TEST BANK

Pharmacology

Try to Read the summaries before Starting

Analgesics.

- Nonnarcotic:
  - NSAIDs
  - Paracetamol / acetaminophen.
- opioids Drugs. (• Morphine.) → Narcotic.
  - Cause :- Tolerance and Dependence.
  - Anti-inflammatory, Antipyretic, Antiplatelets. ← ليست

Share analgesic & antipyretic properties (NSAIDs & Paracetamol).

ولكن paracetamol lacks anti-inflammatory effects, act on the CNS rather than peripherally, and it doesn't commonly cause gastric irritation or nephrotoxicity.

ولكن يزيد الـ Hepatotoxicity Risk

* Zileuton ⇒ 5-lipoxygenase inhibitor.
* -Zafirlukast
- montelukast
- pranlukastare.

→ Selective antagonists of CysLT1 receptor.

* Colchicine ⇒ LTB_4 inhibitor, inhibits phagocyte attraction and it is used in the treatment of Gout.

* Aspirin (Non-selective) ⇒ NSAIDs.
  - At low Doses (more selective to Cox1) → Antiplatelet drug.
  - AT high Doses → Cox1 & Cox_2 inhibition. → Anti-inflammatory drug. → this high dose will Cause GI irritation

↑ Dose ⇝ ↓ selectivity.

COX-(1)	COX-(2).
دائمًا موجود وإله Physiologic functions.	بيجي لمّا يصير inflammation بتحفيز من cytokinase. وهو المسؤول عن الـ inflammation.

* حتّى يتجنبوا GI irritation قرروا يعملوا drug يكون selective against Cox(2) إي بعمل inflammation وما إله أثر على Cox(1) إي بعمل Normal physiological functions.

طلّع ← Selective Cox_2 inhibitors زي:

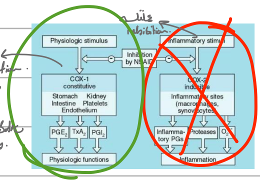
Celecoxib & Rofecoxib

(in our slides.) All NSAIDs are non-selective except :- meloxicam and celecoxib.

* Meloxicam ⇝ NSAID slightly Cox 2 selective, less side effects.

يُستعمل بحالة بدي anti-inflammatory effect بدون ما يصير GI irritation

ويُمنع عند الـ patients with a history of thromboembolic diseases and hypertension.



صار له overactivation وصار عنا بسبب thromboembolic diseases.

بس طلع عليه مشاكل زي إنه بسبب الـ Blood clotting لأنه صار عندي overactivation of the Cox 1 إي عنده (TXA_2) ← فيسبب Thromboembolic Diseases.

NSAIDs

Anti-inflammatory action.

* ↓ vasodilator PG ⇒ PGE_2, PGI_2
- ↓ vasodilation ⇒ ↓ Edema.
* inhibition of adhesion molecule.
* ↓ accumulation of inflammatory cells.

An analgesic effect.

* ↓ PG generation → ↓ sensitivity of nociceptive (pain receptors) nerve endings to inflammatory mediators.
* Relief of Headache (How?) → ↓ PG-mediated vasodilation.

PGE_2 بزيد حساسية الـ Nerve endings → لـ Bradykinin, Histamine, ...

وظيفة الـ NSAID بهادي الحالة → mangement of pain of low to moderate intensity arising from musculoskeleton disorders.

. NSAIDs وليس opioids بروح عند فقط from vicera الألم إلي

Antipyretic effects.

Aspirin Has NO effect on normal Body temperature.

NSAIDs ⇒ Blockage of PG synthesis at the thermoregulatory Centers in the hypothalamus and at peripheral target sites.

Aspirin (Acetylsalicylic acid) → weak organic acid.

Non-selective *
irreversible *
inactivation of Cox_1 & Cox_2 *

Mechanism of action.

MOA

other NSAIDs ... reversible.

* irreversible →
* aspirin rapidly → deacetylated By esterase in the body producing :-
  - Salicylate: Has :- Anti-inflammatory, Anti-pyretic, Analgesic effects.

Respiratory actions.

* Causes Bronchoconstriction in some asthmatic patients through ↑ production of Pro-inflammatory mediators; LT

Decreases | Clinical uses.

