HAEMATOLOGY & ONCOLOGY H+E:

History of presenting complaint

Anaemia

- Fatigue
- SOB/dyspnoea, Chest pain

Uncommon Sx:

- Restless leg
- Tinnitus
- Pruritus
- Hair loss (Fe def. anaemia)
- Mouth ulcers
- Vertigo
- Pica (pregnancy-desire for non-food e.g. dirt)

Anaemia

Common signs

- Pale skin, conj. Pallor, ↑HR, ↑RR
- Confusion
- Koilonychia (spoon-shaped)
- Angular cheilitis
- Atrophic glossitis
- Jaundice (Haemolytic anaemia)
- Oedema, HTN and skin excoriations (CKD)

Thrombocytopenia

Bruising

- ***Petechiae*** *(pinhead red, non-bleeding flat spots)*
- ***Purpura*** *(> 5 mm)*

Bleeding:

- ***Bleeding into joints*** *(haemophilia)*
- ***Epistaxis***

WBC Abnormality

- ***HIGH = leukeamia***
- ***Low = leucopenia***
- **Recurrent Infection** (esp. URT):
  - pneumonia
  - Cold
  - sinusitis
  - HIV etc.
- **Subjective Fevers**
- **Mouth ulcers** /blisters
- **Unexplained constant Rash = l**eukaemia

Hodgkin's Lymphoma

- Fever, UWL, NS, LN
- **Chronic fever** (due to CMV or EBV - infectious mononucleosis)
- **Male (bimodal 15-30s and > 55s)**
- *Pruritus after EtOH consumption*

Non-Hodgkin's Lymphoma

- Fever, UWL, NS, LN

*Symptoms Of Myeloma (**CRABS**)*

- **HyperC**alcium symptoms (e.g. **muscle weakness**, polyuria, polydipsia, N+V, constipation, confusion)
- **R**enal impairment,
- **A**naemia ➔ fatigue, chest pain
- **B**one pain/fractures
- **SoB**and palpitations

Myeloproliferative disease

- **PRV** - RUDDY complexion, facial plethora, splenomegaly
- **ET = Vasomotor symptoms [microvascular] - SPHLECT**
- **Systemic (e.g.** *weight loss, fatigue, fevers, sweats, pruritus***)**

Past MHx

Current Conditions	• **anaemia related (**rheumatoid arthritis or CKD), **hepatitis and HIV status** • **Previous**: haemophilia (coagulation), previous DVT, inherited clotting abnormality
Medications	• Fe supplements + VitB12 injection (anaemia), **erythropoietin (CKD)** • Immunosuppressants (or. HIV) ➔ increased risk of Hodgkin's lymphoma
Surgeries/Treatments	• chemotherapy for malignancy (**leukaemia, myeloma or lymphoma** or MDS) • **regular blood transfusions (MDS, myelofibrosis or bone marrow failure)** • **Colonoscopy (possible anaemia due to** polyps/bowel cancer/malabsorption)
Vaccinations	• *strep. Pneumoniae*, *FluVax***)**

Social Hx

Background	• Thalassaemia (Mediterranean/South Asian) • sickle cell disease (Africans)
Occupation	• **toxin** exposure (e.g. benzene → risk of leukaemia)
Overseas travel	• **malarial infection or intestinal parasitic**

Family Hx

- FHx of **lymphoma** = increased risk of lymphoma (esp. males > females for Hodgkin's lymphoma)
- FHx of **thalassaemia or sickle cell anaemia**
- FHx of **Haemophilia** (sex-linked recessive)
  - **Recombinant and donor-obtained factor IX concentrate is available for patients with haemophilia B**
- **von Willebrand's disease** (autosomal dominant + incomplete penetrance)

SR

- Light-headed & Insomnia, anorexia, vision/hearing
- Back/joint pain/aches
- Chest pain
- Cough
- Bowel Habits (bowel cancer)
- Urination
- feeling cold? (hypothyroid)

Hyperviscosity Syndrome

- Easy bruising
- Easy bleeding
- Reduced or loss of sight due to vascular disease in the eye
- Purple discolouration to the extremities (purplish palmar erythema)
- Heart failure

Bone Marrow failure:

- Anaemia → pallor
- Thrombocytopenia → bruise/bleed
- Leukopenia → ulcers
- Infiltrative (e.g. bone pain)
- Metabolic effects (e.g. gingival)

RED FLAG DDx:

1) **Malignancy**
   - 1° = myeloproliferative, lymphoproliferative, MDS, MM
   - 2° = Bone, breast, prostate, bowel
2) **Plt Issue / Coagulopathy**
   - *ITP, VWF, Haemophilia, chronic liver disease*
   - *Drug-induced (aspirin vs warfarin)*
   - *Autoimmune (SLE)*
3) **Bone Marrow Suppression**
   - Chemo, RT
4) **Acute Trauma**

Primary tumors	Metastatic sites
Colon, rectum, stomach	Liver, lung
Breast	Bone, liver, lung, brain, surrenal
Lung (small cells)	Brain, liver, bone marrow
Lung (non small cells)	Liver, bone, brain
Prostate	Bone
Kidney	Lung, bone, surrenal
Melanoma (skin)	Liver, brain, colon
Melanoma (uveal)	Liver
Neuroblastoma	Liver, surrenal
Thyroid	Bone, lung

Key statistics:

- **Prostate** cancer (leading ***cancer*** cause)
- **Breast** cancer (leading ***female*** cancer)
- **Lung** cancer (highest ***mortality*** cause)

DDx

Specific Sx	Cause
Sepsis +NO fever	Immuncomp (HIV, chemo, steroids,)
Constitutional Sx	Leukemia, lymphoma
Bleeding, bone pain, lump	Solid-organ malignancy
Non-specific	All cancer
Fixed firm non-tender mass	METS

General Work-up

1) **Biomarker** – B-HCG, CA 19.9, CEA
2) **Imaging** – USS, XR, CT-PET, MRI
3) **Biopsy** – solid organ, bone marrow

The Haematological Examination (Lymph node, liver, spleen)

POSTIOIN – LYING SUPINE AT 45°

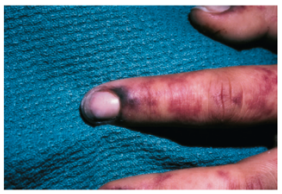
General inspection

1. **Equipment, monitoring treatments** (*e.g. O_2, nasogastric feeds, medications?)*
2. **Vitals**
3. **Weight**
4. **Cachexia**
5. **Bruising** (thrombocytopenia, scurvy)
6. **Pigmentation**: **Petechiae** (pinhead bleeding), **Ecchymoses** (large bruises), Pigmentation (lymphoma)
7. **Rash** (lymphoma)
8. **Ulcers** (neutropenia)
9. **Cyanosis and plethora** (polycythaemia)
10. **Jaundice** (haemolytic anaemia)
11. **Scratch marks** (myeloproliferative diseases, lymphoma)
12. **Racial origin (thalassemia and sickle cell disease)**
13. **Bone deformity** (thalassemia)
14. **Oedema, HTN and excoriations of the skin (CKD)**

Nails/Palms

- **Koilonychia** (Microcytic anaemia)
- **Palmar crease pallor** (anaemia – unreliable)
- **Arthropathy**
  - haemophilia,
  - gouty arthritis: (myeloproliferative disease)
  - drug treatment
  - RA
- **Pulse** *(tachycardia to compensate– anaemia = low O_2 carrying capacity)*
- ***Digital infarction*** *(abnormal globulins – cryoglobulinemia)*
- ***Gout & arthropathy (SLE)***

Raynaud's phenomenon



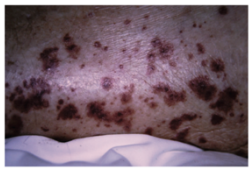
Digital infarction

DDx: BB, scleroderma, perniosis | *DDx: cryoglobulinemia, IE*

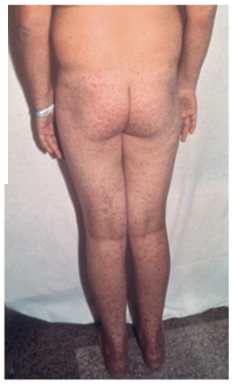
Arms/Axilla

Bruising (e.g. purpura, petechiae)

- **Petechiae** (pinhead red, non-bleeding flat spots) → bleed into skin
  - Leukaemia
  - Meningococcal septicaemia
  - Vasculitis
  - HSP
  - ITP
  - NAI
- **Purpura** (> 5 mm):
  - Trauma
  - Vasculitis (HSP)
  - Thrombocytopenia
  - platelet dysfunction (CKD),
  - if raised = *palpable purpura* (NOT thrombocytopenia but systemic vasculitis and possibly tender)
  - **Senile ecchymoses/bruises**
  - **Coagulation disorders**
    - *Acquired* (Vit k deficiency, liver disease, DIC, anticoagulants)
    - *Congenital* (haemophilia A/B)
- **Bleeding into joints** (haemophilia)



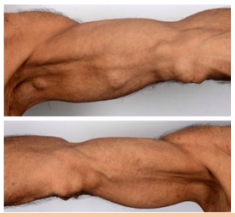
Drug purpura

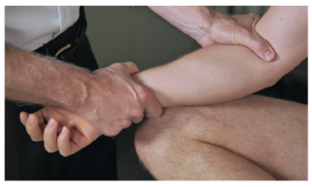


Henoch-Schönlein purpura

Features of bleeding abnormalities

	Platelet abnormalities	Coagulation abnormalities
Family or medication history	Sometimes	Often
Sex	Females>males	Males>females
Petechiae	Usual	Unusual
Superficial ecchymoses (bruises)	Small, numerous	Large, single
Bleeding into joints (haemarthrosis)	Rare	Common
Delayed bleeding after trauma	Rare	Common
Haematoma (deeper bruises)	Rare	Common



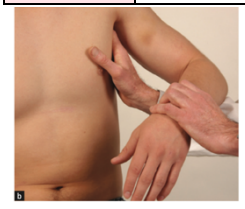


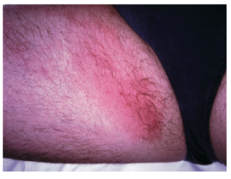
Feeling for the epitrochlear lymph node

LYMPHADENOPATHY:

- **Size:** Large nodes (> 1 cm = abnormal).
- **Consistency:** Hard = tumour, soft = normal, rubbery = lymphoma.
- **Tenderness:** infection or acute inflammation.
- **Fixation:** *fixed nodes* more likely than mobile nodes to be *infiltrated by carcinoma*.
- **Inflammation over Overlying skin:** → infection, and tethering to overlying skin → carcinoma.
- **benign** = lipoma, abscess, sebaceous cyst

Cervical	1=**submental**; 2=**submandibular**; 3=**jugular chain** 4=**supraclavicular** [**shrug shoulders**] ; 5=**posterior triangle**; 6=**postauricular**; 7=**preauricular**; 8=**occipital**	• Head and neck cancer • Lymphoma • 2nd mets: Tap for bony tenderness (in spine, sternum, clavicles, shoulders)
Supra-clavicular	**R supraclav**	Oesophageal cancer
	L supraclav	Abdo cancer (e.g. troisier's sign)
Axillary (C-LPIS)	• central, • lateral (above and latera) • pectoral (medial) • infraclavicular • subscapular (most inferior)	➢ Upper limb infections ➢ Breast Cancer ➢ 2nd mets ➢ Immunisations ➢ Lymphoma
Epitrochlear	*Ask patient to flex elbow at 90° and abduct upper arm a little and place palm of hand under elbow*	➢ Arm infection ➢ Lymphoma ➢ sarcoidosis
Inguinal		➢ Lower limb infections ➢ STD ➢ Abdo/pelvic cancer ➢ Immunisations ➢ Lymphoma



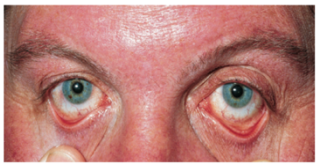


Lymphangitis in the groin

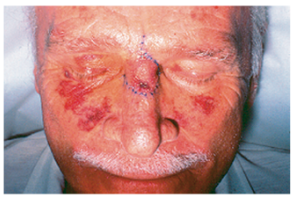
***KEY Differentials of enlarged LN**

- **Infection** (most common) e.g. cellulitis
- **reactive immune response**
- **autoimmune** (e.g. thyroid nodule)
- **malignancy** (least common)
- **benign** = lipoma, abscess, sebaceous cyst

