Medicine summary

(2nd semester)

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L1: Anemia

Anemia: WHO criteria is Hg < 13 in men and Hg < 12 in women, Anemia in patient with Malignancy WHO criteria Hg < 14 in men and Hg < 12 in women.

1- Iron deficiency anemia (microcytic hypochromic): Most common cause of anemia

- Chronic blood loss is the most common cause (GI Bleeding in elderly, menorrhagia in women)

- Investigation:

- ✓ Low Retic Count.
- ✓ High RDW > 14.
- ✓ **Iron profile:** Low iron level, High TIBC, high transferrin receptors, Low ferritin.
- ✓ In peripheral smear: microcytic hypochromic and increase anisocytosis.
- ✓ The gold standard is bone marrow biopsy.

- Treatment:

- ✓ Oral iron (ferrous sulfate or ferrous fumarate) for stable cases.
- ✓ Parenteral iron for severe cases like (chest pain).
- ✓ Blood transfusion is not recommended unless anemia is severe or the patient has cardiopulmonary disease.

2- Anemia of chronic disease:

- Pathophysiology: Any chronic inflammation or diseases will release cytokines, which lead to: decrease EPO production, suppression of erythrocyte progenitor, blockage of reticuloendothelial iron release and increase hepcidin levels**.**

- Investigations:

- ✓ **Iron profile:** Low serum iron, low TIBC, low transferrin 15-20%, normal to increased ferritin.
- ✓ RDW normal**.**
- ✓ Usually normocytic and normochromic, but may be microcytic and hypochromic as well.

- Treatment:

- ✓ Treat the underlying cause
- ✓ EPO in renal failure

L2: Lymphoma

Clinical grouping of lymphoma		
Indolent (low grade)	Aggressive (intermediate grade)	Highly aggressive (high grade)
e.g. Follicular lymphoma Grade 1,2 22%	e.g. Diffuse large B-cell lymphoma 21%	e.g. Burkett's lymphoma 1%.

Lymphoma staging system (Ann Arbour Classification)	
Stage I	Single lymph node region.
Stage II	Two or more lymph node regions.
Stage III	Lymph node regions on both sides of diaphragm
Stage IV	Widespread disease.
A	Asymptomatic
B	Fever (recurrent), night sweats, Wight loss.
X	Bulky disease ≥ 10 cm Or > 1/3 internal transverse diameter at T5-T6 on PA CXR.
E	Limited extra-nodal extension from adjacent nodal site.

Notes:
- Metastatic: Thyroid tumor + nasopharyngeal carcinoma associated with "Epstein-Bar virus"
- Systemic diseases can cause Lymphoma: HIV & SLE
- Drug-induced Lymphadenopathy: Phenytoin and some diuretics.

Non Hodgkin lymphoma NHL:
- Painless lymphadenopathy, nodes are not warm, red or tender.
- Investigation: Core biopsy. CBC is normal in most cases.

Management of NHL	
Indolent	- Old patient → Observe - Young patient with follicular grade I → High aggressive chemo
Aggressive	- Stage I → Aggressive chemo + local radiation - Stage II,III,IV → Chemo 4-6 cycles, if B symptoms add two cycles (6-8 cycles), if there is X (bulky disease) add radiation - We use PET scan to follow up → Residual → chemo, chemo, chemo, chemo, until it disappear

Hodgkin lymphoma:
- shows reed sternberg cells on pathology.
- **The difference between NHL and HL in treatment of residual:**

NHL: aggressive chemotherapy NH: radiotherapy (IFRT).

Management of HL		
Early stage		**Advanced**
FAVOURABLE 1-3 sites, Age ≤ 40	UNFAVOURABLE > 3 sites, Age > 40	- Stage III, IV -Bulky Disease -B Symptoms
Treatment: chemo + radiotherapy		**Treatment**: mainly **chemo** + radiotherapy in case of bulky or residual

MALT lymphoma:
- Associated with H pylori infection.
- Treatment: antibiotics for gastric MALT lymphoma.
- We don't treat lymphoma with surgery except in gastric lymphoma with obstruction.

L3: Leukemias

Acute Leukemias

- The leukaemias are a group of disorders characterized by the accumulation of malignant white cells in the bone marrow and blood. They can be classified into four subtypes on the basis of being either *acute* or *chronic*, and *myeloid* or *lymphoid*.
- Acute leukaemias are aggressive diseases in which transformation of a haemopoietic stem cell leads to accumulation of >20% blast cells in the bone marrow.
- The clinical features of acute leukaemia result from bone marrow failure and include anemia, infection, and bleeding. Tissue infiltration can also occur.
- AML is common in adults (median onset of 65 years), while ALL is the most common malignancy of childhood.
- The diagnosis is made by analysis of blood and bone marrow using microscopic examination (morphology) as well as immunophenotypic, cytogenetic and molecular studies. Cytogenetic and molecular abnormalities are used to classify and indicate prognosis in the majority of cases.
- Acute promyelocytic leukaemia (M_3) is a variant of AML that carries a t(15;17) chromosomal translocation. It commonly presents with bleeding and is treated with retinoic acid and chemotherapy.
- The prognosis for patients with AML has been improving steadily, particularly for those under 60 years of age, and approximately one-third of this group can expect to achieve long-term cure. The outcome for elderly people remains disappointing. Allogeneic stem cell transplantation is useful in treating some subsets of patients and may also be curative for patients with relapsed disease.
- Acute lymphoblastic leukaemia (ALL) is caused by an accumulation of lymphoblasts in the bone marrow. ALL is subclassified according to the underlying genetic defect and a wide variety of genetic lesions are seen. The number of chromosomes in the tumor cell has prognostic importance: *Hyperdiploid* cells have >50 chromosomes and generally have a good prognosis whereas *hypodiploid* cases (<44 chromosomes) carry a poor prognosis. Treatment protocols for ALL are complex and usually have four components – remission induction, intensification, CNS-directed therapy and maintenance. 85% of children can now expect to be cured, while in adults drops significantly to less than 5% over the age of 70 years.

CML

- Chronic myeloid leukaemia (CML) is a clonal disorder of a pluripotent stem cell. The disease accounts for around 15% of leukaemias and may occur at any age (most commonly between 40-60 years).
- All cases of CML have a translocation between chromosomes 9 and 22 (Philadelphia chromosome) resulting in *BCR-ABL1* gene codes for a fusion protein with tyrosine kinase activity. Which is seen by karyotype examination of tumor cells or by FISH or PCR.
- The clinical features include anemia, bleeding and splenomegaly. There is usually a marked neutrophilia with myelocytes and basophils seen in the blood film.
- Treatment is with tyrosine kinase inhibitors such as imatinib, dasatinib or nilotinib. Stem cell transplantation can be curative and may also be useful for advanced disease.
- The clinical outlook is now very good and patients can expect long-term control of disease.

CLL

- Chronic lymphocytic leukaemias (CLL) are characterized by the accumulation of mature B or T lymphocytes in the blood. Chronic lymphocytic leukaemia (CLL, B cell) represents 90% of cases and has a peak incidence between 60 and 80 years of age.
- Individual subtypes are distinguished on the basis of morphology, immunophenotype and cytogenetic.
- Most cases are identified when a routine blood test is performed. As the disease progresses the patient can develop enlarged lymph nodes, splenomegaly and hepatomegaly.
- Immunosuppression is a significant problem because of hypogammaglobulinaemia and cellular immune dysfunction. Anaemia may also develop because of autoimmune hemolysis and bone marrow infiltration.
- Diagnosis is usually performed by immunophenotypic analysis of peripheral blood which reveals a clonal population of $CD5^+$, $CD23^+$ B cells. The best guide to prognosis is the stage of the disease.

L4: Introduction to cancer

- **Cancer** is a term used for diseases in which abnormal cells divide and escape the body's control.
- Cancer arises from the **mutation** of a normal gene; mutated genes that cause cancer are called oncogenes
- Cancer Etiology:
    - DNA mutations: Radiation and other environmental factors (tobacco, alcohol, radon, asbestos, etc.)
    - Genetic predisposition: BRCA1 and BRCA2
    - Infectious agents:
        - HPV – cervical cancer, Hepatitis – liver cancer, H.pylori – stomach cancer, EBV – lymphoma
- Malignant disorders categorized into SOLID and LIQUID
- Solid like Carcinoma. Liquid like LUEKEMIA
- There are NO specific signs or symptoms for malignancy
- There are **clues** for these nonspecific signs and symptoms: progressive, persistent and disabling.
- **Constitutional symptoms:** fatigue, fever, sweating, and weight loss.
- The aim of cancer treatment is to cure cancer (curative) if possible OR control the symptoms and improve the patient's survival if not curable (palliative)
- **Adjuvant treatment:** administered after surgery and its aim is to increase the disease-free and overall survival.
- **Neoadjuvant treatment:** patients receive chemotherapy, radiotherapy, or hormonal therapy before surgery.
- Treatment modalities: local (surgery or radiotherapy), and systemic (chemo).

L5: Common solid tumors:

EPIDEMILOGY OF COMMON SOLID TUMORS:

In the KSA, The three most common cancers:
- Men: 1st colorectal, 2nd Lymphoma, 3rd leukemia.
- Women: 1st Breast, 2nd Thyroid, 3rd colorectal.

BREAST CANCER:

1st most common cancer in females.

- 2nd leading cause of death.
- Wide age range 20 - +70y.
- Associated with BRCA1 and BRCA2.

RISK FACTORS:

- History of breast cancer
- Family history of breast cancer.
- Benign breast diseases / atypical hyperplasia
- Early menarche, late menopause.
- Late first pregnancy/ no pregnancy.
- Exogenous estrogens.

Premalignant in situ breast cancers:

DCIS:

- Arise from ductal elements.
- Found on mammogram.
- Treated by lumpectomy or mastectomy if negative margins.

LCIS:

- Arise from lobular elements.
- Found on biopsy.
- Treatment is variable
- 1. Close observation
- 2. selective estrogen receptor modulators
- 3. prophylactic bilateral mastectomy

✓ Breast cancer is **usually painless**.
✓ It may also be associated with **retraction of the nipple**.

- Fine needle aspiration(FNA): the best initial biopsy.
- Open biopsy : The most accurate diagnostic test.

MANGEMENT:

- **Local therapy: surgery & radiotherapy*:*** Lumpectomy with radiation

- **Systemic therapy: Chemotherapy & hormonal therapy & biological therapy:**

- Estrogen Receptor or Progesterone Receptor: tamoxifen or one of the aromatase inhibitors (anastrazole, letrozole, exemestane)

- HER2/NEU overexpressing: transuzumab.

COLON CANCER:

1st most common cancer in males.

2nd leading cause of death.

RISK FACTORS:

- Age—everyone over the age of 50 years is at increased risk
- Adenomatous polyps .
- Personal history of prior CRC (Colorectal Cancer) or adenomatous polyps
- Inflammatory bowel disease (IBD):

a. Both ulcerative colitis (UC) and Crohn's disease .

- Family history

a. Multiple first-degree relatives with CRC

b. Any first-degree relative diagnosed with CRC or adenoma under age 60

- Dietary factors—high-fat, low-fiber diets associated with a higher risk of CRC
- Major polyposis syndromes:

- Familial adenomatous polyposis.
- Gardner's syndrome.
- Turcot's syndrome.

CLINICAL PRESENTATION:

• A change in bowel habits, including diarrhea or constipation.

• Rectal bleeding (Hematochezia) or blood in your stool.

• Persistent abdominal discomfort, such as cramps, gas or pain.

• Unexplained weight loss.

• Unexplained Fatigue.

• Unexplained iron deficiency anemia.

Colonoscopy:

• **Most sensitive and specific test**. It is a diagnostic and therapeutic.