1- incidence of transient ischemic attacks.
2- Unstable angina, الذبحة الصدرية.
3- Coronary artery thrombosis with MI myocardial infarction.
4- thrombosis after coronary artery bypass grafting.

* GI effects.

PGE_2 → Stimulate synthesis of protective mucus in stomach and small intestine. & ↓ acid secretion.

→ Under physiological conditions.

aspirin → X Prostanoids → ↓ mucus protection → ↑ Gastric acid secretion.

gastric or duodenal ulcers → GI irritation من aspirin

PPIs proton-pump inhibitors. أفضل من PPI ← PG analog يمكن استعمال

* The most common GI effects of the Salicylates are epigastric distress.
* Microscopic GI Bleeding → Universal in Patients treated with Salicylates.

كيف يسبب aspirin حرقة:

→ Stomach → At stomach pH, aspirin is Uncharged.
→ When aspirin crosses into mucosal cells → it ionizes (negatively charged), & Becomes trapped Thus Causing Direct Damage to the cells.

* Effects on platelets.

* irreversible inhibition of platelet Cox
→ Aspirin's anti-platelet effect lasts 8-10 days
New Cox in other tissues. بصير صنع ل inactivated بدل إذا كان
So, ordinary doses have a duration of action of 6-12 hours.

Common Adverse Effects

بشكل عام لكل NSAIDs:

1. Platelet Dysfunction
2. Gastritis and peptic ulceration with bleeding (inhibition of PG + other effects)
3. Acute Renal Failure in susceptible
4. Sodium+ water retention and edema
5. Analgesic nephropathy
6. Prolongation of gestation and inhibition of labor.
7. GIT bleeding and perforation

* Actions on kidney :-

Cox inhibitors prevent the synthesis of PGE_2 & PGI_2 that are responsible for maintaining Renal Blood Flow.

↓ PG → retenation of Sodium and water → Edema & Hyper-Kalemia.

* There is Contraindication between hypertensive drugs and NSAIDs.

Hypersensitivity :-

~ 15% of patients taking aspirin → Experience hypersensitivity reaction.

* symptoms → Urticaria, Bronchoconstriction, angioedema.

*fetal anaphylactic Shock is Rare.

Reye's syndrome.

1. aspirin & other Salicylates During viral infection

- Reye's syndrome is a potentially **fatal disease** that has numerous detrimental effects to many organs, especially the **brain and liver**, as well as causing a lower than usual level of blood sugar (**hypoglycemia**) The classic features are a **rash, vomiting, and liver damage**. The exact cause is **unknown** and, while it has been **associated with aspirin consumption by children with viral illness**, it also occurs **in the absence of aspirin use.**

2. often fetal, fulminating Hepatitis with cerebral edema.

3. Espicially encountered in children.

aspirin بدل acetaminophen للأطفال

Paracetamol.

Drug interactions

distribution in the blood. بصير أثناء

Salicylate is 90 to 95 % Protein Bound. and can be displaced from its protein - binding sites resulting in increased Concentration of free Salicylate. effect صعبي يعني الـ free form

كمان هيك الـ aspirin ممكن يعمل displace لـ drugs تعتبر أيضًا highly protein-bound زي:-

1- Warfarin → مميّع قوي.
2- phenytoin
3- valproic acid → أدوية صرع.

= resulting in Higher free Conc. of these drugs → بزيد تركيزها في الدم فبزيد الـ effect.

!!! **Concomitant use of Ketorolac & aspirin is Contraindicated cuz of increased risk of bleeding and platelet aggregation inhibition.**

Toxicity

- mild form → Salicylism, in Patients with little allergy to aspirin.
- major form → Toxicity

→ nausea, vomiting, Headache, mental Confusion, dizziness, tinnitus And marked Hyperventilation → زيادة التنفس.

Relying on anaerobic respiration → Acidosis

↓ CO_2 Respiratory Alkalosis,

- Uncoupling of oxidative phosphorylation
- Inhibition of krebs cycle enzymes.
- Alterations in lipid metabolism & AA metabolism

→ ↑ metabolic acidosis

Kidney will produce Bicarbonate and will excrete more potassium, ↑ electrolytes loss → Dehydration, ↓ Sodium and loss of buffer capacity

قصان بقل الـ K

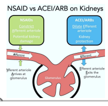
Treatment :- In serious Cases, mandatory measures include:-

1- IV administration of fluid → dehydration إي بقل loss of electrolytes بسبب
2- Dialysis of the kidney → غسيل كلى.
3- Correction of acid-base and electrolyte Balances.

