Oncology Test Review

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2/22/2022

Question 1

- A 64-year-old man is evaluated in the emergency department for 5 days of increasing bouts of diarrhea. He was diagnosed with metastatic melanoma 2 months ago and has received three doses of immunotherapy with ipilimumab and nivolumab. He was seen 3 days ago for diarrhea (two loose stools daily). Evaluation for infectious causes of diarrhea, including *Clostridioides difficile*, was initiated, and loperamide was begun. Today he reports increased diarrhea, with up to five loose stools per day. He takes no additional medications.
- On physical examination, temperature is 36.7 °C (98.0 °F), blood pressure is 95/70 mm Hg, and pulse rate is 100/min. Abdomen is slightly tender and distended without hepatosplenomegaly.
- Complete blood count, metabolic panel, and thyroid-stimulating hormone level are normal, and stool studies, including nucleic acid amplification testing for *Clostridioides difficile* toxin genes, are negative. Fecal calprotectin and fecal lactoferrin levels are elevated.
- Ipilimumab and nivolumab are discontinued. The patient is admitted to the hospital for intravenous fluids and additional treatment.
- Which of the following is the most appropriate additional treatment?

    A. Budesonide

    B. Infliximab

    C. Mesalamine

    D. Methylprednisolone

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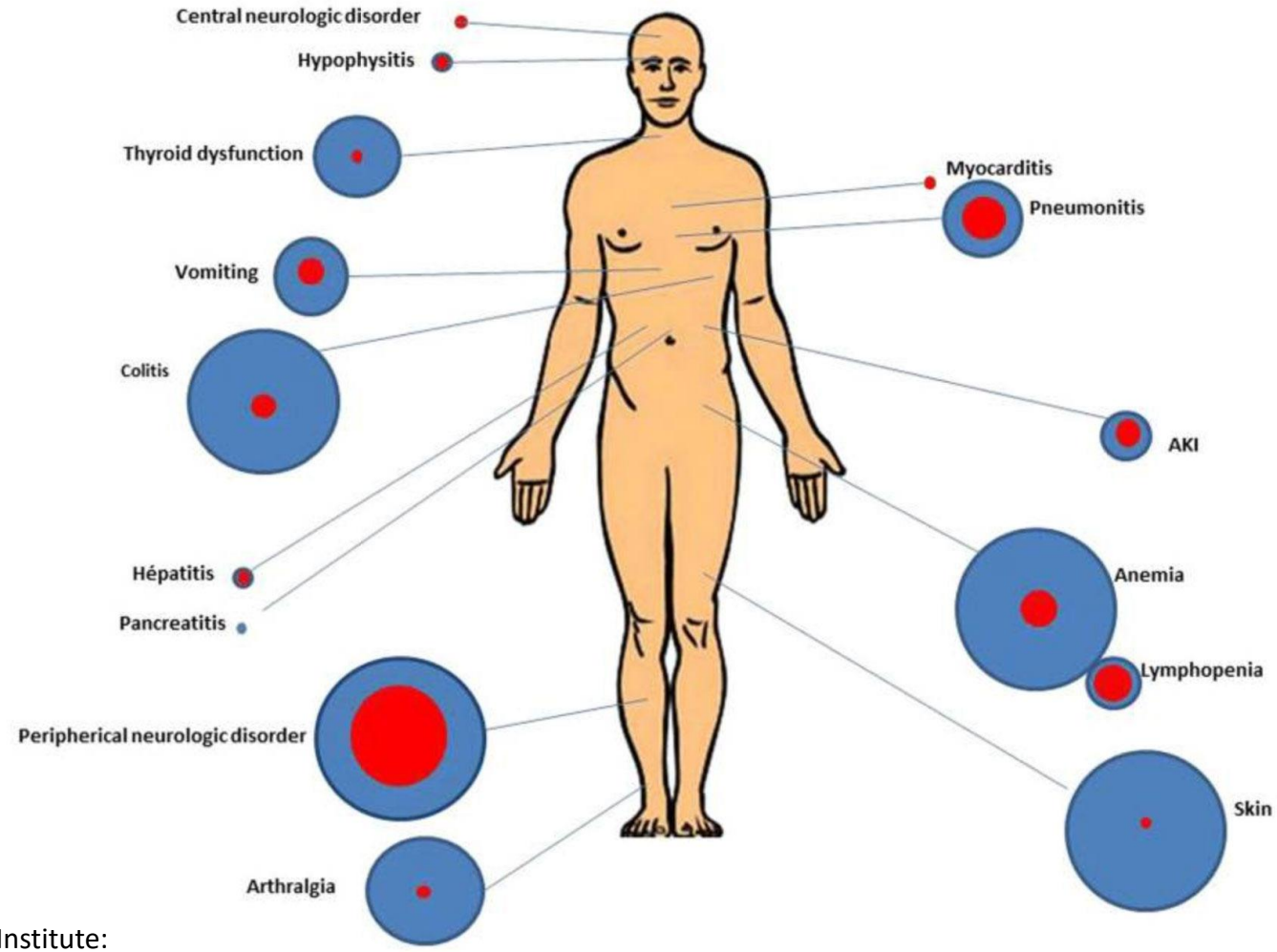
Treat moderately severe diarrhea related to immunotherapy

- Complications of immunotherapy
  - Colitis
  - Dermatitis/mucositis
  - Autoimmune endocrinopathies (thyroiditis, adrenalitis, hypophysitis)
  - Pneumonitis
  - Hepatotoxicity



National Cancer Institute:
Complications of Cancer Immunotherapy, 2019

Treatment of immunotherapy-related colitis

- Rule out infections with enteric pathogens and *Clostridioides difficile*
- Stool testing for lactoferrin and calprotectin suggest bowel inflammation and can be used to monitor disease activity
- Proctoscopy or colonoscopy with biopsy can confirm the diagnosis
- Stop immunotherapy agents and start systemic steroids

- Other answers:
  - Oral budesonide can be considered in patients with mild noninfectious diarrhea (<4 stools daily) associated with immunotherapy but is inadequate for symptomatic patients with moderate to severe diarrhea
  - Infliximab (TNF inhibitor) can be considered for patients not responding to steroids, but is not initial therapy of choice
  - 5-Aminosalicylates such as mesalamine have an anti-inflammatory mechanism of action and are the mainstay of treatment of mild to moderate ulcerative colitis

Question 2

- A 79-year-old man is evaluated in the office following a recent hospitalization for pneumonia. This is his second episode of pneumonia in the past year. Medical history is notable for chronic lymphocytic leukemia. His disease course has been followed without treatment for the past 9 years.
- On physical examination, vital signs are normal. Pulmonary examination is normal. There is diffuse adenopathy and splenomegaly.

Laboratory studies:	
Leukocyte count	46,000/µL (46 × 10^9/L) with 92% lymphocytes, 6% neutrophils, 1% bands, and 1% monocytes
IgG	320 mg/dL (3.2 g/L)
IgA	20 mg/dL (0.2 g/L)
IgM	34 mg/dL (0.34 g/L)

- Which of the following is the most appropriate treatment for this patient?
  - A. Granulocyte-colony stimulating factor
  - B. Ibrutinib
  - C. IV gamma globulin
  - D. Splenectomy

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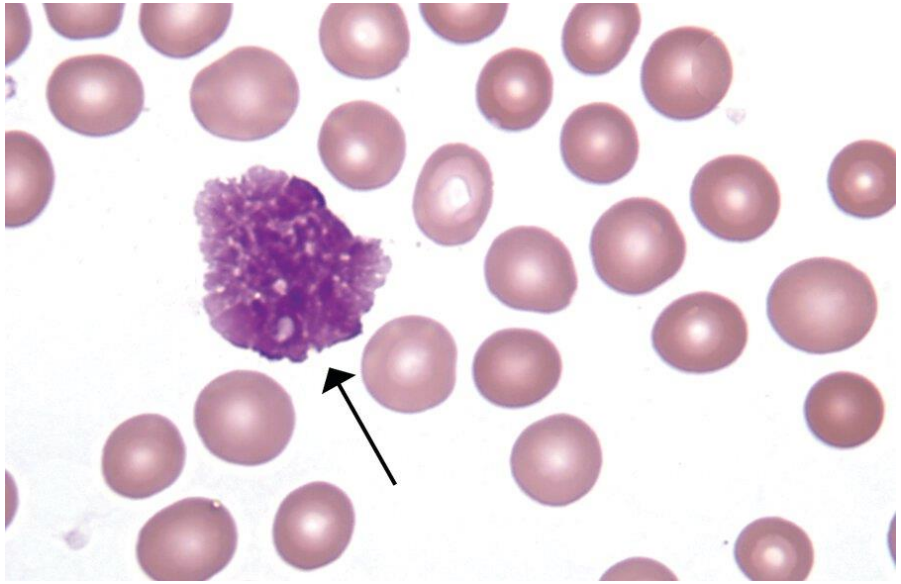
Treat hypogammaglobinemia in a patient with chronic lymphocytic leukemia

- Advanced CLL → decreased antibody levels → recurrent infections
- IV gamma globulin every 3-4 weeks to raise level to at least 600 mg/dL



- Other answers:
  - Neutropenia may complicate CLL or its treatment; however, this patient does not have absolute neutropenia (<1500 cells/µL) and GCSF not indicated
  - Ibrutinib is a first-line treatment as well as later treatment for CLL; however, treatment would have no immediate benefit for this patient's recurrent risk of infection
  - Splenectomy would rarely be performed in patients with CLL, except in circumstances such as for immune thrombocytopenia or immune hemolytic anemia unresponsive to other systemic therapies

Question 3

- A 63-year-old woman is evaluated for a mass in her right axilla. She first noticed the mass 2 months ago. She has also had a persistent cough. She was diagnosed 3 years ago with stage IIB right breast cancer for which she underwent lumpectomy, chemotherapy, and breast irradiation.
- On physical examination, vital signs are normal. There is a firm, fixed, 2-cm mass in the right axilla. Bilateral breast examination reveals no masses or nodules. The remainder of the examination is normal.
- Chest radiograph shows multiple bilateral pulmonary nodules. CT scan of the chest, abdomen, and pelvis shows new right axillary adenopathy and multiple peripheral pulmonary nodules measuring up to 1.5 cm in size. There is no hilar or mediastinal adenopathy.
- Which of the following is the most appropriate management?

