation

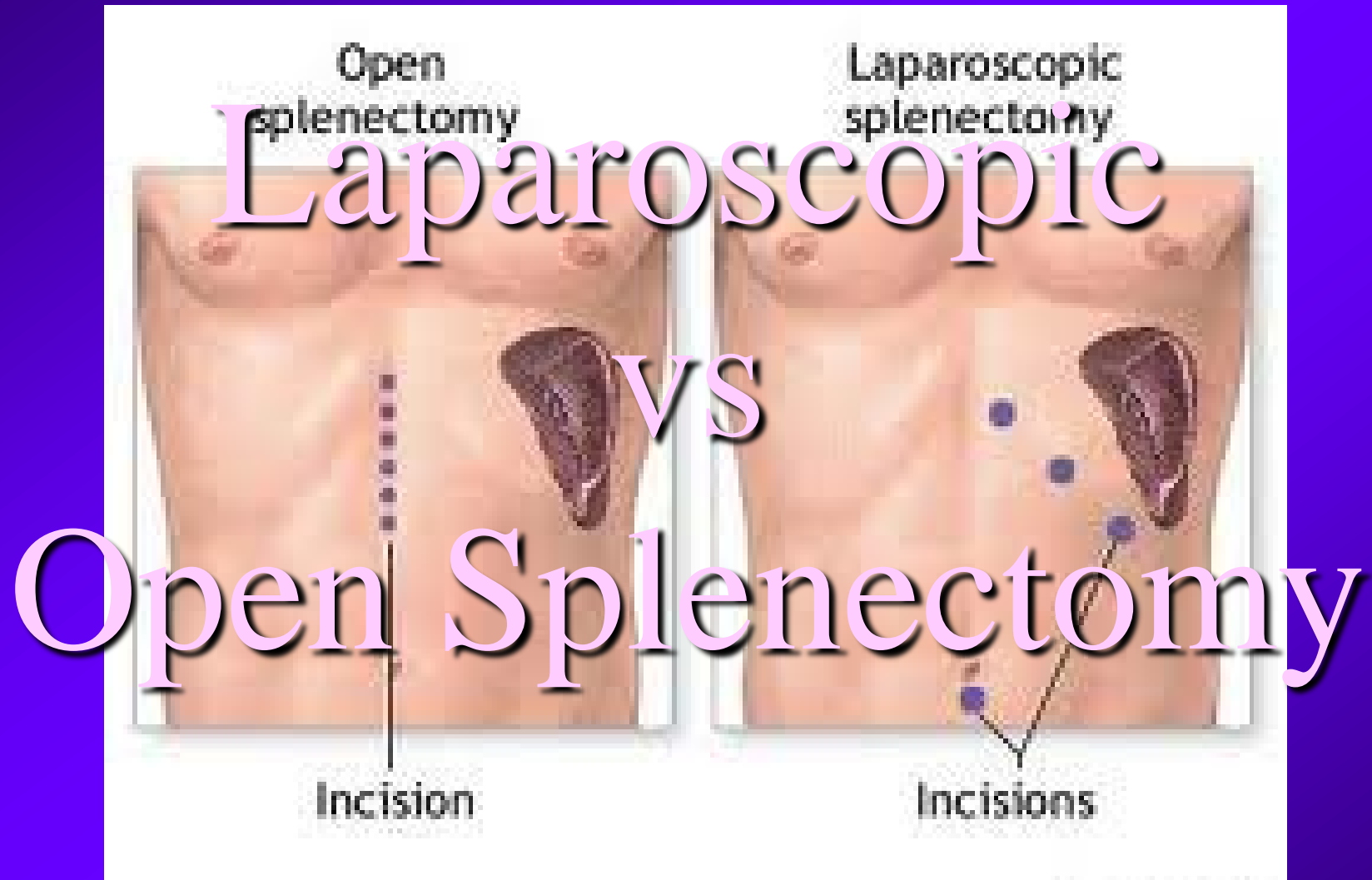
Other Bone Marrow Disorders

- CML
- Polycythemia vera
- Essential thrombocytopenia
- Hypereosinophilic syndromes
- Mast cell disease
- Chronic neutrophilic leukemia
- Splenectomy:
 - Palliative role
 - Massive splenomegaly
 - Cytopenia



Which of the following is an absolute contraindication for laparoscopic splenectomy?

