Hematology Assignment

This unit is big, and mastery of the material requires a combination of reading the book, reviewing lecture notes and especially attention to the online exercises. It covers RBC and WBC disorders, problems of coagulation and diseases of the lymph nodes. Do not wait until week before the exam to try and do the reading.

All of the material in this unit will be covered on the second exam, and it’s a bunch. You’ll be sunk if you put reading and online assignments off until the just few weeks before the exam.

Here’s the scoop on just the hematology unit, the immunopathology comes later.

Big Robbins: chapters 13 and 14.
Little Robbins: Chapter 11

Wheater: Hematopoietic

Slides: For the blood smears, the entire set is online. There are no slides in your box.

For the lymph nodes, there are slides in your box and online.

There are four online exercises for hematology unit, two cases and two tutorials. The tutorials are rather large but absolutely necessary. Don’t flush these or try to rush through them.

Online stuff:

Case 11, Mr. Herbert: A man complaining of lethargy.
Module 24, Coagulation tutorial
Module 19, Leukemia review
Case 17, Mrs. Talbot: Woman with a neck mass.

Slides and TBL stuff:

There are no formal TBLs for this unt. Rather the blood smear section of the slides will serve that purpose. Approach of these cases as if you will see them, their histories and lab values in case studies on the written exam. The reason is, you will.

If you’re having trouble with the reading, please see Dr. Braun or Bauman pronto.
Hematopoietic and Lymphoid Systems
Basic Robbins Chapter 11
Mark E. Bauman, M.D.

Hematopoiesis
(Most material below not in text)

3rd week gestational age
3rd month gestational age
4th month gestational age
18 years

Hb A  Hb A₂  Hb F

red/white marrow
extramedullary hematopoiesis
stem cells

Normal anatomy of bone marrow

Cell/fat ratio
Hypoplasia/hyperplasia
Myeloid/erythroid ratio
Avg life span RBC  Poly  Platelet

Erythroid maturation
Granulocytic maturation

Megakaryocytes

**Normal anatomy of peripheral blood**

**Erythrocytes**

Hb content: Normochromic/ hypochromic/ hyperchromic

Polychromatophilia/polychromasia (standard Wright stain)
Reticulocytes (retic stain showing RNA still synthesizing Hb)

Reticulocyte count
- Percentage: 0.5 – 1.5% (Except in newborns 2.5 – 6.5)
- Absolute: 24 – 84 x 10^9

Reticulocytes production index/Corrected reticulocyte count compensates for
1) decreased # RBC
2) increased life span of reticulocyte (early marrow exit)

Consumption vs Production etiology of anemia

Size: Normocytic/microcytic/macrocytic; variation =

Shape: Elliptocytes, spherocyes, target cells, schistocytes, acanthocytes

Erythrocyte cytoplasmic inclusions:
- Basophilic stippling
- Pappenheimer bodies
- Howell-Jolly bodies

Multiple images
Rouleaux formation

RBC Indices

- RBC count
- Hct
- Hb
- RDW

Leukocytes

<table>
<thead>
<tr>
<th>Total WBC/mm³</th>
<th>% polys</th>
<th>Absolute polys</th>
<th>% lymphs</th>
<th>Absolute lymphs</th>
<th>% monos</th>
<th>% eos</th>
<th>% basos</th>
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</table>

<table>
<thead>
<tr>
<th>Total WBC/mm³</th>
<th>% lymphs</th>
<th>Relative lymphocytosis?</th>
<th>Absolute lymphocyte count</th>
<th>Absolute lymphocytosis?</th>
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<tbody>
<tr>
<td>10,000</td>
<td>70</td>
<td></td>
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<tr>
<td>6,000</td>
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<tr>
<td>10,000</td>
<td>30</td>
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</tbody>
</table>