A. Biopsy pulmonary nodule

B. Biopsy right axillary mass

C. Initiate chemotherapy

D. Initiate endocrine-based therapy

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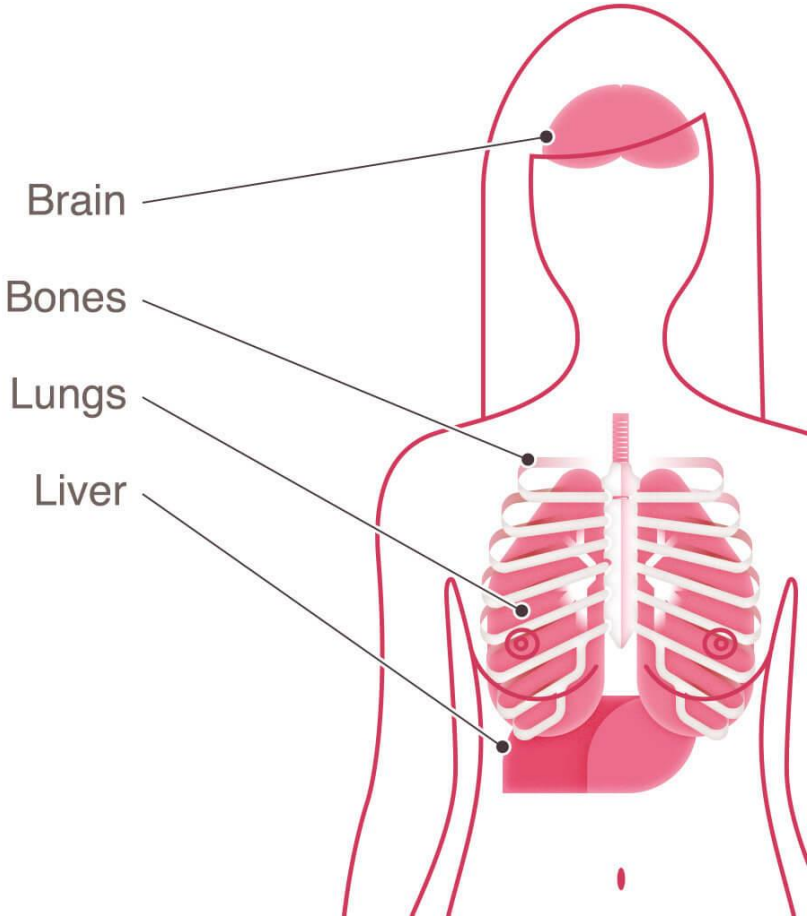
Evaluate metastatic disease in a patient with a history of breast cancer

- Approximately 5% of patients with breast cancer present with metastatic disease
- Up to 30% with early-stage disease develop metastases
- With newly diagnosed metastatic breast cancer, the lesion that upstages the patient to the greatest degree should be biopsied
- There may be treatment altering discordance in the receptors in the metastatic lesion compared with the primary breast cancer in 10% to 15% of patients



Question 4

- A 62-year-old woman was diagnosed 2.5 years ago with left-sided, stage IIB, estrogen receptor–positive, human epidermal growth factor receptor 2–negative breast cancer treated with mastectomy, postmastectomy irradiation, and letrozole, which was started 2 years ago. Medical history is otherwise unremarkable. Current medications are letrozole, a calcium supplement, and cholecalciferol.
- Which of the following is the most appropriate screening or surveillance test to perform at this time?

A. CT of chest, abdomen, and pelvis

B. Dual-energy x-ray absorptiometry

C. Echocardiogram

D. Pelvic ultrasound

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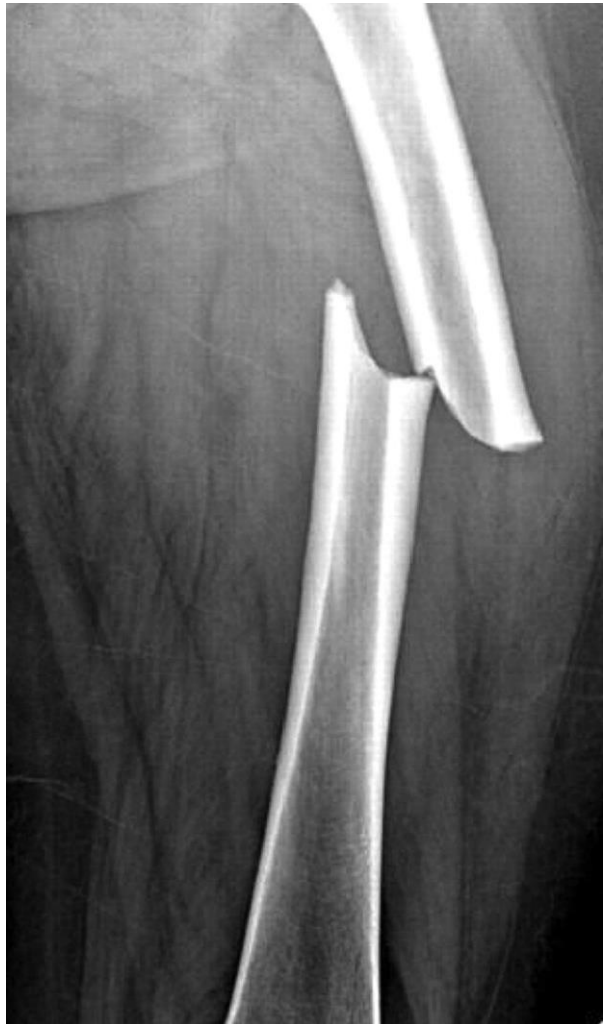
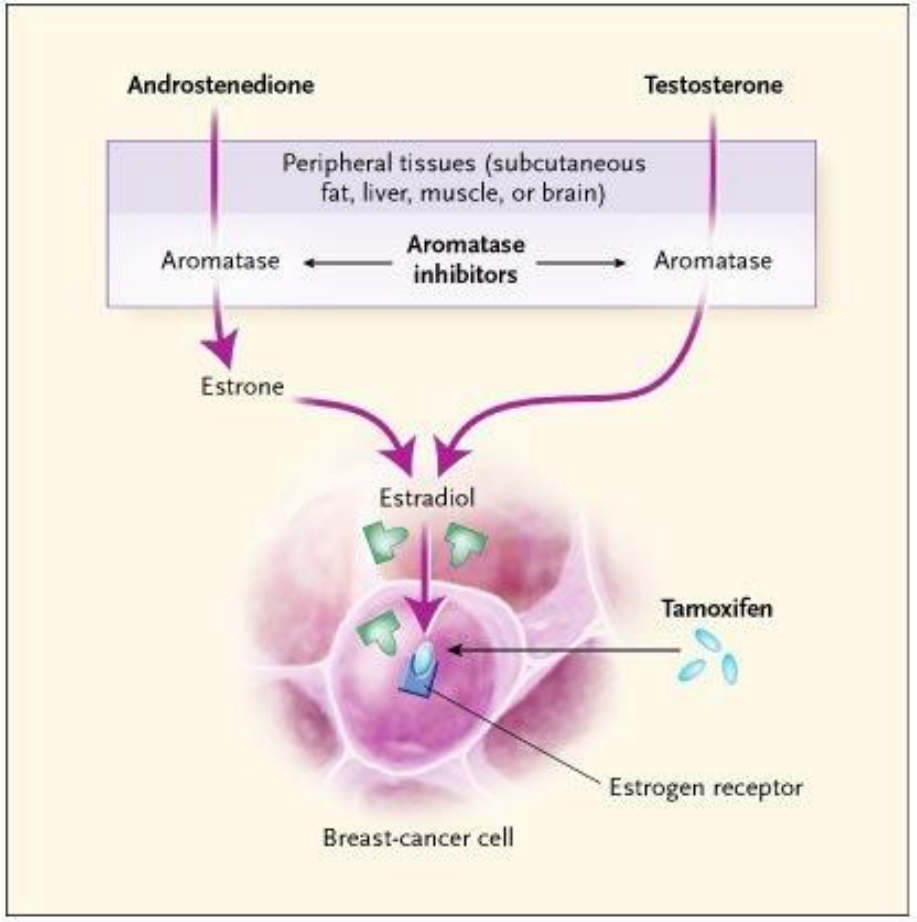
Screen for bone loss in a patient on an aromatase inhibitor

- Patients on aromatase inhibitors should have bone density evaluated with dual-energy x-ray absorptiometry at the start of treatment to establish a baseline and periodically, every 2 years, while on treatment
- Aromatase inhibitors are associated with bone loss and an elevated risk of fracture
- The risk of fracture with 5 years of aromatase inhibitor therapy is about 8% to 10%



Aromatase inhibitors

- Five years of an aromatase inhibitor or 2 years of tamoxifen followed by 3 years of an aromatase inhibitor is associated with a significantly lower risk of recurrence and with improved survival in postmenopausal women with higher-grade ductal cancers or lobular cancers



NEJM, 2003

Question 5

- A 56-year-old woman is evaluated for findings suspicious for inflammatory breast cancer.
- On physical examination, vital signs are normal. The right breast is enlarged, and the skin is thickened and erythematous. There is a 5- × 4-cm mass in the lower outer breast. There is an enlarged right axillary node.
- Right breast mammogram reveals a mass in the lower outer breast with calcifications that span approximately 5 cm in size. Right axillary ultrasound reveals an enlarged axillary lymph node. Core biopsy of the breast reveals estrogen receptor–negative, progesterone receptor–negative, and human epidermal growth factor 2–negative invasive ductal carcinoma. CT of the chest, abdomen, and pelvis and bone scan show no evidence of distant metastatic disease.
- Which of the following is the most appropriate sequence of therapies for this patient?