يمكن استعمال Charcoal as scavenger إي بشتغل and help to eliminate aspirin from GIT, if it hasn't been absorbed.

Drugs	Mechanism of action	Side effect	Other notes
Salicylate • *Aspirin*	• Irreversibly inhibits Cyclooxygenase 1 (COX-1) and COX-2 • Inhibition of COX-2 suppresses prostanoid synthesis providing analgesic, anti-pyretic and anti-inflammatory effects • Aspirin is weakly selective to COX-1	• **Gastrointestinal:** Inhibition of COX-1 causes dyspepsia and if severe gastric bleeding and ulceration • **Rashes:** Morbiliform rash, urticaria, toxic epidermal necrolysis (TEN) • **Acute renal failure** • **Increase blood pressure** • **Reduce effect of anti-hypertensives** (except CCB) • Salicylate poisoning in aspirin overdose (hyperventilation, tinnitus, deafness, vasodilatation)	• Contraindicated in active peptic ulceration, bleeding disorders, children under 16 years (risk of Reye's syndrome), severe cardiac failure
Propionate • *Ibuprofen* • *Naproxen*	• Competitive inhibitors of COX-1 and COX-2 • Both ibuprofen and naproxen are weakly selective to COX-1		• Contraindicated in GI bleed, ulceration, heart failure
Coxibs • *Celecoxib* • *Etoricoxib*	• Competitive inhibitor of COX-2 only at therapeutic dose	• Similar to other NSAIDs • Less gastrointestinal side-effects	• Contraindicated in active GI bleed, ulceration, cerebrovascular disease, inflammatory bowel disease, ischemic heart disease, heart failure, peripheral arterial disease • Monitor blood pressure
Paracetamol	• Exact mechanism unknown but has ability to inhibit COX pathways • Good analgesic and anti-pyretic but poor anti-inflammatory effects	• Paracetamol overdose can cause liver damage • Presents with nausea and vomiting, associated with right subcostal pain and tenderness	**No anti-inflammatory effect** **Works centrally not peripherally** **Can cause hepatotoxic only when taking over dose.**

يُمنَع الـ NSAID مع الـ ACEI & ARB.



OTHER NSAIDs.

* Naproxen and Ibuprofen

both naproxen and ibuprofen should be avoided during pregnancy, especially in the third trimester, unless the benefits outweigh the potential risks and under the guidance of a healthcare professional.

- Pregnancy :- Category C, Category C 3rd trimester
- Side effects :- ↑ Risk of CV thrombotic event, MI and stroke, GI Bleeding.
- Take with food or with water to avoid GI effect.

Acetic acid derivatives → Indomethacin.

* Potent as anti-inflammatory agent.
* The toxicity of indomethacin limits its use to the treatment of
  * acute gouty arthritis.
  * Ankylosing spondylitis.
  * Patent Ductus arteriosus

المفروض الـ BV بسكر لما يقل PG عشان هيك بستعمله لأنه بقلل PG

Patent Ductus Arteriosus (PDA) is a congenital heart defect that occurs when a blood vessel called the ductus arteriosus, which is present in fetuses and normally closes shortly after birth, remains open

Oxicam derivatives

- Piroxicam & meloxicam
  - (meloxicam) inhibit Both Cox1 & Cox2 and at low doses shows (with preferential Binding for Cox2) less GI irritation than piroxicam.

* They have Long half-lives, ONCE daily administration.
* parent drug and its metabolites are renally excreted in the urine
* Used to treat :- 1- RA (Rheumatoid arthritis) 2- Ankylosing spondylitis. 3- osteoarthritis.

Diclofenac Sodium.

* orally (PO) after food and I.M. inj (intramuscular injection)
* Toxicity Similar to others.

- Diclofenac potassium → Prompt Release. (Has quicker onset علاج)
- Diclofenac Sodium → Delayed release.

Cyclooxygenase II inhibitors → Celecoxib.

* selective Cox-2 inhibitor - x10-20 more selective Cox2 than Cox1
* Interacts occasionally with warfarin, As would be expected of a drug metabolized via CYP2C9

If a drug is metabolized via the CYP2C9 pathway, it can potentially interact with other medications that also use this pathway, such as warfarin.

