HST-080

HEMATOLOGY 2019

Wednesday, February 6, 2019 - Wednesday, April 26, 2019

Course Directors: Nancy Berliner MD and Edward Benz MD

SCHEDULES, PROBLEM SETS, AND LECTURES

CONTENTS

I. FACULTY

CORE FACULTY

Nancy Berliner, M.D. Course Co-Director
nberliner@bwh.harvard.edu

Edward J. Benz, M.D. Course Co-Director
Edward_Benz@dfci.harvard.edu

H. Franklin Bunn, M.D.
hfbunn@rics.bwh.harvard.edu

Benjamin L. Ebert, M.D., D. Phil.
Benjamin_ebert@dfci.harvard.edu

Andrew Lane, M.D., PhD
Andrew_Lane@dfci.harvard.edu

Julie Losman, M.D., PhD
julieaurore_losman@dfci.harvard.edu

Ann Mullally, M.D.
ann_mullally@dfci.harvard.edu

Zuzana Tothova, M.D., PhD
zuzana_tothova@dfci.harvard.edu

Teaching Assistant
Sebastian Koochaki, MD-PhD Candidate
sebastian.koochaki@gmail.com

GUEST LECTURERS and PATHOLOGY INSTRUCTOR

Joseph Antin, MD
joseph_antin@dfci.harvard.edu

John Aster, MD, PhD
jaster@rics.bwh.harvard.edu

Kenneth Bauer, MD
kbaur@bidmc.harvard.edu

Jorge Castillo, MD
JorgeJ_Castillo@dfci.harvard.edu

Daniel DeAngelo, MD, PhD
Daniel_Deangelo@dfci.harvard.edu

Walter Dzik, MD
sdzik@mgh.harvard.edu

Mark Fleming, MD, DPhil
mark.fleming@childrens.harvard.edu

John Gansner, MD, PhD
jgansner@partners.org

Christopher Gibson, MD
Christopher_Gibson@dfci.harvard.edu

Marian Harris, MD, PhD
mhharris@partners.org

Ann LaCasce, MD
alacasce@partners.org

Scott Lovitch, MD, PhD
slovitch@bwh.harvard.edu

Ann Mullally, MD
amullally@partners.org

David Scadden, MD
Scadden.david@mgh.harvard.edu

Adam Sperling, MD, PhD
assperling@partners.org

Olga Weinberg, MD
oweinberg@partners.org

SCHEDULE OF HST HEMATOLOGY COURSE 2019

The course will be held on Wednesday and Friday from 8 AM until 10 AM. February lectures will be in **TMEC 209**. Reading assignments listed below are chapters in Pathophysiology of Blood Disorders. All events will begin on time. Please be prompt.

February 6	*Reading Assignment: Chapters 1, 2*
8:00 – 8:15	Introduction to the course – Dr. Benz
8:15 – 9:45	Lecture 1 – Stem cells and hematopoiesis – Dr. Scadden
February 8	*Reading Assignment: Chapter 19*
8:00 – 9:00	Lecture 2 – Hematopoietic growth factors – Dr. Berliner
9:00 – 10:00	Lecture 3 - Introduction to hematologic malignancies – Dr. Berliner
February 13	*Reading Assignment: Chapters 4, 12, 20*
8:00 – 9:00	Lecture 4– Bone marrow failure – Dr. Ebert
9:00 - 10:00	Lecture 5– Myeloproliferative disorders and myelodysplasia--Dr. Ebert
February 15	
8:00 – 10:00	Case Problems 1-4 Berliner, Mullally, Tothova, Benz
February 20	*Reading Assignment: Chapters 21, 18*
8:00 - 9 :00	Lecture 6 – Acute leukemias – Dr. DeAngelo
9:00 - 10:00	Lecture 7 – WBCs and non-malignant WBC disorders– Dr. Berliner
February 22	
8:00 – 10:00	Case Problems 5-8 Losman, Sperling, Tothova, Berliner
February 27	*Reading Assignment: Chapters 22-24*
8:00 – 9:00	Lecture 8 – Lymphomas including Hodgkin disease – Dr. LaCasce
9:00 - 10:00	Lecture 9 – Plasma cell disorders – Dr. Castillo
March 1	*Reading Assignment: Chapter 25, 26*
8:00 - 9:00	Lecture 10– Hematopoietic cell transplantation – Dr. Antin
9:00 - 10:00	Lecture 11 –Transfusion medicine – Dr. Dzik
March 6	Aster, Fleming, Lovitch
8:00 - 10:00	**Laboratory** - Review of normal and abnormal peripheral blood smears– White cell disorders
March 8	
8:00 -10:00	Case Problems 9-12 Sperling, Benz, Lane, Losman
March 13	*Reading Assignment: Chapters 13-16*
8:00 - 9:15	Lecture 12 – Coagulation and coagulation disorders – Dr. Berliner

9:15 – 10:00	Patient presentation
March 15	*Reading Assignment: Chapters 13-16*
8:00 – 9:00	Lecture 11 – The platelet and platelet disorders – Dr. Berliner
9:00 – 10:00	Lecture 12 – Diagnosing hemorrhagic disorders – Dr. Berliner
March 20	*Reading Assignment: Chapter 17*
8:00 -9:30	Lecture 15 – Thrombotic disorders and anticoagulants – Dr. Bauer
March 22	Aster, Weinberg, Harris
8:00 - 10:00	**Laboratory** - Review of normal and abnormal peripheral blood smears– White cell disorders
March 27	*Reading Assignment: Chapters 3, 5, 7*
8:00-9:00	Lecture 16 – Introduction to anemia – Dr. Benz
9:00-10:00	Lecture 17 – Iron homeostasis and iron disorders- Dr. Fleming
March 29	*Reading Assignment: Chapters 6, 11*
8:00-9:00	Lecture 18 – Megaloblastic anemias – Dr. Bunn
9:00-10:00	Lecture 19 – Acquired hemolytic anemias – Dr. Bunn
April 3	
8:00-10:00	Case Problems, 13-18 Mullally, Benz, Lane, Gibson
April 5	*Reading Assignment: Chapters 8, 9*
8:00-9:15	Lecture 20 – Sickle cell anemia and thalassemia – Dr. Benz
9:15-10:00	Patient Presentation—Elyse Mandell
April 10	
8:00 -10:00	Case Problems, 19-24 Berliner, Sperling, Gibson, Bunn
April 12	*Reading Assignment: Chapter 10*
8:00-9:20	Lecture 21 – Inherited hemolytic anemias – Dr. Benz
9:20-9:50	Patient Presentation-Dr. Bunn

April 15-April 19 HST VACATION

April 24	Fleming, Lovitch, Harris
8:00 – 10:00	**Laboratory** – Review of peripheral blood smears – Red cell disorders
April 26	
8:00 – 10:00	Case Problems 25-29 Berliner, Losman, Benz, Tothova
April 30	
1:30-4:00 PM	Final Exam

III. Groups for Case Solving and Labratory Sessions

Small Case Groups:

