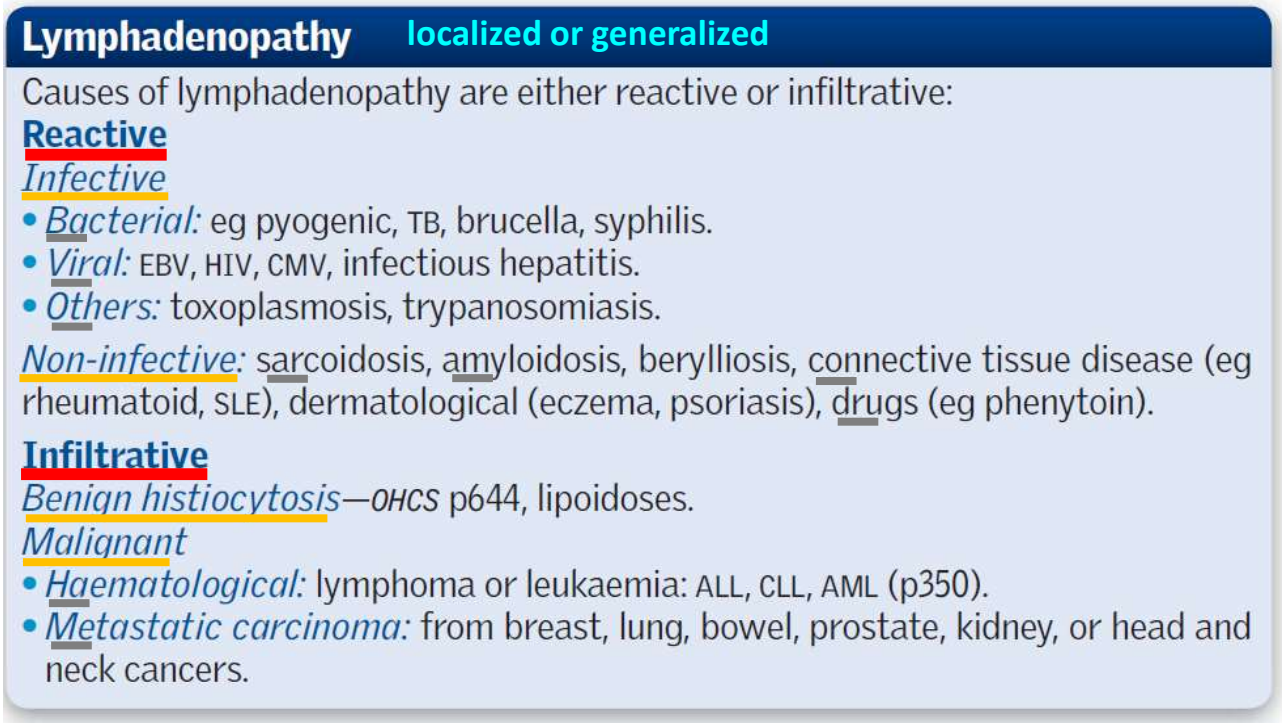


- **Lymph node open biopsy** – The choice in descending order of preference is supraclavicular, neck, axilla, and groin since the chances of a nonspecific result are greatest with axillary and inguinal nodes, and the frequency of the main complications of lymph node biopsy, infection, and damage to the neurovascular structures is higher in the groin and axilla.

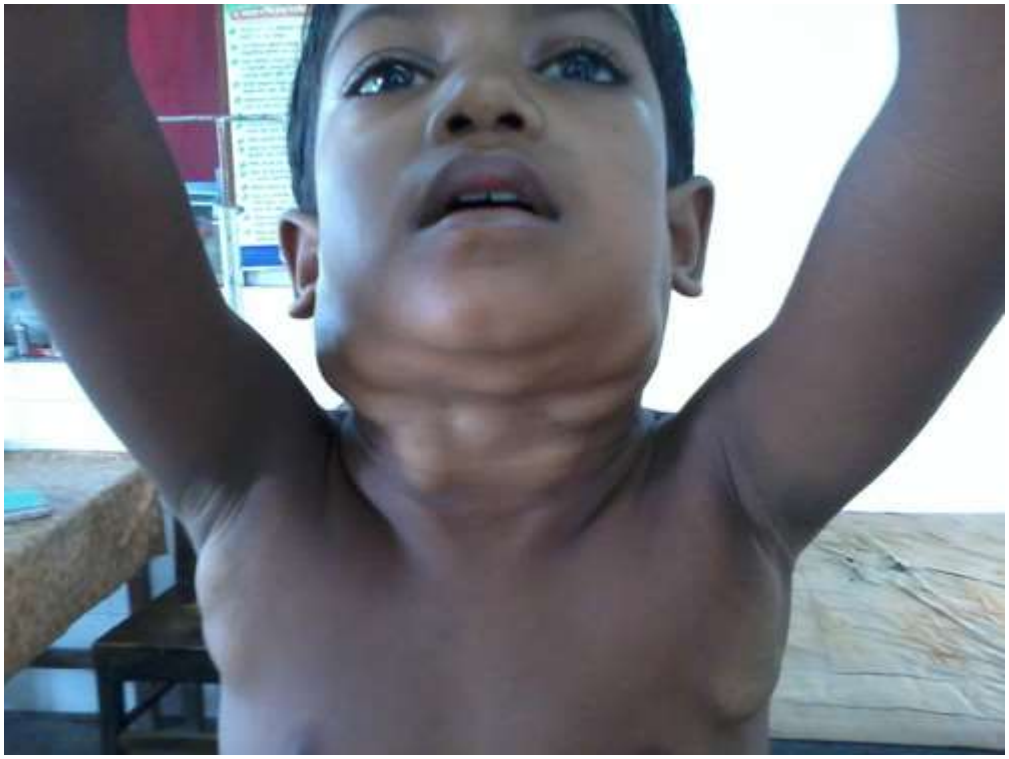
- **Fine-needle aspiration for cytology** –Lack of information on tissue architecture is a specific problem with this technique when lymphoma is suspected.

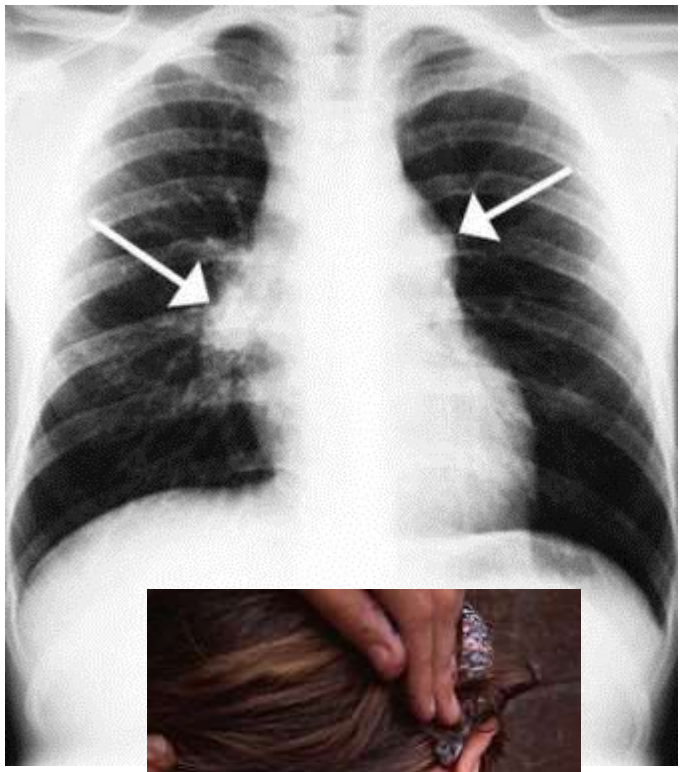
Physical examination:

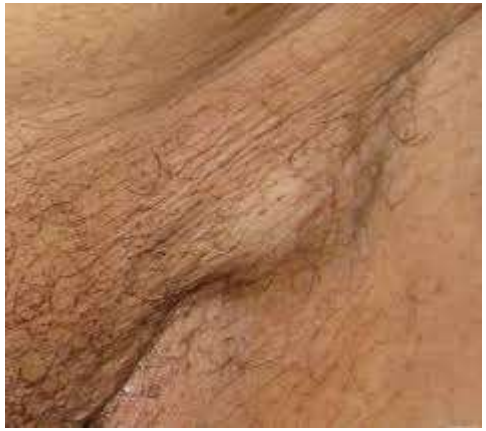
- **Localized versus generalized adenopathy.**
- **Size** – abnormal nodes are generally **>1 cm** in diameter.
- **Consistency** – **hard** nodes are found in cancers that induce fibrosis (scirrhous changes) and when previous inflammation has left fibrosis, **rubbery** nodes are found in lymphomas and chronic leukemia; nodes in acute leukemia tend to be **softer**.
- **Fixation** – Normal lymph nodes are **freely movable** in the subcutaneous space. Abnormal nodes can become **fixed to adjacent tissues** (eg, deep fascia) by invading cancers or inflammation in tissue surrounding the nodes. They can also become **fixed to each other** ("matted") by the same processes.
- **Tenderness** – **suggests recent, rapid enlargement** that has put pain receptors in the capsule under tension. This typically occurs with inflammatory processes but can also result from hemorrhage into a node, immunologic stimulation, and malignancy.
- A complete physical examination should also be performed to look for signs of systemic disease. For example, **associated splenomegaly** suggests lymphoma, chronic lymphocytic leukemia, acute leukemia, or infectious mononucleosis.

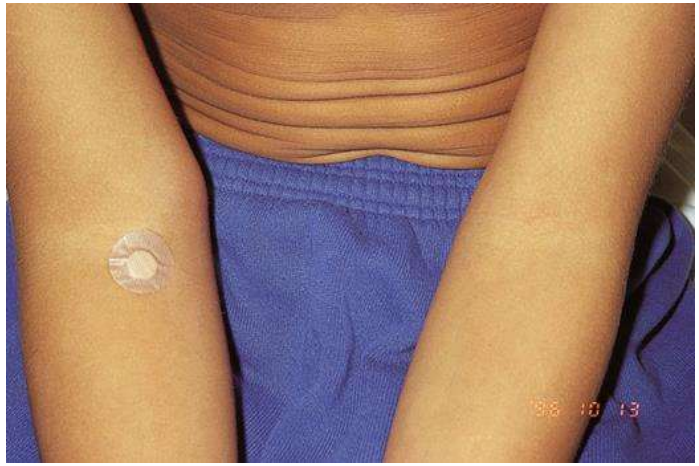
Imaging:
computed tomography (CT), ultrasound, doppler technology, or magnetic resonance imaging (MRI)