Face /eyes /mouth	• Sclera—**jaundice** [scleral icterus], **conjunctival pallor**, **polycythaemia rubra vera** (i.e. prominent scleral BVs since bone marrow overproduces RBCs) • EPISTAXIS - anti-coag, anti-plt, trauma, mucosal oral bleeds • Mouth: **gum hypertrophy** (monocytic leukaemia), **mouth ulcers, , angular chelitis stomatitis** (Fe, vitamin deficiencies) • Tongue—amyloidosis, **atrophic glossitis (anaemia)**
Chest	1. Apex beat + murmurs 2. Bony tenderness = sternum, spine, RIB, clavicle
Abdomen & genitalia	1. GI = distensions, scars and prominent veins 2. Palpate for: While patient under full inspiration o **Hepatomegaly (RIF → RUQ)** o **Splenomegaly (RIF → LUQ)** o **Para-aortic lymph nodes** (rarely palpable) o **inguinal lymph nodes** (i.e. along inguinal ligament + along the femoral vessels) → **lymphangitis** uss for: o **Ascites** o **Traube space** = dull (if splenomegaly) ➔ patient supine → abduct the patient's left arm slightly → breath normally → percuss across the space from its medial to lateral margins o **Castell spot**: dull in inspiration (if splenomegaly) ➔ patient supine → percuss castell spot (lowest left intercostal space in the anterior axillary line—with the patient in full inspiration and expiration. 4. Auscultation – **SBO/LBO** (bruits and rubs), **RAS** (murmur)
Legs	• **Petechiae/ Leg ulcers** (*thalassemia, TTP, Polycythaemia*, **SICKLE CELL anemia) → look for signs of DVT** • **Rash = Vasculitis** (Henoch–Schönlein purpura— buttocks, thighs) • **Bruising + Pigmentation** (due to drugs?) o **Anti-coag (DOAC, warfarin, LMWH)** • **Ulceration** (e.g. haemoglobinopathies) • **Arthropathies** (gout, arthralgia) • **Neurological signs** (subacute combined degeneration, peripheral neuropathy due to *Vit B12 deficiency*) o **Foot drop** (*due to lead poisoning causing anaemia*)
Requests	• **Genital, Rectal and pelvic examination** (for tumour and bleeding) • **Fundoscopy** (*haemorrhages, infection, optic atrophy due to Vit B12 deficiency , increased blood viscosity -macroglobulinemia*) • **Temperature chart** (infection) • **Urine analysis** (haematuria, bile, etc.) • **Urine M/C/S** • **Bloods (FBC, Blood film, EUC, LFT, CRP)** • **CXR** • **LN biopsy** • **Bone marrow biopsy – POSTERIOR ILIAC CREST = NO BV/NERVES**



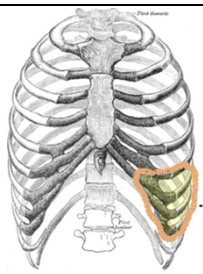
Polycythaemia rubra vera—prominent scleral blood vessels

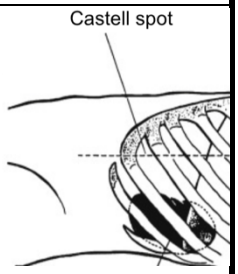


Ecchymoses

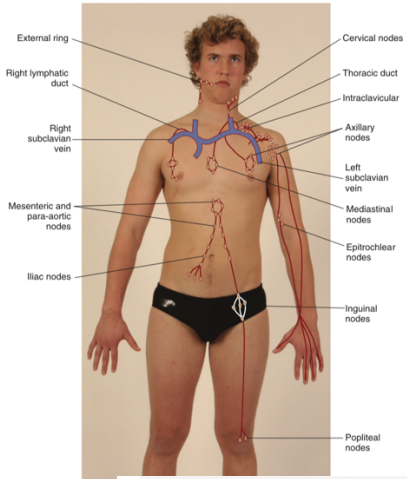
GOOD SIGNS GUIDE 21.2
Splenomegaly

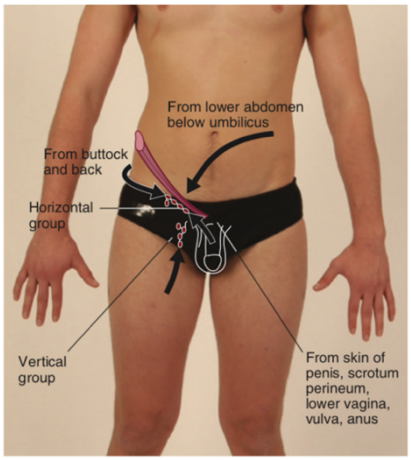
Finding	LR+	LR–
Spleen palpable	8.2	0.4
Spleen percussion positive (Traube space)	2.3	0.48
Spleen percussion (Castell spot)	1.2	0.45



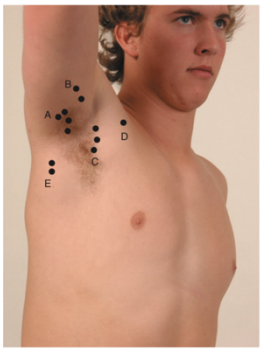


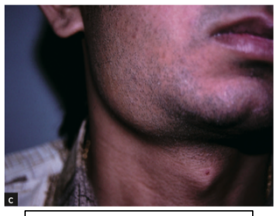
Hepatomegaly	Splenomegaly (CHINA-man)
➢ **Congestive** (cirrhosis, CCF, budd-chiari) ➢ **Infection** (*bacterial cholangitis, hep A/B/C, malaria, black fever, schistosomiasis, histoplasmosis, TB infection, liver abscess -amoebiasis*) ➢ **Infiltrative** o **Malignant** (Mets, primary HCC, polycythaemia, MM, lymphoma) o **Non-malignant** (cyst, Wilson, amyloidosis, myelofibrosis) ➢ **Inflammatory (alcoholic, autoimmune, drug-induced, sarcoidosis)**	➢ **Congestion** (portal HTN - Chronic liver disease) ➢ **Haematological (AHA, sickle cell)** ➢ **Infection** (malaria, EBV, TB, leishmaniasis, black fever, brucellosis – Mediterranean fever) ➢ **Neoplasm = Myeloproliferative** (CML, myelofibrosis) + lymphoma ➢ **Autoimmune (RA, sarcoid, amyloid)** ➢ **MASSIVE SM = malaria, myelofibrosis, CML**



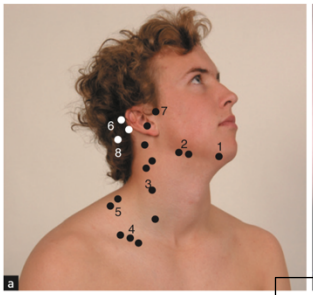


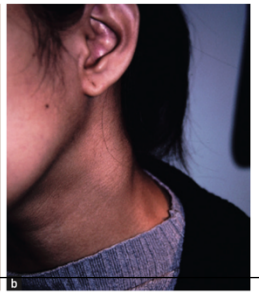
The groups of inguinal lymph nodes and their drainage areas





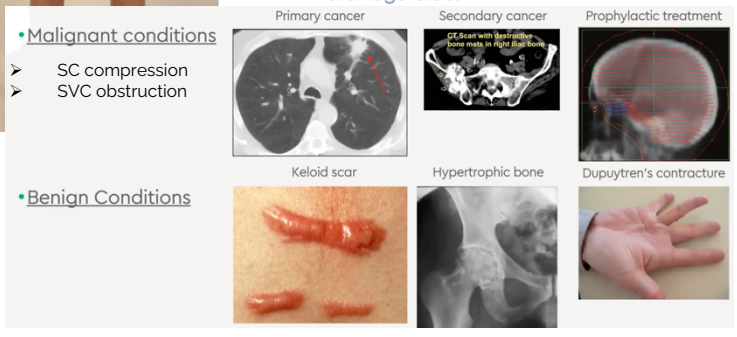
Submandibular lymphadenopathy



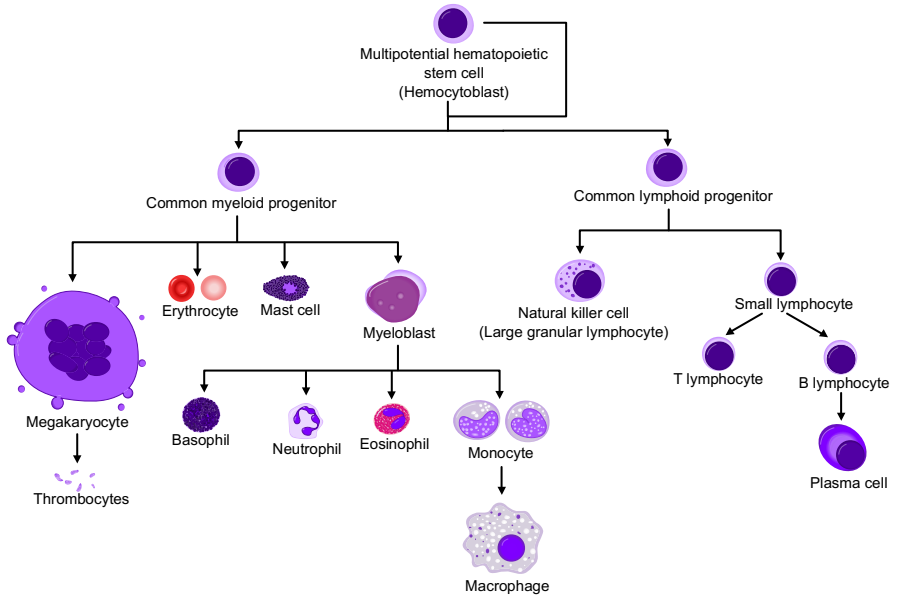


Cervical lymphadenopathy

RADIOTHERAPY INDICATIONS



COMPONENTS OF BLOOD



Leukaemia work-up

- ***FBC (within 48hrs if suspected)*** i
- ***Blood film*** = ***abnormal cells*** and ***inclusions***.
- ***Lactate dehydrogenase*** (***LDH***) = raised in leukaemia (poor specificity)
- ***Bone marrow aspirate*** (liquid sample of bone marrow)
- ***Bone marrow biopsy*** (gold standard – from iliac crest)
- ***CXR*** may show infection or mediastinal lymphadenopathy.
- ***Lymph node biopsy*** = ASSESS LN involvement or investigate for lymphoma.
- ***Lumbar puncture*** = if CNS involvement.
- ***CT***, ***MRI*** and ***PET*** scans = staging and assessing for lymphoma and other tumours.

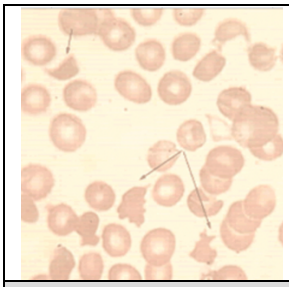
* Children or young adults with ***petechiae*** or ***HSM*** → immediately referred to the hospital.

	High		Low	
Reticulocytes	• **Haemolysis** (autoimmune, mechanical, infection) • **Spherocytosis** • **Bleed**	•	• Reduced erythropoiesis • Aplastic anaemia • CKD	• FBC • EUC (eGFR)
Erythrocytes (RBCs)	**Polycythaemia** • Polycythaemia rubro vera • Chronic hypoxia (↑EPO) • CHF, COPD		**Anaemia (microcytic vs macrocytic)** ➢ Microcytic (TAILS) ➢ Normocytic (chronic disease) ➢ Macrocytic (B12, folate def.)	**Aplastic Anaemia:** • Bone marrow failure • Pancytopenia • Insecticide poisoning?
Basophils	• **Allergies** • **CML**			
Eosinophils	• **Collagen vascular disease** (Churg-strauss) • **Helminths** • **IgE-HYPER** • **Neoplasm** (NHL, HL, CML) • Addison • Allergy		• **Infection** (sepsis, typhoid) • **XS steroids**: o Cushing o Stress o Exogenous glucocorticoids	•
Neutrophils	• **Acute infection** • **Stress** • **Seizure** • **Smoking** • **Steroid**	• Beware of **CRP lag**	• **BMF** (aplastic anaemia, chemo, RT) • **Autoimmune** (SLE, Crohn, Wegener's) • **Previous infection** • **CVID** • **BEN** (benign ethnic neutropenia)	•
Monocytes / Macrophages	• **Chronic bacterial** (TB, syphilis) • **Protozoa** (toxoplasmosis) • **Neoplasm** (CML, HL) • **Autoimmune** (SLE)		• **Infection** (EBV, HIV(• **Aplastic anaemia** • **Neoplasm** (AML, hairy cell leukemia) • **Glucocorticoids** • **Chemo**	•
Megakaryocytes / platelets	• Essential Thrombocytosis • Splenectomy • **Reactive thrombocytopenia** o Pregnancy o Chronic infection o AHA	**Thrombophilia screen** • Factor V leiden (protein C resistance) • Prothrombin genotype • Anti-thrombin III • Protein C/S • APS/SLE (lupus anti-coag, B2GP1, anti-cardiolipin) • Jak2 genotype (ET)	• **Haemodilution** (MTP) • **Plt consumed** o **DIC, HELLP, PE** o **Drug-induced** (NSAID, warfarin, HIT, MTX, PPI, antihistamine, Na valproate) o **Mechanical devices** o **Thrombotic angiopathies** (TTP, HUS) o **EtOH** • **Reduced production** o BMF, Infection o Sepsis o B12, folate deficiency o Liver failure o Leukaemia o Myelodysplastic syndrome • **Increase plt sequestered** o SM (Hypersplenism) o cirrhosis, portal HTN, PCV, CHF) • **TCP in ICU** o DIC (infection, sepsis, shock) o Post-transfusion o Intra-aortic balloon pump, ECMO	• FBC + blood film • LFT • Haemolytic screen • Hep B/C/ HIV serology • ANA/ENA • Folate/B12 • HIT (if suggested) **INDICATIONS FOR BONE MARROW ASPIRATION** 1) Splenomegaly or splenectomy 2) **> 60** (as TCP may be precursor to myelodysplastic syndromes) **IMMATURE PLATELET FRACTION (IPF):** Indicates bone marrow regeneration 1) **High IPF** = active bone marrow (ITP) or increased destruction 2) **Low IPF** = depressed bone marrow **Reference ranges:** • **Plt < 50** = surgical bleed risk, epistaxis, easy bruising • **Plt < 10** = spontaneous bleed risk (ICH, GI bleed)
Lymphocytes (B and T cells)	• **Acute** = EBV, MUMPS, RUBELLA • **Chronic** = TB, syphilis • **Neoplasm** (NHL, HL)	•	• **Immunosuppressed** (Chemo, RT, SCID, Wiscott-Aldrich, DiGeorge) • **Autoimmune** (SLE) • **Neoplasm** (NHL, HL)	•

