



Pharmacology

Subject :

Lec no : 13

Done By : Raneem Azzam

وَقُلْ رَبِّ زِدْنِي عِلْمًا

تجدون في guidance المادة الفارما على موقع النادي :

The screenshot shows a website with a top navigation bar containing 'GUIDANCE', 'SLIDES', 'NOTES', and 'RECORDS'. The 'GUIDANCE' tab is circled in red. Below the navigation bar, the main content area is titled 'GENERAL PHARMACOLOGY (علم الأدوية العام)'. There are three buttons: 'دكتور طارق', 'دكتورة اروى', and 'دكتور شريف'. Below these, there are several sections with red arrows pointing to them: 'شرح دكتور شريف و دكتور طارق للمادة', 'شرح فودة لمادة الميد', 'شرح فودة لمادة الفايصل', 'تفاريغ دفعة اثر جداااا قوية ، خاصة مادة الفايصل لانها بتحتاج تفاريغ كثير ، و برضه تفاريغ جهينة بدفعة وريد قوية', 'جدول رح تساعدكم كتبيبيبيبي بحفظ الأدوية بمادة الفايصل', and 'كويزات الدكاترة'. At the bottom, there are 'QUIZES AND TEST BANKS' and 'Download File' buttons.

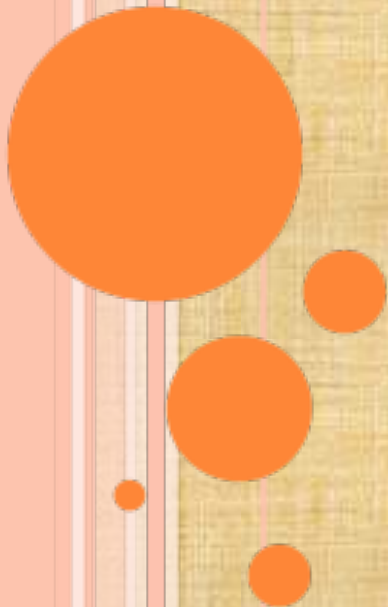
للوصول الى guidance الفارما و تفاريغ المادة كاملة :



كل اعمال الفريق العلمي تنشر على قناة التليغرام

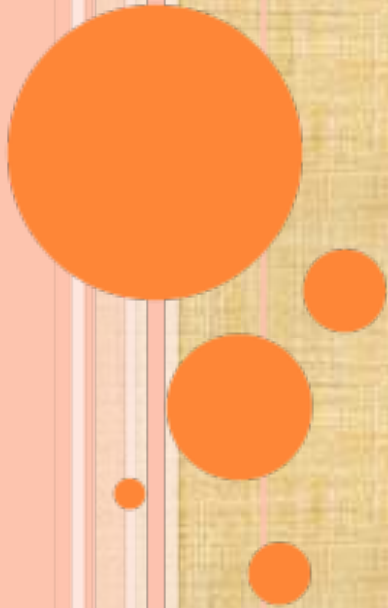


Dr. Yasmeen Mohammed Ismail
Medical pharmacology
Hashemite University



ADVERSE DRUG REACTIONS

التفاعلات الدوائية
الضارة



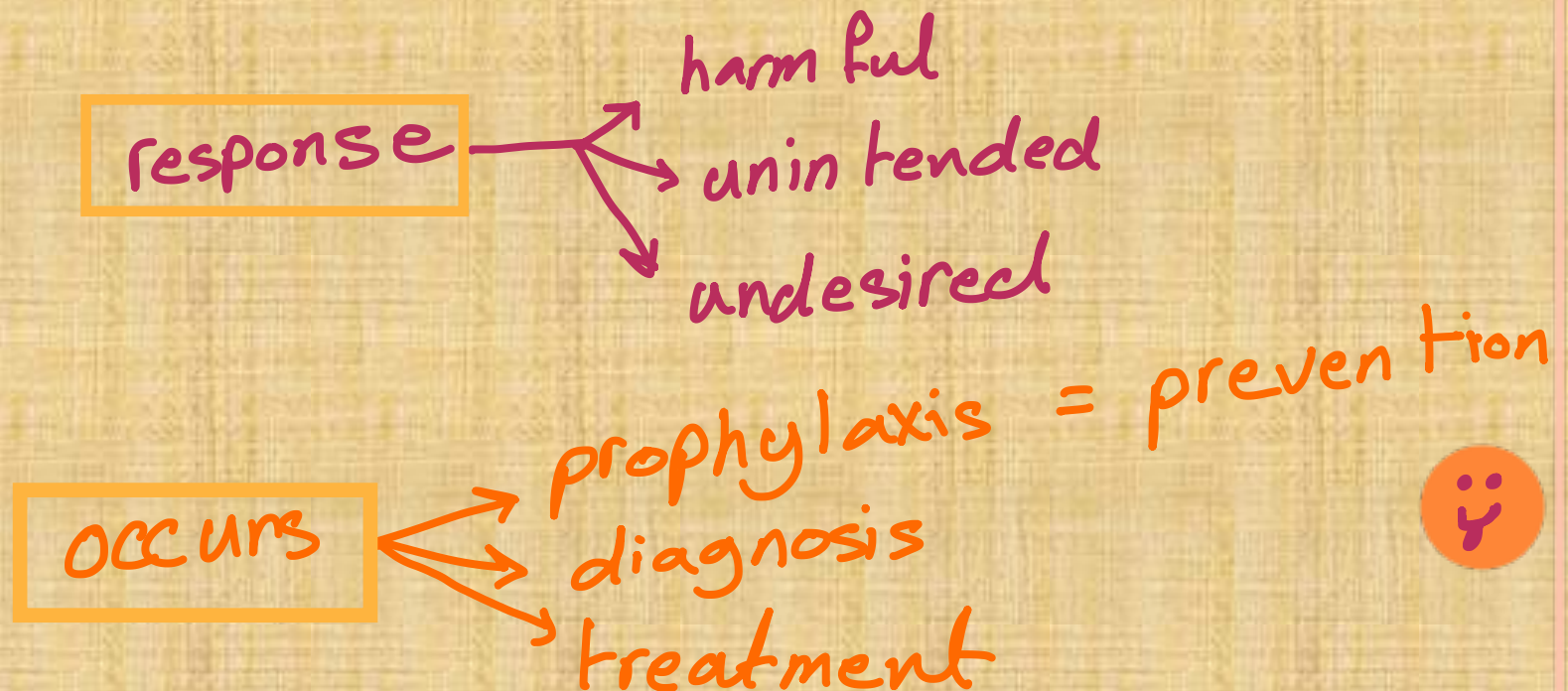
ADVERSE DRUG REACTIONS (ADE)