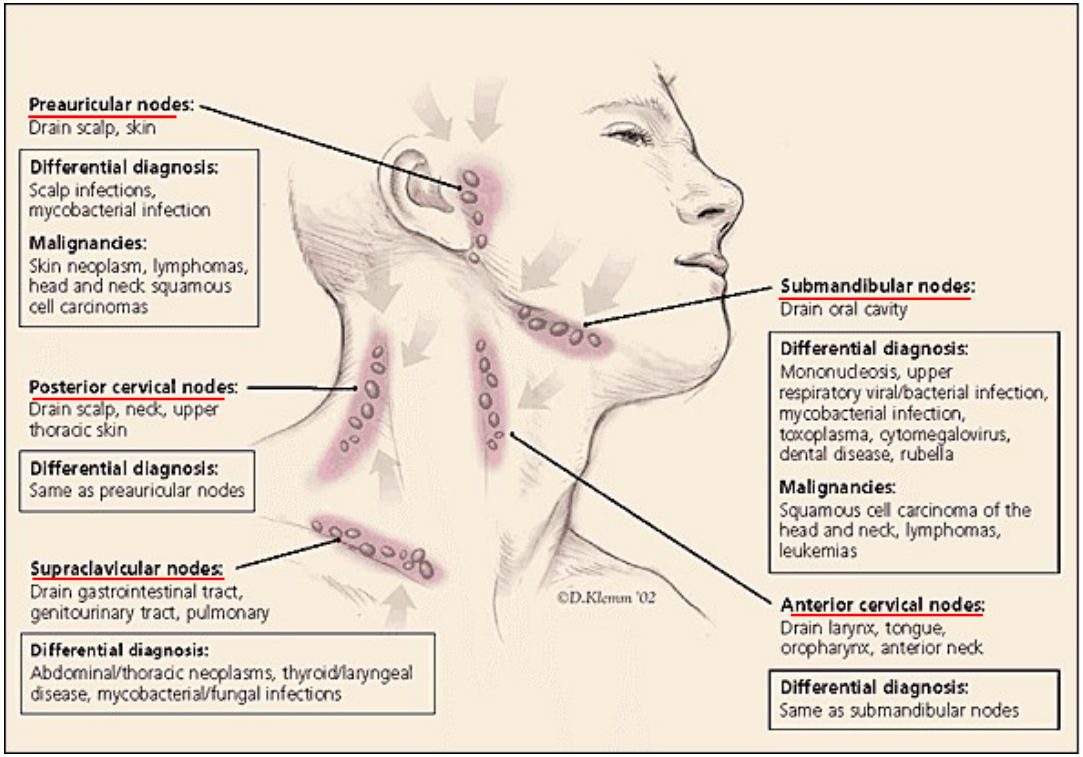
LOCALIZED VERSUS GENERALIZED LYMPHOADENOPATHY

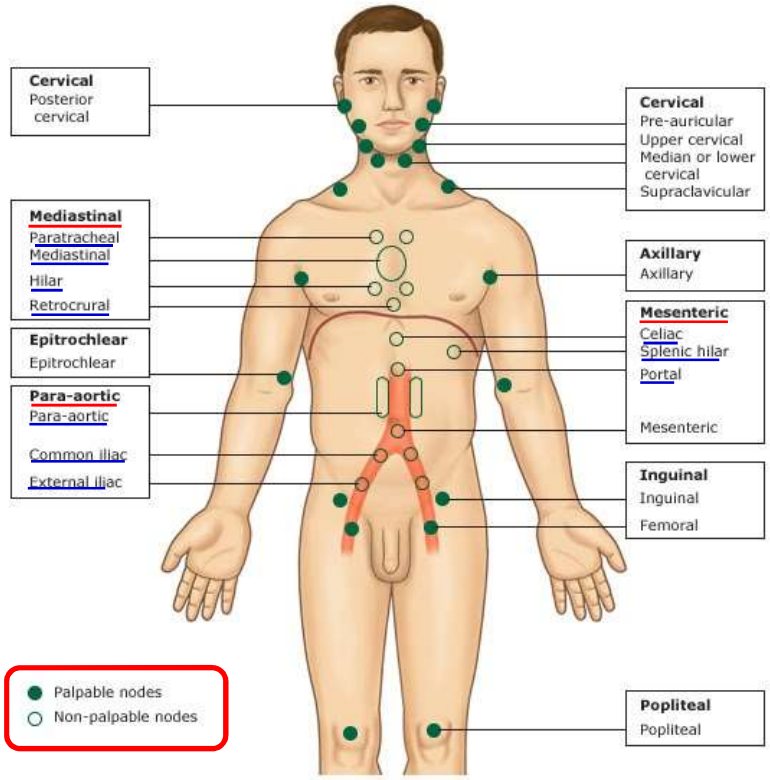


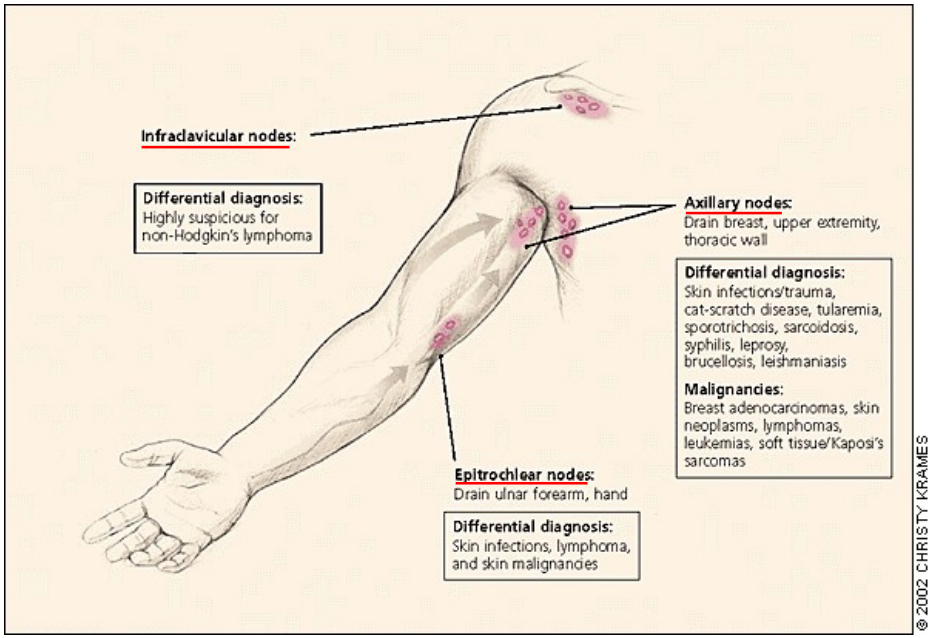







Preauricular nodes:
Drain scalp, skin
Differential diagnosis:
Scalp infections, mycobacterial infection
Malignancies:
Skin neoplasm, lymphomas, head and neck squamous cell carcinomas
Posterior cervical nodes:
Drain scalp, neck, upper thoracic skin
Differential diagnosis:
Same as preauricular nodes
Supraclavicular nodes:
Drain gastrointestinal tract, genitourinary tract, pulmonary
Differential diagnosis:
Abdominal/thoracic neoplasms, thyroid/laryngeal disease, mycobacterial/fungal infections
©D.Klemm '02
Submandibular nodes:
Drain oral cavity
Differential diagnosis:
Mononucleosis, upper respiratory viral/bacterial infection, mycobacterial infection, toxoplasma, cytomegalovirus, dental disease, rubella
Malignancies:
Squamous cell carcinoma of the head and neck, lymphomas, leukemias
Anterior cervical nodes:
Drain larynx, tongue, oropharynx, anterior neck
Differential diagnosis:
Same as submandibular nodes


Cervical
Posterior cervical
Mediastinal
Paratracheal
Mediastinal
Hilar
Retrocrural
Epitrochlear
Epitrochlear
Para-aortic
Para-aortic
Common iliac
External iliac
Palpable nodes
Non-palpable nodes
Cervical
Pre-auricular
Upper cervical
Median or lower cervical
Supraclavicular
Axillary
Axillary
Mesenteric
Celiac
Splenic hilar
Portal
Mesenteric
Inguinal
Inguinal
Femoral
Popliteal
Popliteal


Infraclavicular nodes:
Differential diagnosis:
Highly suspicious for non-Hodgkin's lymphoma
Axillary nodes:
Drain breast, upper extremity, thoracic wall
Differential diagnosis:
Skin infections/trauma, cat-scratch disease, tularemia, sporotrichosis, sarcoidosis, syphilis, leprosy, brucellosis, leishmaniasis
Malignancies:
Breast adenocarcinomas, skin neoplasms, lymphomas, leukemias, soft tissue/Kaposi's sarcomas
Epitrochlear nodes:
Drain ulnar forearm, hand
Differential diagnosis:
Skin infections, lymphoma, and skin malignancies
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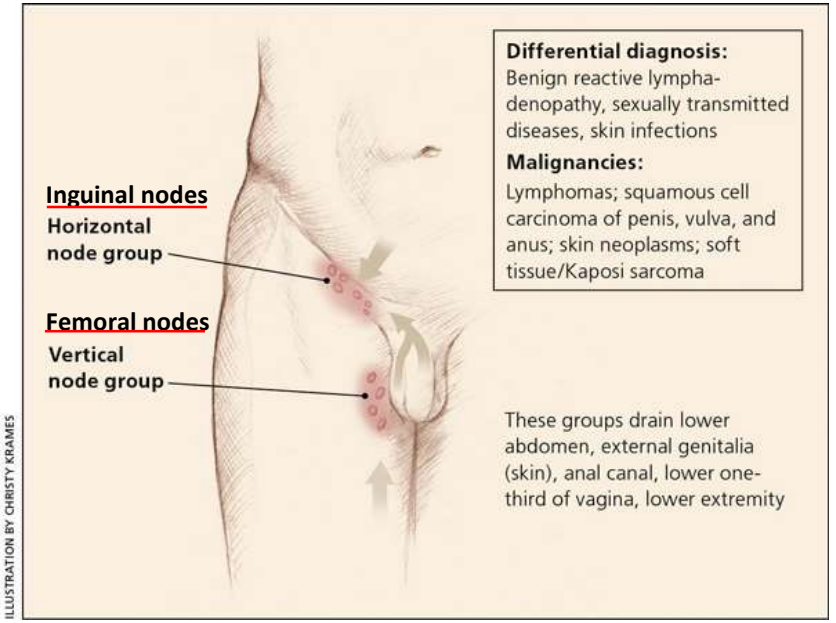

Inguinal nodes
Horizontal node group
Femoral nodes
Vertical node group
Differential diagnosis:
Benign reactive lympha-denopathy, sexually transmitted diseases, skin infections
Malignancies:
Lymphomas; squamous cell carcinoma of penis, vulva, and anus; skin neoplasms; soft tissue/Kaposi sarcoma
These groups drain lower abdomen, external genitalia (skin), anal canal, lower one-third of vagina, lower extremity
ILLUSTRATION BY CHRISTY KRAMES

Lymph node groups: Location, lymphatic drainage and selected differential diagnosis

Location	Lymphatic drainage	Causes
Submandibular	Tongue, submaxillary gland, lips and mouth, conjunctivae	Infections of head, neck, sinuses, ears, eyes, scalp, pharynx
Submental	Lower lip, floor of mouth, tip of tongue, skin of cheek	Mononucleosis syndromes, Epstein-Barr virus, cytomegalovirus, toxoplasmosiss
Jugular	Tongue, tonsil, pinna, parotid	Pharyngitis organisms, rubella
Posterior cervical	Scalp and neck, skin of arms and pectorals, thorax, cervical and axillary nodes	Tuberculosis, lymphoma, head and neck malignancy
Suboccipital	Scalp and head	Local infection
Postauricular	External auditory meatus, pinna, scalp	Local infection
Preauricular	Eyelids and conjunctivae, temporal region, pinna	External auditory canal
Right supraclavicular node	Mediastinum, lungs, esophagus	Lung, retroperitoneal, or gastrointestinal cancer
Left supraclavicular node	Thorax, abdomen via thoracic duct	Lymphoma, thoracic or retroperitoneal cancer, bacterial or fungal infection
Axillary	Arm, thoracic wall, breast	Infections, cat-scratch disease, lymphoma, breast cancer, silicone implants, brucellosis, melanoma
Epitrochlear	Ulnar aspect of forearm and hand	Infections, lymphoma, sarcoidosis, tularemia, secondary syphilis
Inguinal	Penis, scrotum, vulva, vagina, perineum, gluteal region, lower abdominal wall, lower anal canal	Infections of the leg or foot, STDs (eg, herpes simplex virus, gonococcal infection, syphilis, chancroid, granuloma inguinale, lymphogranuloma venereum), lymphoma, pelvic malignancy, bubonic plague

STDs: sexually transmitted diseases.

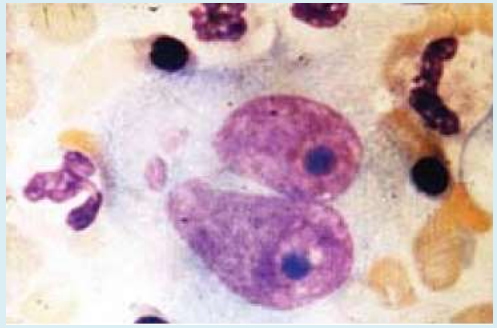
Epidemiologic clues to the diagnosis of lymphadenopathy

Exposure	Diagnosis
General	
▪ Cat	▪ Cat-scratch disease, toxoplasmosis
▪ Undercooked meat	▪ Toxoplasmosis
▪ Tick bite	▪ Lyme disease, tularemia
▪ Tuberculosis	▪ Tuberculous adenitis
▪ Recent blood transfusion or transplant	▪ Cytomegalovirus, HIV
▪ High-risk sexual behavior	▪ HIV, syphilis, herpes simplex virus, cytomegalovirus, hepatitis B infection
▪ Intravenous drug use	▪ HIV, endocarditis, hepatitis B infection
Occupational	
▪ Hunters, trappers	▪ Tularemia
▪ Fishermen, fishmongers, slaughterhouse workers	▪ Erysipeloid
Travel-related	
▪ Arizona, southern California, New Mexico, western Texas	▪ Coccidioidomycosis
▪ Southwestern United States	▪ Bubonic plague
▪ Southeastern or central United States	▪ Histoplasmosis
▪ Southeast Asia, India, northern Australia	▪ Scrub typhus
▪ Central or west Africa	▪ African trypanosomiasis (sleeping sickness)
▪ Central or South America	▪ American trypanosomiasis (Chagas' disease)
▪ East Africa, Mediterranean, China, Latin America	▪ Kala-azar (leishmaniasis)
▪ Mexico, Peru, Chile, India, Pakistan, Egypt, Indonesia	▪ Typhoid fever

HIV: human immunodeficiency virus.

Cervical lymphadenopathy and cyclic fever

A 23-year-old man presented with **malaise**, **night sweats**, **pruritus**, **loss of weight (12 kg in 6 months)** and **cyclic fever** dating from a flu-like illness 3 months previously. On examination, he had **bilateral cervical and axillary lymphadenopathy**; the glands were 2-5cm in diameter, firm, rubbery, discrete and fairly mobile. His *liver and spleen were not enlarged*. Investigation showed that his **haemoglobin** was low (11.3g/dl) and the white-cell count was normal (4200/mm^3) but his **erythrocyte sedimentation rate** (ESR) was 78mm/h; the blood film did not show any abnormal cells. *No enlargement of the hilar glands was seen on chest X-ray*. **A cervical lymph node was removed for histology.** The gross architecture of the node was destroyed; the tissue consisted of histiocytes, eosinophils, lymphocytes and giant cells known as **Reed-Sternberg cells.** These large binucleate cells are characteristic of Hodgkin's disease. A *bone marrow examination was normal* and *computed tomography showed no involvement of other lymph nodes*. This patient had **stage 2 Hodgkin's disease**, because, although only lymphoid tissue above the diaphragm was involved, his ESR was above 40mm/h. In view of his symptoms, the suffix **'B'** was added to the stage which suggests a poorer prognosis associated with systemic symptoms, so he was given **chemoradiotherapy**.