    A. Mastectomy, chemotherapy, irradiation

    B. Preoperative chemotherapy, lumpectomy, irradiation

    C. Preoperative chemotherapy, mastectomy, irradiation

    D. Irradiation, mastectomy, chemotherapy

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Manage a patient with newly diagnosed inflammatory breast cancer

- Diagnostic criteria:
  - Rapid onset of breast erythema, edema, and/or peau d'orange, and/or warm breast, with or without an underlying palpable mass
  - Duration of history no more than 6 months
  - Erythema occupying at least one-third of the breast
  - Pathologic confirmation of invasive carcinoma

- Differential diagnosis:
  - Non-inflammatory breast cancer
  - Infectious mastitis and breast abscess
  - Ductal ectasia
  - Other malignancies (lymphoma)

Treatment of IBC

- Inflammatory breast cancer is usually treated initially with neoadjuvant chemotherapy, followed by surgery, and then radiation therapy
  - **Pre-op chemo** aims to shrink the tumor maximizing the chance that mastectomy will result in negative margins
  - **Mastectomy** is associated with decreased risk of locoregional recurrence and improved disease-free survival

- **Postmastectomy radiation therapy**
  - Tumors > 5 cm in size
  - Inadequate or positive margins or skin involvement
  - IBCs
  - Four or more positive axillary nodes
- Postmastectomy radiation therapy decreases both the risk of local recurrence and the risk of distant metastases and increases overall survival

Question 6

- A 51-year-old man is evaluated for intermittent, bright red blood per rectum of 10 weeks' duration. Medical history is otherwise unremarkable, and he takes no medications.
- On physical examination, vital signs are normal. Digital rectal examination is normal.
- Stool is positive for fecal occult blood.
- A colonoscopy is performed, and a nonobstructing lesion is noted at 10 cm from the anal verge. Examination of the rest of the colon is unremarkable. An MRI scan of the rectum shows the lesion to be invading into but not through the full thickness of the muscularis. No abnormal lymph nodes are seen on MRI. Contrast-enhanced CT scan of the chest and abdomen does not show evidence of metastases.
- Biopsy of the mass shows adenocarcinoma.
- Which of the following is the most appropriate treatment?

    A. Chemotherapy

    B. Irradiation plus chemotherapy

    C. Irradiation, chemotherapy, and surgery

    D. Surgery

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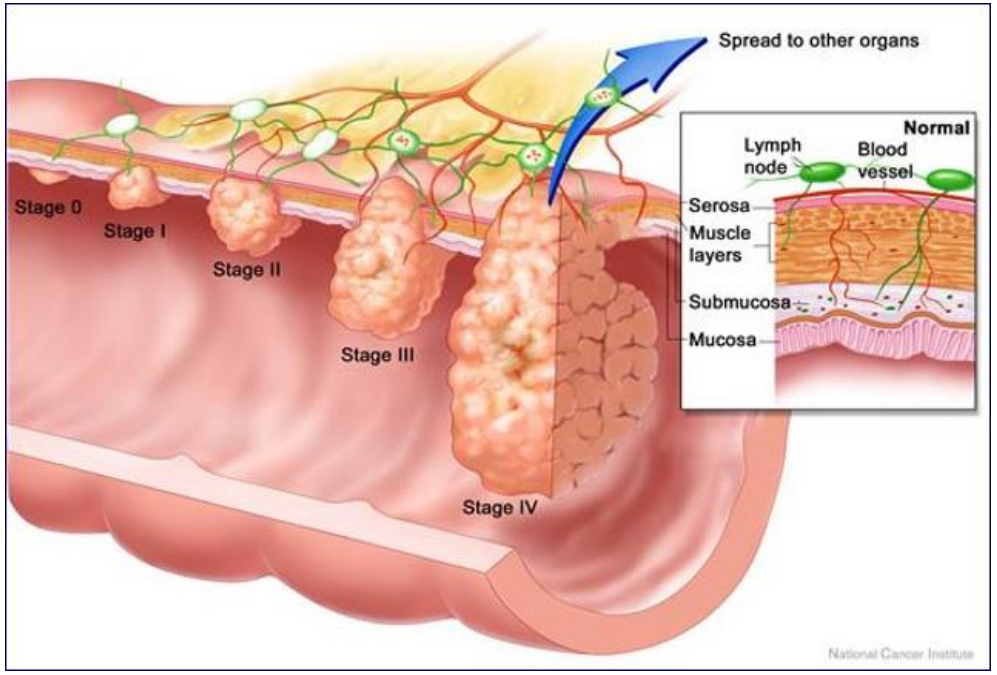
Treat stage I rectal cancer

- Rectal cancers that do not penetrate the full thickness of the bowel wall and do not involve regional lymph nodes are stage I and are treated with surgical resection



- With the tumor located 10 cm from the anal verge, the surgical procedure of choice would be a low anterior resection, with either a direct anastomosis, or, more likely, a temporary diverting ileostomy, which would be reversed after 2 to 3 months
- Such a resection would be anticipated to be sphincter-sparing, and so the patient should not require a permanent colostomy

TNM staging

Table. Colon and Rectum Cancer Staging[6]

AJCC Stage	TNM Stage	Description
0	Tis N0 M0	Tumor is confined to mucosa
I	T1 N0 M0	Tumor invades submucosa
I	T2 N0 M0	Tumor invades muscularis propria
IIA	T3 N0 M0	Tumor invades subserosa or beyond, no other organs involved
IIB	T4 N0 M0	Tumor invades adjacent organs or perforates visceral peritoneum
IIIA	T1-2 N1 M0	Metastasis to 1-3 regional lymph nodes with tumor invasion of submucosa and/or muscularis
IIIB	T3-4 N1 M0	Metastasis to 1-3 regional lymph nodes with tumor invasion of subserosa or adjacent organs
IIIC	Any T, N2 M0	Metastasis to 4 or more lymph nodes
IV	Any T, any N, M1	Metastasis to distant organs

Abbreviations: AJCC, American Joint Committee on Cancer; Tis, tumor (carcinoma) in situ.

Question 7

- A 72-year-old woman is evaluated for rectal bleeding with bowel movements.
- On physical examination, vital signs are normal, and the remainder of the examination, including digital rectal examination, is unremarkable.
- A colonoscopy is performed, and a bulky lesion is noted 10 cm from the anal verge. The rest of the colonoscopy results are normal.
- MRI of the pelvis shows a bulky tumor in the upper third of the rectum, involving the full thickness of the rectal wall, and several enlarged mesorectal lymph nodes of up to 2 cm in diameter are noted. CT scan of the chest and abdomen is normal.
- A biopsy of the mass shows adenocarcinoma.
- Which of the following is the most appropriate treatment?

    A. Chemotherapy followed by irradiation and then surgery

    B. Surgery alone

    C. Surgery followed by irradiation

    D. Surgery followed by irradiation and then chemotherapy

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Treat locally advanced rectal cancer

- Full-thickness rectal tumors (stage II) and/or those with involved lymph nodes (stage III) routinely require irradiation, chemotherapy, and surgery
- Surgery followed by irradiation is avoided when feasible for rectal tumors because of greater toxicity and a higher risk of tumor recurrence in the irradiated field than when irradiation is given before surgery
- Capecitabine, an oral prodrug that is converted into 5-fluorouracil (5-FU), or, less commonly, intravenous 5-FU, is given concurrently with radiation therapy
- If a complete clinical response to TNT is achieved, nonoperative management with close surveillance may be considered
- Attempts are made to preserve anal sphincter function, but if a distal rectal cancer is not fully eradicated by TNT, an abdominal-perineal resection with resultant permanent colostomy is required
- Surgery for tumors of the mid rectum and above rarely require a permanent colostomy

Question 8

- A 65-year-old woman is evaluated for a lung nodule found on a preoperative chest radiograph for upcoming elective surgery. Medical history is significant for a malignant melanoma that was resected from the right chest wall 4 years ago. A right axillary sentinel lymph node was negative at that time. Medical history is otherwise unremarkable, and she takes no medications.
- On physical examination, vital signs are normal. There is a healed incision site from prior right chest wall melanoma resection. There is no evidence of local or in-transit recurrence and no axillary or other adenopathy.
- PET/CT scan shows uptake in the right lung nodule but no other evidence of disease. CT-guided biopsy of the right lung lesion shows *BRAF* V600E–mutated malignant melanoma.
- Which of the following is the most appropriate initial treatment for this patient?

