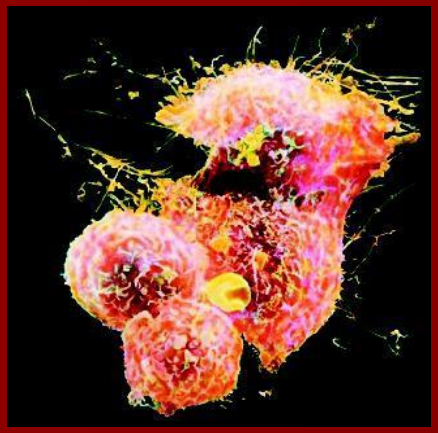


Malignant Lymphomas

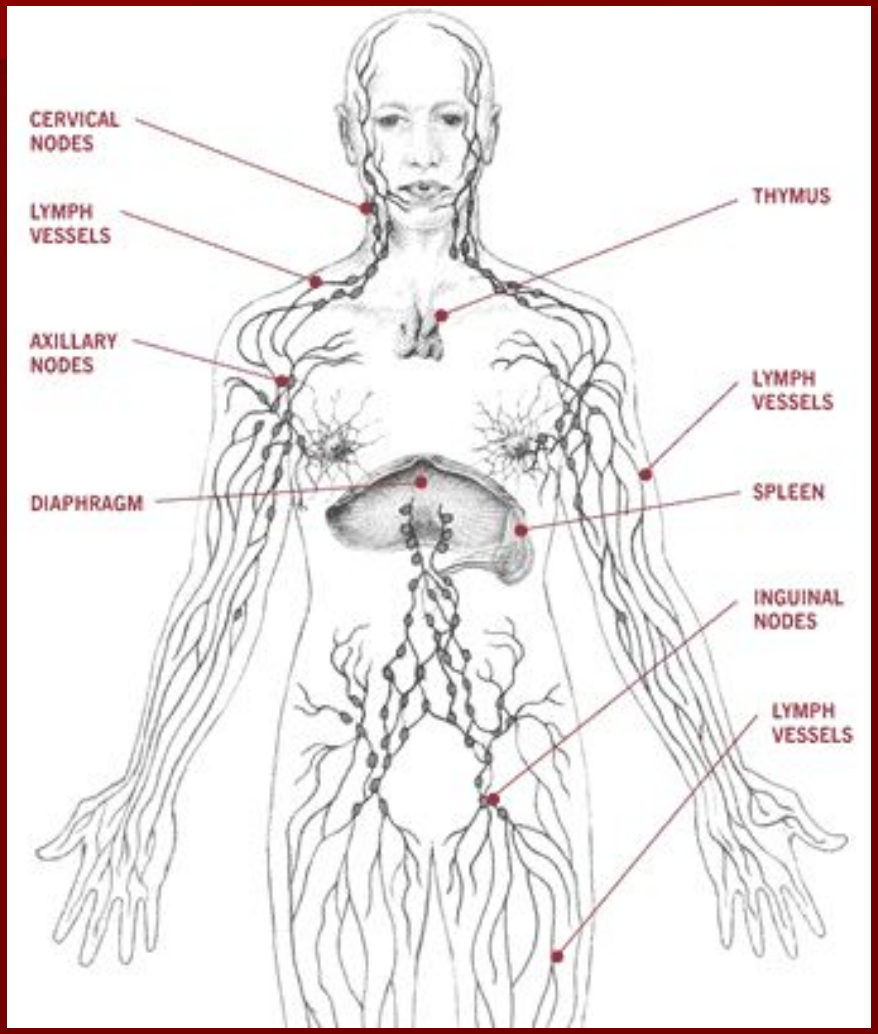
Definition

Lymphoma means a malignant tumor of the lymphatic system. There are two main types of lymphoma

1) Hodgkin's lymphoma
2) Non Hodgkin's lymphoma (NHL)

Most lymphomas are NHL. Only about 1 in 5 are Hodgkin's lymphoma. Hodgkin's disease was named after the doctor who first recognised it in 1832 - Thomas Hodgkin. It is now called Hodgkin's lymphoma.

The lymphatic system



- The lymphatic systemThe lymphatic system is part of the immune systemThe lymphatic system is part of the immune system, which defends the body against infection. The lymphatic system is a network of small lymph nodesThe lymphatic system is part of the immune system, which defends the body against infection. The lymphatic system is a network of small lymph nodes connected by very thin lymph vessels, which branch into every part of the body except the brain and spinal cord. The major nodes can be found in the neck, armpits, chest, abdomen, pelvis and groin. Other parts of the lymphatic system include the spleenThe lymphatic system is part of the immune system, which defends the body against infection. The lymphatic system is a network of small lymph nodes connected by very thin lymph vessels, which branch into every part of the body except the brain and spinal cord. The major nodes can be found in the neck, armpits, chest, abdomen, pelvis and groin. Other parts

