MAYO CLINIC

Oncology and Hematology Review
ACP Puerto Rico Chapter Annual Meeting

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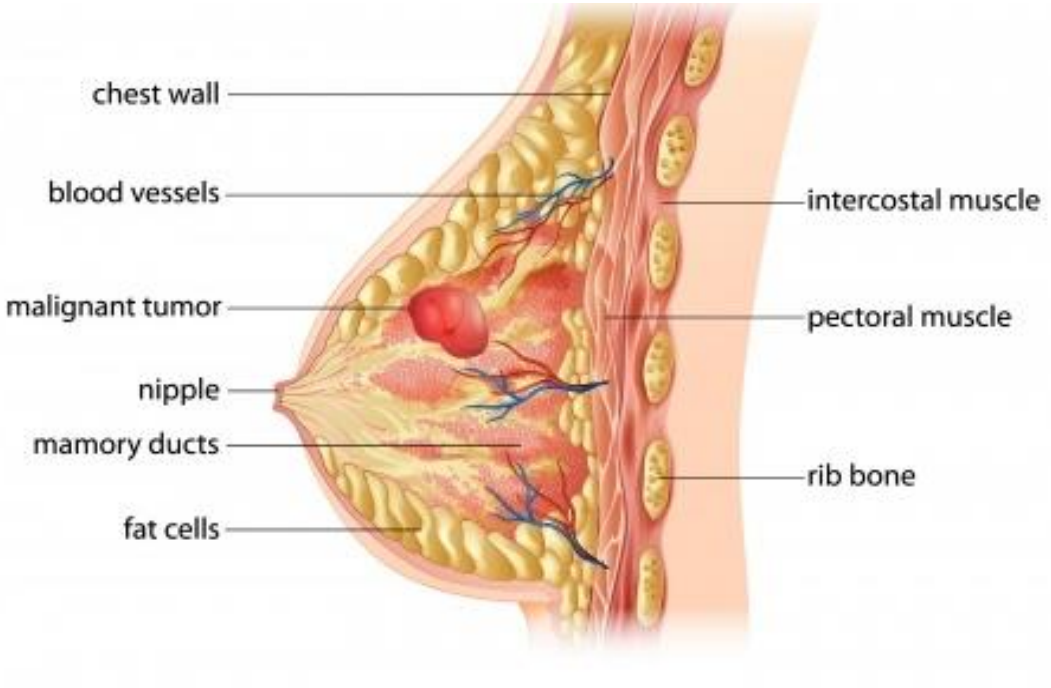
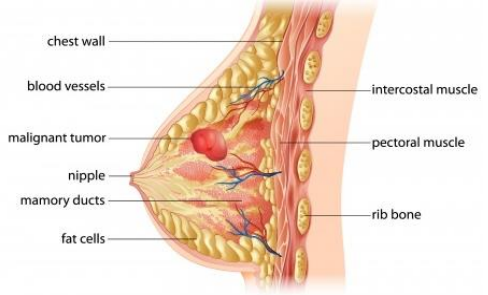
Disclosures

- None



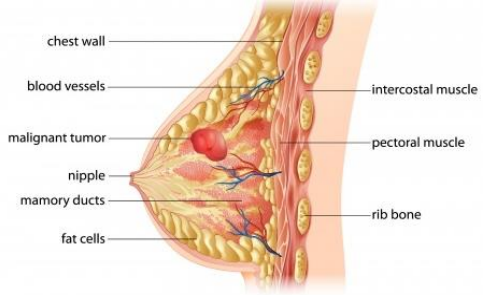
Breast Cancer

Breast Cancer Question 1



- A 57 year old woman is evaluated for a 3 month history of musculoskeletal pain in the right chest wall and ribs, as well as right upper quadrant discomfort
- Medical history significant for Stage II Breast cancer 6 years ago, ER+, PR-, HER2- invasive ductal carcinoma, negative sentinel lymph nodes
- Treated with lumpectomy, radiation, and adjuvant chemotherapy. Continues on anastrozole since completing radiation
- Exam – pain over chest wall and ribs on palpation
- Imaging – CXR and rib views negative. CT abdomen/pelvis shows two 2cm liver lesions and 3 lytic bone lesions in the lumbar spine and pelvis consistent with metastases.

Breast Cancer
Question 1



Which is the most appropriate management?

- A. Anthracycline based chemotherapy
- B. Biopsy liver lesion
- C. Exemestane + Everolimus
- D. PET/CT

Breast Cancer
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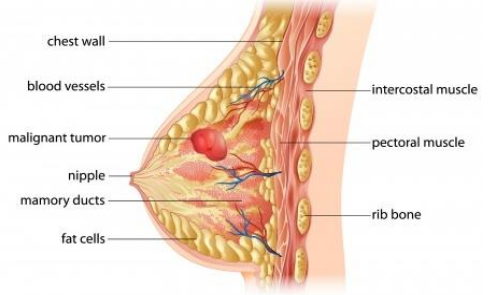

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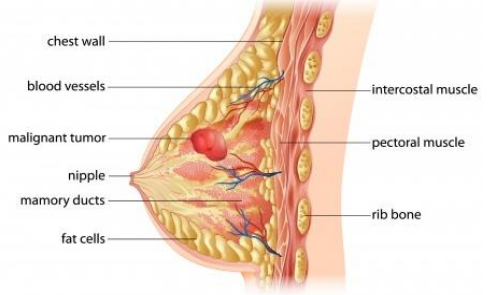
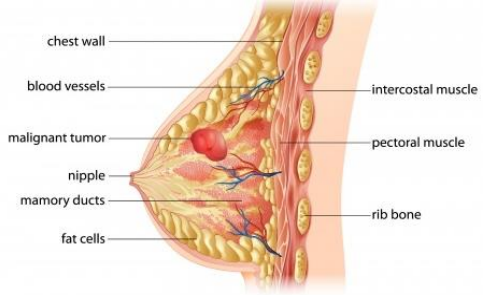


- Key Takeaway: Always consider re-biopsy
- A prospective study* of 121 women showed discordance between primary and metastatic sites:
  - 16% ER
  - 40% PR
  - 10% HER2
- Implication: Re-biopsy let to change in management in 14% of patients!!

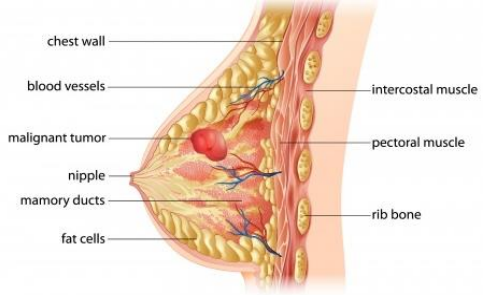
- *Amir E et al. Prospective Study Evaluating the Impact of Tissue Confirmation of Metastatic Disease in Patients with Breast Cancer. JCO Feb 2012.

Breast Cancer Question 2



- A 34 year old female has a 6 week history of tenderness in her right lower breast.
- No family history of breast cancer. Grandmother with ovarian cancer at age 54.
- Exam: 2cm mass left breast
- Mammogram shows increased density and calcifications at mass site
- Ultrasound reveals 2cm hypoechoic mass
- Biopsy: high grade invasive ductal, ER-, PR-, HER2-

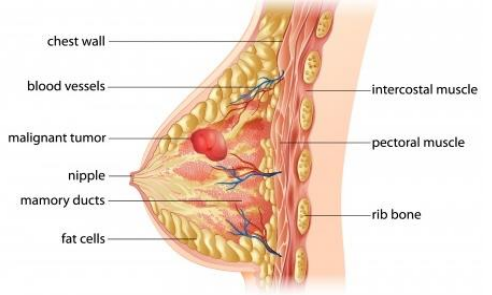
Breast Cancer
Question 2



Which is the most appropriate initial management?

- A. Bilateral mastectomy
- B. BRCA1/2 Testing
- C. Left Mastectomy
- D. Lumpectomy with SNB

Breast Cancer
Question 2



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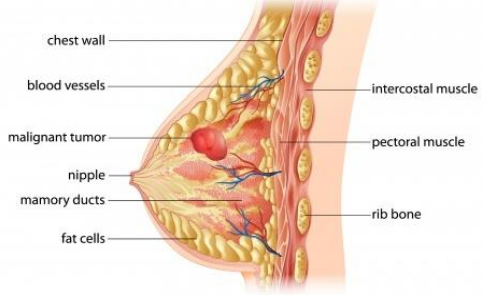

- Key Takeaway: Perform BRCA 1/2 Testing before surgery in women who:
  - Diagnosed with breast cancer **before age 45**
  - Diagnosed at **any age** and **have family history of breast/ovarian cancer**
  - Diagnosed with **triple negative** breast cancer **before the age of 60**

- Why? – Influences what kind of surgery
  - Discussion should include bilateral mastectomy
    - Lifetime risk of contralateral breast cancer is 40-60%
      - Highest in women <40*

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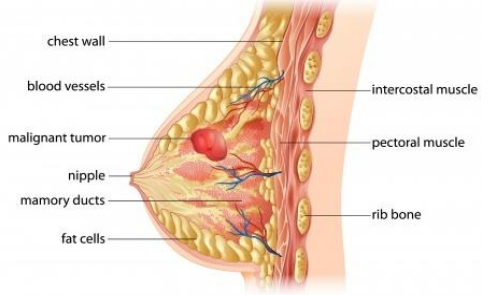
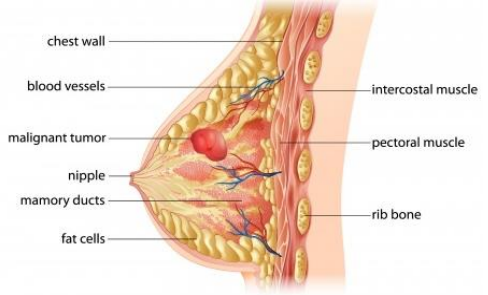
* Malone KE et al. Population based study of the risk of second primary contralateral

Breast Cancer Question 2



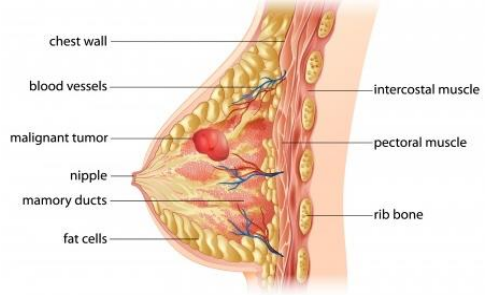
- Should this woman undergo BSO?

Breast Cancer Question 3



- 80 Year old female hospitalized for pneumonia has a history of Stage I ER+ PR+ breast cancer 14 years ago
- Treated with lumpectomy + radiation + tamoxifen 5 years
- On this hospitalization, a palpable lytic lesion on frontal skull, rest of examination normal
- CA 15-3 elevated 4x normal
- MRI head confirms lesion, no intracranial lesions
- CT scans show metastases in spine, sternum, pelvis.
- Biopsy of bony lesion reveals metastatic adenocarcinoma consistent with breast primary, ER+, PR+, HER2-.

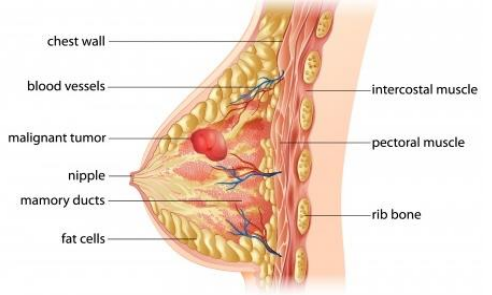
Breast Cancer
Question 3



Which is the most appropriate treatment?

- A. Radium 223 isotope
- B. Chemotherapy
- C. Anastrazole
- D. Radiation

Breast Cancer
Question 3



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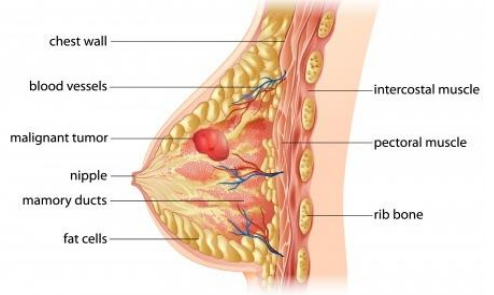
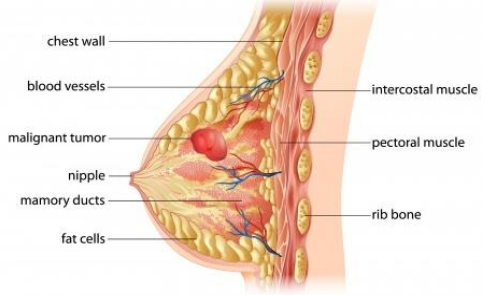


Key Takeaway: patient with ER+ disease metastatic only to bone → Aromatase inhibitor

Rationale:

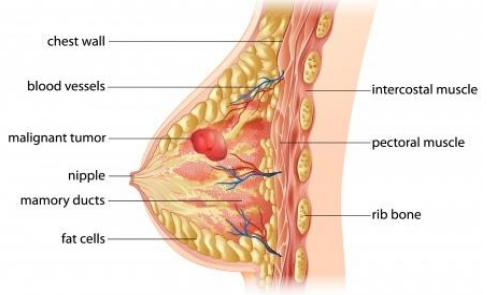
- long disease interval, bone only
- Postmenopausal – therefore AI
  - AI>SERM
- If becomes resistant to AI, may switch to everolimus + exemestane (another AI)

Breast Cancer Question 3



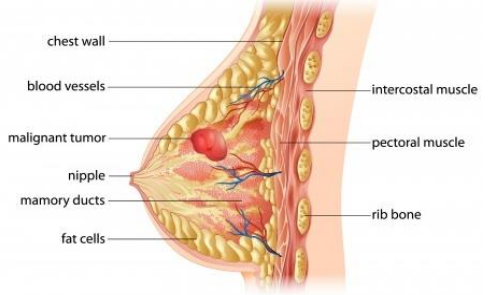
- Radium 223 approved for use in Prostate cancer – studies in breast cancer ongoing
- Chemotherapy if hormone receptor negative, fail hormone therapy, or signification visceral disease
- Radiation not indicated if asymptomatic and bone stable

Breast Cancer Question 4



- 55 year old postmenopausal female is diagnosed with 2.5x2.0cm left breast mass
- Mammogram reveals 2.9 cm spiculated mass
- Ultrasound guided biopsy reveals grade 3 invasive ductal carcinoma ER/PR-, HER2+
- Patient desires best conserving surgery, but surgeon believes mass too large to resect due to mass/breast size ratio and central location

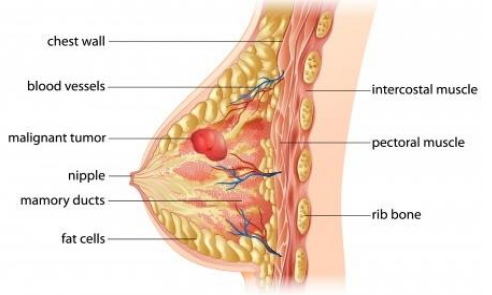
Breast Cancer
Question 4



Which of the following is most appropriate management?