Platelets

- Total

Quality vs Quantity
Red Cell Disorders

Anemia = reduction of O2 transport capacity in blood

Anemias classified by MCV

Anemias classified by Underlying Etiology

***Table 11-1***

1. A. 

2. A. 

3. A. 

B.
**Anemias of Blood Loss: Hemorrhage**

Acute vs chronic blood loss

Het/Hb

Reticulocytes

**Hemolytic Anemias**

Increased RBC destruction: Intrinsic and extrinsic abnormalities

EPO

LDH

Reticulocytes

Bone marrow

Hemoglobin catabolism

unconjugated hyperbilirubinemia

hemoglobinemia

hemoglobinuria

haptoglobin
**Instrinsic (intracorpuscular) hemolysis**

**Hereditary spherocytosis** (Figures 11-1 and 11-2)

Spherical erythrocytes secondary to an inherited defect of red cell membrane skeleton proteins

“Obese man attempting to bend at the waist.”

Osmotic fragility

**Clinical:**

**Sickle Cell Anemia**

Hemoglobinopathy

Hb S  substitution of valine for glutamic acid at amino acid 6 of the β globin chain

Hb SS

Hb AS

HbC substitution of lysine for glutamic acid at amino acid 6 of β globin chain

Chronic hemolytic anemia
Clinical onset in homozygotes
Congestion, thrombosis, infarction
Veno-occlusive crises
Autosplenectomy

DX: Hb electrophoresis/HPLC

Thalassemia Syndromes
Thalassa + emia =
(Figures 11-5 and 11-6, Table 11-3)

Pathogenesis: relative excess of insoluble, unstable chains with ineffective erythropoiesis

Peripheral blood/anemia/splenic sequestration

α Thalassemia

Each chromosome 16 has two genes for alpha; typically loss of entire gene

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Genotype</th>
<th>Condition</th>
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<tbody>
<tr>
<td>I</td>
<td>-α/αα</td>
<td>silent carrier</td>
</tr>
<tr>
<td>II</td>
<td>-/-αα</td>
<td>α-thal trait, Asian</td>
</tr>
<tr>
<td></td>
<td>-α/α</td>
<td>α-thal trait, African</td>
</tr>
<tr>
<td>III</td>
<td>-/-α</td>
<td>Hb H disease, β-globin tetramers = Hb H</td>
</tr>
<tr>
<td>IV</td>
<td>-/- -</td>
<td>Hb Barts, hydrops fetalis, γ-globin tetramers = Hb Barts</td>
</tr>
</tbody>
</table>
**β Thalassemia**

Each chromosome 11 has a single gene for beta. Typically point mutations (promoters, terminators, splicing).

\[ \beta = \text{normal gene} \]
\[ \beta^+ \text{thal} = \text{decreased production (variable amount produced)} \]
\[ \beta^0 \text{thal} = \text{total absence of beta globin chain} \]

\[
\begin{align*}
\beta/\beta &= \\
\beta/\beta^+ \text{ or } \beta/\beta^0 &= \\
\beta/\beta^0 \text{ or } \beta^+/\beta^+ &= \\
\beta^+/\beta^+ \text{ or } \beta^0/\beta^0 &= \\
\end{align*}
\]

Hb electrophoresis/HPLC

\[
\begin{align*}
\beta \text{ minor} & \quad \uparrow \text{Hb A2 (4-8%)} \\
\beta \text{ major} & \quad \text{Hb A2} \uparrow \text{ or } \downarrow; \text{Hb F usually } \uparrow \\
\end{align*}
\]

Clinical course

- Skeletal deformities
- Hemochromastosis

**Glucose-6-phosphate dehydrogenase deficiency**

*One example of an erythrocyte enzyme defect*

Defective hexose monophosphate shunt incapable of regenerating reduced Glutathione (GSH). GSH needed for inactivation of intracellular oxidants, e.g. sulfonamide, primaquine, infectious agents, fava beans, H₂O₂ from phagocytes during infections

Heinz bodies (Figure 11-7)
Bite cells: (Fig 13-8)