PERIPHERAL BLOOD SMEAR/DISORDERS

Indication for blood smear:

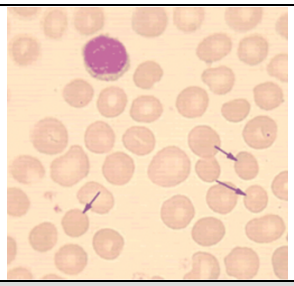
1) Anaemia OR unexplained jaundice
2) Sx of thrombocytopenia
3) Sx of lymphoproliferative disease (LN, + SM, B Sx)
4) Sx of myeloproliferative disease (+SM, plethora, itchy, UWL)
5) Suspected DIC
6) Suspected parasitic disease OR EBV, viral



Schistocytes

Microangiopathic hemolytic anemias (MAHA) = disrupted RBC membrane = intravasc. haemolysis

- **TTP**
- **HUS**
- DIC
- Pre-eclampsia
- Malignant HTN
- Metallic heart valves
- Toxins



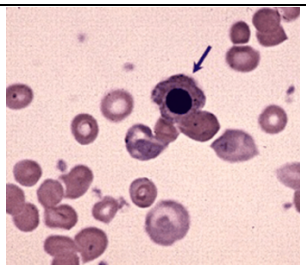
Spherocytes

(1) Hereditary spherocytosis (AD mutation in RBC membrane)

- elevated MCHC
- osmolarity fragility test

(2) ABO incompatible → AHA

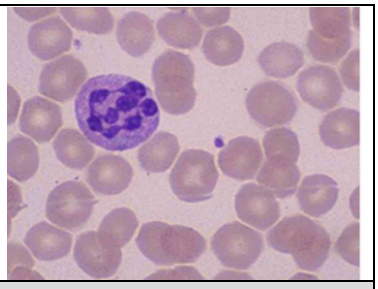
- +ve coomb's test (DAT +ve)



Nucleated RBC (Reticulocytes)

Immature RBCs with RNA material within them → bone marrow that is under stress

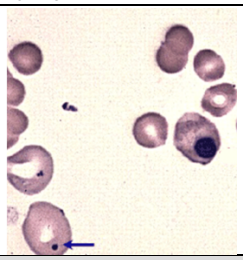
- ➢ haemolytic anaemias
- ➢ reticulocytes



Megaloblastic anaemia with hypersegmented neutrophils

Subacute combined degeneration of spinal cord due to **Vit B12 def.** ➔ symmetrical manifestations:

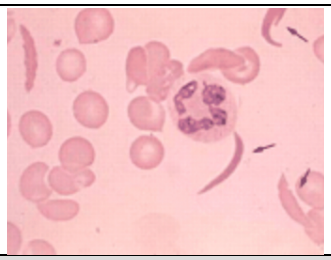
- **Loss of vibratory sensation**, tactile discrimination, and proprioception
- **Spastic paresis**
- **Gait abnormalities** (spinal ataxia, positive Romberg's test – proprioception loss)



Howell Jolly Bodies

inclusions of nuclear chromatin remnant in RBC due to incomplete nucleus expulsion➔ usu. removed by spleen

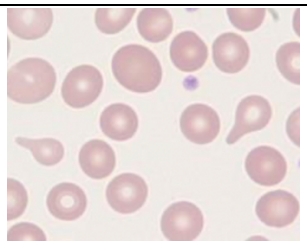
- **Severe haemolytic anaemia**
- **Asplenia – splenectomy →** avoid live vaccines (e.g. MMR, rotavirus, yellow fever, Jap enceph, BCG, VZV)



Sickle cells

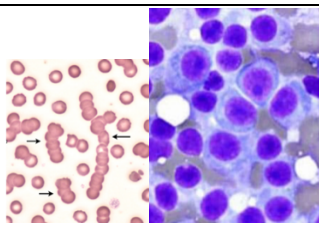
sickle cell anaemia.

- In the setting of low oxygen tension ➔ HbS polymerizes, causing red cell distortion into the sickle shape.
- **Protective against malaria**



Teardrop cells (dacrocytes)

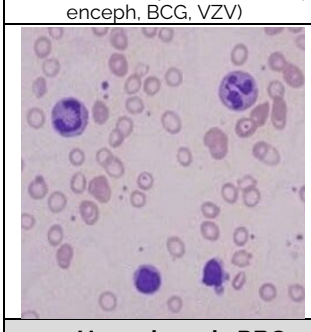
- **Myelofibrosis (mainly)**
- severe Fe deficiency
- megaloblastic anaemia
- thalassemia,
- MDS.



Rouleaux formation

stacked like coins.

- hyperfibrinogenemia or
- hypergammaglobulinemia (e.g. MM).
- MM = fried egg appearance on microscopy

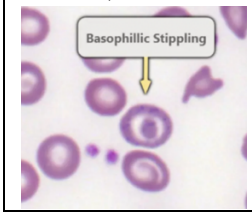


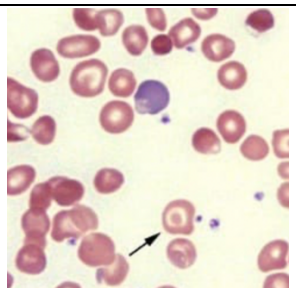
Hypochromic RBC

- Fe def anaemia (microcytic)

Basophilic stripping:

- ➢ Thalassemia
- ➢ Sickle cell
- ➢ Pb poisoning (abdo pain + FND)

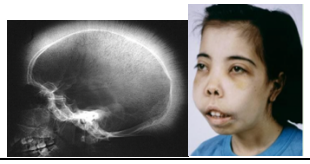




Target Cells

Central pigment area surrounded by pale area

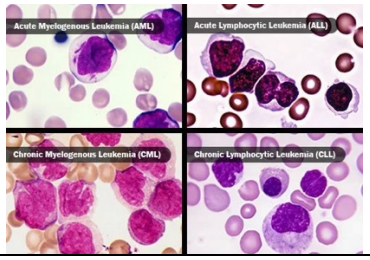
- **Thalassemia** (**very low MCV AND Hb**)➔ chipmunk face + reactive bone produces crew cut appearance
- **Post-splenectomy**
- **Liver disease (high SA ratio)**



Heinz Bodies

Individual blobs inside RBC caused by denatured **globin**

- G6PD
- Alpha-thalessemia



Sideroblasts

Immature RBC that contains blobs of iron (due bone marrow unable to incorporate iron into Hb molecules)

- ➢ **Myelodysplastic syndrome**

AML = auer rods
ALL = many lymphocytes
CML = XS eosinophils
CLL = smudge/smoke cells

Approach to Anaemia (Fatigue pt w/ low Hb)

Microcytic (MCV < 80fl)

- **Thalessemia (AR mutation in a/b globin genes)**
  VERY LOW MCV ≈ 60 (BIGGEST CLUE)
  Minor = *single-gene deletion (asymptomatic)*
  Major = *transfusion dependent (FTT)*
  XS stress on bone marrow – XS bone growth – coarse facial features, prognathism "chipmunks"
- **Fe deficiency anaemia – (low ferritin)** - ***koilonychia, angular stomatitis / glossitis, pale conjunctiva, Plummer-Vinson Syndrome = dysphagia + Fe def. + atrophic glossitis***
  - **Where is the bleeding coming from?**
  - **↓ Fe intake – Vegan (no meat/eggs/dairy), PPI usage** (prevents Fe absorption as Fe2+
  - **Fe loss = Menorrhagia, GI malignancy, GI bleed –** angiodysplasia, PUD rupture
  - **Fe malabsorption – coeliac, IBD, gastric bypass duodenum**
  - **↑Fe usage** = *pregnancy, infection (e.g. Schistosomiasis (parasitic infection – Egypt),*
- **Pb poisoning**
- **Sideroblastic anaemia** - *cannot put heme into RBC (secondary to Pb poisoning)*
- **Hereditary Spherocytosis** - *common inherited hemolytic anemias = ↑ Na and water permeability = rounded RBCs*
- **Haemoglobinopathy**
- **Hereditary haemorrhagic telengiectasias**

Normocytic (MCV < 80fl)

3 A's and 2 H's
- Acute blood loss
- Anaemia of chronic disease
- Aplastic anaemia
- Haemolytic anaemia
- Hypothyroidism

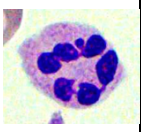
Haematological
- **BMF (primary cause) – Hypoproliferative** (reticulocyte <2)
- **Haemolytic Hyperproliferative** (reticulocyte >2)
  - Autoimmune
  - EBV infection (Fever + Pharyngitis + LN),
  - microangiopathic (HUS, DIC)
  - Mechanical valve

Anaemia of chronic disease (RA, IBD, hypothyroid)
- **↑↑↑ hepcidin/ESR/CRP** = *Fe trapped in macrophages of reticulo-endothelial system, ↓↓Fe absorption in GIT, ↓↓↓ bone marrow response to EPO)*
- *Screen for autoantibodies*

Renal anaemia (low EPO)
- **ADPKD**
- **AV fistula**
- **Renal transplant**
- **CKD (low EPO)**

Macrocytic (MCV < 80fl)

Megaloblastic (impaired DNA synthesis)
- **Pernicious anaemia (most common cause)** (*Antibodies target parietal cells and intrinsic factor = ↓ B12 absorption)*
- **B12 def** *(IBD, gastric bypass, peripheral neuropathy)*
  - ***Elevated Methylmalonic acid (MMA)***
- **Folate def** (*rare = as fortified staple foods)*
  - ***Normal Methylmalonic acid***



Normoblastic
- **Alcohol & Liver Disease**
- **Hypothyroidism**
- **G6PD** (triggered after substrate consumption e.g. flava beans, naphthalene) – normal Hb, ESR, ↑ROS, ↓Glutathione
- **Chemotherapy** (MTX, Anti-HIV, hydroxyurea)
- **Myelodysplastic syndrome (CML, AML)**
  - **Anaemia** = ↑SOB, chest pain, palpitaitons, fatigue,
  - **Thrombocytopenia** = ↑bleeding easily
  - **Leucopenia** = ↑recurrent infection,
  - Rx: supportive, Azacitidine, bone marrow transplant
- **Reticulocytosis**
- **Bone marrow failure**

Key Signs

- **Vitals and fluid status**
- **Physical bleed signs** (internal vs external)
  - Check menstrual pads
  - DRE / Vomiting
  - Bruise/ Haematoma – thighs/legs/head
- **Organomegaly**
- **Lymphadenopathy - L) SCV = gastic ca.**
- **Joint deformity**
- **Palpate uterus** (endometrial ca)
- **Stigmata of chronic liver disease** (gynacomastia , spider naevia, palmar erythema, jaundice ascites)

Anaemia work-up

- Bedside – ECG, DRE
- Bloods
  - FBC – Hb, WCC, MCV
  - EUC
  - LFT
  - CRP/ESR
  - Fe studies, B12, folate
  - TSH
  - Coags
  - Group and Hold (O-ve)

Definitive
- OGD, Colonoscopy or pill-cam (GI bleeding)
- Coeliac serology
- **Blood film → ?MDS, spherocytosis**
- Sickle cell trait
- Autoantibodies (RA, SLE)
- Haemolytic screen
- EPG/IEPG/SFLC (MM)
- **Bone marrow biopsy**

Treating Fe-deficiency anaemia

200mg Oral Fe supp tds – constipation, black stools and abdo pain
- Take w/ meal + vitamin C
- Take thyroxin 4hr before Fe
- A/E = constipation, black stools, cramps and heartburn

IV Fe infusion
- Anaphylaxis
- Permanent hyperpigmented staining
- Headache, flush, chronic muscle ache
- CI: do NOT give in active infection (bacteria EATS Fe +glucose)

Haemolytic anaemias = shortened RBC lifespan

- **Inherited** (spherocytosis, elliptocytosis, thalassemia, sickle cell, G6PD)
- **Acquired** (AHA, HUS/TTP, metallic valve, Paroxysmal nocturnal Haemoglobulinuria)

General Symptoms
- **Jaundice,**
- **Gallstones**
- **Splenomegaly / hypersplenism** (spleen is busy breaking down RBCs)

Haemolytic Anaemia Screen

Test	Results	Reason for screen
Reticulocyte	**+++**	Immature RBC produced to compensate for anaemia (**increased in haemolysis or acute bleeding → +++ bone marrow response**)
Bilirubin + LDH	**+++**	Released when RBC broken down by spleen macrophages
Haptoglobin	**---**	Bound by free Hb released during haemolysis (low)
Coomb's	**+**	Antibodies present on RBC surface
Blood film	polychromasia, spherocytes	Baby RBC w/ loss of membrane