  A. BRAF inhibitor

  B. BRAF inhibitor and a MEK inhibitor

  C. Immunotherapy

  D. Surgical resection

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- Which of the following is the most appropriate initial treatment for this patient?

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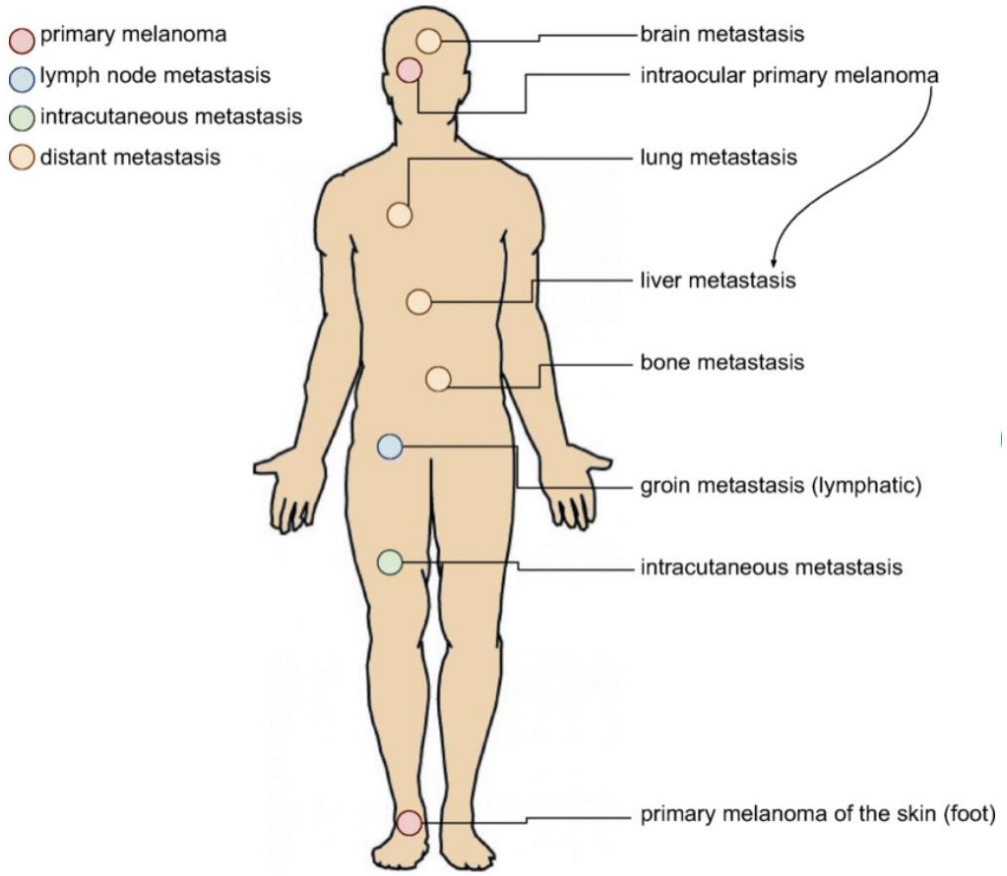
Treat melanoma with a solitary metastasis with surgical resection



- Metastasectomy can be optimal in selected patients with solitary or oligometastatic metastases in a variety of malignancies
  - Melanoma
  - Renal cell cancer
  - Colorectal cancer
  - Sarcomas
- Positive prognostic factors for patients undergoing metastasectomy include:
  - Longer disease-free intervals
  - Fewer than three pulmonary nodules
  - Absence of extrathoracic and lymph node metastases
  - Response to chemotherapy or immunotherapy

Question 9

- A 64-year-old woman is evaluated in the office following a diagnosis of metastatic breast cancer. Six years ago, she was diagnosed with breast cancer and treated with lumpectomy, irradiation, and a complete course of adjuvant hormonal therapy. Two weeks ago, a bone lytic lesion was found on a lumbar spine radiograph taken for low back pain after a fall while playing tennis. Subsequent CT scans revealed diffuse involvement of her axial skeleton with no associated fractures and no epidural extension. The patient is currently asymptomatic. Medical history is unremarkable, and she takes no medications.
- On physical examination, vital signs are within normal limits, and examination findings are unremarkable.
- Systemic therapy for metastatic breast cancer is planned.
- Which of the following is the most appropriate additional treatment?

A. Calcium and vitamin D

B. Spine irradiation

C. Teriparatide

D. Zoledronic acid

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Treat bone metastases from breast cancer

- Bone-modifying agent indicated to prevent the development of skeletal-related events, including bone pain, cord compression, need for palliative radiation therapy, and hypercalcemia

- Zoledronic acid (bisphosphonate)
  - Renally cleared; contraindicated among patients with creatinine clearance less than 30 mL/min
- Denosumab (a receptor activator of nuclear factor κB ligand inhibitor)
  - Dose-adjustment not needed with renal insufficiency
- Both associated with SEs of small risks of osteonecrosis of the jaw
- Given every 3 months

Other answers

- Calcium and vitamin D alone are an insufficient preventive therapy for this patient with metastatic bone disease; often given with bone-modifying agents as can result in hypocalcemia
- Palliative irradiation is useful for patients with focal areas of pain caused by bone metastases but is not indicated in this asymptomatic woman
- Teriparatide is a form of parathyroid hormone and acts as an anabolic agent to promote bone formation for the treatment of osteoporosis; not used to treat bone metastases from solid tumors

Typical radiographic presentation of select tumors in bone*

Predominantly osteoblastic
Prostate
Carcinoid
Small cell lung cancer
Hodgkin lymphoma
Medulloblastoma
POEMS syndrome
Predominantly osteolytic
Renal cell cancer
Melanoma
Multiple myeloma
Non-small cell lung cancer
Thyroid cancer
Non-Hodgkin lymphoma
Langerhans cell histiocytosis
Mixed osteoblastic and osteolytic
Breast cancer
Gastrointestinal cancers
Squamous cancers at most primary sites

POEMS: polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes.

* These represent the most common patterns of metastatic involvement; individual variations may occur.

Question 10

- A 69-year-old woman undergoes follow-up evaluation for stage III colon cancer, which was resected 2 years ago. She is asymptomatic and takes no medications.
- On physical examination, vital signs and examination findings are unremarkable.
- Surveillance CT scan of the chest, abdomen, and pelvis reveals a new 3-cm lesion and a 2.5-cm lesion, both in the right lobe of the liver. No other abnormalities are noted.
- Which of the following is the most appropriate treatment?

A. Hepatic artery embolization

B. Needle biopsy of the largest lesion

C. Resection of the two lesions

D. Systemic chemotherapy

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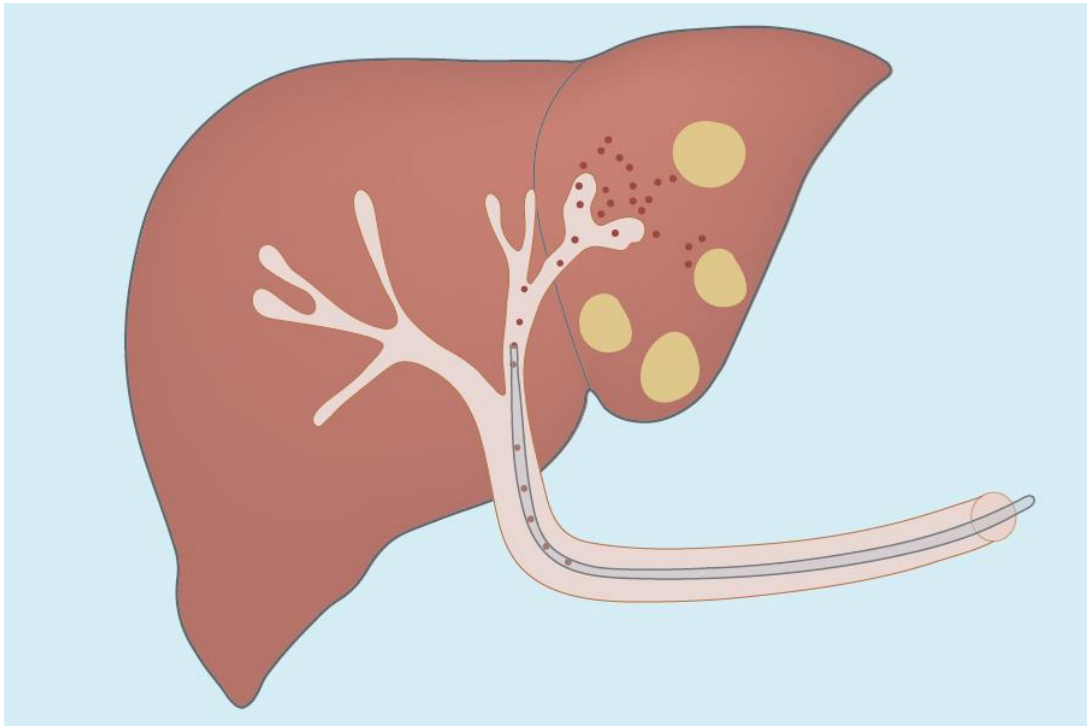
Treat oligometastatic liver metastases