Genetics:

Clinical: enzyme synthesis vs enzyme stability

Paroxysmal Nocturnal Hemoglobinuria

Somatic mutation of pluripotential stem cell → decreased glycosyl phosphatidyl inositol (GPI: a phospholipid anchoring non-transmembrane proteins); decreased GPI → decreased GPI-linked proteins regulating complement → increased sensitivity of RBCs to complement

Misnomer

Ham’s test

Flow cytometry for CD 55 and CD 59 (GPI-linked proteins)

FLAER: fluorescent labeled proaerolysin (binds to PGI)

Extrinsic (extracorpuscular) hemolysis

Immune-mediated hemolytic anemia

Anti-RBC antibodies and complement-mediated RBC hemolysis

Direct Antibody Test (D.A.T.) = Coomb’s test

Indirect Antibody Test (I.A.T.) = Indirect Coomb’s test

Warm Antibody Immunohemolytic Anemia
Temperature
IgG
Idiopathic 75%
Immune disorders
Spherocytes

Cold Antibody Immunohemolytic Anemia
Temperature
IgM
Opsonization
Agglutination

Non-immune hemolytic anemias

Mechanical etiologies

Microangiopathic hemolytic anemia
DIC, TTP
Schistocytes

Malaria
1 million deaths annually; endemic in Asia and Africa
Plasmodium species: P. falciparum, P. malariae, P. vivax, P. ovale
Mosquito
Parasite life cycle

Clinical
Anemias of Diminished Erythropoiesis

Iron deficiency anemia  (Figure 11-9)

Iron functions

Iron absorption and balance  
Ferroportin 1/hepcidin

Serum iron/TIBC/transferrin

Ferritin

Hemosiderin/hemosiderosis

Hemochromatosis (page 629, figure 15-25)

Iron deficiency
Iron deficiency anemia (Figure 11-10)

- MCV
- MCH
- RDW
- Platelets

- Ferritin
- TIBC
- Free erythrocyte protoporphyrin

Anemia of chronic disease

Defective utilization of iron (present in adequate amounts) secondary to a defect in iron transfer from the storage pool to erythroid precursors

Ferroportin 1/hepcidin

Clinical settings

- MCV
- RDW
- Platelets

- Ferritin
- TIBC

Megaloblastic Anemias

Impaired DNA synthesis

Megaloblasts: impairment of cell maturation and division; normal RNA and protein synthesis; nuclear/cytoplasmic dysynchrony; ineffective hematopoiesis

Bone marrow erythroid and granulocyte precursors

- MCV
- Retic
- Platelets

- Neutrophils
B12 (Cobalamin)  
Folate

Sources/storage:

Deficiency:

Pernicious anemia: One form of megaloblastic anemia secondary to defects of intrinsic factor

Physiologic absorption of B12

Serum antibodies: 1. 2. 3.

Additional etiologies of malabsorption

CNS Changes: spinal cord demyelinization of dorsal and lateral tracts (sensory ataxia, paresthesias of extremities)

Aplastic anemia
Trilineal aplasia

Etiologies

Pure red cell aplasia
Association
Virus

**Myelophthisic anemia**

Leukoerythroblastosis

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**Polycythemia**

Polycythemia/erythrocytosis

Relative erythrocytosis

Absolute erythrocytosis
  
  Primary: RBC production not regulated by EPO

Secondary: RBC production regulated by EPO
  
  Appropriate

  Inappropriate
White Cell Disorders

Non-neoplastic Disorders of White Cells

Leukopenia

Neutropenia/agranulocytosis

Decreased production

Increased consumption

Reactive leukocytosis

Review Table 11-6 Causes of Leukocytosis (page 426 in Basic Robbins)

Neutrophilia
Eosinophilia

Basophilia

Monocytosis

Lymphocytosis

Leukemoid reaction

Infectious mononucleosis

EBV

Monospot test (rapid heterophile antibody); serology

Atypical lymphocytosis

Lymphadenopathy, hepatosplenomegaly
Associations

1. Reactive lymphadenitis
   Normal lymph node structure

2. Acute nonspecific lymphadenitis

3. Chronic nonspecific lymphadenitis
   Follicular hyperplasia
   Paracortical hyperplasia
   Sinus histiocytosis

4. Cat scratch disease
   *Bartonella henselae*
   Cervical, axillary adenopathy: stellate necrotizing granulomata
Neoplastic Proliferations of White Cells

(Note: The following material is somewhat different from the order of presentation in the text.)