Group 1, TMEC 115	Group 2, TMEC 116	Group 3, TMEC 117	Group 4, TMEC 118
Alaina Bever	Andres Binker Cosen	Alice Bosma-Moody	Debbie Burdinski
Wan Fung Chui	James Diao	Kathryn Evans	Nicole Gilette
Isobel Green	Jon Hochstein	Samantha Hoffman	Joyce Kang
Minjee Kim	Kameron Kooshesh	Chanthia Ma	William Mannherz
Nicita Mehta	Alexander Munoz	Leonard Nettey	Atousa Nourmahnad
Julia Schiantarelli	Blake Smith	Akansha Tarun	Enrique Toloza
Julie Urgiles	Emory Werner	Ellen Yu	Christina Zeina
Yichen Zhang	Angela Zou		

Laboratory Groups:

Group 1, HST Skills Area	Group 2, TMEC 302	Group 3, TMEC 332
Alaina Bever	Andres Binker Cosen	Alice Bosma-Moody
Wan Fung Chui	James Diao	Kathryn Evans
Isobel Green	Jon Hochstein	Samantha Hoffman
Minjee Kim	Kameron Kooshesh	Chanthia Ma
Nicita Mehta	Alexander Munoz	Leonard Nettey
Julia Schiantarelli	Blake Smith	Akansha Tarun
Julie Urgiles	Emory Werner	Ellen Yu
Yichen Zhang	Angela Zou	Debbie Burdinski
Nicole Gilette	Joyce Kang	William Mannherz
Atousa Nourmahnad	Enrique Toloza	Christina Zeina

IV. NOTES ON COURSE

1. Goals of HST 080. Although most of you will probably not become hematologists, the goal of this course is to supply all of you with those basic pathophysiology principles that enable a solid understanding of blood disorders. Our coverage of the coagulation system and the structure and function of red and white blood cells will provide an understanding of basic cellular and molecular principles that underlie important clinical disorders. We seek to show you the visual beauty of hematology under the microscope and convey some of the scientific and clinical excitement in this field. Finally, through case discussions and patient presentations, we hope to show you how this area relates to a wide range of medical problems, which are both intellectually fascinating and rewarding to treat.

2. Evaluations. This is a "Pass-Fail" course. Evaluation will be based 5% on the completion of daily quizzes, 45% on participation in the case discussions with the instructors, and 50% on the final examination. The final examination will cover all lecture material, case presentations, labs and the assigned contents of Pathophysiology of Blood Disorders.

3. Final examination. The two-hour final examination will be held on **Tuesday** ***April 30 from 1:30 - 4:00 pm.*** All students are required to be present unless illness or family emergency prevent attendance.

4. Attendance. The HST attendance rules are in effect. ***Attendance at all lectures, case discussions, and labs is mandatory.***

5. Lectures will cover a wide range of topics within each general category ranging from current research to clinical fundamentals.

6. Reading assignments. The assignments given in the course schedule (pp. 6-7) are the indicated chapters in Pathophysiology of Blood Disorders, which is available online free of charge to HMS students. It is our expectation that you will read these chapters before class. To facilitate your understanding of the chapter concepts and gain familiarity with how these topics are likely to be tested, a short multiple choice quiz pertaining to the assigned reading will be posted on MyCourses before each class. Completion of these quizzes is expected and will count towards 5% of your total grade.

7. Laboratory sessions. There will be three laboratory sessions. Since laboratory time is severely abbreviated, our goals for this part of the course are limited to acquainting students with basic blood cell morphology. Students will perform enough microscopy to acquire some competence in identifying normal and abnormal blood cells, and to appreciate the importance of examination of

blood smears along with bone marrow and lymph node specimens in the diagnosis of blood disorders.

8. Case-solving problem sets. To develop clinical hematology skills, we will devote considerable time to the case-solving problem sets that begin in Section VIII. Although we will discuss these cases in small groups, please try to review the problems prior to the sessions. During the session the relevant peripheral blood, bone marrow and laboratory findings will be shown.

9. Problems, comments, complaints. The instructors are all here to help you learn what we think is an exciting and enjoyable area of medicine. If there are areas that you would like to hear more about, or problems with lecturers, classmates, etc. please let Dr. Benz or Dr. Berliner know.

10. HST My Courses Website. All lectures will be posted within 12h of their delivery on this Website.

V. COMMENTS ON AVAILABLE HEMATOLOGY BOOKS

The textbook for this course is Pathophysiology of Blood Disorders, 2nd Edition, 2017. This book was written by Dr. Bunn and Dr. Aster with many of the lecturers in the hematology course given to the regular HMS second year students. This book will serve as the major reference outside of the lecture notes. The electronic version of this book is available to all students free of charge through (https://accessmedicine-mhmedical-com.ezp-prod1.hul.harvard.edu/book.aspx?bookid=1900)
For more in-depth reading on specific topics of interest, recent editions of some excellent hematology books are available:

1. Comprehensive reference works on general hematology.

For many years, the only standard text was Wintrobe, M.M., Clinical Hematology, Lea & Febiger, a clinically-oriented book with extensive bibliographies. This mighty work, which appeared in its 8th edition before Wintrobe's death many years ago, has recently been reissued as Wintrobe's Clinical Hematology, 12th ed., by J.P. Greer et al (Eds), Lippincott Williams & Wilkins, 2008 (two volumes). This is an encyclopedic clinical reference book in hematology.

The large multi-authored work, Williams Hematology, 8th ed, MA Lichtman et al (Eds), McGraw-Hill, 2006 is strong on both clinical and pathophysiological matters. This book is as encyclopedic as Wintrobe but is a bit more concisely written. This book is on library reserve.

Blood, edited by three professors at Harvard Medical School, Robert Handin, Sam Lux and Thomas Stossel, and published by Lippincott, Williams and Wilkins (2003) is equally comprehensive and authoritative.

Hematology: Basic Principles and Practice, by Ronald Hoffman, et al (Eds), 5th Ed, 2008, Churchill, Livingstone is multi-authored text that stresses the scientific basis of hematology with less of an effort being placed on providing an encyclopedic listing of clinical details. It provides a thorough scientific explanation for most issues in hematology.

2. Atlases of blood morphology.

A revision of the famous Sandoz Atlas of Haematology, now called Clinical Haematology 3d Ed, by A.V. Hoffbrand and J.E. Pettit, Mosby, 2000.

Kapff, C. and Jandl, J., Blood, Atlas and Sourcebook of Hematology, 2nd ed., Little Brown, 1991.
An excellent atlas with brief informative text. On reserve in the library.