- Patients with oligometastatic lesions confined to the liver or lung should be referred for surgical evaluation; resection can be curative in approximately 25% of these patients
- Previous guidelines defined resectability of hepatic metastases based on the number of lesions, tumor size, and potential for clear surgical margins, but newer approaches define resectable disease as metastatic tumors that can be completely resected while leaving an adequate functional residual liver volume

Colon cancer surveillance

- Postoperative surveillance following curative surgery for colon cancer:
  - Colonoscopy is recommended 1 year after resection (or 3 to 6 months after resection if a complete colonoscopy was not done preoperatively) and then in 3 years, followed by every 5 years, unless abnormalities are found
  - CEA assessment should be done at approximately 6-month intervals
  - Contrast-enhanced CT of the chest, abdomen, and pelvis is recommended annually for up to 5 years postoperatively
  - PET scanning should not be used for routine surveillance

Other answers

- Hepatic arterial embolization can be used for control of more vascular tumors such as hepatocellular carcinoma or neuroendocrine tumors, but it is not routinely used in colorectal cancer because these tumors tend to be relatively low in vascularity
- A needle biopsy should not be done because it will not affect management; this clinical presentation is compelling enough for recurrent colorectal cancer that a negative needle biopsy would be assumed to be a false-negative result, and so would not alter management, and surgical resection would be the appropriate intervention regardless of the biopsy results
- Because this patient is potentially curable, systemic chemotherapy, which is not curative, would not be a correct consideration

Question 11

- A 67-year-old woman is about to begin highly emetogenic chemotherapy with cyclophosphamide and doxorubicin for stage III breast cancer.
- On physical examination, vital signs are normal. There is a healed left lumpectomy incision and a sentinel node sampling incision. The left chest port is in place.
- Which of the following is the most appropriate management of this patient's potential for nausea and vomiting?

A. Lorazepam

B. Medical marijuana

C. Ondansetron, aprepitant, olanzapine, and dexamethasone

D. Ondansetron or dexamethasone

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- A 67-year-old woman is about to begin highly emetogenic chemotherapy with cyclophosphamide and doxorubicin for stage III breast cancer.
- On physical examination, vital signs are normal. There is a healed left lumpectomy incision and a sentinel node sampling incision. The left chest port is in place.
- Which of the following is the most appropriate management of this patient's potential for nausea and vomiting?

A. Lorazepam

B. Medical marijuana

C. Ondansetron, aprepitant, olanzapine, and dexamethasone

D. Ondansetron or dexamethasone

Manage high-emetic-risk chemotherapy

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Antiemesis

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EMETOGENIC POTENTIAL OF PARENTERAL ANTICANCER AGENTS

LEVEL	AGENT		
High emetic risk (>90% frequency of emesis)[a]	• AC combination defined as any chemotherapy regimen that contains an anthracycline and cyclophosphamide • Carboplatin AUC ≥4 • Carmustine >250 mg/m²	• Cisplatin • Cyclophosphamide >1500 mg/m² • Dacarbazine • Doxorubicin ≥60 mg/m² • Epirubicin >90 mg/m² • Ifosfamide ≥2 g/m² per dose	• Mechlorethamine • Melphalan ≥140 mg/m² • Sacituzumab govitecan-hziy • Streptozocin
Moderate emetic risk (>30%–90% frequency of emesis)[a]	• Aldesleukin >12–15 million IU/m² • Amifostine >300 mg/m² • Amivantamab-vmjw • Azacitidine • Bendamustine • Busulfan • Carboplatin AUC[b] <4 • Carmustine[b] ≤250 mg/m² • Clofarabine • Cyclophosphamide[b] ≤1500 mg/m² • Cytarabine >200 mg/m²	• Dactinomycin[b] • Daunorubicin[b] • Dual-drug liposomal encapsulation of cytarabine and daunorubicin • Dinutuximab • Doxorubicin[b] <60 mg/m² • Epirubicin[b] ≤90 mg/m² • Fam-trastuzumab deruxtecan-nxki • Idarubicin[b] • Ifosfamide[b] <2 g/m² per dose • Irinotecan[b]	• Irinotecan (liposomal) • Lurbinectedin • Melphalan <140 mg/m² • Methotrexate[b] ≥250 mg/m² • Naxitamab-gqgk • Oxaliplatin[b] • Romidepsin • Temozolomide • Trabectedin[b]

Adapted with permission from: Hesketh PJ, Kris MG, Grunberg SM, et al. Proposal for classifying the acute emetogenicity of cancer chemotherapy. J Clin Oncol 1997;15:103-109.
Grunberg SM, Warr D, Gralla RJ, et al. Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity--state of the art. Support Care Cancer 2011;19:S43-S47.

Manage high-emetic-risk chemotherapy

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HIGH EMETIC RISK PARENTERAL ANTICANCER AGENTS — ACUTE AND DELAYED EMESIS PREVENTION[f,g,h,i,j]

DAY 1: Select treatment option A, B, or C All treatment options are category 1 and should be started before anticancer therapy[h]	DAYS 2, 3, 4:
Treatment option A (preferred), use the following combination[l]: 1. Olanzapine 5–10 mg oral (PO) once[k] 2. NK1 receptor antagonist (RA) (choose one): ◊ Aprepitant 125 mg PO once ◊ Aprepitant injectable emulsion 130 mg intravenous (IV) once[m] ◊ Fosaprepitant 150 mg IV once ◊ Netupitant 300 mg / palonosetron 0.5 mg (available as fixed combination product only) PO once[n] ◊ Fosnetupitant 235 mg / palonosetron 0.25 mg (available as fixed combination product only) IV once[n] ◊ Rolapitant 180 mg PO once[o] 3. 5-HT3 RA (choose one)[p,q]: ◊ Dolasetron 100 mg PO once ◊ Granisetron 10 mg subcutaneous (SQ) once,[r] or 2 mg PO once, or 0.01 mg/kg (max 1 mg) IV once, or 3.1 mg/24-h transdermal patch applied 24–48 h prior to first dose of anticancer therapy ◊ Ondansetron 16–24 mg PO once, or 8–16 mg IV once ◊ Palonosetron 0.25 mg IV once 4. Dexamethasone 12 mg PO/IV once[s,t]	**Treatment option A:** • Olanzapine 5–10 mg PO daily on days 2, 3, 4[k] • Aprepitant 80 mg PO daily on days 2, 3 (if aprepitant PO is used on day 1) • Dexamethasone 8 mg[s,t] PO/IV daily on days 2, 3, 4

Manage high-emetic-risk chemotherapy

- For patients receiving high-emetic-risk chemotherapy, standard antiemetic treatments include a four-drug combination of an NK1 receptor antagonist, a 5-hydroxytryptamine-3 receptor antagonist, dexamethasone, and olanzapine
- Olanzapine, when added to standard antiemetic regimens, has been found to be effective for the treatment of delayed chemotherapy-induced nausea and vomiting (although some oncologists may not routinely prescribe this as first-line therapy due to the risk of sedation)

Question 12

- A 66-year-old man is evaluated for increased confusion and lethargy over the past 2 days, as well as nausea and vomiting. He has also had diffuse bone pain that began 6 weeks ago and has worsened over the past month. His medical history is otherwise unremarkable, and he takes no medications.
- On physical examination, temperature is 36.4 °C (97.6 °F), blood pressure is 110/60 mm Hg, pulse rate is 110/min, and respiration rate is 16/min. He is somnolent but can be aroused. Mucous membranes are dry, and he has decreased skin turgor. Cardiopulmonary examination is normal.
- Results of laboratory studies show an albumin level of 3.8 g/dL (38 g/L), calcium level of 14.8 mg/dL (3.7 mmol/L), and creatinine level of 2.5 mg/dL (221 µmol/L).
- Which of the following is the most appropriate initial management?

    A. Denosumab

    B. Intravenous isotonic saline and calcitonin

    C. Intravenous isotonic saline and furosemide

    D. Zoledronic acid

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Treat hypercalcemia of malignancy

- 20-30% of patients with advanced cancer
- Most frequent with myeloma and cancer of the lung, breast, kidney, head, and neck
- Isotonic saline volume expansion, which will increase renal perfusion and urine calcium excretion
  - Initial rate of 200 to 300 mL/hour that is then adjusted to maintain the urine output at 100 to 150 mL/hour is a reasonable goal
- Calcitonin increases kidney excretion of calcium and decreases bone resorption; it can decrease calcium within several hours in responsive patients

- Other answers:
  - Denosumab typically reserved for patients who do not respond to bisphosphonate therapy and when denosumab is contraindicated, such as in patients with kidney failure
  - Furosemide is not recommended unless kidney failure or heart failure is present, in which case volume expansion should precede the administration of furosemide to avoid hypotension and further kidney injury
  - Bisphosphonates have maximum effect in 2 to 4 days, so they are usually given in conjunction with intravenous isotonic saline

Hypercalcemia of malignancy

Table 1. Types of Hypercalcemia Associated with Cancer.*

Type	Frequency (%)	Bone Metastases	Causal Agent	Typical Tumors
Local osteolytic hypercalcemia	20	Common, extensive	Cytokines, chemokines, PTHrP	Breast cancer, multiple myeloma, lymphoma
Humoral hypercalcemia of malignancy	80	Minimal or absent	PTHrP	Squamous-cell cancer, (e.g., of head and neck, esophagus, cervix, or lung), renal cancer, ovarian cancer, endometrial cancer, HTLV-associated lymphoma, breast cancer
$1,25(OH)_2D$-secreting lymphomas	<1	Variable	$1,25(OH)_2D$	Lymphoma (all types)
Ectopic hyperparathyroidism	<1	Variable	PTH	Variable

* PTH denotes parathyroid hormone, PTHrP PTH-related protein, $1,25(OH)_2D$ 1,25-dihydroxyvitamin D, and HTLV human T-cell lymphotrophic virus.