- A. Neoadjuvant trastuzumab based therapy
- B. Neoadjuvant anastrozole
- C. Mastectomy with post op chemotherapy
- D. Staging CT and bone scans

Breast Cancer
Question 4



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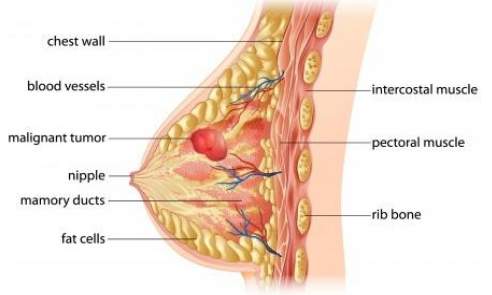
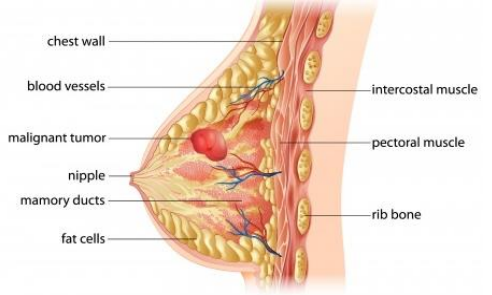


Key Takeaway: In a woman who desires breast conserving surgery, treat with neoadjuvant chemotherapy.

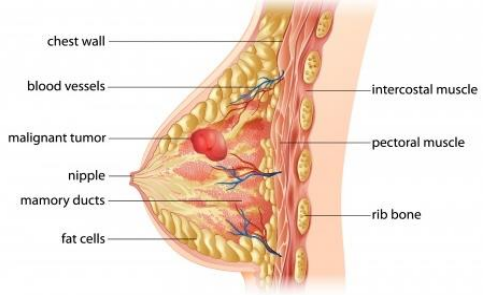
- Should be neoadjuvant trastuzumab based therapy
  - Disease free and overall survival are EQUIVALENT in neoadjuvant and adjuvant chemotherapy
  - Neoadjuvant approach allows for breast conservation
  - Typically have highest response rates
    - Pathologic complete response in 60% of HER2+; 40% in triple negative tumors
- ASCO Guidelines recommend AGAINST PET/CT or bone scans in patients with Stage 0 to II Breast cancer

Breast Cancer Question 5



- 57 year old female underwent bilateral breast reduction surgery 3 months ago
- Bilateral atypical ductal hyperplasia was noted, but no evidence of carcinoma.
- Patient has been on continuous estrogen and medoxyprogesterone HRT since menopause (age 50)
- Tapering HRT with plans to discontinue in one month

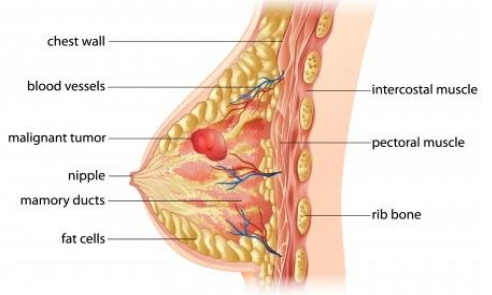
Breast Cancer Question 5



Which of the following is most appropriate breast cancer prevention strategy?

- A. Begin antiestrogen chemoprevention therapy
- B. Begin Vit. D supplementation
- C. Bilateral prophylactic mastectomy
- D. Continue HRT

Breast Cancer Question 5



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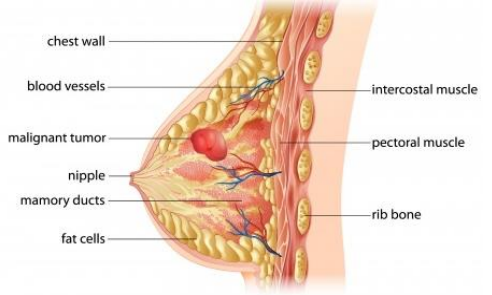
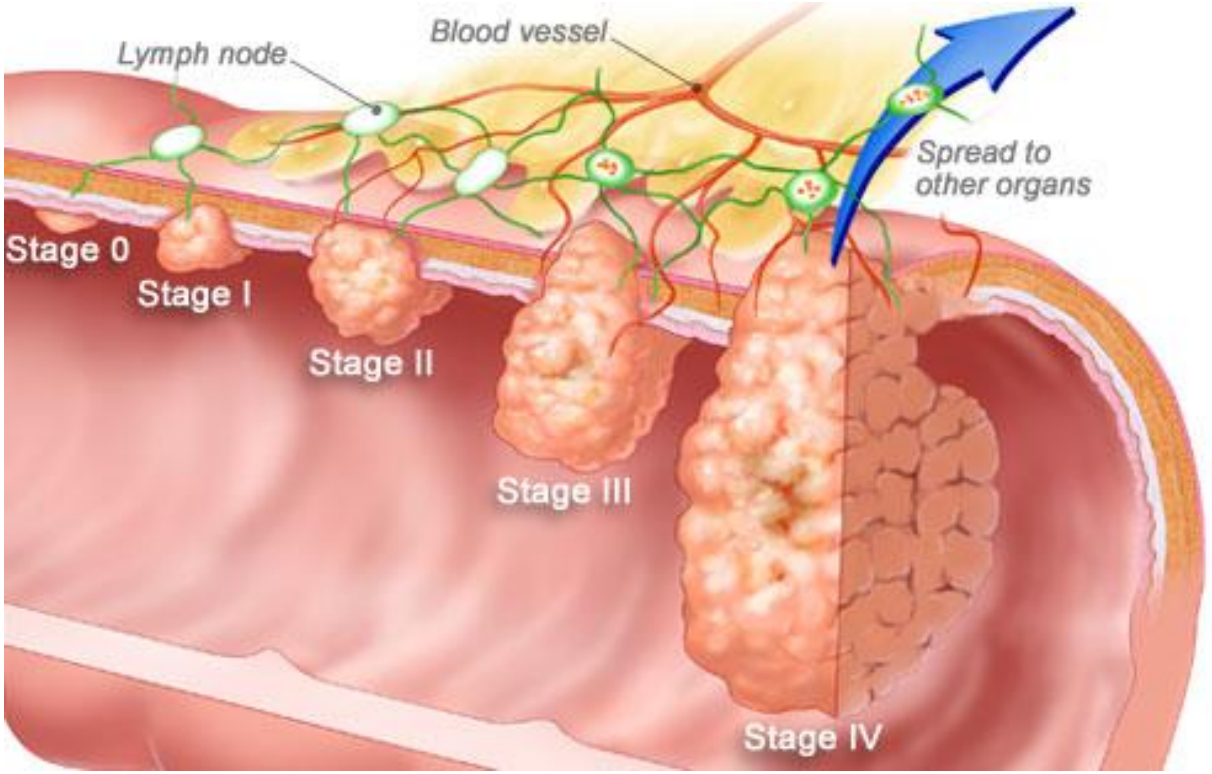
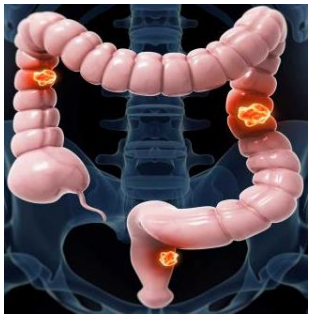


- Key Takeaway: patients with atypical ductal hyperplasia ***should*** be offered breast cancer chemoprophylaxis
- ADH associated with 3-5x increase of breast cancer, 30 year cumulative incidence of 35%
- Exemestane has greatest reduction in risk- 65% relative reduction in annual incidence of invasive breast cancer
  - Tamoxifen and raloxifene decrease the risk, but less so and are accompanied by other risks
- Continuing HRT will increase the risk of breast cancer



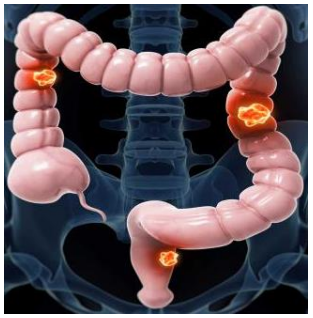
Colorectal and Anal Cancer

CR and Anal Cancer
Question 1



- 69 Year old male diagnosed with Stage II colon cancer 3 years ago, treated with surgery.
- Follow up CT scan shows two new hypodense lesions (6cm and 4cm) in the right lobe of the liver with the largest close to the hilum
- No evidence of vascular invasion
- Liver surgeon believes the larger lesion is unresectable due to proximity to vasculature
- Laboratory studies are normal

CR and Anal Cancer
Question 1



Which of the following is the most appropriate approach to providing chemotherapy in this patient?

- A. Adjuvant Chemotherapy
- B. Conversion Chemotherapy
- C. Neoadjuvant Chemotherapy
- D. Palliative Chemotherapy

CR and Anal Cancer
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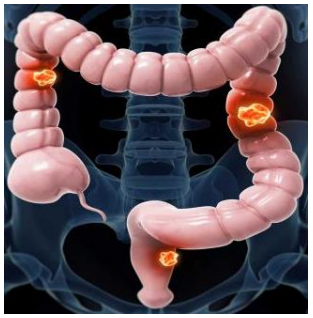

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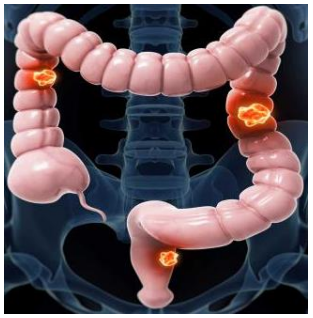
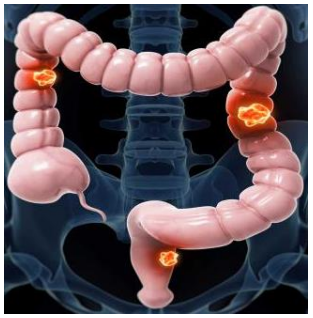


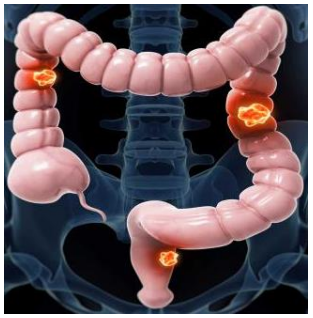
- Key Takeaway: Terminology
- Adjuvant – given ***after*** resection of tumor, ***curative intent***
- Neoadjuvant – given ***before*** resection of tumor, ***curative intent***
- Conversion – given ***before surgery***, intent to ***shrink tumor*** before surgery
- Palliative – given to prolong survival, ***not curative intent***

CR and Anal Cancer
Question 2



- 61 year old woman was diagnosed with Stage II colon cancer, treated with surgery
- Routine follow up CT scan shows 3 new hypodense lesions in the right lobe of the liver, 1-3cm in size.

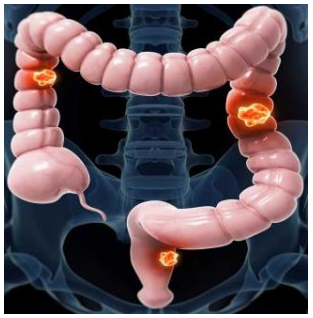
CR and Anal Cancer
Question 2



Which of the following is the most appropriate management?

- A. CT guided biopsy
- B. Hepatic artery embolization
- C. Palliative chemotherapy
- D. Radiation Therapy
- E. Right hepatectomy

CR and Anal Cancer
Question 2



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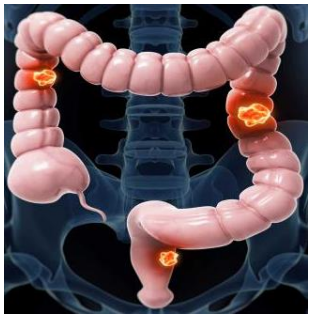
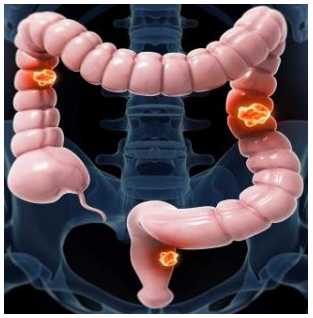


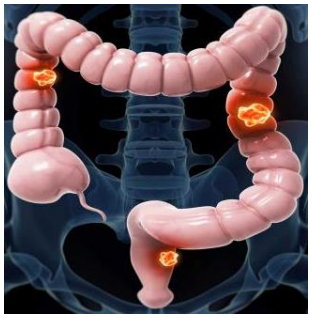
- Key Takeaway: Oligometastatic disease potentially curable with resection.
- Right hepatectomy most appropriate
  - 25-50% of patients cured
- Embolization used in noncurable situations

CR and Anal Cancer
Question 3



- 48 year old has a 6 month history of rectal pain and BRBPR
- Medical history unremarkable
- Examination: no hepatosplenomegaly, lymphadenopathy, genital warts present.
- DRE reveals hard, 2.5 cm tender mass in anal canal
- CT negative for lymphadenopathy
- Biopsy shows invasive squamous cell carcinoma

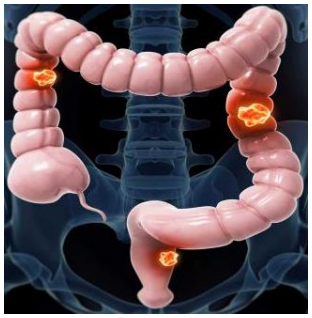
CR and Anal Cancer
Question 3



Which of the following is the most appropriate treatment?