VI. LIST OF NORMAL LABORATORY VALUES

TEST	NORMAL VALUE
WBC	4.3-10.8 th/cumm
PLATELET COUNT	150-350 th/cumm
HCT	42-52% (Men), 37-48% (Women)
HGB	13.0-18.0 g/dL (Men), 12.0-16.0 (Women) g/dL
MCV	86-98 fl
MCH	28.0-33.0 pg/rbc
MCHC	32.0-36.0 g/dL
RBC NUMBER	4.70-5.50 mil/cumm (Men), 4.15-4.90 mil/cumm (Women)
RETIC	0.5-2.5%
THROMBIN TIME (TT)	18 sec
PT	11.2 - 13.2 sec
PTT	22.1 - 34.1 sec
FIBRINOGEN	175 - 400 mg/dL
BLEEDING TIME	2 - 9.5 minutes
LAP	30-160 U
ESR	1-17 mm/h
B12	>250 pg/mL
FOLIC ACID	3.1-17.5 ng/mL
FE	30-160 mcg/dL
TIBC	228-428 mcg/dL
FERRITIN	30-300 ng/mL
VWF ANTIGEN	70-140% (Blood group O=74%, A=105%, B=115%, AB=125%)
FACTOR LEVELS	60 - 140%
BILIRUBIN TOTAL	0.0-1.0 mg/dL
BILIRUBIN, DIRECT	0.0-0.4 mg/dL
LDH	110-210 U/mL
TOTAL PROTEIN	6.0-8.0 g/dL
ALBUMIN	3.1-4.3 g/dL
GLOBULIN	2.6-4.1 g/dL
BUN	8-25 mg/dL
CREAT	0.6-1.5 mg/dL

VII. COSTS OF LABORATORY TESTS*

TEST	PATIENT CHARGE ($)
Room, semi-private	1818
Room, private	2163
Medical ICU	5004
CCU	5004
Fe	51
TIBC	67
Ferritin	73
Erythropoietin level	93
LDH	40
Hct, spun	15
CBC, diff & plt	53
Diff, automated	11
Plt count	23
Sedimentation rate	19
Reticulocyte count	23
TT	152
PT	21
PTT	33
Fibrinogen	40
Factor level	162
VWF antigen	458
Anti-PL antibody, each	194
LAP	87
D-dimer	183
Protein S or C functional	405
ATIII functional	281
Hgb electrophoresis	152
Plt aggregation, each	394
Plt aggregation & risto	495
Ristocetin cofactor	195
Haptoglobin	68
Flow cytometry, 1 marker	146
DAT	104
Cross-match blood	171
Plt transfusion, one unit	390
Plt txf, 1 apheresis unit	3918
RBC transfusion, one unit	637
FFP transfusion, one unit	317
HIV test	162

VIII. CASE-SOLVING PROBLEMS

CASE-SOLVING - PROBLEM 1

HISTORY: A 47-year old white woman consults you complaining of severe fatigue. A physician has told her she is anemic. She had always been in good health. Eight months ago she slipped on the ice and injured her right shoulder. A physician prescribed orange and white pain capsules which she took for 11 days. Four weeks later she developed flu-like symptoms and returned to her doctor. He gave her a 10-day supply of antibiotic capsules. She took them for 4 days and rapidly improved. Three months ago she had a "scratchy" throat and took the remaining antibiotic capsules. One month prior to admission she began to feel tired and was found to be anemic.

PHYSICAL EXAMINATION: Pallor; otherwise normal.

LABORATORY RESULTS:

Hemoglobin: 9.0 g/dL	Hematocrit: 27%	MCV: 100
RBC: 2.95 million	Reticulocyte count: 0.2%	
WBC: 2,400	Platelet count: 25,000	

Differential : bands 1 polys 12 lymphs 86 monos 1

1. Focusing on the red-cell problem, how would you characterize the anemia?
2. What do the other abnormalities suggest regarding the underlying pathophysiology of this disorder?
3. What additional tests are needed?
4. How do you describe the bone marrow (shown on screen)?
5. What is the probable diagnosis?
6. What is the prognosis?
7. What therapy would you consider?
8. What are potential long-term complications of this disorder?

CASE-SOLVING - PROBLEM 2

HISTORY: A 82 year old man was sent to the Hematology Clinic for evaluation of anemia. He had been in good prior health except for hypertension for which he had been taking hydrochlorathiazide for 26 years. Ten years ago his blood counts were noted to be normal. Six years ago his Hct was 29 and an extensive workup including endoscopy of colon and stomach by his internist was negative. Three years ago his Hct was also 29 with a normal platelet and WBC. His internist performed a number of tests all of which were normal. These included a B_{12}, folate, creatinine, iron, total iron-binding capacity. When his daughter who is a nurse found out that her father's Hct was low she insisted that he be seen by a "specialist." The patient reluctantly comes to the clinic and tells you that he feels perfectly well.

PHYSICAL EXAMINATION: Well-appearing man looking younger than his age. No petechia, bruises, scleral icterus. No hepatosplenomegaly. Stools guaiac negative.

LABORATORY TESTS: From the referring physician:

Hct = 28.5	BUN = 19	PT = 12/12
MCV = 102	CREAT = 0.9	PTT = 28
WBC = 3.5	DIFF = normal	Plts = 72,000
Fe = 145	TIBC=208	Retic = 1.2%
B_{12} = 412	Folate = normal	Guaiac = neg
LDH = 310 (normal: 110-210)		

1. What disorders are associated with a normocytic anemia? With a macrocytic anemia?

2. What other blood tests should you order to help distinguish between these disorders?

All of these tests come back normal.

3. What should you do next?

4. The results of this test are shown on the screen. What is depicted?

5. What special tests would help confirm his diagnosis and assess his progrosis?

6. What are the prognostic factors for this diagnosis?

7. What treatment would you recommend?

CASE-SOLVING - PROBLEM 3

HISTORY: A 31-year old insulin-requiring diabetic shoe salesman has developed fatigue, easy bruising and more frequent nosebleeds. He monitors his own insulin and dislikes visiting his physician. Reluctantly he comes to clinic seeking your help.

PE: Afebrile. Sallow, asthenic man. Multiple bruises, some old blood in nares, no petechiae. No "frost" on the skin.

INITIAL LABORATORY RESULTS:

Hematocrit: 21
MCV: 83
WBC: 4.8
Retics: 1.4 %
Platelets: 312,000

1. What are some possible causes for his anemia?

2. What further tests would you like to order?

ADDITIONAL LABORATORY TESTS:

Bun: 212
Creat: 9
TSH: normal
Folate: normal
Blood Smear: shown on next screen

PT: 12/12
PTT: 33/33
B12: normal
Iron/TIBC: normal

3. Describe the blood smear.

4. Why is he bruising? (He denies any medications other than insulin.)

5. What further tests can you do to document the etiology of his bleeding problem?

6. Three weeks after initiating hemodialysis his Creat is 2.4 and his BUN is 45. His Hct has risen to 26. His bruising is better but still present. He still has some nosebleeds but they are not bothersome. He says he has more energy but still is unable to work. Is there anything else that can be done to help him? Are there any tests that might be performed to assess the potential merit of a particular intervention?

7. He responds well to your intervention and his Hct rises to 37. Surprisingly his bleeding also improves. Ten months later he develops a peritoneal abscess that requires surgical drainage. His hematocrit is now down to 25. Why?

CASE-SOLVING - PROBLEM 4

HISTORY: You are asked to see a 56-year old man in consultation because his WBC count has remained at 51,000 ten days after hospitalization for pneumonia.

1. The blood smear is shown on next screen. Describe it.

2. A bone marrow aspirate is performed and looks just like the peripheral blood.

3. What is the differential diagnosis?

4. How would you distinguish between leukemoid reaction and CML?

5. What therapy is indicated?

6. Three days later you learn that the BCR-ABL RT-PCR was negative. Would this alter your diagnosis?

CASE-SOLVING - PROBLEM 5

HISTORY: A 46-year old dentist is admitted to the hospital for evaluation of left-sided abdominal discomfort of three weeks' duration. In the year prior to entry, he noted progressive postprandial bloating and discomfort, urinary frequency and nocturia and intermittent diarrhea. Over this period he also experienced progressive weakness and easy fatigability, intermittent night sweats and a 15-pound weight loss. His prior health was excellent save for the development of gout 3 years ago and the passage of a renal stone 2 years ago.

