

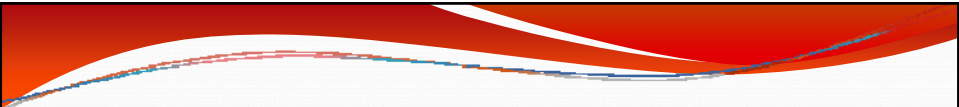
# The Haematology MDT

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12 June 2013

## Haematology – the study of blood

haematology *UK*, **hematology** *US* [hi'mə'tɒlədʒɪ] *n*  
(Medicine) the branch of medical science concerned  
with diseases of the blood and blood-forming tissues  
**haematologic**, **haematological** *UK*, **hematologic**  
*US*, **hematological** *adj*, **haematologist** *UK*,  
**hematologist** *US*

[Collins English Dictionary – Complete and Unabridged](#) © HarperCollins Publishers 1991,  
1994, 1998, 2000, 2003, 2012

- 
- Anatomy & structures involved
  - Functions & Symptomatology
  - Investigations
  - Diseases & disorders
  - Treatment
  - ...
  - Questions



## Anatomy in haematology

- Blood
- Bone marrow
- Lymph nodes
- Spleen & liver

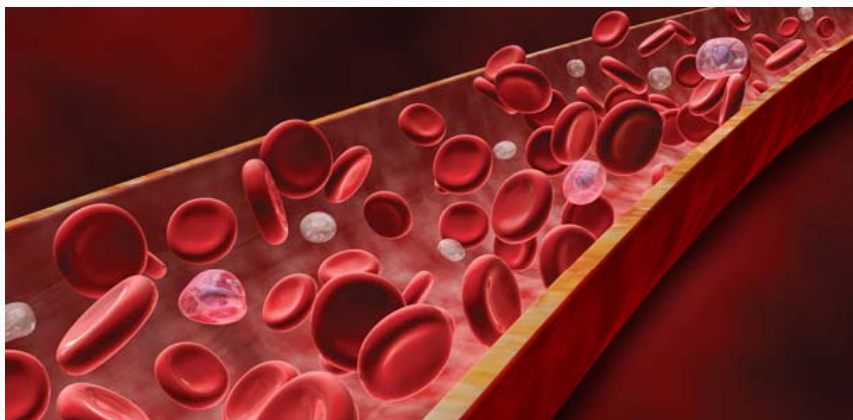
## Blood, bone marrow and lymph nodes/glands

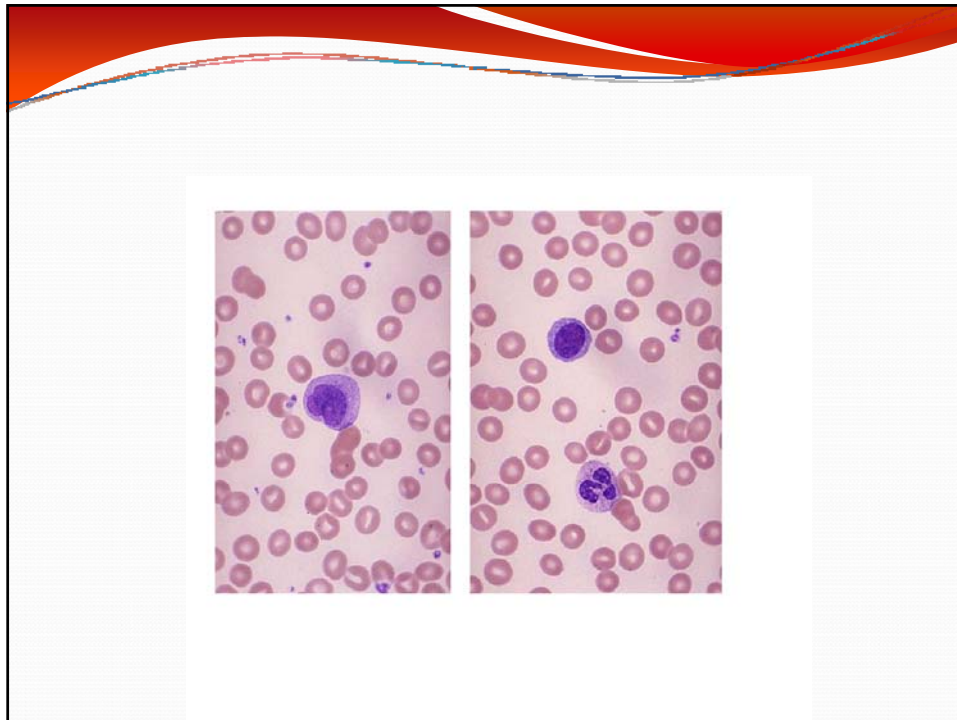
**Blood:** Transports red cells, white cells and blood platelets through the blood vessels