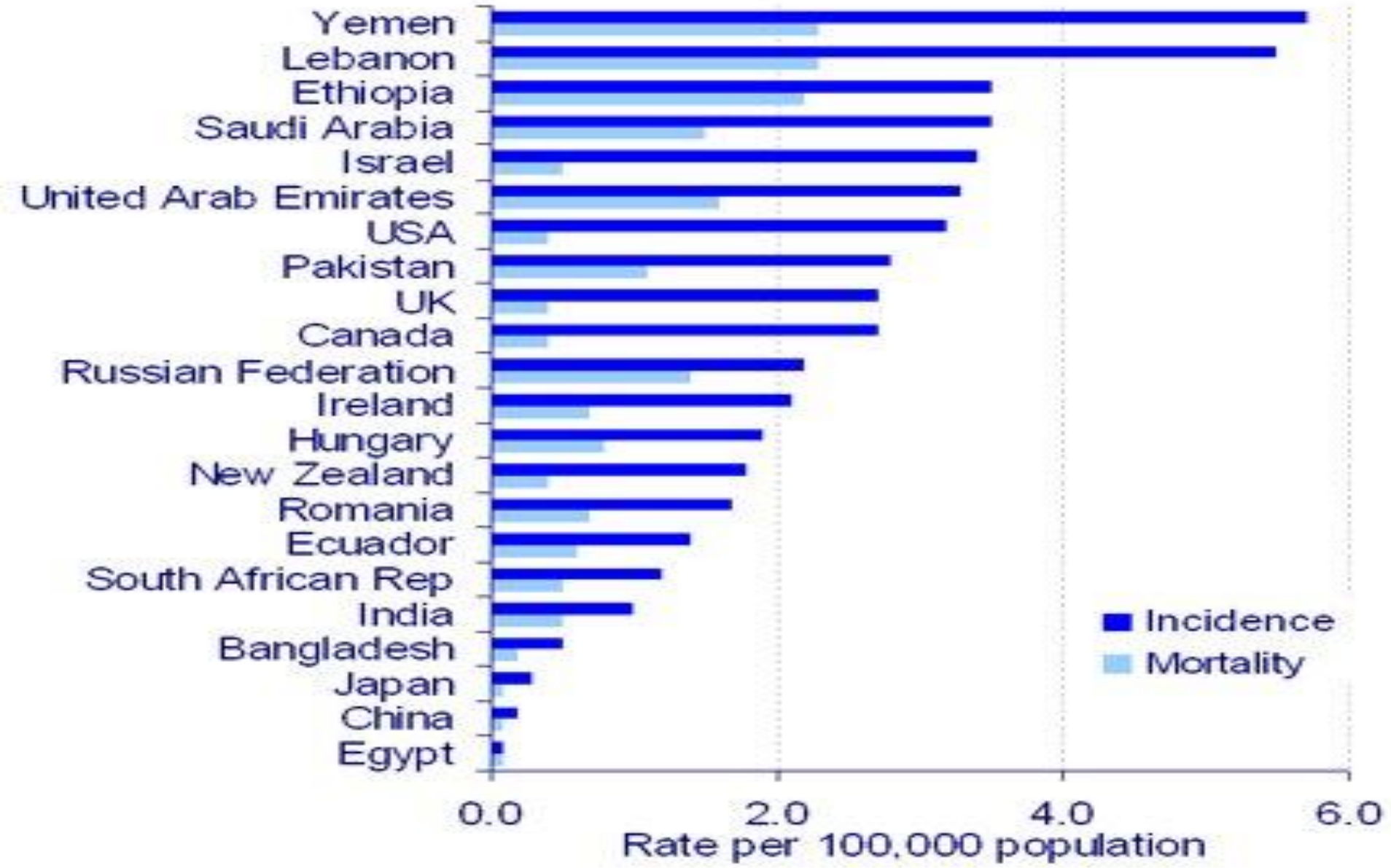
Epidemiology

TABLE 1 Incidence and Mortality by Sex and Cancer Site Worldwide, 2002

	INCIDENCE						MORTALITY					
	MALES			FEMALES			MALES			FEMALES		
	Cases	ASR (World)	Cumulative risk (age 0–64)	Cases	ASR (World)	Cumulative risk (age 0–64)	Deaths	ASR (World)	Cumulative risk (age 0–64)	Deaths	ASR (World)	Cumulative risk (age 0–64)
Oral cavity	175,916	6.3	0.4	98,373	3.2	0.2	80,736	2.9	0.2	46,723	1.5	0.1
Nasopharynx	55,796	1.9	0.1	24,247	0.8	0.1	34,913	1.2	0.1	15,419	0.5	0.0
Other pharynx	106,219	3.8	0.3	24,077	0.8	0.1	67,964	2.5	0.2	16,029	0.5	0.0
Esophagus	315,394	11.5	0.6	146,723	4.7	0.3	261,162	9.6	0.5	124,730	3.9	0.2
Stomach	603,419	22	1.2	330,518	10.3	0.5	446,052	16.3	0.8	254,297	7.9	0.4
Colon/rectum	550,465	20.1	0.9	472,687	14.6	0.7	278,446	10.2	0.4	250,532	7.6	0.3
Liver	442,119	15.7	1.0	184,043	5.8	0.3	416,882	14.9	0.9	181,439	5.7	0.3
Pancreas	124,841	4.6	0.2	107,465	3.3	0.1	119,544	4.4	0.2	107,479	3.3	0.1
Larynx	139,230	5.1	0.3	20,011	0.6	0	78,629	2.9	0.2	11,327	0.4	0.0
Lung	965,241	35.5	1.7	386,891	12.1	0.6	848,132	31.2	1.4	330,786	10.3	0.5
Melanoma of skin	79,043	2.8	0.2	81,134	2.6	0.2	21,952	0.8	0.0	18,829	0.6	0.0
Kaposi sarcoma*												
Breast				1,151,298	37.4	2.6				410,712	13.2	0.9
Cervix uteri				493,243	16.2	1.3				273,505	9.0	0.7
Corpus uteri				198,783	6.5	0.4				50,327	1.6	0.1
Ovary				204,499	6.6	0.5				124,860	4.0	0.2
Prostate	679,023	25.3	0.8				221,002	8.2	0.1			
Testis	48,613	1.5	0.1				8,878	0.3	0.0			
Kidney	129,223	4.7	0.3	79,257	2.5	0.1	62,696	2.3	0.1	39,199	1.2	0.1
Bladder	273,858	10.1	0.4	82,699	2.5	0.1	108,310	4.0	0.1	36,699	1.1	0.0
Brain, nervous system	108,221	3.7	0.2	81,264	2.6	0.2	80,034	2.8	0.2	61,616	2.0	0.1
Thyroid	37,424	1.3	0.1	103,589	3.3	0.2	11,297	0.4	0.0	24,078	0.8	0.0
Non-Hodgkin lymphoma	175,123	6.1	0.3	125,448	3.9	0.2	98,865	3.5	0.2	72,955	2.3	0.1
Hodgkin disease	38,218	1.2	0.1	24,111	0.8	0.1	14,460	0.5	0.0	8,352	0.3	0.0
Multiple myeloma	46,512	1.7	0.1	39,192	1.2	0.1	32,696	1.2	0.1	29,839	0.9	0.0
Leukemia	171,037	5.9	0.3	129,485	4.1	0.2	125,142	4.3	0.2	97,364	3.1	0.2
All sites but skin	5,801,839	209.6	10.3	5,060,657	161.5	9.5	3,795,991	137.7	6.4	2,927,896	92.1	4.9

*Africa only.

Figure 2.4: Age-standardised incidence and mortality rates for Hodgkin's lymphoma in males, selected countries, 2002 estimates

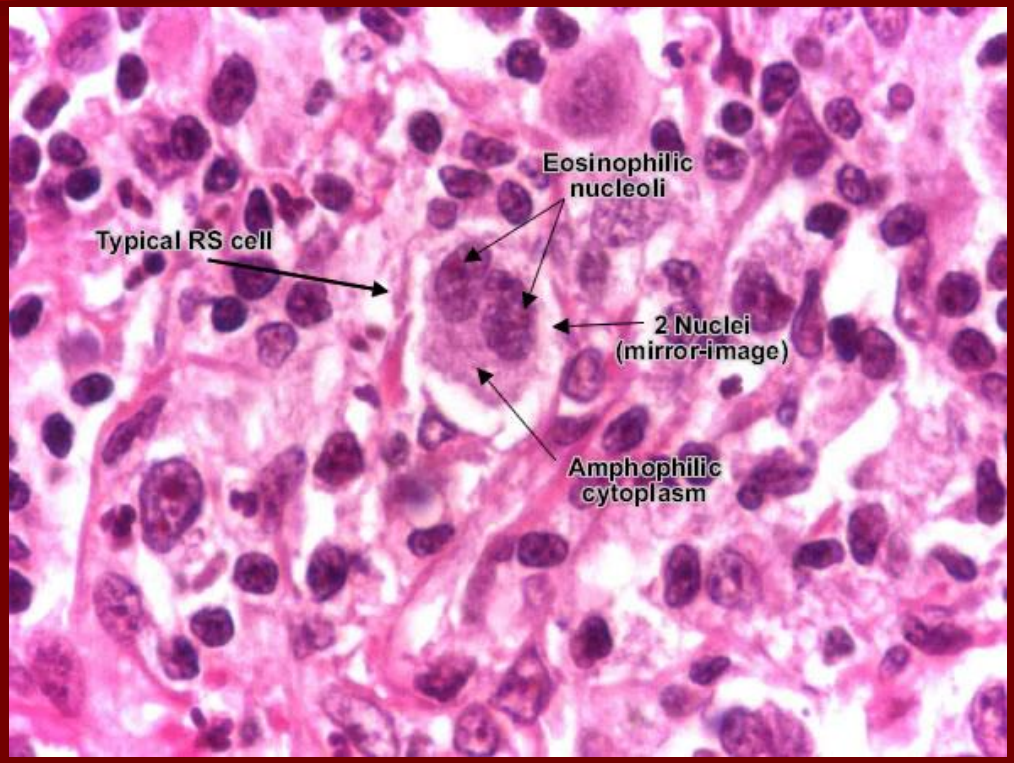


Hodgkin Lymphoma

Sir Thomas Hodgkin (1798-1866)