* Inhibit PG synthesis without affecting the action of Constitutively active Cox1 (Housekeeping isozyme found in GIT, kidney and platelets.)
* Cox2 is Constitutively active within the kidney → Recommended doses of Cox2 inhibitors Cause renal toxicities. → Similar to the traditional NSAIDs.
* Side effects :- ↑↑ incidence of CV thrombotic events → Resulting in their withdrawal from the market.

Analgesics → NSAIDs, Paracetamol, opioids.

Acetaminophen.

* inhibits PG synthesis in CNS (weak PG inhibitor) → also modulates the endogenous Cannabinoid system.
* less effect on Cox in peripheral tissues → Weak anti-inflammatory activity.
* Does NOT affect platelet function.
* NOT :- Ulcerogenic oR teratogenic.

← متى بستخدم الـ acetaminophen بدل الـ aspirin

1- Patients with gastric Complaints. 2- Prolonged bleeding. 3- Don't require anti-inflammatory action.

Adverse effects

- With normal therapeutic doses, acetaminophen is virtually free of any significant adverse effects .
- Renal tubular necrosis and hypoglycemic coma are rare complications of prolonged, large-dose therapy.
- large doses Hepatic necrosis, a very serious and potentially life-threatening condition can result.
- Renal tubular necrosis may also occur .
- Periodic monitoring of liver enzymes tests is recommended for those on high-dose acetaminophen.

- Acetaminophen is the analgesic/antipyretic of **choice** for **children** with viral infections or chickenpox (recall that aspirin increases the risk of **Reye's** syndrome .(

* Toxicity → Severe hepatotoxicity with High doses.

N-acetylcysteine is the antidote when given in the 1st 24 Hours.

علاج الـ Toxicity

* Pharmacokinetics

- Acetaminophen is rapidly **absorbed** from the GI tract. A significant first-pass metabolism occurs in the **luminal** (1) cells of the intestine and in the **hepatocytes** (2).
- Under normal circumstances, acetaminophen is conjugated in the **liver** to form inactive metabolites.
- A portion of acetaminophen is hydroxylated to form **N-acetylbenzoiminoquinone** a highly reactive and potentially dangerous metabolite .

At normal doses of acetaminophen, the N-acetylbenzoiminoquinone reacts with the sulfhydryl group of **glutathione**, forming a nontoxic substance

Acetaminophen & its metabolites are excreted in the Urine.

1)All of the following statements about cyclooxygenase1 (cox1) are correct except:

a. Is constitutively expressed on GIT, kidney and platelets .
b. It is responsible for the PGE2 synthesis which is important in mucus production in the stomach.
c. It is responsible for PGE2&PGI2 synthesis that maintain renal blood flow.
d. COX-1 is only found in inflammatory cells and tissues.

2)NSAIDs should be avoided in which group(s) of patients?

a. Kidney disease.
b. Myocardial infarction.
c. Irritable bowel syndrome.
d. All of the above.

3)Which of the following NSAIDs is a selective COX-2 inhibitor?

a. Indomethacin
b. Meloxicam
c. Celocoxib
d. Mefenamic acid

Note: Meloxicam is slightly COX-2 inhibitor with less side effects.

4)Which of the following statements about NSAIDs is false?

a. NSAIDs are not recommended during pregnancy.
b. NSAIDs increase renal blood flow.
c. NSAIDs have hypocoagulability effect.
d. Most NSAIDs are weak acids.

5)Paracetamol is an NSAID with a comparatively low anti-inflammatory effect compared to other NSAIDs.

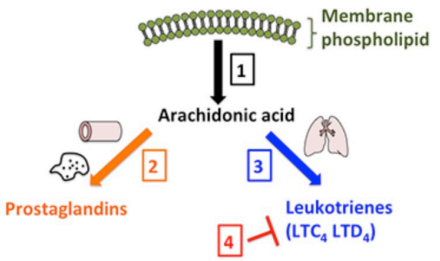
a. True.
b. False.