- A) Massive splenomegaly
- B) Portal hypertension
- C) Malignancy
- D) Morbid obesity (BMI>35)
- E) Platelet count <20,000



After failing medical therapy, a 46-year-old woman with ITP is referred to you for splenectomy. She is very interested in a laparoscopic procedure and was told by her hematologist that she is a good candidate. Review of her CT scan shows a normal-sized spleen and normal splenic vascular anatomy. Which of the following is true about laparoscopic splenectomy?

- **A** Operative mortality rates are the same regardless of the underlying disease type.
- **B** Laparoscopic splenectomy has similar success rates as open splenectomy, except when performed for ITP.
- **C** The rate of conversion from laparoscopic to open splenectomy is 0% to 20%.
- **D** Laparoscopic splenectomy can be considered for spleen sizes up to 35 cm.
- **E** Laparoscopic splenectomy results in a higher incidence of splenosis than does the open approach.

Pre-Op Evaluation

- CT imaging
 - Splenic size
 - Anatomic relationship w/surrounding organs
 - Anatomy of variable splenic blood supply
 - Locate accessory spleens
- Pre-op splenic arterial embolization
 - Massive splenomegaly
 - Portal hypertension



Pre-Op Considerations

- Blood products
 - Especially in thrombocytopenia
 - Transfuse only for bleeding after splenic artery ligation
- Pre-op antibiotics 60 minutes prior
- NG/OG tube
- Stress-dose steroids if chronic use
- Vaccinations 2 wks prior
 - Haemophilus influenzae B
 - Polyvalent Pneumococcus
 - Meningococcus



Splenectomy

➤ Open

- Midline vs left subcostal
- Enter lesser sac
- Dissect vessels at hilum
- Ligate splenic hilum 1st
 - Facilitates plt transfusion in ITP
 - Vascular stapler or suture ligate
- Divide splenogastric ligament
 - Ligate short gastrics

➤ Laparoscopic

- Abdominal vs right lateral decub
- Mobilize splenic flexure
- Splenic pedicle dissected from lower pole
- Ligate vascular pedicle & short gastrics
- Macerate spleen in specimen bag

Laparoscopic Splenectomy

- Spleen size
 - Normal: 11 cm & 100-250g
 - Splenomegaly: >15cm
 - Massive Splenomegaly: >20cm
 - Megspleen: >22cm
- Higher rate of conversion related to increasing size
- Contraindications:
 - Portal hypertension from cirrhosis