- A. Radiation therapy
- B. Radiation therapy with concurrent chemotherapy
- C. Radiation + concurrent chemo→resection
- D. Surgical resection

CR and Anal Cancer
Question 3



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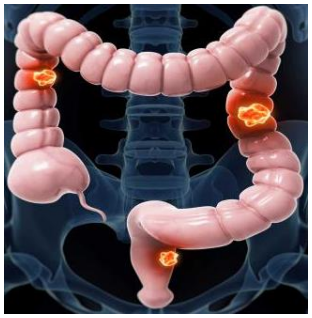
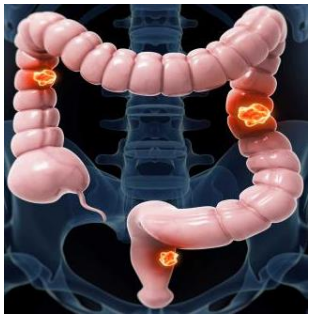


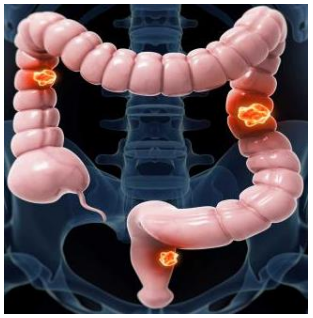
- Key Takeaway: standard treatment for stage I-III anal squamous cell carcinoma is radiation + concurrent chemotherapy.
- Typically arises in squamous epithelium and is associated with HPV exposure
- Contrasts with ***rectal*** adenocarcinoma which rises from columnar epithelium where resection is first step
- Mitomycin + 5-FU
- Surgery is reserved as salvage

CR and Anal Cancer
Question 4



- 77 year old female presents with iron deficiency anemia
- Colonoscopy identifies 7 cm mass in transverse colon
- Biopsy shows poorly differentiated adenocarcinoma
- CT Scan negative for metastatic disease

CR and Anal Cancer
Question 4



Which of the following is likely to be the most important factor in determining her prognosis?

- A. Degree of differentiation
- B. Patients performance status
- C. Size of tumor
- D. Stage of tumor

CR and Anal Cancer
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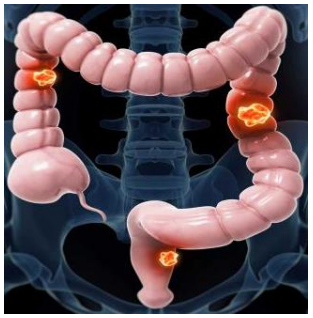

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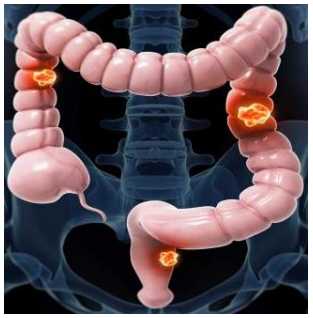
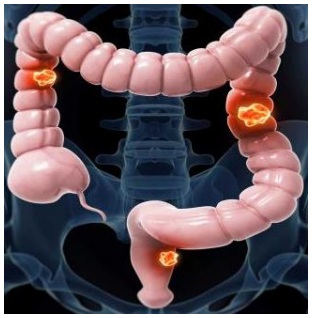
CR and Anal Cancer
Question 4



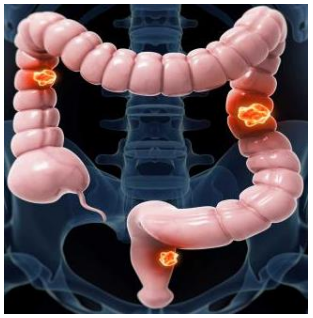
- Key Takeaway: Stage is most important prognostic factor
- Although differentiation has some influence, its outweighed by stage
- Same for performance status

CR and Anal Cancer
Question 5



- 69 year old woman has 3 months of intermittent rectal bleeding and fatigue
- Father died of metastatic colon cancer at age 78
- Rectal exam is positive for blood streaked stools, otherwise unremarkable
- Colonoscopy reveals 4cm mass mid rectum 8 cm from anal verge. Biopsy + for adenocarcinoma
- Pelvic MRI shows penetration into, but not through rectal wall → T2 lesion, no abnormal LN → N0

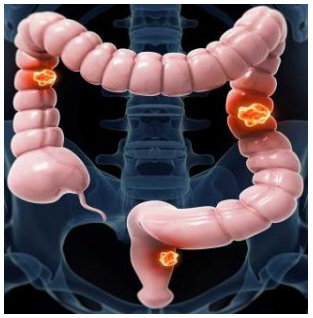
CR and Anal Cancer
Question 5



Which of the following is the most appropriate treatment at this time?

- A. Chemotherapy
- B. Radiation + Chemotherapy
- C. Radiation + Chemotherapy →Resection
- D. Resection

CR and Anal Cancer
Question 5



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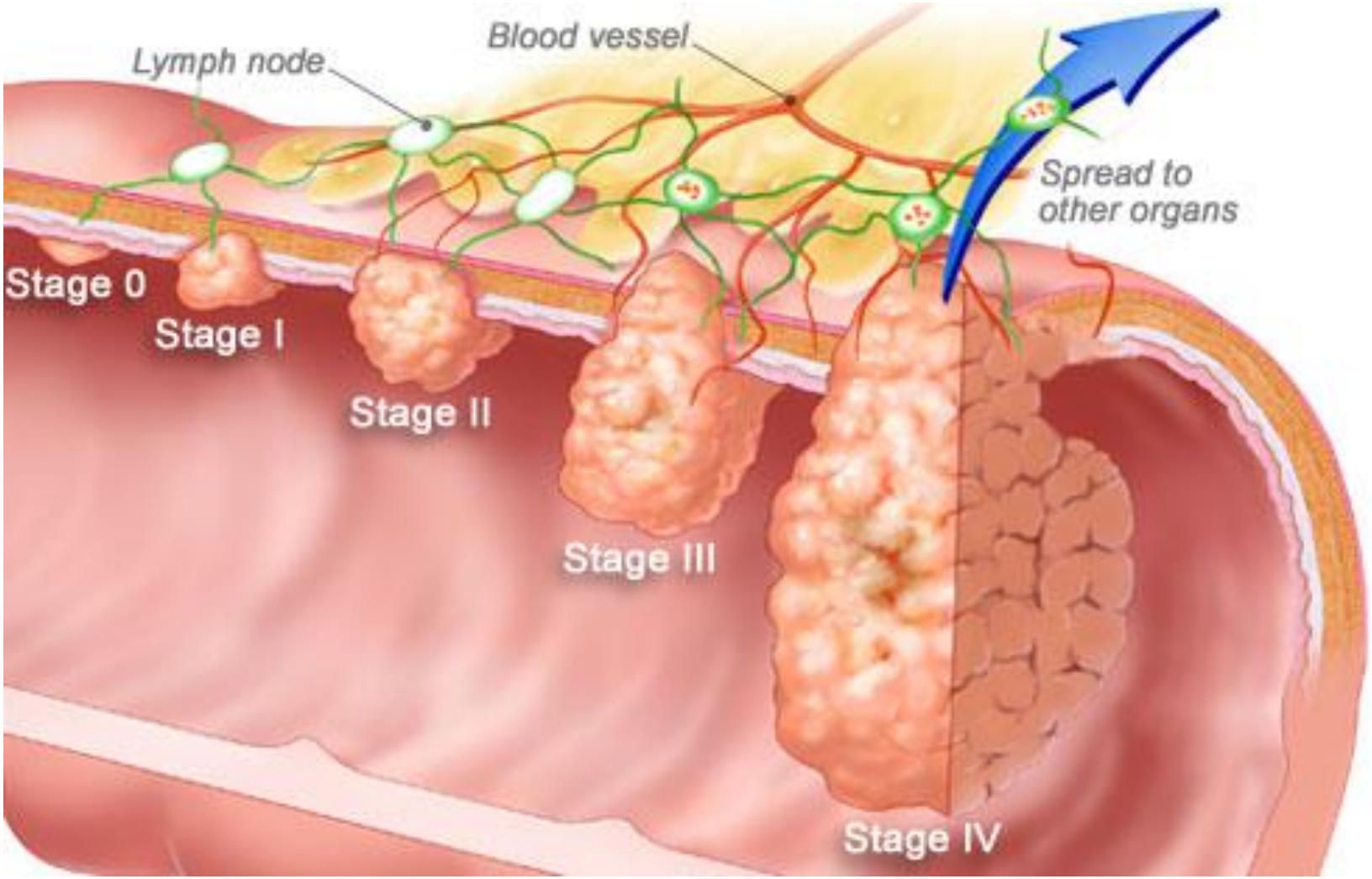
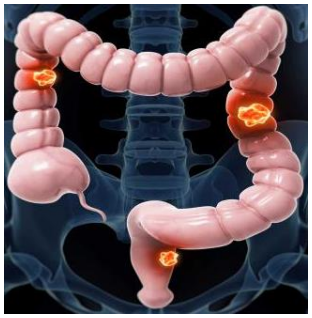
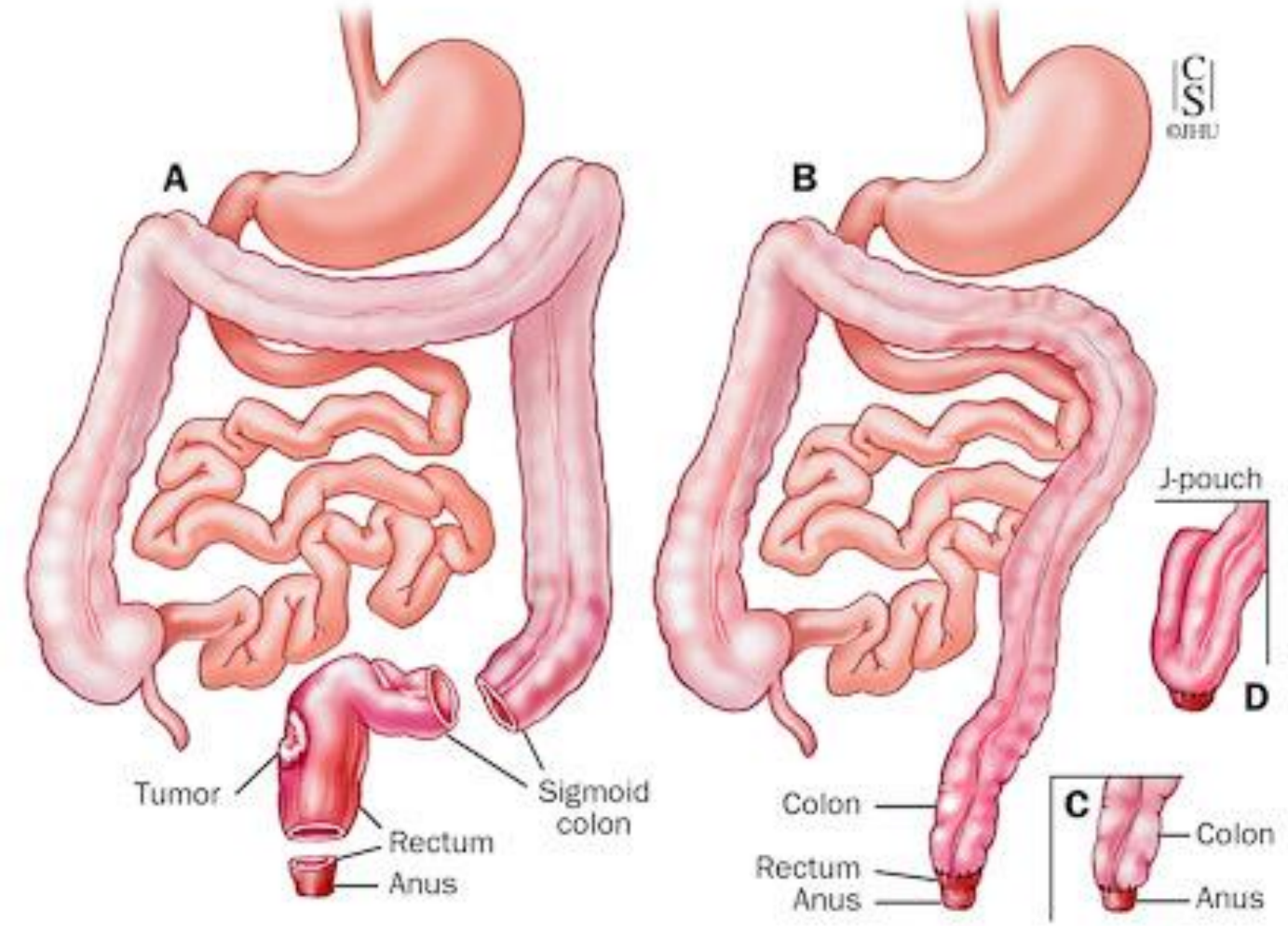


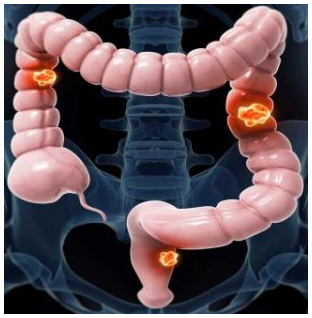
CR and Anal Cancer
Question 5



- Key Takeaway: This is stage I disease, and resection is initial treatment
- Stage I: tumor invades into, but not fully through rectal wall with no abnormal LN
- As this is mid rectum, procedure will be low anterior resection with en-bloc removal of rectum.
- If pathology is found to upstage tumor to T3 or T4, or lymphnodes +,→post op chemoradiation or chemotherapy

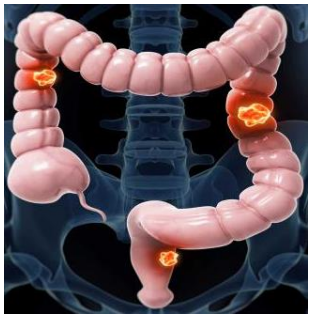


CR and Anal Cancer
Question 6



- 70 year old male underwent left hemicolectomy for 8cm tumor of sigmoid colon.
- Pathology reveals poorly differentiated adenocarcinoma penetrating into pericolonic fat, 1/22 LN + → T3N1; stage III disease.
- Patient completes 6 months of adjuvant chemotherapy

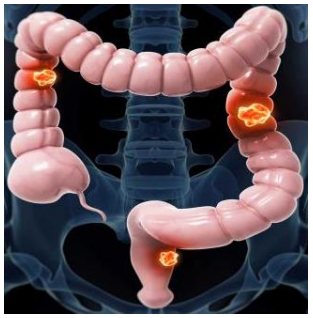
CR and Anal Cancer
Question 6



Which of the following surveillance imaging studies should also be done?