6)Despite aspirin has been found to be effective in reducing CV risk in such patients, it has also been found that other drugs can significantly cause excessive bleeding if taken concomitantly. An example of the type of drug to be avoided in such patients is:

a. Colchicine
b. Ketorolac
c. Prednisone
d. Methotrexate

7)NSAIDs such as aspirin can produce a type of allergic response in some patients. Which step, if blocked, is responsible for causing this drug allergy?

a. Step1
b. Step2
c. Step3
d. Step4



8)Your ten year old son is running a fever of 101°F after developing a cold. To help him feel better you go to the local pharmacy to purchase an a fever-lowering medication. However, as a good parent you recall that there are warnings about the risk of drug-induced Reye's syndrome in children given the wrong type of NSAID. Which NSAID is associated with this potentially serious condition?

a. Acetaminophen
b. Celecoxib
c. Montelukast
d. Aspirin

Note: Instead of aspirin, acetaminophen (paracetamol) is typically recommended for children with symptoms such as fever and pain.

9) John is a 63 year old alcoholic with a 5 year history of ulcers. Recently when self-medicating for a back condition John consumed 5 times the recommended daily dose of an over-the-counter pain reliever. Soon afterwards John developed a severe episode of nausea and vomiting. Twleve hours later his wife brings him to the local Emergency Department. After quizzing John about the identity of his analgesic, the ER physician draws blood samples for drug analysis and administers N-acetyl cysteine (Mucomyst) 140 mg/kg orally to prevent further toxicity. What analgesic did John most likely take to cause this problem?

a. Acetaminophen
b. Aspirin
c. Ibuprofen
d. Naproxen

10)Mikey is a twleve year old boy who has suffered from asthma for the past five years. His asthma has become worse after a recent episode of pneumonia, and now requires some form of chronic, preventative therapy. His parents express concern about the harmful effects associated with the long-term use of inhaled corticosteroids, and ask about possible therapeutic alternatives. After further discussion, it is decided to have Mikey try taking an oral formulation of montelukast for three months until his next regular appointment. The mechanism of action of this drug involves:

a. COX-1 inhibition
b. COX-2 inhibition
c. leukotriene receptor antagonism
d. Lipoxygenase inhibition

11)A premature newborn suffering from cyanosis is found to have a heart murmur upon auscultation. A 2D doppler echocardiogram indicates the presence of a patent ductus arteriosis. A drug is prescribed, and during the next followup exam, the murmur is gone. A new echocardiogram indicates a normal pattern of blood flow inside the heart. The drug prescribed was most likely:

a. Montelukast
b. Acetic Acid derivatives
c. Propranolol
d. Indomethacin
e. B&D

12)Highly selective COX-2 inhibitors are anti-inflammatory drugs with fewer GI side effects compared to traditional non-selective COX inhibitors, such as aspirin. What other effect do COX-2 inhibitors lack, in contrast to aspirin?

a. Analgesics
b. Anti-inflammatory
c. Antipyretic
d. Antiplatelet
e. Lipoxygenase inhibition

13)One of the following statements about NSAIDs is not true :

a. Oxicam derivatives have long half lives which permit once daily administration.
b. Diclofenac potassium is prompt release and has quicker onest where as diclofenac sodium is delayed release.
c. Cause GIT bleeding and perforation
d. Used to induce labor or in abortion.

14)What conditions can be treated by NSAIDs?

a. Muscle injuries
b. Arthritis
c. Headache
d. All of the above .

15)Which one of the following statements is not true about NSAIDs ?

a.Acetyl salicylic acid is an irreversible inhibitor of COX enzyme
b. Salicylic acid reduces in vivo synthesis of prostaglandins
c. Duration of action of aspirin is primarily related to .the pharmacokinetic clearance of the drug from the body
d. Antiplatelet effect of low-dose aspirin is related to presystemic COX inhibition

16)Among NSAIDS ,aspirin is unique because it :

a. Irreversibly inhibits it's target enzyme
b. Prevent gouty arthritis
c. Reduce fever
d. Reduce risk of colon cancer

17)A 16-year old boy comes in emergency with aspirin overdose ,which are the most likely symptoms:

a. Bone marrow suppression ,aplastic anemia
b. Fever,hepatic failure.
c. Hyperthermia,metabolic acidosis,coma
d. Fulminant hepatic failure

18)Indication for aspirin administration are the following, EXCEPT:

a. Inflammatory conditions.
b. Decreasing the incidence of transient ischemic attack, unstable angina, coronary artery thrombosis with myocardial infarction.
c. Relieving severe visceral pain(myocardial infarction, cancer pain condition, renal or biliary colic).
d. Reducing elevated body temperature .