Undulant fever: due to lymphoma

Staging (Ann Arbor system) Influences treatment and prognosis. Done by CXR, CT/PET of thorax, abdo, pelvis ± marrow biopsy if B symptoms, or stage III–IV disease.

- **I** Confined to single lymph node region.
- **II** Involvement of two or more nodal areas on the same side of the diaphragm.
- **III** Involvement of nodes on both sides of the diaphragm.
- **IV** Spread beyond the lymph nodes, eg liver or bone marrow.

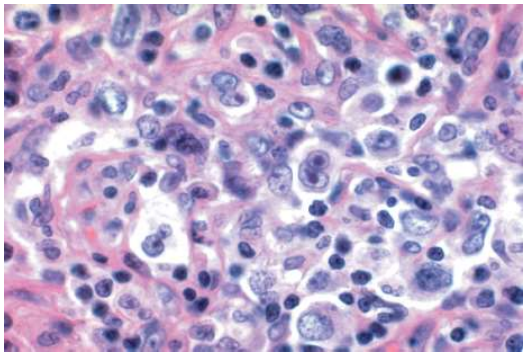
Each stage is either 'A'—no systemic symptoms other than pruritus; or 'B'—presence of B symptoms: weight loss >10% in last 6 months, unexplained fever >38°C, or night sweats (needing change of clothes). 'B' indicates worse disease. Localized extra-nodal extension does not advance the stage, but is indicated by subscripted 'E', eg I-AE.

Characteristics of Hodgkin and Non-Hodgkin Lymphomas

Characteristic	Hodgkin Lymphoma	Non-Hodgkin Lymphoma
Cells of origin	B cells	Lymphocytes (**most commonly B cells**) or natural killer cells
Classification (low to higher grade)	Nodular sclerosis (**most common**, women = men, fibrosis of lymph nodes), mixed cellularity, lymphocyte-rich (rare, best prognosis), lymphocyte-depleted (very rare, worst prognosis)	Many types, common variants include diffuse large B cell (**most common**), follicular small cell (B cells, t[14;18]), small lymphocytic (same disease as CLL), Burkitt (**EBV related**, t[8;14], **"starry sky" pattern**), peripheral (**T cells**)
Risk factors, patient population	Bimodal age distribution (peaks at 20 and 65 yr of age), men > women (except for nodular sclerosis subtype)	EBV, HIV, congenital immunodeficiencies, rheumatic disease
History and physical	Painless lymphadenopathy (**neck**), weight loss, pruritus, night sweats, fever, hepatosplenomegaly	Painless lymphadenopathy (**generalized**), weight loss, fever, night sweats
Labs	Lymph node biopsy shows **Reed-Sternberg cells** (see also Figure 6-14)	Lymph node or bone marrow biopsy shows lymphocyte proliferation (**cleaved cells seen in follicular small cell variant**)
Treatment	Radiation, chemotherapy	Palliative radiation, chemotherapy
Prognosis	**Good**, 80% cure rate unless far progressed	**Poor** (months for aggressive types, years for less aggressive variants), worsens with increasing age

CLL, chronic lymphocytic leukemia; EBV, Epstein-Barr virus; HIV, human immunodeficiency virus.

Hodgkin disease; histologic section of lymph node demonstrates pathognomonic Binucleated Reed-Sternberg cells that resemble owls' eyes.



Lymphoma

1. Malignant transformation of lymphocytes primarily in lymph nodes that can also involve bloodstream or nonlymphatic organs

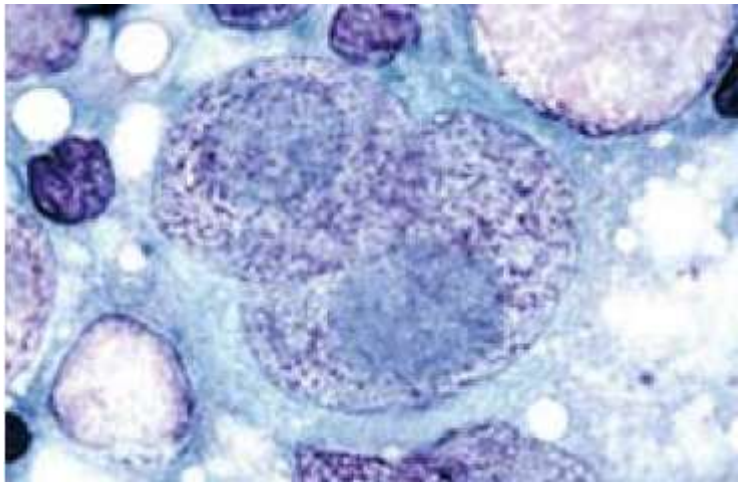
2. Categorized as Hodgkin and non-Hodgkin variants

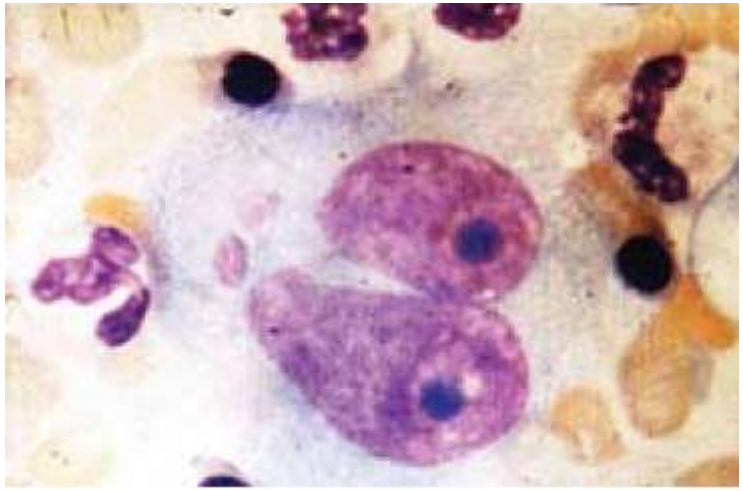
Hodgkin's lymphoma

Lymphomas are disorders caused by malignant proliferations of lymphocytes. These accumulate in the lymph nodes causing lymphadenopathy, but may also be found in peripheral blood or infiltrate organs. Lymphomas are histologically divided into Hodgkin's and non-Hodgkin's types. In Hodgkin's lymphoma, characteristic cells with mirror-image nuclei are found, called Reed–Sternberg cells (figs 1, 2, 3).

Incidence 2 peaks of incidence: young adults[1] and elderly. ♂:♀ ≈ 2:1. Risk↑ if: an affected sibling; EBV (p401); SLE; post-transplantation; westernization;[93] obese.[94]

1 HL is the leading cause of malignancy if aged 15–24yrs (+ gonadal germ-cell tumours♂ and melanoma).[98]





Reed-Sternberg cell with 2 nuclei

Symptoms Often presents with enlarged, painless, non-tender, 'rubbery' superficial lymph nodes, typically cervical (60–70%), also axillary or inguinal nodes (fig 4). Node size may increase and decrease spontaneously, and nodes can become matted. 25% have constitutional upset, eg fever, weight loss, night sweats, pruritus, and lethargy. There may be alcohol-induced lymph node pain. Mediastinal lymph node involvement can cause features due to mass effect, eg bronchial or SVC obstruction (p526), or direct extension, eg causing pleural effusions. *Pel–Ebstein fever* implies a cyclical fever with long periods (15–28 days) of normal or low temperature: it is, at best, rare.[2]

Signs Lymph node enlargement. Also, cachexia, anaemia, spleno- or hepatomegaly.

Tests *Tissue diagnosis:* Lymph node excision biopsy if possible. Image-guided needle biopsy, laparotomy or mediastinoscopy may be needed to obtain a sample. *Bloods* FBC, film, ESR, LFT, LDH, urate, Ca^{2+}. ↑ESR or ↓Hb indicate a worse prognosis. LDH is raised as it is released during cell turnover. PET (p753) also has an uncertain role.[95]

Staging (Ann Arbor system) Influences treatment and prognosis. Done by CXR, CT/PET of thorax, abdo, pelvis ± marrow biopsy if B symptoms, or stage III–IV disease.

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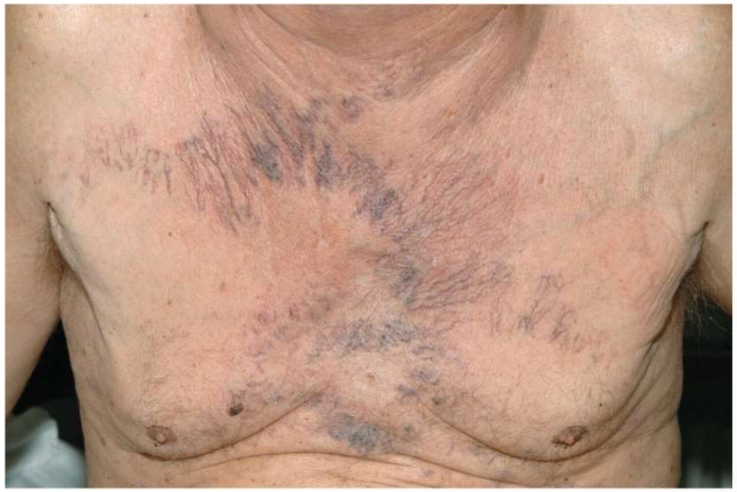
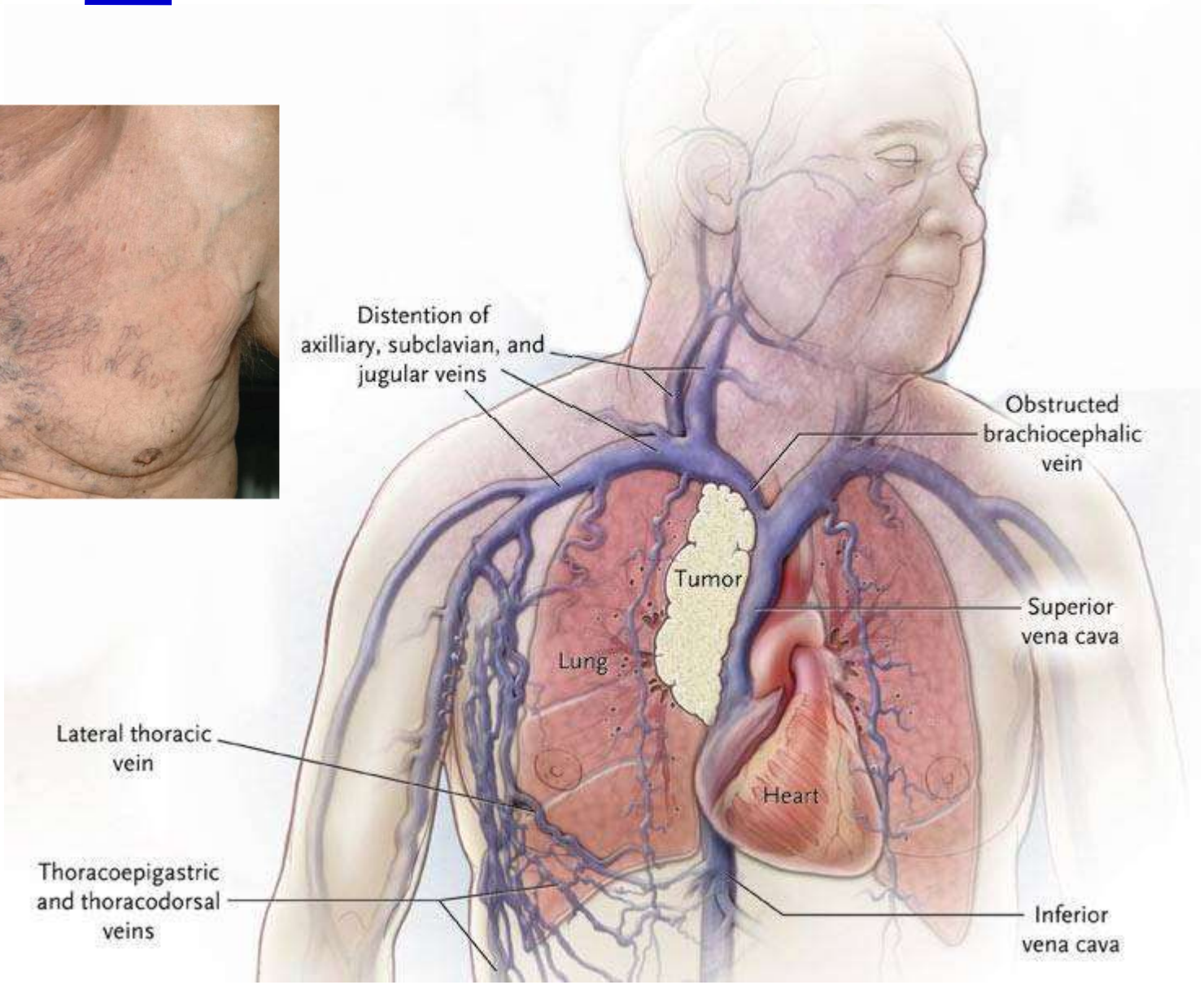
Cervical lymphadenopathy

Emergency presentations Infection; svc obstruction—JVP↑, sensation of fullness in the head, dyspnoea, blackouts, facial oedema (seek expert help; see p526).