	Key findings	Rx
Elliptocytosis /spherocytosis (aut. dominant)	Aplastic crisis (if parvo B19) + jaundice	Folate supp. + splenectomy +/- cholecystectomy
G6PD (X-linked recessive)	Trigger = fava bean, anti-malarials, moth ball, recent infection	Gene test (G6PD assay) Heinz body on blood film Avoid triggers
Autoimmune haemolytic anaemia	**Warm** = IgG on surface of RBCs in DAT **Cold** – IgM on RBC surface → (1° or 2° to myeloproliferative, SLE, infections – EBV, HIV, CMV)	Blood transfusion Prednisone (acute flares) Rituximab Splenectomy
Alloimmune haemolytic anaemia	**Transfusion reaction** **Haemolytic disease of newborn**	Stop transfusion Anti-D in sensitisation events
Paroxysmal nocturnal Haemoglobulinuria	Specific mutation = loss of proteins in RBC surface – inhibit compleent cascade **Red urine AM**	Eculizumab (targets C5 to suppress complement system) BMT (curative)
MAHA	HUS, DIC, TTP, SLE, Cancer	
Prosthetic valve	Metallic valve – shear stress	Monitor + oral Fe Blood transfusion or revision surgery

Interpreting Fe Studies

	Serum Fe Total Fe	Transferrin (TIBC) Total iron binding capacity	Trans Sats Total Fe in body	Ferritin Fe storage	Inflammatory markers Acute phase proteins **(IL-6)** → *elevates*
Fe def. anaemia	↓	↑	↓	↓	• Ferritin • Haptoglobin • Hepcidin • CRP • Serum amyloid • Procalcitonin • fibrinogen
Anaemia of chronic disease (*sideroblastic, thalassemia*)	↓	↓	↓	normal	
Acute reaction	↓	↓	↓	↑	
Fe Overload • *haemochromatosis* • *porphyria cutanea tarda*	↑	↓	↑	↑	

Other common Anaemia

Pernicious Anaemia	Thalessemia	Sickle cell disease
• Autoimmune • B12 def	• Fe overload (faulty RBC creation) • Alpha (Chr 16) • Beta (Chr 11) – minor, intermediate, major	Genetic condition where RBC are sickle chsaped • Malaria = protective • **2x abnormal** copies required for Sx
• PN + parasthesia • Loss of vibration + proprioception • Visual change • Mood changes	• **Anaemia** • **Splenomegaly** • **Bone deformities** (esp. major) – prominent malar eminences (cheekbone) • **Haemochromatosis signs** (ED, fatigue, HF, diabetes, OP, joint pain)	○ Anaemia ○ Infection recurrent ○ **Avascular necrosis** in large joints (hip) ○ **PHTN** ○ **CKD** ○ **Sickle cell crisis** ○ **Acute chest syndrome** ○ **priapism**
Intrinsic factor autoantibody	• FBC • Serum ferritin • Hb electrophoresis • DNA testing	○ Newborn heel prick test
IM **B12 - *Hydroxycobalamin*** injections (3x weekly for 2 weeks then every 3 mths) ?Steroid IgG	*Fe overload signs* ➢ Limit transfusions ➢ Fe chelation *Beta-Minor* ➢ Monitor *Beta-intermediate* ➢ Monitor + ➢ +/- chelation *Alpha or B-Major* ○ Blood transfusion ○ Splenectomy ○ BMT (curative)	*General*: ○ Hydration ○ IUTD ○ Abx prophylaxis (pen V) ○ Hydroxycarbamide (stimulate HbF – reduce sickling of RBC to protect against sickle cell crisis) *Last resorts:* ○ Blood transfusion (if severe anaemia) ○ BMT (curative)

Case studies:

	Case 1 - 23 yo Female	Case 2 – 55-75 Yo M	Case 3 - 65 Yo Male	Case 4: - 32 y.o. F	Case 5:
Lab results	• **Hb 73 g/L ↓** • **MCV 65fL ↓** • WCC 8.0 • **Platelets 450 ↑**	• **Hb 110 g/L ↓** • **MCV 105fL ↑** • WCC 8.0 • Platelets 400	• **Hb 100↓** • MCV 85 • WCC 8.0 • Platelets 400	• **Hb 105 g/L ↓** • MCV 68fL • WCC 5.0 • Platelets 270	• **Hb 105 g/L ↓** • MCV 85fL • **WCC 120↑** • **Platelets 115↓**
Ix	Iron studies ➔ check ferritin • Ferritin < 5µg/L • Decreased ferritin = specific for **Fe deficiency anaemia**	• LFTs normal, • TFTs normal • **↓ B12/Folate test** = pernicious aneamia • If B12/Folate test = **normal** *BUT bilirubin raised* (i.e. > 21) ○ Suggests haemolysis – haem referral	Screen for all anaemia causes: • Iron studies: normal • B12/Folate: Normal • EUC/LFTs: Normal • TFTs: Normal	Fe studies: - NORMAL ***Likely thalassemia*** ○ Mildly low Hb but very low MCV ○ Thalessemia Screen → Hb electrophoresis (EPG, HPLC)	**Leukeamia?** ○ High WCC ○ Chronic → CML vs CLL? *Look at WCC types:* ○ **CML** – high Neutrophils ○ **CLL** – high Lymphocytes
Rx	• **IV iron infusion** – usu. low Hb (< 70) If Still Anaemic: • Retest Fe studies➔ Ferritin 250 g/L • haemoglobinopathy screen • Thalassaemia screen → Comes back normal	**Steroid IgG**	○ **Asymptomatic** ○ **Oral Fe tablets** ○ **Check diet**	○ Blood transfusion ○ Fe chelation therapy ○ Folic acid supp.	**CML = imatinib (TKI)** **CLL** = *only if progressive anaemia + splenomegaly → chemo + rituximab*

What about females with recurrent miscarriages?

- Need to conduct pathology initially
- After 3 miscarriages → investigations may include:
  - **Chromosomal testing** (i.e. abnormal parental or embryonic karyotype)
  - Check for **SLE and antiphospholipid syndrome** (hypercoagulable state – lupus anti-coagulant) → esp. if prior history of DVT
  - **Thyroid** (TFTs - hypothyroidism) & **diabetes** (HbA1c, fasting BSLs)
  - **Uterine bleeds**

Normal Values

- **Hb (120-160µg/L)**
- **MCV (80-100)**
- **WCC (4-11)**
- **Platelets (150-400)**

#1: MRS ES

- 70 year old lady
- Presents with lethargy and fatigue
- History of frequent epistaxis and maleena

What to order?

ferritin study (iron study)

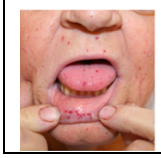
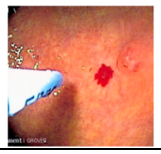
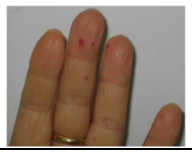
Test	Result	Interpretation
Iron	**2 umol/l**	Low
Transferrin	3.1 g/l	Normal High
Transferrin saturation	**3%**	Low
Ferritin	**9 ug/l**	Low

haemolytic screen (FBC, Hb and MCV data)

Test	Result	Normal Range
WBC	9.2 x 10^9/l	4 - 11 x 10^9/l
Haemoglobin	**64 g/l**	115 – 155 g/l
Platelets	391 x 10^9/l	150 – 400 x 10^9
MCV	**68.1 fl**	80 – 100 fl

Diagnosis: ***Hereditary haemorrhagic telangiectasia***

- Low ferritin = iron deficiency
- Supported by low transferrin saturation

Case Study #2: MR EH

- 40 year old accountant
- Presents with fatigue and difficulty concentrating

What to order?

Haemolytic screen (FBC, Hb and MCV data)

Test	Result	Normal
White cell count	**3.3 x** 10^9/l	4 - 11 x 10^9/l
Haemoglobin	**61 g/l**	115 – 155 g/l
Platelets	**71 x** 10^9/l	150 – 400 x 10^9
MCV	**128 fl**	80 – 100 fl

Other tests:

B12 and folic acid levels test

- critically **low vitamin B12**
- Also: intrinsic factor and gastric parietal cell antibodies

Dx: Pernicious Anaemia → vitamin B12 injections

Possible Causes:

- Faulty mechanical valve (shearing or RBCs)
- G6PD deficiency
- Increased bilirubin production = spleen enlarged

Case Study #3: MR RW

61 year old man

What to order?

Test	Result	Normal Range
WBC	6.8 x 10^9/l	4 - 11 x 10^9/l
Hb	**73 g/l**	115 – 155 g/l
Platelets	205 x 10^9/l	150 – 400 x 10^9/l
MCV	**113 fl**	80 – 100 fl
Reticulocytes	**497 x** 10^9/l	25-100 10^9/l

- high LDH, low haptoglobin and positive DAT (i.e. COOMBs test)

Dx: Immune haemolytic anaemia → 75mg prednisone + 5mg folic acid

Case Studies: Thrombocytopenia

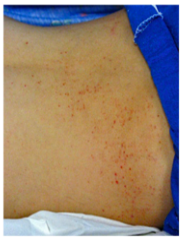
#1: MRS ES	Initial Tests		Special Tests	
➢ 18 y.o. presents to A/E ➢ Large swelling over the lower back after a game of football (swelling is 6cm in diameter and is tender and firm) ➢ Maternal aunt died from bleeding peptic ulcer (12 years ago)	**X-ray**	• large soft tissue swelling over the right psoas muscle	**Mixing study 50:50**	32 seconds Differentiate between deficiency in clotting factor or inhibitor (i.e. lupus anticoagulant)
	Blood tests	• FBC ≈ Hb147g/L • WCC ≈ 10.3x109/L • Platelet Count ≈ 299x109/L	**Factor Assays — FVIII**	• FVIII: 145% (50-200%) • **FIX: 16% (50-200%)** • FXII: 102% (50-200%) • FXI: 85% (50-200%)
	Coagulation studies	• PT: 14 seconds (<15s) • APTT: 42 seconds (<38s) **Hence intrinsic pathway issue**	**Diagnosis**	Mild haemophilia B

Case Studies: Heparin-Induced Thrombocytopenia (HIT)

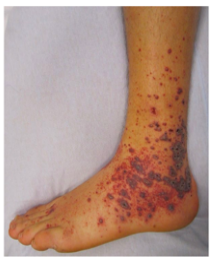
#1: MRS hj	Initial Tests		Management	
➢ 77 y.o. presents to A/E ➢ Acute SOB, pleuritc chest pain ➢ CKD ➢ Maternal aunt died from bleeding peptic ulcer (12 years ago)	**Blood tests**	• hB 127 • WCC ≈ 15 x10^9/L • Platelet Count ≈ 35	**Diagnosis**	HIT + possible PE
	Coagulation studies	• APTT: 48 seconds (<38s) **Hence intrinsic pathway issue**	**Mx**	Stop heparin Haematologist referral Alternative anticoagulation: ➢ Fondaparinux, ➢ **Danaparoid – does not react to hepairin Abs** ➢ rivaroxaban

Bleeding Diathesis & Coagulopathy

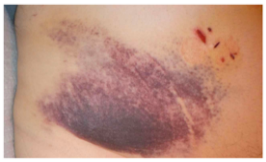
1)	**Trauma Hx**	• possible child abuse (NAI)
2)	**Surgical Hx**	• Circumcision, Dental extractions • Childbirth - PPH
3)	**Bleeding hX**	• Recurrent menorrhagia, epistaxis • Easy mucocutaneous bleed (Lip, skin, GI) • Haemophilia (haemoarthrosis)
4)	**Medications**	• Ginger, gingko, garlic • EtOH, ant-coags, antiplts • Cytotoxic drugs, Na valproate, diuretics • Abx: penicillin, cephalosporin, vancomycin
5)	**FHx**	• Haemophilia (sex-linked) – VWF • F5, F7 and F10 deficiency (aut. recessive)
6)	**Exam**	• Purpura on legs = plt issue, meningococcal, HSP • Gum hypertrophy, monocytic leukaemia (LN, HSM) • Blood filled vesicles = hereditary telenegectasias



Petechiae



Purpura



Ecchymoses

If ACQUIRED diseases suspected:

➢ Malignancy, infection, liver disease and drugs

Bleeding Sx	Bleeding disorder	
	Platelet defects (PETECHIAE) **(qualitative or quantitative)**	**Clotting factor deficiencies (ECCHYMOSES)** **(e.g. factor VIII or factor IX deficiencies)**
Bleeding type	**Mucocutaneous bleedinG**	**Deep tissue bleeding**
Red flags	**XS early bleeding after cuts** (oral cavity, epistaxis, GI and GU sites)	Haemarthroses, muscle haematomas
Bleeding time	*Immediate*	*Delayed*
DDx	• Leukeamia • Vasculitis or HSP • NAI • ITP • Meningococcal septicaemia	• SLE /APS
TESTS	• Plt count • VWF antigen and activity • DATs (+) = autoimmune haemolytic anaemia • DAT (-) = G6PD	• PT / INR, APTT, fibrinogen • F8, F9 screen +/- mixing study • Corrected APTT = haem 8/9 • Uncorrected APTT = APS (lupus anti-coagulant)
Acute Mx	FFP (if severe)	Recombinant Factor 7/8 (NO aspirin)

APTT	PT	Bleeding Time	Cause
Normal	Normal	↑↑↑	• *CKD (less EPO)* • *Thrombocytopenia* • *Haem A/B* • *VWF* • *DIC (secondary to sepsis)*
Normal	↑↑↑	Normal	• *F7 def (Warfarin, mild Vit K def. liver disease)* • *Inherited F7 def.* • *F7 inhibitor*
↑↑↑	Normal	Normal	• *F8, 9, 11 and 12 def.* • ***Inhibitors*** *= Heparin (HIT) , APS* • ***Haem A/B*** **Acquired Haemophilia (does not correct w/ mixing studies)*
↑↑↑	Normal	↑↑↑	• *VWF Disease (most common)*
↑↑↑	↑↑↑	Normal	• *DOAC, severe Vit K def.* • *Advanced liver disease (cirrhosis)* • *Warfarin + heparin* • *TF def (F5, F10, F2, fibrinogen)*
↑↑↑	↑↑↑	↑↑↑	• *DIC (low plts)*

What should I consider if patient presents with "Easy bruising"?