• Carcinoembryonic antigen (CEA): not useful for screening; useful for baseline and recurrence surveillance. CEA does have prognostic significance

Treatment:

1. Surgery is only curative treatment of CRC
2. CEA level should be obtained before surgery.

L6: DM type I

- T1DM is a t-cell mediated autoimmune disease that involves destruction of beta cells resulting in absolute insulin deficiency.
- It develops in genetically susceptible individuals who are exposed to an environmental factor that triggers the immune response:
  - Genetic predisposition: (HLA DR3/DR4).
  - Viruses (Mumps, Coxsackie B, Rubella).
  - Dietary (cow's milk)
- Cardinal symptoms are (polyphagia, polydipsia, polyuria, and weight loss).
- Symptoms often develop quickly over days to weeks.
- Sometimes appear after an illness.
- Labs:
  - Random blood glucose:
    - A sample is taken without regard to last meal.
    - Usually used for screening.
  - Fasting blood glucose (FBG)
    - Patient should be fasting for at least 8 hours. It shows impaired fasting.
  - Oral glucose tolerance test (OGTT)
    - A glucose load of (75grams) is administered as an oral solution. Blood glucose is taken 2 hours postprandial.
  - HbA1C
    - Exposure of hemoglobin A results in nonenzymatic glycation of the protein.
    - Shows the average of the blood glucose for the last 3 months
- Tx:
- Insulin is the mainstay of treatment.
- Education، Physical activity, and diet.

Symptoms of DM	**The cause**
Polyuria	Glucose in renal tubule causes osmotic retention of water, causing a diuresis
Polydipsia	A physiologic response to diuresis to maintain plasma volume
Fatigue	May due to increase glucose in plasma
Weight loss	Due to loss of anabolic effect of insulin
Blurred vision	Swelling of lens due to osmosis (caused by increased glucose)
Fungal infection	Common in mouth and vagina (Candida thrives under increased glucose condition.
Numbness and tingling of hand and feet	Mononeuropathy: due to microscopic Vasculitis leading to axonal ischemia Polyneuropathy: etiology is probably multifactorial

Comparison of type I and II DM		
	Type I	**Type II**
Onset	Sudden	Gradual
Age of onset	Any age (typically young)	Mostly in adults
Body habitus	Usually thin	Frequently obese
Ketosis	Common	Rare
Autoantibodies	Present in most cases	Absent
Endogenous insulin	Low or absent	Can be normal, decreased or increased
HLA association	DR)/Yes (HLA-DQ	No
Genetic factor	Concordance rate between identical twins is 50%	Concordance rate between identical twins is 90% therefore, type II demonstrate a much strong genetic component than type I
Family history	Uncommon	Common

L7: DM type II

- Type two diabetes, once known as adult-onset or noninsulin-dependent diabetes.
- Patients with type two diabetes usually have associated disorders including hypertension, dyslipidemia, non-alcoholic fatty liver, and in women, polycystic ovarian syndrome,
- type two diabetes is much more common in patients who are obese.
- type two diabetes (Insulin IS SECRETED NORMALLY).
- type one diabetes (Insulin IS **not** SECRETED NORMALLY).
- Risk factors of type II Diabetes mellitus: 1- Obesity(most potent) 2- Genetics 3- Age.
- obesity exacerbates insulin resistance in type two diabetes.
- type 1 progresses acutely, while type 2 progresses chronically.
- patient with type 2 diabetes presentation are: polyuria, polydipsia, polyphagia, fatigue, blurred vision, weight loss, and/or candidal vaginitis.

American Diabetes Association, 2011
Diagnostic criteria for Diabetes Mellitus

	Normal Glucose tolerance	Impaired Glucose Tolerance 'PREDIABETES'	Diabetes Mellitus
Fasting plasma glucose	<100mg/dl	100-125mg/dl	*>/=126mg/dl*
2 hr plasma glucose during an OGTT**	<140mg/dl	140-199mg/dl	*>/=200mg/dl*
Random Blood glucose + Symptoms of diabetes*			*>/= 200mg/dl*
A1C	<5.6%	5.7-6.4%	*>/= 6.5%*

*polyuria, polydispsia, weight loss
**after a glucose load of 75g anhydrous glucose dissolved in water

Drugs that are used for type II DM:

- **Metformin** :(Biguanide) :The best initial drug
- **Sulfonylureas**: NOT used as first line therapy
- **Nateglinide** and **Repaginate**: Similar to sulfonylureas (increase insulin release) but do not contain sulfa.
- **Alpha glucosidase inhibitors (Acarbose, Miglitol) :** Can be used with renal insufficiency

L8: Diabetes Complications.

Diabetic complications categorized into two, based on the onset:

1. Acute.
2. Chronic.

Acute Complications	Chronic Complications
A) **Hypoglycemia:** no mortality, and the patient usually able to manage him/herself without need for hospitalization. B) **Hyperglycemia**: I. Simple. II. DKA. (Emergency, mostly with type 1 and caused by severe insulin deficiency.) III. Hyperglycemic Hyperosmolar State (HHS): 50% mortality rate. Mostly in type 2. The patient may lose up to 6 L of fluid and the blood could turn into Jelly-appearance. **Management of DKA & HHS:** 1. Fluid resuscitation. 2. Insulin infusion. 3. K^+ replacement. (not needed in DKA) 4. Heparin as a prophylaxis.	A) **Neuropathy (e.g. loss of sensation, hypersensitivity to touch):** accumulation of sorbitol inside of Schwann cell, pressing on the axon. B) **Retinopathy (e.g. blurred vision, vision loss):** Angiogenesis due to lack of glucose inside of the Rods and Cons → rupture of the vessels after a stress e.g. sneezing. C) **Nephropathy (signs and symptoms of proteinuria):** goes through four phases, from glucose excretion till nephrotic syndrome. The latter will results in Glomerulosclerosis. D) **Vasculopathy (e.g. diabetic foot along with neuropathy, claudication, stroke):** ranging from CAD, CVD and PVD. Caused mainly by dyslipidemia.

L9: Bleeding Disorders

- Platelet bleeding or VWF is superficial (easy bruising, epistaxis, menorrhagia)
- Factor bleeding is deep (Joints and muscles)

Disorder		Signs & symptoms	Investigations and diagnosis:	Treatment
Hemophilia X linked A: ⬇FVIII B: ⬇FIX (Christmas Disease) Autosomal C: ⬇FXI (Rosenthal Syndrome)	✓ A bleeding disorder caused by deficiency of coagulation factors. ✓ Most common inherited bleeding disorders	hematomas, hemarthroses, bruising, bleeding (mucosal, GI, GU) The severity and the degree of bleeding Symptoms correlate with Factor levels (sever if <1 % factor activity)	✓ Prolonged aPTT ✓ low Factor Level (F VIII or FIX or F XI) ✓ Mixing study (corrected) ✓ Normal VWF & PT	✓ Replacement of the deficient coagulation Facto ✓ Adjunctive therapy (Desmopressin (DDAVP) for mild cases
Von Willebrand Disease (VWD)	VWD is the most common inherited bleeding disorder with a decrease of von Willebrand factor (VWF). It is autosomal dominant	Look for bleeding related to platelets (epistaxis, gingival, gums) with a normal platelet count.	✓ VWF (antigen) level may be decreased ✓ Ristocetin cofactor assay ✓ Factor VIII activity ✓ Bleeding time: increased duration of bleeding (rarely done) ✓ PTT may be elevated in half of patients	The best initial therapy is DDAVP (desmopressin) If there is no response, use factor VIII replacement or VWF concentrate.
Disseminated Intravascular Coagulation	Aabnormal activation of the coagulation sequence→ microthrombi throughout the microcirculation. Does not occur in otherwise healthy people.	look for a definite risk such as: sepsis, burns, amniotic fluid embolus, snake bites, trauma, cancer	✓ Elevation in both the PT and aPTT ✓ Low platelet count ✓ Elevated d-dimer and fibrin split products ✓ Decreased fibrinogen level (it has been consumed)	Treat the underlying cause. If platelets are under 50,000/microliter and the patient has serious bleeding, replace platelets as well as clotting factors by using **FFP**
Immune Thrombocytopenic Purpura (ITP): Quantitative	autoimmune antibody formation against host platelets. Diagnosis of exclusion	Petechiae and ecchymoses on the skin. Bleeding of the mucous membranes.	✓ Peripheral smear shows decreased platelets. ✓ Bone marrow aspiration shows increased megakaryocytes. ✓ There is an increased amount of platelet-associated IgG.	Mild<30,000: Glucocorticoids Sever <10,000: IVIG, Anti-Rho Recurrent episodes, steroid dependent: splenectomy

Thrombotic Thrombocytopenic Purpura / Hemolytic Uremic Syndrome (TTP/HUS) Quantitative	TPP: clotting in small blood vessels of the body. HUS: is a clinical syndrome	1. Thrombocytopenia 2. Micro angiopathic haemolytic anemia (MAHA) (100%) 3. Renal Failure (50%) 4. Neurological symptoms (65%) 5. Fever (25%) HUS Triad: 1- Thrombocytopenia 2- MAHA 3- Renal Failure	✓ Thrombocytopenia + MAHA ✓ +ve Schistocytes (> 2-3/hpf), -ve Coombs ✓ Normal PT/aPTT& Fibrinogen ✓ ADAMTS13 Deficiency	✓ Plasma pheresis ✓ Corticosteroids and splenectomy ✓ Eculizumab in HUS Platelet transfusion is contraindicated because that will cause microvascular thrombosis.
Bernard–Soulier Syndrome: Qualitative	Disorder of platelet adhesion due to deficiency of platelet glycoprotein GPIb-IX		On peripheral blood smear, platelets are abnormally large. Platelet count is mildly low.	
Glanzmann'sThrombasthenia: Qualitative	Disorder of platelet aggregation due to deficiency in platelet glycoprotein GPIIb-IIIa		Bleeding time is prolonged. Platelet count is normal.	
Heparin-Induced Thrombocytopenia (HIT)	HIT presents 5 to 10 days after the start of heparin with a marked drop in platelet	Both venous and arterial thrombosis can occur, although venous clots are more common. Rarely leads to bleeding. The platelets just precipitate out.	HIT is confirmed with an ELISA for platelet factor 4 (PF4) antibodies or the serotonin release assay.	Immediately stop all heparin Administer direct thrombin inhibitors: argatroban, lepirudin, and bivalirudin.

L10 Thyroid disorders

- **Thyroid hormone action:** act on the bone and bone development, In brain: cognitive impairment, Regulate metabolic rate and little change in bodyweight and Act on cardiac muscle: tachyand bradycardia
- Assess thyroid function by : Free T4, FT3 ,TSH ,Ultrasound neck

Hyperthyroidism

- Etiology and Diagnosis:

Lab Findings in Hyperthyroidism			
Diagnosis	**TSH**	**RAIU***	**Confirmatory**
Graves disease	Low	Elevated	Positive antibody testing
Subacute thyroiditis	Low	Decreased	Tenderness
Painless "silent" thyroiditis	Low	Decreased	None
Exogenous thyroid hormone use	Low	Decreased	History and involuted, nonpalpable gland
Pituitary adenoma	High	Not done	MRI of head
*RAIU = radioactive iodine uptake			

- Treatment of Acute Hyperthyroidism and "Thyroid Storm":

1. Propranolol
2. Thiourea drugs (methimazole and propylthiouracil)
3. Iodinated contrast material (iopanoic acid and ipodate):
4. Steroids (hydrocortisone)
5. Radioactive iodine: ablates the gland for a permanent cure

What causes goiter:
Goiters can occur when the thyroid gland produces either

- too much thyroid hormone (hyperthyroidism)
- not enough (hypothyroidism)
- Normal production (nontoxic multinodular goiter)

Hypothyroidism

- Etiology: Hashimoto thyroiditis ,
- Occasionally patients have hypothyroidism from Dietary iodine deficiency or Amiodarone
- Diagnostic Tests: TSH levels are markedly elevated if the gland has failed.
- Treatment: Replacing thyroid hormone with thyroxine (synthroid) is sufficient.