Lymphoma

Leukemia

Myelodysplasia

Myeloproliferative neoplasms

1.
2.
3.
4.
Lymphoid neoplasms

Benign vs malignant

Clonality

1. Monoclonal protein (surface antigen receptor or secreted globulin)

2. Genetic rearrangement: PCR/Southern blot
Classification schemes for lymphomas attempt to define distinct clinic-pathologic entities, based on cell morphology, origin, maturity, immunophenotype, genotype, and clinical features.

***Table 11-7 WHO Classification of Lymphoid Neoplasms ***

Most lymphomas resemble some stage of B or T cell differentiation. (Figure 11-13)

B cell: T cell: NK cell:
Nodal: Extranodal:
Non-Hodgkin lymphoma: Hodgkin lymphoma:
<table>
<thead>
<tr>
<th>Precursor (immature)</th>
<th>B cell</th>
<th>T cell</th>
</tr>
</thead>
</table>

**Peripheral (mature)**

Most common lymphomas are derived from germinal center or post germinal center B cells.

Immune abnormalities in lymphomas

NHL lymphomas are systemic

**Precursor (immature) B and T cell leukemia/lymphoma = Acute lymphoblastic leukemia/lymphoblastic lymphoma**

**ALL**

Morphology

Molecular

Clinical

Aleukemic leukemia
Distinguished from AML

**Peripheral (mature) B cell neoplasms**

**CLL/SLL:** Chronic lymphocytic leukemia/small lymphocytic lymphoma

Morphology

- Lymph node
- Blood
- Bone marrow

Immunophenotype

Clinical

- Richter transformation
Follicular lymphoma

Morphology

Immunophenotype

Molecular

Clinical

Mantle cell lymphoma

Morphology

Immunophenotype

Molecular

Clinical

Lymphomatoid polyposis

Blast variant

Diffuse large B cell lymphoma

Morphology (Figure 11-17)
Immunophenotype

Molecular

Clinical

**Burkitt lymphoma**

3 types  
1)  
2)  
3)

**Morphology**

**Molecular**  
c-MYC on 8  
\[ t(8;14) \quad t(2;8) \quad t(8;22) \]

**Multiple myeloma and related plasma cell tumors**  
*Note: The following material is somewhat different from the order of presentation in the text.*

**Morphology**

**Solitary plasmacytoma**

**Multiple myeloma**
Secretory function

Bence Jones protein

MGUS

Clinical

Immunosuppression

Peripheral blood

Pathologic fractures/lytic lesions

Hypercalcemia

Myeloma nephrosis

Light chain (AL) amyloidosis

Prognosis

Lymphoplasmacytic lymphoma

Waldenström macroglobulinemia/hyperviscosity syndrome

Heavy chain disease
Hodgkin lymphoma: a B cell lymphoma

<table>
<thead>
<tr>
<th>Site</th>
<th>HL</th>
<th>NHL</th>
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<tbody>
<tr>
<td>Spread</td>
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<td></td>
</tr>
<tr>
<td>Nodal based</td>
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</table>

Morphology: Reactive cells plus Reed Sternberg cells

5 subtypes: 4 Classical (nodular sclerosis, lymphocyte rich, mixed cellularity, lymphocyte depleted) and Nodular Lymphocyte Predominance

**Classical**
RS cells CD15 and CD30 positive; CD45 and CD20 negative

Nodular sclerosis with “Lacunar cells”