- *Hodgkin's disease is one of two common types of cancers of the lymphatic system. Non-Hodgkin's lymphoma, the other type, is far more common. Hodgkin's disease is named after the British physician Thomas Hodgkin, who first described the disease in 1832 and noted characteristics that distinguish it from other lymphomas.*
- *Advances in diagnosis, staging and treatment of Hodgkin's disease have helped to make this once uniformly fatal disease highly treatable with the potential for full recovery.*

Hodgkin's Disease – Reed Stenberg Cell



- Presence of typical Reed-Sternberg cell and reactive component are mandatory for diagnosis of **Hodgkin's lymphoma**. Characteristics of typical Reed-Sternberg cell : size between 20 - 50 microns; abundant, amphofilic, finely granular/homogenous cytoplasm; two mirror-image nuclei ("owl eyes") each with an eosinophilic nucleolus and a thick nuclear membrane (chromatin is distributed on the inner surface of the nuclear membrane, generating a halo image around the nucleolus). Reed-Sternberg cell has a B-cell origin. (H&E, ob.x40)

Hodgkin Lymphoma

Within the latter, four subtypes have been distinguished:

- nodular sclerosis,
- mixed cellularity,
- lymphocyte-rich
- lymphocyte-depleted.

Cotswolds staging classification for Hodgkin lymphoma

- ***Stage I*** *– Involvement of a single lymph node region (eg, cervical, axillary, inguinal, mediastinal) or lymphoid structure such as the spleen, thymus, or Waldeyer's ring.*

- ***Stage II*** *– Involvement of two or more lymph node regions or lymph node structures on the same side of the diaphragm. Hilar nodes should be considered to be "lateralized" and when involved on both sides, constitute stage II disease. For the purpose of defining the number of anatomic regions, all nodal disease within the mediastinum is considered to be a single lymph node region and hilar involvement constitutes an additional site of involvement. The number of anatomic regions should be indicated by a subscript (eg, II-3).*

Cotswolds staging classification for Hodgkin lymphoma

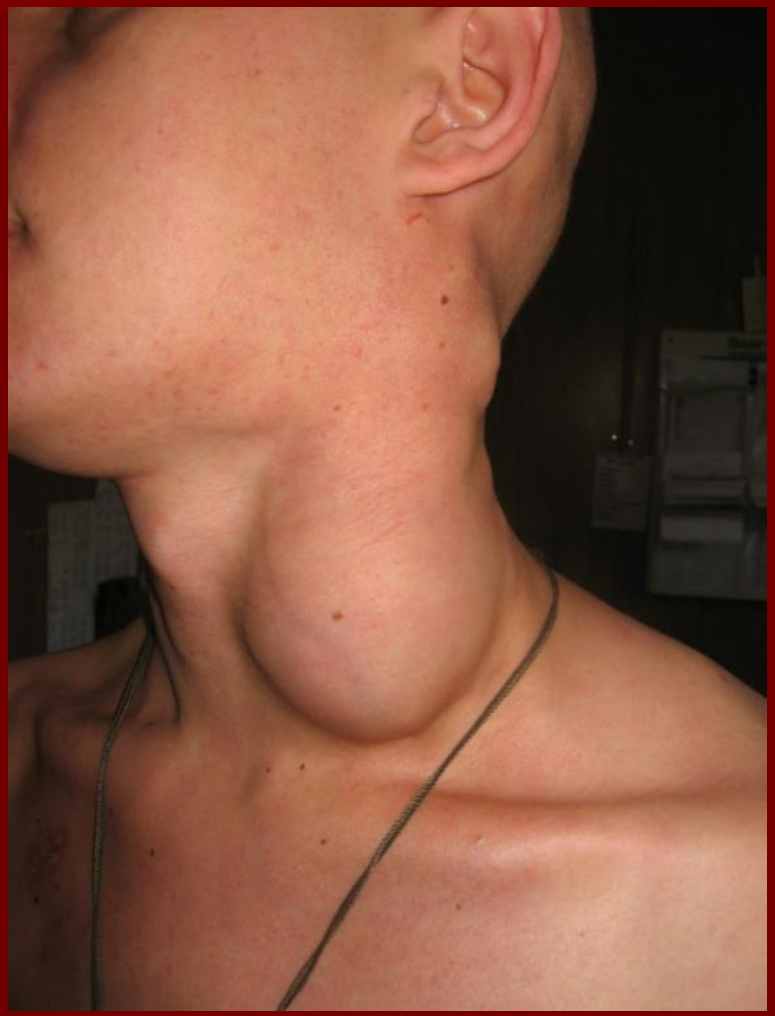
- ***Stage III*** *– Involvement of lymph node regions or lymphoid structures on both sides of the diaphragm. This may be subdivided*
  stage III-1 or III-2: stage III-1 is used for patients with involvement of the spleen or splenic hilar, celiac or portal nodes; and
  stage III-2 is used for patients with involvement of the paraaortic, iliac, inguinal, or mesenteric nodes.

- ***Stage IV*** *– Diffuse or disseminated involvement of one or more extranodal organs or tissue beyond that designated E, with or without associated lymph node involvement.*