What to Look for in Hypothyroidism and Hyperthyroidism	
Hypothyroidism	**Hyperthyroidism**
Bradycardia	Tachycardia, palpitations, arrhythmia (atrial fibrillation)
Constipation	Diarrhea (hyperdefecation)
Weight gain	Weight loss
Fatigue, lethargy, coma	Anxiety, nervousness, restlessness
Decreased reflexes	Hyperreflexia
Cold intolerance	Heat intolerance
Hypothermia (hair loss, edema)	Fever

1-Severe hypothyroidism causes myxedema, but hyperthyroidism is associated with pretibial myxedema.

2-Almost all bodily processes are being slowed in hypothyroidism except the menstrual flow

L11: Parathyroid disorders

- Parathyroid hormone (PTH), calcitonin (CT) and Vit D are tightly regulating the levels of electrolytes (Ca^{++},$Mg^{++}$and phosphate) in the serum by working in bone , kidney and intestine.
- Calcitonin (CT) antagonizing parathyroid hormone and Vit D effects.
- Calcitonin (CT) released when Ca level is high.
- PTH released when Ca level is low.

Hyperparathyroidism

✓ Common in age of 50 and in women

Causes divided to:

- Parathyroid related :
  1. Primary hyperparathyroidism (Solitary or Multiple) **and** Lithium therapy.
- VitD related:
  1. Vitamin D intoxication
  2. granulomatous diseases (TB and sarcoidosis release active VitD)
  3. Idiopathic hypercalcemia of infancy
- Malignancy – related : solid tumor + hematological malignancies
- Associated with renal failure.

Clinical features:

- 90% Asymptomatic discover by routine screening, Vague symptoms (fatigue, weakness, etc..), Bone and kidney complications (rare)

NOTE: in endocrinal disorders never start with imaging !! always start with chemicals level

Diagnostic tests:

- high (Ca)*, (PTH), low serum phosphate.

* If it is normal check vitD level and kidney function

- the most accurate scanning test is Sestamebi scan

Tx: Resection of 3 ½ glands (put the rest half in forearm to be easily reached in case of recurrence).

acute severe:

1. adequate hydration
2. diuretics (furosemide)

Hypoparathyroidism

All four glands become hypo not only one like hyper

Causes

1. Surgical hypoparathyroidism – the commonest (by removal of the gland or interrupting blood supply).
2. Idiopathic hypoparathyroidism.
3. Functional hypoparathyroidism(due to chronic hypomagnesaemia)
4. Radiation
5. Epileptic drugs

DDx of hypocalcemia :

1. hypoparathyroidism
2. Deficiency of vitamin D or calcium
3. Malabsorption disorders .
4. (Pseudohypoparathyroidism) tissue resistance to PTH
5. Tissue resistance to vitamin D
6. Excessive intake of phosphate
7. Severe hypomagnesemia
8. Chronic renal failure

Clinical features:

Neuromuscular hyperexcitability (Parathesia, tetany …etc)

Diagnosis : Hypocalcaemia, hyperphosphatemia, Undetectable serum iPTH

Tx: oral calcium with vitamin D or its potent analogues (active form due to PTH def. which activate inactive vit D) **and** phosphate restriction.

L11: Metabolic bone diseases

Osteomalacia:

- Failure of organic matrix (osteoid) of bone to mineralize normally.
- Disease of adults , Disease of children called Rickets which has bone deformity unlike Osteomalacia.

Causes :

1. Vitamin D deficiency:

Inadequate sunlight exposure. 90% , Gastrointestinal diseases (malabsorption) , Impaired synthesis by the kidney, Target cell resistance, Dietary, Impaired renal tubular reabsorption of phosphate.

2. Systemic Acidosis: get the Ca out of bone (kidney diseases and soft drinks)
3. drugs induced

Patients with osteomalacia go through three phases .

Clinical Features:

- non-specific skeletal pain and muscular weakness.
- fractures
- waddling gait.

Treatment:

Oral calcium **and** Vit D supplementation (inactive :Cheap , more physiological / indication of active form only in kidney and liver diseases)

hypophosphataemicrickets :phosphate , vit D to prevent hypocalcaemia and secondary hyperparathyroidism.

Follow up: Normalized Ca then VitD then ALP+PTH then radiological changes is the final restore to normal

Osteoporosis

Decrease in bone mass (not mineralization) and strength .

Clinical Features:

It is usually an asymptomatic disease until fractures occur.

It could lead to many complications:

- chronic back pain., dorsal Kyphosis , loss of height occurs, Hip fractures

	Type I	Type II
Name	Post Menopausal	Senile
Type of bone loss	Mainly trabecular	Trabecular & Cortical
Fracture site	Vertebrae (Crush) & distal radius (Colle's)	Vertebrae (Multiple wedge), hip, pelvis, proximal humerus
Main causes	Factors related to menpause	Factors related to aging

Diagnosis:

- sex hormones deficiency.
- X-rays decreases in osseous density means 30% of bone mass lost
- SPA,DPA and CT (compare it with peak bone density skeleton which in age 20 -30)

Treatment:

- calcium intake, vit D supplementation, exercise
- Avoidance of osteopenia-producing conditions/medications/lifestyles: Smoking & excessive alcohol intake, excessive caffeine/protein intake, Amenorrhea/oligomenorrhea and Cortisone.

L12: Pituitary Disorders

Hypopituitarism:

Caused by any conditions that compresses or damages the pituitary gland. Hypothalamic or pituitary tumor is the most common cause

Clinical features: Depends on the hormones that are lost

Prolactin:	**LH and FSH:**	**GH:**
no symptoms in men, inability to lactate in women	Infertility, loss of secondary sex characteristics and decreased libido, Women: amenorrhea, Men : erectile dysfunctions	children: short stature and dwarfism, adult: central obesity, increased LDL and cholesterol levels and reduce lean muscle mass

Diagnosis:
Hypernatremia, MRI of the brain (may miss micro adenomas)
And specific diagnosis tests for each hormones

Treatment:
Replacement of appropriate hormones

Diabetes insipidus:

Decrease in ADH from the pituitary (Central DI) or decrease in ADH effect in kidneys (Nephrogenic DI)

	Central DI	**Nephrogenic DI**
Causes	Idiopathic, destruction of brain or infiltration of gland from sarcoidosis, infection	kidney diseases , Lithium use, Hypercalcemia and Sickle cell anemia
Clinical feature	Polyuria, Thirst and polydipsia, Hypernatremia, Neurological symptoms (when volume losses are not matched)	
Diagnosis:	Decreased: Urine osmolality and urine sodium. Increase: Serum osmolality. Different between central and Nephrogenic DI by response to vasopressin:	
	volume decrease + osmolality increase	no effect
Treatment	vasopressin	correcting the underlying cause, Diuretic , NSAIDs

Acromegaly:

It is Overproduction of GH leading to soft tissue overgrowth throughout the body.

Causes: pituitary adenoma

Clinical features: Soft tissue and skeleton overgrowth, carpal tunnel syndrome, Coarsening of facial features, Enlarged jaw, Increasing glove/ring/shoe/hat size, Arthralgia, Body odor from Hyperhidrosis, Sleep apnea,Deep voice ,Colonic polyps, HTN, Hypertrophic cardiomyopathy

Diagnosis:
The best initial test is level of insulin-like growth factor (IGF-1). Most accurate is the glucose suppression test.

Treatment:
The first line therapy: transsphenoidal resection

Medications: Octreotide or lanreotide, Pegvisomant

If don't respond to surgery or medications: Radiotherapy

"Most common cause of death in an acromegaly patient is cardiovascular disease (CHF) "

Hyperprolactinemia

Causes: pituitary adenoma, primary hypothyroidism, Medications (verapamil) , Pregnancy, Renal failure

Clinical features:
1) Men: Hypogonadism, decreased libido and infertility, rarely Glactorrhea and gynecomastia
2) Women: amenorrhea, infertility, and Glactorrhea

Diagnosis:
After prolactin level is found high, perform: Thyroid function test, Pregnancy test, BUN/Creatinine, Liver function test
MRI (done after: High prolactin level is confirmed, Secondary causes are excluded, and patient is not pregnant)

Treatment:
First drug of choice: Dopamine agonists: Cabergoline
If not responding to medications: Transsphenoidal surgery

"Always exclude pregnancy first in any women with high prolactin "

L13: Adrenal disorders

Primary adrenocortical insufficiency "**Addison's Disease**"	**Secondary** adrenocortical Insufficiency	**Cushing's Disease**
Main event: Damaged Adrenals → ↓ **Adrenal hormones.** **Major Causes :** 1- Autoimmune (80%). 2-Tuberculosis (20%). **Symptoms** usually appear after the loss of 90% of both adrenals: **1-Hyperpigmentation** (↑ACTH&BLPH) 2-Fatigue, anorexia & weight loss 3- GI disturbance 4-postural hypotension 5-craving salt 6-Amenorrhea 7-Loss of body hair 8- Hypoglycemia Lab Findings: **Hyponatremia**, **hyperkaliemia,** anemia, neutropenia, eosinophilia, **Azotemia** and **metabolic acidosis**. Diagnostic test: **Rapid ACTH stimulation test (Cosyntropin Or Tetracosactrin).** Results:↓Adrenal reserve Treatment: **Hydrocortisone** & Fludrocortisone.	Main event: ↓ ACTH →↓ Cortisol & Androgen but **normal Aldosterone**. **Causes:** 1-Exogenous glucocorticoid administration. 2-Pituitary /hypothalamic tumors. **Symptoms** same as the primary except that there is **No Hyperpigmentation, Hypotension or Salt craving.** Lab Findings: Only **Hyponatremia** and **Hypoglycemia**. Diagnostic test: **Plasma ACTH Level** Results: Primary: ↑ ACTH Secondary: ↓ ACTH Treatment: **Hydrocortisone.**	Main event: Chronic **glucocorticoid EXCESS**. **Causes:** Iatrogenic (**chronic steroid ingestion**.) -**ACTH Dependent**: • pituitary adenoma• Ectopic ACTH syndrome. -**ACTH Independent:** • Adrenal Adenom • Adrenal Carcinoma. **Symptoms:** - **Central obesity** - **Stria** - **Hypertension** - **Hirsutism** - Gonadal Dysfunction - Psychological Disturbances Lab findings: High normal hemoglobin, hypokalemic alkalosis, **hyperinsulinism** & **hypercortisolism**. Diagnostic test: **1-** first test for the presence of **hypercortisolism**. Best initial test for that is **24-hour urine cortisol.** Or Second option **OVERNIGHT 1 MG DEXAMETHASONE SUPPRESSION TEST.** **2- The second test is for determine the Cause** of hypercortisolism**, wither it caused by Pituitary or Ectopic production (tumor)** Best initial **ACTH level , if** ↑ then the cause either **Pituitary** (suppresses with high dose dexamethasone) or **Ectopic production**; lung cancer or carcinoid (Doesn't suppress). Treatment: Transphenoidal surgery → **pituitary sources.** laparoscopic removal → **adrenal sources**.

- **Primary Hyperaldosteronism:** ↑ **aldosterone** → **hypokalemia & sodium retention**→ Volume expansion, hypertension& metabolic alkalosis. Causes: 1- **aldosterone producing adenoma (Conn's syndrome**) 2- Bilateral Adrenal hyperplasia. Symptoms: **HTN with hypokalemia** – headache & fatigue – Polydipsia, nocturnal polyuria –Absence of peripheral edema.
    - Diagnostic tests: *best initial;* plasma aldosterone to plasma renin level→high renin **exclude** the disease Most accurate test*;* adrenal venous blood sample→ high aldosterone level **confirm** unilateral adenoma. Treatment: Laparoscopy →Unilateral adenoma, Eplerenone or Spironolactone → bilateral hyperplasia.

