Lymphoma and multiple myeloma

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

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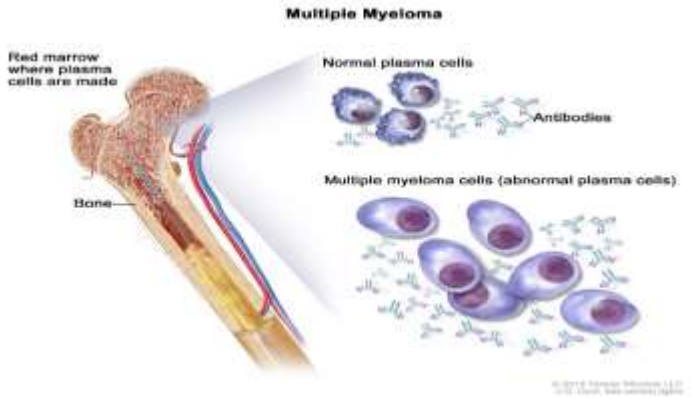
Plan of the lecture

- Lymphoma' modern understanding
- Hodgkin lymphomas (HL)
- non-Hodgkin lymphomas (NHL)
- Multiple myeloma



- Definition
- Epidemiology
- Risk Factors and etiology
- Mechanisms
- Classification
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic guidelines

https://www.cancer.gov/images/cdr/live/CDR763079.jpg

Lymphoma' modern understanding

- Lymphoma is any of a group of blood cell tumors that develop from lymphatic cells with the enlarged lymph nodes and signs and symptoms that may include enlarged lymph nodes, fever, night drenching sweats, unintended weight loss, itching, and feeling tired
- The two main categories of lymphomas are Hodgkin (HL) and the non-Hodgkin (NHL) lymphomas
- The World Health Organization (WHO) includes two other categories as types of lymphoma: multiple myeloma and immunoproliferative diseases

https://en.wikipedia.org/wiki/Lymphoma

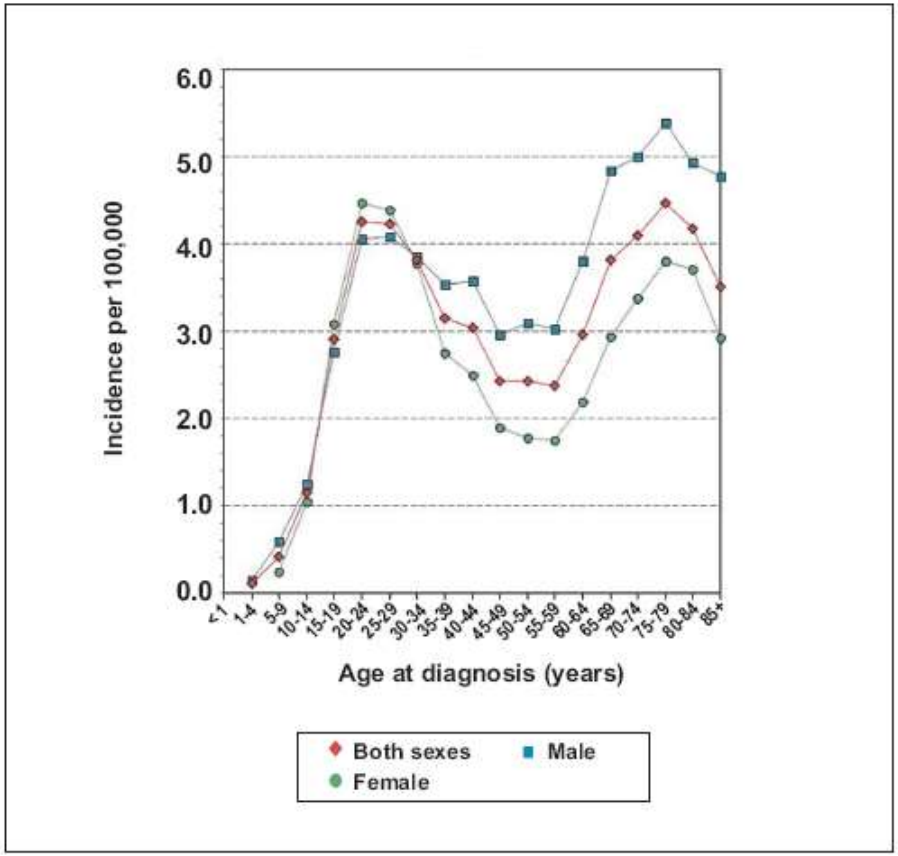
HODGKIN LYMPHOMA

Definition

- Hodgkin (Hodgkin's) lymphoma or Hodgkin's disease, is a type of the most curable forms of lymphoma, in which cancer originates from the lymphocytes
- Hodgkin Lymphoma is named for Dr. Thomas Hodgkin, who first noted a trend of cancer cases in the lymph nodes in 1832
- The disease was called Hodgkin's disease until it was officially renamed Hodgkin lymphoma in the late 20th century

https://www.lls.org/lymphoma https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Epidemiology



Incidence of Hodgkin Lymphoma in the United States, by age

http://www.cancernetwork.com/articles/hodgkin-lymphoma-older-patients-uncommon-disease-need-study

Risk factors and etiology 1

- Epstein-Barr virus infection/mononucleosis (sometimes called *mono* for short)
- Age (HL is most common in early adulthood (ages 15 to 40, especially in a person's 20s) and in late adulthood (after age 55))
- Gender (HD occurs slightly more often in males than in females)
- Geography (HD is most common in the United States, Canada, and northern Europe, and is least common in Asian countries)

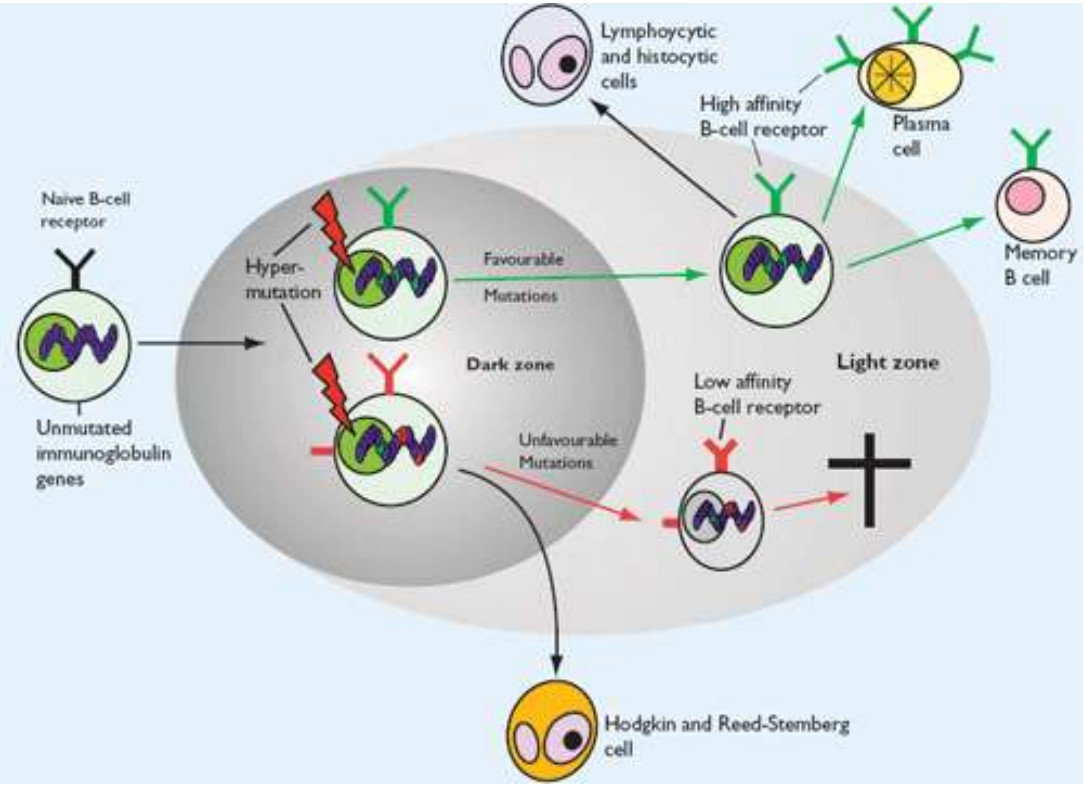
http://www.cancer.org/cancer/hodgkindisease/detailedguide/hodgkin-disease-risk-factors

Risk factors and etiology 2

- Family history (brothers and sisters of young people with HD have a higher risk for Hodgkin disease)
- Socioeconomic status (the risk is greater in people with a higher socioeconomic background)
- HIV infection (the risk is increased in people infected with HIV)
- In most cases, the etiology of HL is unknown

http://www.cancer.org/cancer/hodgkindisease/detailedguide/hodgkin-disease-risk-factors

Mechanisms 1



The derivation of Hodgkin and Reed-Sternberg cells in classic HL and lymphomatic and histiocytic cells in noduler lymphocyte-predominant HL

http://www.medscape.com/viewarticle/559870_4

Classification

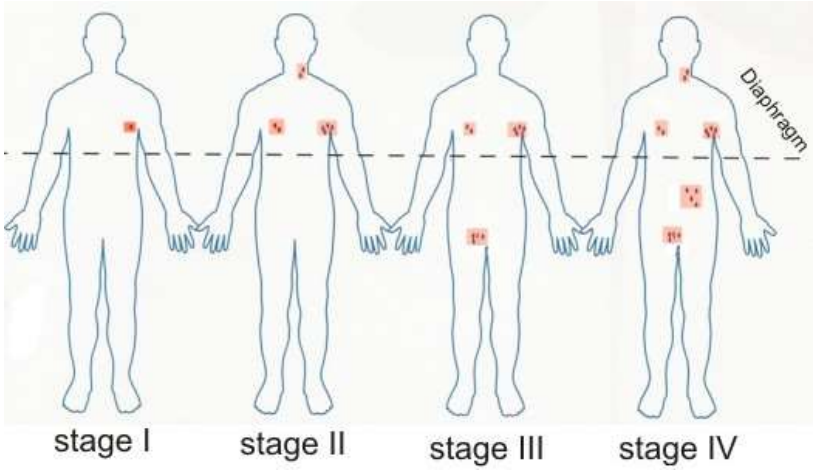
Four pathologic subtypes of HL based upon Reed–Sternberg cell morphology and the composition of the reactive cell infiltrate seen in the lymph node biopsy

- Nodular sclerosing
- Mixed-cellularity subtype
- Lymphocyte-rich
- Lymphocyte depleted
- Unspecified

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma#Classification

Classification

the Ann Arbor staging classification scheme 1

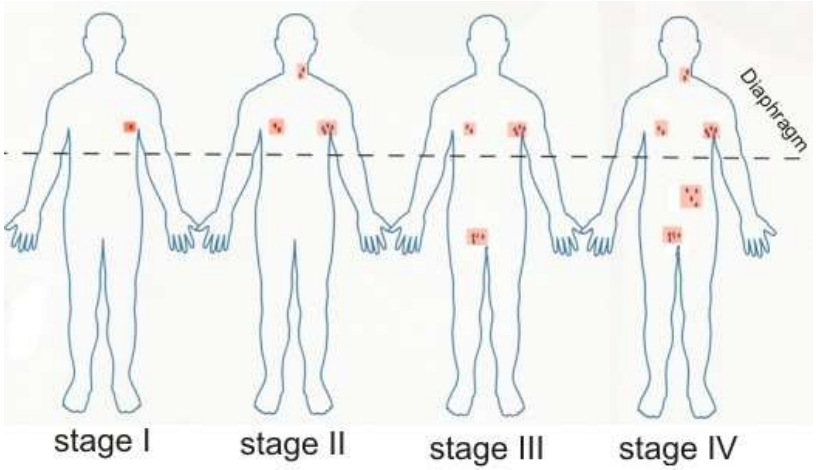


I - is involvement of a single lymph node region (I) (mostly the cervical region) or single extralymphatic site

http://www.lymphomation.org/stage.htm https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma#Classification

Classification

the Ann Arbor staging classification scheme 2

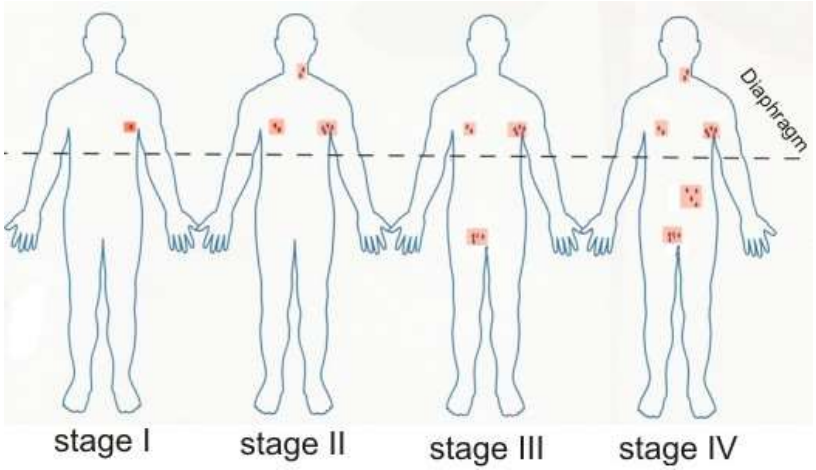


II - is involvement of two or more lymph node regions on the same side of the diaphragm or of one lymph node region and a contiguous extralymphatic site

http://www.lymphomation.org/stage.htm https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma#Classification

Classification

the Ann Arbor staging classification scheme 3

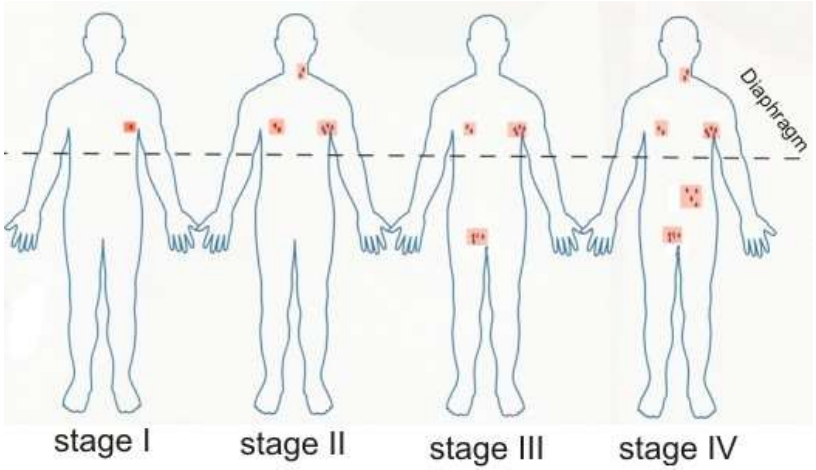


III - is involvement of lymph node regions on both sides of the diaphragm, which may include the spleen and/or limited contiguous extralymphatic organ or site

http://www.lymphomation.org/stage.htm https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma#Classification