Chemoradiotherapy Radiotherapy[2] ± short courses of chemotherapy for stages I-A and II-A (eg with ≤3 areas involved). Longer courses of chemotherapy for II-A with >3 areas involved through to IV-B. '**ABVD**': **A**driamycin, **B**leomycin, **V**inblastine, **D**acarbazine (+ radiotherapy in younger patients) cures ~80% of patients.[96] More intensive regimens are used if poor prognosis or advanced disease.[3] In relapsed disease, high-dose chemotherapy with peripheral stem-cell transplants may be used, involving autologous (or occasionally allogeneic) transplantation of peripheral blood progenitor cells to restore marrow function after therapy.[97]

Complications of treatment: See p528-9: Radiotherapy may ↑ risk of second malignancies—solid tumours (especially lung and breast, also melanoma, sarcoma, stomach and thyroid cancers), ischaemic heart disease, hypothyroidism and lung fibrosis due to the radiation field. Chemotherapy SE include myelosuppression, nausea, alopecia, infection. AML (p350), non-Hodgkin's lymphoma and infertility may be due to both chemo- and radiotherapy—see p531.

5-year survival Depends on stage and grade: >95% in I-A lymphocyte-predominant disease; <40% with IV-B lymphocyte-depleted.

3 Eg BEACOPP (bleomycin/etoposide/doxorubicin/cyclophosphamide/vincristine/procarbazine/prednisone). In IIB, III, or IV, BEACOPP gives better initial control, but 7yr event free survival is similar: 78% *vs* 71%.[100] ***Radiotherapy*** can be guided by PET: extended field is no better (and has more SE) than involved field.[101]

A large inguinal lymph node with splenomegaly

A 59-year-old man presented with a **gradually increasing lump in his right groin** of 6 months duration, which he thought was a 'hernia'. This was **a large inguinal lymph node**. He had suffered repeated urethritis in the past. He had no other symptoms, but was found on examination to have **splenomegal**y (7cm below the costal margin) without hepatomegaly.
On investigation, his **haemoglobin** was low (11.8g/dl) but his white-cell count and differential were normal. His **ESR** was 58mm/h and the **lactate dehydrogenase** level was also high. His **serum immunoglobulins were all reduced**: his IgG was 5.2g/l (NR 7.2-19.0g/l); IgA 0.3g/l (NR 0.8-5.0g/l); and IgM 0.3g/l (NR 0.5-2.0g/l). Serum electrophoresis showed no monoclonal bands. **The lymph node was excised**; light microscopy showed irregular follicles with mixtures of small and large cells throughout but no organized germinal centres. Reactive follicular hyperplasia was a possibility but immunophenotyping of tissue sections showed monoclonality, with strong cellular staining of the multiple follicle cells with anti-IgG and anti-k antisera. Normal interfollicular T-cell staining was present. This patient had a ***follicular type of non-Hodgkin's lymphoma***.

Non-Hodgkin's lymphoma

This includes all lymphomas without Reed-Sternberg cells (p354)—a diverse group. Most are derived from B-cell lines; diffuse large B-cell lymphoma (DLBCL) is commonest.[106] Not all centre on nodes (extranodal tissues generating lymphoma include mucosa-associated lymphoid tissue, eg gastric MALT, below). Incidence has doubled since 1970 (to 1:10,000). *Causes:* Immunodeficiency—drugs; HIV (usually high-grade lymphoma from EBV transformed cells, p401); HTLV-1, p376; *H. pylori*; toxins; congenital.

The patient *Nodal disease (75% at presentation): superficial lymphadenopathy.

*Extranodal disease (25%)—*Skin:* T-cell lymphomas: Sézary syndrome (p598 & fig 1).
Oropharynx: Waldeyer's ring lymphoma causes sore throat/obstructed breathing.
Gut: 1 *Gastric MALT* is caused by *H. pylori*, and may regress with its eradication (p401). Symptoms: like gastric Ca, with systemic features (fever, sweats). MALT usually involves the antrum, is multifocal, and metastasizes late.
2 Non-MALT gastric lymphomas (60%) are usually diffuse large-cell B lymphomas—high-grade and not responding well to *H. pylori* eradication.
3 *Small-bowel lymphomas* are IPSID (immunoproliferative small intestine disease), MALT or enteropathy/coeliac-associated intra-epithelial T-cell lymphoma—presents with diarrhoea, vomiting, abdominal pain, and weight↓. Poor prognosis.
Other possible sites: Bone, CNS, and lung.

*Systemic symptoms—fever, night sweats, weight loss (less common than in Hodgkin's lymphoma, and indicates disseminated disease).

*Pancytopenia from marrow involvement—anaemia, infection, bleeding (↓platelets).

Overview: Non-Hodgkin's Lymphoma (NHL)

- Most commonly occurring hematological cancer
- Fifth leading cause of cancer death in the US (SEER)
- Second fastest-growing cancer in the US (in terms of mortality rate)
- 85% of all NHLs are B-cell lymphomas

Major Non-Hodgkin's Lymphoma Types

Category	Percentage Incidence
Diffuse large B-cell	31
Follicular small B-cell	22
Marginal zone B-cell, MALT	8
Peripheral T-cell	7
Small B-lymphocytic (CLL)	7
Mantle Cell Lymphoma	6
Primary mediastinal large B-cell	2
Anaplastic large T/null cell	2
High grade B-cell, Burkitt-like	2
Marginal Zone B-cell, nodal	2
Precursor T-lymphoblastic	2

Tests *Blood:* FBC, U&E, LFT. ↑LDH≈worse prognosis, reflecting ↑cell turnover. *Marrow and node biopsy* for classification (a complex, changing quagmire, based on the WHO system of high- or low-grade). *Staging* Ann Arbor system (p354)—CT/MRI of chest, abdomen, pelvis. Send *cytology* of any effusion; LP for CSF cytology if CNS signs.

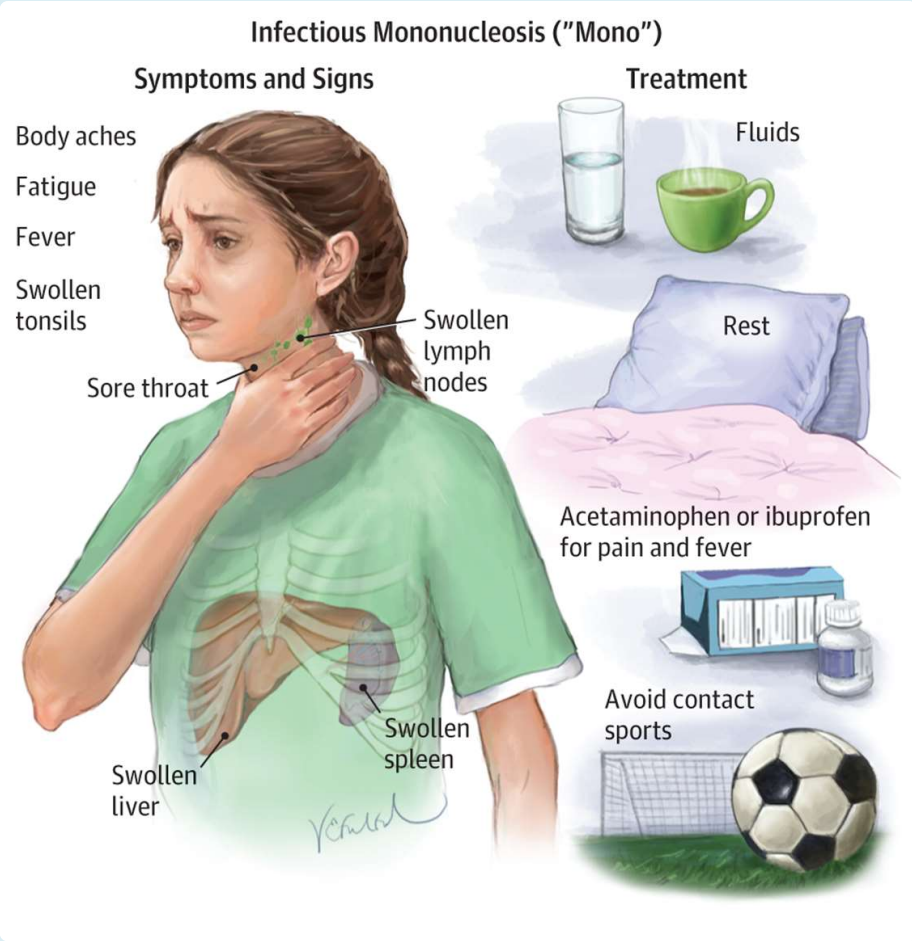
Diagnosis/management is multidisciplinary, synthesizing details from clinical evaluation, histology, immunology, molecular genetics, and imaging. *Generally:*

- Low-grade lymphomas are indolent, often incurable and widely disseminated. Include: follicular lymphoma, marginal zone lymphoma/MALT, lymphocytic lymphoma (closely related to CLL and treated similarly), lymphoplasmacytoid lymphoma (produces IgM = Waldenström's macroglobulinaemia, p364). *See* fig 2.
- High-grade lymphomas are more aggressive, *but often curable*. There is often rapidly enlarging lymphadenopathy with systemic symptoms. Include: Burkitt's lymphoma (childhood disease with characteristic jaw lymphadenopathy; figs 3 & 4), lymphoblastic lymphomas (like ALL), diffuse large B-cell lymphoma.

Treatment Depends on disease subtype. *Low grade:* If symptomless, none may be needed. Radiotherapy may be curative in localized disease. *Chlorambucil* is used in diffuse disease. Remission may be maintained by using α-*interferon* or *rituximab* (see below). *Bendamustine* is effective both with rituximab and as a monotherapy in rituximab-refractory patients.[107] *High grade:* (eg large B-cell lymphoma, DLBCL), **'R-CHOP' regimen**: *R*ituximab *C*yclophosphamide, *H*ydroxy-*d*aunorubicin, *v*incristine (*O*ncovin®) and *P*rednisolone. Granulocyte colony-stimulating factors (G-CSFs) help neutropenia—eg filgrastim or lenograstim (at low doses it may be cost-effective).[108]

Survival Histology is important. Prognosis is worse if at presentation: • Age >60yrs • Systemic symptoms • Bulky disease (abdominal mass >10cm) • ↑LDH • Disseminated disease. Typical 5-yr survival for treated patients: ~30% for high-grade and >50% for low-grade lymphomas, but the picture is very variable.

A 18-year-old student presented with a 1-week history of a **sore throat**, stiffness and tenderness of his neck, and extreme malaise. On examination, she was mildly pyrexial with posterior **cervical lymphadenopathy**, palatal petechiae and pharyngeal inflammation without an exudate. Abdominal examination showed **splenomegaly**. There was no evidence of a skin rash or jaundice. Her bilirubin and albumin levels were normal with raised liver enzyme levels (**aspartate transaminase 195 iu/l** (NR 5-45); **alanine transaminase 176 iu/l** (NR 5-30). The INR was normal. Hepatitis B surface antigen, IgM antibodies to hepatitis A virus and hepatitis C antibody were not detected.

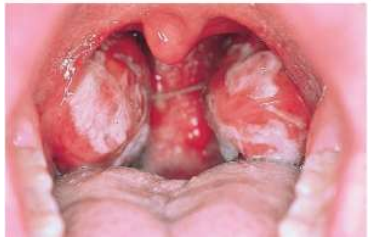


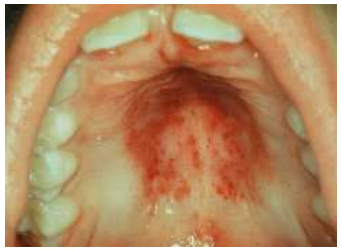
A **monospot test** for infectious mononucleosis was positive. The clinical diagnosis of infectious mononucleosis ('glandular fever') was confirmed on investigation. Her *white cell count was 13 x 10^9/l (NR 4-10 x 10^9/l) with over 50% of the lymphocytes showing atypical morphology* (**'atypical lymphocytosis**'). Her serum contained **IgM antibodies to Epstein-Barr viral capsid antigen** (VCA), the most specific test for acute infectious mononucleosis .

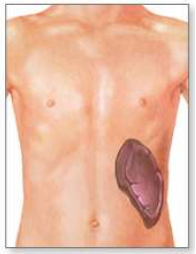
Abnormal liver test: mild acute hepatitic pattern

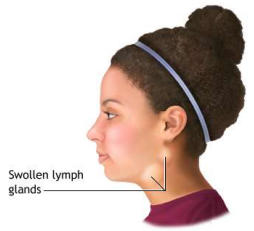
EBV and infectious mononucleosis (glandular fever)

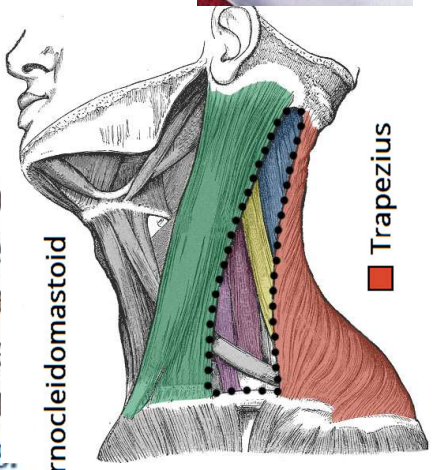
Epstein-Barr virus (EBV) infects 90% of people at some point during their lives.[144] Spread: saliva or droplet (presumed). Incubation 4–5wks. In early childhood it causes few symptoms, but adolescents/young adults may develop infectious mononucleosis. EBV also is associated with several cancers (stomach; nasal/ENT; lymphoma). EBV is a DNA herpesvirus with a predeliction for B-lymphocytes, and causes proliferation of T cells ('atypical' mononuclear cells) which are cytotoxic to EBV-infected cells. The latter are 'immortalized' by EBV infection and can, very rarely, proliferate in a way indistinguishable from immunoblastic lymphoma in immunodeficient individuals (whose suppressor T cells fail to check multiplication of these B cells).