**Lymphocyte Predominance** HL
Lymphohistiocytic variant RS cells (popcorn cells)

CD15 and CD30 negative; CD45 and CD20 positive

EBV

Clinical

Staging and “B” symptoms

Prognosis

Extranodal marginal zone lymphoma
Morphology
MALToma
Sites
Associations

Hairy cell leukemia
Morphology
Immunophenotype
TRAP (outdated)
Clinical
Splenomegaly
Bone marrow involvement
Prognosis

Mycosis fungoides
Cutaneous T-cell lymphoma: patches, plaques, tumors
Pautrier microabscesses
Sezary syndrome

Adult T cell leukemia/lymphoma
HTLV-1: Japan, Caribbean, West Africa
Myeloid neoplasms

(Note: The material on Myelodysplasia in this handout precedes that of acute myeloid leukemia. The text presents AML before Myelodysplasia.)

Myelodysplastic syndromes

WHO definition: A group of clonal myeloid neoplasms characterized by ineffective hematopoiesis that present clinically as cytopenia(s), dysplasia in one or more hematopoietic cell lines in the bone marrow, and risk of transformation to acute myeloid leukemia.

Morphology

Molecular: monosomy 5, monosomy 7; 5q-, 7q-, 20q-

Subtypes: Refractory cytopenia with unileage dysplasia (RCUD), Refractory anemia with ring sideroblasts (RARS), Refractory cytopenia with multilineage dysplasia (RCMD), Refractory anemia with excess blasts-1 (RAEB-1), Refractory anemia with excess blasts-2 (RAEB-2), Myelodysplastic syndrome unclassified (MDS-U), MDS associated with isolated del (5q), Therapy-related MDS (t-MDS).

Clinical

Acute myeloid leukemia = Acute myelogenous leukemia = AML

At least 20% marrow blasts.

Morphology(Figures 11-14, 11-25)

Auer rods

Immunophenotype

Molecular

Clinical
WHO Classification based on cell lineage, cell maturation, molecular changes

**AML with recurrent chromosomal translocations**
- AML with a translocation between chromosomes 8 and 21
- AML with a translocation or inversion in chromosome 16
- AML with changes in chromosome 11
- APL (M3), which usually has translocation between chromosomes 15 and 17

**AML with multilineage dysplasia (more than one abnormal myeloid cell type is involved)**

**AML related to previous chemotherapy or radiation**

**AML not otherwise specified** (includes cases of AML that don't fall into one of the above groups; similar to the FAB classification)
- Undifferentiated AML (M0)
- AML with minimal maturation (M1)
- AML with maturation (M2)
- Acute myelomonocytic leukemia (M4)
- Acute monocytic leukemia (M5)
- Acute erythroid leukemia (M6)
- Acute megakaryoblastic leukemia (M7)
- Acute basophilic leukemia
- Acute panmyelosis with fibrosis
- Myeloid sarcoma (also known as granulocytic sarcoma or chloroma)

**Undifferentiated or biphenotypic acute leukemias** (leukemias that have both lymphocytic and myeloid features). Sometimes called ALL with myeloid markers, AML with lymphoid markers, or mixed lineage leukemias.

**FAB M3**

- t(15;17) retinoic acid receptor α (RARA) gene on 17
- PML gene on 15

**FAB M4**

**FAB M6**

**Chronic Myeloproliferative Neoplasms**

Clonal hyperproliferation of myeloid cells retaining capacity for terminal differentiation

Peripheral blood

Bone marrow

Hepatosplenomegaly
“Spent phase” and “blast crisis”