- A. Chest/Abd CT annually for 3-5 years
- B. Chest/Abd CT annually for 10 years
- C. PET/CT scan annually for 5 years
- D. No additional studies

CR and Anal Cancer
Question 6



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CR and Anal Cancer
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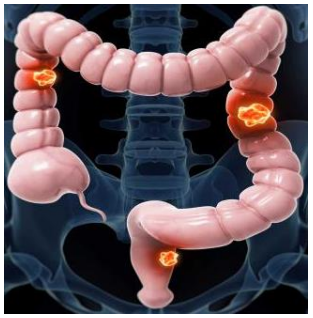
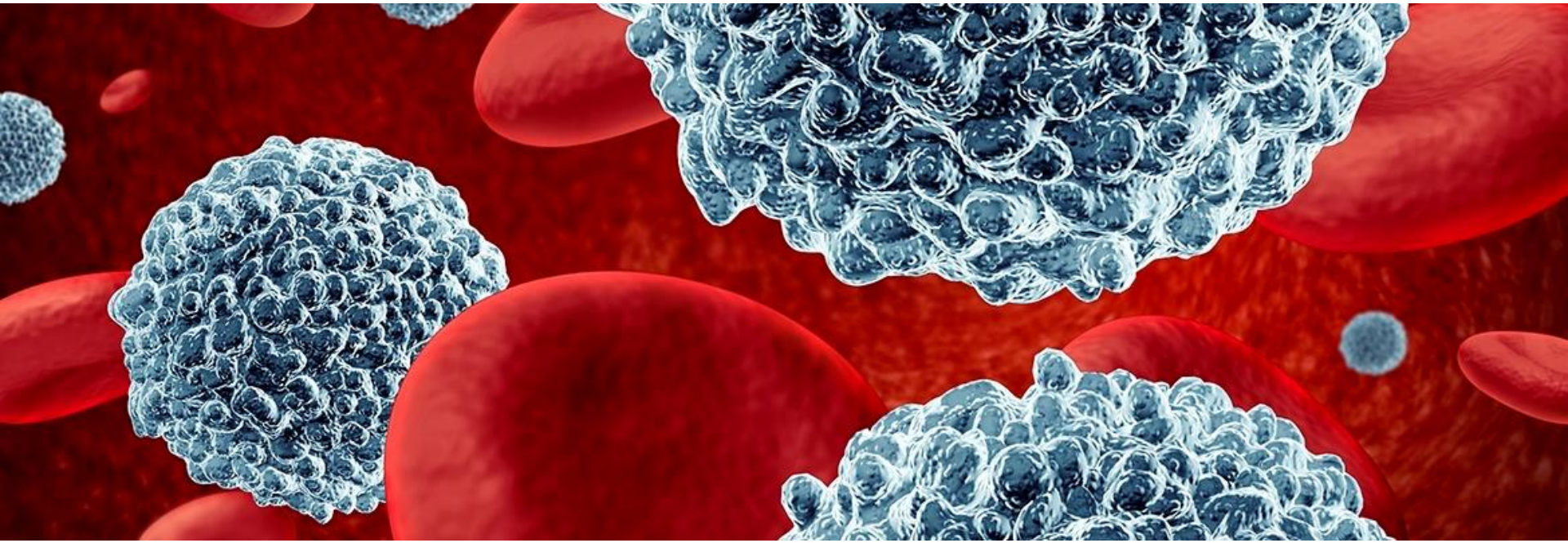
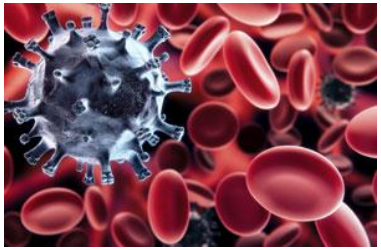


- Key Takeaway: understand post-op surveillance for stage III colon cancer
- Physical exam and CEA every 3-6 months for 3-5 years
- CT chest/abd/pel annually for 3-5 years
- Colonoscopy 1 year after resection



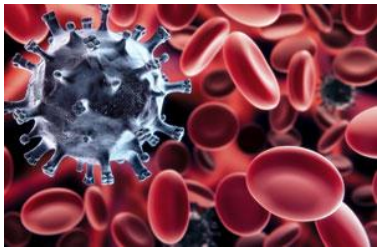
Hematology

Hematology
Question 1



- 36 year old woman present to the ER with 1 month history of abdominal pain, 1 week history of abdominal swelling.
- Examination reveals tender hepatomegaly and ascites. No jaundice
- Hg 11.5, WBC 12,000, Plt 335,000
- Abdominal ultrasound reveals hepatic vein thrombosis and elevated portal pressures

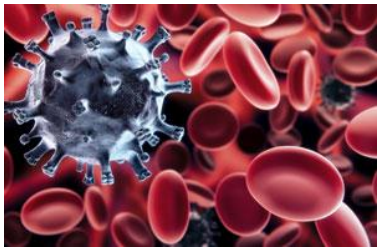
Hematology
Question 1



Which of the following tests likely explains the cause of her condition?

- A. Antiphospholipid antibody
- B. Factor V Leiden
- C. *JAK2 V617F* activating mutation
- D. Prothrombin gene mutation (G20210A)

Hematology
Question 1



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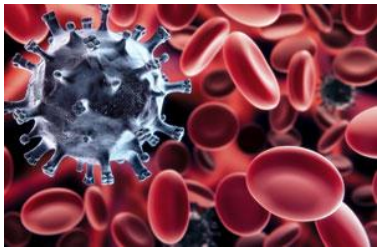
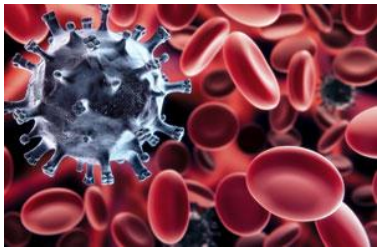
Hematology Question 1



- Key Takeaway: diagnosing Budd-Chiari syndrome and association with *JAK2 V617F*
- Approximately 50% of patients with idiopathic Budd-Chiari have *JAK2* mutation→ most appropriate initial step
- AP Ab have been associated with Budd-Chiari, but nonspecific.
  - Diagnosis requires 1) persistent elevation of antibodies, 2) consistent clot presentation
    - I.E. DVT, PE, arterial thrombus
- Factor V Leiden → present with DVT/PE, less commonly with mesenteric, cerebral, portal vein thrombosis

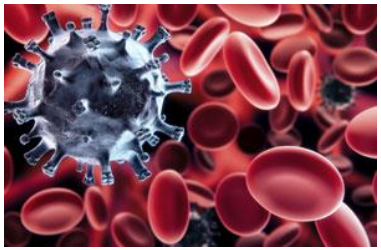
Hematology Question 2



- 27 year old female presents with 9 months of fatigue and pica. She has heavy, irregular menstrual cycles.
- Medications are OCPs, daily iron supplementation

	3M Ago	2M Ago	Current
Ferritin	6	16	45
Hemoglobin	8.7	10.1	13
MCV	71	77	88
Platelet	800K	790K	775K

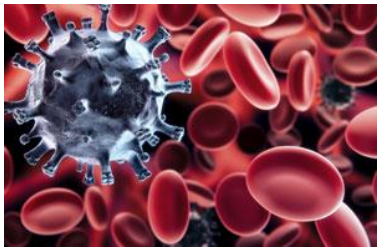
Hematology
Question 2



Which is the most appropriate diagnostic test to perform next?

- A. *BCR-ABL* analysis
- B. *JAK2 V617F* analysis
- C. PT and APTT
- D. von Willebrand Factor antigen

Hematology
Question 2



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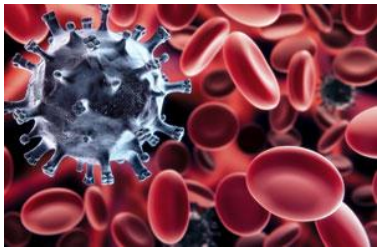
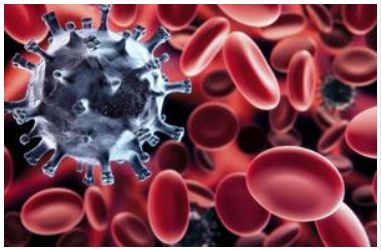


- Key Takeaway: diagnosing Essential Thrombocythemia
- Initially, presented with iron deficiency anemia due to menstrual cycles
  - Elevated platelets can be expected
- Issue is that as anemia corrected, platelets ***remained elevated***
- First step →check *JAK2*
  - 50% of patients with ET will be positive for *JAK2*
- *If JAK2 negative:*
  - *MPL, CALR, BCR-ABL, bone marrow biopsy*

PLT count ≥ 450 x10^9/L



CBC count
Examination of peripheral blood smear
CRP & body iron status
BCR-ABL1 rearrangement
JAK2/CALR/MPL mutation status

Iron deficiency and/or inflammatory state

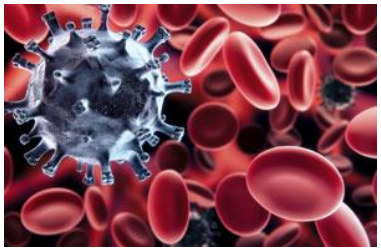
Reactive thrombocytosis (to be re-evaluated following treatment of the underlying disorder)

Presence of *JAK2* (V617F), or a *CALR* exon 9 indel, or an *MPL* exon 10 mutation

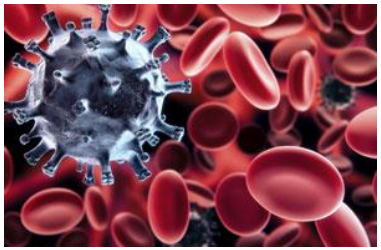
Diagnosis of essential thrombocythemia is probable but bone marrow biopsy (H&E or Giemsa, Gomori, and Perls staining) is required to confirm it, excluding other myeloid neoplasms (e.g., polycythemia vera, primary myelofibrosis, myelodysplastic syndromes, or the myelodysplastic/ myeloproliferative neoplasm with ring sideroblasts and thrombocytosis)

Absence of *JAK2* (V617F), *CALR* exon 9 indels, and *MPL* exon 10 mutations

These patients have no evidence of reactive thrombocytosis and are triple negative, that is, negative for canonical mutations in the 3 driver genes. They include: (i) cases of essential thrombocythemia associated with noncanonical somatic mutations of *MPL* (outside exon 10); (ii) subjects with hereditary thrombocytosis attributable to germline mutations of *JAK2, MPL or THPO;* (iii) individuals with nonclonal disorders

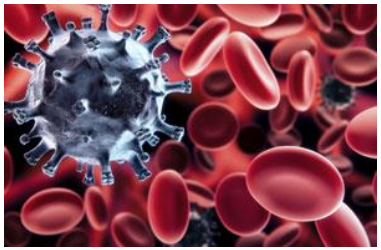


Hematology
Question 3



- 67 year old male diagnosed with Essential Thrombocythemia
- Past medical history unremarkable
- Hg 15; WBC 5.5; Plt 770K

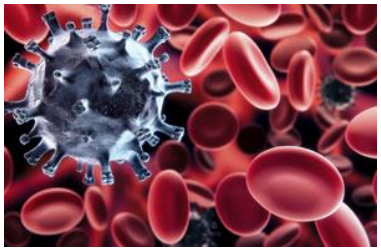
Hematology
Question 3



Which of the following is the most appropriate treatment?