Classification

the Ann Arbor staging classification scheme 4



IV - is disseminated involvement of one or more extralymphatic organs

http://www.lymphomation.org/stage.htm https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma#Classification

Clinical presentation 1

- The painless enlargement of one or more lymph nodes, or lymphadenopathy
- Itchy skin
- Night sweats
- Red-coloured patches, easy bleeding and petechiae (low platelet count)
- Cyclical high-grade (Pel-Ebstein or simply P-E) fever
- Unexplained weight loss

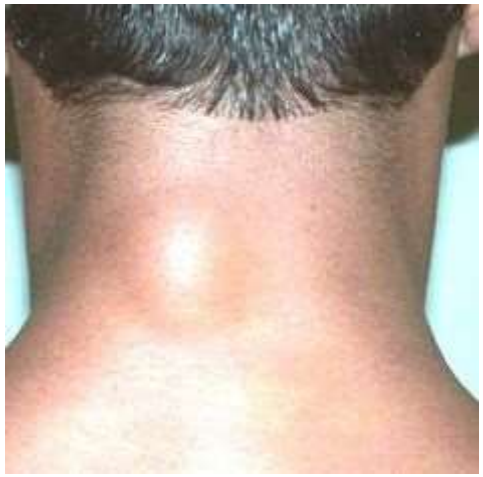
https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Clinical presentation 2

- Splenomegaly in about 30% of cases
- Hepatomegaly in about 5% of cases
- Pain following alcohol consumption
- Lower back pain
- Nephrotic syndrome

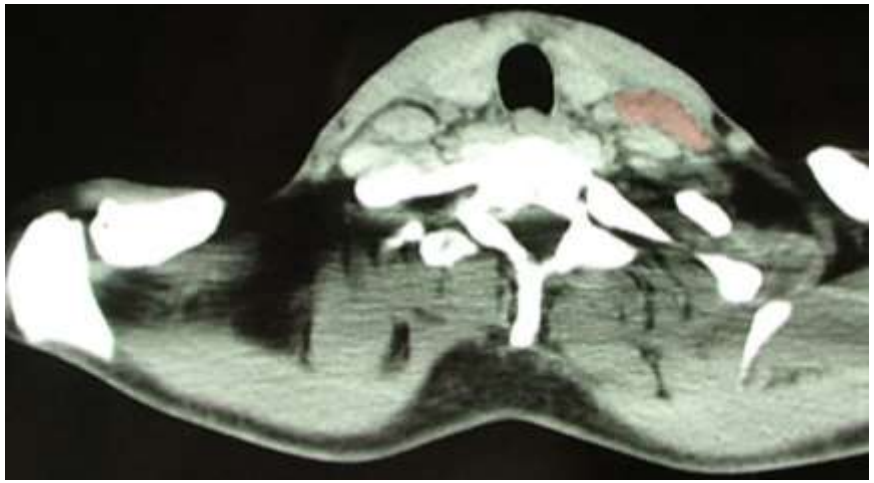
https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Clinical presentation 3



Lump in Neck

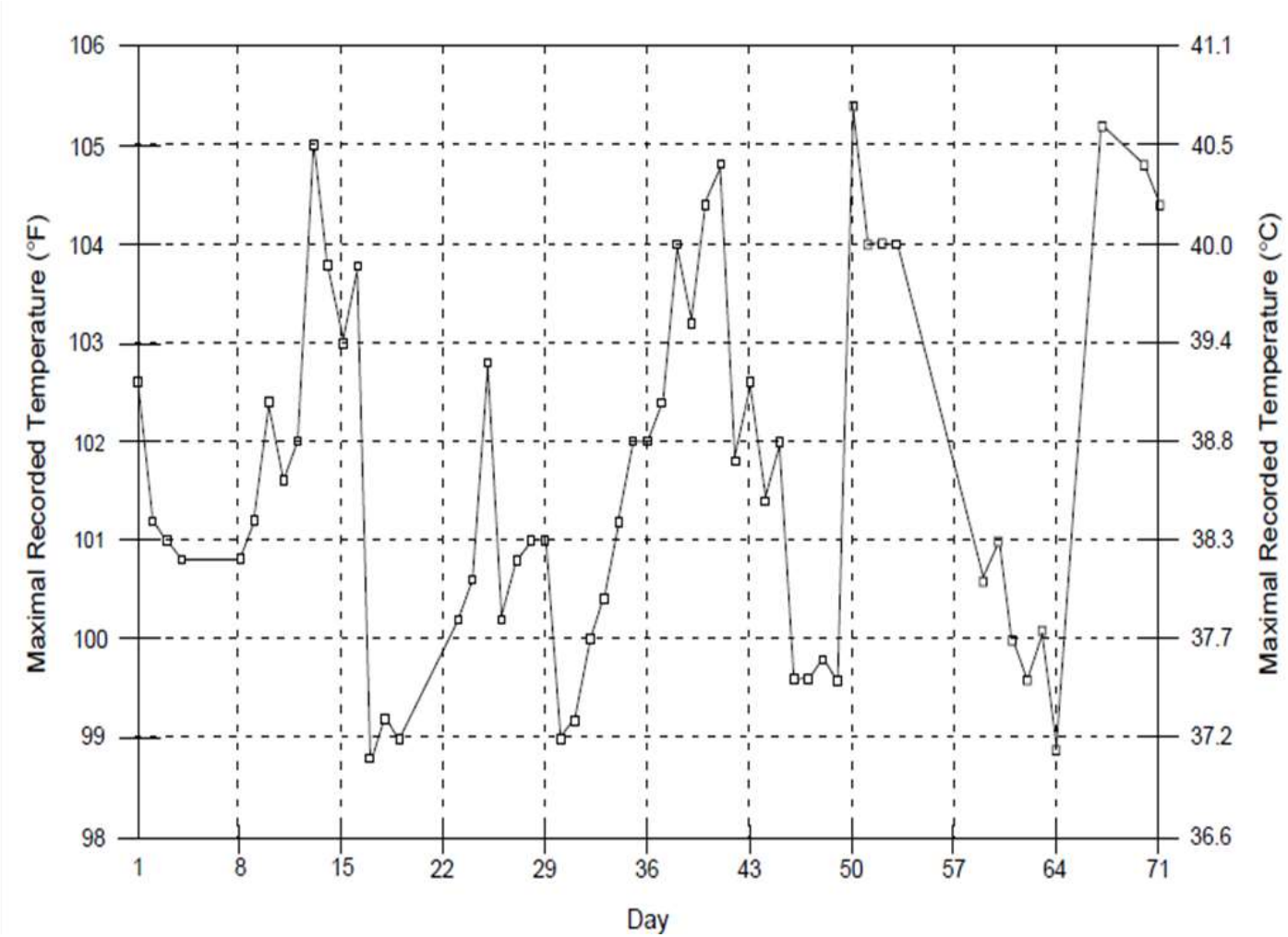
Itchy skin



On the left side of the patient's neck enlarged lymph node

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Clinical presentation 4



Pel-Ebstein Fever

http://3.bp.blogspot.com/-QPLZFoWiVvs/Ufp1Y44yiqI/AAAAAAAAAxM/5RvtHq3FGlY/s1600/Pel-Ebstein.png

Diagnosis 1

- HL must be distinguished from non-cancerous causes of lymph node swelling and from other types of cancer
- Definitive diagnosis is by lymph node biopsy with microscopic examination:
  - effacement of the lymph node architecture by scattered large malignant Reed-Sternberg cells (RSC) admixed within a reactive cell infiltrate of lymphocytes, histiocytes, eosinophils, and plasma cells

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Diagnosis 2

- RSC are identified as large often bi-nucleated cells with prominent nucleoli and an unusual CD45-, CD30+, CD15+/- immunophenotype
- in 50% of cases, the RSC are infected by the Epstein–Barr virus
- the cell histology in HL is not as important as it is in non-Hodgkin's lymphoma

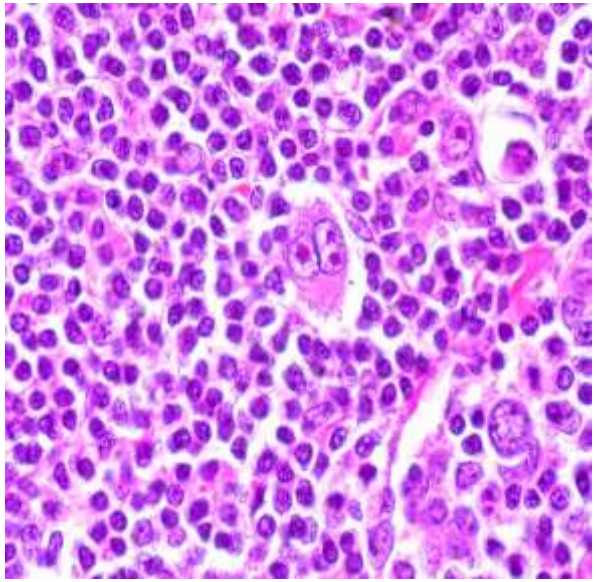
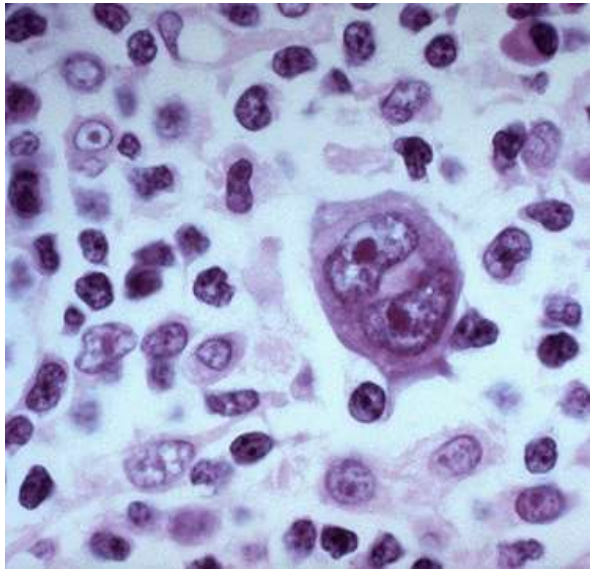
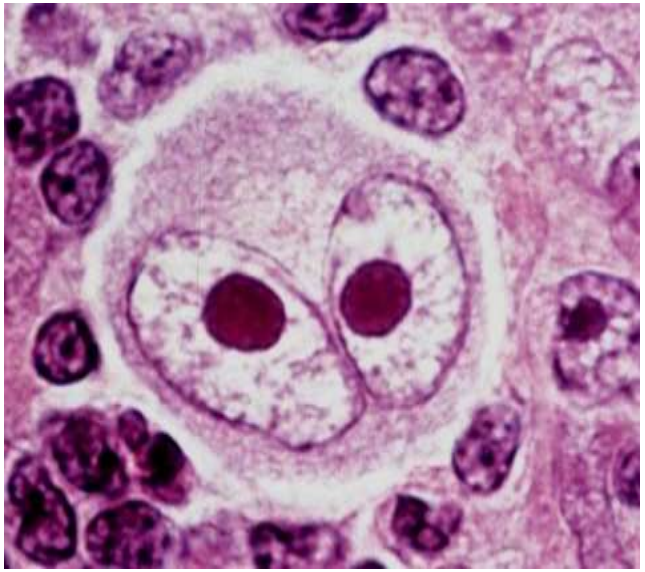
https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Diagnosis 3

- Blood tests are performed to assess function of major organs and to assess safety for chemotherapy
- Positron emission tomography is used to detect small deposits that are not shown on CT scanning

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

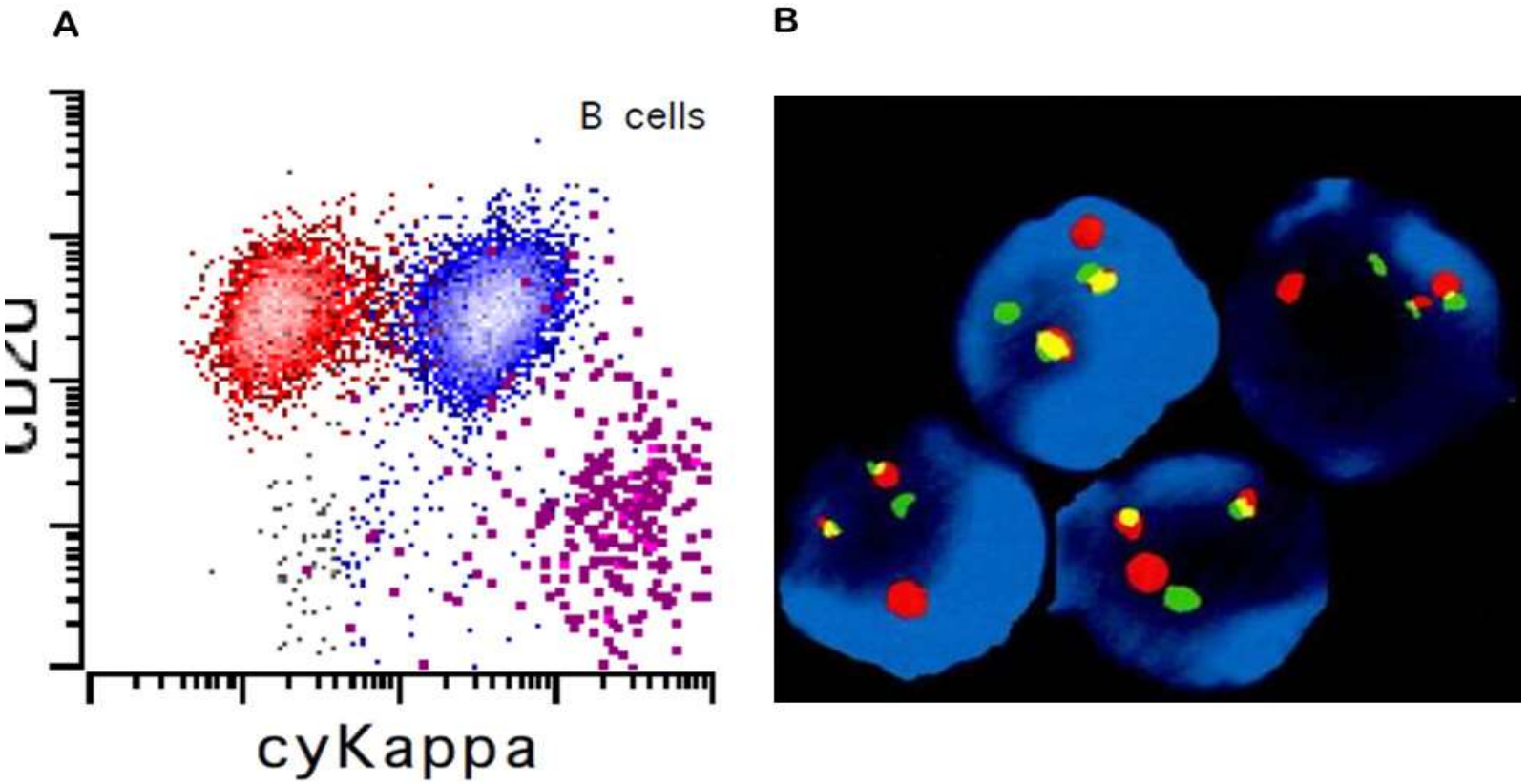
Diagnosis 4

Reed-Sternberg cells

http://library.med.utah.edu/WebPath/jpeg5/HEME045.jpg https://s-media-cache-ak0.pinimg.com/736x/ac/06/20/ac0620621ea55abba1545f8bdf0711ee.jpg