PHYSICAL EXAMINATION: A reasonably healthy-looking, slightly pale man who shows evidence of recent weight loss. A firm, non-tender spleen was palpable 20 cm beneath the left costal margin, and the liver edge was 4 cm below the right costal margin. The remainder of the examination was normal.

LABORATORY RESULTS:

Hematocrit: 30% WBC: 24,500

Platelet count: 611,000 MCV = 90

Reticulocyte count 2.4 %

Blood smear: shown on next screen

1. Describe the blood smear.

2. What is the differential diagnosis?

3. What further tests would be useful in establishing the diagnosis?

ADDITIONAL DATA:

Ph[1] chromosome: negative

JAK2 mutation analysis: both normal and mutant JAK2 alleles are present

Bone marrow: on next screen.

4. What is the most probable diagnosis?

5. What treatment would you offer?

CASE-SOLVING - PROBLEM 6

HISTORY: A healthy 58-year old man is seen in clinic because a routine blood test revealed a hemoglobin of 20 g/dL (Hct = 60). He had a chronic cough but no sputum or shortness of breath. Exercise tolerance was essentially normal. He had smoked 3 packs of cigarettes daily for 30 years and, in addition, 15 large cigars a week for the last 10 years. His hemoglobin 4 years earlier was 15 g/dL.

PHYSICAL EXAMINATION: Ruddy complexion (slide). Heart normal. No enlargement of liver, spleen or lymph nodes.

LABORATORY RESULTS:

Hematocrit: 62% Hemoglobin: 21.6 g/dL

WBC: 7,600 Reticulocytes – 1.3%

Differential: polys 68% lymphs 28% monos 4%

Platelets: 250,000

1. What disorder (s) might explain the elevated hematocrit?

2. What tests would help you to evaluate this problem?

ADDITIONAL LABORATORY DATA:

Hemoglobin electrophoresis (cellulose acetate): normal

Arterial oxygen saturation: 78% (normal 95-99%)

Carboxyhemoglobin (HbCO): 17.8% (normal <1%) (slide)

Serum erythropoietin: 107 mIU/mL (normal 7-30)

JAK2 mutation analysis: no mutation detected by PCR

3. What is the diagnosis?

4. How would you treat this patient?

5. Why is this NOT polycythemia vera?

CASE-SOLVING - PROBLEM 7

HISTORY: A 4-year old boy is brought to your office by his mother because he has been irritable for a week and was noted that day to have a rash. For the past 36 hours he has had a cough and a sore throat. The child was previously in good health.

PHYSICAL EXAMINATION: Temperature 103.5 F. Pale skin with scattered petechiae, especially on the legs. Small hemorrhage in left fundus. Petechiae on buccal mucosa and conjunctivae. Small-moderate-sized lymph nodes (1 cm) in cervical regions, both axillae and both inguinal areas. Neck supple. Chest clear. Heart normal to examination. Spleen felt 2 cm below the left costal margin. Liver edge palpable. Remainder of examination normal.

LABORATORY RESULTS:

Hematocrit: 23%	MCV = 84
WBC: 1,900	Hemoglobin: 7.6 g/dL
Platelet count: 11,000	Reticulocyte count: 0.4%

1. What is the differential diagnosis?

2. What tests will aid you in the differential diagnosis?

ADDITIONAL DATA:

All cultures negative.

Blood smear: shown on next screen.

Bone marrow aspirate: shown on next screen.

Flow cytometry: 96% of blasts are CD10+ ("CALLA") positive and terminal deoxyribonucleotidyl transferase (TdT) positive

3. What is the most probable diagnosis?

4. What forms of therapy are indicated?

5. What is the prognosis for this child?

CASE-SOLVING - PROBLEM 8

HISTORY: A 34-year old lawyer developed an extensive hematoma following body contact in a squash game. He later developed gingival bleeding (slide), and he was referred to you by his dentist for evaluation. He had been previously well and had undergone appendectomy without complications.

PHYSICAL EXAMINATION: Petechiae and purpura, including mucus membranes.

1. Outline your approach to the problem.

LABORATORY RESULTS:

Hematocrit: 26 with 3% retics; Platelets: 50,000 (nl=150,000-350,000)

PT: 18/12 PTT: 62/34

WBC: 35,000 (normal=5,000-12,000)

Blood smear: many promyelocytes, nucleated red cells, schistocytes, red cell fragments, decreased platelets.

2. What is the most likely hematologic disorder (to account for blood smear)?

3. What further diagnostic tests should be done to resolve that issue?

The bone marrow aspirate is shown on the next screen.

4. Before reaching a final hematologic diagnosis, you elect (wisely) to elucidate the hemostatic defect. What disorders can affect both the PT and PTT?

5. What further clotting tests would you order at this point?

ADDITIONAL DATA:

Fibrinogen level: 80 mg/dL (normal >150)
TT: 40/20
FSP: 1:128 (normal < 1:4) D-dimer: > 10,000 ng/mL (normal < 500 ng/mL)

7. Why is the TT prolonged?

8. What diagnosis can tie this picture together?

9. What therapy would you recommend?

CASE-SOLVING - PROBLEM 9

HISTORY: A previously healthy 19-year old high school girl gives a 6-month history of malaise. Three months before hospital admission she noticed night sweats and shortly afterward her mother observed a swelling in the left side of her neck. She consulted a doctor who biopsied a left supraclavicular lymph node. Histology was reported "reactive hyperplasia" and was considered non-diagnostic.

Night sweats continued and she experienced chills. She soon developed lymphadenopathy on the right side of the neck, and she was referred to the hospital for study.

PHYSICAL EXAMINATION: A 19-year old white girl with a temperature of 102˚F. Other vital signs normal. Bilateral 2-3 cm rubbery supraclavicular lymph nodes. Healed biopsy scar. Discrete 2 cm node in left axilla. Heart and lungs normal. Liver and spleen could not be felt. No other adenopathy.

LABORATORY RESULTS:

Hemoglobin: 10.1 g/dL Hematocrit: 31%

WBC: 12,500 Platelets: 432,000

Differential: polys 83%, lymphs 7%, monos 4%, eos 5%, basos 1%.

Serum BUN, creatinine, electrolytes, bilirubin, alkaline phosphatase, LDH and uric acid normal.

Direct Coombs and heterophile negative.

Chest CT scan: enlarged paratracheal lymph nodes; no hilar adenopathy or pulmonary infiltrate.

CT scan of abdomen: enlarged para-aortic lymph nodes and splenomegaly.

1. What diagnoses would you consider in this clinical situation?

Repeat biopsy from the right supraclavicular region was performed. The biopsy is shown on the next screen.

2. What does the biopsy show?

3. What further tests would you consider essential for adequate staging?

Bone marrow biopsy is seen on the next screen.

Note the appearance of the Reed-Sternberg cells.