- drug use
- bone marrow disease = fatigue, infections and bleeds
- haemophilia A/B

Anticoagulant therapy

Drug	MoA	Route	T1/2	Dose	Monitor	Reversal
Heparin	**Enhance antithrombin III**	**IV**	**0.5**	**varies**	**APTT**	**Protamine**
LMWH (-aparins)		**SC**	**9**	**Wt-based**	**No**	**Protamine (mild)**
Warfarin	**inhibit vit K factors**	**Oral**	**40**	**varies**	**INR/PT**	**Prothrombinex (short-acting) Vit K (long-acting)**
Dabigatran	**Direct thrombin inhibitor**	**Oral**	**9-13**	**Fixed**	**No**	**Idarucizumab →** *if prolonged thrombin time or if ICH suspected*
Rivaroxaban	**Anti-Xa**	**Oral**	**7-11**	**Fixed**	**No**	**No reversal → if bleeding → stop either → ABCD → tranexamic acid** *for mucosal bleeding*
Apixaban	**Anti-Xa**	**Oral**	**8-15**	**Fixed**	**No**	**Andexanet alfa *(andexanet)***

**Warfarin for APS, prosthetic heart valve*

- ➢ *Both NOACs and warfarin associated with higher risk of in hospital death*
- ➢ *Less risk with NOACs compared to warfarin*
- ➢ *AVOID LMWH if eGFR < 30 (stage 4 CKD*

67 y.o. male w/ AF on warfarin + dizzy

Clinical Setting		Action
INR	**Sig. Bleeding**	
High but <4.5	No	Lower dose/omit warfarin
5-9	No	If high bleed risk give vit. K
>9	No	Low risk – vit. K High risk – PTX
Any	Yes	Vitamin K + PTX+/- FFP

When do I transfuse?

Indications

Hb > 90g/L	Transfuse ONLY if Hb 90-100g/L for ACS
Hb 71-90 g/L	• Transfusion if symptomatic (i.e. chest pain, SOB, tachypnoea) • Acute bleed during surgery or marrow suppression due to haematological disease or chemotherapy • Sudden drop in Hb • Acute haemolysis (i.e. anaemia w/ heart, lung or organ failure)
Hb < 70g/L	• Transfusion given → Accept lower Hb if patient has no symptoms •

NB: 1 x pRBC = ↑↑ 10g/L

Mx for coagulopathy with bleeding

FFP (clotting factors ONLY)

- Must address underlying cause
- If INR<2 probably OK for most invasive procedures

CryoPPT (contains fibrinogen)

- Must address underlying cause

Platelets indications

- **Any adults plt <10 (or prophylaxis)**
- **Severe bleed <20 x 10^9/L** in critically ill
- **Major surgery needed** and Plts >50 x 10^9/L

Risk of platelet transfusion:

1) Higher incidence than RBC transfusions
2) TRALI
3) Post-transfusion purpura
4) infections

Massive transfusions protocol (MTP)

4 units RBC in < 4 hrs for

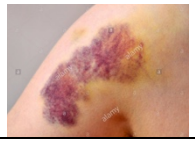
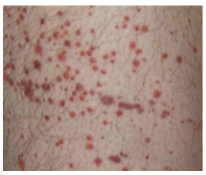
- *hemodynamically unstable,*
- *Major obstetric, GI or surgical bleeding*
- *anticipated ongoing bleeding*

1st shipment:	4 units of packed red cells + 2 FFP
2nd shipment:	4 units of packed red cells + 4 FFP + 1 pooled plts
3rd shipment:	4 units of packed red cells + 4 FFP + 10 units cryoprecipitate
	Alternate 2nd and 3rd shipment

Main issue:

- **Risk of dilutional coagulopathy as giving lots of RBCs→ need to add plts**

Bleeding Disorders/Diseases

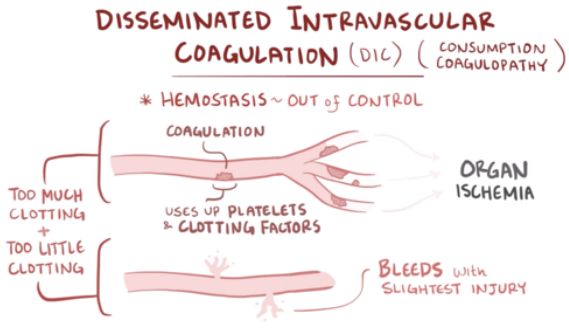
	Types	Sx	Ix – severity	Rx
Haemophilia (Factor 8, 9) ♂ [X-linked recessive = Males] *for females affected – need affected father + carrier/affected mother	• Factor VIII def (haem A) = more common • Factor IX def (haem **B**) • *Acquired* ***(pregnancy, autoimmune, drugs)***	• Usu. present at 12-18 months • **Spontaneous Bleeding,** • **Painful haemothroses →** *progressive joint deformity = non wt bearing = atrophy of distal limb – worse if obese* • **UTI – haematuria** • Gum bleeds	*Check:* ➢ COAGs ➢ Bleeding time ➢ Genetic test *Inherited haemophilia* • **Mild**: 5-40% activity • **Mod**: 1-5% activity • **Severe**: <1% activity → high-risk spontaneous bleeding	• **Expensive IV recombinant factor VIIa** (NOT donors – risk of HIV/hep C Tx) • **Desmopressin (DDAVP) –** stimulate VWF release • **TXA** (anti-fibrinolytics) • MDT care in haemophilia centre • **Gene therapy ?**
Von Willebrand's Disease ♀ [Autl dom. inheritance] 	• **Deficiency or abnormally functioning glycoprotein (vWF)**	• Easy bruising and mucosal bleeding • young women w/ menorrhagia • Epistaxis • Heavy bleed in operations	*Check:* ➢ COAGs (APTT may be prolonged) ➢ Bleeding time ➢ **VWF** screen to diagnose **Classification of VWD** **Type I** Partial deficiency **Type II** Functional abnormality **Type III (rare)** Complete deficiency	• **Expensive IV recombinant VWF or F8** • **Desmopressin (DDAVP) –** stimulate VWF release • **TXA** (anti-fibrinolytics) • **For women w/ menorrhagia** → COCP, mirena, TXA "hysterectomy = last resort"
Thrombocytopenia [< 150 x 10^9/L] 	**Immune / idiopathic thrombocytopenic purpura (ITP)** • Antibodies against platelets → low plt count		• Isolated low plt – only bleeding • Normal bone marrow • **NO splenomegaly** • **Blood film = large plts**	• 2mg/kg **Prednisone** • 0.8-1g.kg **IVIg** • Rituximab (MAB against B cells) • Splenectomy
	Haemolytic uraemic syndromeΔ • E. coli or Shigella (shiga toxin)	• Bruising • HTN, oedema, • Bloody diarrhoea • reduced UO • Abdo pain, lethargy	• Low plts • Anaemia • Ureamia	• Urgent ED (10% mortality) • Renal dialysis • Anti-HTN • Fluid balance +/- transfusion
	Thrombotic thrombocytopenic purpura ⬟ • ADAMTS13 mutation – cannot inactivate VWF – XS clot formation (using up platelets	• Bruising • **Fever** • **Neuro symptoms**	• **Low plts** • **Anaemia** • **Renal failure (ureamia)** • **Fever** • **Neuro symptoms**	• Heamatologist referral • Prednisone • Plasma exchange • Rituximab (MAB against B cells)
	Heparin induced thrombocytopenia • Heparin binds to plt factor 4 (PF4) – conformational change targeted by anti-PF4 antibodies		• 14 C serotonin release assay (100% Sn, 97% Sp) • ELISA for heparin dependent antibodies (91% sn)	• *Stop heparin* • *Use alternative – start* ***danaparoid*** *+ warfarin* • *Avoid plt transfusion*
	Drug induced thrombocytopenia - Drug binds to GPIIB-IIIA - conformational change expose a neoepitope = new target for antibodies → plt consumed		None	• Removing suspected drug = resolves thrombocytopenia • Steroids +/- transfusion (if plt < 10)
Disseminated intravascular coagulation (DIC) [*acquired*]	• Widespread abnormal activation of coagulation and fibrinolytic systems **Clotting and bleeding** • **Arterial clot = systemic** • **Veinous clot = cancer**	*Triggers of DIC:* • **Sepsis** • **Malignancy** (Metastatic adenocarcinoma, APML • **Eclampsia** • **Trauma, Burns, Snakebite** • **ABO incompatibility**	**Tests / TTP / DIC** **Plt** ↓↓↓ / ↓↓↓ **Blood smear** Schistocytes / Schistocytes **PT/APTT** Normal / +++ **LDH** +++ / +++ **Fibrinogen** Normal / ↓↓↓ **D-dimer** Normal / +++ (most specific)	• Urgent medical help • **Rx cause** – sepsis, trauma, malignancy, obstetric comp. intravascular haemolysis • **Prepare for Transfuse?**

How do we approach thrombocytopenia in critically ill patients?

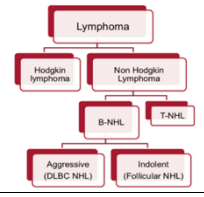
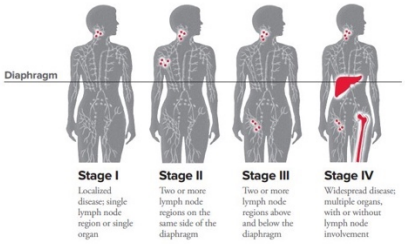
Platelet count less than 100 x 10^9/l	Exclude laboratory artefacts
Acute drop (more than 50% in 24-48 h)	Drug-induced ITP, HIT, PTP
Surgery less than three days ago	Postoperative drop
Clear evidence of sepsis (e.g., culture +ve)	Sepsis-associated thrombocytopenia
Abnormal coagulation profile (PT/APTT)	Sepsis, DIC, Liver disease
Blood contact with devices	Dialysis, Cardiac assist device or ECMO-related
Blood film shows microangiopathy	Thrombotic microangiopathy
Large amount of fluids given	Haemodilution
Recent extensive thrombosis	Clot thrombocytopenia
Recent blood transfusion	Post-transfusion purpura

Plt count monitor in surgical pts:

- Plt counts frequently dip on days 1-4 (due to peri-op consumption) = greater drop = greater extent of tissue damage and blood loss
- If **plt count blunted after day 4** → consider critical illness
- If **plt count drops after day 4** → acute illness (e.g. infection, drug-induced bone marrow suppression)



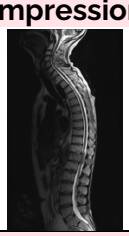
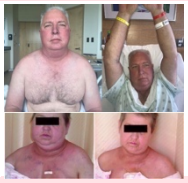
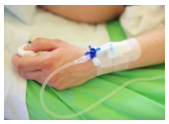
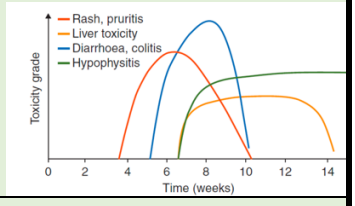
Leukaemia vs Lymphoma