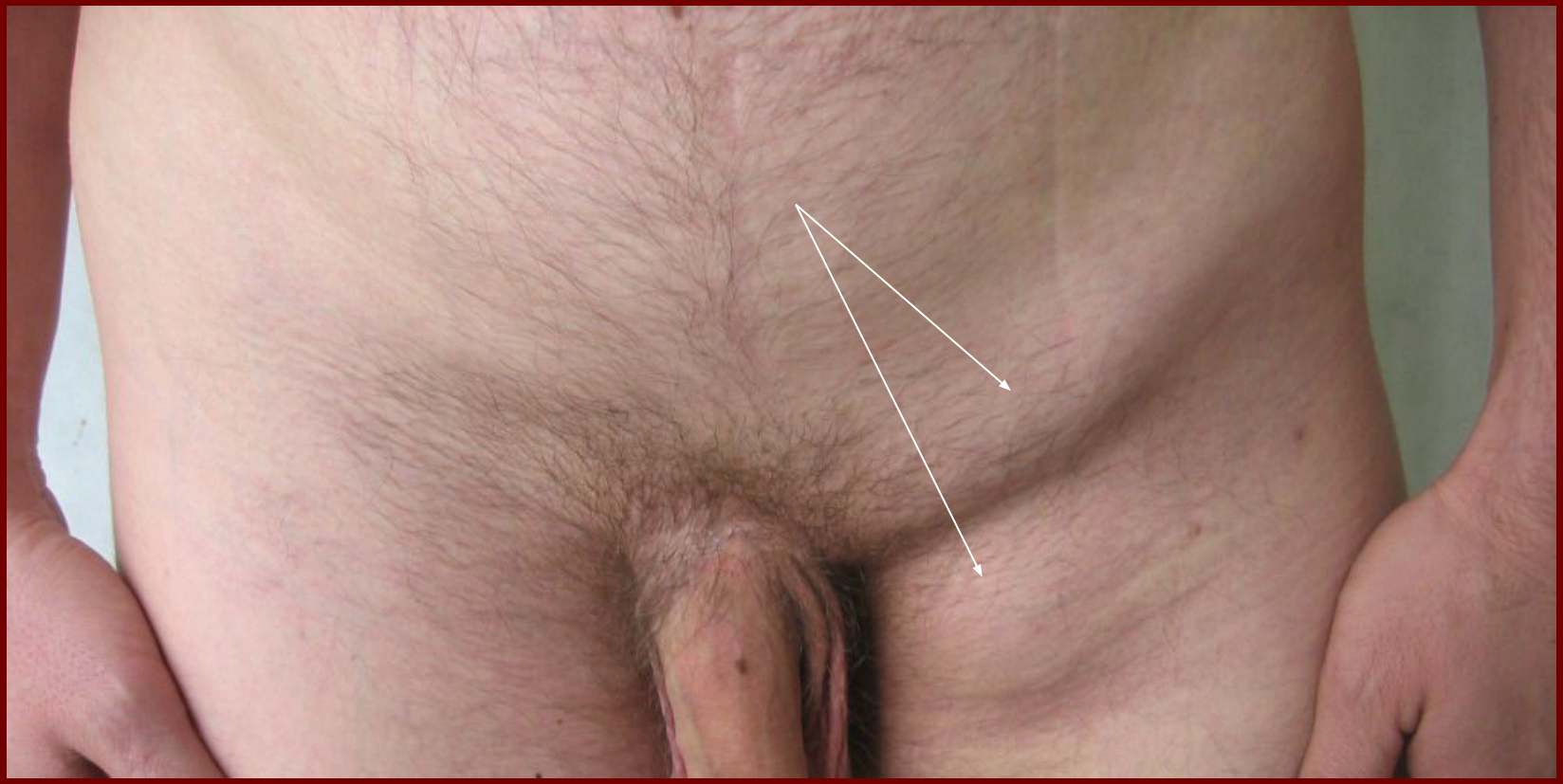
- *All cases are subclassified to indicate the absence (**A**) or presence (**B**) of the systemic symptoms of significant unexplained fever, night sweats, or unexplained weight loss exceeding 10 percent of body weight during the six months prior to diagnosis.*

- *The designation "**E**" refers to extranodal contiguous extension (ie, proximal or contiguous extranodal disease) that can be encompassed within an irradiation field appropriate for nodal disease of the same anatomic extent. More extensive extranodal disease is designated stage IV.*