NEJM, 2005

Question 13

- A 68-year-old man is evaluated for shortness of breath, headache, and swelling of the neck. He first noticed symptoms 3 weeks ago, which have worsened over the past 2 days.
- Medical history is significant for a 25-pack-year history of smoking.
- On physical examination, temperature is 36.5 °C (97.8 °F), blood pressure is 110/65 mm Hg, pulse rate is 112/min, and respiration rate is 18/min. Oxygen saturation is 92% breathing ambient air. The patient is cachectic but appears comfortable. His face is plethoric, and there are distended cutaneous vessels over the anterior thorax. An enlarged right supraclavicular lymph node is palpable. Pulmonary examination is normal.
- CT scan of the chest reveals bulky mediastinal adenopathy compressing the superior vena cava, right supraclavicular adenopathy, and a small right-sided pleural effusion.
- Which of the following is the most appropriate management?

    A. Biopsy of the supraclavicular node

    B. Glucocorticoids

    C. Radiation therapy

    D. Surgical resection of the mediastinal lymphadenopathy

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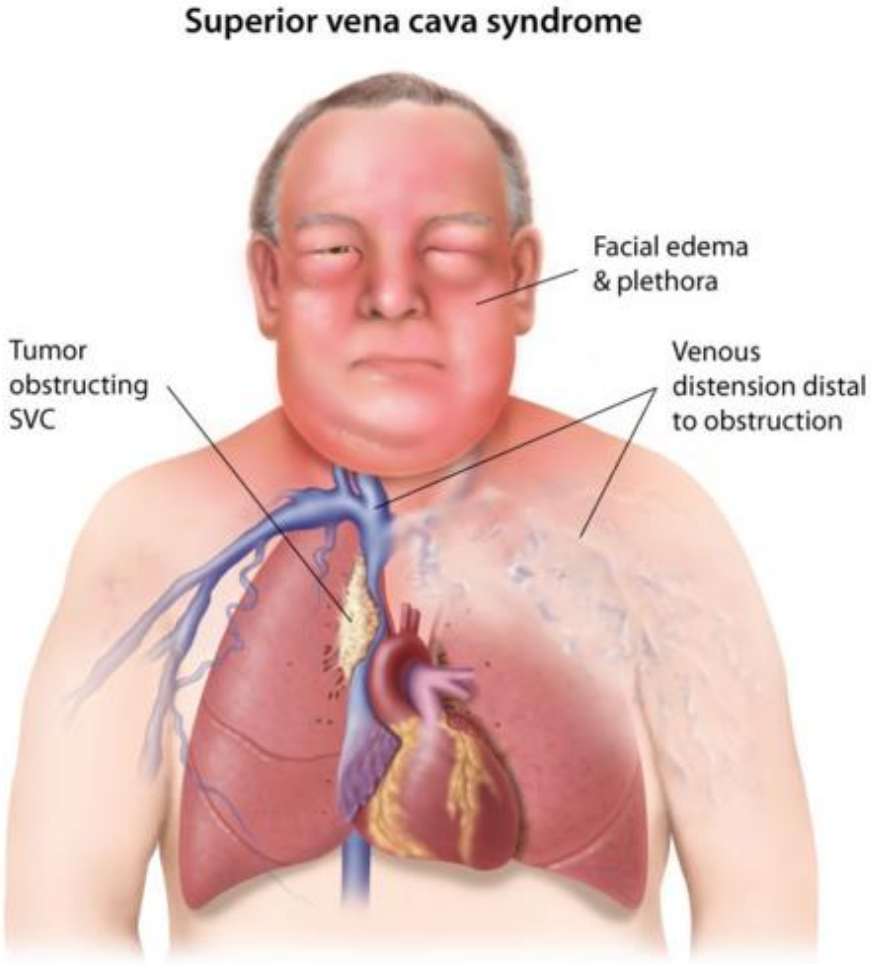
Manage a patient with superior vena cava syndrome

- Most cases of superior vena cava syndrome are caused by malignancies with large mediastinal masses, and most patients do not require emergency intervention
- For superior vena cava syndrome, a tissue biopsy should be obtained to determine the underlying malignancy and guide further management
- Many patients with SVC syndrome have highly chemotherapy-sensitive malignancies, such as small cell carcinoma of the lung or aggressive non-Hodgkin lymphoma
- Even those who present with a heavy burden of symptoms or vital sign abnormalities such as hypoxia may be treated with standard chemotherapy to obtain shrinkage of the tumor and improvement in SVC syndrome



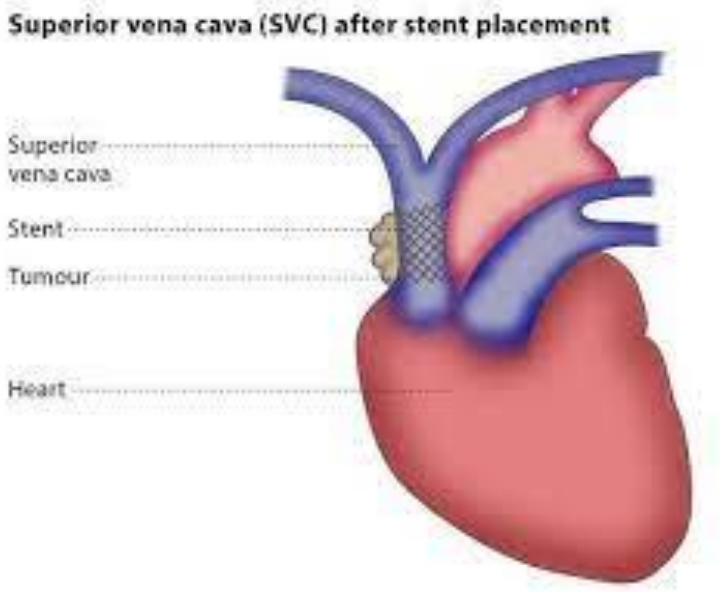
Manage a patient with superior vena cava syndrome

- Patients who require urgent treatment:
  - Stridor
  - Respiratory compromise
  - Depressed CNS function
  - Significant hemodynamic compromise

Grading the severity of malignant superior vena cava syndrome

Grade	Findings	Estimated incidence (%)
0	Asymptomatic – Radiographic superior vena cava obstruction in the absence of symptoms	10
1	Mild – Edema in head or neck (vascular distention), cyanosis, plethora	25
2	Moderate – Edema in head or neck with functional impairment (mild dysphagia, cough, mild or moderate impairment of head, jaw, or eyelid movements, visual disturbances caused by ocular edema)	50
3	Severe – Mild or moderate cerebral edema (headache, dizziness), mild/moderate laryngeal edema, or diminished cardiac reserve (syncope after bending)	10
4	Life-threatening – Significant cerebral edema (confusion, obtundation), significant laryngeal edema (stridor), or significant hemodynamic compromise (syncope without precipitating factors, hypotension, renal insufficiency)	5
5	Fatal – Death	<1

- Urgent treatment consists of endovenous recanalization (mechanical or pharmacologic thrombolysis, balloon angioplasty) and SVC stenting



Other answers

- Glucocorticoids should not be administered routinely to patients with SVC syndrome; pretreatment with glucocorticoids can obscure the tissue diagnosis, particularly for patients with aggressive lymphomas, which may be very sensitive to glucocorticoids
- Radiation therapy should only be performed after a tissue diagnosis is obtained and if it is otherwise indicated for management of the underlying disease; can be considered if highly symptomatic SVC syndrome in the setting of a malignancy that is unlikely to respond quickly to systemic therapy, or if the patient is not fit to receive systemic therapy
- Surgical resection of the mediastinal adenopathy to relieve SVC syndrome is not appropriate in this patient because treatment should be tailored to the underlying malignancy

Question 14

- A 62-year-old woman is evaluated in the office following a diagnosis of atypical ductal hyperplasia. She underwent a right total hip replacement 2 years ago complicated by deep venous thrombosis. Medical history is otherwise unremarkable, and she takes no medications.
- On physical examination, vital signs are normal. There is a well-healed left breast incision with no skin changes and no palpable mass or nodule.
- Which of the following is the most appropriate breast cancer chemoprevention for this patient?