- **Pheochromocytoma:** Tumors that secret catecholamine by chromaffin cells of the **adrenal medulla.**
  Symptoms: **persistent HTN**– headache – sweating – palpitation – anxiety.
  Treatment: - **Phenoxybenzamine.**

L14 Obesity

Definition by WHO: "Abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired"

- High BMI or even BMI below 20 is associated with high mortality, but high BMI can increase the risk for CVS diseases (↑LDL,↑ Total cholesterol ,↑TGA) stroke, osteoarthritis, liver disease, cancer, obstructive sleep apnea and depression.
- We can measure the amount of adipose tissue in the body by :
  Calculating BMI=weight (Kg)/ height $(m)^2$ Recommended by WHO relatively reliable except in:

☒ Extremes of age or height
☒ Very fit individuals with muscular build

Ethnicity can affect the cut off points.

Classification	BMI(kg/m^2)	Risk of co-morbidities
Underweight	<18.5	Low (but risk of other clinical problems increased)
Normal range	18.5-24.9	Average
Overweight	>25.0	
Pre-obese	25-29.9	Mildly increase

Classification	BMI(kg/m^2)	Risk of co-morbidities
Obese	>30	
Class I	30-34.9	Moderate
Class II	35-39.9	Severe
Class III	>40.0	Very severe

- Measurement of waist-hip ratio Measures central adiposity reflecting visceral Adiposity (central obesity is associated with DM2,HTN,Dyslipedimia).
- Growth charts are used for children (BMI<25 is normal , BMI>30 obese)
- Body weight is ultimately determined by the interaction of: Genetic , Environmental and Psychosocial factors, acting through several physiological mediators of food intake and energy expenditure.
- Obesity causes are classified into: Neuroendocrine (e.g. Hypothyroidism or any disease in pituitary), Drug-induced(e.g. Antidepressants, Antiepileptic, Insulin), Diet (high fat or carbohydrates diet), Reduced energy expenditure, and Genetic factors.
- Hypothalamic modulators of food intake: ↑ food intake Orexigenic (e.g. Ghrelin) and ↓ food intake Anorexigenic (e.g. GLP-1).

Ghrelin is one of the 9 hormones that increase when body trying to lose weight.

- Factors participating in body-weight maintenance : Metabolic utilization of nutrients, Dietary habits, Physical activity and they are affected by genetic factor.
- In the assessment of an obese patient you first need to:
  Measure BMI, body weight, waist to hip ratio. Then you will rule out any secondary causes like neuroendocrine or drug. Next you will assess the diet, physical activity, and the genes.
- Management:
  - Referral to dietitian with follow up
  - Behavioral or cognition therapy (e.g. telling the pt. to eat slowly)
  - Medication when patient lose 5-7% of weight (e.g. Orlistat lipase inhibitor, reduces the absorption of dietary fat) it is prescribed with multivitamins due to incontinence.
  - Bariatric surgery is the last choice.

Problems of surgery:

Its effect mainly in the first year of surgery.

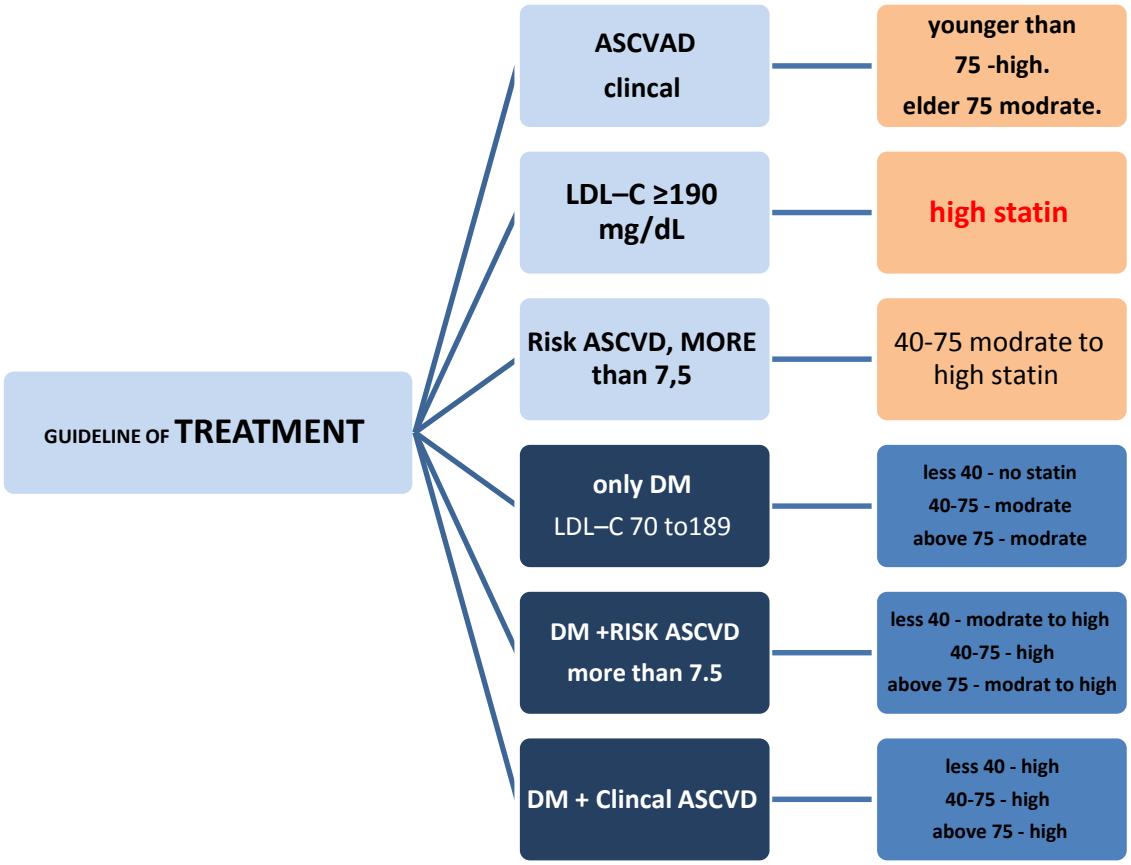
Dietary malabsorbtion such as vit B12 deficiency and Iron deficiency.

L15 Hyperlipidemia

1. Hyperlipidemia is one of the most important (and modifiable) risk factor for CAD. It causes accelerated atherosclerosis
2. There a different type of lipoprotein but the most important is :
    - A. LDL cholesterol: two third of the total cholesterol, CAD risk is primarily due to the LDL component (most atherogenic)
    - B. HDL cholesterol: it's a protective effect (removes excess cholesterol from the arterial walls).
    - C. Triglyceride: elevated TGs are associated with coronary risk and pancreatitis.
3. Most patients are asymptomatic but in sever hyperlipidemia they might have:
Tendon xanthomas, tuberous xanthomas, and xanthelasmas of eyes.
4. Lipid screening is either by
    - **Non-fasting lipid** (measures HDL and total cholesterol)
    - **Fasting lipid panel** (Measures HDL, total cholesterol and triglycerides LDL cholesterol is calculated).
5. The long-term goal of treatment is to reduce the coronary heart disease the short term goal is to reduce the LDL level.
6. Rather than LDL–C or non-HDL– C targets, new guideline uses the intensity of statin therapy as the goal of treatment.
7. The 4 Statin Benefit Groups:

    - Individuals with clinical ASCVD
    - Individuals with primary elevations of LDL–C ≥190 mg/dL
    - Individuals 40 to 75 years of age with diabetes and LDL–C 70 to189 mg/dL without clinical ASCVD
    - Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age with LDL–C 70 to 189 mg/dL and have an estimated 10-year ASCVD risk of 7.5% or higher.

8. Keep that in mind that what we mean by "high intensity" statin, is the daily dose of statin that lowers the LDL by approx **greater than 50%,** and what we mean by moderate intensity statin, is the daily dose of statin that lowers the **LDL by approx 30-50%.**



L16: CNS Infections

1/Meningitis:

- Inflammation of the leptomeninges (Pia and Arachnoid), CSF can also be involved by suppuration (Filled with pus). Not every meningitis is an infection, it can be also a result of non-infectious conditions (e.g. medications, SLE, sarcoidosis, and carcinomatosis)
- Microorganisms reach the meninges by hematogenous spread, retrograde spread through olfactory or peripheral nerves or by contagious spread after sinusitis, otitis media or trauma.
- It's classified as acute (hours to days) and chronic (weeks-months) or infectious and non-infectious.
- The type of bacteria causing the infection vary with age:

Group	Microorganisms
Neonates	Group B streptococci (50%), Escherichia coli, Listeria monocytogenes Enterococci, Klebsiella, Enterobacter, Salmonella, and Serratia.
Children	Neisseria meningitides, Streptococcus pneumoniae and H.influenzae
Adults	S.pneumoniae, N.meningitides, L.monocytogenes and H.influenzae
Elderly	S.pneumoniae, N.meningitidis, L.monocytogenes Other strept.species , Gram negative H.influenzae ,TB and Brucella

- L.monocytogenes, gram-negative bacilli, S.pneumoniae are common in immunocompromised hosts.
- Symptoms include: Headache, Fevers, Nausea and vomiting, stiff painful neck, Malaise, Photophobia, Altered mental status, Seizures, Bulging fontanel in infants.
- Common signs are: Nuchal rigidity, Kerning's and Brudzinki's signs (Both are specific but not sensitive which means they are not seen in every case of meningitis but if present they highly indicate meningitis), Jolt accentuation maneuver(most useful sign, highly sensitive with low specificity).
- Absence of each of fever, neck stiffness, and an altered mental status rule out meningitis.
- Diagnosis: The best initial test and most accurate test is an LP (CSF analysis). However, CT is done first is ICP is high, In this case giving antibiotics is the best initial step in management.
  Others: CBC, creatinine, electrolytes: Na, BloodCulture, CXR, and bacterial Antigen Detection (When the patient has received antibiotics prior to the LP and the culture may be falsely negative).
  As well as organism-specific tests (e.g. Acid fast stain, PCR, ELISA, serology, western blot ... etc.).
- Treatment (usually large doses). Best initial treatment is Ceftriaxone + Vancomycin + Dexamethasone. (Add ampicillin if Listeria is suspected).
  After that, treatment can be based on culture results.
- Non-treated meningitis leads to a wide range of complications including: Seizures, Coma, Brain abscess, Subdural empyema & effusions, DIC, Respiratory arrest, SIADH, cortical vein thrombosis, Arterial ischemia, infarction, multi-organ failure, adrenal hemorrhage (WaterhouseFriderichsen syndrome) Deafness (cranial nerve 8) , Brain damage, Hydrocephalus.
- Prognosis depends on causative organism and time of starting therapy (earlier is always better).

2/Encephalitis:

- Diffuse inflammation of the brain parenchyma, usually comes along with meningitis, most common cause is viruses (HSV-1, Arbovirus, Enterovirus and others). Non-viral causes can be Toxoplasmosis or Aspergillosis. Immunocompromised patients and travelers are more vulnerable. Diagnosis is made by Head CT or PCT. Treated by Acyclovir (Foscarnet in case of resistant herpes)
- Symptoms include: Headache, malaise, and myalgias. Patient is usually severely ill.

3/Brain Abscess: caused by bacteria *Streptococci* (60-70%),. Diagnosed by CT. Treated by drainage if >2.5cm, otherwise Ceftriaxone with metronidazole.

4/Subdural empyema: usually follows sinusitis or otitis media. Treated surgically (drainage).

L17: STROKE

Stroke: is when poor blood flow to the brain results in cell death. There are two main types of stroke: ischemic 85%, due to lack of blood flow, and hemorrhagic 15%, due to bleeding.