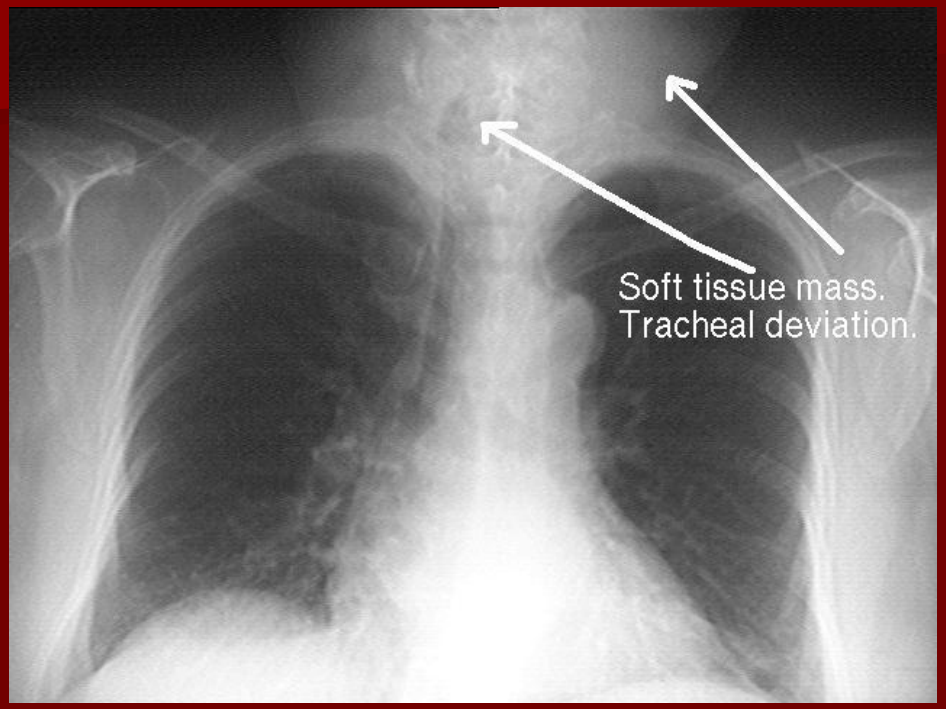
Hodgkin lymphoma



Hodgkin lymphoma

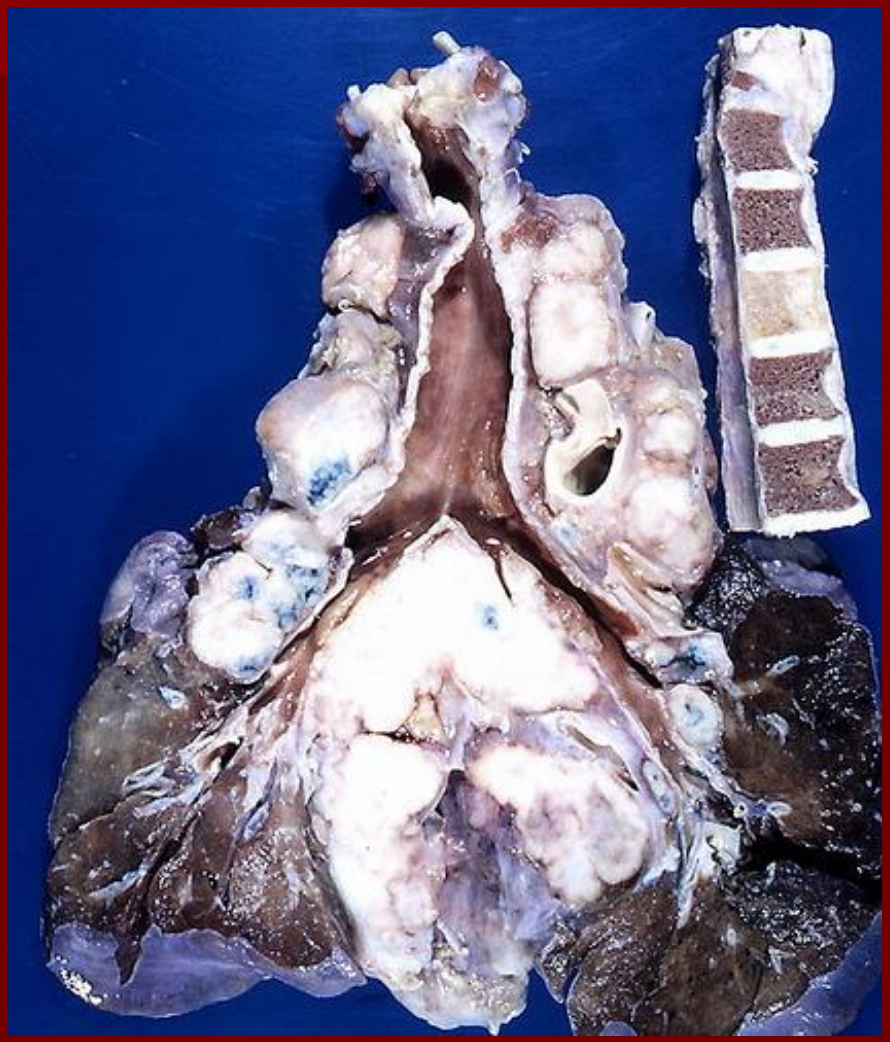


Hodgkin Lymphoma



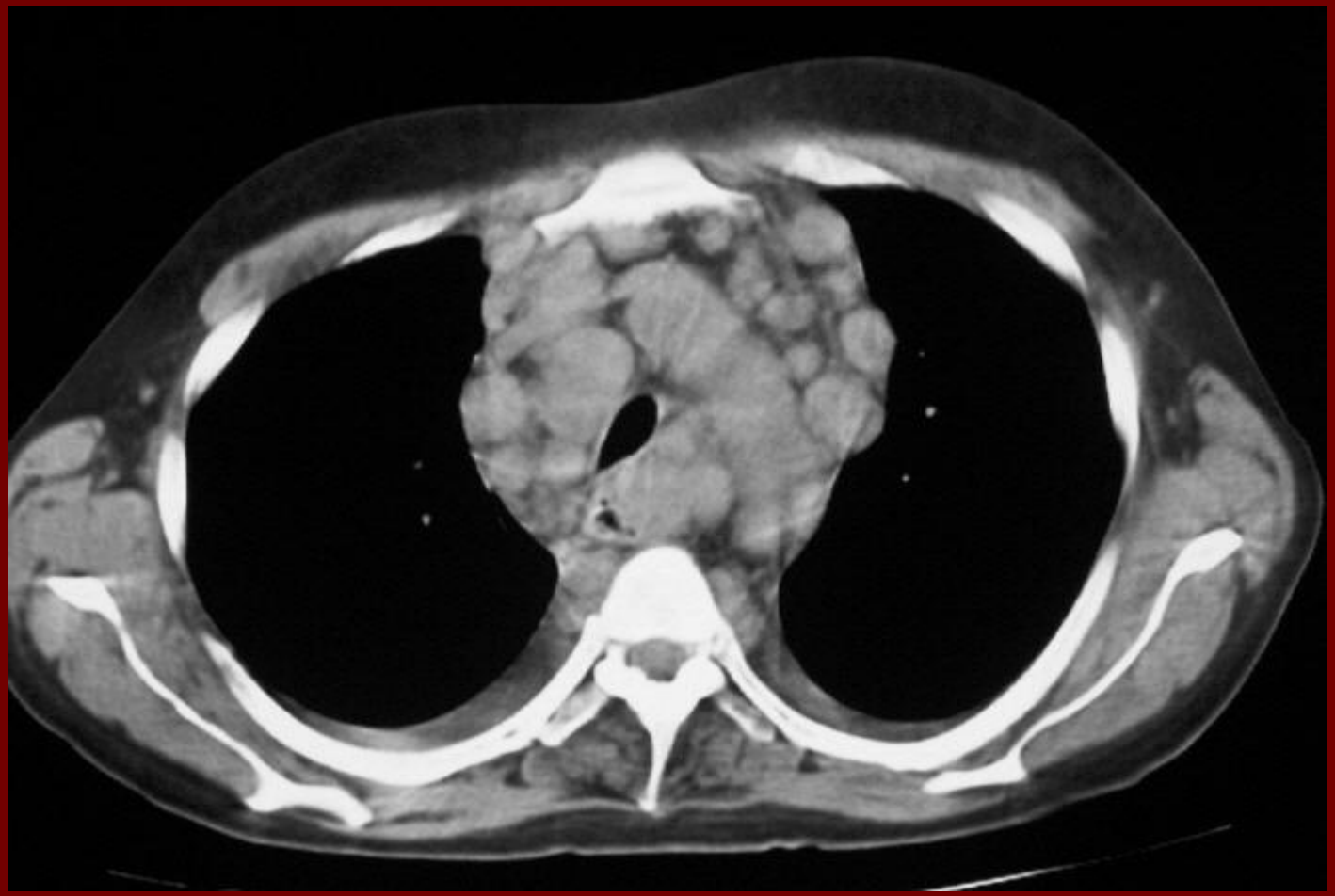
- Findings:
- Subtle soft tissue swelling is present along the left side of the patient's neck.
  - The trachea is deviated to the right.
- Lung fields are clear.
- There is no definite evidence of mediastinal or hilar adenopathy.
- Radiographic findings are consistent with a neck mass, subsequently proven to be **Hodgkin's Lymphoma**.

Hodgkin disease

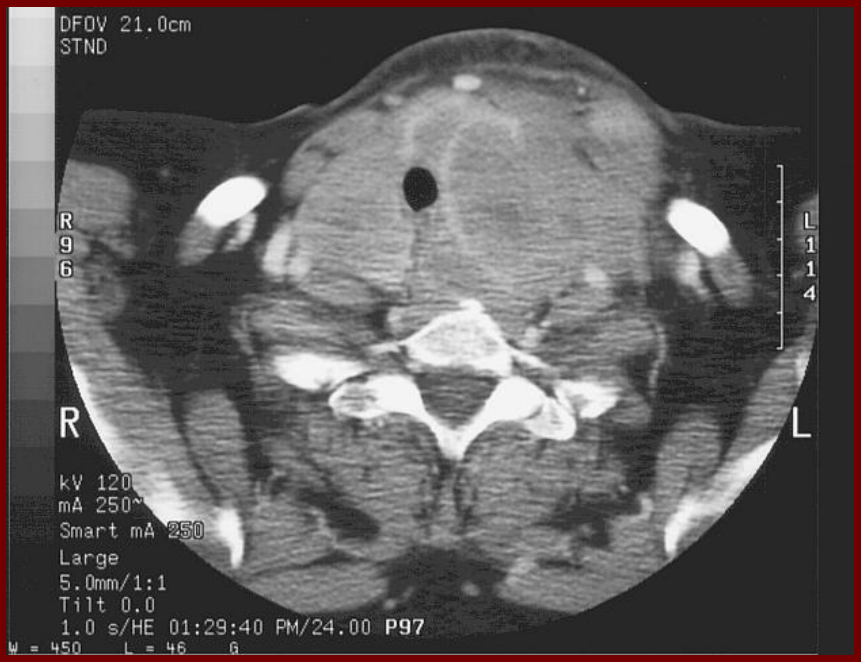


- Massive involvement of paratracheal, hilar and subcarinal lymph nodes as well as two vertebral bodies.