    A. Aspirin

    B. Exemestane

    C. Raloxifene

    D. Tamoxifen

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Prevent breast cancer with an aromatase inhibitor in a high-risk woman with previous deep venous thrombosis

- USPSTF recommends that clinicians offer to prescribe risk-reducing medications, such as tamoxifen, raloxifene, or aromatase inhibitors, to women who are at increased risk for breast cancer and at low risk for adverse medication effects
- Women ≥ 35 with prior benign breast lesions on biopsy (such as atypical ductal or lobular hyperplasia and lobular carcinoma in situ)
- Does not apply to women who have a current or previous diagnosis of breast cancer or ductal carcinoma in situ

- Other answers:
  - Tamoxifen shown to reduce the risk of breast cancer by approximately 30%, but associated with a significantly increased risk of VTE and has a black box warning for use among patients with a previous history of VTE
  - Raloxifene, effective in breast cancer chemoprevention for postmenopausal women, also increases the risk of VTE, although not to as great an extent

Question 15

- A 60-year-old woman is evaluated for right-sided mid back pain of 2 months' duration. Medical history is significant for hypertension treated with hydrochlorothiazide. She takes no other medications.
- On physical examination, vital signs are within normal limits. Oxygen saturation is 99% with the patient breathing ambient air. The remainder of the examination is normal.

Hemoglobin	20 g/dL (200 g/L)
Leukocyte count	7200/µL (7.2×10^9/L)
Platelet count	295,000/µL (295×10^9/L)
Urinalysis	3+ blood; no protein; 30 erythrocytes/hpf; no casts or dysmorphic erythrocytes

- Subsequent measurement of erythropoietin level was 180 mU/mL (180 U/L).
- Which of the following is the most likely diagnosis?

A. Lung cancer

B. Myelodysplastic syndrome

C. Polycythemia vera

D. Relative erythrocytosis

E. Renal cell carcinoma

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Diagnose renal cell cancer in a patient with secondary erythrocytosis

- Secondary erythrocytosis defined by the presence of erythrocytosis and an elevated erythropoietin level

Secondary polycythemia (elevated serum erythropoietin [EPO])
Hypoxia/cardiopulmonary-associated
Chronic pulmonary disease
Right-to-left cardiac shunts
Sleep apnea
Obesity hypoventilation syndrome (Pickwickian syndrome)
High altitude
Chronic carbon monoxide poisoning (including heavy smoking)
Kidney-associated causes
Following renal transplantation
Others (eg, renal artery stenosis, cysts, hydronephrosis)
Autonomous EPO production
EPO-producing tumors (eg, hepatocellular carcinoma, renal cell carcinoma, hemangioblastoma, pheochromocytoma, uterine leiomyomata)

- Other answers:
  - Lung cancer associated with a variety of paraneoplastic syndromes, including hypercalcemia and SIADH, but it has not been associated with ectopic erythropoietin production and would not be expected to cause hematuria
  - Myelodysplastic syndrome is a stem cell disorder that results in ineffective hematopoiesis and various cytopenias, the most common of which is anemia, often macrocytic; myelodysplastic syndrome is not a cause of erythrocytosis
  - Polycythemia vera is a myeloproliferative disorder that is caused by a mutation in the *JAK-2* gene; leukocytosis and thrombocytosis are often seen as well; hematuria would not be expected

Question 16

- A 37-year-old woman is seen for follow-up evaluation 6 months after resection of cutaneous melanoma. It had a 0.45-mm depth of invasion by Breslow microstaging (stage IA).
- On physical examination, vital signs are normal. There is a healed incision on the right thigh from resection of the melanoma. There is no evidence of cutaneous or in-transit recurrence and no femoral or inguinal adenopathy.
- Which of the following is the most appropriate cancer surveillance for this patient?

  A. Annual chest radiograph

  B. Brain MRI every 6 months for 3 years; PET/CT annually for 5 years

  C. Complete blood count, biochemistry profile, and lactate dehydrogenase measurement every 6 months

  D. Physical examination and dermatologic evaluation every 6 months

  E. PET/CT annually for 5 years

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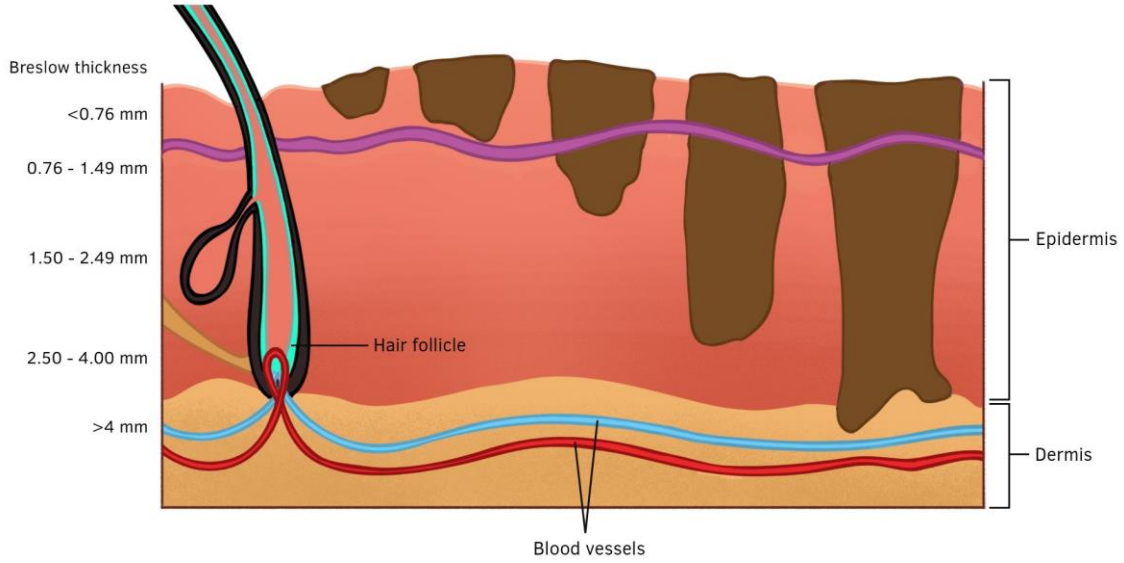
D. Physical examination and dermatologic evaluation every 6 months

E. PET/CT annually for 5 years

Manage low-risk melanoma with appropriate posttreatment surveillance

- Patients with low-risk (thin; <0.8 mm Breslow depth) melanoma should be encouraged to perform skin self-examinations as well as receive skin evaluations by a dermatologist regularly for life
- Particular attention directed at primary resection site for evidence of local recurrence (satellite lesions), in-transit metastases (looking for disease traveling along the course of draining lymphatics), and regional nodal involvement

- Patients who have had one melanoma have a significantly higher risk of developing second primary melanomas
- Risk of recurrence ↑ with depth of invasion, ulceration and high mitotic rate



Other answers

- In the absence of signs or symptoms of recurrence, routine laboratory evaluation or imaging with chest radiograph, PET/CT, or brain MRI have a very low yield and are not routinely recommended
- However, in patients with higher stages of disease (stage IIB-IV), serial imaging with CT or whole-body fluorodeoxyglucose-PET with or without brain MRI may be considered appropriate for 3 to 5 years

Question 17

- A 61-year-old woman is evaluated following a diagnosis of colon cancer. A colonoscopy performed for iron deficiency anemia revealed an adenocarcinoma at the splenic flexure. The patient is asymptomatic and otherwise has no medical problems. Oral iron replacement therapy has been initiated.
- On physical examination, vital signs are normal, and the remainder of the examination is noncontributory.
- Results of laboratory studies show a hemoglobin level of 9.9 g/dL (99 g/L). A comprehensive metabolic profile and carcinoembryonic antigen measurement are within normal limits.
- Which of the following imaging studies should be performed next?

    A. Contrast-enhanced CT of the chest, abdomen, and pelvis

    B. CT colonography

    C. Whole-body PET/CT

    D. No additional imaging studies

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B. CT colonography

C. Whole-body PET/CT

D. No additional imaging studies

Evaluate a patient with newly diagnosed colon cancer for metastatic disease

- Staging evaluation of newly diagnosed colon cancer includes measurement of serum carcinoembryonic antigen level and contrast-enhanced CT of the chest, abdomen, and pelvis
- PET/CT is not recommended for either preoperative staging or for postoperative surveillance in patients with colon cancer; higher false-positive and false-negative rates than acceptable

- CEA
  - Elevated level indicates a worse prognosis for patients at any stage of colon cancer compared to patients with normal levels
  - Failure of an elevated CEA level to normalize after resection suggests the continued presence of metastatic disease and need for additional evaluation
  - Rising CEA level during the surveillance period after surgical resection indicates recurrent disease and the need for diagnostic imaging

Question 18

- A 66-year-old woman is evaluated following completion of therapy for locally advanced squamous cell carcinoma of the hypopharynx. She was treated with combined cisplatin chemotherapy and irradiation. One month ago, imaging with PET/CT revealed a complete response. She is a former smoker with a 40-pack-year history who quit 7 years ago. She takes no medications.
- On physical examination, vital signs are normal. She has dry oral mucosa and post-irradiation induration to the right of the neck. No cervical adenopathy is noted.
- Which of the following imaging tests is most appropriate?