1. Chronic myelogenous leukemia (CML)
   - Peripheral blood (Figure 11-26)
   - Philadelphia chromosome

   Rx

   Prognosis

2. Polycythemia vera
   - Peripheral blood
   - EPO
   - JAK2
   - Thromboses/infarctions/ erythromelalgia

   Rx

3. Primary myelofibrosis
   - Peripheral blood
   - Bone marrow
   - JAK2

   Prognosis

4. Essential thrombocythemia
   - Peripheral blood
Bone marrow

JAK2

Histiocytic neoplasms

Two types of histiocytes: macrophages/histiocytes and dendritic cells

Dendritic cells present antigens to initiate an immune response

Two types of dendritic cells:
1. Follicular dendritic cells within germinal centers
2. Langerhans cells – a dendritic cell within the dermis

CD1a positive
Birbeck granules: pentalaminar tubular structures on EM (tennis rackets)

Langerhans cell histiocytoses (LCH)

Children and adults

Unisystem LCH
Unifocal unisystem LCH (“eosinophilic granuloma”)  
Erosive aggregates of LC’s, often in bone, skin or lungs

Multifocal unisystem LCH
Multiple bony masses, often extending into soft tissues
Hand-Schüll-Christian triad: calvarial bone defects, diabetes insipidus (posterior pituitary stalk involvement), exophthalmos

Multisystem LCH (Letterer-Siwe disease)
Seborrheic skin eruptions, hepatosplenomegaly, pulmonary lesions, destructive bone lesions
Myeloid and lymphoid neoplasms

Based on and

Pluripotent stem cell

Myeloid stem cell
  Polys, basos, eos, monos, plts, rbc
  Acute

Lymphoid stem cell
  Bcells
  T cells
  Chronic

Myeloid and lymphoid neoplasms

Based on and

Pluripotent stem cell

Myeloid stem cell
  Polys, basos, eos, monos, plts, rbc
  Acute

Lymphoid stem cell
  Bcells
  T cells
  Chronic
Bleeding Disorders

(Note: The material presented below draws from chapters 3 and 11 of Basic Robbins. The order of this material does not follow the text. Some of the material is not in the text.)

Hemostasis

Petechiae  Purpura  Echymosis  Contusion  Hematoma

Primary Hemostasis  (Fig 3-7)

1. Adhesion

2. Activation
   
   \( \alpha \) (alpha) granules

   \( \delta \) (delta) granules/dense bodies

   TxA\(_2\)

   Shape change

3. Aggregation
**Secondary Hemostasis**: Coagulation System
Transformation of plasma proenzymes → activated enzymes with cofactors → conversion of prothrombin → thrombin → conversion of fibrinogen → fibrin with crosslinking by XIII

Intrinsic and extrinsic pathways (Figures 3-8, 3-9, 3-5)
Antithrombotic mechanisms
Inhibitory effects on platelets (primary hemostasis)

Intact endothelium
Endothelial products
Drugs

Inhibitory effects on coagulation (secondary hemostasis) (Figure 3-6)

Anti-thrombin III
AT III is activated by
Activated AT III functions to

Thrombomodulin
Thrombomodulin functions to
1.
2. activate Protein C

Activated Protein C inactivates
Activated Protein C Resistance/Factor V Leiden

Normal        APCR
               PTT
               PTT w/ act Protein C

Protein S is a cofactor for Protein C
Tissue Factor Pathway Inhibitor (TFPI)

Drugs

Fibrinolysis (Figure 3-11)

Plasminogen
activated to
activated by
1.  2.  3.

Plasmin produces

Fibrinolysis is controlled by
1.  2.

With bleeding disorders, history comes first: onset, type of bleeding, family history

<table>
<thead>
<tr>
<th>Platelet disorder</th>
<th>Coag disorder</th>
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<tbody>
<tr>
<td>Petechiae</td>
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</tr>
<tr>
<td>Deep hematomas</td>
<td></td>
</tr>
<tr>
<td>Hemarthroses</td>
<td></td>
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<tr>
<td>Delayed bleeding</td>
<td></td>
</tr>
<tr>
<td>Mucosal bleeding</td>
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</table>