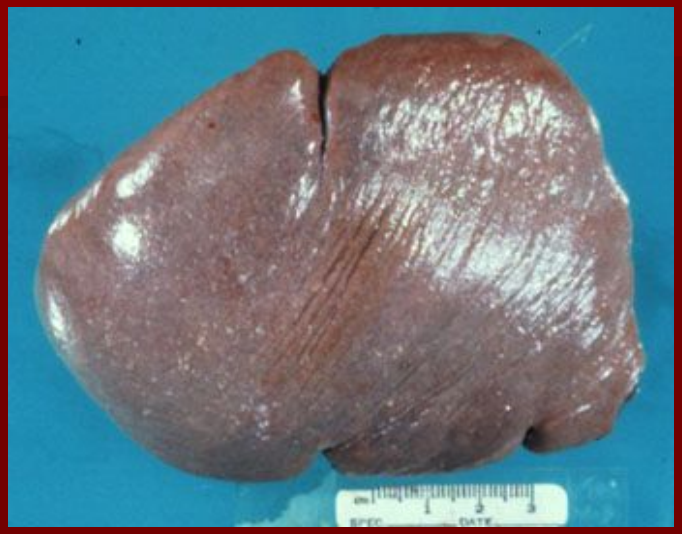
Nonenhanced CT scan through the mediastinum shows multiple enlarged lymph nodes in the prevascular space, in the right and left paratracheal region. Nodes in the left paratracheal region cause the trachea to be indented and narrowed on the left side. Note the small, bilateral pleural effusion.

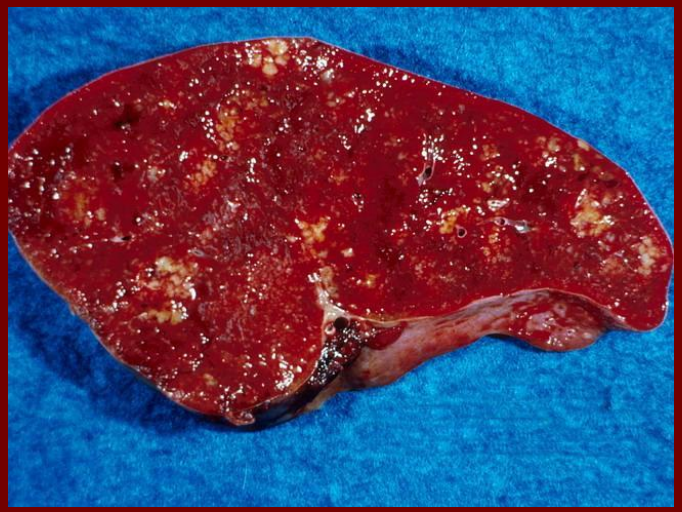


CT scan



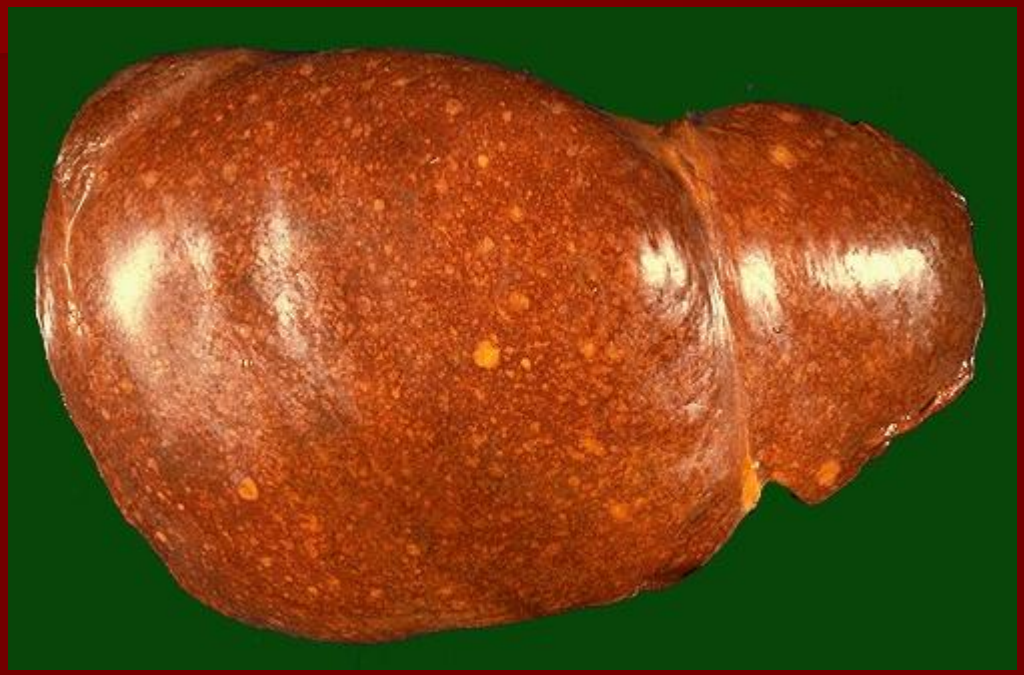
- Can demonstrate the relationship of the mass to vessels and other structures.
- Can help characterize the lesion.
- Can serve as a guide for biopsy.





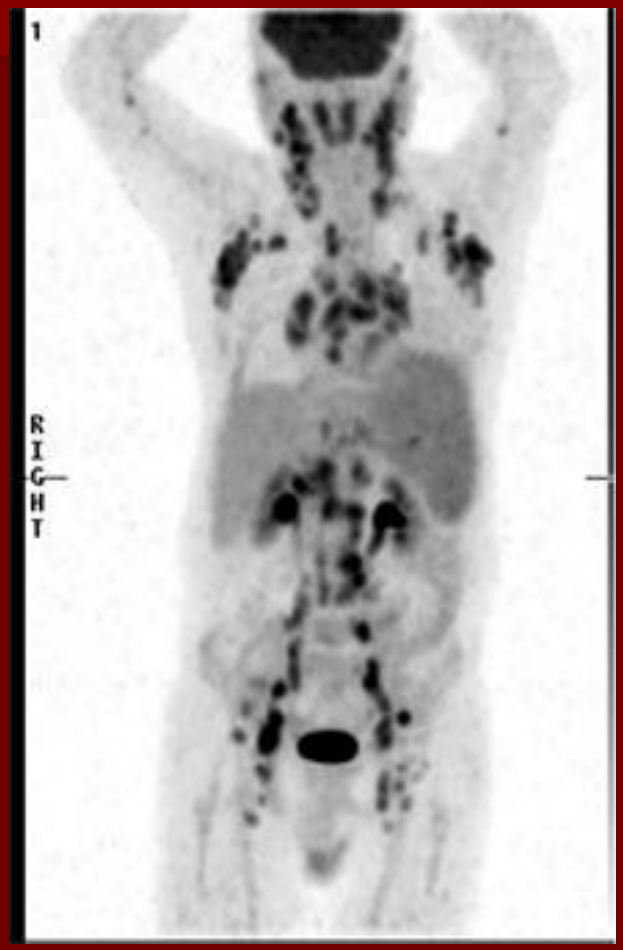
- **Comments:**
  78 y/o man with hepatosplenomegaly. Splenectomy specimen showed scattered gray-white nodules. The tumor cells were **positive for CD15, CD30, CD20 (partial) and negative for CD45**. Spleen is the most common extranodal site of involvement in Hodgkin's lymphoma. Primary Hodgkin's lymphoma of spleen is rare.