	Leukaemia "ALL CeLLmates have CoMmon AMbitions" When single cell type suppresses other cell lines – causing bone marrow failure – anemia, leucopenia, thrombocytopenia				**LYMPHOMA** When cancerous cells proliferate within lymph nodes = lymphadenopathy	
	Acute lymphoblastic leukaemia (ALL)	***Chronic lymphocytic leukaemia (CLL)***	***Chronic myeloid leukaemia* (CML)**	**Acute myeloid leukaemia (AML)**	**Hodgkin's (10%)**	**Non-Hodgkin's (90%)**
Onset	Under 5 and over 45 *(Most common leukaemia in children)*	Over 55 *(Most common leukaemia in adults).- insidious onset*	Over 65 (3 *phases inc. a 5 year "asymptomatic chronic phase".*	Over 75	**Bimodal (20 and 75yo)** ➢ Localised to single axial group of nodes ➢ Orderly spread ➢ Rare extranodal involvement ➢ mesenteric and Waldeyer ring rarely affected	• **Follicular** t(14:18) • **Burkitt** (EBV, malaria, HIV) – t(8:14) • **MALT** (H. pylori) • **Diffuse large B cell** (painless mass in 65yo)
Risk factors	***Down syndrome***	***warm haemolytic anaemia***		***Transforms from a myeloproliferative disorder (PRV, myelofibrosis)***	➢ HIV, EBV ➢ Autoimmune (RA, sarcoidosis) ➢ FHx	➢ HIV, EBV, hep B/C ➢ H. pylori (MALT) ➢ **Pesticide** (trichloroethylene) ➢ FHx
Sx	**Non-specific** ➢ MALAISE ➢ Pallor ➢ Bone pain ➢ pancytopenia	**Non-specific** ➢ LN + organomegaly +systemic Sx ➢ *Richter's transformation into high grade lymphoma*	**Non-specific** ➢ Early satiety (+ SM) ➢ Fatigue ➢ Symptomatic during accelerated phase ➢ Severe pancytopenia during blast phase	**Non-specific** ➢ Malaise, ➢ pallor, ➢ oral issue	➢ **systemic Sx** ➢ **LN – non-tender rubbery** o **Upper body** (Hodgkin's) o Any LN (NHL) ➢ **Itchy** (after EtOH -Hodgkin's) ➢ **SOB, Cough** ➢ **Abdo pain** ➢ **Recurrent infection**	
Ix	**FBC + blood film** ➢ B lymphocytes ➢ Blasts (CD10 +ve)	**FBC + blood film** ➢ B lymphocytes ➢ LOW plts ➢ ***smudge / smear cells***	**FBC + blood film** ➢ *accelerated phase (high % of blasts)* ➢ *blast phase (> 30% blasts) = fatal* ***PCR + FISH*** ***Philadelphia chromosome*** *t(9;22) – BCR:ABL Fusion gene*	**FBC + blood film** ➢ blasts ➢ **Auer rods** **DDx:** **APML: (good prognosis)** • **DIC** + pancytopenia + epistaxis • ↑ **PT, D-dimer** • ↓ fibrinogen, APTT, PT • T(15,17) → PML-RARA fusion gene • Rx: Retinoic acid	➢ **LDH** (raised – not specific) ➢ **Flow cytometry (anormal antigens on cell membrane)** ➢ **Fungal and bacterial M/C/S +/-** ACID FAST BACILLI ➢ **LN biopsy** (gold-standard test) to ddx o **Hodgkin's = Reed Sternberg cells** (large B cells w/ multiple nuclei) ➢ **CT, MRI, PET = Ann-Arbor staging** 	
Mx	• MDT • Chemo (vincristine) • Steroids (prednisone)	• MDT • Conservative (indolent) • Aggressive → chemo + rituximab	• MDT • Imatinib (TKI) • STEM CELL TRANSPLANT	➢ MDT ➢ BMT ➢ RT)	*CURATIVE INTENT*: • **Chemo** (leukeamia, infertility) ***AVBD (keep fertility)*** ***RCHOP (higher cure)*** • **RT** (cancer, tissue damage, hypothyroidism)	**Depends on stage/type** • Chemo • Rituximab • RT • Stem-cell transplant **Beware of neutropenic sepsis** ➢ Rx: IV Tacosin + blood cultures

Myeloproliferative vs Myelodysplastic syndrome (MDS) vs Myeloma

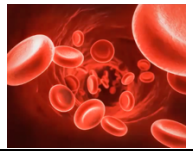
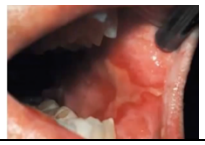
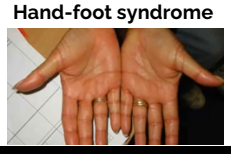
	Myeloproliferative Disorders				**Myelodysplastic syndrome (MDS)**	**Multiple myeloma** *(1% of all cancers)*
	Myelofibrosis	**Primary Myelofibrosis**	***Polycythaemia Vera***	***Essential* thrombocythemia**		
Define	Proliferating cell line causes bone marrow fibrosis	Haemotopoetic stem cell proliferation	Erythroid cell proliferation	Megakaryoctyes proliferation	Myeloid bone marrow cells NOT maturing (no healthy cells produced)	Proliferation of plasma B cells -
Risk factors	**Primary, PRV, ET**		***95% JAK2***	***50% JAK2, CALR, PML***	Previous chemo or RT	Old age, male, Afro-american FHx, obesity
Sx	**Scar tissue in bone marrow** – stimulates RBC production in liver and spleen (extramedullary haematopoesis) ➢ HSM → portal HTN ➢ SC compression	**Non-specific** ➢ Fatigue, UWL, NS, ➢ fever ➢ *Anaemia* ➢ *Neutropenia* ➢ *Thrombocytopenia*	**Non-specific** ➢ **Conjunctival plethora (**XS redness) ➢ **Ruddy complexion** ➢ **Splenomegaly** ➢ **Erythromelalgia** ➢ **VTE clots** **DDx** • 1° = PRV (↑ bone marrow activity) • 2° = COPD, high alt, R→L shunts, neoplasms	**Non-specific** ➢ Syncope, paraesthesia, headache, lightheaded, erythromelalgia ➢ chest pain ➢ transient visual disturbance ➢ **VTE clots (thrombosis)** DDX: Infection, splenectomy, bleed	➢ Anaemia ➢ Neutropenia ➢ Thrombocytopenia	➢ CRAB Sx ➢ Recurrent infections **MGUS** ➢ XS single antibody type without CRAB sx < ➢ 5% paraprotein ➢ Can progress to myeloma **Smouldering myeloma** ➢ 5-10% paraprotein ➢ Pre-malignant **Waldenstrom's macroglob. (type of smouldering myeloma)** ➢ XS IgM paraprotein → hyperviscosity ➢ **Rx**: BTK inhibitors
Ix	**FBC + blood film** ➢ Blasts (Immature RBC, WBC) ➢ Target cells + polychromasia ➢ Dacrocyte ➢ Teardrop poilkilocytes (different size) **Bone marrow aspirate and biopsy** (confirm Dx)		**FBC + blood film** ➢ NO anaemia ➢ Hb > 185 (men), > 165 (women) **Bone marrow aspirate and biopsy** (confirm Dx) ***JAK2, CALR, PML testing***	**FBC + blood film** ➢ Plts > 600 **Bone marrow aspirate and biopsy** (confirm Dx) ***JAK2, CALR, PML testing***	• **FBC** • **Blood film** = blasts • **Bone marrow aspirate and biopsy** (confirm Dx)	• **FBC/EUC**: anaemia, low WBC, hypercalcemia • **LFT:** + albumin • **UA:** cast nephropathy • **EPG / FLC (bence-jones)** • **Film: rouleax form** • **CT survey:** *punched out lytic lesions*
Mx	• **Allogenic stem cell transplant** (BMT) • **Chemo** (not curative) • **JAK2 inhibitor – Ruoxitinib (primary myelofibrosis)** • Monitor if progress to AML		• **Venesection** (1st line) • **Aspirin** (reduce clots) • **Chemo** • Monitor if progress to AML	• **Hydroxyurea** (makes RBC bigger) • **Aspirin** (reduce clots) • Monitor if progress to AML	• Conservative • Supportive Rx • Chemo • Stem-cell transplant (BMT)	• **MDT** • **Chemo** (thalidomide + dexamethasone) • **+/- BMT** – stem cell • **VTE prophylaxis** • **Bisphosphonates** to reduce fracture risk

Oncological Emergencies

Condition	Cause	S+S	Ix	Rx
Febrile neutropenia *(Neutropenic sepsis)* (neutrophil <1 x 10^9 cells/L)	• **Solid organ or haematological malignancies** who are receiving chemotherapy • bone marrow failure *Medications = agranulocytosis* • **RA** – MTX, Hydroxy, SSZ • **Hyperthyroid** – carbimazole • **Malaria** – quinine • **MAB** -infliximab, rituximab • **Shizo** – clozapine	**Prolonged fever** *(> 2-10 days) > 38* ***Haem compromise***: • hypoTN <90mmHg • tachycardia • (Temperature ≥ 38.0°C) • Reduced UO • low Sats • Confused + altered mental state	• FBC =neutrophil <0.5 x 10^9 cells/L • EUC – renal failure? • LFT – liver failure? • COAGS → abnormal APTT/PT (DIC?) • **2x set blood cultures** (aerobic and anaerobic) from each lumen of CVAD • **Gram -ve most common = E.coli, Pseudomonas, Klebsiella** • **Culture** – sputum, blood, feaces, MSU, CVC, wounds • ECG • CXR	• ABCDE • Anti-pyretic • Anti-emetics • 2x large bore cannula Empirical Abx within 30mnis • **Stable** = tazocin or cefepime (if allergy) • **Unstable** = + vancomycin • **Cellulitis or skin breaks** = + vancomycin • **Suspected abdo or perineal infection** = + metronidazole
Malignant HyperCa • Mild 2.6- 2.9 mM • Mod 3.0 - 3.5 mM • Severe >3.5 mM	• Cancer = breast, renal, breast, lung, MM • Poor prognostic factor **Assoc. w/:** 1) High PTHrP 2) Bone mets 3) Tumour producing calcitriol	• Polydipsia • Polyuria • Confusion • Myalgia • A/N/V • Constipation • Lethargy • Obtundation	• FBC • EUC – 24hr urine Ca:Cr • CMP (corrected Ca) • LFT • PTH – check for PTHrP (assoc. w/ SCC) • Vit D & calcitriol levels • Check ECG = shortened QT intervals • MYELOMA screen	• **Fluid hydration**: IV NaCl 0.9%; to increase renal Ca excretion (may be as high as 4 – 6 L over 24 hours) – dialysis if renal failure • **Bisphosphonate + adequate hydration**: IV zoledronic acid or IV pamidronate • **Denosumab (RANKL mAB):** if renal impairment or if refractory to bisphosphonate • **Calcitonin**: blocks osteoclasts and renal resorption; effect is transient; useful add on in severe hypercalcaemia
Spinal cord compression 	**Commonest solid** organ cancers – 1) prostate cancer, 2) lung cancer, 3) breast cancer, 4) renal cell carcinoma **Location:** • thoracic (70%) • lumbar (20%) • cervical (10%)	• Back / abdo pain • Myalgia • Trouble ambulating • PN • Sphincter dysfunction	• Manage whole spine • Check if known active malignancy • CT-CAP	• **Dexamethasone** (16mg/day) • Radiation oncology and neurosurgical consult • If SCC → **radiotherapy** **Neurosurgical decompression** if: • Single site compression only • < 48 hrs of symptoms • Radioresistant tumour • Displaced spinal cord
SVC obstruction 	**Cancer mass effect** • **Lung** (50-80%) -NSCLC • **Lymphoma** (2-20%) • **METs**	Symptoms worse supine, bending forward, cough, sneeze • Headache • Syncope • Stridor + SOB • Dysphagia • Cough • Dilated chest veins • Swelling of neck and upper limbs • Facial plethora • Pemberton's sign	• **ECHO** • **CXR** – may show mediastinal masses, pleural effusions, mediastinal widening • **CT Chest** – as above; also can guide tissue biopsy if required	• Send for help • ABCD **Definitive Mx:** • Radiotherapy = most tumours causing SVCO are sensitive to RT • High dose Steroids • Chemo for some tumours • Resection
Infusion reactions 	**HOST antibodies attack donor RBCS:** IV anticancer agents • taxanes, • platinums, • doxorubicin, • L- asparaginase, procarbazine, etoposide, • bleomycin, cytarabine • **MABs**	Few hours of the drug infusion or after 1st or 2nd exposure • Skin rash • Flushing • Throat tightness • SOB chest pain • Back or abdo pain • Dizzy or seizures • N/V diarrhoea	• FBC • EUC + CMP • LFT • ESR/CRP • ABG • UA	• Stop infusion + maintain IV access • Send for help → ABCDE + Vitals *If anaphylaxis* ➢ IM adrenaline *If cytokine release:* ➢ IV steroids *AFTERMATH:* 1) Explain reaction to patient 2) Double check pt details, blood bank labels (any clerical error) 3) Report incidence to blood bank (do not throw away tubing/lines) 4) Check expiry date 5) Clinical incident report form
Tumour lysis syndrome (C-KUP)	**High grade, high burden malignancies** (e.g. Burkitt's, ALL, large cell lymphoma, solid tumours w/ high proliferation rate – SCLC) **Death of large numbers of cancer cells usu. after chemo or RT**	Hyperuricaemia Hyperkalaemia Hyperphosphataemia Secondary hypocalcaemia Uraemia Renal failure Cardiac arrhythmias Seizures Sudden death	➢ FBC ➢ **EUC – hyperK = arrythmias, muscle cramps, twitch, seizures** ➢ **CMP – hyperPO4 → HypoCa** = ↓QT interval ➢ LFT (↑LDH) ➢ **Uric acid – hyperUric**	**Initial management = prophylaxis!** • Adequate hydration - excrete uric acid + PO4 • Maintain urine output • Pre-emptive **hypouricaemic** agents e.g. allopurinol AND rasburicase • HDU support
Immune-related toxicities	• Anti-CTLA4 antibodies (ipilimumab) • Anti-PD1 antibodies (nivolumab)	• Patient on immunotherapy • Rash • Diarrhoea (?colitis) • Abnormal LFT • Fatigue	• Remove immunotherapy • Check for: o cortisol AM o autoimmune hepatitis (LFT) o autoimmune colitis (ESR/CRP)	• 
Chemo toxicities	•	• FTT (stunted growth) • Neuro/cardiotoxicity • Infertility • Tumour lysis syndrome	•	•