- A. Anagrelide + low dose aspirin
- B. Hydroxyurea + low dose aspirin
- C. Ruxolitinib
- D. Warfarin
- E. Observation

Hematology
Question 3



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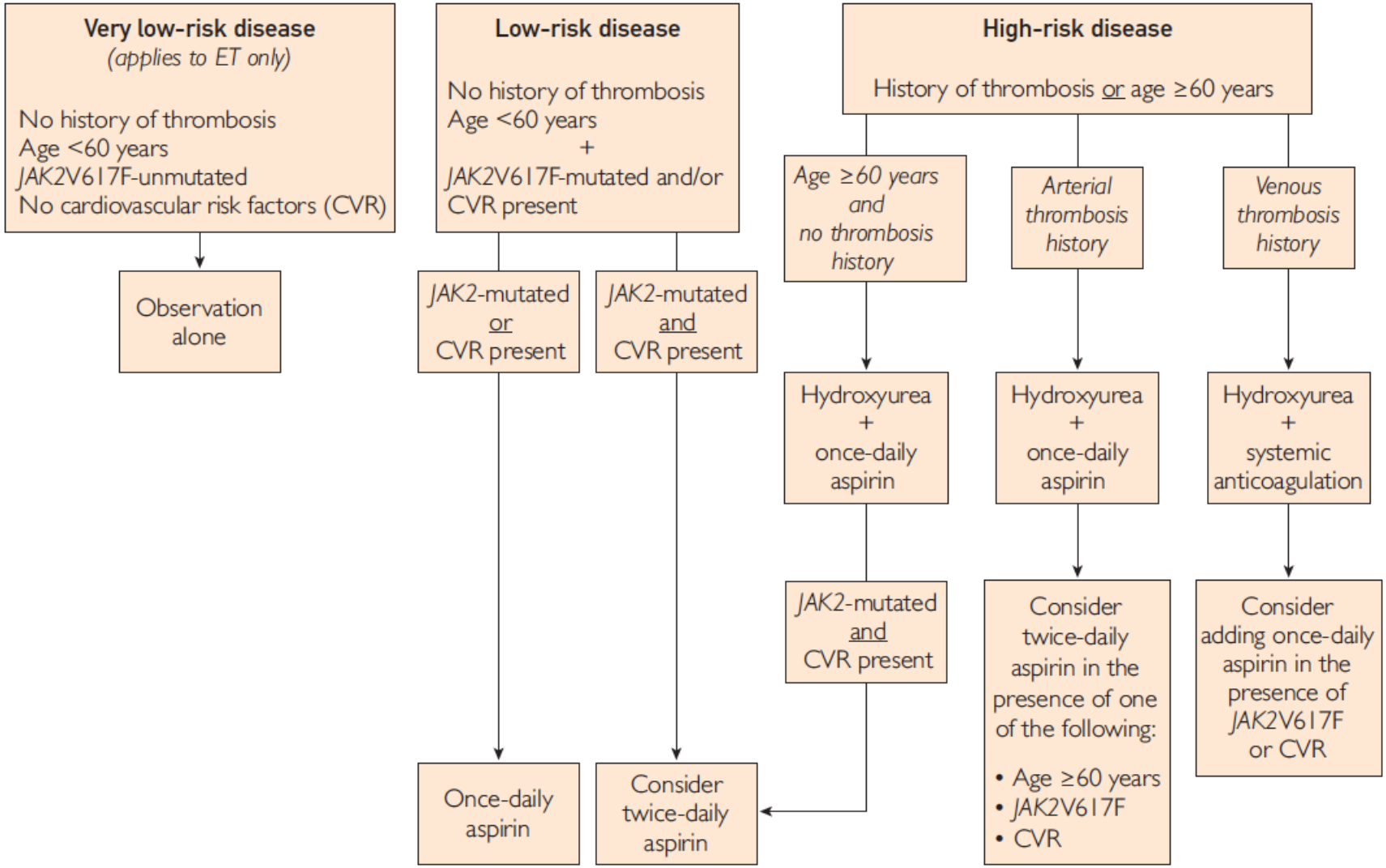
Contemporary treatment algorithm for essential thrombocythemia (ET) and polycythemia vera (PV)

(all patients with polycythemia vera require phlebotomy to a hematocrit target of <45%)



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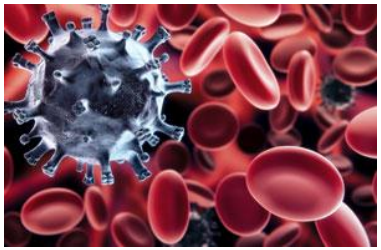
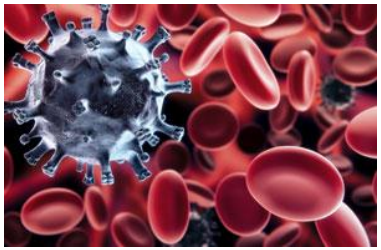
Hematology Question 3



- Key Takeaway: treatment is based on risk stratification → main risk is thrombosis
  - Age >60
  - History of thrombosis or bleeding

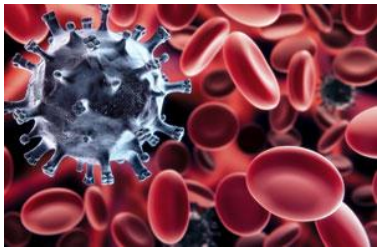
- One or more risk factor – cytoreduce with hydroxyurea
- No risk factors – low dose aspirin or observation

Hematology
Question 4



- 32 year old woman diagnosed with bilateral PE at 25 weeks gestation
- Treated with therapeutic LMWH, discontinued at onset of labor, restarted after delivery.
- She wishes to breastfeed her newborn

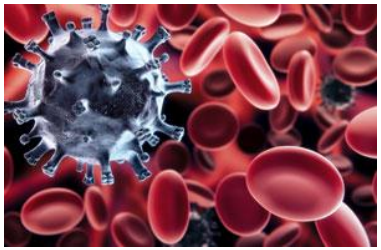
Hematology
Question 4



Which of the following is the most appropriate anticoagulation for this patient?

- A. Apixaban
- B. Dabigatran
- C. Fondaparinux
- D. Rivaroxaban
- E. Warfarin

Hematology
Question 4



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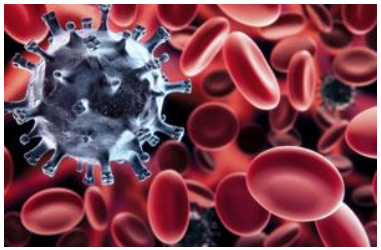
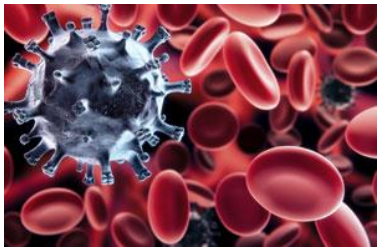
Hematology Question 4



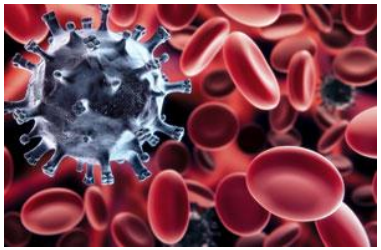
- Key Takeaway: If breastfeeding, which drug is not excreted in breastmilk?
- Apixaban, dabigatran, rivaroxaban → excreted in breast milk
- Fondaparinux→ excreted in milk in lab rats, not sure in humans
- However, warfain and LMWH do not pass into breast milk

Hematology
Question 5



- A 48 year old male presents to the ER for fever and cough for 7 days
- Takes warfarin
- Physical exam reveals ill appearing slightly jaundiced, febrile, hypotensive, tachycardic. Coarse rhonchi right lung base. RUQ tenderness and mutiple ecchymoses noted

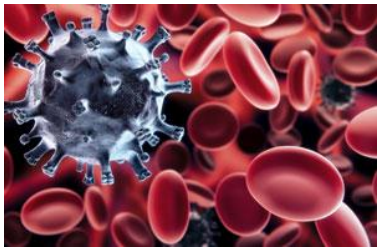
Hematology Question 5



- Labs:

D-dimer	5800	Prothrombin time	58s
WBC	22,000	Fibrinogen	110 mg/dL
PLT	95,000	INR	8.8
Factor V	20%	Factor VIII	200
Factor VII	5%		

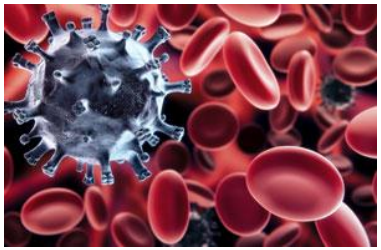
Hematology
Question 5



Which is the most likey cause of the patients' coagulopathy?

- A. DIC
- B. Liver failure
- C. Vit. K deficiency
- D. Warfarin overdose

Hematology
Question 5



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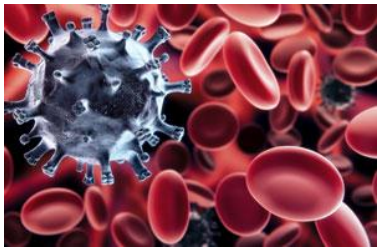
Hematology Question 5



- Key Takeaway: identify coagulopathy of liver disease
- Characterized by:
  - Elevated PT
  - Elevated APTT
  - Elevated VIII level
- Why?
  - All factor levels decrease, except factor VIII
    - Synthesized in endothelial cells
    - Good hepatic function needed to clear Factor VIII

Hematology
Question 5

How to differentiate between warfarin overdose, DIC, Liver disease?

- DIC consumes coagulation factors → should see **LOW FVIII**
- Warfarin OD→ FV synthesized in liver, but NOT Vit K dependent. Thus, FV levels decreased in liver failure, normal in warfarin OD.

Hematology
Question 6

- 76-year-old woman is seen for an annual physical. ROS is only positive for fatigue.
- Physical exam with conjunctival pallor
- No lymphadenopathy or splenomegaly
- CBC:
  - Hemoglobin 8.8 g/dl, MCV 102
  - WBC 2.0 $X10^9$/L , ANC 1000
  - Platelets 75 X10/L

Q6a: What is the next step in evaluation?

- A. B_{12} and folate levels
- B. Bone marrow biopsy with cytogenetics
- C. Peripheral blood flow cytometery
- D. PML-RARA PCR

Q6a: What is the next step in evaluation?

- **A. B_{12} and folate levels**
- B. Bone marrow biopsy with cytogenetics
- C. Peripheral blood flow cytometery
- D. PML-RARA PCR

Case continued

- B_{12} and folate are normal
- Bone marrow biopsy results:
  - Hypercellular marrow (~90%) with trilineage dysplasia
  - Blasts are present ~10%
  - Cytogenetics: del(11q)

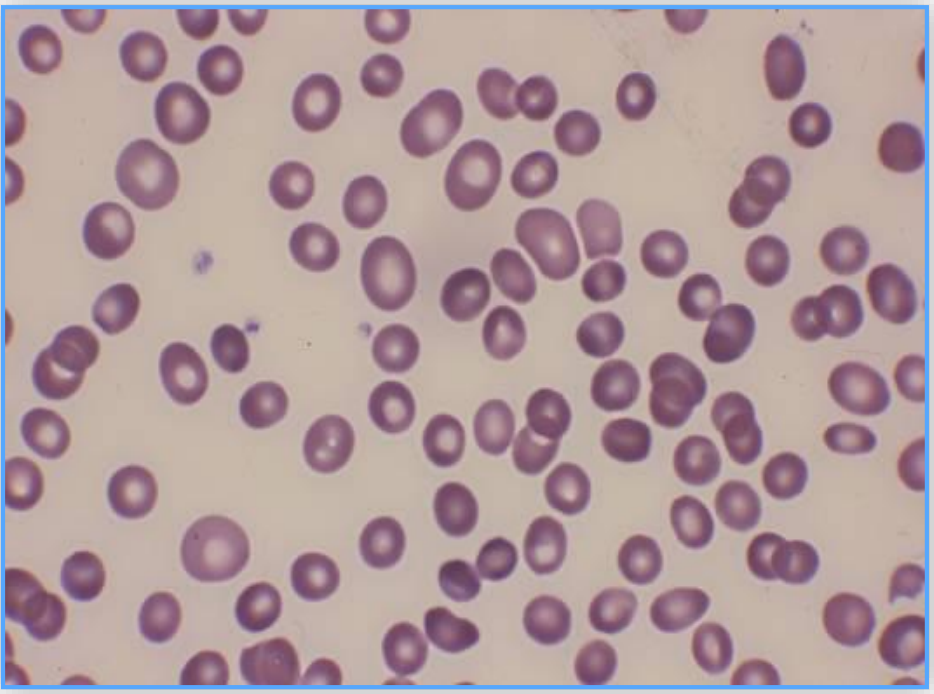
Q6b: Which of the following is the most appropriate management?

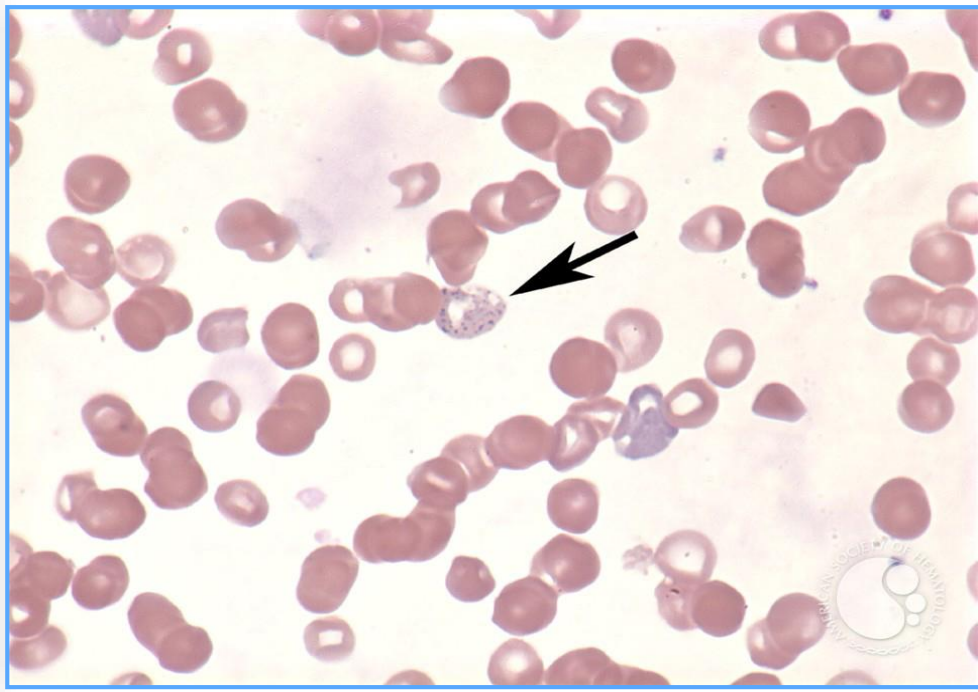
- A. Supportive care
- B. Erythropoietin
- C. Decitabine or Azacitidine
- D. Bone marrow transplant
- E. Lenalidomide

Q6b: Which of the following is the most appropriate management?