19)Paracetamol has the following advantage(s) over NSAIDs

a. It is the first choice analgesic for majority of osteoarthritis patients.
b. It can be given safely to all age groups from infants to elderly
c. It is contraindicated in pregnant or breastfeeding women.
d. All of the above

20)Which of the following NSAIDs is available in a delayed-release formulation?

a. Ibuprofen
b. Diclofenac sodium
c. Meloxicam
d. Piroxicam

21)Which of the following NSAIDs is typically used for acute gouty arthritis?

a. Ibuprofen
b. Naproxen
c. Indomethacin
d. Celecoxib

22)A 65-year-old male presents to the emergency department with complaints of severe abdominal pain, vomiting, and black tarry stools. He has a history of osteoarthritis and has been taking over-the-counter ibuprofen for the past month for pain relief. On physical examination, he appears pale and is in distress due to abdominal pain. Laboratory tests reveal a decreased hemoglobin level and evidence of gastrointestinal bleeding.Based on the clinical presentation, what is the most likely cause of the patient's symptoms?

a. Peptic ulcer disease
b. Acute pancreatitis cholecystitis
c. Diverticulitis
d. Acute cholecystitis

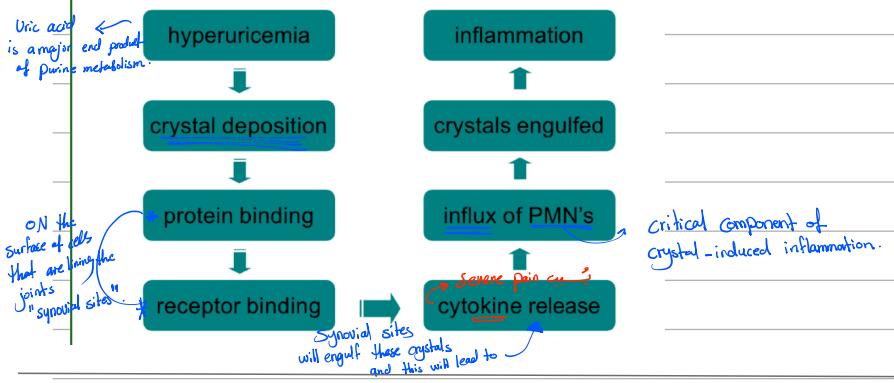
1)d	7)b	13)d	19)d
2)d	8)d	14)d	20)b
3)c	9)a	15)c	21)c
4)b	10)d	16)a	22)a
5)b	11)e	17)c	
6)b	12)d	18)c	

Drug therapy of Gout.

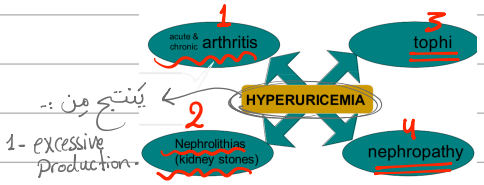
* Characteristics of Gouty (arthritis):-
  * Sudden onset.
  * Distal joints.
  * influenced By diet.
  * middle aged males.
  * Intense inflammation.
  * Bony erosions on x-ray.
  * Severe pain.
  * recurrent episodes.

Chronic tophaceous gout.
X-ray → changes of distal interphalangeal joint, joint destruction and formation of cysts in the Bone.
→ Bony erosions.

Crystal-induced inflammation



What are the Cardinal manifestations that make a person characterized of gout & needing to pharmacological treatment?



يُنتج من :-
1- excessive Production.
2- inadequate excretion.

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dietary intake → Purine Base ← cell Breakdown

Diet is a major influence on levels of uric acid, which will ultimately affect the condition of gout.

↓
Hypoxanthine.
↓ Xanthine oxidase
Xanthine
↓ Xanthine oxidase
(Uric acid)

How is uric acid handled in the kidney?
↓ glomerular filtration → ↓ Conc. of uric acid in plasma.
in Proximal convoluted tubule we have Reabsorption ↑
↓ tubular excretion. ↑ post-secretory reabsorption.

Reabsorption معناه أنا بدي أمنع الـ excretion وبدي أزيد الـ return to the Bloodstream.

* Treating acute gouty arthritis.