The risk factors includes :

Non-modifiable Risk Factors	**Well documented modifiable Risk Factors**	**Potentially modifiable risk**
age	**Hypertension** : It is a major risk factor for stroke	Obesity : ABMI >30 kg/m2 predisposes to cardiovascular disease and stroke in particular
sex	Smoking	Physical Inactivity
Race	Diabetes	Poor Diet/Nutrition
Family history	Hyperlipidemia	Hormone Replacement Therapy
Birth weight	Asymptomatic carotid stenosis	Oral Contraceptive Use
	Sickle cell anemia	Alcoholic abuse
	Atrial fibrillation	Hyperhomocystenemia

Classes of ischemic stroke

1. Transient ischemic attack (TIA) **2.** Evolving stroke **is a stroke that is worsening. 3.** Completed stroke **is one in which the maximal deficit has occurred.**

TIA is a warning sign of stroke

common stroke presentation based on arterial distribution :

ACA : Sudden contralateral leg weakness and personality changes. **MAC:** Contralateral hemiparesis and hemisensory loss, Aphasia, Apraxia, contralateral body neglect, confusion (if nondominant hemisphere is involved). **PCA:** ipsilatral sensory loss of the face, 9th and 10th cranial nerves, contralatral sensory loss of the limbs and limb ataxia.

Diagnostic tests of stroke

The best **initial** test in any kind of stroke is a CT scan of the head without contrast, Positive in hemorrhagic stroke. However the most **accurate** test is an MRI.

Penumbra is zone of reversible ischemia around core of irreversible infarction—salvageable in first few hours after.

The best initial therapy for a nonhemorrhagic (Ischemic) stroke is:

Less than 3hours since onset of stroke: thrombolytic

More than 3hours since onset of stroke: aspirin

Hemorrhagic stroke: nothing

*** If the patient is already on aspirin at the time of the stroke?**

Add dipyridamole OR Switch to dopidogrel.

Treatment for prevention of a stroke is with either aspirin or clopidogrel. **DO NOT COMBINE THEM**. It causes bleeding. You can combine dipyridamole with aspirin as an equivalent of clopidogrel.

Common complication of ischemic stroke:

- ✓ Progression of neurologic insult
- ✓ Cerebral edema occurs within 1 to 2 days and can cause mass effects for up to 10 days. Hyperventilation and mannitol may be needed to lower intracranial pressure.
- ✓ Seizures (fewer than 5% of patients).

Complications of Hemorrhagic stroke

1. Intracerebral hemorrhage (ICH) Increased ICP/Seizures / Rebleeding/ Vasospasm e/ Hydrocephalus/ SIADH

2. Subarachnoid hemorrhage (SAH) : Rerupture: occurs in up to 30% of patients.

L18: Peripheral neuropathy

is any damage to peripheral nerve system, can be pseudoneuropathy like in (Hyperventilation or psychogenic)

Sign and symptoms:

	Loss of function "Negative"	Altered function "Positive"
Motor nerves	Muscle wasting, Hyopotonia, Weakness, Hyporeflexia	Fasciculations (Tiny movement caused by activation of single motor unit), Cramps
Sensory (Large fibers) Dorsal column	↓ Vibration, Proprioception, Hyporeflexia, Sensory ataxia	Paresthesias
Sensory (Small fibers) Spinothalamic tract	↓ Pain, and temperature	Dysesthesias (Abnormal sensation such as pain, burning, or itching) Allodynia (severe pain from normally nonpainful stimuli)
Autonomic nerves	↓ Sweating, Hypotension, Urinary retention, Impotence	↑ Sweating, Hypertension

Peripheral neuropathy classified to:

1- According to lesion site:

A- Mononeuropathies is a type of neuropathy that only affects a single nerve (Usually due to compression)

- Median nerve (Carpal tunnel syndrome) is the most common cause.
- Ulnar nerve lesion usually in condylar groove and causing claw hand.
- Radial nerve cause Saturday night palsy characterized by wrist drop.
- Common peroneal nerve causing foot drop.
- Multi mononeuropathies usually caused by DM or Vasculitis

B- mononeuropathy multiplex is a damage of at least two separate nerve areas

C- polyneuropathy is the involving of multiple nerves in the same areas on both sides, divide into Demyelinating and axonal

- All heredity disease cause uniform demyelination polyneuropathy, While AIDP (Guillain-Barre Syndrome GBS) is autoimmune that cause non uniform demyelination polyneuropathy.
- We use EMG to differentiate between axonal and Demyelinating (small fiber neuropathy shows normal EMG because it lack of myelin sheath)
- Usually it affect the distal lower limbs before the upper limbs.
- GBS is autoimmune (usually caused by campylobacter jejuni) that cause demyelination of peripheral neuropathy, result in symmetric ascending muscle weakness or paralysis with areflexia, EMG shows demyelination, CSF shows high protein, usually treated with IV immunoglobulin or plasmapheresis (Steroid have no role).

2- Radiculopathy is any damage to nerve root (e.g. herniated disc)

- C8 damage present with Horner's syndrome.
- **Dermatome**: you should only know the major dermatome, like (T_4 in nipple, T_{10} in umbilical, L_1 in groin area).

3- Plexopathy: it can be brachial or lumbosacral plexuses.

- There is motor, and sensory deficit.

*We recommend you to listen to Dr.Alqattan lecture (peripheral nerve injuries).

L19: CNS Demyelinating Disease

Multiple sclerosis: A chronic autoimmune inflammatory demyelinating disorder of the CNS of uncertain etiology, likely autoimmune leading to Destruction of myelin sheaths and axons. it's a Progressive disease and there is Multifocal areas of demyelination.

Risk factors:
1-fisrt degree relative
2-vit.d deficiency
3-infectous mononucleosis and Ebstin bar virus
4-genetic
5-obesity.

Common presentations:
-focal sensory symptoms with gait and balance disorders
-Blurry vision or visual disturbances from optic neuritis. Other manifestations such as spasticity and hyperreflexia.
-Internuclear ophthalmoplegia (INO) (Strongly suggest MS).
-types of MS: 1-Clinically silent 2-relapsing and remitting (most common) 3-secondry progressive(gradual worsening) 4-primary progressive (steady progressive).

Diagnostic tests:
1- MRI is both the best initial and the most accurate test.
2- Lumbar puncture shows:
- CSF with mild elevation in protein and fewer than 50 to 100 WBCs.
-Elevated IgG Index >0.7: Increased CNS IgG synthesis, with normal serum IgG consistent with MS.
- Oligoclonal Bands: Presence of 2 or more distinct bands in CSF is consistent with MS.

Management:
-Acute exacerbations: 1 high dose steroids is the best initial therapy 2. Plasma exchange.
-Drugs that prevent relapse and progression:
• Glatiramer • Beta interferon (These two are the best first choice for prevention of relapse).
-Mitoxantrobe and Natalizumab are for aggressive MS .Natalizumab WORSENES the neurological defect.

L20: Malaria

- Malaria is a life-threatening protozoal infection caused by one of four organisms :
  - Plasmodium falciparum - P. ovale - P. vivax - P. malariae
- Transmitted via mosquito bite in endemic tropical countries (e.g. Part of Africa, Asia …).
- Most important parasitic infection affecting humans, and cause 1-3 million deaths per year.

Pathogenesis

- Following mosquito's bite, sporozoites reach the liver within 1-2 hours, and patient still asymptomatic for 12-35 days.
- P. Falci. invades RBCs at all ages, P. Malar. invade old RBCs, P. ovale and P. vivax invade young RBCs.
- Causes microvascular Ischemia & Adherence of non-deformable parasitized RBC to endothelium.

Clinical Features

- Symptoms may include recurring fever, chills, myalgia, headache, nausea/vomiting and diarrhea.
- Fever pattern depends on the organism:
  - P. falciparum : constant fever
  - P. ovale and vivax : fever spikes every 48 hours
  - P. malariae : fever spikes every 72 hours
- Malaria fever paroxysms has 3 phases :

- I : Rigor & headache > II : Delirium, tachypnea & hot skin > III : Fever, sweating and fatigue

Diagnosis

- Dx is made by detailed Hx including travel, PEx and peripheral blood smear.
- Blood smear must have Giemsa stain and can identify different malaria species.
- Correct identification of malaria sp. is important in treatment (e.g. P. falci. is resistant to chloroquine)

Complications

- Complications include cerebral malaria, pulmonary edema, anemia, renal problems, and hypoglycemia.
- Majority of complications (apart from anemia) are associated with P. falciparum.
- Anemia in most severe infections are caused by hemolysis of infected RBCs while non-infected RBCs undergoes immune-mediated hemolysis.
- Tissue hypoxia related complications are caused by altered microcirculation + anemia.

Management

- Treatment should be guided by three main factors (CDC):

1. The infecting Plasmodium species.
2. The clinical status of the patient.
3. The drug susceptibility of the infecting parasites as determined by the geographic area where the infection was acquired and the previous use of antimalarial medicines.

- If no organism identified treat as P. falci. and should be presumed to be chloroquine resistant.
- Drugs include : quinine sulfate, tetracycline, atovaquone-proguanil, mefloquine, primaquine.
- Other measures in treating severe malaria :

- Antibodies against TNF-a
- Steroids
- Reducing mosquito-human contact
- Malaria vaccine

- Prophylaxis is important for travelers to endemic regions. Mefloquine is the agent of choice in chloroquine-resistant areas. Chloroquine can be used in areas where chloroquine resistance has not been reported.

L21: Dementia

- **Delirium**= acute confusional state + encephalopathy
    - Some causes of Delirium: hyponatremia, hypocalcemia, UTI, pneumonia, renal and liver impairments, post-surgery and CNS disorders like multiple stroke and post seizure
- **Alzheimer's disease AD:** decreased memory and new learning is the hallmark, apraxia (inability to do a certain skill that you used to do) and delusions also are included
    - Increasing age, APOE E4 and Down syndrome are causes of AD
    - Tangles (from tau) and senile plaques (from amyloid beta) are pathological hallmarks in Alzheimer's disease

- **Lewy Body Dementia**: 2nd most common
    - visual hallucinations, Parkinsonism, and fluctuations in cognitive ability and level of consciousness.

- **Vascular dementia**: due to recurrent strokes or single stroke that affects important region to cognition such as hippocampus and thalamus
    - Associated with vascular risk factors (HTN, DM, Hyperlipidemia, & smoking)

- **Frontotemporal dementia:** involves frontal and temporal lobes
    - Primary Progressive Aphasia: left frontal atrophy
    - Semantic dementia (Usually have intact fluency, but comprehension is impaired and decreased naming ability): left temporal lobe

- Normal pressure hydrocephalus: magnetic gait

- Creutzfeldt-Jakob Disease: prion disease
    - Rapidly progression dementia plus myoclonic jerks

- Dementia is not curable. But there medications may help, such as cholinesterase inhibitors (Donepezil, rivastigmine) or memantine in advanced AD

L22: Myopathies

Are Disorders in which there is a primary functional or structural impairment of skeletal muscle.
Symptoms: **POSITIVE**: Myalgia Myotonia. Cramps. Contractures. Myoglobinuria. Weakness.
NEGATIVES: Atrophy. Exercise intolerance. Periodic paralysis

Classification

Hereditary :Channelopathies Congenital myopathies Metabolic myopathies Mitochondrial myopathies Muscular dystrophies Myotonias
Acquired : Drug-induced myopathies Endocrine myopathies Inflammatory/immune myopathies Myopathies associated with other systemic illness Toxic myopathies

Muscular Dystrophy: is Inherited, progressive degeneration of the muscles with connective tissue replacing muscle fibers with systemic involvement (variable age of onset).
Types: Dystrophinopathies: Duchenne and Becker (DMD, BD). Most common
X linked recessive disorders caused by mutation in the dystrophin gene.
Its absence causes digestion of the glycoprotein complex. This initiates degeneration of the muscle fiber resulting in muscle weakness.
1-Duchenne Muscular Dystrophy (DMD): Motor developmental delay.
Onset: age 3-6 years. -
- Toe walking, as a compensation for the progressive weakness of the knee extensors. Difficulty rising from sitting position.
Difficulty rising from sitting position. -
Gower's sign. -
Lumber lordosis. -
waddling gait. -
pseudohypertrophy of the calves. -
Cardiomyopathy : CHF and arrhythmias. -
- Investigations: • CK is markedly elevated early in the disease. • Electromyography: myopathic potentials.