Lab tests for platelet function

Bleeding time

Platelet function analyzer (PFA)
Platelet aggregation studies

(Selected) Lab tests for coagulation function
Activated partial thromboplastin time (PTT)

Prothrombin time (PT)

INR

Thrombin time

Mixing Studies:
**Platelet Disorders**

Platelet Quantity: production vs consumption

Production problem

- Bone marrow

Consumption problem

- Sequestration/hypersplenism

  Neonatal and post-transfusion immune reaction

  ITP (Immune Thrombocytopenic purpura)
  Immunologically mediated destruction of platelets

  - Acute
  - Chronic

  Autoantibodies

  PT/PTT/BMBx

  HIT (Heparin-induced Thrombocytopenia)

  HIV-associated Thrombocytopenia

  CD 4 receptors on megakaryocytes
TTP/HUS (Thrombotic Thrombocytopenia Purpura/Hemolytic Uremic Syndrome) Thrombotic Microangiopathies

TTP Pentad

Formation of

VWF metalloprotease defect

ADAMTS 13 (A Disintegrin-like And Metalloprotease With ThromboSpondin, the 13th member)

Therapy:

HUS etiology

PT/PTT

Platelet Quality
Bernard Soulier Disease

Glanzmann’s thrombasthenia

Storage pool disorder

Von Willebrand Disease (Figure 11-29)
VWF functions:
1.

2.

$t\frac{1}{2}$ for VIII with vWF = without vWF =
Inheritance

Clinical findings

<table>
<thead>
<tr>
<th>Platelet count</th>
<th>PT</th>
<th>PTT</th>
<th>Platelet function assay</th>
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<tbody>
<tr>
<td>FVIII activity</td>
<td>vWF Ag</td>
<td></td>
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</tr>
<tr>
<td>vWF activity/Ristocetin test</td>
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Multimer studies/Subtypes of vWD:

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**Coagulation Disorders**

Factor VIII Deficiency (Hemophilia A)

Inheritance

Clinical findings

Range of VIII activity

<table>
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<th>Platelet count</th>
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<th>PTT</th>
<th>Platelet function assay</th>
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<td>FVIII activity</td>
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<tr>
<td>Rx</td>
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</table>
Factor IX Deficiency (Hemophilia B, Christmas Disease)

Clinical findings

Lab testing

Disseminated Intravascular Coagulation (DIC) (Figure 11-28)

Activation of coagulation with microthrombi formation with microangiopathic hemolytic anemia, coupled with active fibrinolysis

<table>
<thead>
<tr>
<th>PT</th>
<th>PTT</th>
<th>Platelet count</th>
<th>Fibrinogen</th>
<th>D-dimer</th>
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<tbody>
<tr>
<td>I</td>
<td>N</td>
<td>Common Factor VII deficiency</td>
<td>early liver disease, early vitamin K deficiency, early warfarin therapy</td>
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<td></td>
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<td>Rare Factor VII inhibitor, dysfibrinogenemia</td>
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<td>I</td>
<td>Common Deficiency or inhibitor of factor VIII, IX, or XI, vWD, lupus, lupus inhibitor with qualitative platelet defect</td>
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<td>Rare Deficiency or inhibitor of factor VIII, IX, or XI, vWD, lupus, lupus inhibitor with qualitative platelet defect</td>
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<td></td>
</tr>
<tr>
<td>I</td>
<td>I</td>
<td>Common Vitamin K deficiency, liver disease, warfarin, heparin</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Rare Deficiency or inhibitor of factor VIII, IX, or XI, vWD, lupus, lupus inhibitor with qualitative platelet defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>D</td>
<td>Common Increased platelet destruction, decreased platelet production, splenomegaly, hemodilution</td>
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<tr>
<td></td>
<td></td>
<td>Rare Myeloproliferative disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>N</td>
<td>Common Mild vWD, acquired qualitative platelet disorders (uremia)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare Inherited qualitative platelet disorders, vascular disorders, fibrinolytic disorders, factor XIII deficiency, lupus inhibitor with qualitative platelet defect</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Etiologies