**Bone marrow:** factory of the blood

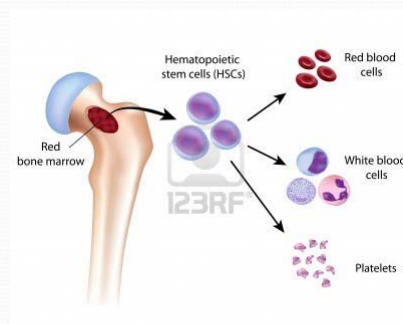
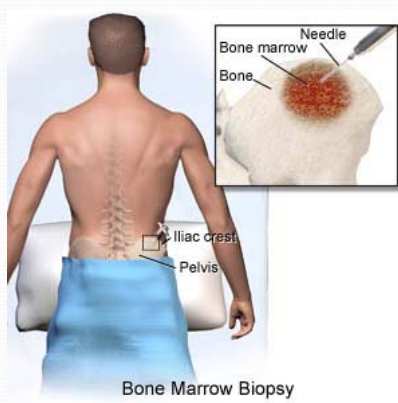
**Lymphatic system:** Runs alongside the blood vessels.

## Blood system



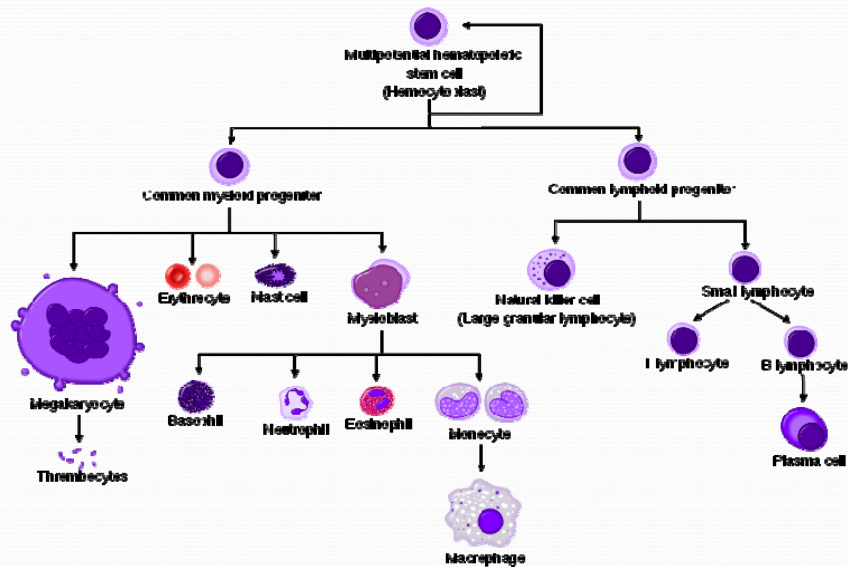
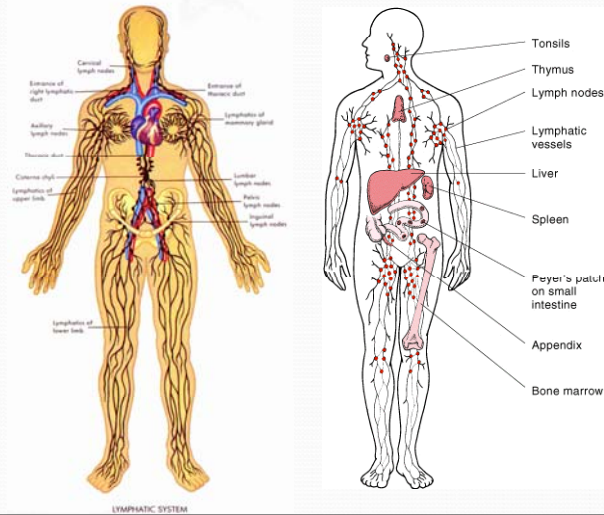