2-Becker Dystrophy :

Less severe symptoms -
-Older age at onset.
- Most between ages 5 and 15.
- Onset in the third or fourth decade or even later can occur Loss of ambulation is usually in the 4th decade.
- Muscle biopsy shows decreased staining patterns rather than complete absence of dystrophin.

Myotonic Dystrophy:

The most prevalent inherited neuromuscular disease in adults. Autosomal dominanat. Age of onset average is 29 years.
Diagnosis: can usually be made clinically in a patient with the characteristic presentation and a positive family history.

Clinical features: ¬ Myotonia. ¬ Weakness of the forearms and peroneal muscles. ¬ Ptosis and weakness of other facial muscles. ¬ Characteristic facial appearance: The face is long and narrow and the palate is high arched. The cheeks are hollowed and the jaw sags. ¬ Frontal bolding. ¬ Mild axonal neuropathy. ¬ Heart involvement. ¬ GIT dysmotility, constipation and diarrhea. ¬ Cataract. ¬ Endocrine abnormalities. ¬ Low IQ.

Ocular muscular dystrophy:

(Autosomal dominant myopathy with complete penetrance) Middle age with ptosis
Ocular and pharyngeal muscle involvement. Typically presents with ptosis, dysarthria, and dysphagia. It can also be associated with proximal and distal extremity weakness.

Muscle Channelopathies:

Nondystrophic Myotonias and Periodic Paralyses A group of rare inherited diseases caused by mutations in muscle ion channels (sodium, chloride, potassium, and calcium). Mutations cause an increase or decrease in muscle membrane excitability.

Flaccid paralysis – mild focal weakness to severe generalized weakness ¬ Occur anytime of the day; more common in morning ¬ Absence of myotonia ¬ Proximal > distal weakness; legs > arms ¬ Sparing of facial, ventilatory and sphincter muscles ¬ Attacks may be preceded by sensation of heaviness and or aching in the low back

Inflammatory Myopathies (Polymyositis and Dermatomyositis)

Definitions: The Term **POLYMYOSITIS** is used when the condition does not involve the skin.

The Term **DERMATOMYUOSITIS** is used when polymyositis is associated with a characteristic skin rash.

-Symmetrical proximal muscle weakness that develops subacutely over weeks or several months. ¬ The earliest and most severely affected muscle groups are the neck flexors, shoulder girdle, and pelvic girdle muscles. ¬ Distal extremity weakness is less frequent and less severe.

Features unique to dermatomyositis:

a. Heliotrope (butterfly) rash b. Gottron's papules: popular, erythematous, scaly lesions over the knuckles. c. V sign: rash on the face, neck, and anterior chest. d. Shawl sign: rash on shoulders and upper back, elbows, and knees.

- **The best initial test is CPK and aldolase.**
- **The most accurate test is a muscle biopsy**
- Steroids are usually sufficient

L23: Epilepsy

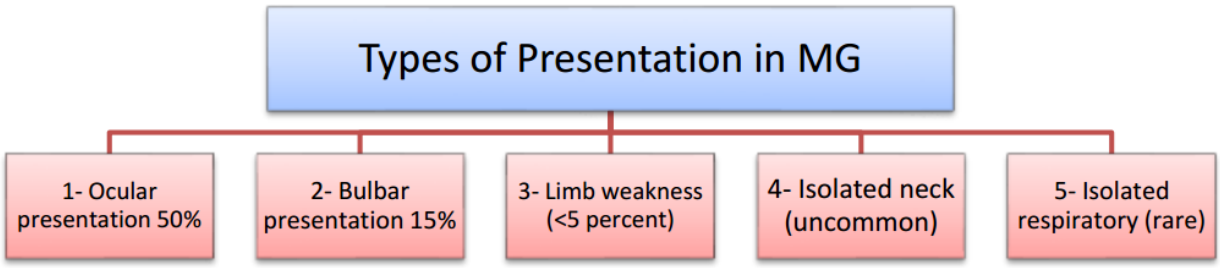
- **Epilepsy:** recurrent of two or more unprovoked seizure.
- **Status epilepticus:** recurrent convulsion lasts >20 minutes. (medical emergency)
- **Risk factors:**
    - Febrile Convulsion (in children)
    - CNS infection
    - CNS mass
    - Perinatal insult
    - Family history
    - Stroke
    - Gestation and delivery abnormalities
- **Triggers:**
    - Poor medication compliance
    - Sleep deprivation
    - Stress
    - Alcohol
    - Infection
    - Menstrual cycle
- **Classifications:**
    - **Partial**
        - **Simple:** No loss of consciousness
        - **Complex:** Impair of consciousness
        - **Secondary-generalized.**
    - **Generalized**
        - **Absence:** Patient stops his activity and does not obey any command.
        - **Myoclonic** Shock-like jerk affects one group of muscle or more.
        - **Tonic-clonic**
- **Investigations:**
    - **CBC:** to rule out metabolic and infectious diseases
    - **MRI and CT scan:** to rule out masses and lesion
    - **EEG:** to confirm epilepsy
- **Treatment:** Either medical or surgical
- **Partial (focal) seizures:** carbamazepine, valproate; clonazepam
- **Tonic-clonic (grand mal) seizures:** phenytoin, valproate.
- **Absence seizures (petit mal):** ethosuximide or valproate.
- **Myoclonic seizures:** valproate or clonazepam.

L24: Myasthenia Gravis

- Myasthenia Gravis is a post-synaptic NMJ disorder that is Caused by an immunoglobulin G(IgG) that attacks the NMJ nicotinic ACH receptor
- MG doesn't affect sensation and doesn't cause autonomic dysfunction.
- Myasthenia weakness is often exacerbated by infections and can lead to myasthenia crisis.
- Clinical features of MG:

Fluctuating weakness (the hallmark of MG).

Ocular: Ptosis, diplopia (double vision) and blurred vision. (Commonest symptoms)



- Unlike true 3rd nerve palsies MG never affects pupillary function

- Diagnosis: Best initial test: acetylcholine receptor antibodies (80%- 90% sensitive). This is a better first answer than edrophonium testing.

- Treatment of MG: (Pyridotgmine, neostigmine) Best initial therapy. Thymectomy: is an absolute indication in case of thymoma.

- Drugs that unmask and exacerbate myasthenia gravis: Antibiotics- aminoglycosides and tetracycline.

Myasthenic Crisis

- Myasthenic crisis is a life-threatening condition due to weakness of respiratory muscles .
- It is managed by Plasmapheresis and IV immunoglobulin therapy.

Lambert Eaton Myasthenic Syndrome

- - Presynaptic NMJ disorder that is Associated with Small Cell Lung Cancer. (Paraneoplastic manifestation of SCC).
- Fluctuating proximal muscle weakness and hyporeflexia abscent of tendon reflexes (AN IMPORTANT SIGN and it differentiate it from MG).

Botulism

Presynaptic NMJ disorder - Caused by toxin produced by Clostridium Botulinum [present in certain food e.g. honey]

L25: Tuberculosis.

- Mycobacterium Tuberculosis primary affects the lung but it can also affect any other tissue.

- The way it spreads and damage the body **depends on host-immunity.**

- Any factor or agent that disrupt the host-immunity specially **cell-mediated immunity** & decreases eradication of the mycobacterium, or increase in contact with those who have active disease, increase the risk for having TB.

Pathogenesis:

1. Exposure (usually with inhalation of droplets nuclei which will travel to **lower and middle zone**)→ No specific immunity in the host → The inhaled bacteria infiltrates neutrophils and macrophages.
    - Because of the **virulence** of the bacteria, they are not destroyed by phagocytosis.
    - In the affected locus, there will be pneumonitis with neutrophils and edema.
2. Multiplication in the macrophages.
3. The bacteria travel through lymphatics and blood stream to affect other organs.
4. Some of the macrophages succeed in phagocytosing and travel toward local lymph node → present parts of the bacteria to T-helper cells.
5. Multiplication of T-helper cells → searching for bacteria and to activate macrophages against the mycobacterium.
6. Macrophages attack the bacteria and causes damage to the local tissue → Caseous necrosis → Granuloma. Within the granuloma, is where the bacteria kept.
    - A calcified tubercle is called Ghon focus. Ghon focus accompanied by perihilar lymph node calcified granuloma is called Ghon complex or Ranke complex.
7. They could break out if there's any assault or depression in the host-immunity. (secondary or reactivation of TB)

- Primary tuberculosis could be asymptomatic (commonly, latent TB) or symptomatic (rare, it occurs in children or those with impaired immunity).

Pulmonary TB; The most common. The patient present with chronic lowgrade fever, night sweats, weight loss and hemoptysis	**Lymph node infection**; most common extrapulmonary manifestaion. Lymph node tuberculosis is called Scrofula.	**Pleural & pericardial infection**; infection in these spaces result in infected fluid.	**Kidney**; patients will have RBCs and WBCs in the urine without bacteria.
Skeletal TB; usually involves the thoracic and lumbar spine. (Pott's disease)	**Miliary TB**; small granuloma dissemenated to all over the body.	**Joint TB**; chronic arthritis usually affecting 1 joint.	**CNS**; causing subacute meningitis and granuloma formaion in the brain.

L26: Healthcare-associated infections (HAIs)

Localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s).

Colonization The presence of microorganisms on the body but are not causing adverse clinical signs and symptoms.

Source of infection could be **endogenous** Or **exogenous** **(the worse).**

Mode of transmission could be

- **Contact** (**the commonest**) : **Direct** (contact with affected person) _ **Indirect** (contact with contaminated surface).
- **Airborne (like TB).**
- **Blood exposure (like HIV).**
- **Consuming contaminated water or food**

Types of Healthcare-associated Infection

Catheter-associated Urinary Tract Infection:

✓ **Most common type** of healthcare-associated infection

✓ **The Source of microorganisms could be : Endogenous** (meata) Or **Exogenous** (contaminated hands).

✓ **The criteria of symptomatic UTI is one of Fever (.38.8C,), urgency, frequency, dysuria, or suprapubic tenderness**.....**and positive urine culture that is more than 105 microorganisms per cc of urine with no more than 2 species of microorganisms.**

✓ The most important risk factor for developing a catheter associated UTI (CAUTI) is **prolonged use of the urinary catheter.**

- **Blood stream infection:**

✓ **Neutropenia is the commonest risk factor.**

✓ **Central Line-associated Bloodstream Infection:**

Laboratory-confirmed bloodstream infection

LCBI must meet **at least 1 of the following criteria**:

Recognized pathogen cultured from 1 or more blood cultures and is not related to an infection at another site **with one of the following :** Fever , chills, or hypotension which is not related to other source or infection at another site.

- **Ventilator-associated pneumonia:**

✓ LOWER RESPIRATORY TRACT INFECTIONS 13%

Or pneumenia. (**NOT a chest infection**).

✓ Antibiotics (kills the normal flora) and anti-acids (decreasing acid ph of stomach) are examples of risk factor to have ventilator pneumonia**.**

- **Surgical site infection : superficial or deep.**

✓ **The most common pathogenesis is Staphylococcus aureus (normal flora in the skin)**

Transmission of multidrug-resistant/marker organisms

1. **MRSA (methicillin-resistant *S. aureus)*:**
   - ✓ **Second most common overall cause of healthcare associated infections reported.**
   - ✓ **Most common cause of**
     a) surgical site infections(30%)
     b) ventilator associated pneumonia (24%)
2. **C. difficile.**
3. **Aspergillus in immunocompromised patient.**
4. **Tuberculosis (MDR).**
5. **VRE (Vancomycin-Resistant Enterococci (VRE):**
6. **Carbapenem-resistant Acinetobacter.**

L27: HIV & AIDS

- ✓ HIV: Infection with Human Immunodeficiency Virus. It's RNA icosahedral virus belong to retrovirus family, which means RNA transcribed into DNA at the host cell.
- ✓ It's characterized by Progressive immunodeficiency, Long latency period and Opportunistic infection.
- ✓ The most common virus associated with HIV is HIV1
- ✓ The hallmark of HIV Disease: is Infection and viral replication within T-lymphocyte expressing the CD4 antigen causing progressive depletion and defect at CD4 that will increase the risk of getting
  1. Opportunistic infection as **Pneumocystis Jiroveci (PCP).**
  2. Neoplasm such as Lymphoma and Kaposi sarcoma.

