



Pharmacology

Subject : Adverse drug reactions

Lec no : 13

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وَقُلْ رَبِّ زِدْنِي عِلْمًا

تجدون في guidance مادة الفارما على موقع النادي :

The screenshot shows the website medclubhuweebly.com with the following sections and annotations:

- Navigation Tabs:** GUIDANCE (circled in red), SLIDES, NOTES, RECORDS.
- GENERAL PHARMACOLOGY (علم الأدوية العام):** Includes a welcome message and a list of lecturers: دكتور طارق, دكتورة اروى, دكتور شريف.
- PHARMA LECTURES:** A section for general pharmacology lectures.
- FOUDA GENERAL PRINCIPLES:** A section for general principles of pharmacology.
- FOUDA ANTIMICROBIAL CHEMOTHERAPY:** A section for antimicrobial chemotherapy.
- NINJA NERD:** A section for general principles of pharmacology.
- SCIENTIFIC TEAM:** A section for the scientific team.
- JOSEPH ABULAIL:** A section for Joseph Abulail.
- ATHAR NOTES:** A section for Athar Notes.
- VEIN NOTES:** A section for Vein Notes.
- EXTERNAL SOURCES:** A section for external sources.
- QUIZZES AND TEST BANKS:** A section for quizzes and test banks.
- Download File:** A button to download a file.

شرح دكتور شريف و دكتور طارق للمادة

شرح فودة لمادة المييد

شرح فودة لمادة الفايبل

تفاريغ دفعة اتر جداااا قوية ، خاصة مادة الفايبل لانها بتحتاج تفاريغ كثير ، و برضه تفاريغ جهينة بدفعة وريد قوية

جداول رح تساعدكم كتيييبيير بحفظ الأدوية بمادة الفايبل

كويزات الدكاترة

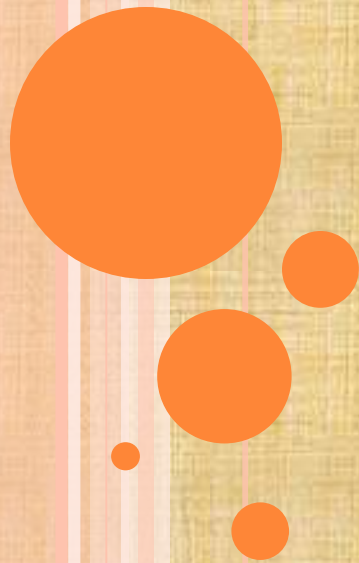
للوصل الى guidance الفارما و تفاريغ المادة كاملة :



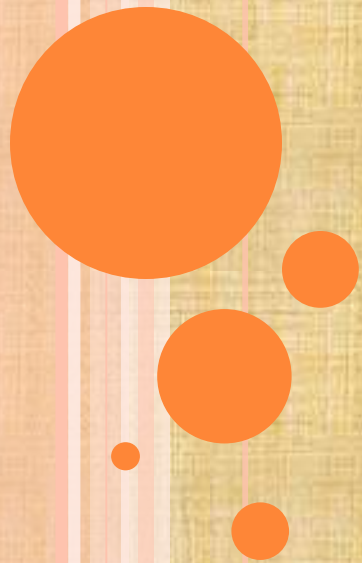
كل اعمال الفريق العلمي تنشر على قناة التليغرام



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Medical pharmacology
Hashemite University



ADVERSE DRUG REACTIONS



ADVERSE DRUG REACTIONS (ADE)

○ Definition

- Any response to a drug which is harmful, unintended, undesired & which occurs at doses in man for prophylaxis, diagnosis or treatment.

غير مقصود

عس كركون

وقاية

في فرق بين side effect و adveres effect
ال adveres effect يعني اثر عكسي للدواء مؤذي لو صار
أما ال side effect اثر جانبي انا متوقعة انه يصير ومو مؤذي بشكل كبير



- Incidence of ADR more الفئات المعرضة للADR أكثر ولازم اكون حذرة وانا بعطيهم دواء
 - Polypharmacy
 - Elderly
 - Children } ↓ metabolism
 - Patient with multiple diseases
 - Pregnancy
 - Malnourished بجانوا من سوء تغذية (↓ plasma protein)
 - Immunosuppression
 - Drug Abusers and addicts
- Develop حتى بصير ردة فعل ADR
 - Immediately فوراً
 - or
 - Prolonged medication ممكن بعد شهر من الالتزام بالدواء فجأة بصير ال ADR
 - or
 - After stopping.