## Bone marrow – factory of the blood





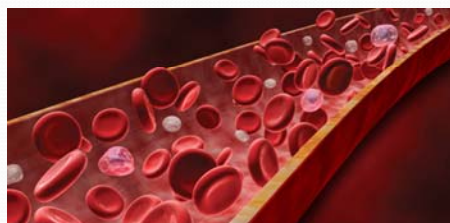
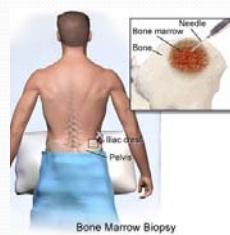
# Lymphatic system



# Functions

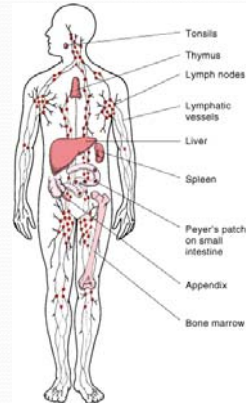
## Function

- Bone marrow
  - Factory of the blood
- Blood
  - Red cells
  - White cells
  - Blood platelets



## Function

- Lymphatic system
  - Lymph 'vessels'
  - Lymph glands/nodes
  - Spleen...!
- Organs
  - Liver
  - Bowels
  - Brain
  - ...



## Symptoms

## Symptoms

- Bone marrow
  - Over-production of red cells
  - Over- production of white cells
  - Over-production of platelets
  - Not enough production of red cells
  - Not enough production of white cells
  - Not enough production of platelets
- Blood
  - Only reflects what's going on in the bone marrow!!!

## Symptoms

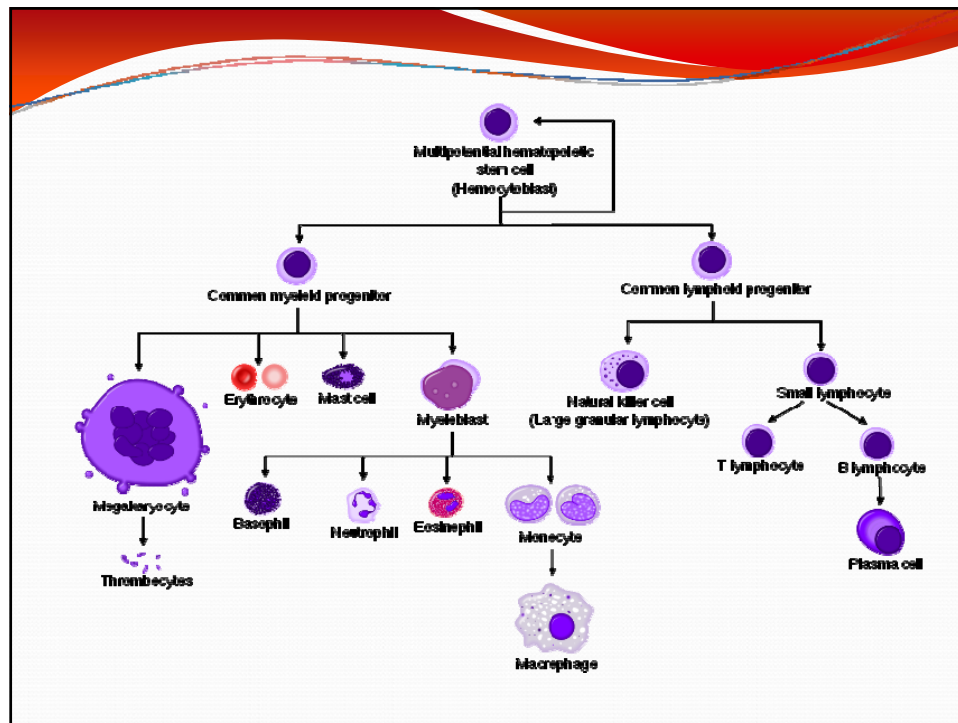
- Lymphatic system
  - Lymphadenopathy: 'swollen glands'/abnormal glands
  - Splenomegaly: large spleen
- ***B-SYMPTOMS (constitutional symptoms)***
  - ***Night sweats***
  - ***Weight loss***
  - ***Unexplained fevers***
- Organs