Diagnosis 5



A) Flow cytometric immunophenotyping

B) Fluorescence in situ hybridization (FISH)

https://www.mskcc.org/clinical-updates/diagnostic-accuracy-enhanced-genomic-profile-immunophenotyping

Treatment 1

- Treatment is tailored to HL type, disease stage, and an assessment of the risk of resistant disease
- Patients with early stage disease are effectively treated with radiation therapy or chemotherapy: adding localised radiation therapy after the chemotherapy regimen controls the tumors better and provides a better chance for survival than chemotherapy alone

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Treatment 2

- Patients of any stage with a large mass in the chest are usually treated with combined chemotherapy and radiation therapy, and stem cell transplantation
- Radiation oncologists typically use external beam radiation therapy
- The high cure rates and long survival of many patients has led to a high concern with late adverse effects of treatment, including cardiovascular disease and second malignancies such as acute leukemias, lymphomas, and solid tumors within the radiation therapy field

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Prognosis

- Treatment of HL has been improving over the past few decades
- New types of chemotherapy have indicated higher survival rates than have previously been seen, and the 5-year survival rate for those patients with a favorable prognosis was 98%, while that for patients with worse outlooks was at least 85%

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

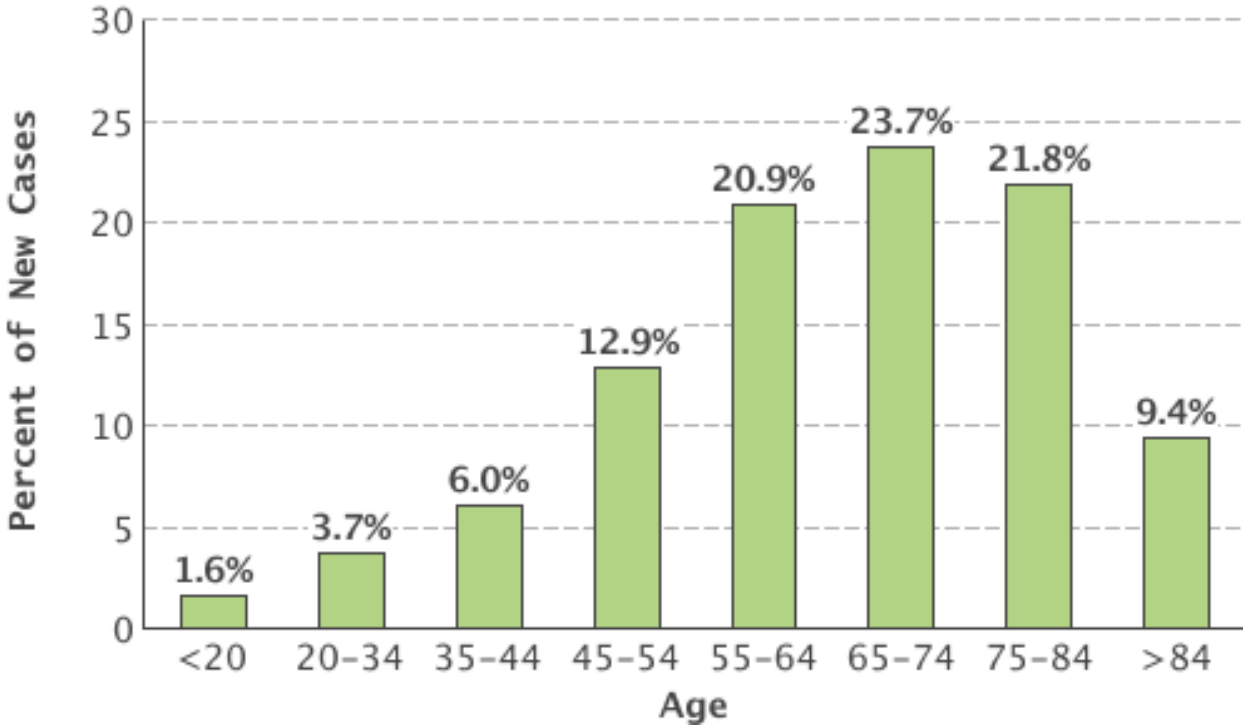
NON-HODGKIN LYMPHOMA

Definition

- Non-Hodgkin lymphomas (Non-Hodgkin's lymphoma, Non-Hodgkin lymphomas, non-Hodgkin disease - NHL) are diverse group of blood cancers that include any kind of lymphomas except HL, and vary significantly in their severity, from slow growing to very aggressive types
- NHL affects the lymphatic system, generally develops in the lymph nodes and lymphatic tissues, and in some cases, involves bone marrow and blood

https://en.wikipedia.org/wiki/Non-Hodgkin_lymphoma https://www.lls.org/lymphoma

Epidemiology



Percent of New Cases by Age Group: Non-Hodgkin Lymphoma

http://seer.cancer.gov/statfacts/html/nhl.html#

Risk factors and etiology 1

There are many types of NHL, and some of the risk factors and etiology factors have been linked only to certain types:

- Getting older is a strong risk factor for NHL overall, with most cases occurring after 60s
- The risk is higher in men than in women, but there are certain types that are more common in women

http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-risk-factors

Risk factors and etiology 2

There are many types of NHL, and some of the risk factors and etiology factors have been linked only to certain types:

- In the USA, whites are more likely than African Americans and Asian Americans to develop NHL
- NHL is more common in developed countries
- Some types of NHL that have been linked to specific infections are more common in certain parts of the world

http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-risk-factors

Risk factors and etiology 3

- Some chemicals (benzene and certain herbicides and insecticides) and some chemotherapy drugs may be linked with an increased risk of NHL
- Studies of survivors of atomic bombs and nuclear reactor accidents have shown they have an increased risk of developing several types of cancer, including NHL
- Patients treated with radiation therapy for some other cancers, have a slightly increased risk of developing NHL later in life

http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-risk-factors

Risk factors and etiology 4

- People with weakened immune system including people infected with HIV have an increased risk for NHL
- Some genetic (inherited) syndromes can cause children to be born with a deficient immune system and a higher risk of developing NHL

http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-risk-factors

Risk factors and etiology 5

- Some autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, Sjogren disease, gluten-sensitive enteropathy, and others) have been linked with an increased rate of NHL
- Some types of infections may raise the risk of NHL in different ways
- Some viruses (the human T-cell leukemia/lymphoma virus (HTLV-1) and the Epstein-Barr virus (EBV) and human herpes virus 8 (HHV8)) can directly affect the DNA of lymphocytes, helping to transform them into cancer cells

http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-risk-factors

Risk factors and etiology 6

- Some long-term infections (*Helicobacter pylori*, *Chlamydophila psittaci, Campylobacter jejuni*) may increase a person's risk of NHL by forcing their immune system to be constantly activated
- The hepatitis C virus (HCV) also can lead to the development of cancer, particularly hepatocellular carcinoma and non-Hodgkin lymphoma

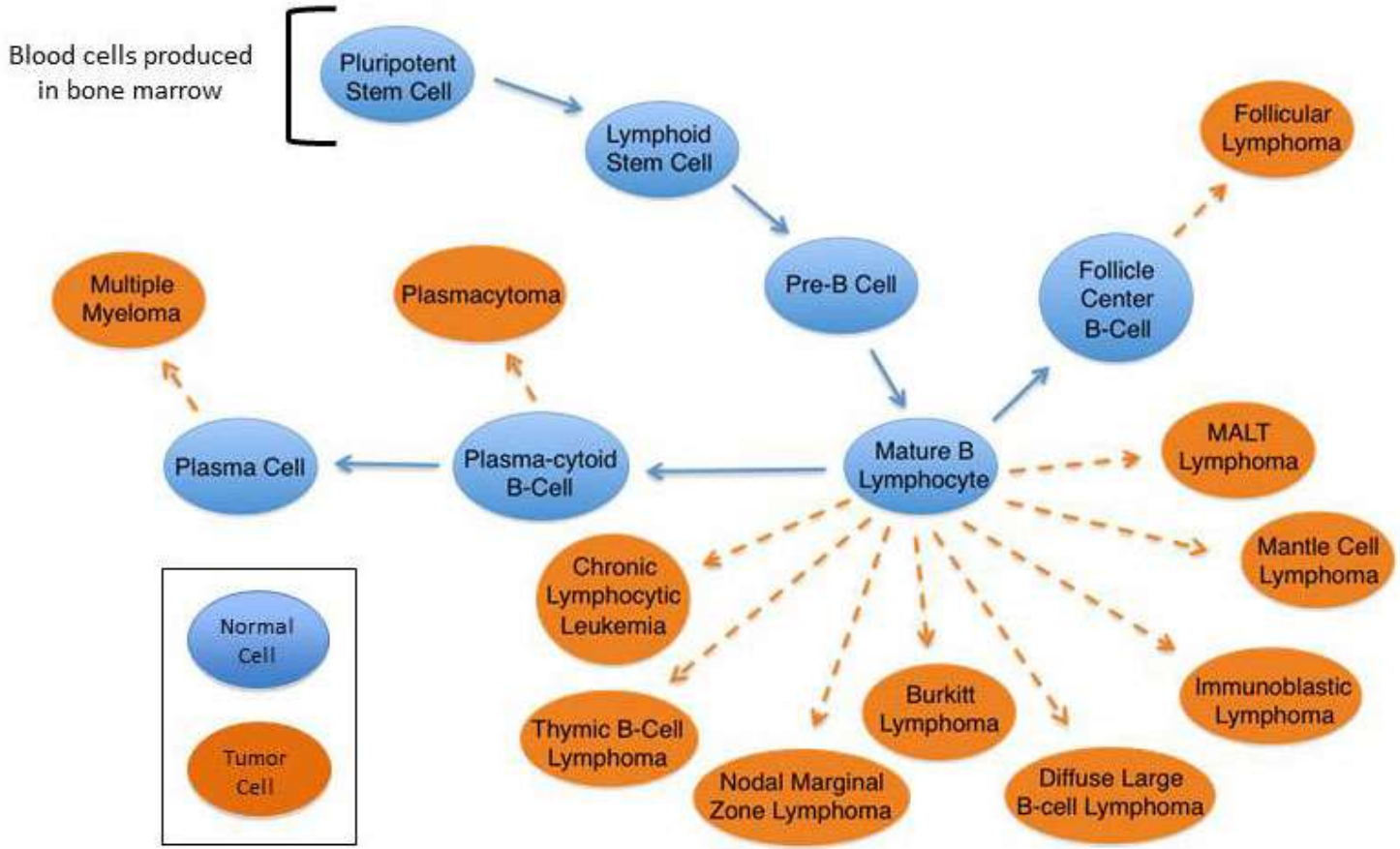
http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-risk-factors

Risk factors and etiology 7

- Some studies have suggested that being overweight or obese may increase patient's risk of NHL
- Other studies have suggested that a diet high in fat and meats may raise NHL risk
- Some women develop anaplastic large cell lymphoma in the scar tissue around their breast implants

http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-risk-factors

Mechanisms



NHL does not involve Reed-Sternberg cells

http://www.shaltech.com/about-lymphoma/

Classification 1

WHO

B-cell neoplasms: chronic lymphocytic leukemia/small lymphocytic lymphoma, prolymphocytic leukemia, lymphoplasmacytic lymphoma/immunocytoma, Mantle cell lymphoma, follicular lymphoma, extranodal marginal zone B-cell lymphoma of mucosa-associated lymphatic tissue (MALT) type, nodal marginal zone B-cell lymphoma (± monocytoid B cells), splenic marginal zone lymphoma (± villous lymphocytes), hairy cell leukemia, plasmacytoma/ plasma cell myeloma, diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma

http://www.cancer.med.umich.edu/news/moj00fa4.shtml

Classification 2

WHO

Peripheral T-cell and NK-cell neoplasms: T-cell chronic lymphocytic leukemia/prolymphocytic leukemia, T-cell granular lymphocytic leukemia, mycosis fungoides/ Sézary syndrome, peripheral T-cell lymphoma not otherwise characterized, hepatosplenic gamma/delta T-cell lymphoma, subcutaneous panniculitis-like T-cell lymphoma, angioimmunoblastic T-cell lymphoma, extranodal T-/NK-cell lymphoma, nasal type, enteropathy-type intestinal T-cell lymphoma, adult T-cell lymphoma/leukemia (human T-lymphotrophic virus [HTLV] 1+), etc.

http://www.cancer.med.umich.edu/news/moj00fa4.shtml

Clinical presentation 1

- The clinical presentation varies tremendously depending upon the their type and the areas of involvement
- Some NHLs behave indolently with lymphadenopathy waxing and waning over years, and others are highly aggressive, resulting in death within weeks if left untreated
- Indolent NHL are often insidious, presenting only with slow growing lymphadenopathy, hepatomegaly, splenomegaly, or cytopenias