CLASSIFICATIONS OF ADR

يصنف حسب قوة ال ADR وسببه وعلاقته بال receptor

- A (Augmented) *بزيد الماكشن تبغ الدواء*
- B (Bizarre) *غريب*
- C (Continuous)
- D (Delayed)
- E (Ending Use)
- F (Failure of Efficacy)

Broadly

Type- A (Predictable)- Based on pharmacological properties

Type- B (Non-predictable) – Based on Immunological response
and genetic makeup of person

TYPE A- AUGMENTED

- These are based on the pharmacological properties of the drug so can be predicted.
- They are common and account for 75% of ADRs
- Dose related and preventable mostly reversible.

مثل دواء باخده كمسكن (aspirine) وهو بيستخدم لسيولة الدم بيمنع يصير thrombosis وهو بالأصل
بزيد ال gastric secretion فبسببلي peptic ulcer
فهو اشتغلي الشغل المطلوب (كمسكن) بس كان في اثار مؤذية وغير مرغوبة (peptic ulcer)

Examples:-

- Anticoagulants (e.g., warfarin, heparin) – bleeding
ال heparin يستخدم ك antihypertensive
- Anti-hypertensives (e.g.. α 1-antagonists) – hypotension
- Anti-diabetics (e.g. insulin) - hypoglycemia

Predictable

TYPE B- BIZZARE OR UNPREDICTABLE

يعني دواء ممكن اخده لفترة بدون اي اثر عكسي وفجأة بيظهر effect غريب كثير وعشوائي

- Have **no direct relationship** to the dose of the drug or the pharmacological mechanism of drug action.
- Develop on the basis of:
 - Immunological reaction on a drug (**Allergy**)
 - Genetic predisposition (**Idiosyncratic reactions**)
- More serious clinical outcomes with higher mortality and morbidity.
- Mostly require immediate withdrawal of the drug.

الحل الوحيد انه توقف استخدام الدواء

Un-predictable

TYPE C – CHRONIC (CONTINUOUS) USE

مريض بياخذ دواء لعلاج مرض chronic فهاد الدواء بعد فترة طويلة من الاستخدام رح يضل يشتغل ع نفس المكان ونفس الاسلوب فيعمل نفس ال injury

- They are mostly associated with **cumulative-long term exposure**

Example:-

Analgesic (NSAID)– interstitial nephritis, papillary sclerosis, necrosis

أدوية nonsteroidal مثل morpholine و voltaren الناس الي عندهم مشاكل بالمفاصل بيستخدموهم كثير فانه ممكن تعلمي مشكلات في kidney بعد فترة طويلة من استخدامه



Predictable

TYPE D – DELAYED

تحصل بعد فترة طويلة من استخدام الدواء

- They manifest themselves with significant delay
 - **Teratogenesis** -Thalidomide – Phocomelia (flipper-like fore limbs)
 - **Mutagenesis/Cancerogenesis**

Others:

شکل رعاشي

Tardive dyskinesia – during L-DOPA Parkinson disease treatment

وتمكن اعتبارها un-predictable

Predictable

TYPE E – END OF USE

أعراض انسحابية

- Drug withdrawal syndromes and rebound phenomena

في أدوية ما يينفع تتوقف فجأة... بصير في effect عكسي للدواء

- Example – sudden withdrawal of long term therapy with **β -blockers** can induce rebound tachycardia and hypertension

ال B-blocker يستخدم لعلاج hypertension ويقللي ضغط الدم وما يينفع اوقفه فجأة بصير لانه ممكن يصير عندني tachycardia و hypertension

Predictable

PREVENTION OF ADVERSE EFFECTS TO DRUGS

- **Avoid inappropriate use of drugs .**
- **Appropriate drug administration (Rational Therapeutics)** في أمور لازم اخدها بعين الاعتبار قبل استخدام اي دواء
 - Dose
 - Dosage form
 - Duration
 - Route
 - Frequency
 - Technique
- **Ask for previous history of drug reactions and allergies** لازم قبل ما اعطي المريض اي دواء أسأله اذا في ادوية بياخذها حاليا واذا في عنده اي مشاكل مع ادوية معينة
- **Always suspect ADR when new symptom arises after initiation of treatment.** هلا ممكن تعطي مريض دواء وبعد فترة بييجي بيحكيك انه وضعي تمام وانه اتحسن ع الدواء الي اعطيته اياه... بس صار عندي مثلا طفح جلدي او احمرار وهيك اشياء فمباشرة اتوقع انه يكون ADR
- **Ask for laboratory findings like serum creatinine etc.**