## Back to basics

## The origin defines the problem

Bone marrow problems	
Over production of white cells	LEUKAEMIA Chronic or acute
Over production of white cells	MYELOMA Symptomatic or Asymptomatic (indolent, 'smouldering')
Over production of red cells	Polycythaemia ('a lot of cells'), Polycythaemia Rubra Vera (PRV), Part of the Myeloproliferative neoplasms (MPNs)
Over production of platelets	Essential Thrombocythaemia (ET), MPN
Reduced production	Myelodysplasia, Myelodysplastic Syndrome (MDS)
Reduced production	Aplastic Anaemia



Lymphatic system	
Enlarged lymph-nodes	LYMPHOMA
Enlarged Spleen	Lymphoma
Organs enlarged	Lymphoma

## The diagnoses

## Haematological cancers

- Bone marrow disease: can be affected in all haematological conditions!!!
  - Always in Leukaemia, Myeloma and Myeloproliferative neoplasms
  - Sometimes: lymphoma
- Lymph glands: no changes in blood!
  - Almost always in Lymphoma
  - Only rarely in Leukaemia



# Investigations



# Investigations

- Blood tests
- Bone marrow test
- Biopsy
- Immunophenotyping
- Cytogenetics



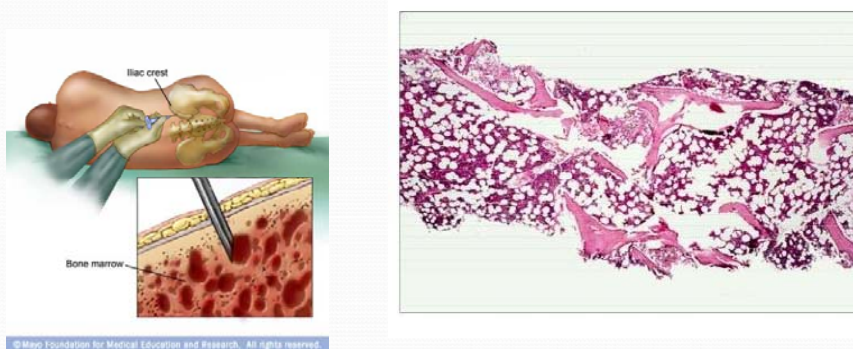
# Investigations

- Blood tests



- Bone marrow investigation

- Aspirate & trephine