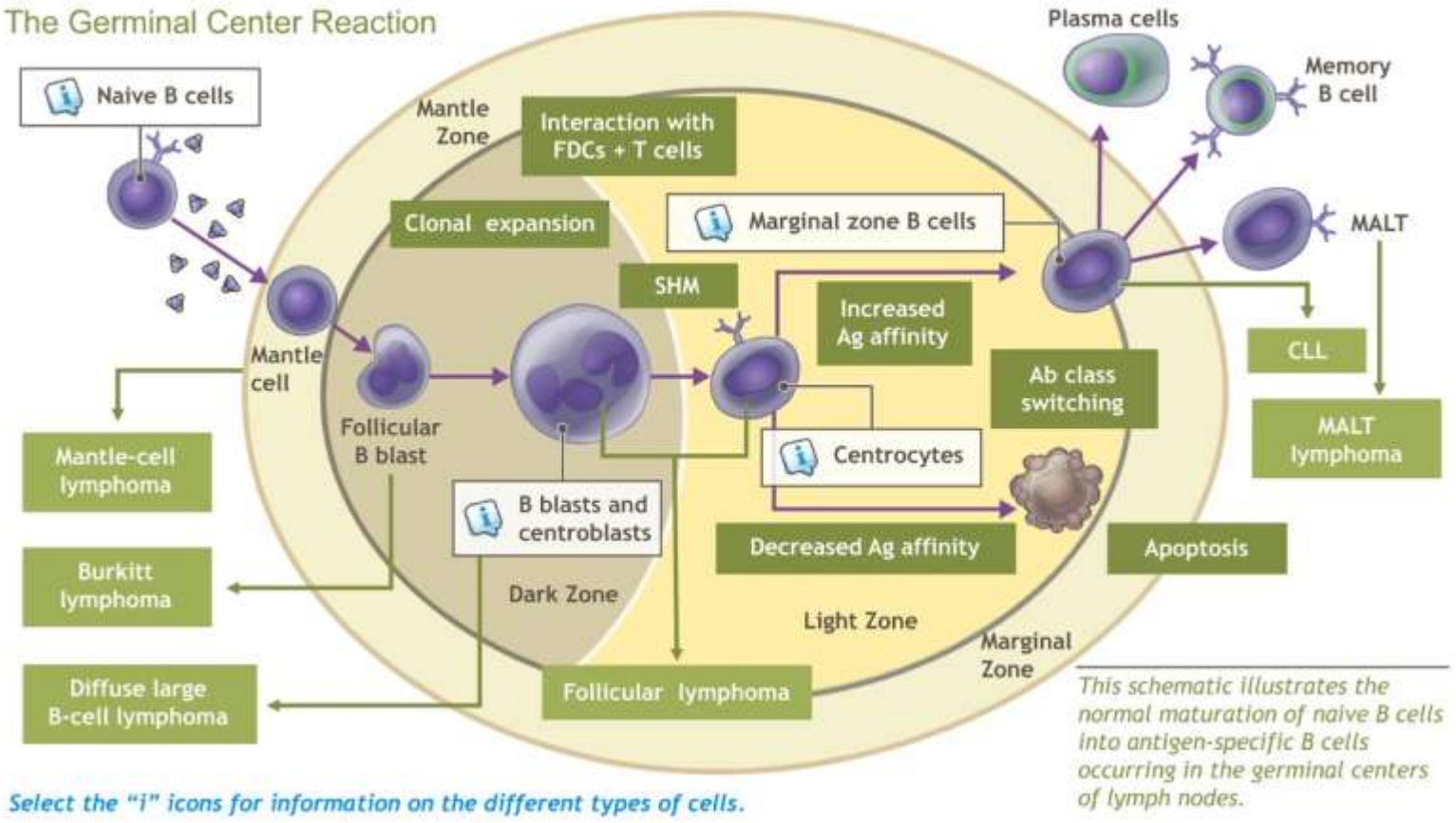
http://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-non-hodgkin-lymphoma

Clinical presentation 2

- Aggressive NHL commonly present acutely or subacutely with a rapidly growing mass, systemic B symptoms (i.e., fever, night sweats, weight loss), and/or elevated levels of serum lactate dehydrogenase and uric acid

http://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-non-hodgkin-lymphoma

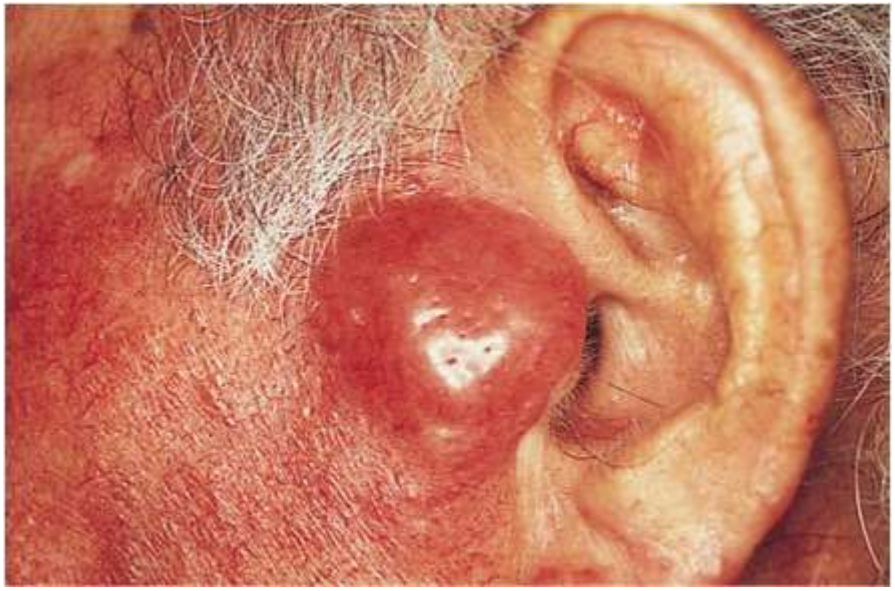
Clinical presentation 3



Indolent NHL

http://www.adamondemand.com/wp-content/themes/ADAMOnDemand2014/images/courses/screenshots/08035509/08035509_06.jpg

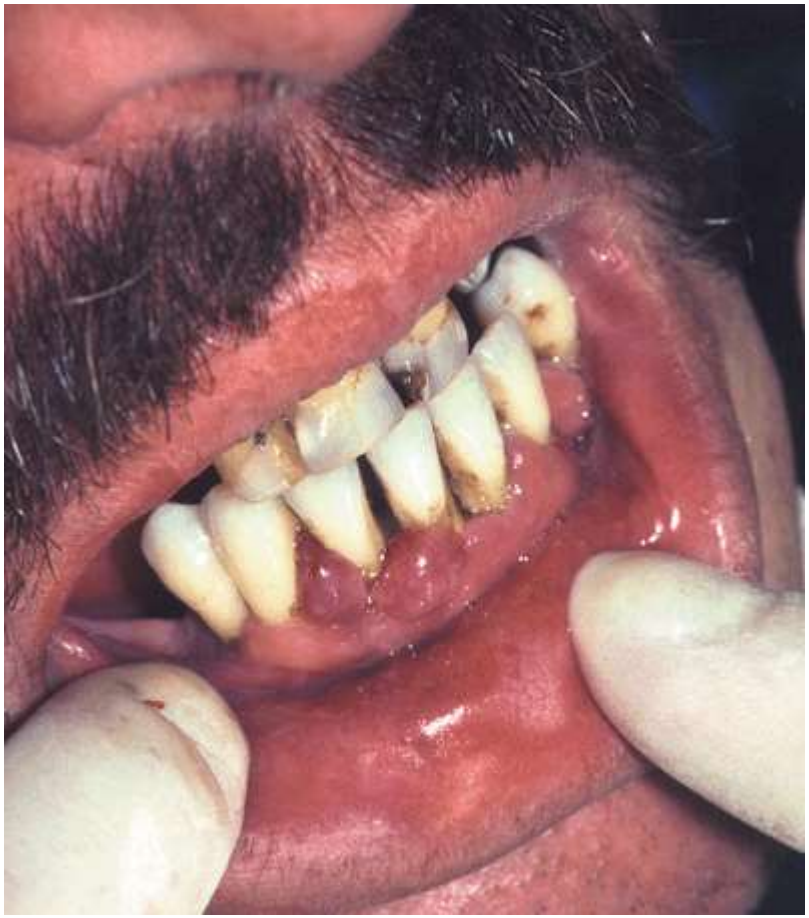
Clinical presentation 4



Peripheral adenopathy in indolent NHL

https://quizlet.com/21608719/oncology-lymphomas-flash-cards/

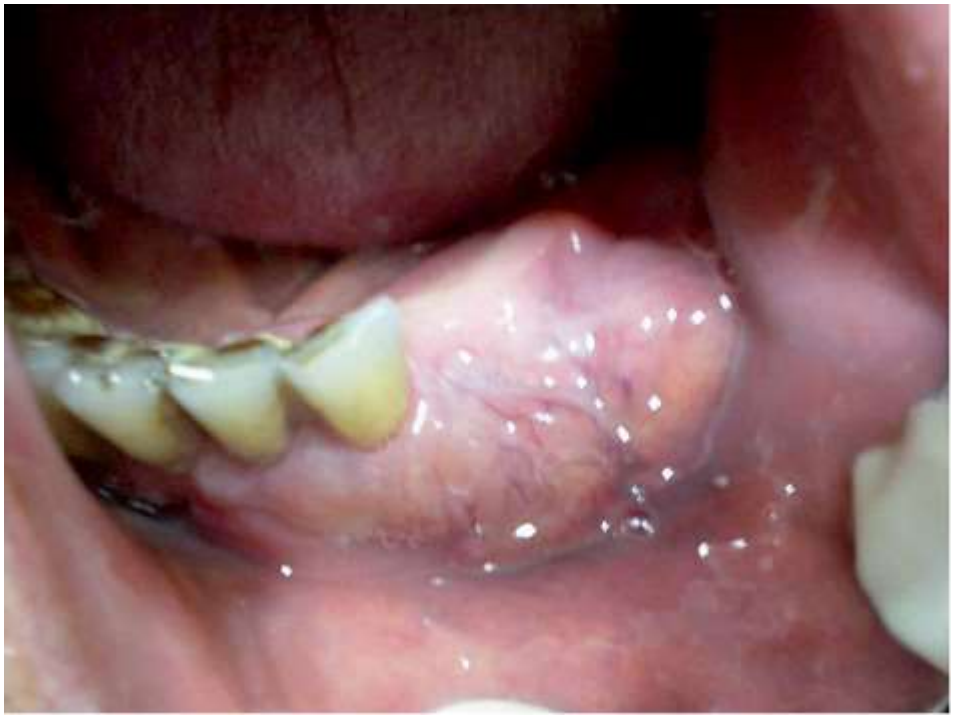
Clinical presentation 5



Aggressive NHL

https://www.withfriendship.com/images/c/14437/Non-Hodgkin-lymphoma-picture.jpg

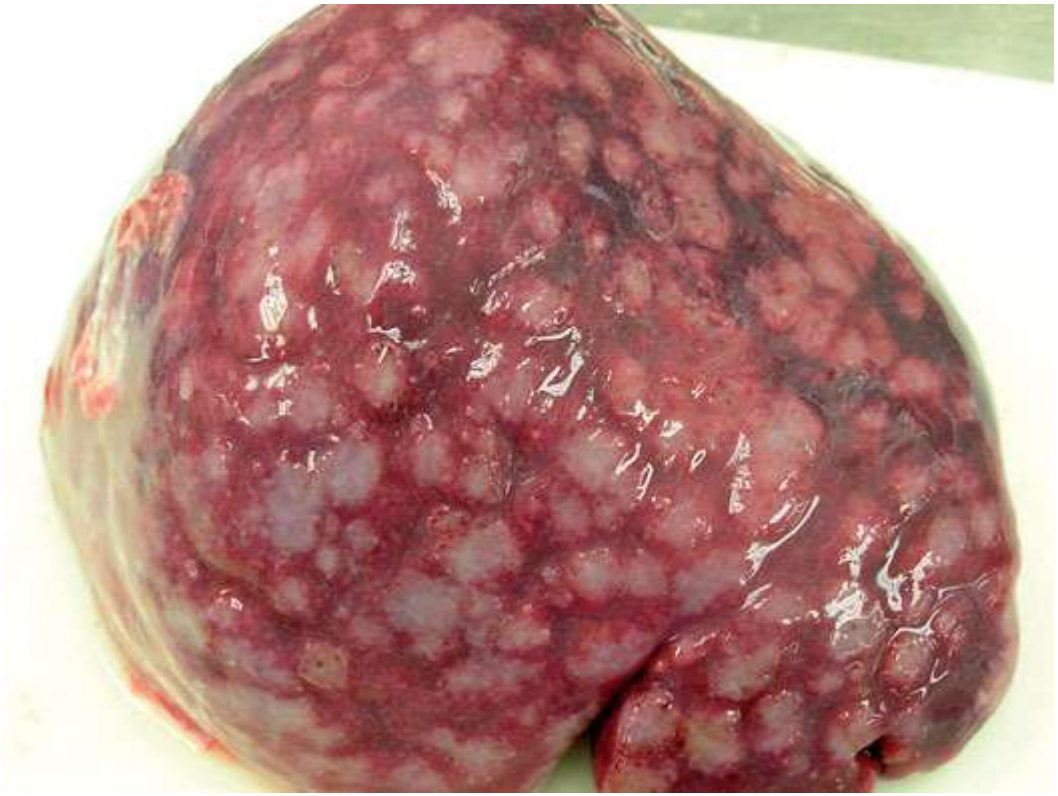
Clinical presentation 6



Gingival appearance of patient with NHL

http://exp-oncology.com.ua/article/3228/primary-extranodal-non-hodgkin-s-lymphoma-presenting-as-painful-gingival-swelling

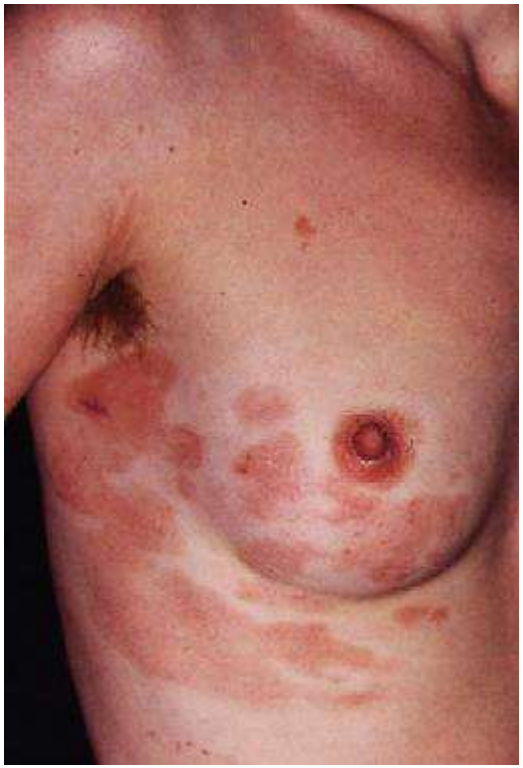
Clinical presentation 7



Spleen, NHL: uniform multicentric involvement of the white pulp by a malignant lymphoma

http://2.bp.blogspot.com/-r0dcUiAFTB4/UXVoP3AC_KI/AAAAAAAAJuE/9aI3qgWHV6g/s640/Spleen,+non-Hodgkin+lymphoma.png

Clinical presentation 8



Cutaneous T-Cell NHL

http://img.medscapestatic.com/pi/meds/ckb/55/36955tn.jpg

Diagnosis 1

- NHL is diagnosed by a tissue biopsy of an enlarged, painless lymph node, without of an infection
- Patient will need some or all of the following tests depending on symptoms and the type of the NHL:
- Lymph node biopsy
- Imaging tests (X-rays, computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI)
- Blood tests