Posterior Triangle of the Neck

The patient Sore throat, T°↑, anorexia, malaise, lymphadenopathy (esp. posterio triangle of neck), palatal petechiae, splenomegaly, fatigue/↓mood (risk is ~5–6 time that of other common upper respiratory tract infections,[145] depending in part on fea tures present at onset, eg less fit premorbidly, no delay in Monospot® becoming +ve and need for bed rest).[146] Fatigue is also part of 'severe chronic active EBV infection rare, eg with anaemia, platelets↓ & hepatosplenomegaly.[147] *Severe complications*. Meningoencephalitis, cerebellitis, Guillain-Barré, myeloradiculitis, cranial nerve lesions (eg VII, bilateral in 40%[148]), fulminant hepatitis, respiratory distress syndrome, severe thrombocytopenia/aplastic anaemia, acute renal failure, myocarditis.

Blood film Lymphocytosis and atypical lymphocytes (large, irregular nuclei, fig 1). These may occur in: viral infections (CMV, HIV, parvovirus, dengue); toxoplasmosis; typhus; leukaemia; lymphoma; drugs; lead poisoning.

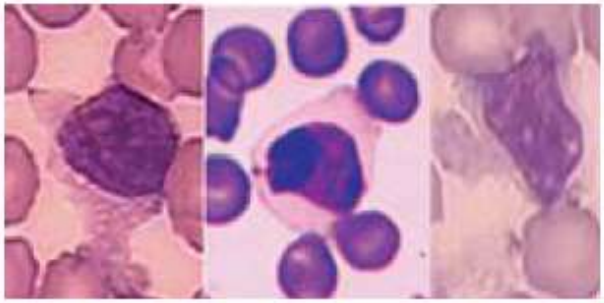


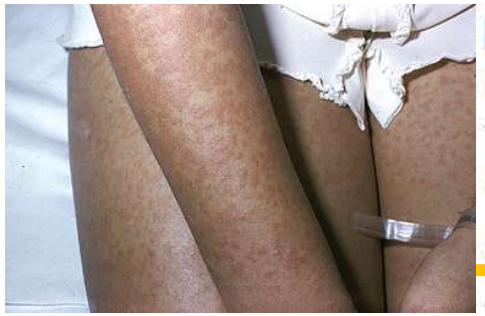
Fig 1. Atypical lymphocytes flowing round RBCs; abundant cytoplasm (dark at contact points). ©JML & A Schneider.

Heterophil antibody test (Monospot®, Paul-Bunnell) 90% show heterophil antibodies by 3wks, disappearing after ~3 months (≤1yr).[149] They agglutinate sheep RBC but are absorbed (and thus agglutination is prevented) by ox RBC, but not guinea-pig kidney cells. This pattern distinguishes them from other heterophil antibodies. They don't react with EBV or its antigens. *False +ve Monospot® tests:* Hepatitis, rubella, parvovirus, lymphoma, leukaemia, malaria, ca of pancreas, and SLE.[150] If serology is difficult, try PCR.[151]

Other false trails: Older patients may have little pharyngitis or adenopathy, but more prolonged fever and LFT↑, often with no telltale lymphocytosis or atypical lymphocytes.[152] So, if Monospot-ve, they may be subjected to dangerous over-investigation unless you request EBV-specific IgM—implies current infection (IgG reflects past infection). PCR may reveal ↑↑serum EBV DNA levels and warn of fulminant infection.[153]

ΔΔ: Streptococci (colonization seen in 30% of EBV, so throat swabs often mislead), CMV (if pregnant do CMV serology, p404, as CMV in pregnancy has important implication), viral hepatitis, HIV seroconversion, toxoplasmosis, leukaemia, diphtheria.

A generalized, erythematous, maculopapular eruption is often seen in patients with infectious mononucleosis after the administration of ampicillin.



℞: None usually needed. Patients may expect chronic fatigue when they hear the diagnosis; don't go along with this! Be optimistic (avoid *vigorous* sport; spleen rupture is reported). Avoiding alcohol 'to protect the liver' is controversial. Steroids[154] ± aciclovir[155] (p400) are sometimes used for the severest signs, listed above.[156]

Never give ampicillin or amoxicillin for sore throats as they often cause a severe rash in those with acute EBV infection (this does not indicate a life-long allergy).

Guillain-Barré syndrome

1. Autoimmune demyelinating disorder of peripheral nerves associated with recent **viral infection**, surgery, or vaccination (rare)
2. H/P
   a. Rapidly progressive **bilateral weakness** initially in distal extremities in "**stocking-glove**" distribution and extending proximally with **decreased sensation** and possible absent DTRs; possible severe neuropathic pain
   b. Recent history of viral infection, vaccination, or surgery
   c. Blood pressure, heart rate, or core temperature may be labile.
   d. Severe cases may include respiratory muscle weakness.
3. **Labs** = LP shows increased protein with normal pressure and glucose
4. **EMG** = consistent with widespread demyelination
5. **Treatment** = self-resolving within 1 month; plasmapheresis or IV immunoglobulin may accelerate resolution; patients must be watched for signs of **respiratory failure**; adequate analgesia for neuropathic pain
6. **Complications** = respiratory failure requires intubation and ventilation; most patients recover fully

EBV oncogenicity Lymphoma[157] (eg post-transplant),[158] nasopharyngeal cancer (esp. in Asia), leiomyosarcoma[159] and oral hairy leucoplakia (p238; aciclovir-responsive). A vaccine to prevent EBV cancers is being developed.[160]

Other EBV-associated diseases Crescentic glomerulonephritis;[161] haemophagocytic syndrome (EBV over-activates T cells & macrophages, with over-production of cytokines, eg causing fatal coagulopathy[162] ± central pontine myelinolysis).[163] The EBV Gianotti-Crosti rash (self-limiting papular acrodermatitis of childhood) consists of pale or red monomorphous 1–10mm papules and plaques placed symmetrically over extensor surfaces of limbs, buttocks, and face (also caused by streps, hep B, HIV, echo, Coxsackie, and respiratory syncytial viruses). forlag.fadl.dk/sample/derma/images/447.htm

Cytomegalovirus (CMV)

CMV (fig 2) is acquired by direct contact (doctors are at ↑risk),[183] blood transfusion, or organ transplantation. After acute infection, CMV becomes latent but the infection may reactivate at times of stress or immunocompromise. If immunocompetent, primary infection is usually asymptomatic, but an illness indistinguishable from glandular fever or acute hepatitis may occur. In transplant recipients or post marrow transplantation: fever > pneumonitis > colitis > hepatitis > retinitis (figs 3–5). In AIDS: retinitis > colitis > CNS disease ('>' means 'is commoner than').

Diagnosis of acute CMV infection is hard; virus growth is slow and there may be prolonged CMV excretion from past infection. Serology helps; specific IgM indicates acute infection (unreliable if HIV +ve). CMV PCR (including quantitative tests) of blood, CSF and bronchoalveolar lavage is available.

Treat only if serious infection (eg immunocompromised), with *ganciclovir* 5mg/kg/12h IV over 1h via central line, or oral *valganciclovir*, *foscarnet*, *cidofovir*. Immunization is being explored. CMV in HIV, see p410.

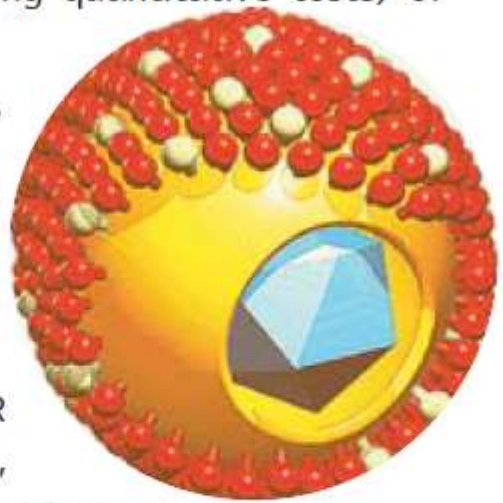


Fig 2. CMV, a herpesvirus.

Post-transplant prevention[180] Weekly PCR for 14wks to detect CMV antigenaemia/viraemia; if +ve, get help; *ganciclovir* starting dose example: 5mg/kg/12h IV if eGFR OK). Use CMV-ve, irradiated blood if transfusing transplant, HIV, or leukaemia patients. Alternative strategy: pre-emptive anti-CMV Rx (can lead to improved graft survival).[184]

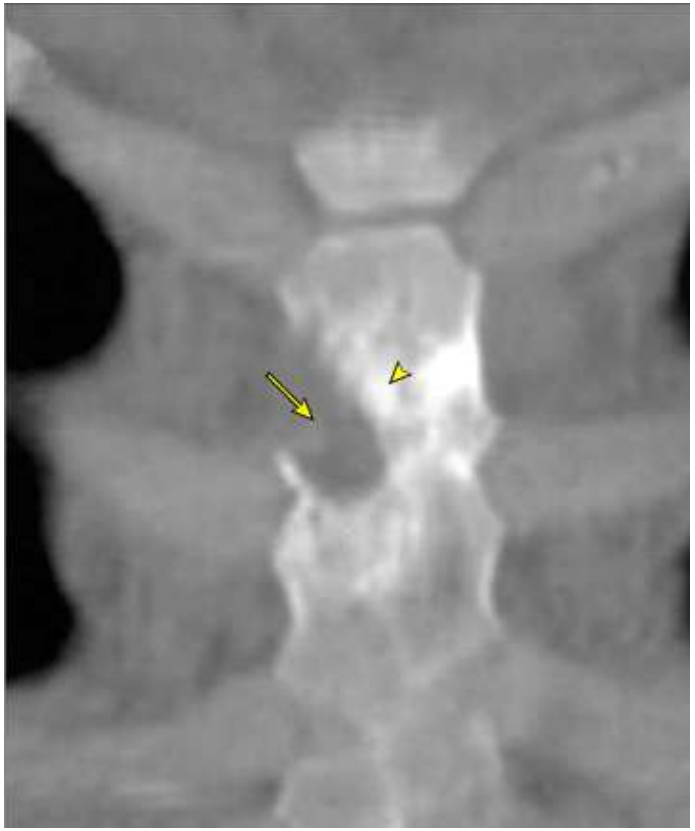
Congenital CMV (*OHCS* p34) Jaundice, hepatosplenomegaly, and purpura. Chronic defects: IQ↓, cerebral palsy, epilepsy, deafness, and eye problems. There is no treatment.

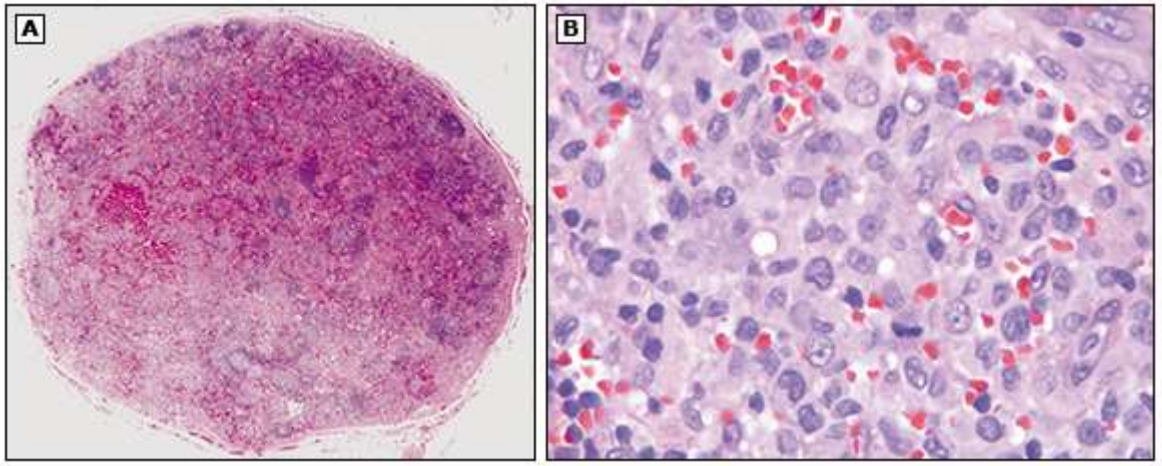
3-5 cases per million children; 1-2 cases per million adult

Langerhans cell histiocytosis (histiocytosis X) A group of disorders, either single- (in 73%, eg bone) or multisystem (in 27%; at-risk organs are liver, lung, spleen, marrow) with infiltrating granulomas containing dendritic (Langerhans) cells. ♂:♀≈1.5:1. Pulmonary Langerhans cell histiocytosis presents with pneumothorax or pulmonary hypertension. CXR/CT: nodules and cysts + honeycombing in upper and middle zones. Δ: Biopsy (skin, lung). ℞: Local excision, steroids, *vinblastine* ± *etoposide* if severe.[81] *OHCS* p644.