Table 45.1 Profiles of Hemostasis Screening Tests in Patients With Bleeding Disorders

<table>
<thead>
<tr>
<th>PT</th>
<th>PTT</th>
<th>Platelet Count</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>N</td>
<td>Common Factor VII deficiency, early liver disease, early vitamin K deficiency, early warfarin therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare Factor VII inhibitor, dysfibrinogenemia</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>I</td>
<td>Common Deficiency or inhibitor of factor VIII, IX, or XI, vWD, lupus, lupus inhibitor with qualitative platelet defect</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare Deficiency or inhibitor of factor VIII, IX, or XI, vWD, lupus, lupus inhibitor with qualitative platelet defect</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>I</td>
<td>Common Vitamin K deficiency, liver disease, warfarin, heparin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare Deficiency or inhibitor of factor VIII, IX, or XI, vWD, lupus, lupus inhibitor with qualitative platelet defect</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>D</td>
<td>Common Increased platelet destruction, decreased platelet production, splenomegaly, hemodilution</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rare Myeloproliferative disorders</td>
<td></td>
</tr>
<tr>
<td>N</td>
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<td>Rare Inherited qualitative platelet disorders, vascular disorders, fibrinolytic disorders, factor XIII deficiency, lupus inhibitor with qualitative platelet defect</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: PT = prothrombin time; PTT = partial thromboplastin time; I = increased; N = normal; vWD = von Willebrand's disease; DIC = disseminated intravascular coagulation

Spleen and Thymus

Spleen
Splenomegaly ≠ hypersplenism

Common causes of massive, moderate and mild splenomegaly: page 456 Basic Robbins

Thymus
Bone marrow progenitor cells migrate to the thymus and give rise to mature T-cells

Thymic hypoplasia: DiGeorge syndrome

Thymic hyperplasia associated with
Thymomas

Mediastinal tumors
T   T   T   T
Transfusion Medicine
M.E. Bauman, M.D.

Donor Restrictions

Med Hx:

Brief Physical Exam:

No possibility of infectious risk to the donor; sterile equipment used once

Autologus Donations

Directed Donations

Blood Bank Testing

Blood Type: Front and Back Typing

<table>
<thead>
<tr>
<th>Type</th>
<th>Antigen</th>
<th>Antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Universal donor: Universal recipient:
Coomb's Test = Direct Antibody Test = D.A.T.

Indirect Coomb's Test = Indirect Antibody Test = I.A.T. = Antibody Screen

Autoantibody and Alloantibody screen

  Type and Screen

  Type and Cross

Infectious Disease Testing

Risks: Hep B: Hep C: HIV:

Components from Whole Blood

Red Blood Cells

  Indications:

    "transfusion trigger".

  ABO Crossmatched:
**Post Transfusion Hb**

Shelf life:

Rate of infusion:

**Platelets**

Indications:

"transfusion trigger":

ABO Crossmatched:

Volume: Single donor vs. pooled random platelets vs. apheresis single donor unit

Expected rise:

**Post Transfusion Count**

Shelf life:

Rate of infusion:

Pooled random platelets vs. single donor platelets (HLA matched)
Fresh Frozen Plasma (FFP)

Contents:

Indications:

ABO Crossmatched:

Volume:

Dosage:

**Post Transfusion PT/PTT**

Shelf life:

Cryoprecipitate

Contents:

Indications:

Dosage: depends on factor to replace and on recipient's level of factor

Transfusion Reactions

Hemolytic Reactions

Definition:

Fatalities:

Reason for error:
Antibodies:
Clinical aspects:

**Delayed Hemolytic Reaction**

Definition:

**Non-Hemolytic Reactions**

**Febrile**

Etiology:

Rx:

**Allergic**

Etiology:

Rx:

**Circulatory Overload**

**Bacterial Contamination**