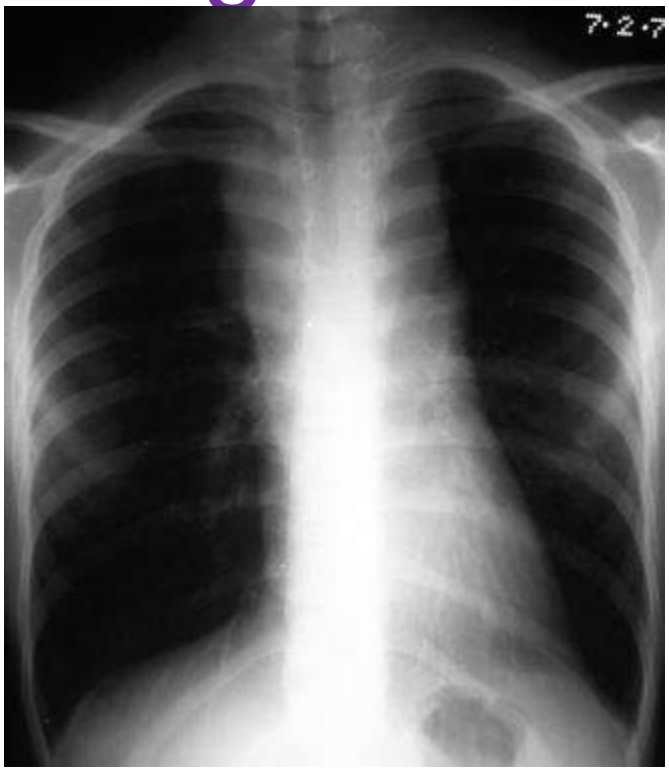
http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/non-hodgkins-lymphoma/diagnosis/index.html

Diagnosis 2

- Bone marrow aspiration and biopsy
- Liver and kidney function tests
- Spinal tap (lumbar puncture)
- Immunophenotyping of cells from a lymph node, blood or bone marrow to determine what type of non-Hodgkin's lymphoma cells are present.
- Echocardiogram
- Pulmonary function test

http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/non-hodgkins-lymphoma/diagnosis/index.html

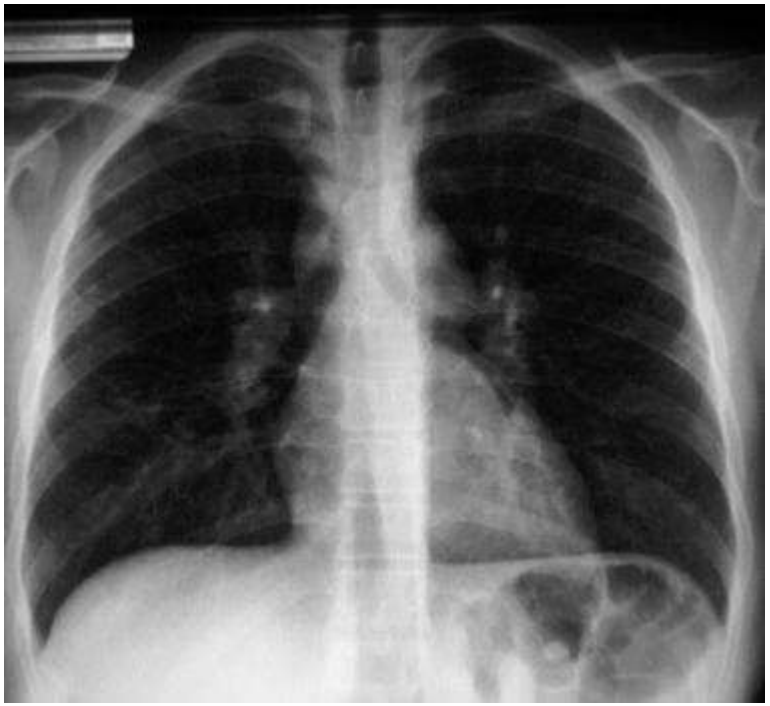
Diagnosis 3



Posteroanterior (PA) chest radiograph in a man with thoracic NHL shows mediastinal widening due to grossly enlarged right paratracheal and left paratracheal nodes

http://emedicine.medscape.com/article/203399-workup#c9

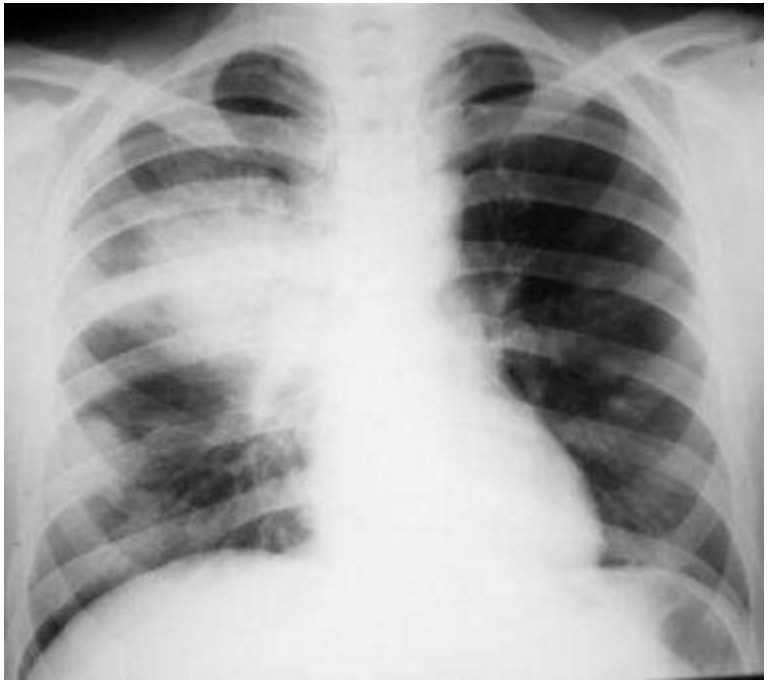
Diagnosis 4



Posteroanterior (PA) chest radiograph in a 16-year-old male adolescent with thoracic NHL shows subtle enlargement of the lower paratracheal lymph nodes

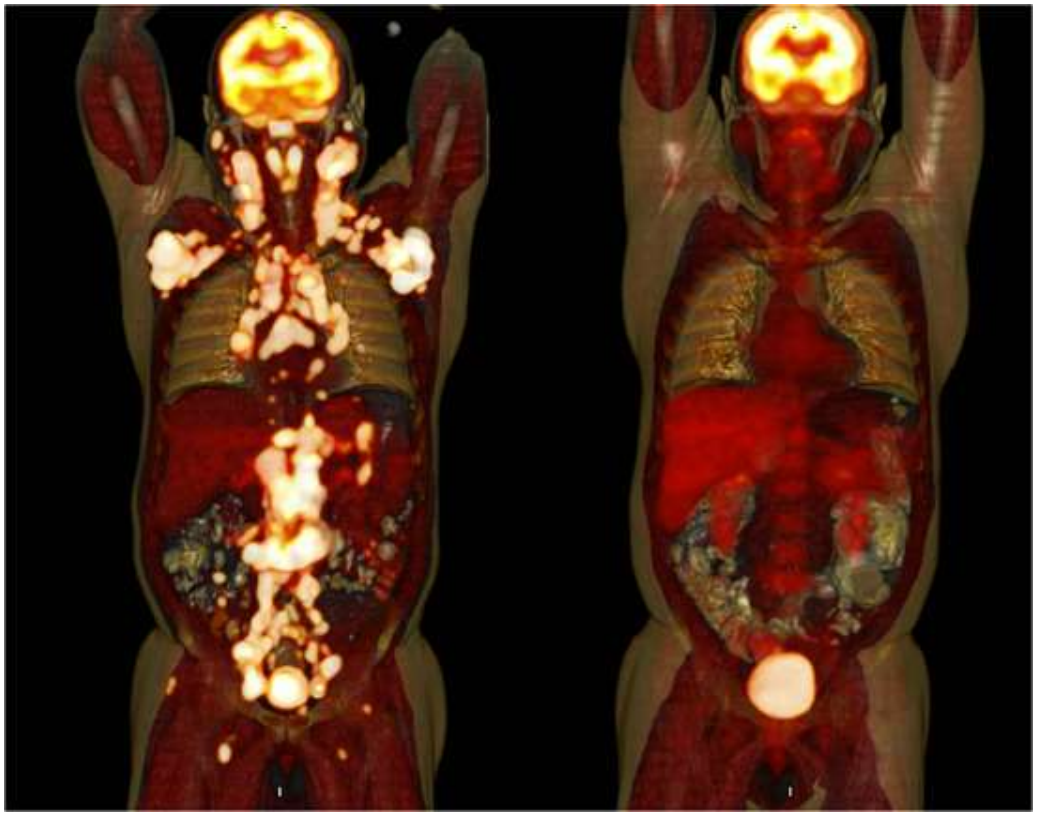
http://emedicine.medscape.com/article/203399-workup#c9

Diagnosis 5



A large mass in the right parahilar region extending into the right upper and middle zones; smaller mass is seen in the periphery of the right lower zone; core-needle biopsy of the larger lesion revealed NHL deposits in the lung http://emedicine.medscape.com/article/203399-workup#c9

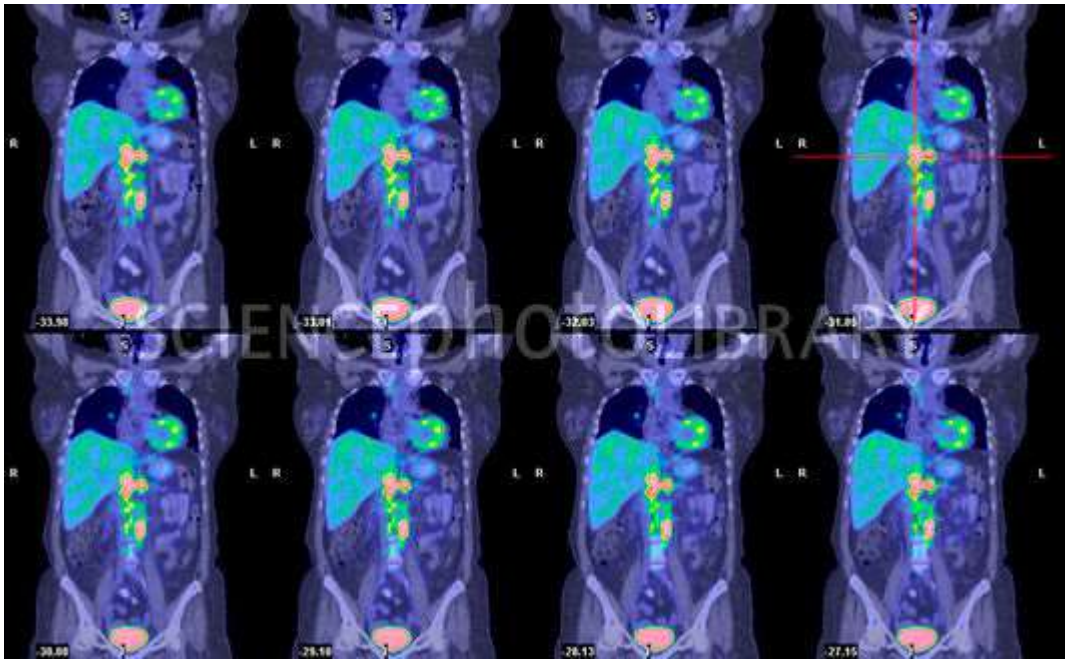
Diagnosis 6



PET/CT images of a patient with NHL before (left) and after (right) chemotherapy, showing complete response

http://www.nature.com/onc/journal/v30/n40/fig_tab/onc2011169f2.html

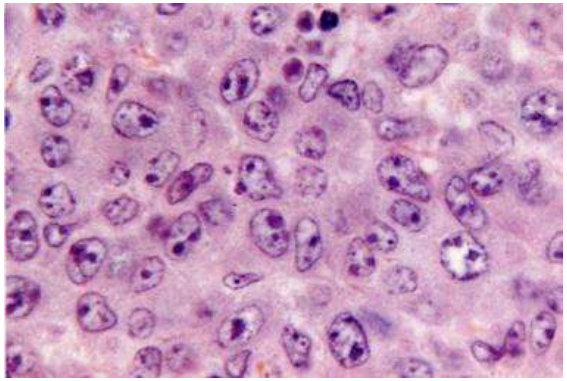
Diagnosis 7



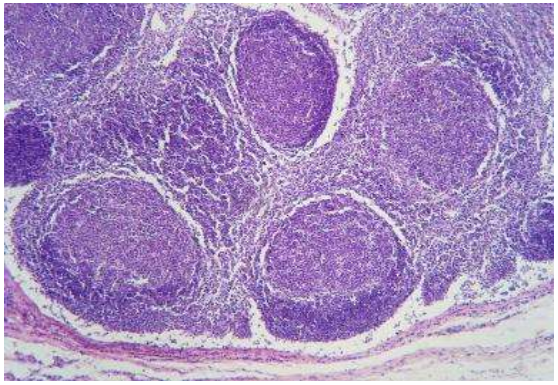
Coloured composite computed tomography (CT) and positron emission tomography (PET) scans of sections through a patient with growths in the abdomen and chest due to NHL

http://www.nature.com/onc/journal/v30/n40/fig_tab/onc2011169f2.html

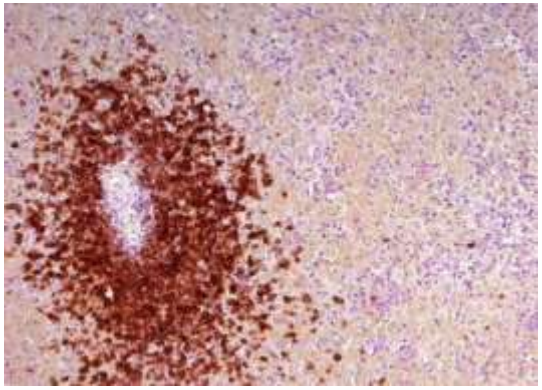
Diagnosis 8



Diffuse large B-cell NHL



Aggressive NHL



Aggressive NHL

http://img.medscapestatic.com/pi/meds/ckb/55/13655tn.jpg http://f.tqn.com/y/lymphoma/1/W/A/3/-/-/GettyImages-121823109.jpg
http://www.humpath.com/IMG/jpg_spleen_gamma-delta_lymphoma_06_cd20.jpg

Treatment 1

- The main types of treatment are chemotherapy (intravenously e.g. CVP (cyclophosphamide, vincristine, prednisolone) with monoclonal antibody drug rituximab, CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone), FAD (fludarabine, doxorubicin, dexamethasone), or FMD (fludarabine, mitoxantrone and dexamethasone), radiotherapy (often used as a local treatment), and biological (e.g. rituximab, ibritumomab, tositumomab, epratuzumab, alemtuzumab) therapy

http://www.cancerresearchuk.org/about-cancer/type/non-hodgkins-lymphoma/treatment/types/

Treatment 2

- Some people may have surgery to remove a tumour or the spleen
- Sometimes high dose chemotherapy with a stem cell transplant may be used to try to increase the chance of curing NHL
- Some people need only one type of treatment and others need more than one

http://www.cancerresearchuk.org/about-cancer/type/non-hodgkins-lymphoma/treatment/types/

Prognosis

- Survival rates for NHL vary widely, depending on the lymphoma type, stage, age of the patient, and other variables
- The overall 5-year relative survival rate for patients with non-Hodgkin's lymphoma is 63% and the 10-year relative survival rate is 51%
- Survival rates for patients with NHL have greatly improved since the early 1990s, especially for patients under age 45
- Advances in treatment have contributed to this improvement

http://www.nytimes.com/health/guides/disease/non-hodgkins-lymphoma/prognosis.html