Hodgkin Lymphoma

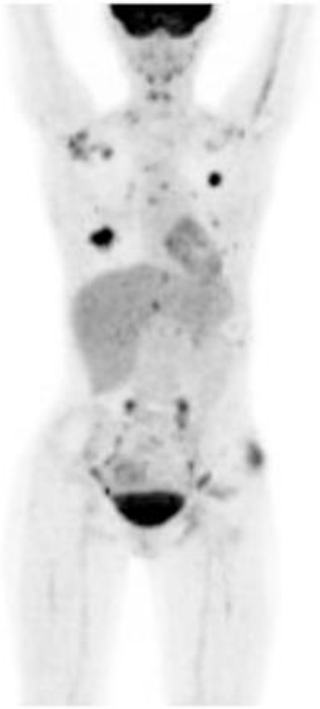


- This is a liver that is involved with Hodgkin's disease. The staging of Hodgkin's disease is very important in determining therapy. Thus, it is important to determine whether the patient has only a single lymph node region involved, multiple node regions, or extranodal involvement. This picture could probably suffice for non-Hodgkin's lymphomatous hepatic disease as well.

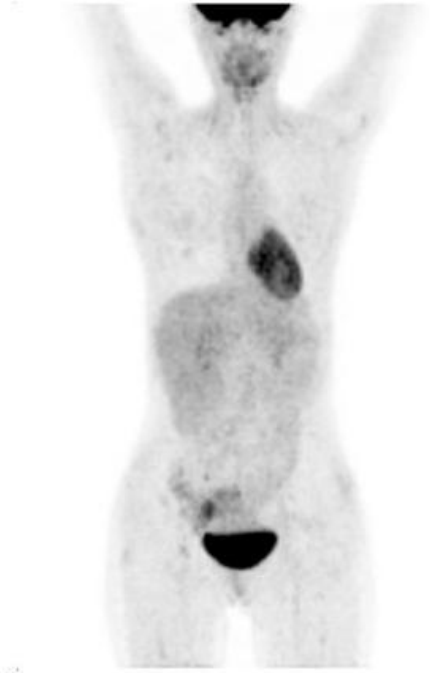
Staging of Hodgkin's lymphoma using FDG-PET



- Maximum intensity projection image of a staging FDG-PET scan of a 68-year-old man with newly diagnosed Hodgkin's lymphoma. There are markedly FDG-avid lymph nodes in a symmetrical pattern above and below the diaphragm. Note the pathological diffusely increased uptake in the spleen (more than liver uptake). FDG-PET is a more sensitive indicator of diffuse splenic involvement, which is not possible to diagnose in the absence of splenomegaly on CT.
- FDG-PET F-18 fluorodeoxyglucose positron emission



30 October 2008,
before therapy



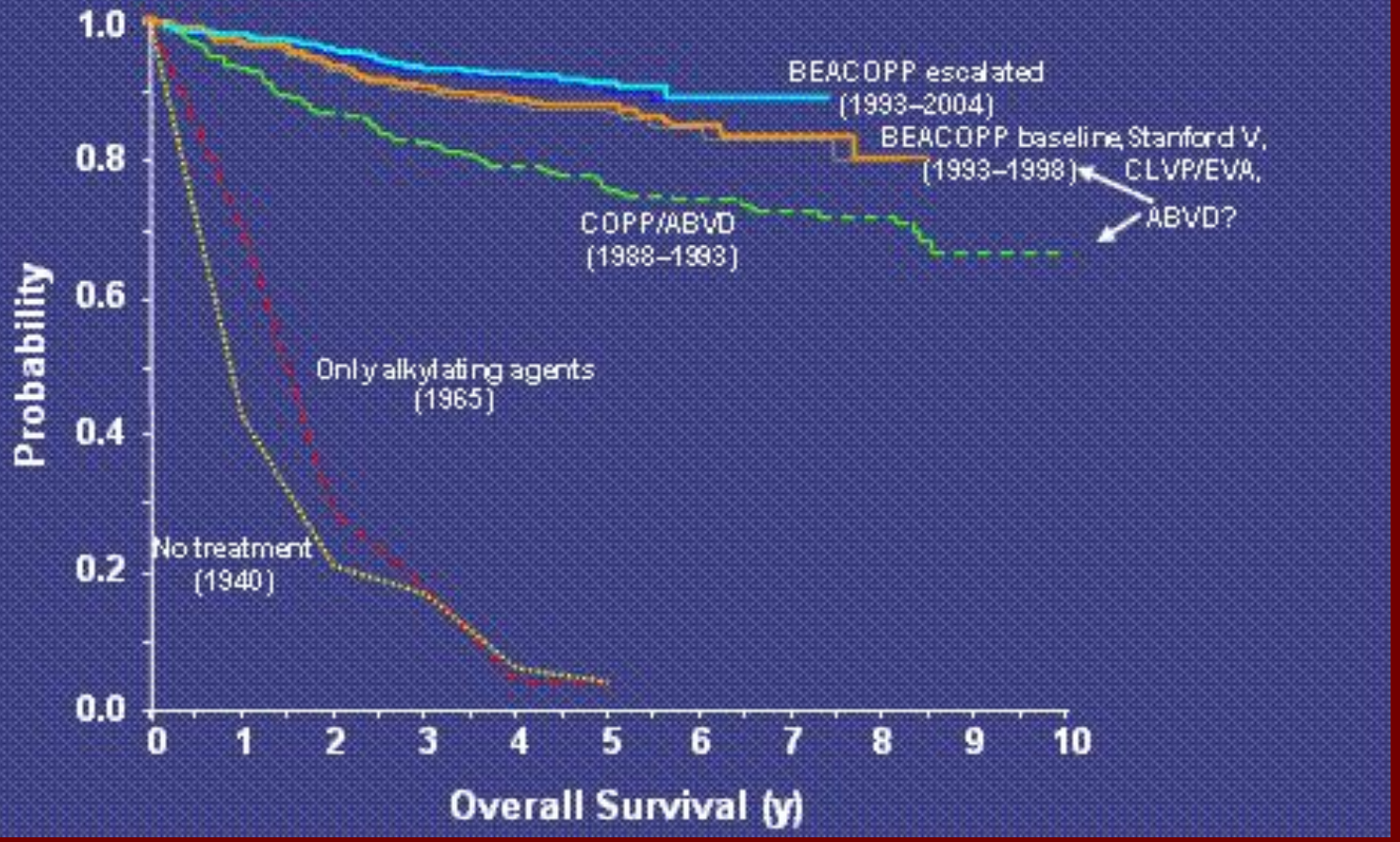
5 December 2008,
40 days after therapy

Positron emission tomography/computed tomography images of Hodgkin's disease staging

- Clinical stage I left axillary disease was upstaged to stage IIIs because of mediastinal nodal and splenic involvement detected on PET/CT.