  A. Low-dose CT of the chest in 1 year

  B. MRI of the neck in 3 months

  C. PET/CT in 3 months

  D. No additional imaging is required

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Screen for lung cancer in a former smoker diagnosed with head and neck cancer

- Up to 20% of head and neck cancer survivors develop a second primary cancer related to smoking and alcohol exposure
- USPSTF lung cancer screening recommendations (updated 3/2021):

Recommendation Summary

Population	Recommendation	Grade
Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

Head and neck cancer

- Squamous cell carcinoma most common form of head and neck CA
- Tobacco is #1 RF and ETOH + tobacco synergistically increases the risk
- HPV increasing important cause (prognosis of HPV-associated CA of the oropharynx is significantly better than for non-HPV related CA)
- Presenting symptoms include LN enlargement, unilateral hearing loss or ear pain, oral pain/ulcers, dysphagia/odynophagia, hoarseness
- Work-up includes referral to ENT for direct laryngoscopy, FNA of suspicious neck masses
- Once malignancy confirmed, MRI preferred for assessment of primary tumor; PET/CT useful to evaluate regional nodes and r/o distant mets, but limited with small LNs (< 5mm)
- Small head and neck tumors without LN mets are effectively treated with surgery or irradiation

Question 19

- A 77-year-old woman undergoes follow-up evaluation for recently diagnosed stage I adenocarcinoma of the lung. Medical history is notable for very severe COPD that limits her ability to dress unaided. Her medications are an inhaled corticosteroid, salmeterol, tiotropium, roflumilast, and an albuterol inhaler as needed.
- On physical examination, respiration rate is 25/min; other vital signs are normal. Oxygen saturation is 91% breathing 3 L/min of oxygen by nasal cannula. BMI is 20, and she is thin with significant muscle wasting. She has a prolonged expiratory phase of respiration and decreased breath sounds bilaterally.
- Surgical and pulmonary consults concur that the patient is too chronically disabled to safely undergo elective thoracic surgery.
- Which of the following is the most appropriate treatment?

    A. Combination platinum-based chemotherapy

    B. Combined chemotherapy and radiation therapy

    C. Immunotherapy

    D. Stereotactic radiation therapy

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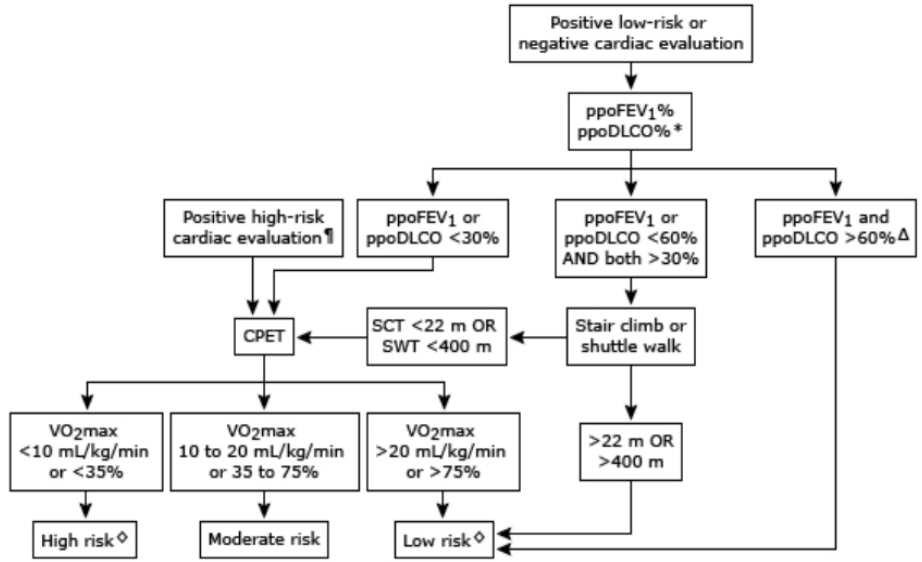
Treat stage I non–small lung cancer with stereotactic radiation therapy

- Surgery is the standard treatment for stage I and some stage II non–small cell lung cancers, and in patients treated with surgery, 5-year survival is about 60% to 70%
- For patients with non–small cell lung cancer who are not candidates for surgery, stereotactic radiation therapy can be used to treat stage I cancers

Algorithm for pulmonary preoperative assessment of patients requiring lung resection



Physiologic evaluation resection algorithm.

Actual risks affected by parameters defined here and:

- Patient factors: Comorbidities, age.
- Structural aspects: Center (volume, specialization).
- Process factors: Management of complications.
- Surgical access: Thoracotomy versus minimally invasive.

Question 20

- A 74-year-old woman is evaluated for cough and dyspnea on exertion, which has progressed over the past 6 months. Medical history is otherwise unremarkable, and she takes no medications.
- On physical examination, vital signs are normal. There are scattered crackles throughout the left chest. There is no adenopathy.
- CT scan of the chest, abdomen, and pelvis shows only patchy, nodular infiltrates in the left upper and left lower lobes of the lung.
- Transbronchial lung biopsy shows non-Hodgkin, mucosa-associated lymphoid tissue lymphoma.
- Which of the following is the most appropriate management?

    A. Combination chemoimmunotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone

    B. Left pneumonectomy

    C. Helicobacter pylori eradication treatment

    D. Rituximab

Question 20

- A 74-year-old woman is evaluated for cough and dyspnea on exertion, which has progressed over the past 6 months. Medical history is otherwise unremarkable, and she takes no medications.
- On physical examination, vital signs are normal. There are scattered crackles throughout the left chest. There is no adenopathy.
- CT scan of the chest, abdomen, and pelvis shows only patchy, nodular infiltrates in the left upper and left lower lobes of the lung.
- Transbronchial lung biopsy shows non-Hodgkin, mucosa-associated lymphoid tissue lymphoma.
- Which of the following is the most appropriate management?

A. Combination chemoimmunotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone

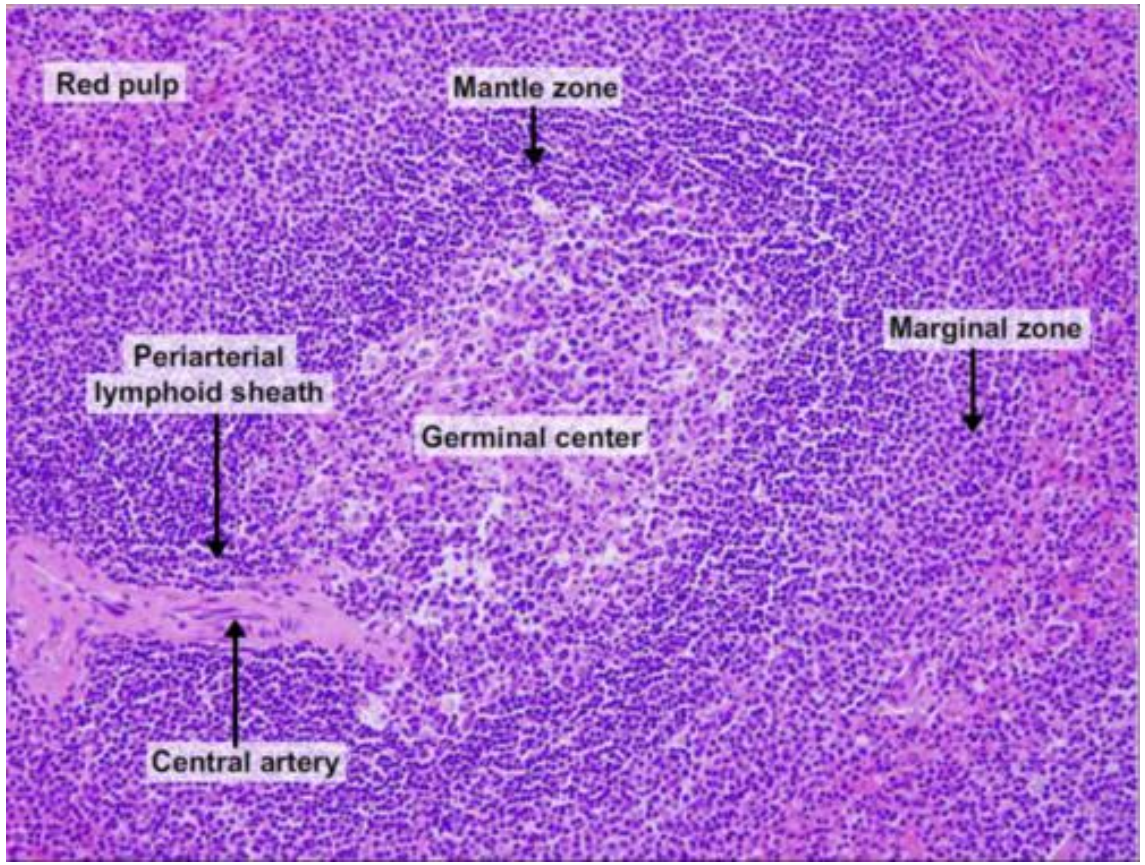
B. Left pneumonectomy

C. Helicobacter pylori eradication treatment

D. Rituximab

Treat a low-grade mucosa-associated lymphoid tissue lymphoma involving the lung

- MALT lymphomas are low-grade B lymphomas of the marginal zone type
- Account for 5% to 8% of B-cell lymphomas and arise from B cells in the “marginal zone,” the external part of secondary lymphoid follicles
- Stomach is the most common site for MALT lymphomas, and it has been linked to infection with *Helicobacter pylori*



MALT lymphomas

- Antibiotic therapy has only been definitively proven to be effective for *H. pylori*–associated gastric MALT lymphomas
- MALT lymphomas typically have a relatively indolent course, and asymptomatic patients may be observed without treatment, although radiation therapy can be considered for those with localized disease
- For other MALT lymphomas, such as in this patient who is symptomatic and has disease in multiple lobes of the lung, single-agent rituximab, an anti-CD20 monoclonal antibody, would be an appropriate treatment