ACUTE LEUKAEMIAS: AML + ALL
- critically ill >30% blasts in bone marrow
  - ass/w Down’s, radiation/chemical exposure, blood disorders, PNH
- Uncontrolled clonal proliferation of haematopoietic cells results in
  replacement of normal bone marrow with malignant leukemic tissue
  → anaemia, neutropenia, thrombocytopenia, DIC 2° to procoagulant
- Clinical features: very vague until bone marrow fails
  → Fatigue, malaise, FLS, fever, night sweats, LOA, weight loss
  → Tissue infiltration: lymph nodes, skin, gums, CNS
  → Marrow failure: pain, infections, fevers, bruising, bleeding

Acute myeloid leukaemia
- Incidence 3.7/100,000, median onset age 70
- 80% of adult acute leukemias, 20% of childhood ones
- Supportive: Myxopancytopenia, fluid, antiemetics, allopurinol
- Chemotherapy: induce CR with combination chemotherapy
  (5-10% mortality) then two courses of different drugs to consolidate and intensify remission → 60% CR, 25% 5yr DFS
- BMT may be offered: 50% DFS, 30% mortality, 20% relapse

Acute lymphoblastic leukaemia
- Incidence 1/100,000, peak age 2-4 (smaller peak at age 50)
- 80% of childhood acute leukemias, 20% of adult ones
- Supportive measures as above, BMT not usually indicated
- CHILDREN: induction of combination chemo (inc. intrathecal) followed by consolidation and intensification +/- radio to sanctuary sites in brain/eye/ovary/testis + oral maintenance for 2-3yrs to consolidate cure → 90% CR, >70% 5yr DFS
- ADULTS: combination chemo +/- BMT → 40% 5yr DFS

HODGKIN’S LYMPHOMA
“rubbery” lymphadenopathy HSmegaly itch
- 20-25 cases per million each year, M=F, peak in 20-30s, ass/w EBV
- Rare lymphoid tumour characterised by presence of malignant Reed-Sternberg cells (birefringent cells of B cell origin) in lymph nodes
- Histology: >90% nodular sclerosing or mixed cellularity
- Clinical features
  → Localised or generalised painless “rubbery” lymphadenopathy
  → Systemic symptoms: itch, alcohol-induced lymphadenitis
  → B symptoms*: fever, night sweats, weight loss >10% in 6m
  → Metastatic symptoms: HSmegaly, SOB, bone pain, bm failure
- Investigations
  → FBC and blood film: microcytic anaemia, 1+/WCC, bm failure
  → ferritin, ESR, U+E, LFT, albumin, LDH, β₂-microglobulin, EBV
  → FNA of lymph node for morphology, immunohistochemistry + cytogenetics; Reed-Sternberg cells, reactive cell infiltrate
- Staging: Ann Arbor system (Ix: CXR, WBCT, PET +/- bm biopsy)
  → I – localised single area
  → II – ≥2 adjacent areas on same side of diaphragm
  → III – ≥2 areas on both sides of diaphragm
  → IV – maldistribution with extranodal infiltration of liver/lungs/bm
  → "A" or "B" depending on presence or absence of B symptoms
- Treatment: >80% overall survival rate, but risk of secondary cancer in 5-10%
  → I/IIa – localised radio +/- chemo (2xABVD) → 95%-100% cure
  → IIb / IIIa – primary chemo (4xABVD) with regional radiotherapy
  → IIIb / IV – intensive chemo (8xABVD/MOPP) then radiotherapy to residual tumours >1.5cm in size → 40-50% 5yr DFS

NON-HODGKIN’S LYMPHOMA
lymphadenopathy can cause ANYTHING
- 5-6/100,000, M=F, age >50, ass/w EBV, HIV, immunosuppression
- A spectrum of haematological cancers arising from lymphocytes and their precursors, representing up to 75% of all lymphomas
- histology: 90% B cell NHL, 31% diffuse large B cell, 22% follicular
- Clinical features
  → 67% present with lymphadenopathy +/- HSmegaly
  → 5% have primary disease affecting bone marrow
  → Extracranial presentations: (can be ANYTHING) 33% GI, 10% skin, 6% endocrine, 5% bone, 4% lung, 4% parotid, 3% CNS
- Investigations
  → FBC and blood film +/- bone marrow biopsy
  → U+E, LFT, Ca²⁺, urate, LDH, β₂-microglobulin, EBV, HTLV-1
  → Tissue biopsies of affected sites +/- relevant fluid samples
- Staging: Ann Arbor system (Ix: CXR, WBCT, PET, MRI, LP, DEXA)
  → I – single lymph node region or single extranodal organ/site
  → II – ≥2 areas on same side of diaphragm +/- adjacent organ
  → III – both sides of diaphragm +/- adjacent organs and/or spleen
  → IV – disseminated or multifocal lymph nodes +/- two extranodal sites
  → “A” or “B” depending on presence or absence of B symptoms
- Treatment: according to histological type rather than stage
  → Localised disease - surgical excision may be recommended
  → Low-grade - watch + wait, only treat if symptomatic
  → Intermediate-grade - CHOP + RITUXIMAB → 60-70% 5yr DFS
  → High-grade e.g. Burkitt’s - aggressive chemotherapy regimes