Categorized into:

- Side effects-
- Secondary effects
- Toxic effects
- Intolerance
- Idiosyncrasy
- Drug allergy
- Photosensitivity
- Drug dependence
- Drug withdrawal reactions
- Teratogenicity
- Mutagenicity and Carcinogenicity
- Drug induced diseases (Iatrogenic disorders or Iatrogenicity)

Beware of – Iatrogenic, Idiosyncrasy, Idiopathic, Intolerance

SIDE EFFECTS

- Unwanted often unavoidable Pharmacodynamic effects(not harmful).
- Occur at therapeutic doses.
- Predictable

Examples.

-H1 Anti-histaminics- Sedation

-Depression of A-V conduction is the desired effect of **digoxin** in atrial fibrillation, but the same may be undesirable when it is used for CHF.

أغلب ادوية الحساسية بتتوم (هاد النعاس هو side effect لانه effect مش مؤذي)



TOXIC EFFECTS (Poisonous effect)

- An adverse effect of a drug produced by an **exaggeration of the effect that produce the therapeutic response.**
- **Predictable**
 - Dose dependent
- **Unpredictable**
 - Allergy
 - Idiosyncrasy
- Over dose or prolonged use.
- The **CNS, CVS, kidney, liver, lung, skin and bone marrow are most commonly involved in drug toxicity.**




- Toxicity may result from extension of the therapeutic effect itself, e.g. complete A-V block by digoxin, bleeding due to heparin.

دواء digoxin يستخدم لعلاج heart failure مشكلته انه يقلل AV conduction بصير عندي heart block

- **Poisoning:** Poison is a substance which endangers life by severely affecting one or more vital functions.



Predictable toxic effects

- □ Dose dependent adverse effect may be:
 - □ **Direct damaging effect to tissue:** Paracetamol overdose leads to hepatotoxicity, Aminoglycoside (Gentamicin) causes nephrotoxicity.
 - □ **Rebound response:** abrupt withdrawal after chronic use. Glucocorticoid withdrawal leads to acute adrenal insufficiency.
 - **Excess pharmacological effect:**
 - Result of excessive pharmacological action of the drug due to overdose or prolonged use.
 - □ Excess insulin-hypoglycemia even death from hypoglycemics shock
 - □ Antihypertensive-hypotension
 - □ Anticoagulant-severe bleeding.
- 

Unpredictable toxic effects

- □ **Dose independent:**
- □ **Less than the therapeutic dose may lead to toxic effect**



○ ^{تَعَوُّد} Tolerance

- □ ↓ pharmacological effect on repeated administration of the drug.
- □ **Pharmacokinetic Tolerance**: ↑ the enzymes responsible for **metabolizing** the drug.
- e.g. Phenobarbitone induces metabolism of its own by increasing its own metabolic enzyme.
- □ **Pharmacodynamic Tolerance**: Cellular tolerance, due to **down-regulation of receptors**.

ال tolerance يعني باخذ دواء أول مرة بتحسن كثير منيح المرة الثاني يعني التحسن ببلش يقل بعد 5 مرات ببطل في تأثير او تحسن ع الدواء

هو نوع ال Tolerance أخذناه من قبل المحاضرات د. شريف



الجسم ما تعود على الدواء

INTOLERANCE

- It is the appearance of characteristic toxic effects of a drug in an individual at therapeutic doses
- **Intolerance**
- □ Converse of tolerance
- □ Indicates a low threshold of the individual
- □ **E.g.**
- □ Chloroquine (single tablet) □ Vomiting and abdominal pain in some individuals

نادر جدًا

Un-Predictable

Tachyphylaxis:

- □ When responsiveness diminishes rapidly after administration of a drug, the response is said to be subject to tachyphylaxis.
- □ Tachyphylaxis to the Action of Topically Applied Corticosteroids
- **Difference between Tachyphylaxis and Tolerance**
- □ Tachyphylaxis is the result of frequent doses over a short period of time and tolerance is the result of chronic administration over a long. A typical example of tachyphylaxis is epinephrine's action on vessels (blood pressure). Repetitive stimulus over a short time causes the depletion of a vasoconstricting substance.