4. What therapy would you advise? Why?

5. How successful do you expect her therapy to be?

CASE-SOLVING - PROBLEM 10

HISTORY: A 64-year old man consults you because of back pain. He had been well all of his life except for an inguinal hernia which was repaired 17 years previously. For the past year he has felt "run-down" without any specific complaints, and for the past 6 weeks he has had pain in his lower back aggravated by movement.

PHYSICAL EXAMINATION: The only positive findings are pallor and tenderness over the lower spine.

LABORATORY RESULTS:

Hemoglobin: 9.6 g/dL	Hematocrit: 30%
MCV = 87	Retic: 1.3%
WBC: 8,400	Platelets: 186,000
Blood Smear: shown on next screen	
ESR = 140	

1. Explain the abnormalities noted on the blood smear.

2. What laboratory test(s) might explain why rouleaux formation is present on the smear?

3. What is the most probable diagnosis?

4. What other tests would you order to confirm the diagnosis?

OTHER DATA:

Fibrinogen: normal

Serum protein (total): 12 g/dL (normal = 6-8 g/dL)

Serum globulins: 9 g/dL (normal = 2.6-4.1 g/dL)

Serum protein electrophoresis: monoclonal (M) spike

Bence-Jones protein in urine: positive

Bone marrow exam: (see slide)

X-rays: diffuse osteoporosis with "punched-out" lesions in ribs, skull and pelvis. L1 collapsed.

5. In addition, the following test results were obtained. Explain each:

Immunofixation: IgA (kappa) M spike

IgA = 5700 mg/dL (normal = 69-309 mg/dL), IgG = 210 mg/dL (normal = 614-1295 mg/dL), IgM = 46 mg/dL (normal = 53-334 mg/dL)

Serum free kappa and lambda light chains: kappa = 3690 mg/L (normal: < 26 mg/L); lambda = 4 mg/L (normal: < 26 mg/L)

Negative urine protein as measured by "Chemistix" and "Albustix" but +++ protein when tested with sulfosalicylic acid.

Serum calcium: 14.7 mg/dL (normal 8.5-10.5 mg/dL)

Serum alkaline phosphatase: 185 U/L (normal 45-115 U/L)

Serum electrolytes: Na = 142, K = 3.5, HCO_3 = 28, Cl = 110.

Serum creatinine: 3.2 mg/dL (normal 0.6-1.5 mg/dL)

6. Would it be worthwhile to treat this man? If so, how (in general terms)?

7. What are his odds for survival?

8. What is amyloid?

CASE-SOLVING - PROBLEM 11

John is a 59-year-old man who presents with "lump" in his right inguinal region. On questioning, he states that he first noticed non-painful swelling in this area 2-3 months ago, and that since then the lump has slowly increased in size. Otherwise, the patient feels well. He denies weight loss, fever or night sweats. Past medical history is significant for a stage B1 colorectal carcinoma, which was resected 5 years previously. He keeps three cats at home.

On physical examination, several firm, matted lymph nodes, 2-3 cm in size, are palpable in the right inguinal region, as is a single 2 cm left inguinal lymph node and a small right axillary lymph node. No organomegaly is appreciable. There is no leg swelling. At this time the CBC is normal.

1. What additional social history might be relevant? What is your differential diagnosis at this point?

A surgeon performs a right inguinal lymph node biopsy. A 2 cm lymph node is removed and immediately transported to the frozen section room where a pathologist is waiting. Two days later, the pathologic results are ready.

2. What tests would you like to perform in order to arrive at a diagnosis? Based on the review of the histology and additional laboratory data (to be performed in the laboratory), what is your diagnosis? Discuss the molecular pathogenesis of this disorder.

3. What additional clinical studies may be useful in further evaluating the patient? What stage is the patient? What treatment options are available?

The patient's local hematologist/oncologist elects to follow the patient, who continues to feel reasonably well for seven years despite waxing and waning inguinal and axillary lymphadenopathy. He now returns to you with a history of recent weight loss and rapid increase in size of a lump in his right axilla, where a 6 cm mass is palpable. A biopsy of the mass is performed.

4. Compare the histology in this biopsy to that of the previous biopsy, evaluating the same histological features. What is your diagnosis on the new biopsy?

5.. What therapy is now indicated?

CASE-SOLVING - PROBLEM 12

HISTORY: A 66-year old grandmother underwent successful replacement of an aortic valve. She was transfused with 4 units of blood during surgery. She was then started on Coumadin therapy. Recovery was uncomplicated until the ninth post-operative day when she appeared slightly icteric and complained of weakness.

PHYSICAL EXAMINATION:

Pallor and slight icterus. Otherwise negative

LABORATORY RESULTS:

Hematocrit: 25% (nine days earlier had been 33%).

Reticulocyte count: 12%

1. What additional tests would you perform?

2. The blood smear is shown on next screen. Describe it.

3. What is the most likely diagnosis?

4. A reference laboratory reports that the patient's serum has developed an anti-Jk^a (anti-Kidd) antibody. What precautions are necessary in the future?

5. Why did it take 9 days for this to occur?

CASE-SOLVING - PROBLEM 13

HISTORY: A Scandinavian representative to the United States, age 52, was visiting in Boston and had a minor automobile accident. Soon afterward he developed multiple ecchymoses over both arms and legs. He also had severe epistaxis. He reported that although he bruises easily and has experienced several episodes of prolonged epistaxis in the past, he has not previously had difficulties with abnormal bleeding. However, his son bled profusely after a tonsillectomy. His daughter also bruises easily and has frequent epistaxis. He reports that a "bleeding time was greater than 15 minutes" on several prior occasions.

LABORATORY RESULTS:

CBC: Normal

PT: 11/11 PTT: 52/31 Platelet count: 220,000 (Nl: 150-350,00)

1. What sort of hemostatic disorder is suggested by these results?

2. What further tests are needed?

ADDITIONAL DATA:

Platelet aggregation: normal with ADP, epinephrine and collagen, abnormally low with ristocetin

Ristocetin cofactor: 30%

VWF antigen: 33%

Factor VIII activity: 36%

3. What diagnosis is most likely?

4. How should he be treated?

5. What is the risk that his children will have this problem?

CASE-SOLVING - PROBLEM 14

HISTORY: A 58-year old man noted a "rash" on his lower legs and consulted his physician. He had been in excellent health and had no other complaints.

PHYSICAL EXAMINATION: Petechiae on lower legs and torso (see slide). Bruise over venipuncture site. No splenomegaly.

LABORATORY RESULTS:

Hematocrit: 46% Platelet count: 5,000 (Nl: 150-350,000)

WBC: 8,600

Differential: polys 80% lymphs 16% monos 4%

Blood smear: shown on next screen.

1. Does the blood smear confirm the platelet count?

2. What additional history might be useful?

3. What other studies are indicated?

The bone marrow aspirate is shown on the next screen.

4. Interpret the bone marrow.

5. What is the most likely diagnosis? What are the possible underlying etiologies for this diagnosis?

6. What initial therapy is indicated?

Four weeks later the platelet count is 13,000.