Systemic Toxicities or ADR in Cancer treatments

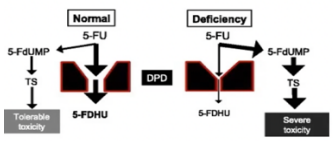
	Type A (augmented) ADR	Type B (bizarre) ADR
Cause	Predictable	Unpredictable
Dose	Dependent	Independent
	Common	Rare
Rx	May respond to dose adj.	Need to stop drug

ADR	Cause	RF	Ix	Rx
Myelosuppression (Damaged stem cells)	• 10-14 day post chemo (e.g. carboplatin, alkylating agents) • PARP inhibitors • TKI • **5-FU toxicity**	• Adv. Age • Extent of bone inv. in cancer • Prior chemo/RT • Nutritional status • Hepatic/renal dysfn caused by drug	• Neutropenia 1st → Fever, septic shock • Leukopenia 2nd	• Abx
Anaemia 	• Chemo/RT • Blood loss • Hypersplenism • BM infiltration • Fe, B12, Folate def. • Chronic disease		• FBC – low Hb • Fe studies (low ferretin) • Blood film (↓reticulocytes) • Low epo	• Oral Fe *(constipation and black stools)* • Fe transfusion (*skin staining + constipation)*
Mucositis 	• 5-16 days post chemo • TKI or oral chemo (folate-based e.g. MTX) • **5-FU toxicity**	• Poor oral hygiene • Immunosuppressed • Prior RT to mouth (head and neck cancers) • Pre-existing mouth damage	• Clinical • Swab – M/C/S	•
Diarrhoea (Colitis)	• Overflow diarrhoea (constipation or obstruction) • Infectious OR inflammatory • Immuno/chemo/RT • Malabsorption • Metabolic – TFT • Carcinoid • **5-FU toxicity**	**Early diarrhoea** • Irontecan (pro-cholinergic) → SLUDGE → Rx w/ atropine prior to usage	• FBC (WCC) • CRP – faecal calprotectin • TFT	• Hydrate + *Treat reversible cause* ➢ **1st line = atropine (pre-med esp. for pro-cholinergics such as irontecan)** **For uncontrolled (late) diarrhoea:** 1. **Loperamide** (2mg after each stool) → opioid agonst → slow Gi motility 2. **Codeine 30mg qid** 3. *ABx if neutropenic or symptoms persist* • **Specialist advice**
Alopecia 	• PolyChemo (cyclophos, ironetecan, anthacyclins, bleomycin)			• Scalp cooling • Scalp care
Hand-foot syndrome 	• Unclear • **5-FU toxicity**		• Dysesthesia (oedema + erythema) → fissuring and ulceration • Hyperkeratosis • Increased dermal vascularity	

Specific ADRS:

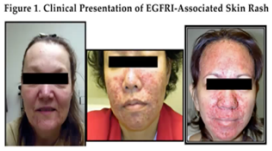
5-FU toxicity

- Colitis
- Mucositis
- Hand foot syndrome
- Bone marrow suppression



EGFR toxicity

- Xerosis → eczema → fissures
- Telangiectasisas
- Hyperpigmentation
- Hair changes



Anthracyclines

Cardiac toxicity

Monitor high-risk
- HF patients
- Congenital heart disease
- Adv. age

Immunotherapy toxicity

(anti-CTLA14 and Anti-PD1

- **Thyroiditis** → *Metoprolol + clexane +/- cardioversion → 10mg carbmiazole tds*
- **Colitis** → stool and blood M/C/S + viral multiplex + faecal calprotecin→ colonoscopy → IV methylpred → 2nd line: infliximab → tapered pred (100mg/day → 25mg/week)
  - **+++ steroids = +++ C. difficile → check C. difficile toxin → oral metro +/- oral vanco + wean steroids**
- **Myocarditis** → NSAID
- **Pleuritis**

Hepatitis

Long-term steroids

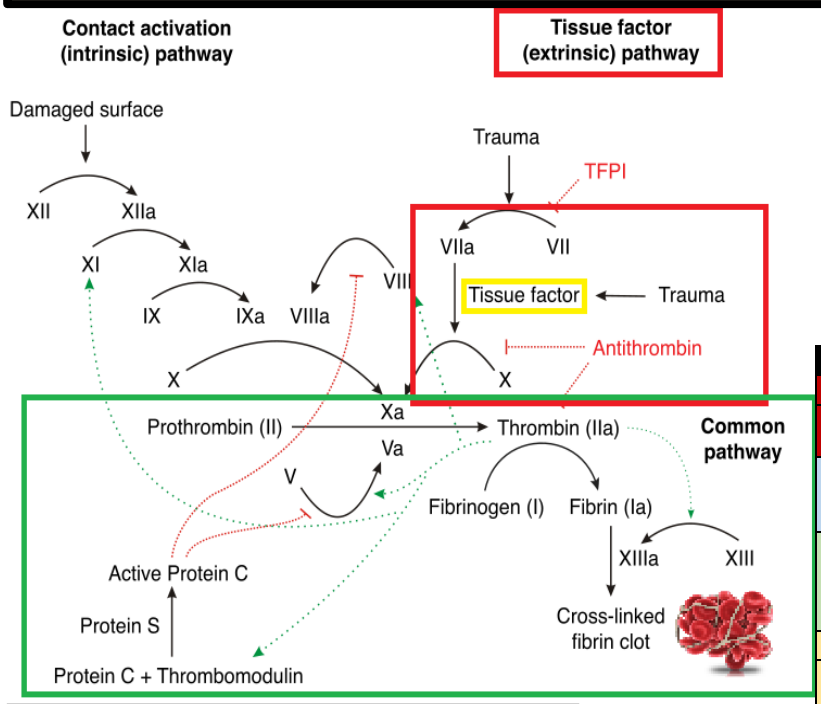
- Wt gain
- Fluid retention
- Gastric upset (diarrhoea)
- Proximal myopathy

- Lethargy
- Insomnia
- Hyperglycemia
- Immunosupp. → **oral thrush,**
- Skin thinning / easy bruising
- **Colitis = +++ C. difficile → C. difficile toxin → oral metro +/- oral vanco + wean steroids**

Risk factors for VTE:

- **General**: BMI>30, smoker, pregnancy (>3 parity), FHx of VTE, age >35, immobile, pre-clampsia
- **Co-morbidities**: malignancy, HF, APS (SLE), PRV, Sickle cell, nephrotic, Factor V lieden
- **Meds:** COCP, HRT, anti-psychotic, tamoxifen

APTT	PT / INR	Bleed	Cause
Normal	Normal	↑↑↑	• *CKD (less EPO)*
Normal	↑↑↑	Normal	• *F7 def.(acq = warfarin, liver disease, mild Vit K def)* • *Inherited F7 def.* • *F7 inhibitor*
↑↑↑	Normal	Normal	• *F8,9, 11, 12 def.* • ***Inhibitors**: Heparin (HIT), APS* • ***Haem A/B** (Nb: if acq. = won't correct w/ mixing studies)*
↑↑↑	Normal	↑↑↑	• *VWF Disease*
↑↑↑	↑↑↑	Normal	• *DOAC, severe Vit K def.* • *Advanced liver disease(cirrhosis)* • *Factor V def. (or combined F def.)* • *Warfarin + heparin* • *Def/inhibitor to F5, 10, 2 fibrinogen*
↑↑↑	↑↑↑	↑↑↑	• *DIC (low plts)*



Drug	MoA	Route	T1/2	Dose	Check	Reversal
Heparin	+++ anti-thrombin III	IV	0.5	varies	APTT	Protamine
LMWH (-aprarins)		SC	9	Wt-based	No	Protamine (mild)
Warfarin	inhibit vit K factors	Oral	40	varies	INR/PT	Vit K (long)-prothrombinex (SA)
Dabigatran	Direct thrombin inhibitor	Oral	9-13	Fixed	No	Idarucizumab → *if prolonged thrombin time or ICH suspected*
Rivaroxaban	Anti-Xa	Oral	7-11	Fixed	No	No reversal if bleeding → stop Med → ABCD → TXA *for mucosal bleeding* ***Andexanet Alfa***
Apixaban	Anti-Xa	Oral	8-15	Fixed	No	

Platelet issue:

➢ Petechiae + spontaneous bleed (DDx: vwf, G6PD, autoimmune haemolytic)

Factor deficiency issue (PT = F7, APTT = F8,9, 11, 12)

➢ Delayed Soft tissue bleed /ecchymoses + haemoarthroses (DDx: Haem A/B, APS)

Inherited thrombophilia:

1) **Factor V leiden** = causes protein C resistance
2) Prothrombin gene mutation
3) Anti-thrombin III or protein S de
4) **Protein C def:** blood clotting (hypercoagulable) = skin

Collagen	Location	Assoc. conditions
Type 1	Bone, skin, tendons	Osteogenesis imperfecta "brittle bone"
Type 2	Hyaline cartilage, vitreous humour	
Type 3	Reticular fibres, granulation tissue	*Vascular* Ehler Danlos Syndrome
Type 4	Basal lamina, lens, basement membrane	Alport and Goodpasture's
Type 5	Interstitial tissue, placental tissue	*Classic* Ehler Danlos Syndrome

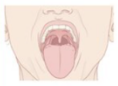
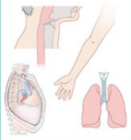
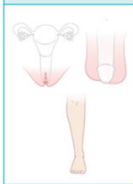
Vitamins	Name	Assoc. conditions with deficiency
A – fat sol.	Retinoic acid	Night-blindness, poor vision + xerosis + keratomelacia
B1	Thiamine	Encephalopathy, beri-beri, extreme weakness
B2	Riboflavin	Angular stomatitis, glossitis, keratitis [**bad skin]** ➔ retarded growth
B3	Niacin	Pellagra (3 D's = dementia, diarrhoea, dermatitis) -
B6	Pyridoxine	Isoniazid, alcohol, bariatric surgery, malabsorption ➔ DRG damage
B7	Biotin	Alopecia [Nb: ↑ ↑ biotin = false +ve ↑ ↑T3/T4 ➔ misdiagnose hyperthyroid]
B9	Folate	IBD, MTX, phenytoin → macrocytic anaemia + cobalamin deficiency
B12 – needed to convert folate for DNA	Cobalamin	Pernicious anaemia, vegans, malabsorption (IBD), drugs (metformin, PPI) ➔ anaemia, CST signs and Wernicke's encephalopathy ➔ SUBACUTE SC DEGENERATION (SPARES STT) + UMN signs (absent ankle reflex)
C	Ascorbic acid (↑ Fe absorption)	Scurvy = gingival inflammation, excess bleeding (epistaxis, heamaturia) ➔ poor collagen formation **Eat peppers, tomatoes, oranges, cauliflower*
D– fat sol.	Calciferol	Rickets (children), osteomalacia (adults) ➔ 90% produced by skin
E– fat sol.	a-tocopherol	Lipid malabsorption | bariatric surgery ➔ tremor, myopathy, cerebellar
K– fat sol.	Phylloquinone	Haemorrhages (epistaxis, heamaturia?)
Copper	~~Leafy veges~~	Zn toxicity, bariatric surgery, malnutrition (retaraded growth) → CST signs, macrocytic anemia, neutropenia
Iodine	~~*Fish, seawater*~~	Goitre, enlarged thyroid gland → cretenism (untreated congenital hypothyroid)
Phosphorus	~~Cereal, milk~~	Weak bones + poor dentition
Zn		Growth retardation, anorexia, ↓ immune, ➔ if severe: *alopecia, dermatitis, diarrhoea*
selenium		Keshan disease (myocardial necrosis)

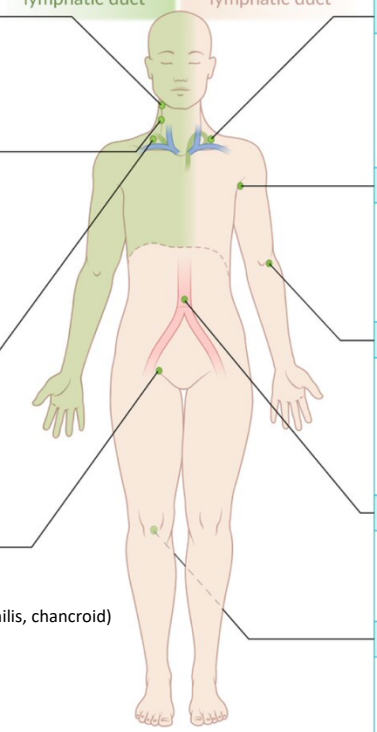
- **Fe = duodenum**
- **Folate = jejunum**
- **Vit B12 (bile salt) = ileum**

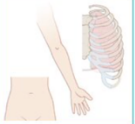
Malnutrition

- **Kwashiorkor = severely protein def. = hypoalbuminemia (*oedema*)**

PALPABLE LYMPHATIC DRAINAGE

Drained areas	Associated conditions
Submandibular lymph nodes	
	• Malignancies of the oral cavity • Tonsillitis
Cervical lymph nodes	
	• Infections of the upper respiratory tract • Infectious mononucleosis • Kawasaki disease • Malignancies of the head, neck, or oropharynx
Right supraclavicular lymph nodes	
	• Mediastinum • Malignancies of the lungs or esophagus
Superficial inguinal lymph nodes	
	• STDs (LGV, genital herpes, syphilis, chancroid) • Malignancies of the pelvis • Infections of the leg • Melanoma of the leg • Cellulitis of the leg or foot