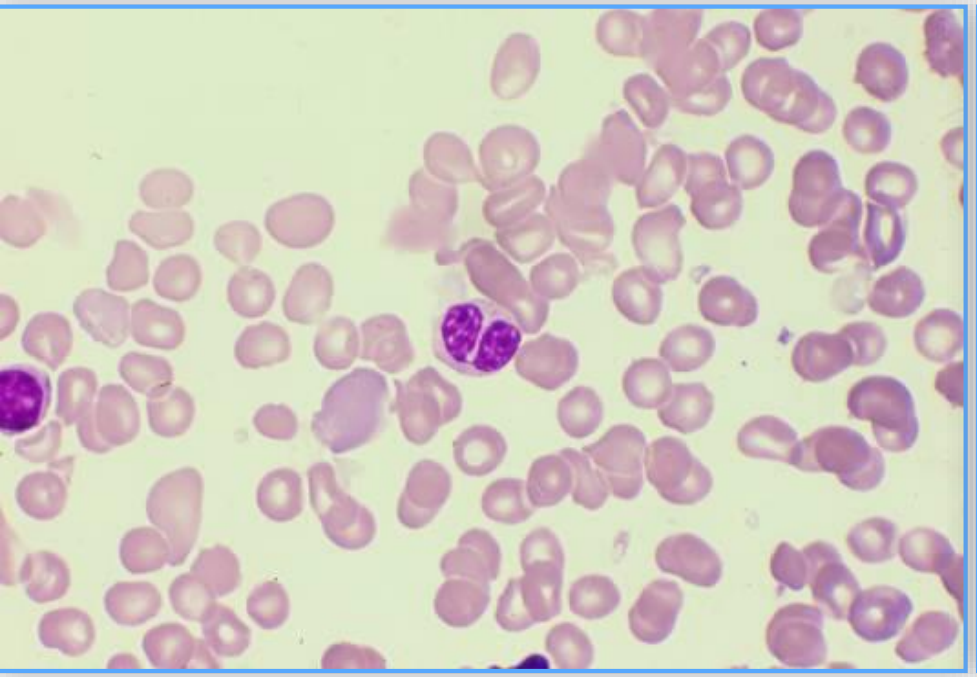
- **A. Supportive care**
- B. Erythropoietin
- C. Decitabine or Azacitidine
- D. Bone marrow transplant
- E. Lenalidomide

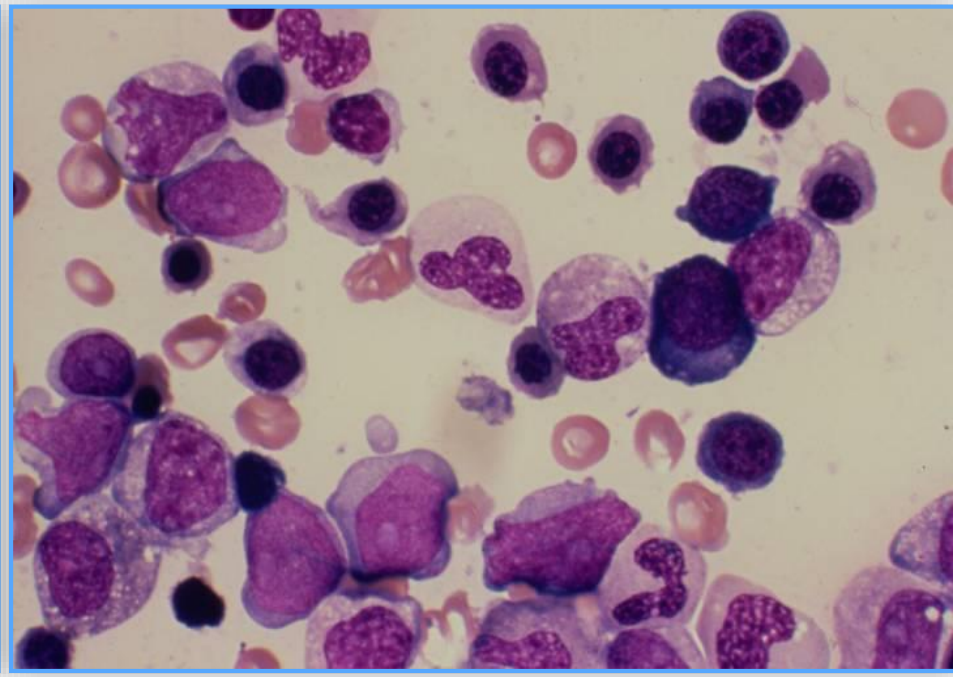
Myeloid Malignancies
MDS – morphology





Myeloid Malignancies
MDS – morphology





WHO Classification of MDS (2016).

MDS with out excess blasts <5%:

- MDS with single lineage dysplasia (MDS-SLD).
- MDS with multilineage dysplasia (MDS-MLD).
- MDS with ring sideroblasts (MDS-RS).
  - Single or multiple lineage dysplasia.
- MDS with isolated del 5q.
- MDS-unclassifiable (MDS-U).

Arber et al Blood 2016

2016 WHO Classification of MDS.

MDS with excess blasts ≥5%:

- MDS-EB-1 :

<5% blasts in PB, 5-9% BM blasts.

- MDS-EB-2 :

5-19% blasts in PB, 10-19% BM blasts.

Diagnosis of AML: Bone Marrow Blasts ≥ 20%

Cytogenetics in MDS

Cytogenetic prognostic subgroups	Cytogenetic abnormalities
Very good	-Y, del(11q)
Good	Normal, del(5q), del(12p), del(20q), double including del(5q)
Intermediate	del(7q), +8, +19, i(17q), any other single or double independent clones
Poor	-7, inv(3)/t(3q)/del(3q), double including -7/del(7q), Complex: 3 abnormalities
Very poor	Complex: >3 abnormalities

Myeloid Malignancies
MDS – Risk Assessment (IPSS-R)

IPSS-R prognostic score values

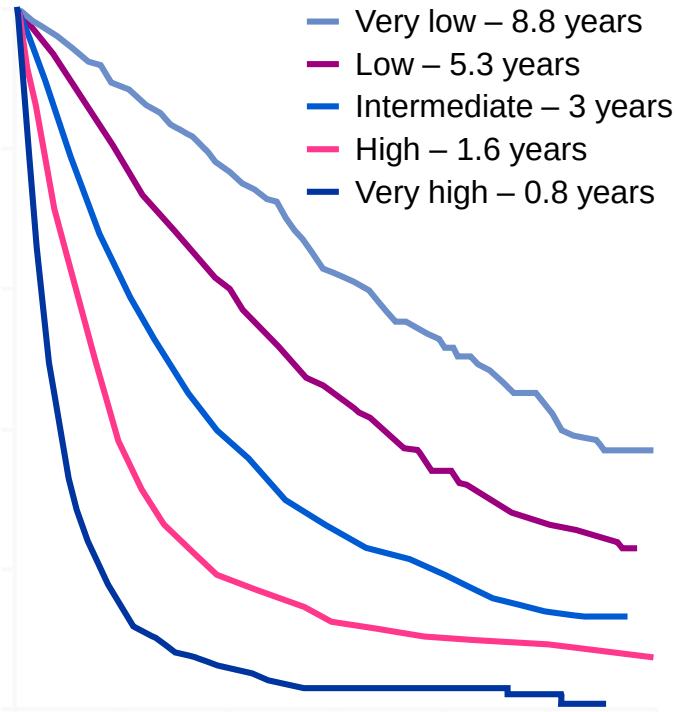
Prognostic variable	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics	Very good	–	Good	–	Intermediate	Poor	Very poor
BM blast, %	≤2	–	>2% <5%	–	5%-10%	>10%	–
Hemoglobin	≥10	–	8 <10	<8	–	–	–
Platelets	≥100	50 <100	<50	–	–	–	–
ANC	≥0.8	<0.8	–	–	–	–	–

IPSS-R prognostic risk categories/score

Risk category	Risk score
Very low	≤1.5
Low	>1.5-3
Intermediate	>3-4.5
High	>4.5-6
Very high	>6

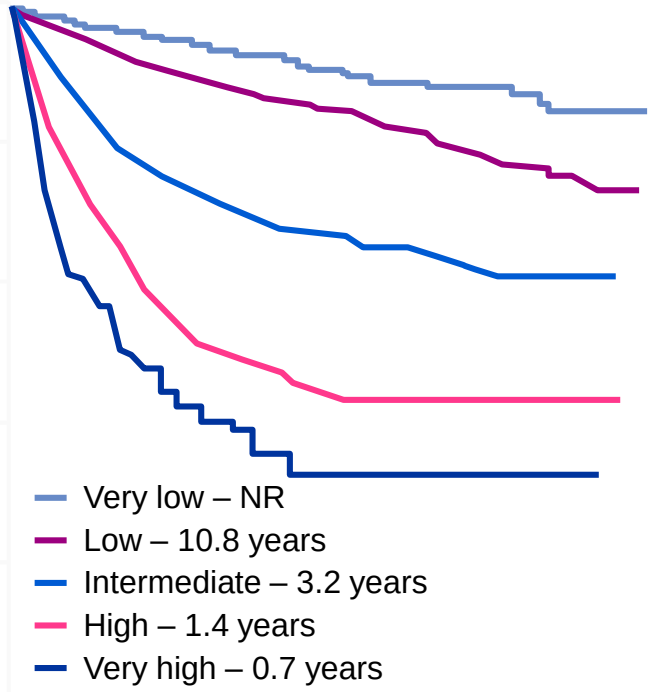
MDS – Prognosis

Median Survival



Years

Progression to AML



Years

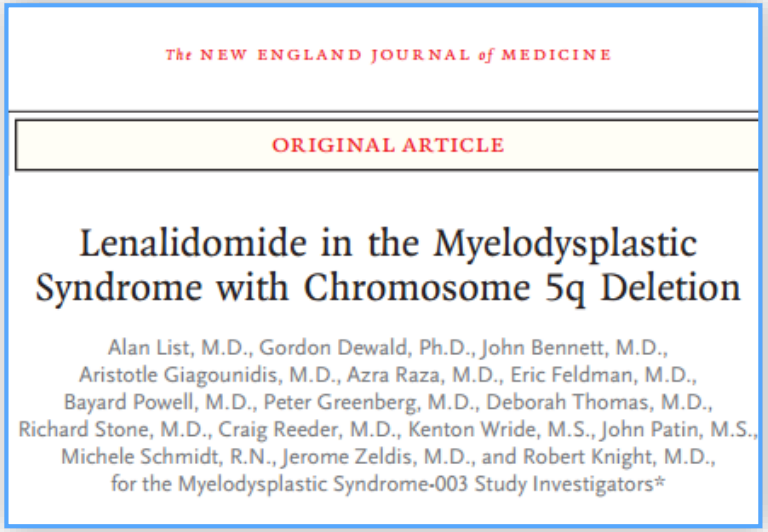
Treatment

- 1. Relieve transfusion dependence
- 2. Prevent transformation to AML

Myeloid Malignancies

MDS – Treatment

- Supportive care
  - RBC transfusions, erythropoietin, antibiotics, G-CSF
- Chemotherapy
  - Del (5q): Lenalinomide
    - 2/3 become transfusion independent
- Hypomethylating agents
  - 5-azacitidine, decitabine
  - Generally reserved for those who are transfusion-dependent or >5% blasts
  - Cause prolonged cytopenias, require prolonged therapy for response
- Allogeneic stem cell transplantation
  - Only curative option



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lenalidomide in the Myelodysplastic Syndrome with Chromosome 5q Deletion

Alan List, M.D., Gordon Dewald, Ph.D., John Bennett, M.D., Aristotle Giagounidis, M.D., Azra Raza, M.D., Eric Feldman, M.D., Bayard Powell, M.D., Peter Greenberg, M.D., Deborah Thomas, M.D., Richard Stone, M.D., Craig Reeder, M.D., Kenton Wride, M.S., John Patin, M.S., Michele Schmidt, R.N., Jerome Zeldis, M.D., and Robert Knight, M.D., for the Myelodysplastic Syndrome-003 Study Investigators*

Myeloid Malignancies
MDS – Review

Patients

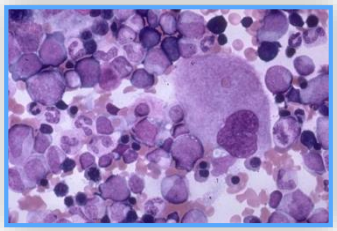
Median age 65-70

Prior chemotherapy

Prior radiation exposure

Disease features

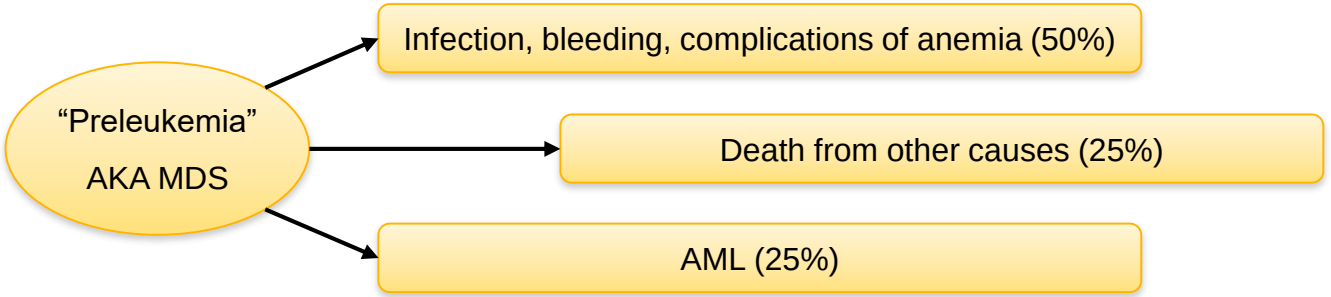
>95% of patients cytopenias, mostly anemia



Bone marrow usually hypercellular, Cells look abnormal ("dysplastic"), Blasts may be increased

50% have abnormal chromosomes, usually numeric anomalies

Clinical course



MDS – Pearls

- Key Takeaways:
- Acquired bone marrow failure syndrome
- Bone Marrow is HYPERCELLULAR
- Suspected in patients with MACROCYTIC anemia or PANCYTOPENIA
  - Where B_{12} and folate deficiencies excluded
- Incidence increases with age
- IPSS-R score needs to be calculated
- FOUR modalities of treatment:
  - Supportive care
  - Chemotherapy
  - BM Transplant
  - Lenalidomide

Myeloid Malignancies
MDS – Risk Assessment (IPSS-R)

IPSS-R prognostic score values

Prognostic variable	0	0.5	1.0	1.5	2.0	3.0	4.0
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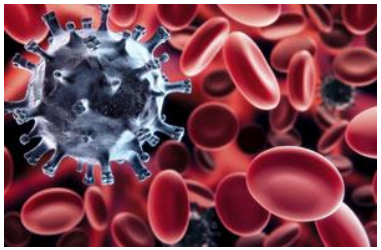
Patients should be treated

Hematology
Question 7



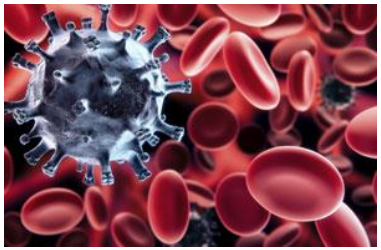
A 58 year old female is being evaluated for syncope. Occurs on changing posture, not associated with urination.