7. What would be your next move?

CASE-SOLVING - PROBLEM 15

HISTORY: A 54 year old man was admitted for chest pain and was found at catheterization to have a 95% obstruction of the mid-LAD. He was stented and placed on iv heparin, clopidrogrel and aspirin. Because of persistent, intermittent chest pain he was kept on iv heparin and had several repeat catheterization procedures over the next 7 days. On admission the platelet count was 230,000. On hospital day 7 it was 109,000. On the 8th hospital day it was 49,000 and the patient complained of right foot pain. The hematocrit remained normal. The foot was examined and found to be cold and ischemic. While waiting to go to the OR for revascularization of the right leg, he developed left hemiparesis.

The patient had a strong family history of cardiac disease and had undergone prior cardiac catheterization one year previously. He had been hospitalized for one week two years previously for pneumonia and had antibiotics administered via a Heplock.

1. Why has this person become thrombocytopenic?

2. What tests could you order to prove your hypothesis?

3. Why is the leg ischemic? Why is he having a stroke? What do you expect the surgeons found in the patient's leg in the OR?

The patient eventually loses the toes on the right leg and undergoes adequate rehabilitation after his stroke. He is discharged home on warfarin. Six months later as a outpatient he develops more angina that is refractory to medical management. He is referred to the cardiac surgeons for a 4-vessel graft.

3. The surgeons tell you he will require a 2 hour bypass time and ask your advice about anticoagulation during that time. What would you recommend?

CASE-SOLVING - PROBLEM 16

HISTORY: A 35 year old woman is undergoing evaluation for infertility. She has had multiple miscarriages (all in the first trimester) in the past 6 years. Her six sisters all have had multiple children. Prior to undergoing laparoscopic evaluation, her gynecologist checked some "routine" pre-op tests.

LABORATORY TESTS:

PTT = 85/35	plts = 125,000
PT = 14/12	fibrinogen = 216
TT = normal	

Platelet aggregation tests = normal except for mild "aspirin effect"
Lab director suggests repeat.

1. What is the "appropriate" pre-op hematological evaluation for surgical patients?

The patient had had multiple prior surgical procedures (wisdom teeth removed, appendectomy, tonsillectomy, D&C) without bleeding. She had never had easy bruising or bleeding problems. She took one ASA a day for her headaches.

The patient provided some additional history: She has frequent Raynaud's phenomenon. Several years ago she has a right lower leg DVT and was treated with warfarin for 3 months. She has frequent migraine headaches and a CT scan done several years ago to evaluate these showed multiple small cerebral infarcts. Her HMO internist refused to send her to a neurologist because she had a "normal neuro exam." She also complained of multiple "blind spots" in her visual field that were bothersome only when she read. She has had no serositis, pleuritis, pericarditis, arthritis or skin rash. Her ESR is 6 and her complement levels have been normal.

2. What are the possible causes of an elevated PTT?

3. The 1:1 mix "fails to correct". What does this mean? What tests should be done next?

4. What is her most likely diagnosis? Does this explain her symptoms?

5. Is it safe for her gynecologist to perform a laparoscopy with this elevated PTT?

6. What does the future hold for this woman re: pregnancy? thrombosis? bleeding?

7. Is there any intervention you can offer her?

CASE-SOLVING - PROBLEM 17

HISTORY: A 20-year old football player sprained his ankle and was told to use crutches and rest the leg. Three days later he developed a swollen calf and thigh, chest pain and hemoptysis.

1. How would you approach the problem?

The chest X-ray is normal but the PE protocol CT scan showed a right pulmonary artery clot and a clot in the left leg extending from the femoral vein down to the popliteal vein.

2. What is the most likely diagnosis?

3. What therapy would you recommend?

Before starting therapy, the patient recalls that his father and two brothers have had similar problems.

4. What potential underlying coagulation disorders should be considered?

5. For how long a time should he be treated with warfarin?

6. His lower leg nearly returns to normal but remains slightly swollen 6 months later. Why? Is there anything that can be done to prevent the swelling? What happens to clots in the leg after anticoagulation therapy?

CASE-SOLVING - PROBLEM 18

HISTORY: A 68-year old woman who has been well all her life enters the hospital with extensive ecchymoses, swelling of the flanks and hemorrhage into the right hip and left knee. Two weeks prior to admission her private physician had given her some penicillin tablets for an upper respiratory infection. There is no family history of bleeding disorder and the patient had undergone prior surgery and two pregnancies without incident.

PHYSICAL EXAMINATION: Hematomas, large ecchymoses and two hemarthroses, swollen L. knee. No petechiae. Normal range of motion in other joints.

1. What further diagnostic steps would you take?

LABORATORY RESULTS:

Hematocrit: 30% (was 42% 3 months before)

WBC: 8,700 Platelet count: 320,000

Differential: 65% polys, 30% lymphs, 5% monos

PT: 11/10 PTT: 54/25 TT: 20/20 fibrinogen: 400 mg/dL

Serum bilirubin: total 2.8, D-dimer: > 10,000 ng/mL

Liver chemistries: normal Stool guaiac: positive

2. What is the significance of these findings?

Factor assays gave the following results:

(Factor XII: 100% - not necessary)
Factor XI: 87%
Factor IX: 154%
Factor VIII: 1%

3. Does the patient have hemophilia? What other studies are indicated?

When this was done, the prolonged PTT of patient plasma was not corrected by admixture with normal plasma.

4. What is the diagnosis?

5. What treatment is indicated?

CASE-SOLVING - PROBLEM 19

HISTORY: A 32-year old woman of Italian ancestry is referred to you because a mild anemia was detected on a routine examination. The patient says she was told she was anemic in childhood, while in college and again during her only pregnancy. In each case, she was given iron pills, but no follow-up evaluations were ever obtained. She thinks her mother has also had intermittent mild anemia. The patient feels entirely well and denies indigestion, melena or excessive menstrual bleeding.

LABORATORY RESULTS:

Hematocrit: 34% WBC: 6,700

Platelet count: 192,000 Reticulocyte count: 1.6%

Red cell indices: MCV 73fl MCHC 32 g/dL

Blood smear: shown on next screen.

1. Describe the blood smear.
2. What is the differential diagnosis?
3. What is the probable diagnosis?
4. What laboratory tests would be indicated?
5. What results would confirm the diagnosis?
6. What genetic counseling would you provide?

CASE-SOLVING - PROBLEM 20

HISTORY: An 8-year old girl who was brought to the emergency room because of sore throat is admitted for 10th time. She was the product of a normal pregnancy and weighed 5.5 lbs at birth. Her growth was slow (15th percentile) but development was normal. At age 18 months she received oral iron for "anemia." At age 3 the hemoglobin level was 8 g/dL. Her mother reports occasional episodes of scleral icterus. Except for recurrent viral infections she has been in reasonably good health. Her usual Hct is 26-28 and her reticulocyte count is usually 6-10%. She is of Italian and English ancestry. Her mother and brother have mild anemias. The mother's sister died at age 12 of anemia. The Hct was 27 one month ago.

PHYSICAL EXAMINATION: Temperature 103° F. Patient is small for her age. Her cheek bones and upper teeth are prominent. Scleral icterus is present and the spleen and liver are palpable 2 cm below the costal margins. Tonsils are inflamed and covered with exudate. Tender cervical adenopathy.

LABORATORY RESULTS:

Hemoglobin: 6.6 g/dL	Hematocrit: 20.5%	MCV: 60 fL
RBC: 3.0 million	Reticulocyte count: 2.5	
WBC: 16,000	Platelet count: 286,000	

Blood smear: shown on next screen.