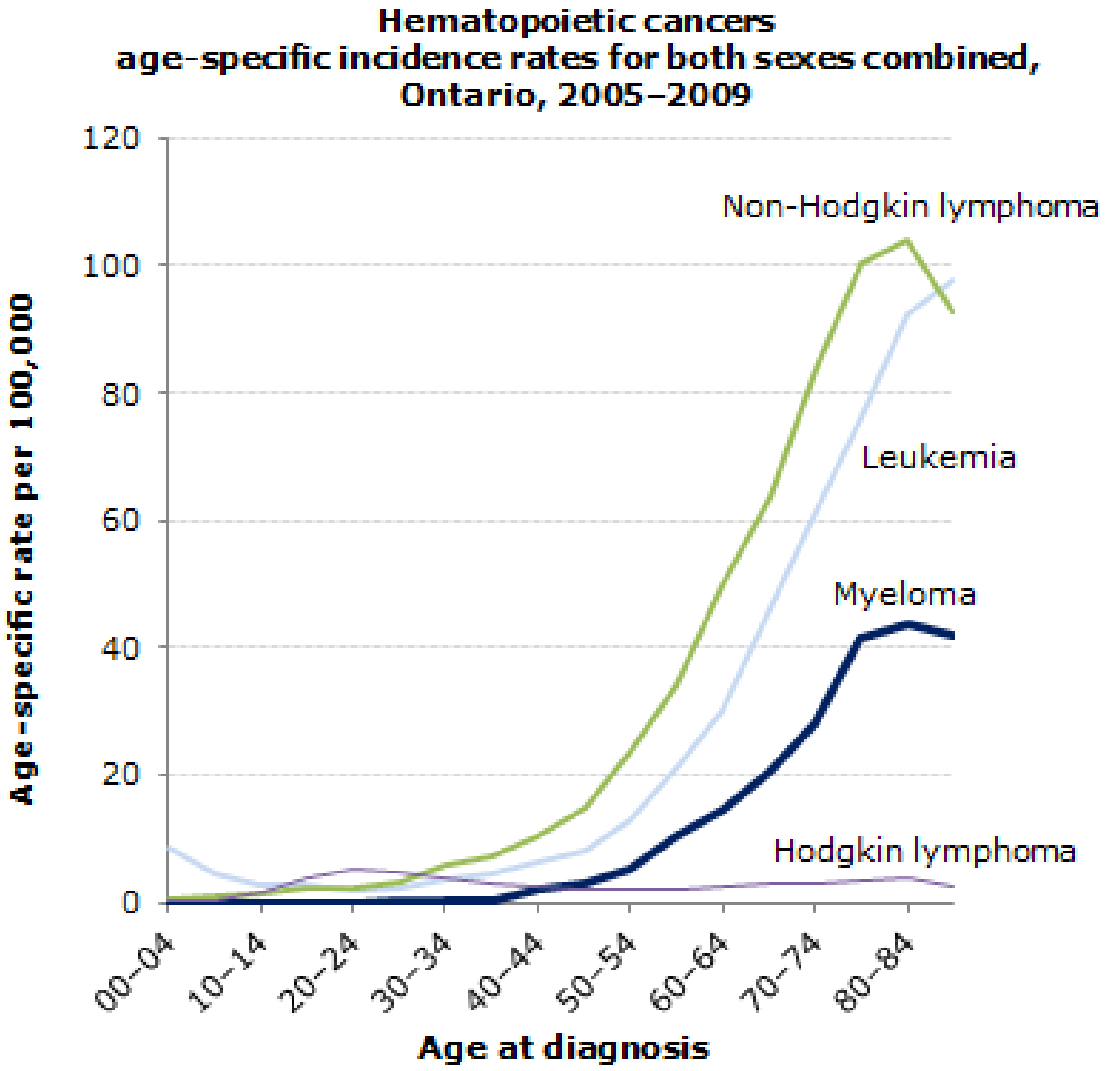
MULTIPLE MYELOMA

Definition

- Multiple myeloma (plasma cell myeloma, myelomatosis, Kahler's disease - MM), is a cancer of plasma cells, in physiological conditions responsible for producing normal antibodies, wherein collections of their abnormal forms accumulate in the bone marrow and interfere with the normal blood cells
- In most cases of MM abnormal plasma cells produce a paraprotein, which can cause kidney failure
- Bone lesions in MM can lead to hypercalcemia (high blood calcium levels)

https://en.wikipedia.org/wiki/Multiple_myeloma

Epidemiology



https://www.cancercare.on.ca/cms/one.aspx?portalId=1377&pageId=254171

Risk factors and etiology 1

- The risk of MM goes up as people age, most cases diagnosed at least after 65 years
- Men are slightly more likely to develop MM than women
- MM is more than twice as common in African Americans than in white Americans, the reason is not known
- Exposure to radiation may increase the risk of MM

http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-risk-factors

Risk factors and etiology 2

- Family history
- Someone who has a sibling or parent with MM is 4 times more likely to get it than would be expected
- Being overweight or obese increases a risk of developing MM
- Having other plasma cell diseases
- People with monoclonal gammopathy of undetermined significance (MGUS) or solitary plasmacytoma may will develop MM

http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-risk-factors

Mechanisms 1

- B- lymphocytes start in the bone marrow and move to the lymph nodes
- As they progress, they mature and display different proteins on their cell surface
- B-lymphocytes activated to secrete antibodies are known as plasma cells

https://en.wikipedia.org/wiki/Multiple_myeloma#Pathophysiology

Mechanisms 2

- The normal cell line most closely associated with MM cells is generally taken to be either an activated memory B cell or the precursor to plasma cells, the plasmablast
- The immune system keeps the proliferation of B cells and the secretion of antibodies under tight control

https://en.wikipedia.org/wiki/Multiple_myeloma#Pathophysiology

Mechanisms 3

- When chromosomes and genes are damaged, often through rearrangement, this control is lost
- The result is proliferation of a plasma cell clone and genomic instability that leads to further mutations and translocations
- Production of cytokines (especially IL-6) by the plasma cells causes much of their localised damage, such as osteoporosis, and creates a microenvironment in which the malignant cells thrive

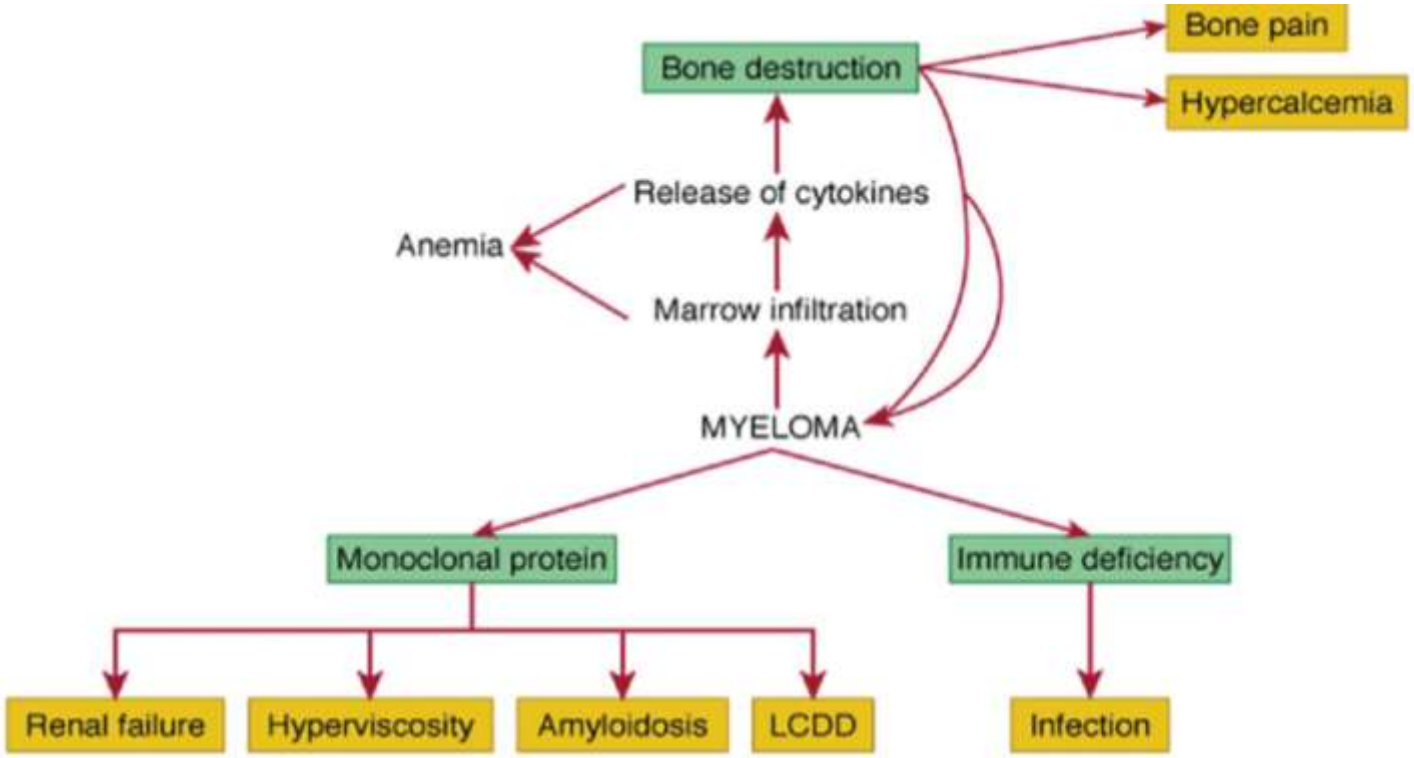
https://en.wikipedia.org/wiki/Multiple_myeloma#Pathophysiology

Mechanisms 4

- Angiogenesis (the attraction of new blood vessels) is increased
- The produced antibodies are deposited in various organs, leading to kidney failure, polyneuropathy and various other myeloma-associated symptoms

https://en.wikipedia.org/wiki/Multiple_myeloma#Pathophysiology

Mechanisms 5



Manifestations of MM

http://www.jahjournal.org/article.asp?issn=1658-5127;year=2015;volume=6;issue=2;spage=58;epage=63;aulast=Olaniyi

Classification

International Staging System

- Stage I: Serum beta-2 microglobulin < 3.5 mg/L and serum albumin ≥ 3.5 g/dL
- Stage II: Neither stage I nor stage III
- Stage III: Serum beta-2 microglobulin ≥ 5.5 mg/L

http://emedicine.medscape.com/article/2007195-overview

Clinical presentation 1

- Bone pain
- Pathologic fractures
- Spinal cord compression (back pain, weakness, numbness, or dysesthesias in the extremities)
- Bleeding resulting from thrombocytopenia, and monoclonal protein absorption of clotting factors
- Hypercalcemia (confusion, somnolence, bone pain, constipation, nausea, and thirst)
- Infection through abnormal humoral immunity and leukopenia

http://emedicine.medscape.com/article/204369-clinical

Clinical presentation 2

- Hyperviscosity (generalized malaise, infection, fever, paresthesia, sluggish mentation, sensory loss, headaches, somnolence, hazy vision, etc., when serum viscosity is greater than 4 times that of normal serum)
- Neurologic symptoms (carpal tunnel syndrome, meningitis (especially that resulting from pneumococcal or meningococcal infection), some peripheral neuropathies, etc.)

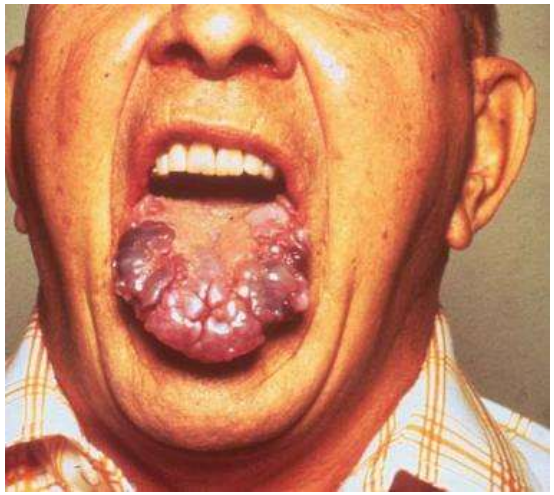
http://emedicine.medscape.com/article/204369-clinical

Clinical presentation 3

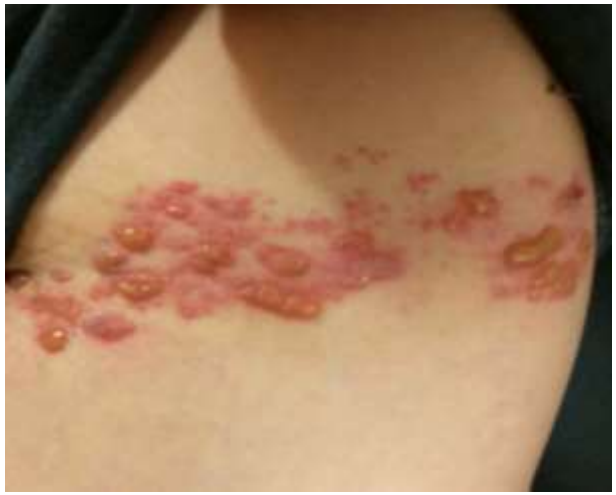
- Kidney problems, that can lead to symptoms like weakness, shortness of breath, itching, leg swelling
- Anemia, which may be quite severe
- Signs and symptoms of light chain amyloidosis (heart problems, enlarged liver and spleen, enlarged tongue, bleeding into the skin around the eyes (“raccoon eyes”),diarrhea)