Hodgkin's Lymphoma

Progress in the Treatment of Advanced Stages Since 1940



The 301,000 cases of non-Hodgkin Lymphoma (NHL) that occurred in 2002 (2.8% of all cancers) comprise an extremely heteroge-neous group of malignancies displaying distinct behavioral, prognostic, and epidemiological characteristics. Advances in molecular biology, genetics, and immunology have resulted in extensive changes in the classification of lymphoid tumors in the last few decades. The WHO classification74 distinguishes tumors primarily by cell lineage defined by immunophenotype and groups together lymphomas and leukemias, acknowledging that some solid tumors also pass through circulating leukemic phases. Three broad categories are now recognized: B-cell neoplasms, T/NK-cell neoplasms, and Hodgkin disease. Lymphocytic leukemias fall within the B-cell neoplasm group.

NHLs are slightly more common in developed countries (50.5% of cases worldwide), with rates highest in Australia and North America, intermediate in Europe (except eastern Europe) and the Pacific islands, and relatively low throughout Asia and eastern Europe. In most African populations, incidence of NHL is not high overall, but the relative frequency is above the world average in sub-Saharan Africa because of the high incidence of Burkitt lymphoma in children in the tropical zone of Africa. The relatively high esti-mated incidence in females in central Africa is a consequence of high relative
frequency of such cancers in the few available datasets from this area.

There have been marked increases in the incidence of NHL in many parts of the world. While this may in part be due to improved diagnostic procedures and changes in classification, there can be little doubt that much of the change is real and the reasons for it have been the subject of much debate. The increase is seen in both sexes across Europe since the 1960s. Increases of about 1% to 2% per year in incidence rates in both sexes by period of diagnosis are seen in Australia and, at a lower level, in South America and Asia. In the United States, the rapid rises (particularly in younger men) may be partially attributable to the onset of the AIDS epidemic in 1981, while the declines during the 1990s may be due in part to a decrease in the incidence of HIV infection and successful antiretroviral therapies.

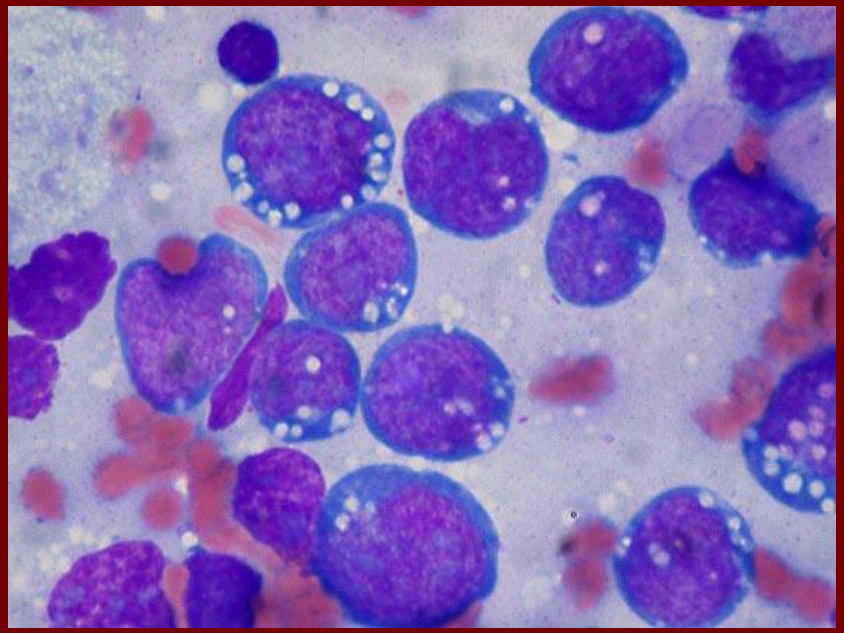
REAL: Classification for Non-Hodgkin's Lymphoma

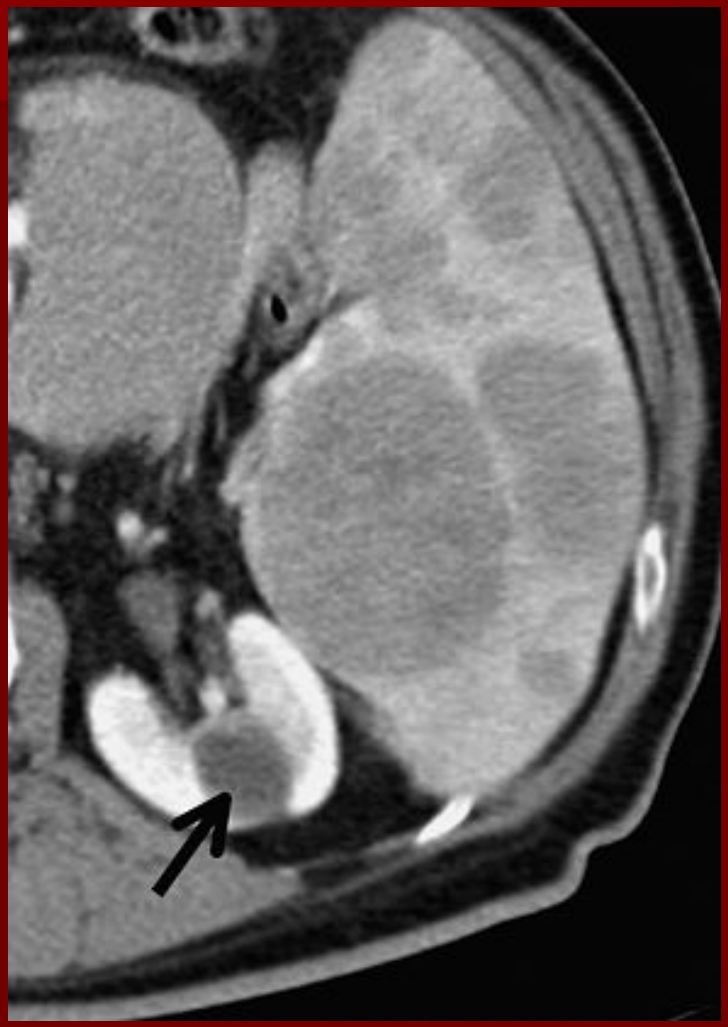
Indolent lymphomas
- Follicular lymphoma
- B-chronic lymphocytic leukemia/small lymphocytic lymphoma
- Lymphoplasmacytic lymphoma
- Marginal zone lymphoma (nodal, extranodal, splenic)
- T/natureal killer large cell granular lymphocyte leukemia
- T-chronic lymphocytic leukemia/prolymphocytic leukemia

Aggressive lymphomas
- Mantle cell lymphoma
- Diffuse large B-cell lymphoma
- Peripheral T-cell lymphoma (unspecified)
- Peripheral T-cell lymphoma (angioimmunoblastic, angiocentric
- T/natural killer cell, hepatosplenic γ/δ, intestinal T cell lymphoma,
- Anaplastic large cell lymphomas

Highly aggressive lymphomas
- Precursor T or B lymphoblastic leukemia/lymphoma.
- Burkitt and Burkitt-like lymphoma.
- Adult T-cell leukemia/lymphoma (HTLV-1+)

BURKITT LYMPHOMA





- Non-Hodgkin lymphoma. Contrast-enhanced CT shows multiple low-attenuation nodules replacing most of them splenic parenchya. Also note renal involvement (*arrow*) by lymphoma

Stenting Through a Portacath for Totally Occluded Superior Vena Cava in a Case of Non-Hodgkin's Lymphoma