Paul Langerhans, 1847–1888 (German pathologist)

- **Bone**
- **Skin** (eczematous rash or ulcerative lesions)
- **Lung**
- **Central nervous system**
- **Lymph nodes and bone marrow**
- **Liver and spleen**





Langerhans cell histiocytosis extensively involving **lymph node** in a patient with widespread disease and symptoms. The Langerhans cells have inconspicuous nucleoli, thin nuclear membranes, and prominent folding of their nuclear contours, imparting a "twisted towel" appearance. (A) Low-power view showing subtotal replacement of lymph node. (B) High-power magnification showing cytologic features of Langerhans cells and a mitotic figure. Hematoxylin-eosin stains.

Thoracic CT scan shows a **solitary osteolytic lesion of the sternum** (arrow) with sclerotic margins (arrowhead) in a 38-year-old woman presenting with chest pain. A bone scan was positive in this area, as well. The resected surgical specimen showed Langerhans cell histiocytosis.

Yersinia pestis causes plague[ND], a disease of small animals and their fleas (fig 1) that can also infect us by flea bite, direct contact, or droplet. *Incubation:* 1–7d.
Signs: Flu-like symptoms, sudden fever, chills, head and body-aches, weakness, and nausea/vomiting. 3 types:

1 *Bubonic plague* is the most common form. *Yersinia pestis* enters the skin from the site of the bite and travels via lymphatics to the nearest node. Swollen nodes ('buboes') are very painful and can suppurate.
2 *Septicaemic plague* is a late complication.
3 *Pneumonic plague* is the worst kind and can be transmitted via droplets without involving fleas or animals. Untreated, it has a high mortality rate.

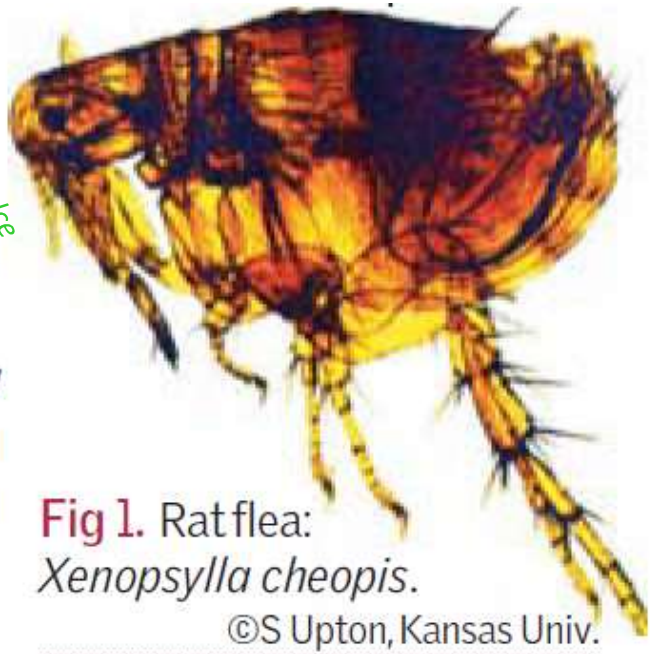
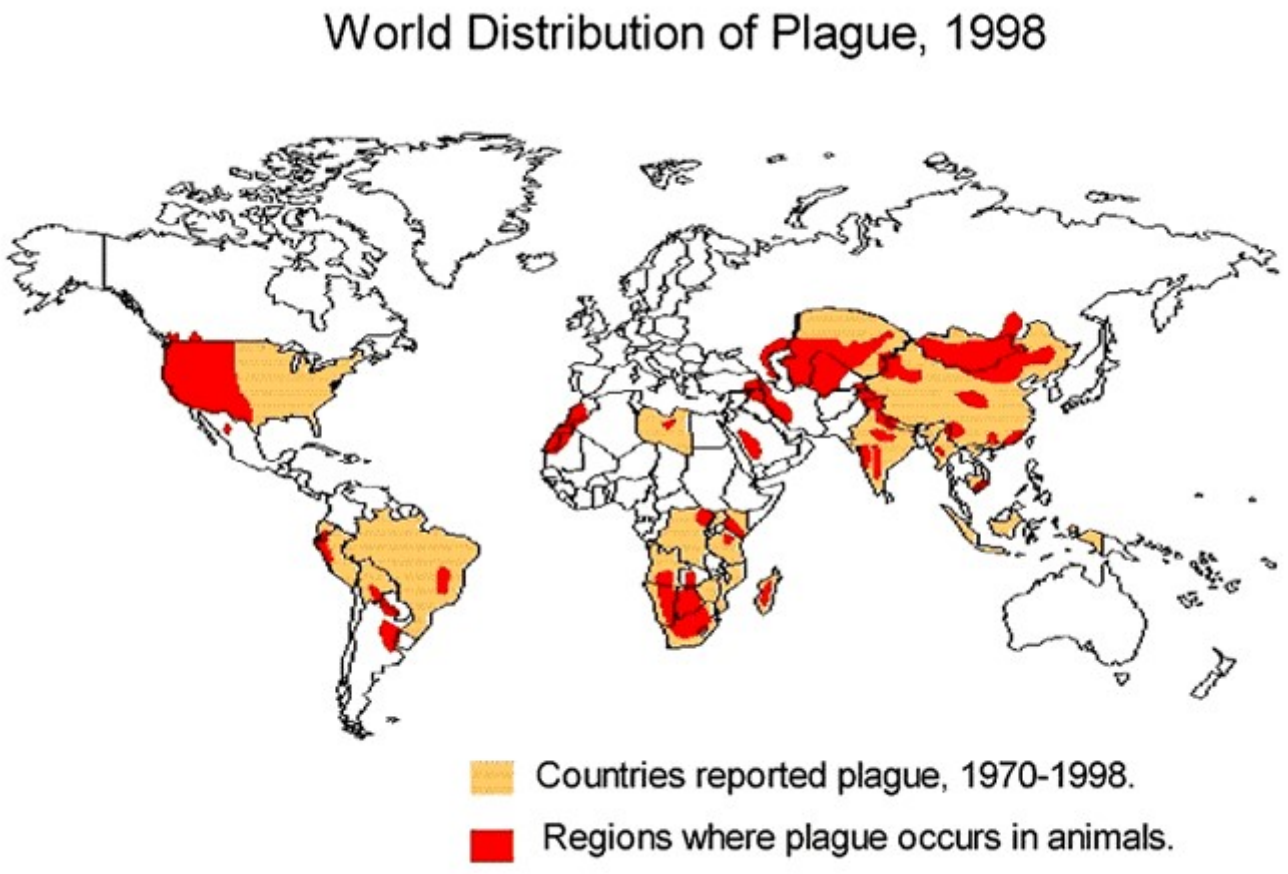


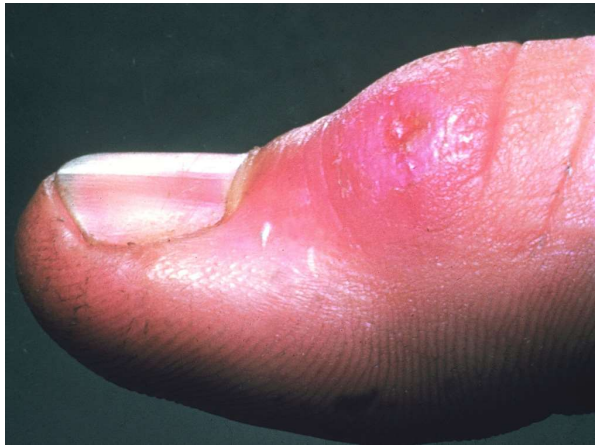
Fig 1. Rat flea: *Xenopsylla cheopis*.

Δ: Phage typing of bacterial culture, or 4-fold ↑ in antibodies to F antigen.
℞: Isolate suspects; *streptomycin* up to 15mg/kg/12h IM for 10d. If in 1st ⅓ of pregnancy, amoxicillin 500mg/8h PO; if later, co-trimoxazole 480mg/12h PO. Children: co-trimoxazole.[309] Staying at home, quarantine (inspect daily for 1wk), insect sprays to legs/bedding, and avoiding dead animals helps stop spread.
Vaccination doesn't offer instant protection, so is not recommended for immediate protection in outbreaks. It is reserved for high-risk groups (eg lab personnel).[310]

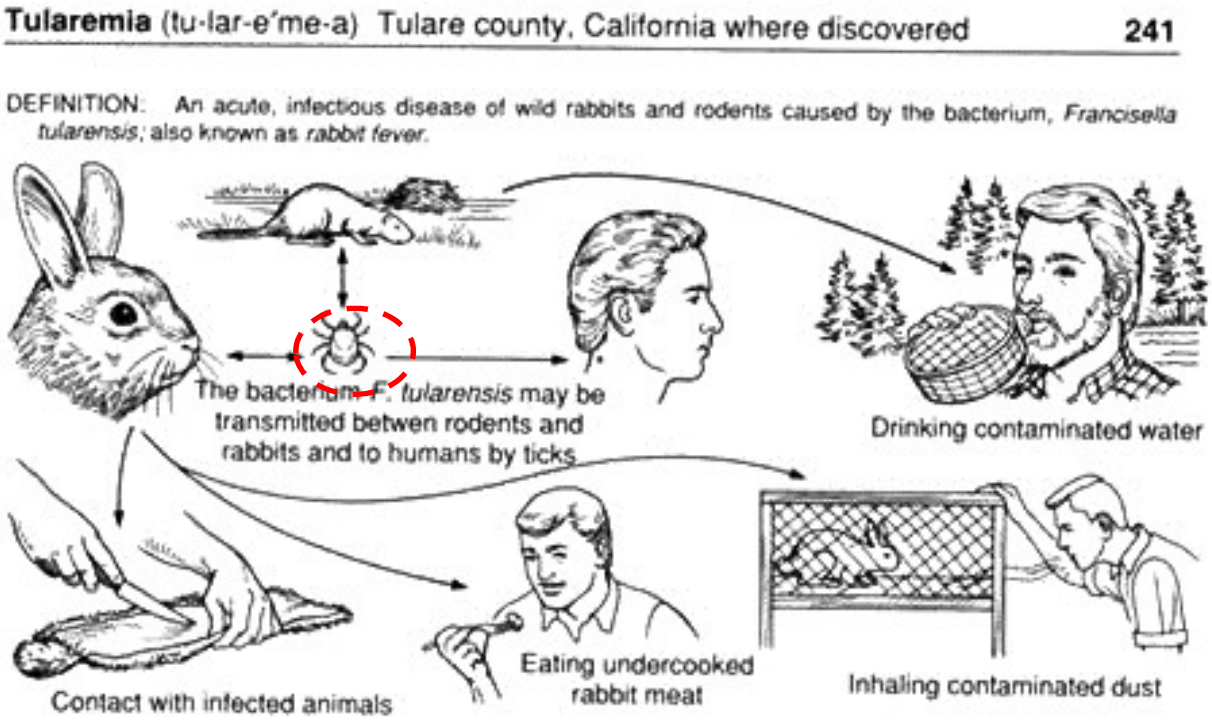


La peste è assente in Europa e in Australia.

Tularaemia (*Francisella tularensis* Gram -ve bacillus; acquired by handling infected animal carcasses). It causes rash, fever, malaise, tonsillitis, headache, hepatosplenomegaly, and lymphadenopathy ± papules at sites of inoculation (eg fingers).
Complications: Meningitis, osteomyelitis, SBE/IE, pericarditis, septicaemia.
Δ: Contact local microbiologist for advice. Only use labs with safety cabinets for dangerous pathogens. Swabs and aspirates must be transported in approved containers.
℞: Gentamicin or tobramycin. Oral tetracycline may be good for chemoprophylaxis.
Prevention: Find the animal vector; reduce human contact with it as far as possible. Vaccination may be possible for high-risk groups.

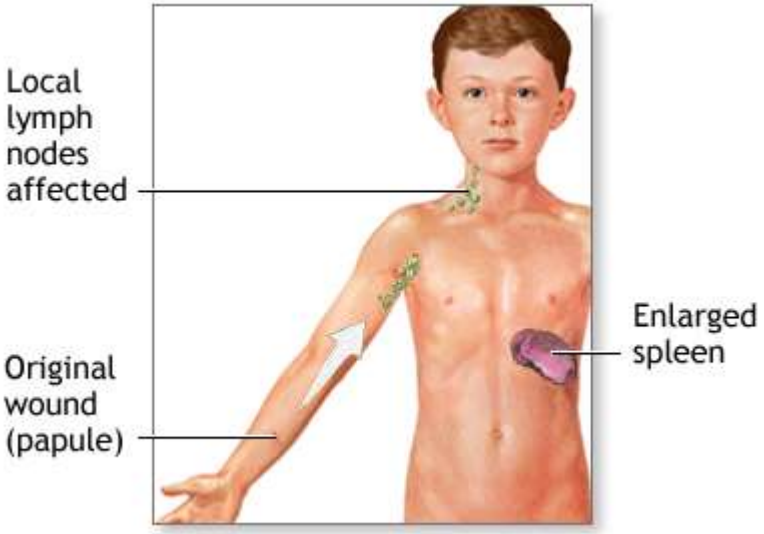


The diagnosis is usually confirmed serologically by detecting antibodies to F. tularensis



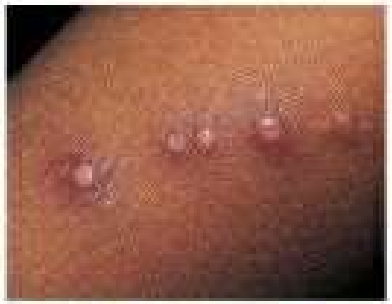
In Italia, dal 1992 al 1998, sono stati segnalati al ministero della Sanità 61 casi di tularemia, per una morbosità media pari a 0,02 casi per 100.000 abitanti

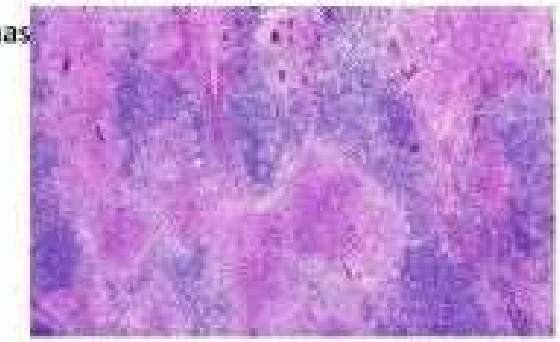
Cat-scratch disease Cause: *Bartonella henselae* (small, curved, Gram-ve rod or *Afepilis felis*—suggested by: 1 Recent cat scratch 2 Regional adenopathy (-ve tests for other causes, p29) 3 +ve cat scratch skin test antigen response 4 Microabscesses in nodes. If HIV+ve, skin lesions are like Kaposi's sarcoma. *Rx:* (Often not needed or unresponsive) Azithromycin,[319] or ciprofloxacin, rifampicin and co-trimoxazole.