IDIOSYNCRASY

- It is **abnormal reaction to a drug due to genetic abnormality.** ردة الفعل مختلفة من شخص للتاني

Example :-

-Succinylcholine can produce **apnea** in people with **abnormal serum cholinesterase.** Their **cholinesterase** is **incapable of degrading the succinylcholine,** thus sustained **NMB results.** حكيئا عنه بالمحاضرة الماحنيه

-Chloramphenicol produces non dose-related serious aplastic anaemia in rare individuals.

الدكتورة بتحكي انه هيك المحاضرة مختصرة 😂🙄



DRUG ALLERGY

It is abnormal reaction to a drug due to antigen-antibody reaction.

- Acquired, altered reaction of the body to drug.
- □ Immunologically mediated reaction.
- □ occur even with much smaller doses
- □ Also called Drug hypersensitivity
- □ Not genetic, not occurred in all *ممكن، الألب عنده حساسية بس، المابن ها عنده*
- □ Occurs on reexposure
- □ E.g. penicillin → 1st time → stimulate antibody → Ag-Ab reaction → allergy *لازم اعمل اختبار حساسية قبل كل مرة*
- □ Chief organ: Skin, respiratory tract, GIT, Blood & blood vessels

كثير نادر بس احنا عاملين حساب لحدوثها

Un-Predictable

- Allergic reactions occur only in a **small proportion of the population** exposed to the drug .
- The drug or its metabolite acts as antigen (AG) or more commonly **hapten** (incomplete antigen) and induce production of antibody (AB)/sensitized lymphocytes.

الدكتورة عملت سكيب بس أكيد لازم نقرأهم



○ Grading system for hypersensitivity reactions

○ 1-Mild

○ Cutaneous and subcutaneous only *مثل قرصبة النحلة*

○ Generalized erythema, periorbital edema, urticaria.

○ 2-Moderate *أعراض بتلحق تتصرف معها*

○ Cardiovascular, respiratory, or gastrointestinal involvement

○ Dyspnea, stridor, wheeze, nausea, vomiting, dizziness, diaphoresis, chest or throat tightness, or abdominal pain

○ 3-Severe *يا بتلحق تتصرف يا لا*

○ Hypoxia, hypotension, or neurologic compromise , confusion, collapse, loss of consciousness, or incontinence Cyanosis.

○



PHOTOSENSITIVITY

- It is a cutaneous reaction resulting from drug induced sensitization of the skin to **UV radiation**.
- The reactions are of two types:
 - a) **Photo-toxic :- (T-S)**
 - a) Drug or its metabolite **Accumulates** in the skin,
 - b) absorbs light and undergoes a **Photochemical reaction** followed by
 - c) **Photobiological reaction** resulting in
 - d) Tissue damage (sunburn-like),
 - a) i.e. erythema, edema, blistering , hyper pigmentation, desquamation.



(b) Photo-allergic: (A-L)

Drug or its metabolites induce a cell mediated immune response which on exposure to

Light of **longer wave lengths (320-400 nm, UV -A)**

Produces a papular or eczematous contact dermatitis.

Drugs involved are sulfonamides, sulfonylureas, griseofulvin, chloroquine, chlorpromazine



مثل الادمان

DRUG DEPENDENCE

مش لاخراجن كليه

- Use of drugs for personal satisfaction

Physical dependence It is an altered physiological state produced by repeated administration of a drug which necessitates the continued presence of the drug to maintain physiological equilibrium.

- Discontinuation of the drug results in a characteristic **withdrawal (abstinence) syndrome.**
- Drugs producing physical dependence are **opioids, barbiturates and other depressants including alcohol and benzodiazepines**



○ Drug abuse : أدوية ممكن الشخص يوقفها

- It is an illegal use of drug for non medical purposes despite physical, social or psychological problems that may result from that use.