* Colchicine → ONLY effective in gouty arthritis. NOT an analgesic.
Does NOT affect Renal excretion of uric acid and does not alter plasma Solubility of uric acid. (serum في الـ uric acid ما بتأثر على مستوى)
↓ inflammatory response and blocks cellular response to deposited crystals.
* inhibits microtubule polymerization (By binding to tubulin) → ↓↓ PMN phagocytosis of crystals.
→ Dose: High :- treatment of acute gouty arthritis. → Declining use, it is replaced now By NSAIDs (as 1st line drugs for those acute conditions).
Low :- prevention of recurrent gouty arthritis. Useful for daily prophylaxis.

Toxicity: ① GIT "Nausea, vomiting, cramping, diarrhea, abdominal pain.
② hematologic "agranulocytosis, aplastic anemia and thrombocytopenia".
③ muscular weakness

These adverse effects are dose-related, More Common a patient who has adrenal or hepatic disease.

* Urate lowering drugs
  * allopurinol
  * probenecid.
  * febuxostat.

* rest, analgesia, ice and time.
* steroids
* NSAIDs → indomethacin, Naproxen, Ibuprofen, Sulindac, Ketoprofen.

* Aspirin is NOT used because:-
- At Low Doses:- it can cause renal retention.
- At high Doses:- It is uricosuric

Block Production → * Urate lowering drugs: * allopurinol * probenecid * febuxostat → enhance excretion

* No Role to play in managing acute gout.
* NOT indicated after first attack.
* Prevents arthritis, tophi and stones → By lowering total Body pool of uric acid.
* initiation of therapy can worsen.

Drugs that blocks production of uric acid.

* **Allopurinol** → inhibit xanthine oxidase.
- Pregancy category C → Would interfere with uric acid synthesis affecting purine metabolism, it can pose some risk to fetus.
→ adverse effects: * diarrhea, nausea, abnormal liver tests.
* acute attacks of gout & Rash.
* hepatotoxicity, bone marrow suppression. (aplastic anemia can occur.)
* Necrotizing vasculitis, Drug interaction (ampicillin, thiazides, mercaptopurine, azathioprine)
* Death. * (epidermal necrolysis: Stevens-Johnson syndrome.
- target skin lesions, mucous membrane erosions and epidermal necrosis with skin deattachment.

Allopurinol Hypersensitivity:-
* Serious problem. First sign usually skin rash.
* Progression to toxic epidermal necrolysis and death.
* Common with impaired renal function.

* **febuxostat**
- oral xanthine oxidase inhibitor.
MOA يختلف كيميائيًا عن allopurinol لكن نفس
- 94% of patients ↓↓ urate < 6.0 mg/dl
- minimal adverse events.

* **PEGLOTICASE**
* Treatment - resistant gout.
→ Refractory chronic gout.
* Recombinant porcine uricase (found in mammalian attached to MPEG monomethoxy-polyethylene glycol to minimize ← يُغلف antibody response in the Body.)
* IV drug.
* This drug should be avoided in patients with glucose-6-phosphate dehydrogenase deficiency, because of the formation of hydrogen peroxidase by Uricase.

Drugs that enhance excretion of Uric acid.

Uricosuric therapy
probenecid زي ال
MOA → Block tubular reabsorption of Uric acid. → excretion زي ال
وبقل نسبة Uric acid في ال serum
↑↑ Risk of nephrolithiasis.
• NOT used in patients with renal disease, History of nephrolithiasis and patients with elevated urine uric acid level.
* moderately effective BUT less effective in elderly patients.

Gout

Acute arthritis → acute synovitis in ankle + inflammation in MTP joints and articulations. (metatarsophalangeal)

Acute bursitis → acute olecranon bursitis. (inflammation in Bursa → fluid filled Sac)

* Case presentation - therapy.
- from day 1 to 10.
NSAID, we can give steroid.
as maintenance therapy: Colchicine قبل ما أوقف NSAIDs ببدأ بتراجيز قليل
immediately after an acute attack: allopurinol بس ما بعطيه ← لأن بدي أعطي
NSAIDs بوقف allopurinol بعطي إياه أيضًا NSAIDs & Colchicine بعطي
* after the attack is subsides & we maintain the patient on colchicine and allopurinol.

* LT-1 receptor antagonist.
- Anakinra.
- Canakinumab.
- Rilonacept.
هادي أدوية تستخدم لعلاج RA ~ gout بتعالج ال
-Suppression of inflammation.