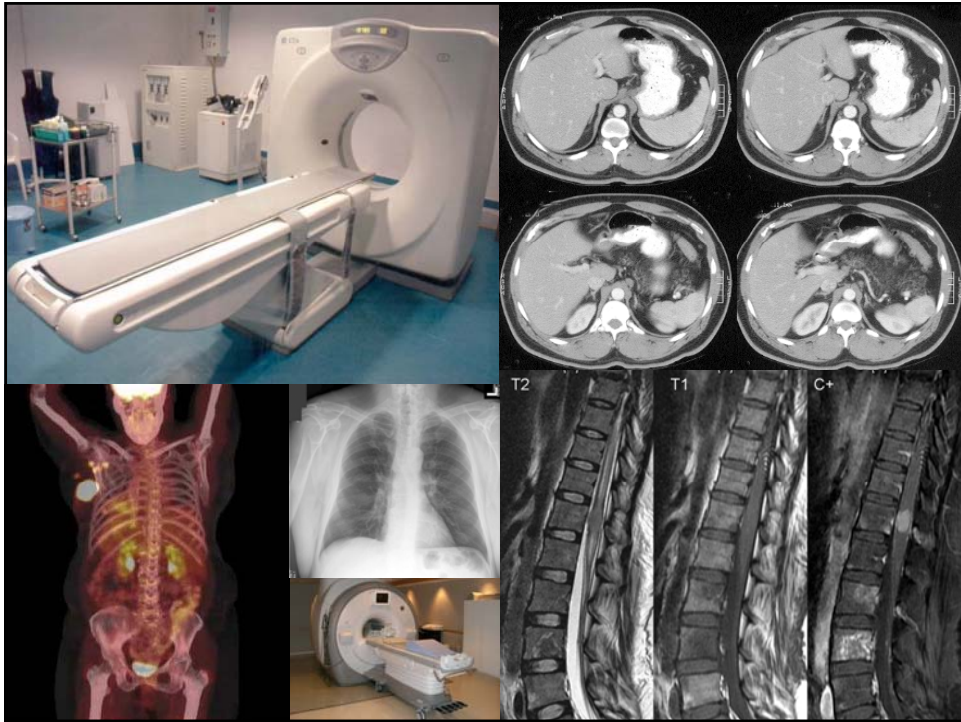


- Biopsy



## Investigations

- CT
- PET/CT
- MRI
- Skeletal Survey
- Others: CXR, USS, ...

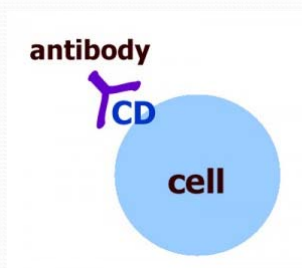




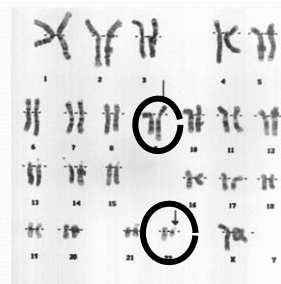
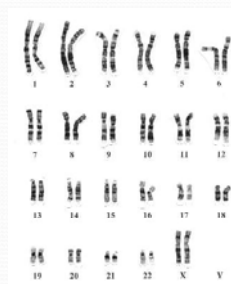
# Investigations

- Immunophenotyping ('flow')
  - Looks at markers on the outside of the cell to see what type of cell it is. These tests can be done on blood and bone marrow and are *diagnostic*.
- Cytogenetics
  - Chromosome tests. Are there any changes in the chromosomes/DNA that have caused a disease? These tests are done on bone marrow and are *diagnostic and prognostic*.

## Immunophenotyping



## Cytogenetics



The abnormality seen by Nowell & Hungerford on chromosome 22. Now known as the Philadelphia Chromosome.





## Investigations

- Other
  - Jak-2
  - BCR-Abl ('Philadelphia chromosome')



## The Haematological cancers

# The haematological cancers

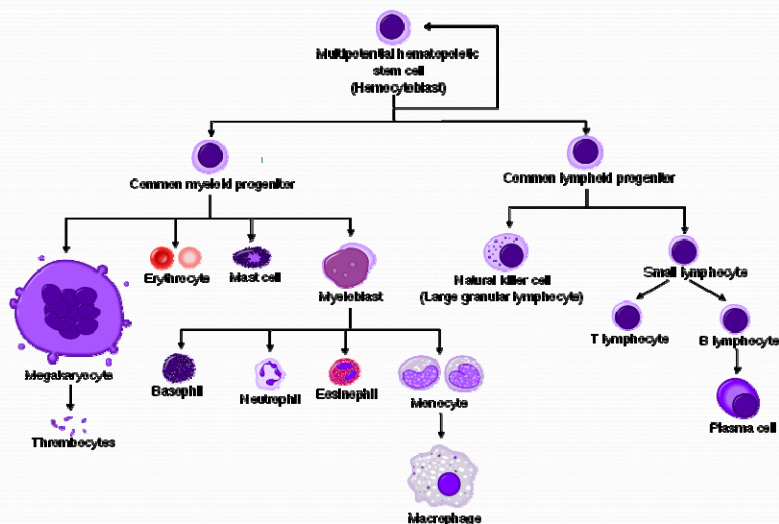
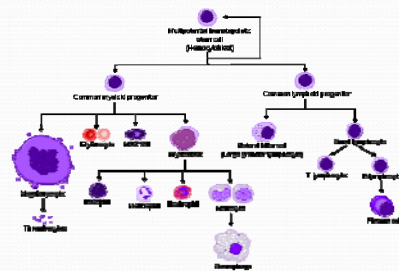
- Common features & Common investigations!
- Overlap symptoms
- Disease specific symptoms
- Many ways for the patients to come to us (GP, hospital teams, MDT, ...)
- Questions so far?