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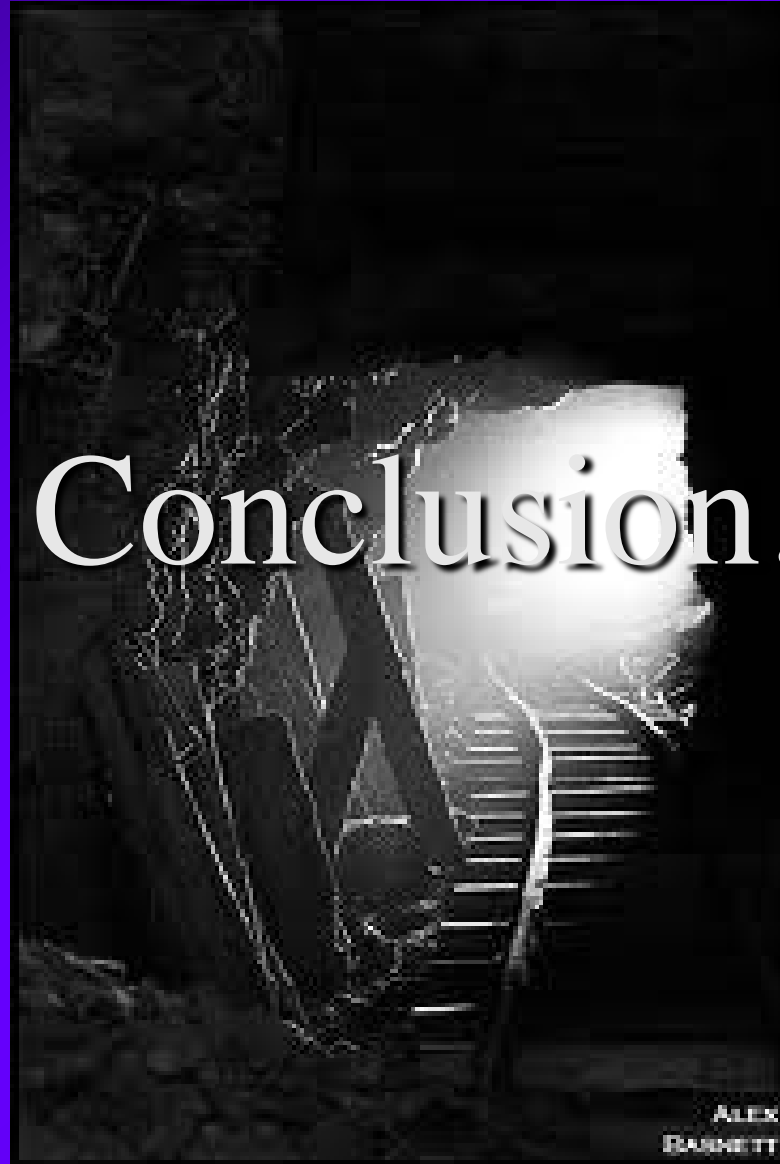
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Laparoscopic splenectomy is increasingly being selected as the technique when elective splenectomy is indicated. The **operative morbidity and mortality rates after splenectomy are higher for patients with malignant hematologic disease than for those with benign disease**. The risk for postoperative **portal venous thrombosis** is greatest for patients with myeloproliferative disorders. For **idiopathic thrombocytopenic purpura**, **laparoscopic splenectomy has success rates similar to those of open splenectomy**. Regardless of the surgical approach, when splenectomy is performed for hematologic disease, a careful search for **accessory spleens** must be performed. Their appearance may mimic that of a lymph node, and they may more easily be palpated than visualized, thus giving rise to concern that the laparoscopic approach may overlook some accessory spleens. **The conversion rate to an open procedure is reported to range from 0% to 20%**. Conversion is usually secondary to bleeding, but extensive adhesions, obesity, and splenomegaly may also be factors. **Spleens up to 20 to 25 cm in size are amenable to laparoscopic splenectomy**. A splenic size of 35 cm is generally too large for a laparoscopic approach. The **laparoscopic approach does not result in a higher incidence of splenosis** (autotransplantation and subsequent growth of splenic fragments from an injured spleen that may remain functional and occasionally cause pain or symptoms related to a mass effect).

Six months after laparoscopic splenectomy for ITP, a 38 yo woman with lupus remains thrombocytopenic (plt 42,000/mm³). The next step should be...

- A) Platelet transfusion
- B) Evaluation for accessory spleen
- C) Plasmapheresis
- D) Bone marrow biopsy
- E) Aspirin
- F) I give up!!!

In Conclusion....



ALEX
BARNETT

Primary therapy for a 5 yo girl w/new-onset petechiae & ecchymosis, platelet count 45,000/mm³, and normal-size spleen...

- A) Corticosteroids
- B) Splenectomy
- C) Plasmapheresis
- D) Chemotherapy
- E) Enzyme Replacement
- F) None of the Above

Primary therapy for a 56 yo man
w/pancytopenia, blood smear showing
circulating cells with cytoplasmic
protrusions, & splenomegaly...

- A) Corticosteroids
- B) Splenectomy
- C) Plasmapheresis
- D) Chemotherapy
- E) Enzyme Replacement
- F) None of the Above

Primary therapy for a 35 yo man w/mental status changes, hemoglobin of 7 g/dL, fever, renal failure, platelet count of 40,000/mm³ and splenomegaly...

- A) Corticosteroids
- B) Splenectomy
- C) Plasmapheresis
- D) Chemotherapy
- E) Enzyme Replacement
- F) None of the Above

Primary therapy for a 10 yo girl
w/recurring episodes of severe anemia with
jaundice, red cells with osmotic fragility &
normal-size spleen...

- A) Corticosteroids
- B) Splenectomy
- C) Plasmapheresis
- D) Chemotherapy
- E) Enzyme Replacement
- F) None of the Above

Primary therapy for a 21 yo woman w/skin discoloration, fatigue, and hepatosplenomegaly...

- A) Corticosteroids
- B) Splenectomy
- C) Plasmapheresis
- D) Chemotherapy
- E) Enzyme Replacement
- F) None of the Above



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