Cat Scratch Disease

- Self-limited lymphadenitis usually of head and neck
- *Bartonella henselae*
- Cat scratch, splinter or thorn
- Primarily in children
- Rarely encephalitis, osteomyelitis, or thrombocytopenia
- Initially, **sarcoid-like granulomas**
- Later **stellate necrotizing granulomas**





DIAGNOSTIC TESTS

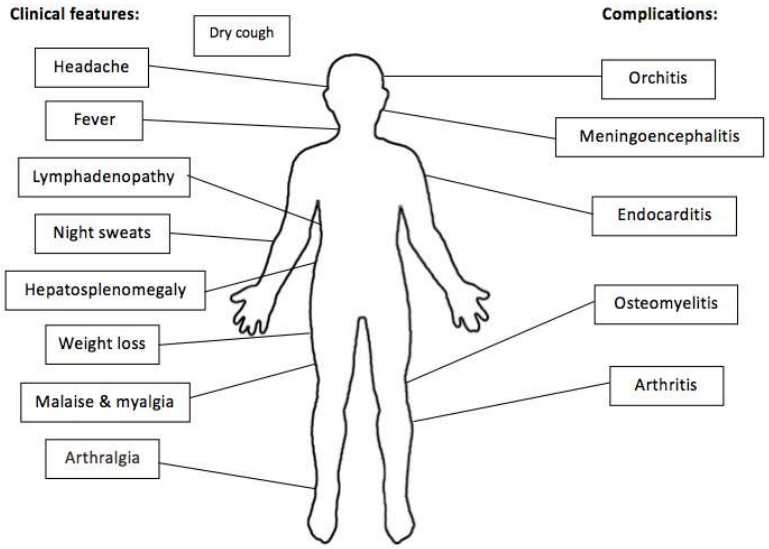
Serology — Several reference labs perform serologic testing for Bartonella.

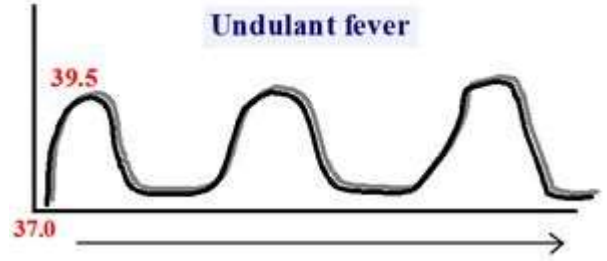
Polymerase chain reaction — Polymerase chain reaction (PCR) based tests for Bartonella on tissue or blood are available commercially.

Skin testing — The CSD skin test, which was one of the original diagnostic criteria of CSD, is no longer used since other more specific and sensitive diagnostic tools are preferred.

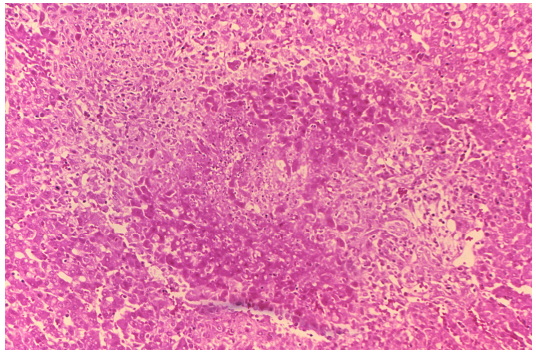
Si stima che l'8% dei gatti domestici sia infetto così come il 13% dei gatti randagi.

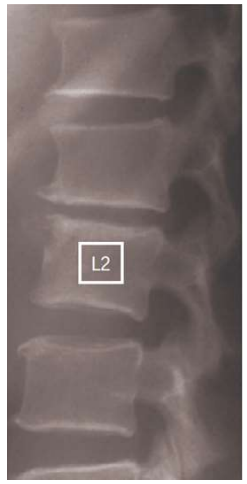
Brucellosis This zoonosis (p446) from contact with animals, their droplet exhalations, or other products, eg unpasteurized goat (or human) milk. It is common in the Middle/Far East and Bosnia, eg in vets or farmers. *Cause:* *B. melitensis* (worst sort); *B. abortus*; *B. suis/canis*. *Symptoms* may be indolent and last years: eg PUO, sweats, malaise, anorexia, weight↓, hepatosplenomegaly, rash, D&V, myalgia, backache, arthritis, spondylodiscitis (fig 2),[314] sacroiliitis, bursitis, orchitis, TIA,[315] cranial palsies (II, VI, VII), urinary retention, depression, hallucinations.[316]
Complications: Osteomyelitis, SBE/IE (culture -ve; a big cause of brucella deaths);[317] abscesses (liver, spleen, lung, breast, psoas), meningoencephalitis, myelitis, aortitis.
Δ: Pancytopenia; blood culture (≥6wks; rapid culture systems exist, contact lab); serology: if titres equivocal (≥1:40 in non-endemic zones) do ELISA ± immunoradiometric assay.
℞: ~6wks *doxycycline* 100mg/12h PO + *rifampicin* + *gentamicin* (for 7d).[318] Oral pills might engender more relapses, a *big* problem, but not, ironically, if IM leads to ↑defaulting: either way, the best doctors negotiate ~100% concordance. *Surgery:* For abscesses or SBE/IE.





The classic tissue response to Brucella is granuloma formation →





Loss of joint space between L1 & L2 + destruction of L2's anterior body.

Toxoplasmosis

The protozoan *Toxoplasma gondii* infects via the gut (poorly cooked meat; soil-contaminated vegetables), lung, or broken skin. Lifecycle: fig 1. In humans, the oocysts release trophozoites, which migrate widely (esp. to eye, brain, and muscle). Toxoplasmosis occurs worldwide. Infection is lifelong. HIV may reactivate it.

The patient ►*In any undiagnosed lymphadenopathy or any granulomatous uveitis or retinitis, think of toxoplasmosis, esp. if immunosuppressed (HIV, pregnancy).* Most infections are asymptomatic: in the UK >50% are infected by 70yrs. Symptomatic acquired toxoplasmosis resembles infectious mononucleosis, and is usually self-limiting. Eye infection, usually congenital, presents with posterior uveitis, eg in the 2nd decade of life, and may cause cataract. In the immunocompromised (eg AIDS), myocarditis, encephalitis, focal CNS signs, stroke or seizures may occur.

Tests Acute infection is confirmed by a 4-fold rise in antibody titre over 4wks or specific IgM (unreliable if HIV+ve). Reactivation of latent toxoplasmosis in HIV presents problems (you may need to look for toxoplasma antigen and IgG).[178] PCR may be rewarding.[179] Parasite isolation is difficult; lymph node or CNS biopsy may be diagnostic. CT: characteristic multiple ring-shaped contrast-enhancing CNS lesions.

Treatment Often not needed (get help).[180] If the eye is involved, or if immunocompromised, *pyrimethamine + sulfadiazine*. ►If pregnant, get help. Sampling of fetal cord blood at ~21wks for IgM indicates severe infection. For HIV, see p410.

Prevention Cook food to >63°C/145°F. Does this mean no rare meat? Perhaps only if you are immunocompromised; abandoning rare meat might not have much impact as vegetable sources still abound, and peeling and washing *everything* is impractical. Freezing meat may ↓infectivity. Wash hands after contact with soil.

Advice in pregnancy/immunosuppression: Don't change cat litter. Don't handle stray cats (esp. kittens).[181] Antenatal screening may be worthwhile in areas of high prevalence (eg in Riyadh 38% of antenatal samples are +ve for anti-T gondii IgG antibodies, indicating past exposure but not current risk).[182]

Congenital toxoplasmosis (*OHCS* p34) Abortion, seizures, choroidoretinitis (fig 2), hydrocephalus, microcephaly, cerebral calcification. Worse prognosis if early infection.

***Toxoplasma gondii*: a subtle parasite**

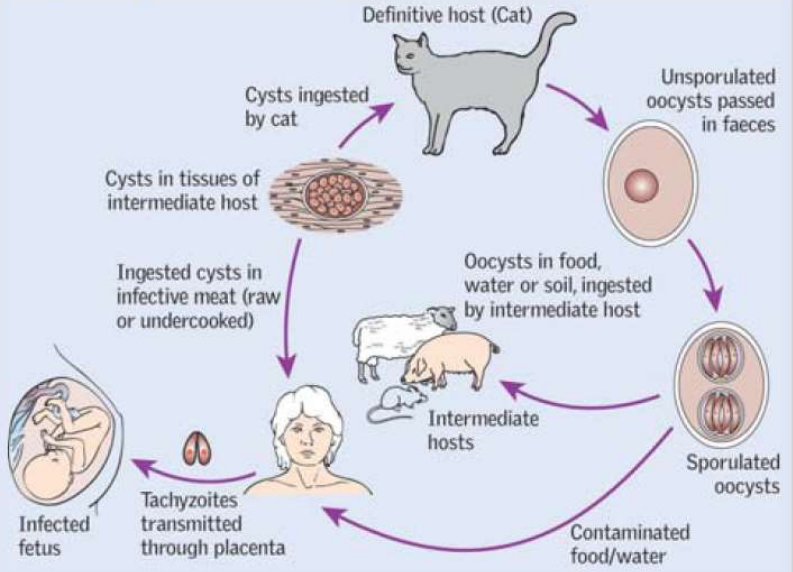


Fig 1. Oocysts in cat faeces can stay in the soil for months, where animals such as rats eat them. They get infected, and, under the direction of *Toxoplasma* in the amygdala, these rats lose their innate fear of cats, and so tend to get eaten. So parasites ensure their success by facilitating their jump from the intermediate to the definitive host. How does the parasite overwhelm the innate fear of cats? By causing a type of sexual attraction to the normally aversive cat odour (through limbic activity).[185]

Data from Fernando Monroy; www2.nau.edu/~fpm/research/res.html

Immunocompromised humans with toxoplasmosis may show these signs:

- Confusion, seizures, and signs of brainstem or spinal cord injury.
- Meningoencephalitis + localizing signs (fever+headache→drowsiness→coma→death, eg over days or weeks). CSF: mild lymphocytic pleocytosis and protein↑. Abnormal MRI, eg multifocal myelin loss; microglial nodules; ring-enhancing lesions often at the grey-white junction with subcortical white matter perifocal oedema. Within large diffuse lesions look for discrete small haemorrhagic lesions. Contrast medium may reveal fine-beaded parallel lines or small discrete nodules traversing the white matter suggesting perivenous spread.[186]
- *Pseudotumour cerebri* syndrome (p502): transient intracranial hypertension.
- ICP↑/space-occupying mass mimicking a tumour or a brain abscess.
- Multiple mass lesions that can be the cause of hemisensory abnormalities, hemiparesis, cranial nerve palsy, aphasia, and tremors.
- Acute psychosis (rare; there may be no other signs of immunodeficiency).[187]
- In some areas, eg India, toxoplasmosis is *the* major HIV-associated CNS infection.[188]

Syphilis: the archetypal spirochete

►*Any anogenital ulcer or sore is syphilis until proven otherwise.* UK incidence: >2250 infections/yr.[351] Serious outbreaks exist in the UK and USA[352–354] as safe-sex messages are forgotten, ignored, or trounced (some clubs ban condoms on 'raw nights').[355] ~70% are in men who have sex with men (rates rising since 2001, esp if black or Hispanic, aged 15–19yrs).[356] Female prevalence (screening in London antenatal clinics): 0.44% (*vs* 0.34% for HIV & 1.1% for hepatitis B).[357]

Treponema pallidum (fig 1) enters during sex, via a graze, forming the very infectious hard ulcer (chancre) of *primary syphilis*. All 4 stages are due to an endarteritis obliterans. *Incubation:* 9–90d.