## Diagnoses

- Leukaemia
  - AML
  - ALL
  - CLL
  - CML
- Myeloma
- Lymphoma
  - NHL
  - HL
- MDS
- MGUS
- MPN
  - ET
  - PRV

# Leukaemia

- Problem of the white cells: over production
- Acute or Chronic
- Bone marrow affected therefore bloods abnormal





AML – ACUTE MYELOID  
LEUKAEMIA

CML – CHRONIC MYELOID  
LEUKAEMIA



ALL – ACUTE LYMPHOBLASTIC  
LEUKAEMIA

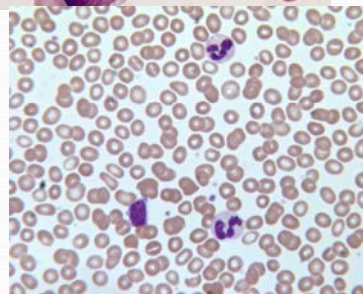
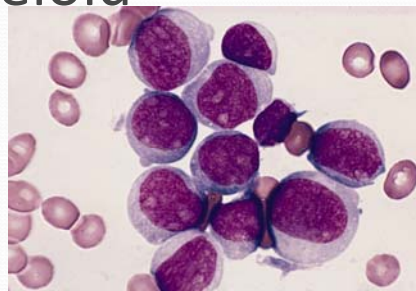
CLL – CHRONIC LYMPHOCYTIC  
LEUKAEMIA



## Individual diagnoses – Diagnosis, prognosis and treatment

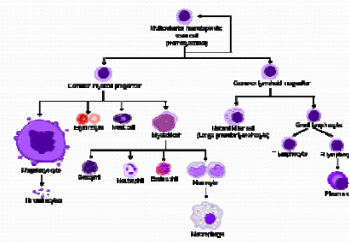
### AML – Acute Myeloid Leukaemia

- Problem of white cell over production (acutely)
- Problem of the BM
- Very abnormal blood tests
- Patients usually very unwell
- Referred through hospital teams
- Diagnostic tests:
  - BM & blood
  - Immunophenotyping (flow)
  - Cytogenetics: often abnormal.
    - Determines prognosis.



## AML - treatment

- Younger patients: 50% long term survival
  - Intensive chemotherapy (in hospital)
  - Standard 4 cycles (one cycle = 3-4 weeks in hospital)
  - Standard treatments:
    - DA (Daunorubicin and Cytarabine)
    - AML17 trial
    - FLAG-Ida: For relapsed AML
    - Vancouver DA: For relapsed AML
    - ...
  - Bone marrow transplant = stem cell transplant



## AML - treatment

- Older patients: palliative...
  - Low dose cytarabine
  - Azacitidine

## ALL

- White cell over-production
- Problem of the BM
- Blood tests very abnormal
- Patients unwell
- Referred through hospital teams
- Diagnostic tests:
  - BM & blood tests
  - Immunophenotyping (flow): always abnormal
  - Cytogenetics: often abnormal. Determines prognosis.

## ALL

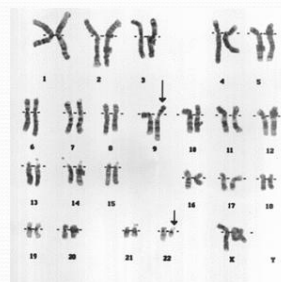
- Very poor prognosis in adults
- Very intensive chemotherapy schedules (UKALL protocol)
- Adult patients will require a bone marrow transplant after chemotherapy to prevent relapse
- Palliative in elderly (older) patients

## CML

- Chronic Myeloid Leukaemia
- White cell overproduction: slowly (chronic!)
- Bone marrow problem; abnormal blood tests
- Usually diagnosed accidentally!
- Referred by GP (2 week -rule)
- Diagnostic tests:
  - Blood tests
  - Bone marrow
  - Cytogenetics: BCR-Abl

## CML - treatment

- **VERY good prognosis (normal!)**
- Imatinib (Glivec)
  - the first (and only?) wonder drug....
  - One tablet a day for life
  - Not chemotherapy
- Dasatinib/Nilotinib
- Spirit study
- Bosutinib, ...



The abnormality seen by Nowell & Hungerford on chromosome 22, Now known as the Philadelphia Chromosome.