1. Describe the blood smear.

2. What is the general type of anemia?

ADDITIONAL DATA:

Throat culture: beta-hemolytic streptococci

Total bilirubin: 4.4 mg/dL (normal: 0.0-1.0 mg/dL)

Iron studies:
- Serum iron: increased
- Iron saturation: increased
- Serum ferritin: increased

3. What is the probable hematological diagnosis?

4. What clinical tests would confirm the diagnosis?

5. What mechanisms underlie the hyperbilirubinemia?

6. Why is the WBC elevated?

7. Why is the hematocrit lower than it was a month ago?

8. How should she be treated today?

9. What complications are likely in the future?

10. What are long-term treatment options?

11. Were iron treatments a good idea?

CASE-SOLVING - PROBLEM 21

HISTORY: A 23-year old black woman is referred to you because splenomegaly and mild anemia had been found on a pre-employment physical examination. She denied illness or significant symptoms in the past. She has not had bouts of joint or abdominal pain, nor was she a "sickly" child. Several doctors had told her she was anemic and gave her iron therapy. She has not experienced abnormal bleeding. Menstrual periods are regular, occurring at normal intervals and lasting 3 days. She has never been pregnant. She does not take alcohol.

PHYSICAL EXAMINATION: An enlarged spleen is easily felt extending 2 cm below the left costal margin. There is no icterus, purpura or lymphadenopathy. The liver is not enlarged.

LABORATORY RESULTS:

Hemoglobin: 10.2 g/dL	Hematocrit: 31%	MCV = 82
RBC: 3.1 million	Reticulocyte count: 7.2%	
WBC: 9,500	Platelet count: 165,000	

A panel of liver function tests gave normal results.

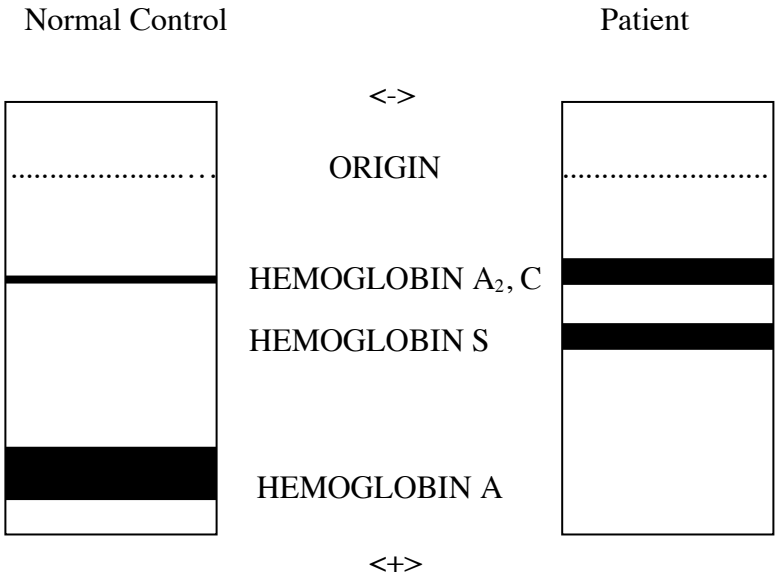
1. The blood smear is shown on next screen. Describe it.

2. What is the differential diagnosis (i.e. the major diagnostic possibilities that must be ruled in or out)?

3. What test would help in sifting through the diagnostic possibilities?

4. The sodium metabisulfite test was positive, indicating decreased solubility of deoxyhemoglobin.

5. A routine cellulose hemoglobin electrophoresis preparation had the following pattern:



6. What is the probable diagnosis?

7. Why is SC a disease whereas AS (sickle trait) is benign?

8. How would you explain the patient's benign course?

9. What complications might be anticipated in the future?

CASE-SOLVING - PROBLEM 22

HISTORY: A 28-year old housewife in the eighth month of pregnancy is referred to you for evaluation and treatment of her anemia. This is the third pregnancy in 5 years. Patient nursed her first baby and was never previously given any type of prenatal supplements.

PHYSICAL EXAMINATION: Patient is carrying what appears to be a normal pregnancy. She is pale and has koilonychia (spoon-shaped fingernails), atrophic glossitis (smooth, sore tongue), angular stomatitis (ulcers at corner of mouth), and brittle hair.

LABORATORY RESULTS:

Hemoglobin: 5.6 g/dL Hematocrit: 20%

RBC: 3.1 million Platelet count: 560,000/mm^3

WBC: 9,000 MCV: 62 fl

Differential: polys 67% lymphs 26% monos 7%

Blood smear: shown on next screen.

Stool guaiacs are repeatedly negative. Urine is free of red cells.

1. Describe the blood smear.

2. What is the differential diagnosis?

3. How would you approach this problem?

ADDITIONAL LABORATORY RESULTS:

Reticulocyte count: 1.9% (normal: 0.8-1.5)
Serum iron: 22 ug/dL
Iron-binding capacity: 482
Iron saturation (calculated): 5% (normal >15%)
Serum ferritin: 3 ng/mL (normal >20 ng/mL)

4. Would you do a bone marrow aspirate and/or biopsy on this patient? If it was done, what would you expect it to show?

5. What is the most likely diagnosis?

6. What points in history should be carefully evaluated?

7. What response would be expected to $FeS0_4$, 300mg three times a day orally?

8. Are there other options for iron supplementation?

9 What would explain a failure of oral iron therapy to completely correct her anemia?

10. Why is her platelet count elevated?

11. What other diseases are associated with microcytic anemia but with excessive iron stores in the bone marrow and failure to respond to oral iron therapy. What cell type may be seen in the bone marrow of most of these patients.

CASE-SOLVING - PROBLEM 23

HISTORY: A 57-year old pharmacist is seen in the outpatient department because of dyspnea on exertion. He had been well until 4 years ago when he was assaulted and robbed. He received stab wounds to the left thigh requiring 18 stitches and to his abdomen resulting in the resection of 5 ft of terminal ileum. He recovered and returned to work after a year's convalescence. For the past 6 months he felt progressively more tired and for 1 month has been unable to climb more than 1 flight of stairs without resting. The patient insists that he has a good diet and is on no medication.

PHYSICAL EXAMINATION: Pallor, faint icterus, well-nourished, atrophic glossitis, signs of previous surgery. Otherwise normal.

LABORATORY RESULTS:

Hemoglobin: 3.8 g/dL	Hematocrit: 12%	MCV: 123 fl
RBC: 1.0 x $10^6/\mu L$	Reticulocyte count: 0.4%	
WBC: 3,500/μL	Platelet count: 70,000/μL	

Blood smear: shown on next screen.

1. Describe the peripheral blood smear.
2. What is the general type of this anemia?
3. What is the differential diagnosis of macrocytosis?
4. What tests will aid in making the diagnosis?

ADDITIONAL DATA:

Serum vitamin B12: 60 (normal 250-800) Serum folate: 15 (normal 5-20)

Serum methylmalonate: 15,000 nM (normal 150-600)

5. What would the bone marrow look like in this patient?
6. What is the diagnosis?
7. What therapy is indicated? Transfusions?