Exam:

BP: 146/80 lying, 90/50 standing

LE: +2 pitting edema bilat to knee

Hematology
Question 7a



You suspect amyloidosis. Which of the following tests are needed to confirm the diagnosis?

A. Bone marrow biopsy & fat aspirate

B. 24 hour urine

C. Echo

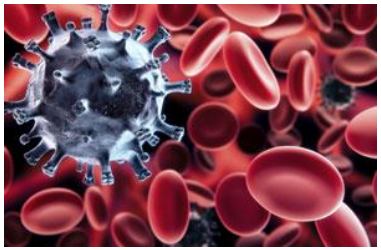
D. EMG

E. Amyloid typing

F. A and E

G. All of the above

Hematology
Question 7a



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C. Echo

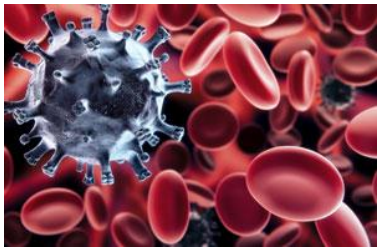
D. EMG

E. Amyloid typing

F. A and E

G. All of the above

Hematology
Question 7b



Testing is positive for amyloidosis. Additional testing reveals an M-spike of 1.4 g/dL on serum protein electrophoresis (SPEP), and no evidence of heart, kidney, or liver end organ damage. What is the next step?

A. Chemotherapy

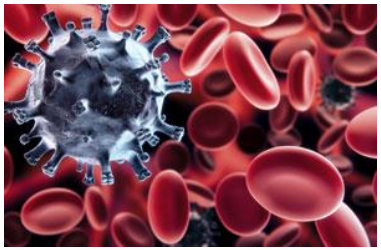
B. High dose chemotherapy with stem cell rescue (AKA Autologous stem cell transplant)

C. Amyloid typing

D. All of the above

E. None of the above

Hematology
Question 7b



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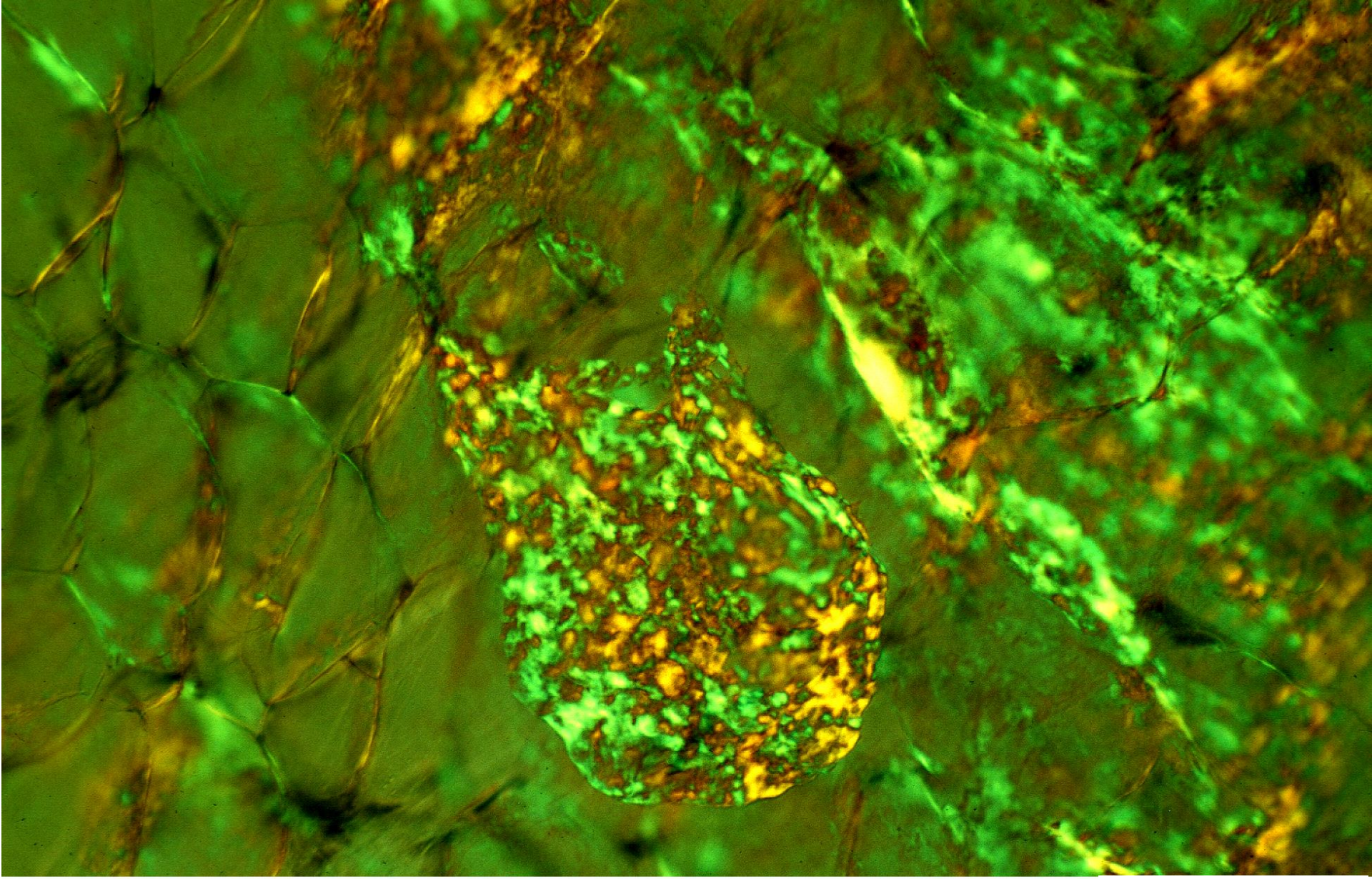
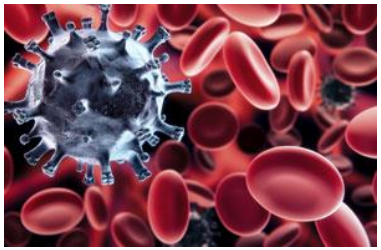


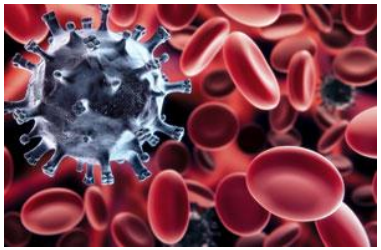
Courtesy: Morie Gertz

Amyloidosis



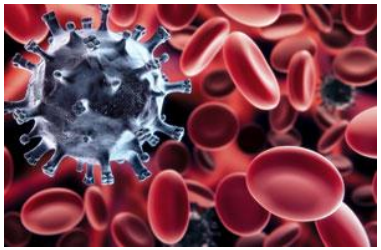
- Key Takeaway: amyloid typing is ***necessary*** to make diagnosis
- Systemic disease
- Deposition of amyloid - variety of serum proteins
- More than 30 proteins recognized to form amyloid fibrils

Amyloidosis

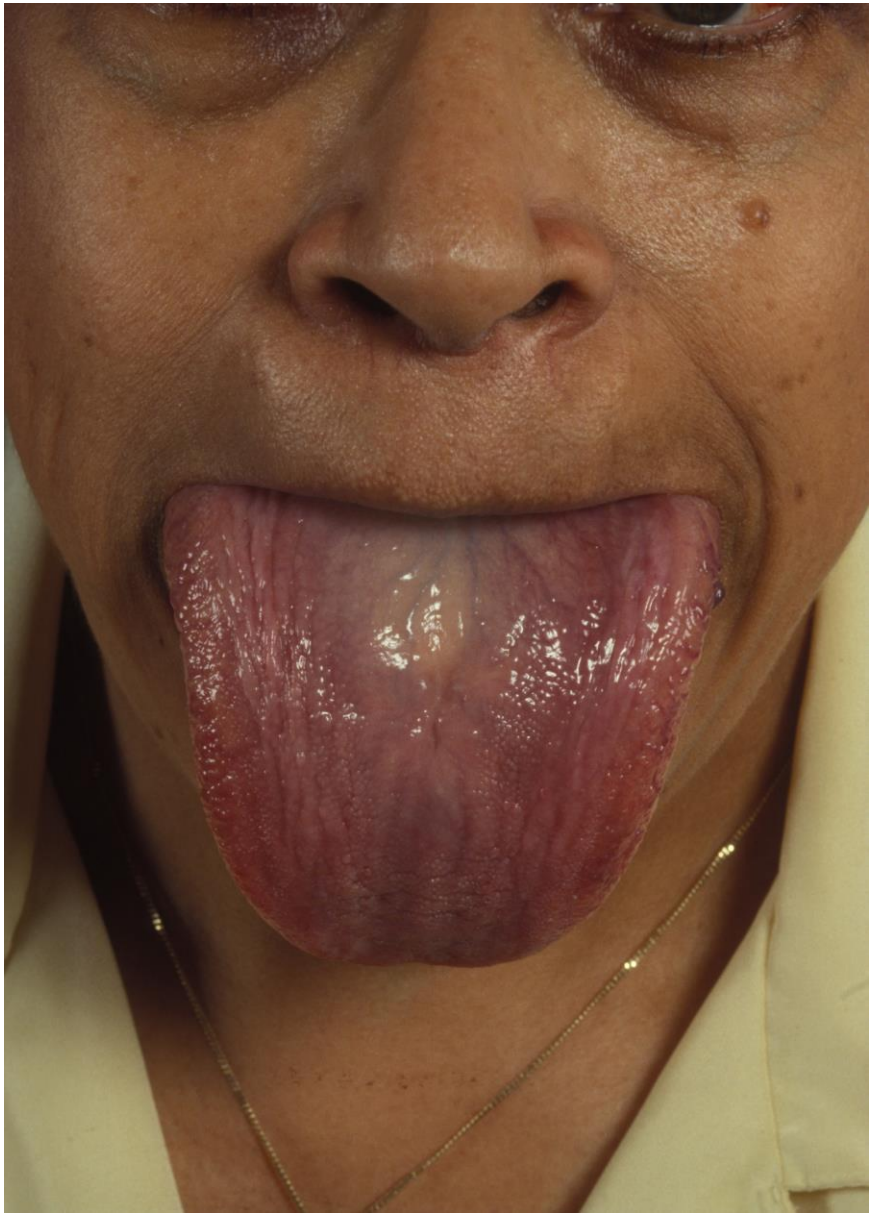


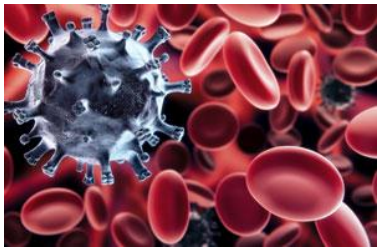
	Component
AL Amyloid	Fragments of monoclonal light chains
Wild Type Transthyretin (ATTRwt)	Unmutated Transthyretin
Hereditary Amyloidosis (ATTRmt)	Mutations of genes coding for several different proteins
AA Amyloid	Serum amyloid A (acute phase reactant)

Amyloidosis

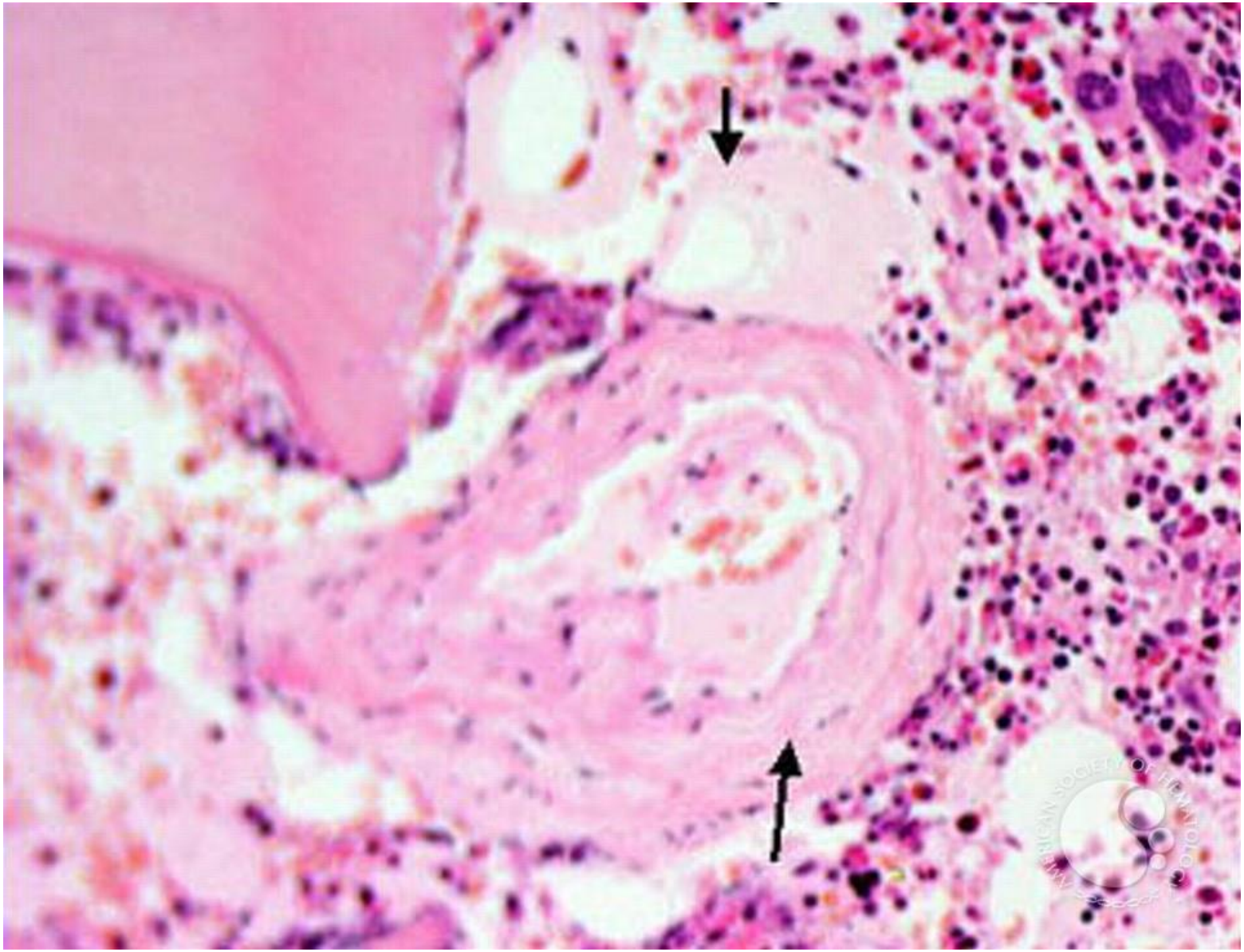


Target Organ Involvement		Presentation
Renal	70%	Nephrotic syndrome
Cardiac	60%	Thickening of IV septum and wall → HF, Arrhythmia
Neuropathy	15-20%	Carpal tunnel, autonomic dysfunction, bladder/bowel dysfunction
Hepatomegaly	70%	Elevated liver enzymes, possibly cholestatic
Macroglossia		Pseudohypertrophy
Bleeding diathesis		Factor X deficiency binding, decreased production, blood vessel fragility