## CLL

- Chronic Lymphocytic Leukaemia
  - SLL: small lymphocytic lymphoma
- White cell overproduction (slowly)
- Bone marrow problem
- Almost always diagnosed accidentally
- Referred by GP (2WR)
- Incurable BUT prognosis usually good
- Can have: Enlarged lymph nodes, large spleen

## CLL

- Diagnostic tests:
  - Blood tests
    - Bone marrow: Not routinely done or needed (only if patient needs treatment!!!)
  - Staging: A-B-C

Table 2. Binet classification system\*\*†

Stage	Description
A	Hemoglobin $\geq 10$ g/dL and platelets $\geq 100,000/\text{mm}^3$ and $< 3$ involved nodal areas
B	Hemoglobin $\geq 10$ g/dL and platelets $\geq 100,000/\text{mm}^3$ and $\geq 3$ involved nodal areas
C	Hemoglobin $< 10$ g/dL and/or platelets $< 100,000/\text{mm}^3$ and any number of involved nodal areas

## CLL - treatment

- **Watch and Wait: refer back to GP!!**
- **Treatment only if symptomatic**
- Treatments: patient (physician?) dependent
  - R-FC = FCR (Rituximab, Fludarabine, Cyclophosphamide)
  - R-Chlorambucil
  - R-Bendamustine
  - Campath
  - Others: Ofatumumab, Methyl-prednisolone, trials, ...

# Myeloma

- Chronic but progressive
- Myeloma cells in the bone marrow are called 'Plasma-cells'
  - These cells produce a 'protein', called the 'paraprotein'.
  - These cells can 'migrate' and go to the bones and cause myeloma problems there.
- Specific symptoms: Can be asymptomatic!!!
  - Pain, backpain, anaemia, kidney problems, high calcium, ...

# Myeloma

- Investigations:
  - Bone marrow
  - Blood tests
  - Skeletal survey
  - MRI spine



## Myeloma – treatment

- The worst disease?
- Incurable disease, but median survival 5 years.
  - Most improved in the last decade
  - Most new drugs in the last decade
- Asymptomatic myeloma: Watch and wait

## Myeloma -treatment

- CTD (Cyclophosphamide, thalidomide, dexamethasone)
  - First line
- Velcade (Bortezomib)
  - Second line
  - First line in renal impairment
- Revlimid (Lenalidomide)
  - Second relapse
- Radiotherapy!!!
  - Spinal Cord Compression
  - Pain relief
  - Palliative





## Myeloma – treatment

- Stemcell transplant: 'Autologous' or 'autograft' (stemcells from patient him/herself)
- Trials
- New drugs