http://emedicine.medscape.com/article/204369-clinical

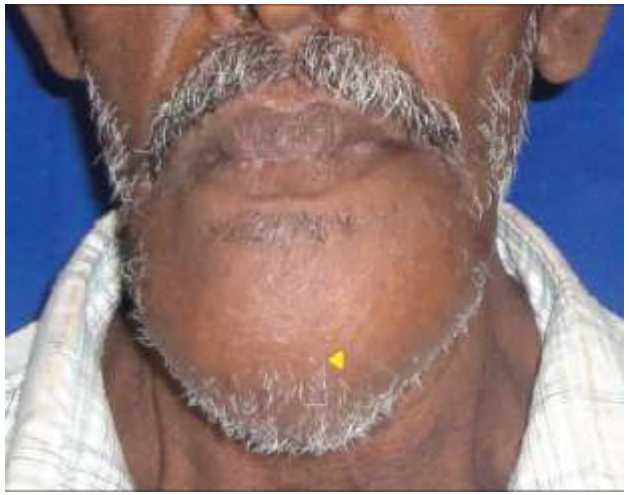
Clinical presentation 4



Amyloidosis infiltrating the tongue



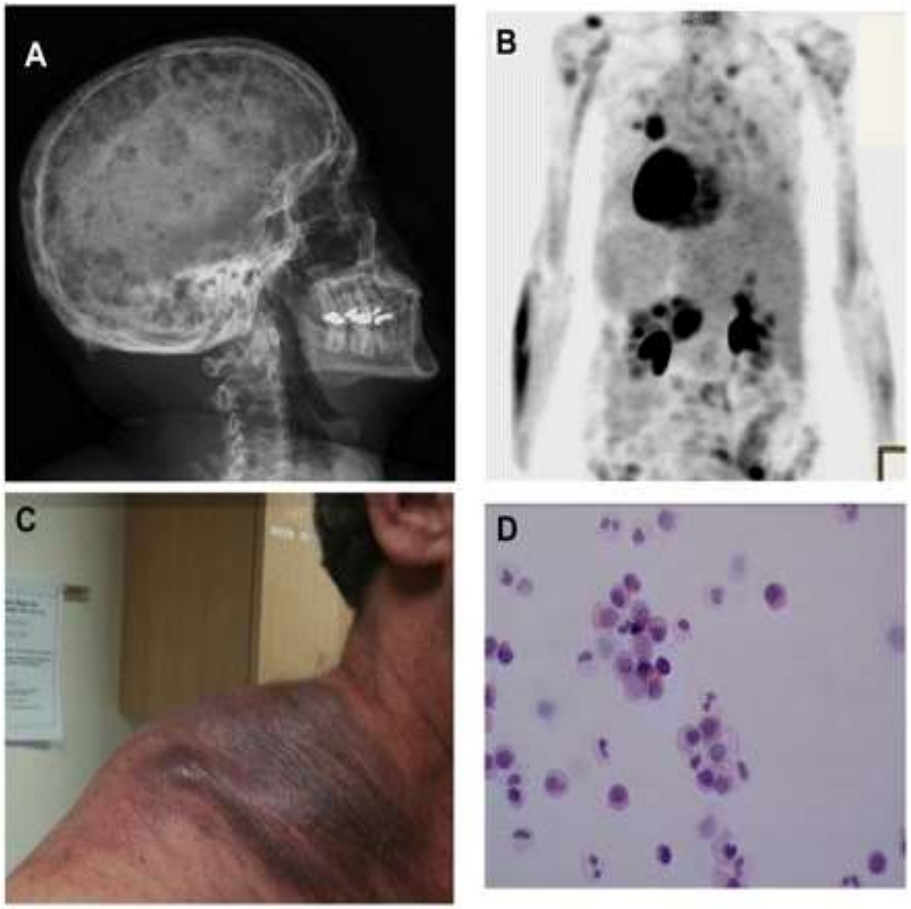
Herpes zoster (shingles)



Swelling in the mandible

myelomapennstate.net/Contents/04c-ClinManifest.htm linicalimagingscience.org/article.asp?issn=2156-7514;year=2013;volume=3;issue=2;spage=6;epage=6;aulast=Vinayachandran

Clinical presentation 5



Cell dissemination and metastasis in MM: (A) Multiple lytic lesions in the skull; B) MM cells metastasize to areas outside the BM; (C) A large subcutaneous mass on the shoulder (D) Circulating tumor plasma cells in the peripheral blood

http://www.bloodjournal.org/content/120/1/20?sso-checked=true

Diagnosis 1

Diagnosis should be based on the following tests:

- Detection and evaluation of the monoclonal (M-) component by serum and/or urine protein electrophoresis (concentrate of 24 h urine collection); nephelometric quantification of IgG, IgA and IgM immunoglobulins; characterisation of the heavy and light chains by immunofixation; and serum-free light-chain (FLC) measurement

http://www.esmo.org/Guidelines/Haematological-Malignancies/Multiple-Myeloma

Diagnosis 2

Diagnosis should be based on the following tests:

- Evaluation of bone marrow (BM) plasma cell infiltration: BM aspiration and/or biopsies are the standard options to evaluate the number and characteristics. Moreover, the BM sample should be used for cytogenetic/fluorescence *in situ* hybridization (FISH) studies and also has the potential for immunophenotypic and molecular investigations

http://www.esmo.org/Guidelines/Haematological-Malignancies/Multiple-Myeloma

Diagnosis 4

- Fluorodeoxyglucose positron emission tomography
- Complete blood cell count, with differential
- Serum creatinine and calcium level
- Evaluation of lytic bone lesions
- A magnetic resonance imaging (MRI) or computed tomography (CT) scan

http://www.esmo.org/Guidelines/Haematological-Malignancies/Multiple-Myeloma

Diagnosis 5

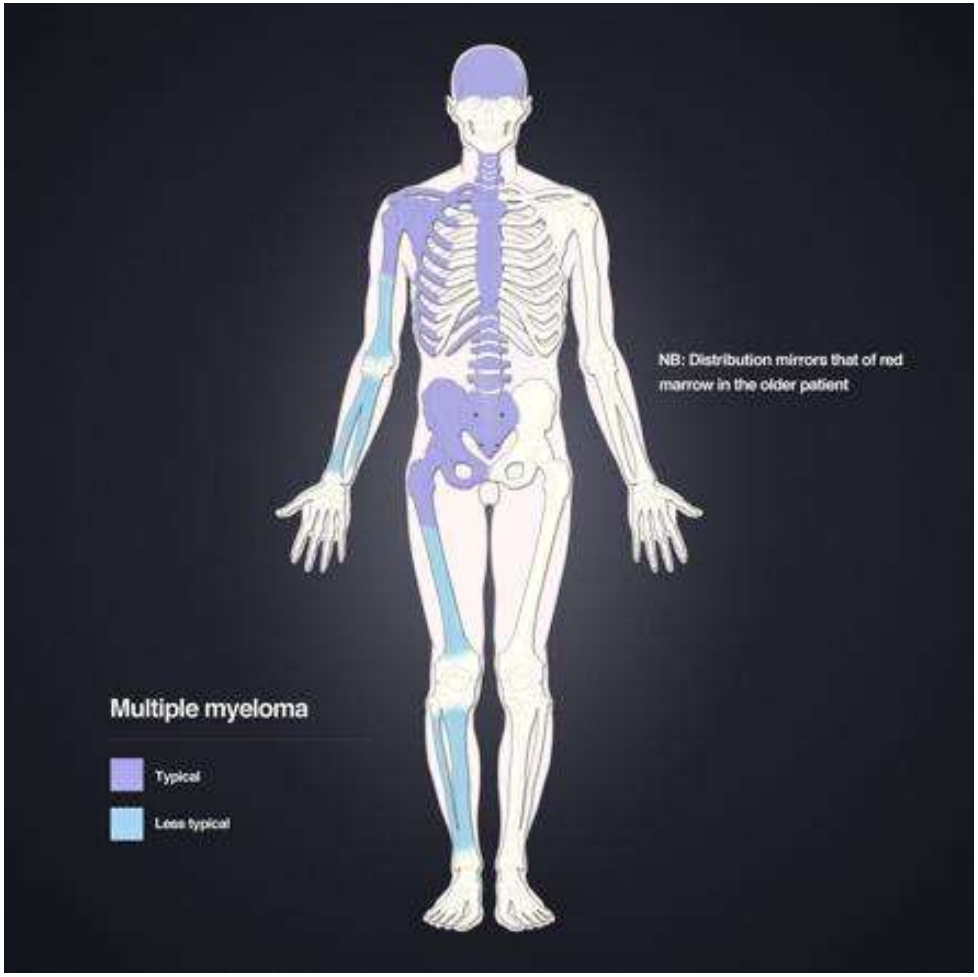
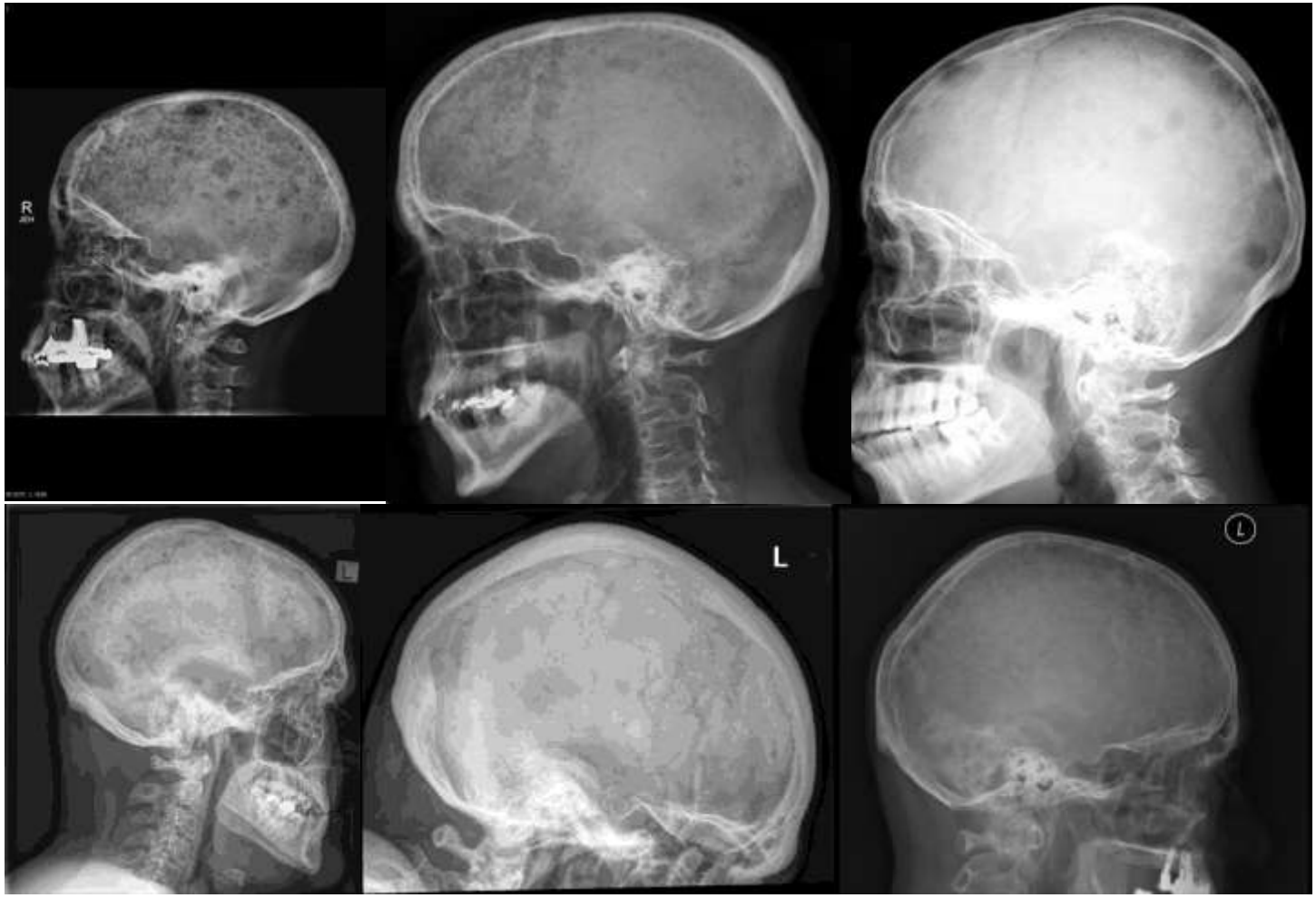