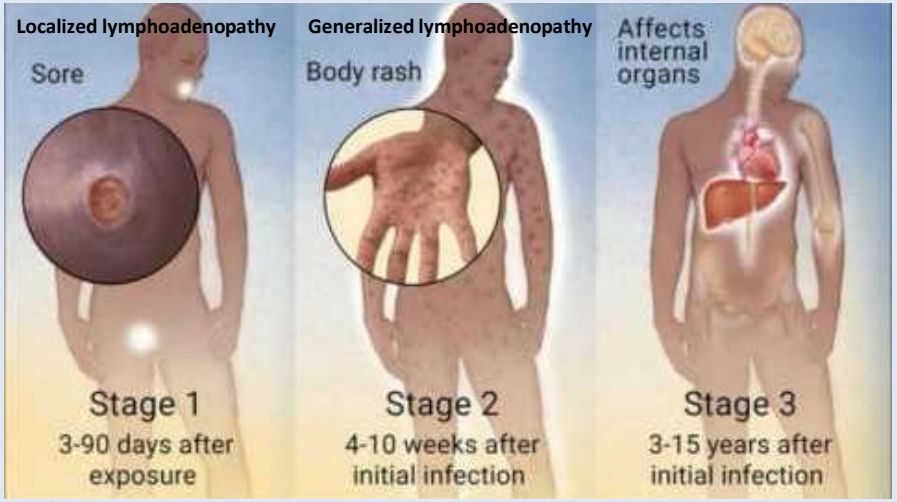
Fig 1. *T. pallidum.* ©Prof S Spilatro.

Secondary syphilis: 6 weeks to 6 months after infection: rash (trunk, face, palms, soles; may be scaly), malaise, lymphadenopathy, T°↑, tonsillitis, condylomata lata (flat papules around/beyond genitals),[358] oral snail-track ulcers, alopecia, hepatitis (in up to ⅓, esp. if HIV +ve too[359]), hepatosplenomegaly, uveitis, optic neuritis, meningism, glomerulonephritis ± periosteitis.

Tertiary syphilis follows ≥2yrs latency (when patients are non-infectious): there are *gummas* (granulomas in skin, mucosa, bone, joints, viscera, eg lung, testis).

Quaternary Vascular: Ascending aortic aneurysm/aortic regurgitation. Neurosyphilis (Δ: CSF analysis; consider if RPR titre ≥1:32) *(a) Meningovascular:* Cranial nerve palsies (eg vision↓), stroke *(b) General paresis of insane (GPI):* Dementia, psychoses/reversible dementia (fatal if untreated) *(c) Tabes dorsalis*: Ataxia, numb legs, chest & bridge of nose, lightning pains ("like a bolt from the blue"), gastric crises, reflex loss, plantars↑↑, Charcot's joints (p520). Argyll Robertson pupil (p79).

- Because **treponemal tests** have become cheaper and are more sensitive during early infection, these tests constitute the preferred **initial diagnostic test**.
- **Positive results on both a treponemal test and a nontreponemal test** are recommended to confirm the diagnosis.



Cardiolipin antibody: Not treponeme-specific. Detectable in primary disease but wanes in late syphilis. Indicates active disease and becomes -ve after treatment. *False +ves* (with -ve treponemal antibody): pregnancy, immunization, pneumonia, malaria, SLE, TB, leprosy. Examples: **Venereal Disease Research Laboratory slide test** (VDRL), **rapid plasma reagin** (RPR), **Wassermann reaction** (WR).

Treponeme-specific antibody: Positive in 1° disease, remains so despite treatment. Examples: ***T. pallidum* haemagglutination assay** (TPHA), **fluorescent treponemal antibody** (FTA), ***T. pallidum* immobilization test** (TPI). Non-specific, also +ve in non-venereal yaws, bejel, or pinta. *ELISA:* Syphilis ELISA IgG and ELISA IgM.

Other tests: In 1° syphilis, treponemes may be seen by *dark ground microscopy* of chancre fluid; serology at this stage is often -ve. In 2° syphilis, treponemes are seen in the lesions and both types of antibody tests are positive. In late syphilis, organisms may no longer be seen, but both types of antibody test usually remain +ve (cardiolipin antibody tests may wane). In neurosyphilis, CSF antibody tests (particularly FTA and TPHA) are +ve. ►*Look for other STIs.* If HIV+ve, serology may be negative during syphilis reactivation. PCR may help. Do contact tracing.

℞: Simplest regimen: 2–3 doses (1wk apart) of benzathine penicillin G 1.8g:[360] As this is only available in the UK on a named-patient basis (see *BNF*) an alternative is benzylpenicillin 0.6–1.2g/24h IM for ~28d (17d in early syphilis) + probenecid, eg 500mg/6h (to prevent penicillin loss in urine):[360]

Or doxycycline: early syphilis, 100mg/12h for 14d; late latent syphilis, 100mg/12h for 28d. Neurosyphilis, **ceftriaxone** (unlicensed) 2g/d IM for 14d. *If pregnant:* **erythromycin** 500mg/6h PO (*OTM* dose).

Beware *Jarisch-Herxheimer reaction:* T°↑, pulse↑, and vasodilatation hours after the 1st dose of antibiotic (? from sudden release of endotoxin). Commonest in 2° disease; most dangerous in 3°. Consider steroids. If HIV+ve, penicillin may not stop neurosyphilis; consult microbiologist. *Congenital syphilis: OHCS* p35.

African trypanosomiasis (sleeping sickness)

In West and Central Africa, *Trypanosoma gambiense* (fig 1) causes a slow, wasting illness with long latency. In East Africa, *T. rhodesiense* causes a more rapidly progressive illness. Uganda is the only country where both species are endemic.[397] Trypanosome parasites, spread by tsetse flies, proliferate in blood, lymphatics, and CNS, causing progressive dysfunction, then death. Prevalence: ≲70,000 in the early 2000s, but active surveillance has now stopped in some areas and mortality is increasing (now probably ~10% *vs* 5% earlier)[397] despite great work done by Stamp Out Sleeping Sickness (SOS) interventions, WHO, the Gates Foundation, Aventis, and Médecins sans Frontières.[398] Wars and famines can cause upsurges.

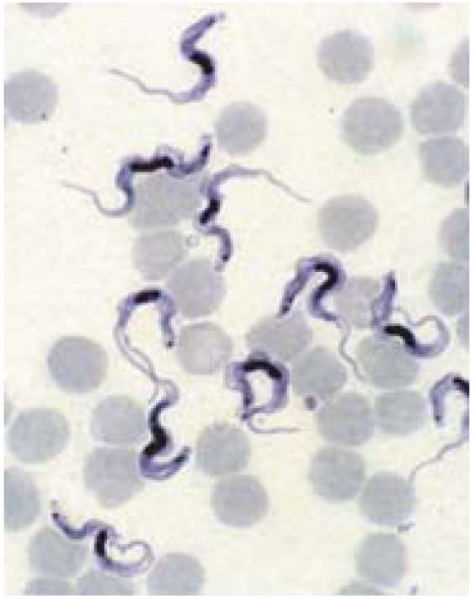


Fig 1. *T. gambiense.*
©S Upton, Kansas Univ.

Staging: A tender subcutaneous nodule *(chancre)* develops at the infection site, then...

Stage I (haemolymphatic): Non-specific fever, rash, rigors, headaches, hepatosplenomegaly, lymphadenopathy, and joint pains. Winterbottom's sign (posterior cervical nodes↑) is a reliable sign (esp. in *T. gambiense*). In *T. rhodesiense* infections, this stage may be particularly severe, with potentially fatal myocarditis.

Stage II (meningoencephalitic): Weeks (*T. rhodesiense*) or months (*T. gambiense*) after initial infection, convulsions, agitation, and confusion—and then apathy, depression, ataxia, dyskinesias, dementia, hypersomnolence, and coma occur.

Diagnosis: Microscopy shows trypomastigotes in blood film, lymph node aspirate, or CSF. Serology (eg card agglutination text) is reliable in *T. gambiense* infections.

Treatment: ►Seek expert help. Treat anaemia and other infections first; then: early (pre-CNS) phase: pentamidine isethionate 4mg/kg/d deep IM for 10d. SE: WCC↓, BP↓, Ca^{2+}↓, GFR↓, platelets↓. Alternative: suramin; SE: proteinuria, GFR↓.

CNS disease: get help. MSF regimen:[Médecins sans Frontières] **nifurtimox** 5mg/kg/8h PO for 10d + **eflornithine** 200mg/kg/12h IVI in 250mL of 0.9% saline over 2h for 7d. SE: Hb↓, diarrhoea, fits, leucopenia, hair loss. ~8% relapse (risk↑ if CSF leucocytes >20×10^9/L or ♂).[399]

American trypanosomiasis (Chagas' disease) is caused by *T. cruzi*. Spread: blood-sucking reduviids (triatomine bugs, fig 2) in Latin America and southern USA. ►Emigration means that chronic Chagas disease could turn up today in your heart or GI clinic: keep alert! Acute disease mostly affects children. A red indurated nodule (*chagoma*) forms at the site of infection; it may scar. *Signs:* (mild/insidious over 2 months): T°↑, myalgia, rash, lymphadenopathy, hepatosplenomegaly ± unilateral conjunctivitis ± periorbital oedema (*Romaña's sign*) ± myocarditis/meningoencephalitis. Chronic disease occurs after a latency of 20yrs. Multi-organ invasion causes serious dilated cardiomyopathy (p146), mega-oesophagus (dysphagia, aspiration), mega-colon (abdominal distension, constipation) + CNS lesions, eg if HIV +ve.

Fig 2. The blood-sucking vector (*Triatoma*) hides in thatch or cracks in walls (rural & urban). Transmission occurs if its faeces are rubbed into wounds or mouths (or via infected blood). ©S Upton, Kansas Univ.

Δ: (no gold standard): *Acute:* trypomastigotes seen in or grown from blood, CSF, or node aspirate. *Chronic:* serology (Chagas' IgG ELISA).

℞: Unsatisfactory. **Benznidazole** (2.5–3.5mg/kg/12h PO for 60d) or **nifurtimox** 2mg/kg/6h PO pc for 120d in acute disease (toxic, and eliminate parasites in ≤50%). Chronic disease can only be treated symptomatically. Surgery may be needed.

Prevention: Better housing, spraying houses with insecticides.

Gram-positive cocci

Staphylococci (including MRSA, p420):
- coagulase +ve, eg *Staph. aureus*
- coagulase –ve, eg *Staph. epidermidis*

Streptococci (see fig 2 and p420):
- β-haemolytic streptococci, eg *Strep. pyogenes* Lancefield group A
- α-haemolytic streptococci
  - *Strep. mitior, Strep mutans*
  - *Strep. pneumoniae* (pneumococcus)
  - *Strep. sanguis*
- Enterococci (non-haemolytic):
  - *E. faecalis* (not a typical strep)
- Anaerobic streptococci

Gram-positive bacilli (rods)

Aerobes
- *Bacillus anthracis* (anthrax: p420)
- *Corynebacterium diphtheriae* (p421)
- *Listeria monocytogenes* (p421)
- *Nocardia* species

Anaerobes:
- Clostridium
  - *C. botulinum* (botulism: p421)
  - *C. perfringens* (gas gangrene: p421)
  - *C. tetani* (tetanus: p424)
  - *C. difficile* (diarrhoea, p247)
- Actinomyces: *Actinomyces israelii* (p421), *A. naeslundii*, *A. odontolyticus, A. viscosus*

Intracellular bacteria: (o=obligate)

Chlamydia ° (p416, p162, OHCS p286)
- *C. trachomatis:* Tropical eye disease trachoma (*OHCS* p450)=serovars A–C
- GU/cervicitis (p417)=serovars B–K[10]
- lymphogranuloma ven. (p416)= L1–3[11]
- *Chlamydophila psittaci* (p162)
- *Chlamydophila pneumoniae* (p162)

Coxiella burnetii ° (p434)

Bartonella ° and *Ehrlichia* ° (p434)

Rickettsia ° (typhus, p435)

Legionella pneumophilia (p162)

Gram-negative cocci

Neisseria: *Neisseria meningitidis* (meningitis, septicaemia)
- *N. gonorrhoea* (gonorrhoea, p418)

Moraxella: *Moraxella catarrhalis* (pneumonia, p423)

Gram-negative bacilli (rods)
- *Escherichia coli*
- *Shigella* species (p426)
- *Salmonella* species (p426)
- *Citrobacter freundii; C. koseri*
- *Klebsiella pneumoniae; K. oxytoca*
- *Enterobacter aerogenes; E. cloacae*
- *Serratia marascens; Proteus mirabilis*
- *Morganella morganii*
- Providencia species; *Yersinia (Y. pestis, Y. enterocolitica, Y. paratuberculosis)*
- *Pseudomonas aeruginosa* (p422)
- *Haemophilus influenzae* (p422)
- *Brucella* species (p423)
- *Bordetella pertussis* (p422)
- *Pasteurella multocida* (p447)
- *Vibrio cholerae* (p426)
- *Campylobacter jejuni* (p390)
- Enterobacteriaceae (p390 & p422)

Anaerobes:
- *Bacteroides* (wound infections, p572)
- *Fusobacterium*
- *Helicobacter pylori* (p242)

Mycobacteria: *M. tuberculosis* (TB, p398)
- *M. bovis & M. leprae* (leprosy, p428)
- Atypical mycobacteria: ▶Suspect if immunocompromised
- *M. avium intracellulare* (p411)
- *M. scrofulaceum* — *M. kansasii*
- *M. malmoense* — *M. marinum*
- *M. xenopi* — *M. gordonae*
- *M. smegmatis*, *M. phlei*, *M. flavescens*

Spirochetes (p430): *Borrelia burgdorferi* (Lyme dis., p430); *Bor. recurrentis*
- *Treponema* (syphilis; yaws; pinta)
- *Leptospira* (Weil's dis.; canicola fever)