Drained areas	Associated conditions
Left supraclavicular lymph nodes (Virchow node)	
	• Malignancies of the abdomen and pelvis • Sarcoidosis
Axillary lymph nodes	
	• Infections of the arm • Metastasis (breast cancer) • Mastitis
Epitrochlear lymph nodes	
	

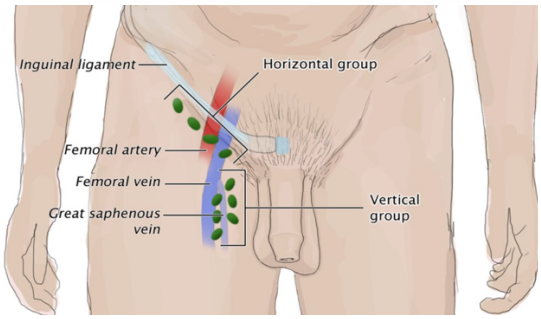
Drainage	DDx
• Ulnar forearm /hand • Drain into axillary LN	• Melanoma • Lymphoproliferative • 2º syphilis • Hand and forearm infection • Tularemia (rabbit fever)

Periumbilical lymph node (Sister Mary Joseph node)

Drainage	DDx
• Abdo-pelvis • Drain into axillary, inguinal, para-aortic LN	• GASTRIC, pancreatic ovarian mets

Popliteal lymph nodes

Drainage	DDx
• Dorsolateral foot & posterior calf • Drain into deep inguinal LN	• Infection/cellulitis (lateral leg or foot) • Melanoma



Superficial inguinal LN
(superficial fascia of femoral triangle)

- All drain into deep inguinal lN

Drainage of horizontal
• Inguinal region • Inferior abd wall (below umbilicus) • Gluteal region • Vulva, lower 1/3rd vagina • Scrotum & Penis exc. glans • Distal anal canal (below dentate)
Drainage of vertical
• Lower limb exc. gluteals

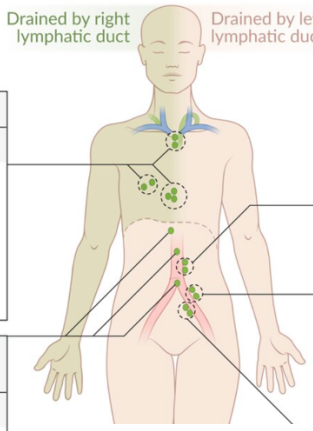
Deep inguinal LN
(femoral triangle parallel to saphenofemoral junction)

- All drain into deep inguinal lN

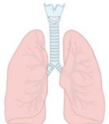
Drainage of horizontal
• Lower limb • Glans, penis or clitoris • Lymph from superior inguinal and popliteal LN • Drain into external iliac LN
Drainage of vertical
• STD • Infection/cellulitis (leg or foot) • melanoma

The testicles, epididymis, and seminal ducts are drained by the deep, iliac, and lumbar lymph nodes.

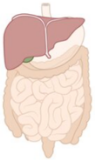
NON-PALPABLE LYMPHATIC DRAINAGE



Paratracheal, mediastinal, hilar lymph nodes

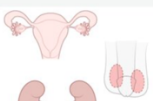
Drained areas	Associated conditions
	Lung carcinoma Esophageal carcinoma Hodgkin lymphoma Metastasis Granulomatous pulmonary diseases

Celiac, superior mesenteric, inferior mesenteric lymph nodes

Drained areas	Associated conditions
	Celiac disease Ulcerative colitis Mesenteric lymphadenitis Colon cancer Focal infections

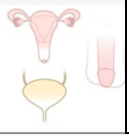
Para-aortic lymph nodes

Drainage
*All drain into cisterna chylli via lumbar lymphatic trunk

Drained areas	Associated conditions
	Endometrial cancer Ovarian cancer Testicular cancer Metastasis

External iliac lymph nodes

Drained areas



Drainage	DDx
• Lower rectum • Anus (above dentate) • Bladder (exc. fundus) • Cervix, lower uterus, middle 1.3rd vagina • Prostate, CC	• STI • Bladder, cervical, prostate mets

Internal iliac lymph nodes

Drained areas	Associated conditions
	Sexually transmitted infections Cervical cancer Bladder cancer Prostate cancer

- Uterus body → upper 1/3rd vagina
- bladder fundus
- Lymph from deep inguinal LN

Pre-aortic LN

Drainage
Coeliac LN (foregut) • Stomach, duo, pan, spleen, liver, biliary tract **SM LN (midgut)** • Lower duo → splenic flex **IM LN (hindgut)** • Splenic flexure → upper rectum *All drain into cisterna chylli via

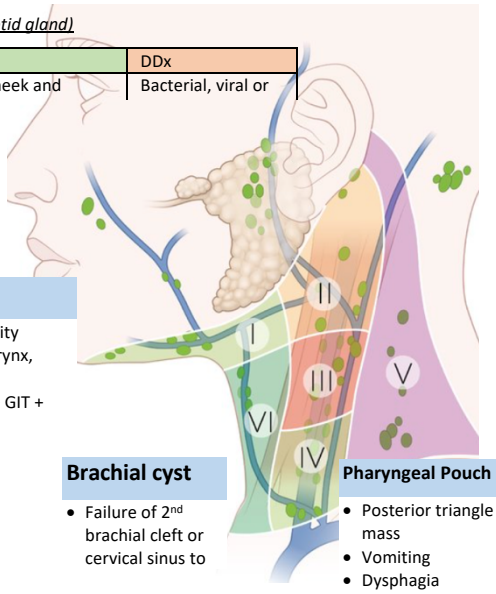
Common iliac LN

Drainage
• Internal and external LN • DRAIN into para-aortic LN
DDx
• Mets

LYMPHATIC DRAINAGE ZONES (HEAD & NECK)

Parotid LN (*paotid gland)*

Drainage	DDx
Skin of ear, cheek and	Bacterial, viral or



Drainage Levels

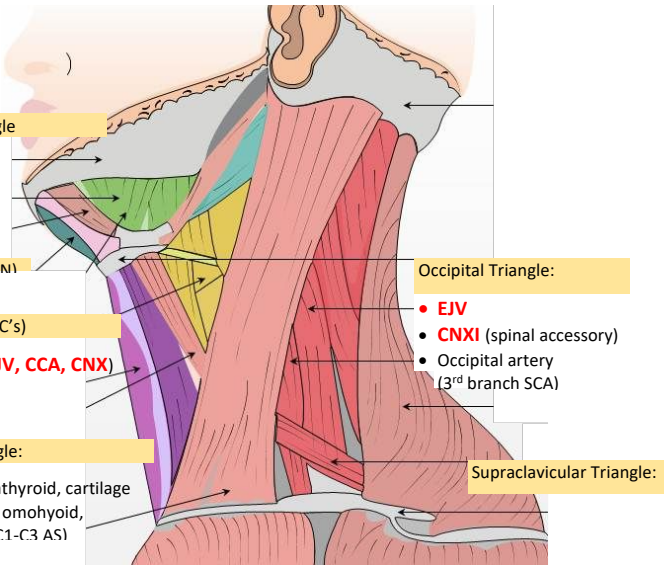
- **Level 1-3** = oral cavity
- **Level 2**-4 = oropharynx, larynx
- **Level 4-6** = larynx + GIT + subglottal

Brachial cyst

- Failure of 2nd brachial cleft or cervical sinus to

Pharyngeal Pouch

- Posterior triangle mass
- Vomiting
- Dysphagia



Submandibular Triangle

- Submand. Gland
- CNXII (hypoglossal)
- Mylohyoid nerve

Submental Triangle (LN)

Carotid Triangle: (3 C's)

- Carotid sheath (**IJV, CCA, CNX**)
- Ansa cervicalis

Muscular Triangle:

- Thyroid, parathyroid, cartilage
- Sternohyoid, omohyoid, thyrohyoid (C1-C3 AS)

Occipital Triangle:

- **EJV**
- **CNXI** (spinal accessory)
- Occipital artery (3rd branch SCA)

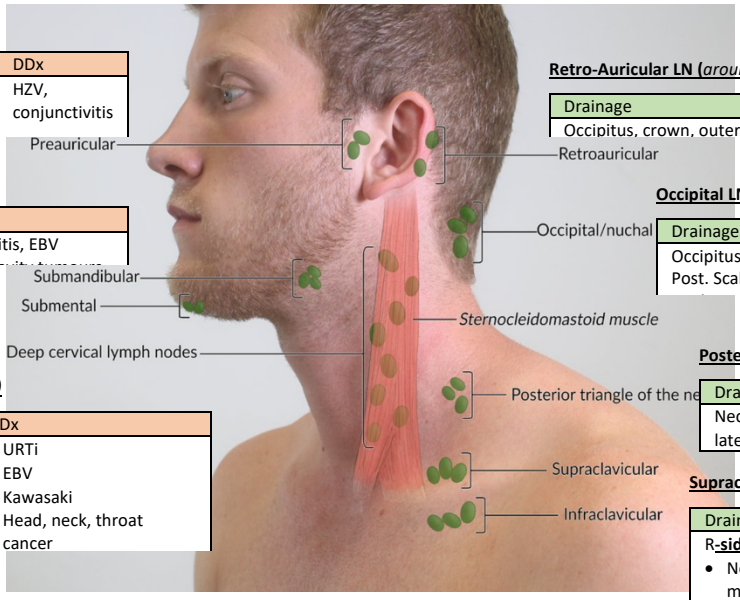
Supraclavicular Triangle:

Pre-Auricular LN (in front of tragus)

Drainage	DDx
Superficial = eyelid, temple, auricle **Deep** = middle ear, soft palate, post. nasal cavity, external auditory meatus	HZV, conjunctivitis

Retro-Auricular LN (*around mastoid process)*

Drainage	DDx
Occipitus, crown, outer ear	Rubella



Submandibular LN

Drainage	DDx
Lateral Tongue, upper lip, gingiva (gum), cheeks	Tonsilitis, EBV Oral cavity tumours

Occipital LN (*NECK and back of head)*

Drainage	DDx
Occipitus Post. Scalp	• Localised scalp infection (e.g. lice, fungal)

Submental LN

Drainage	DDx
Tongue tip, base of	Local infection (EBV)

Posterior Triangle LN

Drainage	DDx
Neck and lateral cervical	Localised infections

Deep Cervical LN (*ventral & dorsal to SCM)*

Drainage	DDx
• Superficial LN groups of head and neck • Drains into Right lymphatic or thoracic duct	• URTi • EBV • Kawasaki • Head, neck, throat cancer

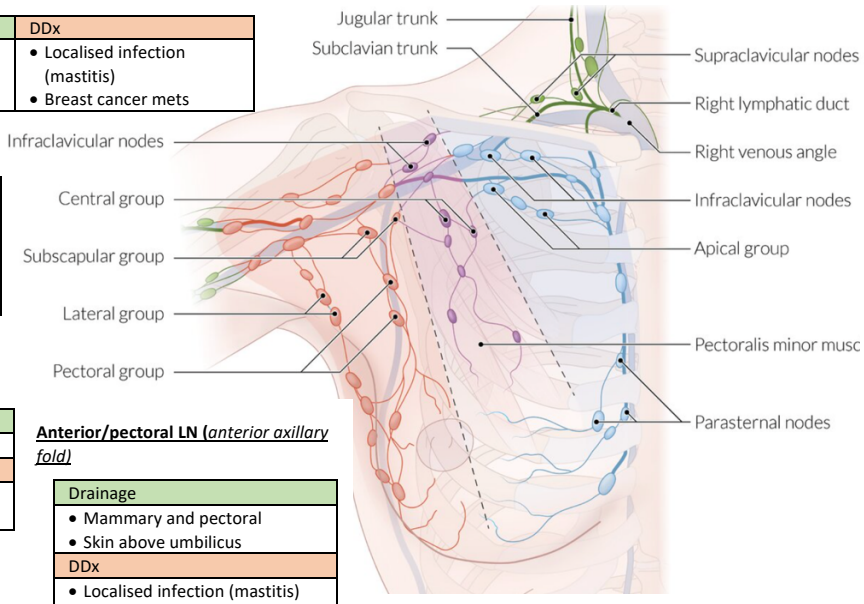
Supraclavicular LN

Drainage	DDx
R-**side:** • Neck, lung, right mediastinum, oesophagus • R upper extremity **L-side: (Virchow's)** • L upper extremity • L thorax	• Lung cancer • Sarcoidosis • **Trosier's** sign = upper GI cancer (gastric, pancreas)

LYMPHATIC DRAINAGE ZONES (Breast)

Central LN (*axillary fat)*

Drainage	DDx
• Lymph from ant. Post, lateral axillary LN • Drain into apical LN	• Localised infection (mastitis) • Breast cancer mets



Posterior (subscapular) LN (*posterior axillary fold)*

Drainage
• Upper back • Posterior neck
DDx
• Localised infection of upper extremity/chest wall

Apical (sub or infraclavicular)

Drainage
• Lymph from central LN • Upper outer quadrant of breast • Drain into right lymphatic or thoracic
DDx
• Localised infection (mastitis) • Breast cancer mets

Lateral (brachial) LN (*medial, proximal upper arm)*

Drainage
• Majority of upper limb
DDx
• Localised infection of upper extremity

Anterior/pectoral LN (*anterior axillary fold)*

Drainage
• Mammary and pectoral • Skin above umbilicus
DDx
• Localised infection (mastitis) • Breast cancer mets