Glucocorticoids → e.g. → prednisone. → During acute gouty arthritis.
"orally, intra-articular, subcutaneously"

1) Allopurinol decreases the plasma concentration of:

a. Hypoxanthine
b. Xanthine
c. Uric acid
d. Purine bases

2) Strong nonsteroidal anti-inflammatory drugs are more commonly used than colchicine in acute gout because:

a. They are more effective.
b. They are better tolerated.
c. They act more rapidly.
d. They have additional uricosuric action.

3)Which of the following statements is correct about the mechanism of action of Probenecid

a. Inhibition of cyclooxygenase enzymes
b. Inhibition of uric acid reabsorption in the kidney
c. Stimulation of insulin secretion
d. Inhibition of monoamine oxidase enzymes

4)All the following drugs will be useful in the treatment of an acute attack of gout; EXCEPT:

a. Indomethacin
b. Prednisone.
c. Colchicine.
d. Allopurinol.

5) Colchicine is best described as it:

a. Enhances uric acid excretion.
b. Is an effective analgesic in osteoarthritis.
c. Is used for treatment and prevention of acute gouty arthritis.
d. All of the above

6)To lower uric acid levels in blood and urine you should use:

a. Colchicine
b. Indomethacin
c. Allopurinol
d. Corticosteroids

7)Which of the following drugs is not used for acute gouty arthritis?

a. Probenecid
b. Steroids
c. Ibuprofen
d. Colchicine

8)Which of the following drugs could be used to decrease rate of production of uric acid:

a. Naproxen
b. Aspirin
c. Colchicine
d. Febuksostat

9)Which of the following agents binds to tubulin leading to depolymerization and disrupting neutrophils mobility:

a. Colchicine
b. Febuxostat
c. Sarilumab
d. Abatacept

10)A 45-year-old man with a history of severe tophaceous gout presents to the rheumatology clinic for evaluation. Despite maximum doses of allopurinol and febuxostat, his serum uric acid levels remain elevated, and he continues to experience debilitating gout flares. His medical history is significant for glucose-6-phosphate dehydrogenase (G6PD) deficiency. The rheumatologist is considering Pegloticase therapy as a potential treatment option .Which of the following statements regarding the use of Pegloticase in this patient is most accurate?

a. Pegloticase should be initiated cautiously with close monitoring of renal function.
b. Pegloticase is contraindicated due to the risk of severe allergic reactions.
c. Pegloticase should be avoided due to the risk of inducing hemolytic anemia in patients with G6PD deficiency.
d. Pegloticase may be considered but requires concurrent administration of corticosteroids to prevent immune-mediated adverse effects

11)Which of the following is a symptom of gout?

a. Purple or red skin

b. Severe pain, warmth and swelling in joints

c. Itching skin, peeling at the site of a gout attack

d. All of these

12)This is not a first-line option for pharmacological treatment of gout

a. Corticosteroids

b. Aspirin

c. Oral colchicine

d. NSAIDS

13) ice packs can be effective adjuncts to the management of an acute gout attack.

a. True

b. False

14)Which of the following best describes the mechanism of action of Acyclovir?

a. Inhibition of viral DNA polymerase
b. Stimulation of host immune response against the virus
c. Disruption of viral protein synthesis
d. Inhibition of viral RNA synthesis

15)Which of the following statements about Ganciclovir is correct?

a. The most common adverse effects of Ganciclovir include gastrointestinal disturbances and hepatotoxicity.
b. Ganciclovir is well-tolerated, with few patients experiencing adverse effects, primarily limited to mild headaches.
c. Ganciclovir is contraindicated in CMV infections and should only be used for other viral infections.
d. Ganciclovir is the drug of choice for CMV infections,but one-third of patients may have to discontinue treatment due to adverse effects

16) Which of the following statements regarding Foscarnet is correct?

a. Foscarnet works by inhibiting viral protein synthesis.
b. Foscarnet is well-absorbed orally, making it suitable for outpatient treatment.
c. Resistance to Foscarnet primarily occurs due to mutations in viral surface proteins.
d. Foscarnet must be administered intravenously due to poor oral absorption and is eliminated primarily via glomerular filtration

1)c	5)c	9)a	13)a
2)b	6)c	10)c	14)a
3)b	7)a	11)d	15)d
4)d	8)d	12)b	16)d