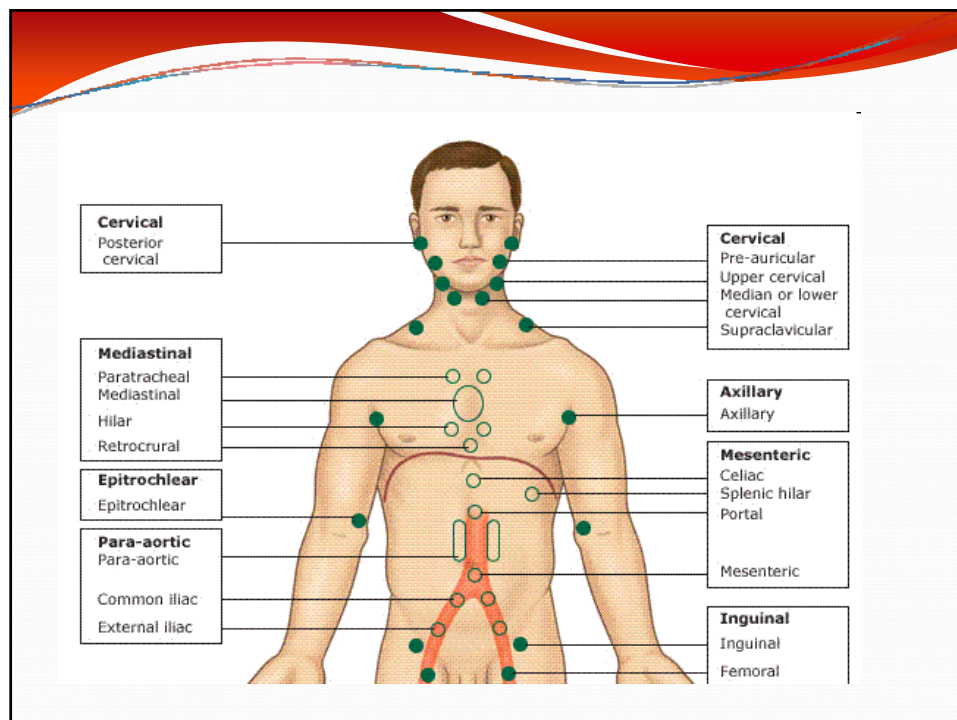
## LYMPHOMA

## Lymphoma

- Not a bone marrow disease!
- Blood tests almost always normal!
- Healthy white cells in bone marrow, go into the bloodstream and from there to:
  - Lymph nodes
  - Organs
  - Everywhere!
- Cell change/mutation leads to lymphoma
- Can arise anywhere....

## Lymphoma

- Non-Hodgkin's Lymphoma (NHL)
- Hodgkin's Lymphoma (HL)
- Swollen lymph nodes, usually not painful!
- Symptoms ranging from unwell to asymptomatic
- B-symptoms: Nightsweats, weightloss, fevers
- Symptoms relating to where the lymphoma is
- NHL: more common with age
- HL: often young patients



**Ann Arbor staging system**

Stage	Definition
I	Lymphoma in 1 lymph node region or a single localized extranodal site, ie, thyroid
II	Lymphoma in 2 or more lymph node regions situated either above or below the diaphragm
III	Lymphoma in lymph node regions situated both above or below the diaphragm
IV	Lymphoma in 1 or more extralymphatic organs with or without associated lymph node involvement (diffuse or disseminated)

stage I      stage II      stage III      stage IV

# Non-Hodgkin's lymphoma

- High-grade lymphoma: Aggressive lymphoma
  - DLBCL: Diffuse Large B-cell Lymphoma
    - RCHOP, RICE, IVE, ESHAP, ...
  - Burkitt's Lymphoma
    - CODOX-M/IVAC
  - MCL: Mantle Cell Lymphoma
    - 'Nordic': R-maxiCHOP & high dose Cytarabine
  - High grade T-cell lymphoma: CHOP
    - Angio-immunoblastic lymphoma
    - Peripheral T-cell Lymphoma



# Non-Hodgkin's lymphoma

- Low-grade lymphoma: **OFTEN NOT TREATED**
  - Follicular lymphoma
  - Marginal zone lymphoma, MALT lymphoma, Splenic Marginal zone lymphoma, Waldenstroms macroglobulinaemia/ Lymphoplasmacytoid lymphoma

Treatments:

- WATCH & WAIT!!
- R-CVP, R-CHOP, FCR, R-CBL, mono-rituximab, ...
- maintenance Rituximab for FL for 2 years



## Hodgkin's lymphoma

- Treatments
  - ABVD
  - ChlVPP
  - IGEV
  - BEACOPP
  - Gem-P
  - Brentuximab
  - ...
  - Radiotherapy!!

## Lymphoma - prognosis

- High grade lymphoma: high cure rate
- Low grade lymphoma: incurable but still good prognosis
- Hodgkin's lymphoma: Very good prognosis

## The others

## MDS

- Myelodysplasia = Myelodysplastic syndrome
- Bone marrow problem
  - Under production of cells!!!
  - Elderly patients
  - High risk of changing to AML ('transformation')
  - Often not treated...

## MDS

- Treatments
  - 'Best supportive care': transfusions!
  - Azacitidine
  - Rarely: treated as AML

## Myeloproliferative neoplasms (disorders)

- Over production of red cells: **polycythaemia**
  - Venesections = blood lettings
- Over production of platelets: **ET** (Essential thrombocythaemia)
  - Hydroxycarbamide
  - Anagrelide
- **Myelofibrosis**
  - Hydroxycarbamide

## And finally

- **MGUS** = monoclonal gammopathy of uncertain significance
  - Found by accident!
  - Pre-malignant/pre-cancerous
  - Can change into Myeloma (10% over 10 years)
  - Back to GP!!



# Questions