MULTIPLE MYELOMA
Bence-Jones protein lytic bone lesions >20% plasma cells in marrow
- 1% of UK cancers, M=F, 60% aged >70, ass/w farming and radiation
- Uncontrolled plasma cell proliferation results in:
  → Excess production of a single Ig class with a single light chain (paraprotein) to the detriment of normal antibody production
  → Depression of normal bone marrow function
  → Destruction of bone
- Clinical features
  → 10% incidental finding
  → 70% bone pain
  → 20% hypercalcaemia
  → 15% infections
  → 15% anaemia
  → Pathological fractures
- Investigations: FBC, blood film, ESR, U+E, Ca²⁺, LFT, albumin, lg electrophoresis for paraprotein (60% IgG type), β₂-microglobulin, urinary Bence-Jones protein, bone marrow biopsy, skeletal survey
- Diagnoses (3°) requires 2 of
  → Paraprotein in blood and/or urine (aka Bence-Jones protein)
  → Plasma cells >20% marrow nucleated cells
  → Lytic lesions on skeletal survey – common in skull
- Treatment: start when patients become symptomatic
  → Supportive: analgesia, IV bisphosphonates, electrolyte Mx
  → Chemotherapy for painful bone lesions and cord compression
  → Chemotherapy e.g. melphalan or combination regimes
  → BMT: for younger patients – not spectacularly effective

CHRONIC LEUKAEMIA
lymphadenopathy HSmegaly AIHA ITP
- Commonest leukaemia, 2.5/100,000, M:F 1.7:1, age >50, ?? genetics
- Spectrum of disorders with malignant monoclonal proliferation of mature lymphocytes which accumulate in the blood, bm, LN, spleen and liver.
  There is immunodeficiency as the cells cannot produce antibodies.
  → Cells fail to respond to apoptotic signals due to ↑Bcl-2 surface proteins
- Investigations
  → FBC: WCC >30% with >80% mature lymphs, normocytic anaemia
  → Blood film: B lymphocyte appearance of cells, “smear cells”
  → Bone marrow: >50% lymphs with evidence of infiltration
  → Treatment: median survival ~10yrs, 5-10% transform to lymphoma
  → cycles of chemotherapy
  → 2° line fludarabine, CAP, CHOP, alectuzumab, radio (no BMT)

CHRONIC MYELOID LEUKAEMIA
anaemia fatigue/malaise splenomegaly
- 1/100,000, age 40-60, ass/w Philadelphia chromosome, atomic bomb
- Rare myeloproliferative disorder arising from a single mutated haematopoietic stem cell which proliferates within the bone marrow
- Reciprocal (t(9;22) → Philadelphia chromosome which produces chimeric fusion gene BCR-ABL → encodes p210 which produces tyrosine kinase activity → uses ATP as phosphate donor to add phosphate to tyrosine residues → unregulated cell proliferation → ca.
  → Histology: 95% Philadelphia chromosome, 2.5% occult (t(9;22)
- Clinical features
  → May be asymptomatic depending on degree of anaemia
  → Non-specific fatigue, malaise, FLS/sweats, LOA, weight loss
  → Bruising
  → Splenomegaly → LUQ abdominal discomfort, early satiety
- Investigations
  → FBC: WCC >50, normocytic anaemia, 1tlasts, 1tbasophils
  → Blood film: resembles bm, all stages of myeloid differentiation
  → Bone marrow: hypercellular with ↑granulocytopenies
  → PCR for BCR-ABL: cytogenetics & FISH for t(9;22)
  → Treatment: 89% overall 5yr DFS, may progress to blast crisis
  → Oral hydroxyurea immediately to control proliferation, then ...
  → Imatinib acts as a tyrosine kinase inhibitor by inhibiting ATP binding to p210 → >95% complete response but lifelong Tx
  → Alternatively, BMT offers definitive cure but with ↑↑risks → 60% cure rate with sibling graft but 20% die and 20% relapse

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HAEMATOLOGICAL MALIGNANCIES