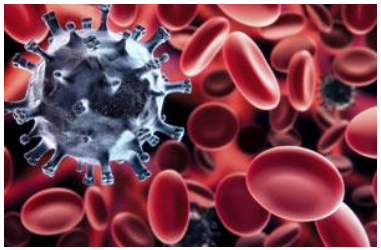




Courtesy: Morie Gertz



Credit: John Lazarchick

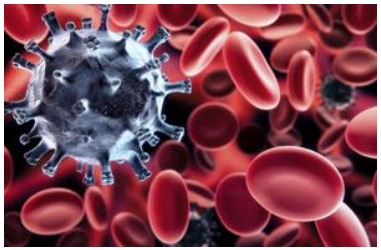


AL Amyloidosis

- Treatment
  - Depends on organ involvement
  - If eligible →autologous stem cell transplant
  - If not → bortezomib based chemotherapy

- MUST be treated at a multidisciplinary center with amyloidosis expertise for optimal outcome

Hematology
Question 8

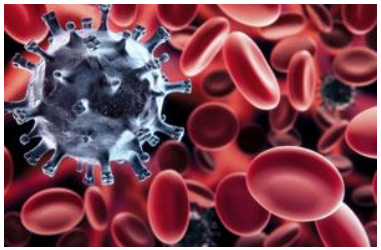


56 year old male undergoing evaluation for peripheral neuropathy has the following test results:

Hg: 15g/dL
WBC: 8.3
PLT: 165K
ESR 135mm/hr
Ca: 10.5mg/dL (nrml)
Cr: 1.0

SPEP: M spike 1.3g/dL in gamma region, IgGκ

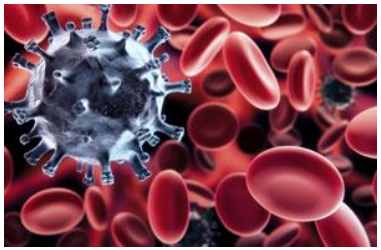
Hematology Question 8a



What are the next steps in evaluation?

- A. Serum free light chains
- B. Urine Protein Electrophoresis
- C. Beta-2 microglobulin
- D. Skeletal survey
- E. Low dose CT/MRI/PET
- F. Bone marrow biopsy & fat aspirate
- G. A, B, D, and F
- H. A, B, E, and F
- I. All of the above

Hematology Question 8a



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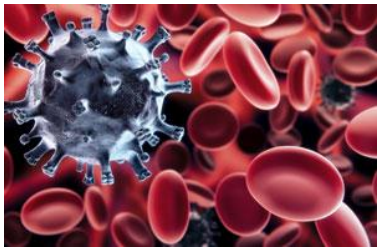
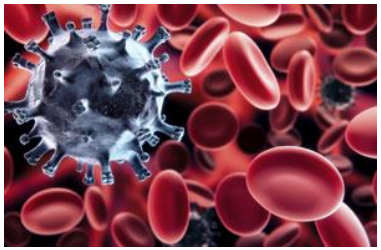
Hematology
Question 8



Here are the results of his further testing:

- FLC: normal
- UPEP: normal
- Low dose CT: no lytic lesions
- Bone marrow biopsy:
  - 8% monoclonal plasma cell population
  - Congo red staining negative



Question 8b

What is the diagnosis?

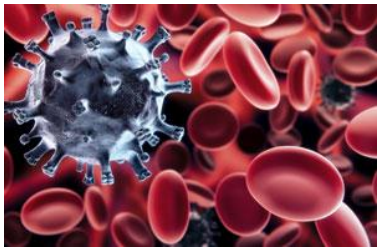
A. MGUS

B. Smoldering MM

C. Multiple myeloma

D. Waldenstroms

E. Amyloidosis



Question 8b

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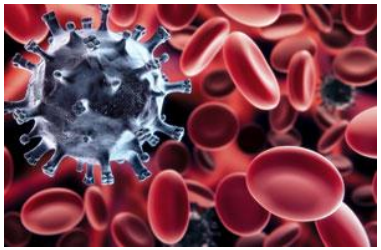
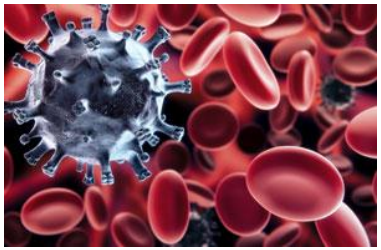
MGUS vs SMM vs MM



	M Spike	BM plasma cell %	End organ involvement
MGUS	<3g/dL	<10%	-
Smoldering MM	≥3g/dL	≥10-60%	-
Multiple Myeloma	Any	≥10%	+



Question 8c

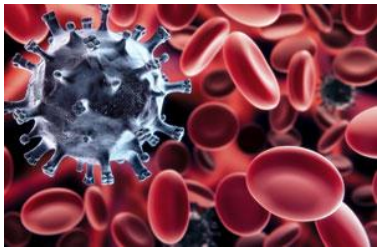
How soon should the patient return for follow up?

A. 3 months

B. 6 months

C. 12 months

D. None needed



Question 8c

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B. 6 months

C. 12 months

D. None needed

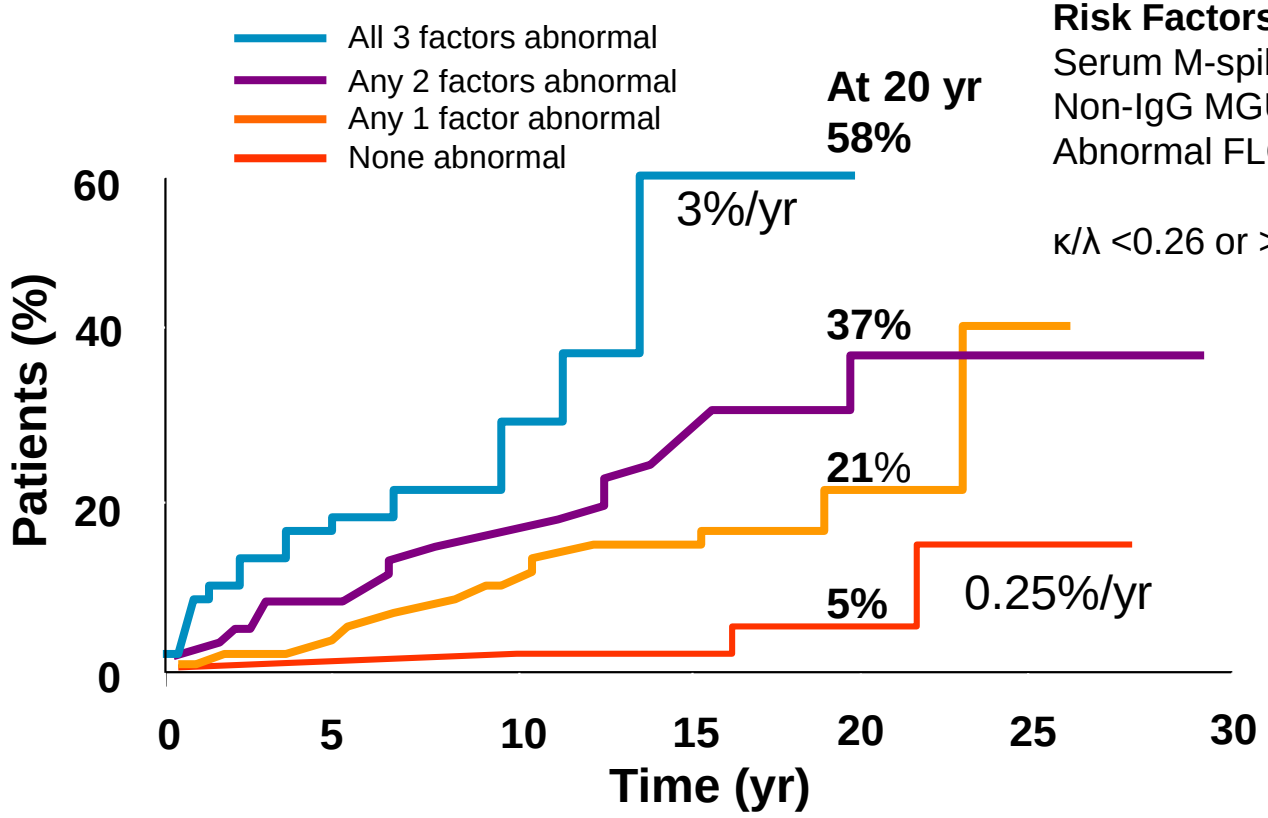
Mayo Clinic Risk-Stratification Model to Predict Progression of MGUS

Risk group	Patients (n)	Relative risk	Absolute risk at 20 yr (%)
Low-risk (no abnormal factors)	449	1.0 (ref)	5
Low-intermediate risk (any 1 factor abnormal)	420	5.4	21
High-intermediate risk (any 2 factors abnormal)	226	10.1	37
High-risk (all 3 factors abnormal)	53	20.8	58

Factors: Non-IgG MGUS, M-protein >1.5 g/dL, abnormal FLC ratio (ref 0.26–1.65)

Rajkumar SV et al. *Blood*. 2005;106(3):812

… however, “individual risk” for myeloma transformation varies!

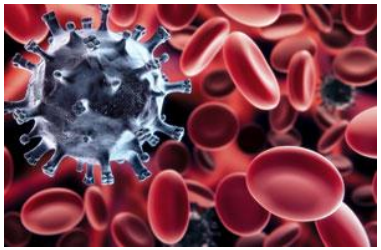


Risk Factors
Serum M-spike >1.5 g/dL
Non-IgG MGUS isotype
Abnormal FLC ratio

κ/λ <0.26 or >1.65

FLC = free light chain

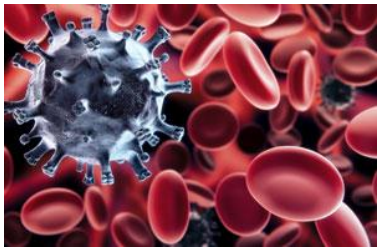
Rajkumar SV et al. *Blood*. 2005;106(3):812



How Often do I need to Follow My Patient?

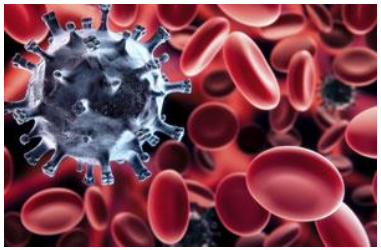
- Low-risk MGUS patients: rechecked in 6 mo, then once every 2 yr
- All other subsets of MGUS patients: rechecked in 6 mo, then yearly thereafter

MGUS/SMM → MM



- Evolution can be abrupt

- Red Flags
  - New bone pain
  - Fatigue/weakness
  - B symptoms
  - CRAB



Multiple Myeloma

- Hallmark:
  - End organ damage
    - C: hypercalcemia
    - R: renal insufficiency (Cr>2.0)
    - A: anemia (Hg<10)
    - B: bone disease ≥1 lytic lesion
  - Myeloma defining biomarkers:
    - ≥60% plasma cell on bone marrow
    - Involved:uninvolved FLC ratio ≥100
    - ≥ focal lesion on MRI

There's More!

- Hemoglobinopathies – Sickle Cell, Thalassemias, Hereditary Spherocytosis
- Anemia – iron deficiency, chronic disease
- Malignancy – Multiple Myeloma, CLL
- Bleeding disorders – Hemophilia, Von Willebrands disease, DIC, ITP
- Thrombotic disorders – TTP, HIT, VTE
- Bone Marrow disorders – MDS, aplastic anemia, pure red cell aplasia, PV, ET, Myelofibrosis
- Acute Leukemias

Review

- Breast Cancer
- Colorectal and Anal Cancer
- Anal Cancer
- Essential Thrombocytosis
- MDS
- Amyloidosis
- MGUS/Smoldering Myeloma/Multiple Myeloma

There's More!

- Emergencies – SVC syndrome, Neutropenic fever, cord compression, effusions, hypercalcemia, tumor lysis
- Lung Cancer – particularly staging
- Head and Neck Cancer – surgery vs chemo radiation
- Ovarian Cancer – screening, BRCA
- Survivorship – cardiac disease, pulmonary disease, second malignancies, bone health

Thank You

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