CASE-SOLVING - PROBLEM 24

HISTORY: A 78-year old woman comes to your office because of the recent onset of fatigue, epigastric distress and weight loss. Physical examination is notable only for pallor. The patient had been told 16 years ago that she has pernicious anemia, and she has been receiving monthly vitamin B12 injections ever since.

LABORATORY RESULTS:

Hematocrit: 25%	Reticulocyte count: 1.4%
WBC: 7,100	Platelet count: 240,000
MCV: 71 fl, MCHC: 30 g/dL	

1. What kind of anemia is suggested by these findings?

2. Is there a diagnosis which might unify her present and past history?

3. What additional studies should be performed?

4. Is it possible after 16 years of vitamin B12 injections to confirm whether or not the patient has pernicious anemia?

5. What medication(s) might correct her anemia? What are your options if she cannot take medication po?

CASE-SOLVING - PROBLEM 25

HISTORY: You have been asked to evaluate a 36-year old black man who was given a course of "sulfa" tablets for prostatitis. Four days later he experienced severe palpitations, fatigue and yellowish sclerae.

PHYSICAL EXAMINATION: Normal except for scleral icterus.

LABORATORY RESULTS:

Hemoglobin: 7.0 g/dL	Hematocrit: 24%	MCV = 108
RBC: not done	Reticulocyte count: 18%	
WBC: 13,600	Platelet count: 190,000	

1. In general terms, what sort of anemia is this?

2. What further laboratory tests would you order at this point?

3. A supravital stain of a blood smear was prepared. It is shown on next screen. Describe the findings.

4. What would routine Wright's stained blood smear look like?

5. A G-6-PD screening assay is reported as normal. What other tests would you request?

6. What is the pathophysiologic mechanism of the anemia?

7. What are the chances that the patient's sister would develop significant hemolysis if she were given a similar course of sulfa tablets?

8. What would you expect to happen if the patient continued to take sulfa tablets?

CASE-SOLVING - PROBLEM 26

HISTORY: A 17-year old woman is referred to you because of mild jaundice which may have been present for many years. When questioned she admits that she never had the physical stamina of her friends. Nonetheless, she jogs several miles each day. Sometimes she has right upper quadrant abdominal pain that may be related to running. She was given iron pills for anemia, at least twice in the past, once in childhood.

PHYSICAL EXAMINATION: The only positive findings are scleral icterus and a palpable spleen tip 1 cm below the left costal margin.

LABORATORY RESULTS:

Hemoglobin: 11.2 g/dL	Hematocrit: 31%	Bili total: 3.3
RBC: 3.0 million	Reticulocyte count: 9.8%	MCV = 85 fl
WBC: 9,600	Platelet count: 256,000	

Differential: polys 61 lymphs 33 monos 6

Blood smear: shown on next screen.

1. Describe the blood smear.

2. What general type of anemia might explain these values? Why do you think so?

3. What additional history might be helpful in supporting your impressions?

4. What other laboratory tests would you order? Why? Are there any tests that might validate your impressions of the blood smear? (slide)

5. What is the diagnosis? What is the underlying pathophysiology?

6. What is the MCHC? Is it normal? If not, explain why.

7. What treatment would you recommend? How might this help this asymptomatic young woman? How might it harm her?

8. What hematologic findings do you expect to encounter in this patient one year after treatment?

CASE-SOLVING - PROBLEM 27

HISTORY: A 45-year old black woman was referred to you because of anemia of recent onset. Except for occasional early morning wrist and finger pain, she was well until 3 months ago when she began to have headaches. A physician found her blood pressure elevated and prescribed anti-hypertensive medication (which she took faithfully). One month ago she noticed shortness of breath on climbing stairs, intermittent palpitations and then generalized weakness. Her family called her attention to a yellowish tint of the whites of her eyes. Her urine and stool were normal in color. Her personal physician again found mild hypertension, but this time he observed scleral icterus and slight enlargement of the liver and spleen. For these reasons he sent her to you. There is no family history of anemia or jaundice.

PHYSICAL EXAMINATION: Your examination confirms that of her own physician.

LABORATORY RESULTS:

Hemoglobin: 9 g/dL	Hematocrit: 28%	MCV = 112
RBC: 2.8 million	Reticulocyte count: 10.2%	
WBC 4,000	Platelet count: 230,000	

Blood smear: shown on next screen.

1. Describe the blood smear.
2. How would you now classify the anemia?
3. What additional history might help you narrow the diagnostic possibilities?
4. What additional laboratory tests will you perform?
5. What is the diagnosis?
6. How should the patient be treated?
7. Why is the MCV increased?

CASE-SOLVING - PROBLEM 28

HISTORY: A 61-year old man who has enjoyed good health consults you because of large lymph nodes in his neck. In addition, you detect splenomegaly. The patient has recently recovered from a "cold" but has no other complaints.

LABORATORY RESULTS:

Hematocrit: 28% Reticulocyte count: 14.0%

WBC: 110,000 MCV = 105

Differential: polys 10% lymphs 89% monos 1%

Total bilirubin: 2.2 mg/dL LDH = 369 (normal = 110-210 U/mL)
Blood smear: shown on screen.

1. What are the findings on the blood smear?

2. What is the most likely diagnosis?

3. What is the cause(s) of the anemia? How would you confirm this?

4. What therapy would be indicated?

5. What potential complications might you expect in the future?

6. Is he neutropenic?

7. Why is the MCV increased?

CASE-SOLVING - PROBLEM 29

HISTORY: A 29 year old female comes to the Emergency Room complaining of malaise. She is an organ grinder who works with her monkey at Quincy Market. She has had no prior medical problems, has not been sexually active or used illicit drugs. Ten days ago she had a bout of profuse, intermittently bloody diarrrhea, cramps and mild fever. The diarrhea has resolved but for the past three days she has felt weak and has been told that her eyes were "yellow." She describes a few bruises on her lower extremities. The monkey has been well.

1. How would you approach this problem?

PHYSICAL EXAMINATION: Petechiae on lower legs, a large bruise on the thigh and scleral icterus. She is afebrile.

2. What laboratory tests would you ask for?

LABORATORY TESTS: Your medical student provides the following test results:

Hct 21; retics 15% WBC 12,000 Platelets 27,000
PT = 12.1 (normal) PTT = 28.9 (normal) DD < 500 (normal)
LDH 2700
Total bilirubin 5.6

3. What is the most likely general diagnosis?

4. What tests should you now consider to clarify and prove this diagnosis?

Schistocytes are present and the platelet count is low. While you are reviewing the smear, the nurses inform you that the patient has lost consciousness.

5. While you are examining your comatose patient, you tell the medical student to draw some more blood. What tests should your HST student ask for?

Twenty minutes later the student reports the following "Stat" values:

BUN	40
Creat	2.5
Na	131
K	5.1
CO2	23
Cl	99

6. What is the final diagnosis and how would you treat this patient?

7. Consider that the patient has the same peripheral smear, but the following laboratory values. How would that change your thinking about the case and how would it alter treatment?

	Hct	Platelets	INR/PTT	d-dimer	Creatinine
This case	21	27,000	1.2/28.9	<500	2.5
2	21	97,000	1.2/28.9	<500	6.8
3	21	50,000	2.6/43	3200	2.5