- ✓ Mood of transmission: **sexual**, vertical transmission (from mother to fetus), **blood** and body fluid transfusion, IV drug abusers.
- ✓ Pathophysiology: In the lymph nodes, it replicates and causes massive viremia that goes to the whole body and spreads everywhere causing activation of immune system which eventually destroy it by keeping proviral DNA in the latent T cell or macrophages.
- ✓ **Diagnostic tests are:**

  1. ELISA: The best initial test which is the screening test for patient and blood product.
  2. Western blot: to confirm.
  3. PCR: Confirmatory test, to assess the viral load, babies born to HIV-positive mothers and response to therapy.
  4. LIA: Confirmatory, for antibodies against HIV 1and HIV 2 with sensitivity 100% and specificity: 96%.

- ✓ **Immunological staging:**

  1. 350-500 cells/mm3 mild deficiency.
  2. 200-350 cells/mm3 moderate immune deficiency.
  3. <200 cells/mm3 sever immune deficiency

- ✓ Clinical presentation

  Skin (seborrheic dermatitis), Oropharynx (oral thrush, hairy leukoplakia and mucosal Kaposi sarcoma), lymph node (TB, Lymphoma) and eyes (Fundoscopy: CMV retinitis. (CD4 less than 50)), genital exam (ulcers, condylomatous lesions). Discharge and cervical lesions in women.

Treatment: Dual – nucleoside reverse transcriptase inhibitor (NRTI) + None-nucleoside reverse transcriptase inhibitor (NNRTI) or Protease inhibitor (PIs)/ Strand- Transfer Integrase Inhibitor (INSTI).

- **The best initial: mtricitabine, tenofovir, and efavirenz (**combination in one pill called →**(Atripla))**
- Resistance, alternate regimens are based on a combination of 3 drugs from at least 2 different classes. The first choices are either atazanavir, darunavir, or raltegravir combined with emtricitabine/tenofovir.

The only exception is the use of efavirenz, which should be avoided in pregnancy because it is associated with teratogenicity in animals. **Protease inhibitors** are safe during pregnancy.

L28-Infections in Immuno-compromised hosts

Neutropenia:

- Neutrophils count of < 500 cells/mm3
- Neutropenia is associated with **fever**, which is defined as Oral temperature of 38c for more than two hours or single temperature of 38.3c or more
- common after chemotherapy
- Pseudomonas species are associated with the highest mortality rate in neutropenia
- Obtain the following for any neutropenic patient with a fever: CXR, panculture (blood, urine, sputum, wound) CBC, complete metabolic panel.
- In neutropenic patients with fever, elevated procalcitonin suggest bacteremia.
- The most common infections seen in neutropenic individuals are; septicemia, cellulitis and pneumonia.
- **Treatment:**

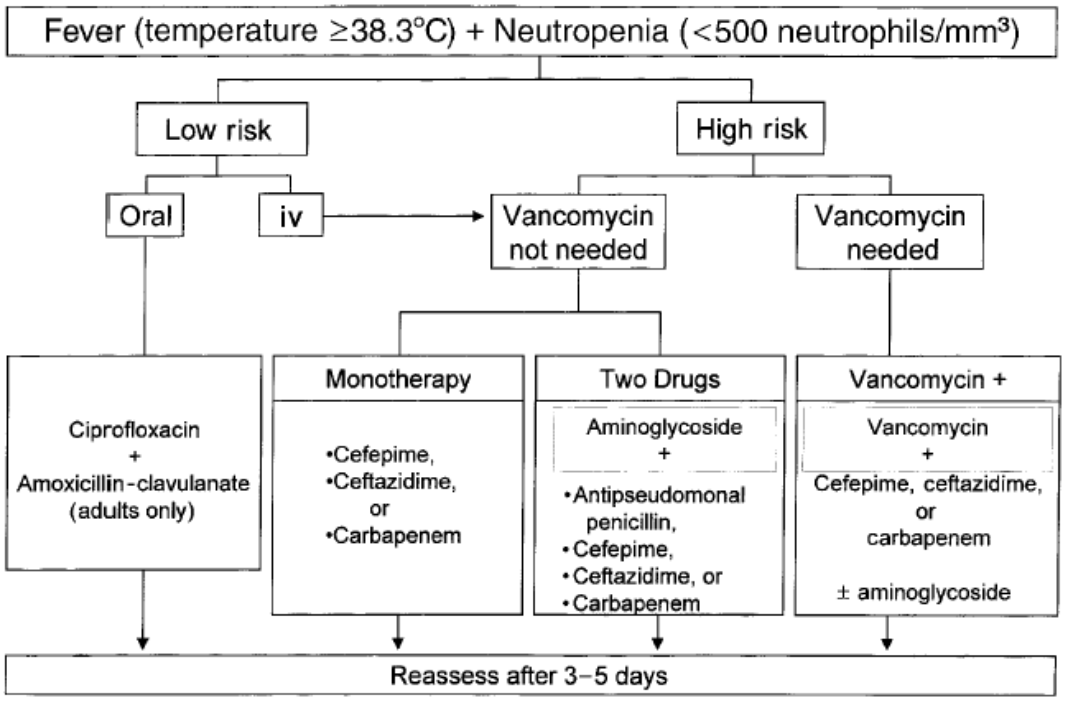


Figure 1. Algorithm for initial management of febrile neutropenic patients. See tables 3 and 4 for rating system for patients at low risk. Carbap

Administration of Granulocyte colony-stimulating factor with chemotherapy can prevent neutropenia

L29: Rheumatoid arthritis & Osteoarthritis

	Rheumatoid Arthritis	Osteoarthritis
Type	- inflammatory autoimmune disease	- degenerative disease of the cartilage
pathology	IL-1 +TNF Pannus : T-lymphocytes – macrophages Synovial fluids: neutrophils	Obesity, trauma, sports
Age	20 to 40 years	Old
Gender	Female >male	Female >male
Joint involvement	Symmetrical + small joints except the DIP- Symmetrical pattern	Weight bearing joints
Symptoms and signs	• Tender, warm and soft swollen joints • Morning stiffness • hand deformities - Ulnar deviation of the MCP joints - Boutonnière deformities - Swan-neck contractures - 'Z' deformity of the thumb - WRIST joint Prominent ulnar styloid and Radial deviation • Small vessels vasculitis • Felty's syndrome. • muscle wasting • Subcutaneous nodule • Anemia(normocytic normochromic) • Cervical spine subluxation C1–C2 • Drying of mucous membranes: Sjögren's xerostomia • cardiac diseases (cause death) • pulmonary diseases • constitutional symptoms	• Pain – worse on use of joint • Stiffness after immobility • Loss of movement • Tenderness • Bony swelling • Soft tissue swelling • Joint crepitus • no systemic manifestations
Diagnosis	• Anti-CCP(specific) • Rheumatoid factor RF(IgM) • CPR • ACPA	• x-ray findings (Narrowing of joint space , Osteophytosis ,Altered bone contour, Bone sclerosis)
Treatment	• initial :(NSAIDs) or (COX-2) inhibitors for pain • Disease-modifying agents(DMARDs): hydroxychloroquine, sulfasalazine, methotrexate and anti TNF (role out TB) to stop progress	no cure for OA palliative /NSAIDs + acetaminophen

L30: SLE & scleroderma

	SLE	Scleroderma
	Autoimmune disorder leading to inflammation and tissue damage involving multiple organ systems.	Generalized disorder of connective tissue affecting the skin, internal organs and vasculature.
Clinical features	A patient has SLE if 4 or more of these 11 criteria are present at any time. 1- 4. skin manifestations : malar rash, Photosensitivity, Oral ulcers, Discoid rash 5. Arthritis (1st symptoms that brings patients to seek medical attentions)(normal x-ray) 6. serositis : Pericarditis, pleuritic 7. Hematologic disease 8. Renal disease 9. neurologic 10. Immunologic manifestations—positive LE preparation, false-positive test result for syphilis, anti-ds DNA, anti-Sm Ab 11. ANAs additional findings: Raynaud phenomenon , Alopecia is common in SLE but is not one of the "official" diagnostic criteria, Antiphospholipid syndromes	a. limited cutaneous systemic sclerosis also known as CREST syndrome (Calcinosis cutis, Raynaud phenomenon, Esophageal dysmotility, Sclerodactyly, and Telangiectasia) **B.** diffuse cutaneous systemic sclerosis (DCSS: 30% of cases). 1. Raynaud phenomenon 2. Skin thickening and hardening involving the hands, fingers, and face. 3. Skin manifestations : fibrosis, pigmentations 4. GI manifestations: Esophageal dysmotility with GERD 5. Renal manifestations: sudden hypertensive crisis 6. Lung manifestations: restrictive lung disease, pulmonary hypertension (PAH). **7.** Cardiac manifestations: myocardial fibrosis, pericarditis, and heart block.
Diagnosis test	**ANA:** found in 95% to 99% of cases. **Anti-double-stranded (DS) DNA (60%) and anti-Sm (30%):** These are found only in SLE. They are extremely specific for SLE. **Decreased complement levels:** They can correlate with disease activity.	**ANA:** positive in 85% to 90%, but nonspecific **SCL-70:** the most specific test is the SCL-70 (anti-topoisomerase), but present in only 30% of those with diffuse disease and 20% of those with limited disease **Anti-centromere:** antibodies are extremely specific for CREST syndrome
Treatment	Acute lupus **flare** is treated with high-dose **boluses of steroids**. mildly chronic disease limited to skin and joint manifestations: Hydroxychloroquine Controls progression of the disease: Belimumab. Lupus nephritis: need steroids either alone or in combination with cyclophosphamide or mycophenolate. Don't treat an asymptomatic ANA	Methotrexate slows the underlying disease process of limited scleroderma. Renal crisis: ACE inhibitors (use even if the creatinine is elevated) Esophageal dysmotility: PPIs for GERD Raynaud: calcium channel blockers and avoidance of cold exposure Pulmonary fibrosis: Cyclophosphamide improves dyspnea and PFTs. Pulmonary hypertension: Bosentanambrisentan (endothelin antagonist), Sildenafil, Prostacyclin analogs: iloprost, treprostinil, epoprostenol

L31: Low back pain

- The initial test to request for back pain is **lumbosacral x-ray**, most accurate **MRI.**
- Red flags 🚩 when they are presents this indicate serious condition that need immediate assess such as malignancy, fracture, infection of the bone, Cauda Equina Syndrome or Ankylosing Spondylitis.
- The most important point to ask about in Past medical history; **history of malignancy** 🚩 **(due to bone metastasis)**, also weight loss 🚩.
- **Compression fracture** is an important cause of back pain, it can happen usually due to osteoporosis 🚩 in elderly by **trauma** 🚩, **chronic cough**, **carrying heavy things specially while taking 'corticosteroids** 🚩 '.
- Bacteremia can lead to acute (**S.Aureus & E. Coli**) or subacute (most common, usually **TB** & **Brucella**) para-spinal abscess. Risk factors: – **IV drug abusement.** 🚩 – Immunosuppressed patients 🚩 – recent infection🚩. **Severe back pain** 🚩 usually **localized in thoracic area. Fever** 🚩**, chills** 🚩 **and night sweats** 🚩 are also present. Complications: **incontinence**, **numbness** & **paraplegia.**
- **Cauda Equina Syndrome** is a **surgical emergency** that need to be investigated by **MRI** ASAP because there is a compression on lumbosacral nerve roots. Symptoms: **Low back pain, saddle** 🚩 **(anal) sensory disturbance**🚩**, incontinence or retention** 🚩 & lower extremity weakness 🚩.
- Young patient, long history of back pain *pain characteristic: **gradual**, nocturnal &alternating* radiating to the buttocks, with early morning stiffness, relieved by movement & NSAIDs, with underlying IBD or psoriasis -> most likely diagnose **Ankylosing Spondylitis**.
- **Sacroiliac joint MRI** is the gold standard test for AS, **positive schober test** will be present in examination.
- Achilles enthesitis & Dactylitis might be present in AS.
- Unclear cause of back pain is associated with **nonspecific back pain,** usually it's managed by **physiotherapist** in addition to **exercise, weight loss** and also **muscle relaxants** or **'NSAIDS** for period of 2-3 weeks continually**'. No imaging is needed.**
- **Radiculopathy (**could be: disc prolapse, osteoarthritis or facet arthropathy.) Usually it is a structural damage that's causing **nerve compression** manifested as **pain, paresthesia or decreased reflex or weakness.** In this condition after the disappearance of back pain**, leg pain will start. The pain is sudden and exacerbated by sitting or coughing due to increase of pressure.**
- **Spinal stenosis**: **narrowing of spinal canal** with or without disc herniation. Symptom: **back pain** with **neurogenic claudication** which is pain in lower thigh while walking, relived by **flexion of the spine or resting.**

Both radiculopathy and spinal stenosis are investigated by **MRI** and managed **conservatively** like non-specific back pain.