حسب فهمي وبعد طلب المساعدة من اختي 😊
هنا مثلا ال steroid او (corticosteroid) في ناس بتستخدمه لعلاج اي مرض ما عرفوله دواء (ع قولت اختي الكورتيزون دواء الدكاترة الي ما بتفهم لانه اي شي ما بيعرفوله علاج بيعطو كورتيزون للمريض) وممكن في بنات بيستخدموه عشان يوصلو لل moon face وفي كمان ال androgen الي هو هرمون ال testosterone في شباب بيستخدموه لنفخ العضلات وهالقصص بدون اي اعتبار للاضرار الي بيعملها

○ Drug addiction

أدوية مش ممكن الشخص يوقفها

It is a pattern of compulsive drug use characterized by overwhelming involvement with the use of a drug.

Procuring the drug and using it takes precedence over other activities

أولويته

استخدام قهري



عادة

○ Drug habituation (Psychological dependence)

ارتباط نفسي

It denotes less intensive involvement with the drug, so that its withdrawal produces only mild discomfort.

- Consumption of tea, coffee, tobacco, social drinking are regarded habituating, physical dependence is absent

ال tobacco ال physical dependence و psychological dependence



DRUG WITHDRAWAL REACTIONS

- Sudden interruption of therapy with certain other drugs results in adverse consequences, mostly in the form of worsening of the clinical condition for which the drug was being used
- **Example:** Acute adrenal insufficiency may be precipitated by abrupt cessation of corticosteroid therapy.



TERATOGENICITY (Teratos- Monster)

- Drug to cause foetal abnormalities when administered to the pregnant mother.

- Drugs can affect the foetus at 3 stages-

(i) **Fertilization and implantation(1-14 days):all or none.**

هون لسا ما بتعرف انها حامل (التأثير قوي جدا)

(ii) ^{أخطر مرحلة} **Organogenesis-18 to 55 days** (3-12 weeks) of gestation **most vulnerable period, deformities are produced.**

(iii) **Growth and development-56 days(12-38 weeks)** onwards developmental and functional abnormalities can occur, e.g. ACE inhibitors , **Thalidomide, Warfarin, Barbiturates,**.....

الأعضاء بتعمل تنمو للشهر التاسع يعني الخطر لسا موجود



Drugs known to be **teratogenic**

- □ Oral anticoagulants—bony abnormality, mental retardation.
- □ Oral hypoglycemic agents-multiple deformity.
- □ Tetracycline—inhibit bony growth.
- □ **Diethylstilbestrol**-Oral contraceptive is no longer used because it causes **reproductive cancers in daughters born to mother taking the drug.**
- □ **Aminoglycosides, Chloroquine**—Deafness
antibiotic



MUTAGENICITY AND CARCINOGENICITY

- Cause genetic defects and cancer respectively.
- Reactive intermediates which affect genes and may cause structural changes in the chromosomes
- Even without interacting directly with DNA.
Examples- anticancer drugs, radioisotopes, estrogens, tobacco.....

ال anticancer drugs هي ادوية بتعالج الكانسر الحالي بس مع الوقت بتعمل كانسر بمكان ثاني



DRUG INDUCED DISEASES

بتعطي دواء وانت عارف انه ممكن يسبب مرض معين بس مضطر تعطيه ما فيك تستغني عنه
ف بتحاول تتجنبها ممكن انك تعطي دواء وقائي او علاجي للمرض الي ممكن تعمله

- These are also called **iatrogenic (physician induced)** diseases, and are functional disturbances (disease) caused by drugs .
- Hepatitis by isoniazid and Rifampicin
- Peptic ulcer by salicylates and corticosteroids *بيعمل قرحة بالمعدة*
- **Retinal damage by chloroquine**



INDIVIDUAL VARIATION IN RESPONSE TO DRUG

بتصير عن شخص بشكل وبتصير عن شخص تاني بشكل اخر وشخص تالت ما بتصير عنده أساساً

- A) Alteration in concentration of drug that reaches the receptors
- Variation in concentration of an endogenous receptor ligand–
- C) Alteration in number or function of receptor
- D) Changes in components of response distal to the receptor



ملاحظات

١) كل التعاريف مع الامثلة مهم

٢) الاشياء التي ذكرتها أو قرأتها، الدكتورَة تعتبر مثل التريجة 😊

٣) مراحل الحل مهم

٤) risk Factors معلومات عامة لنا بس هي مستحيل تجيبهم بالامتحان

THANKS