Diagram Distribution of MM

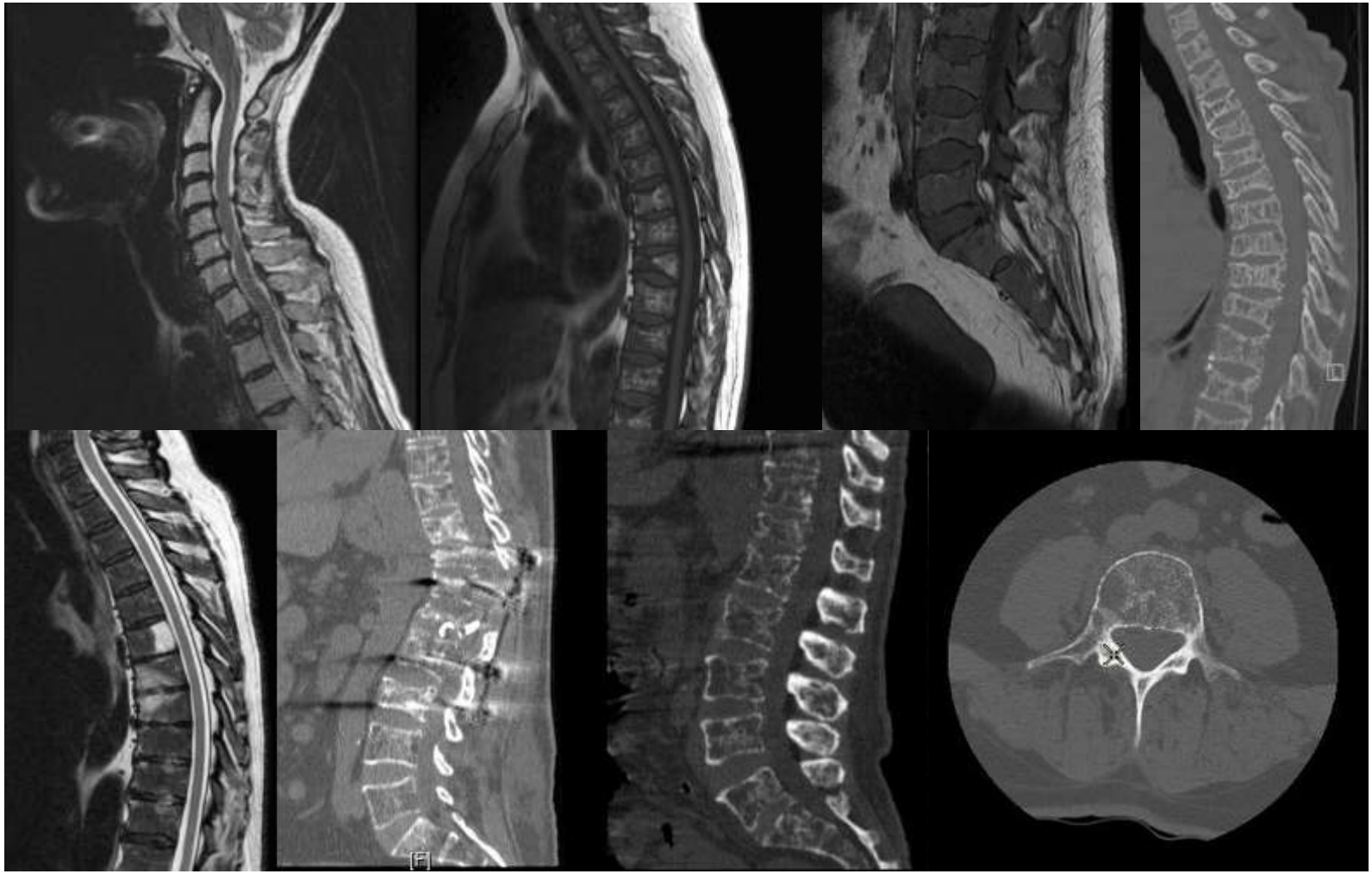
http://radiopaedia.org/images/1696350

Diagnosis 6



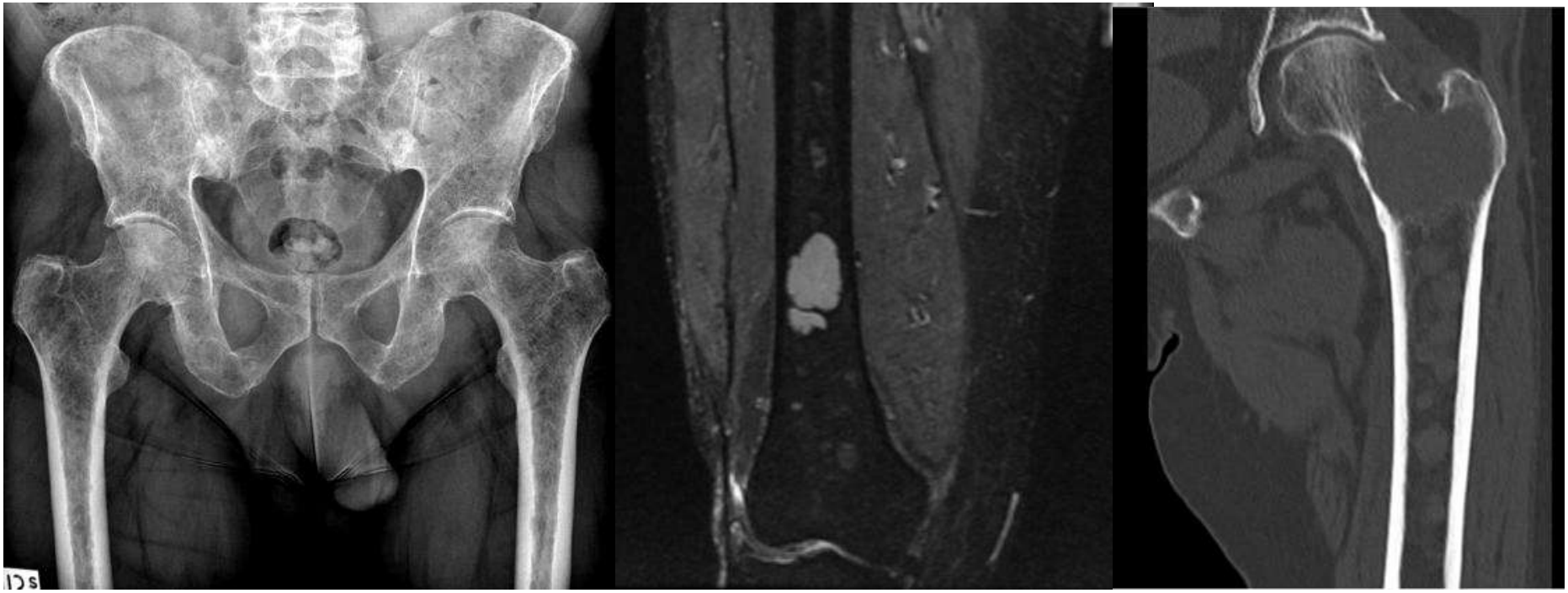
http://radiopaedia.org/images/

Diagnosis 7



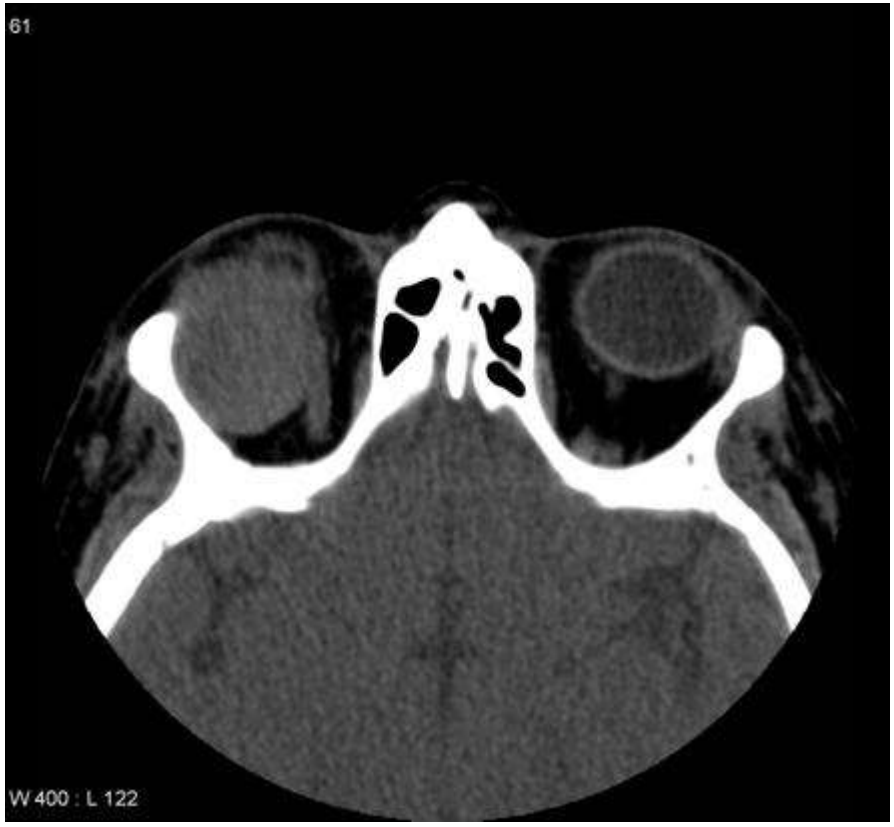
http://radiopaedia.org/images/

Diagnosis 8



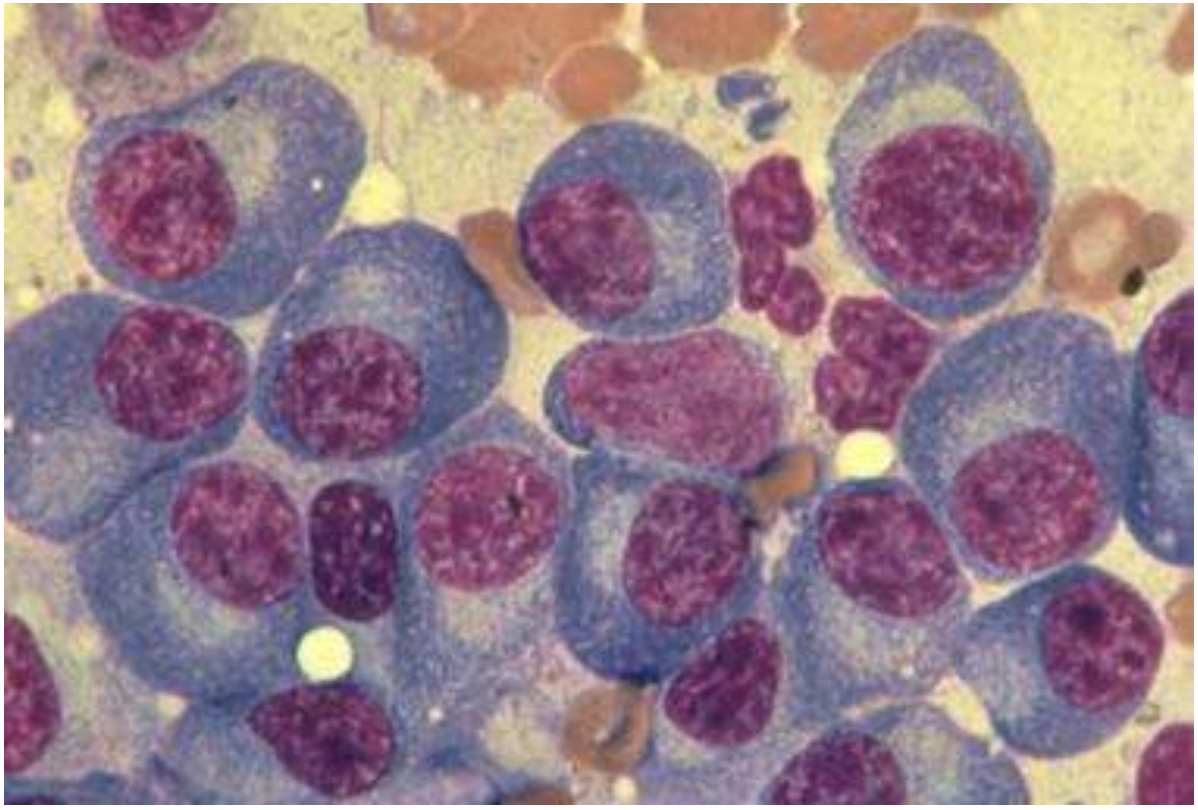
http://radiopaedia.org/images/

Diagnosis 9



http://radiopaedia.org/images/

Diagnosis 10



Bone marrow aspirate demonstrating plasma cells of multiple myeloma

http://emedicine.medscape.com/article/204369-overview

Diagnosis 11

- **Genetic testing**
- Some myeloma centers now employ genetic testing, which they call a “gene array”
- By examining DNA, oncologists can determine if patients are high risk or low risk of the cancer returning quickly following treatment

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Diagnosis 12

- **Genetic testing**
- Cytogenetic analysis of myeloma cells may be of prognostic value, with deletion of chromosome 13, non-hyperdiploidy and the balanced translocations t(4;14) and t(14;16) conferring a poorer prognosis. The 11q13 and 6p21 cytogenetic abnormalities are associated with a better prognosis

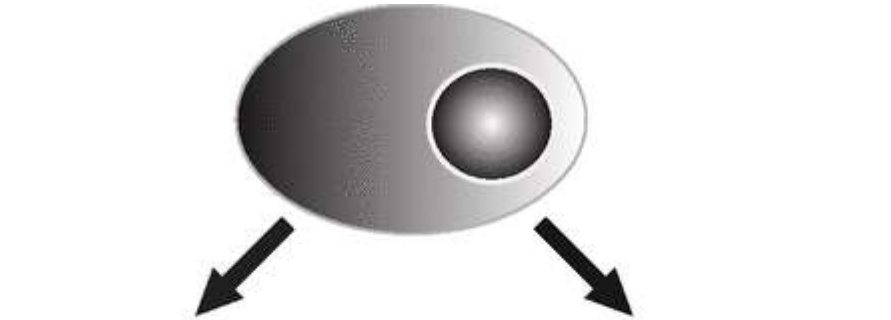
https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Diagnosis 13

- **Genetic testing**
- Prognostic markers such as these are always generated by retrospective analyses, and it is likely that new treatment developments will improve the outlook for those with traditionally "poor-risk" disease

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Diagnosis 14



Genetic classifications of MM

http://www.bloodjournal.org/content/121/6/884?sso-checked=true

Treatment 1

- Focused on therapies that decrease the clonal plasma cell population and consequently decrease the signs and symptoms of disease
- If the disease is completely asymptomatic, treatment is typically deferred, or restricted to clinical trials
- In addition to direct treatment of the plasma cell proliferation, bisphosphonates are routinely administered to prevent fractures

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Treatment 2

- If needed, red blood cell transfusions or erythropoietin can be used for management of anemia
- Bortezomib has the first therapeutic proteasome inhibitor approved by the U.S. FDA for treating relapsed multiple myeloma

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Treatment 3

Initial therapy

- High-dose chemotherapy (lenalidomide–dexamethasone, bortezomib based regimens, and lenalidomide–dexamethasone) with autologous hematopoietic stem-cell transplantation has become the preferred treatment for patients under the age of 65
- Allogeneic stem cell transplantation, has the potential for a cure, but is used in a very small percentage of patients

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Treatment 4

Initial therapy

- Patients over age 65 and patients with significant concurrent illness often cannot tolerate stem cell transplantation, and for them the standard of care has been chemotherapy with melphalan and prednisone, with bortezomib
- Deep venous thrombosis and pulmonary embolism are the major side effects of high-dose chemotherapy

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Treatment 5

Maintenance therapy

- Sometimes after the initial treatment an ongoing maintenance therapy is offered
- In younger patients, maintenance therapy with thalidomide appears to increase tumor burden reduction further, which translates into prolonged progression-free survival
- Maintenance therapy with thalidomide, lenalidomide, or bortezomib is still of questionable benefit

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Treatment 6

- **Relapse**
- The natural history of MM is of relapse following treatment
- For patients with relapsed disease, proteasome inhibitor bortezomib is a recent addition to the therapeutic arsenal (lenalidomide, thalidomide), especially as second line therapy

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Treatment 7

- **Palliative care**
- Multiple national cancer treatment guidelines recommend early palliative care for people with advanced MM at the time of diagnosis as well as for anyone who has significant symptoms
- Palliative care is appropriate at any stage of MM and can be provided alongside curative treatment
- In addition to addressing symptoms of cancer, palliative care helps manage unwanted side-effects, such as pain and nausea related to treatments

https://en.wikipedia.org/wiki/Multiple_myeloma#Treatment

Prognosis

- With high-dose therapy followed by autologous stem cell transplantation, the median survival has been estimated to be approximately 5 years
- The International Staging System can help to predict survival
- The prognoses for patients with MM, as those with other diseases, are not the same for everyone: older patients often are experiencing other serious diseases, which affect survival and younger patients might have much longer survival rates

https://en.wikipedia.org/wiki/Hodgkin%27s_lymphoma

Prophylaxis

- Prophylaxis is treatment that aims to stop a lymphoma elsewhere in the body
- It can be difficult to treat once it develops, so sometimes needs a preventive treatment
- This treatment may be given as well as the usual chemotherapy for the lymphoma or may already be part of a particular regimen

https://www.google.com.ua/webhp?sourceid=chrome-instant&ion=1&espv=2&ie=UTF-8#q=secondary+prophylaxis+of+lymphoma

Abbreviations

- CT - computed tomography
- EBV - Epstein-Barr virus
- FDA - U.S. Food and Drug Administration
- FISH -fluorescence in situ hybridization
- HCV - hepatitis C virus
- HHV8 - human herpes virus 8
- HIV - human immunodeficiency virus
- HL - Hodgkin lymphoma
- HTLV-1 - human T-cell leukemia/lymphoma virus
- IWF - National Cancer Institute's Working Formulation
- MRI - magnetic resonance imaging
- NHL - non-Hodgkin lymphoma
- PET - positron emission tomography
- REAL - Revised European-American Classification of Lymphoid Neoplasms
- RSC - Reed-Sternberg cells
- WHO - World Health Organization
- MGUS - monoclonal gammopathy of undetermined significance
- MM - multiple myeloma

Diagnostic guidelines

Best practice in lymphoma diagnosis and reporting

- Control of pain in adults with cancer: a national clinical guideline
- Referral guidelines for suspected cancer
- Consensus recommendations for the management of cutaneous B-cell lymphomas
- Diagnosis and treatment of primary CNS lymphoma in immunocompetent patients: guidelines from the European Association for Neuro-Oncology
- Hodgkin's lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up
- NCCN clinical practice guidelines in oncology: non-Hodgkin's lymphoma