L32: Endemic Infections in Saudi Arabia

1-Typhoid Fever:

- It is an acute febrile disease, caused by *Salmonella typhi* and *S. paratyphi* A, B, C (lives only in human).
- Sanitation for water decrease it. It transmitted by the fecal–oral route. When patient recovers, it still in patient's body (carrier): this is the source to infect others.
- It invades the ileal mucosa (Peyer's patches to multiply)►Blood stream►Reticlo-endothelial system►Secondary bacteremia
- Gradual onset with intermittent fever + relative bradycardia (↑ fever and no increase in heart rate)
- **Investigations**: WBC could be ↓, Most important are **blood and** bone tests or stool culture.
- **Treatment:**
  1- 3rd generation cephalosporin **(ceftriaxone) I.V** then change to (**cefixime**) orally.
  2- Fluroquinolones (ciprofloxacin) drug of choice.
- **Complications:** Pneumonia, meningitis, osteomyelitis. Severe intestinal hemorrhage and intestinal perforation If not treated can be fatal. Prevention by vaccine for travelers.

2- Brucellosis: called" multa-fever and undulant fever**"**

Systemic febrile illness Zoonosis. B. melitensis and B. abortus are the most frequent

It transmitted through ingestion of infected meat, inhalation and food products such as unpasteurized milk. It can invade any organ.(Low back pain common)

- Clinically it has three patterns: 1-similar to typhoid. 2-Fever & acute mono-arthritis (hip/knee). 3-low grade fever, low back pain, hip pain.
- Brucellosis locally divided into: Osteoarticular (sacroiliac joint), Genitourinary, Neurobrucellosis and Abscess.
- **Investigation:** WBC ↑, ESR ↑ (maybe), Blood culture (slow growth need 4 wk), Serology (SAT +ve should be less than 1:360).
- **Treatment:**
  - Uncomplicated Brucellosis: **1-** Streptomycin I.V. + Doxycycline. **2-**Rifampicin + Doxycycline. **3-** TMP/SMX + Doxycycline.
  - Complicated brucellosis: Usually 3 antibrucella drugs for 3 months.

3-Dengue fever:

- Transmitted by mosquito: Aedes Aegypti. Single-RNA and has 4 serotypes (DEN-1, 2, 3, 4).
- Repeated exposure can result in severe form.
- **Dengue Clinical Syndromes**: Undifferentiated fever, Classic dengue fever, Dengue hemorrhagic fever, Dengue shock syndrome.
- It can cause neutropenia, thrompocytopenia and rash. Only symptomatic management

4- Rift Valley Fever:

- Most commonly associated with mosquito-borne epidemics during years of unusually heavy rainfall. The disease is caused by the RVF virus.
- **Treatment** is symptomatic. Vaccines for veterinary use are available.

5-Leishmaniasis :

- Protozoal disease caused by Leishmania parasite, which is transmitted by the sand fly.
- Three types; cutaneous leishmaniasis, muco-cutaneous and the visceral (Kala-azar).
- Cutaneous types: Hyperkeratotic, Mucosal, Plaque, Recidivans, Erysipeloid.

6- Middle East Respiratory Syndrome Coronavirus MERS-COV:

- Transmission likely occurring from camel to human.
- **Diagnosis:** Real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) for respiratory secretions.
- **Treatment** is mainly Supportive No vaccine available.

7- Gastroenteritis: Main feature is diarrhea. Not all gastroenteritis have fever.

A-parasitic infection:

1. Intestinal Amebiasis	Giardiasis
• Transmission : by cysts • Causes invasive colitis • Presentation: asymptomatic • Complications: liver abscess • Diagnosis: stool microscopy , serology • Treatment: metronidazole.	• Transmission: Colonies upper small intestine • Presentation: asymptomatic-mild To moderate: May become chronic • Diagnosis: stool microscopy • Treatment: metronidazole

B- Bacterial infection:

- Salmonella enteritides (most important), Shigella spp, cholera.
- Food poisoning by clostridium perfeinges.
- Bacteria Gastroenteritis Present with abdominal pain and Diagnosis by stool
- Microscopy & culture and Treat it by fluids.

C-Viral infection:

- Rotavirus = infect children = most important cause of infant mortality in the world = die from dehydration = hydrate to treat them.

L33: Herpes Viruses

They are a family of viruses; in which they share the same characters:

- DNA Encapsulated viruses. –Latency after the initial infection.

1st: Herpes Simplex Viruses: HSV-1 & HSV-2.

Transmitted by close contact of body secretions.

-The initiation of replication happens in the dermis and epidermis. Then the virus travel along the **autonomic and sensory nerves to become dormant in the ganglion.**

HSV-1 = Trigeminal nerve ganglia.	HSV-2: In the Sacral root.

-They present with **painful vesicles but in different places.**

HSV-1 is usually known as the **non-genital type.** **-Gingivostomatitis.** **-Herpes Labials (cold sores).** **-Finger infection (whitlows).** **-Keratoconjunctivitis.** **-Encephalitis.**	HSV-2 is usually known as the **genital type** and can present with **tender inguinal lymphadenopathy.** **-Genital infections.** **-Neonatal infection (vertical transmutation from an infected mother).**

Diagnosis: Can be diagnosed **clinically**.

-**Tzanck smear** is the initial investigation. Will show **multinucleated giant cells**.

-Viral culture is the gold standard.

Treatment: Acyclovir, Famciclovir or Valaciclovir for 5 days. If resistant to the ciclovirs we can use Foscarent.

2nd: Varicella Zoster Virus.

-Primary infection is **Chicken pox** and the recurrent infection is **Herpes zoster (shingles).**

–Transmitted through **Respiratory route.**

–Establishes latency in **the dorsal root ganglia.**

Treatment: Same as HSVs.

Prevention: VZV live attenuated vaccine and VZV Igs for the immunocompromised.

3rd: Cytomegalovirus – CMV.

-Primary infection: Asymptomatic – Infectious Mononucleosis like syndrome.

-Secondary infection: Disease in immunocompromised patients: Pneumonitis, Retinitis, Enteritis and multisystem involvement.

Diagnosis: Viral culture, Serology and PCR.

Treatment: Ganciclovir, Foscarnet or Cidofovir.

4th: Epstein - Barr virus – EBV.

Can cause: Asymptomatic infections, African Burkett's lymphoma, nasopharyngeal carcinoma and Oral hairy leukoplakia in AIDS patients.

Also, Infectious Mononucleosis (Fever, Sore throat, Lymphadenopathy, >50% mononuclear cells, >10% atypical lymphocytes).

Diagnosis: Heterophile Antibodies, Lymphocytosis, neutropenia, thrombocytopenia, EBV specific antibodies.

Treatment: supportive and sometimes corticosteroids.

L34: Use of antibiotics

- Globally, 50% of the time, antibiotics are prescribed either when not needed or misused. Therefore, (Infectious Diseases Society of America) was established to put guidelines for proper antibiotics use.
- Before any use of antibiotics, it's important to determine site of infection, host status and to establish a microbiological diagnosis by lab results especially in serious illness (e.g. endocarditis, sepsis), preferably before the initiation of an antimicrobial therapy. However, antibiotic selection can sometimes be based on clinical suspicion (Empirically) such as in cellulitis and C.A.Pneumonia.
- Empirical antibiotics use is also indicated in urgent cases (e.g. Sepsis, Febrile neutropenia and meningitis). In this case, Empiric therapy should be initiated immediately after or concurrently with collection of diagnostic specimens, while in stable cases such as osteomyelitis and subacute endocarditis, antibiotics should be withheld till specimen is collected and sent to lab.
- A common approach it to use a combination of antibiotics sometimes to cover multiple possible pathogens commonly associated with a specific clinical syndrome (e.g. the use of 3rd generation cephalosporin plus vancomycin against *Streptococcus pneumoniae* and *Neisseria meningitides*).

-Antimicrobial susceptibility testing: the ability of an organism to grow in a media filled with drugs in vitro.
-Minimal inhibitory concentration: the minimal concentration at which the drug inhibit organism's growth.
Results of (MIC) is either, Susceptible, Intermediate or Resistant.

- Always consider the bioavailability of the drug at the target side (e.g. cefazolin is not used in meningitis caused by MRSA, although it is an excellent agent against MRSA).
- The combination of antibiotics can produce synergistic activity (e.g. β-lactam and aminoglycosides), this is essential for rapid killing, shortening the coarse, critically ill patients, polymicrobial infections and to prevent resistance.
- Patients with renal or hepatic impairments should receive reduced dose.
- Take precautions in case of pregnancy, lactation, history of allergy and previous antibiotic use when selecting the antimicrobial agent (certain antibiotics are contraindicated in these cases).
- Mild to moderate infections (e.g. pyelonephritis) can be treated orally (e.g. oral fluoroquinolones) while severe ones only respond for intravenous preparations such as meningitis.
  - Fluoroquinolones, linezolid, trimethoprim-sulfamethoxazole, and metronidazole are examples of drugs that have good bioavailability and can be used orally.
- Certain antibiotics are excellent for specific body sites while others don't reach certain sites.
  - 1st and 2nd generation cephalosporin and macrolides aren't used for nervous system infections.
  - Fluoroquinolones are excellent for prostatitis.
  - Distamycin and Vancomycin aren't used for lung infections
  - Aminoglycosides can't be used in abscesses.
  - Moxifloxacin isn't able to reach urine and thus not used for UTIs.
- Certain drugs should be monitored by drug serum levels, either because of their toxicity (e.g. aminoglycosides) or their therapeutic failure (e.g. Vancomycin) or both (e.g. Voriconazole).
- Response assessment to an antibiotic is by: clinical improvement, lab results and by imaging.
- Infections due to the presence of foreign bodies (e.g. prosthetic valves) are treated by removing the implant. If patient can't tolerate implant removal, long-term suppressive antibiotics are indicated.
- Prophylactic antimicrobial therapy is indicated in pre-surgical patients, preventing transmission (e.g.in close contact to meningitis patients) and in patients undergoing dental procedures.
- Antibiotics shouldn't be used inappropriately or without clear evidence of an infection.
- Inappropriate use of antibiotics is the most important cause of the emergence of drug resistance.