Definition

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

غير مقصود

غير مطلوب



occurrence

- Incidence of ADR more

- Polypharmacy → الإفراط الدوائي

- Elderly

- Children

- Patient with multiple diseases

- Pregnancy

- Malnourished → suffering from سوء التغذية

- Immunosuppression → نقص المناعة

- Drug Abusers and addicts

- * Develop

- ① Immediately

or

- ② Prolonged medication

or

- ③ After stopping.

ردت فعل السبي لا ADR

حتمن تحصل:



CLASSIFICATIONS OF ADR

* على أي أساس
بفحصها؟

- **A (Augmented)** → increase the action
- **B (Bizarre)** → very strange or unusual
- **C (Continuous)**
- **D (Delayed)**
- **E (Ending Use)**
- **F (Failure of Efficacy)**

* * *
فهم تعريفهم *
كلا وحدة

Broadly

مفهوم

Type- A (Predictable)- Based on pharmacological properties

Type- B (Non-predictable) – Based on Immunological response
and genetic makeup of person ②

TYPE A- AUGMENTED

تُضَاعَفُ أَوْ زَوَّدُ
ال action

- 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.) →

الميزة فيها

Examples:-

- مُزَانٌ → Anticoagulants (e.g., warfarin, heparin) – bleeding
حَدُولٌ → Anti-hypertensives (e.g., α 1-antagonists) – hypotension
• Anti-diabetics (e.g. insulin) - hypoglycemia

inhibits blood coagulation

Predictable ✕

TYPE B- BIZZARE OR UNPREDICTABLE

عشوائی / رد فعل عزیز

حالة ملصاش دعوة

→ في

pharmacological

بحيث بتعرف

احياناً بشكل

عشوائی

- 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.

❖ هي حاجة مفاجأة
بس انت ك طبيب
مفروض تكون مش
مفاجأة ليك ❖

ليه؟
لأنها في نسبة خفيفة في البشر
بس يتعملها حساب

Un-predictable

TYPE C – CHRONIC (CONTINUOUS) USE

تأثير الدواء تراكمي

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

Example:-

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

NSAID → non-steroidal anti-inflammatory drug.

احنا دكاترة وعارفين ال سايد
ايفكت ومشاكل كل دوا

ليه؟
←

Predictable

TYPE D – DELAYED

* يتحصل بعد فترة طويلة جدًا

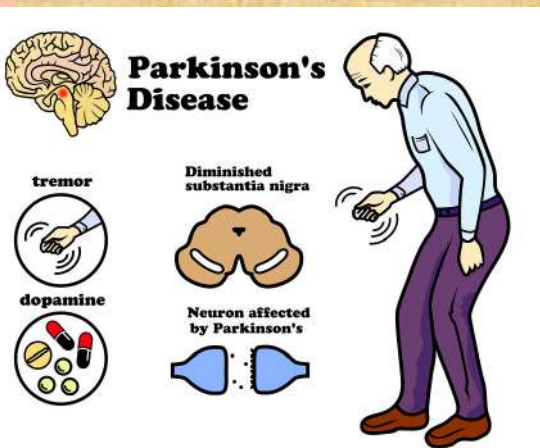
They manifest themselves with significant delay

فترة طويلة

Teratogenesis - Thalidomide – Phocomelia (flipper-like fore limbs)
Mutagenesis/Cancerogenesis

Others:

Tardive dyskinesia – during L-DOPA Parkinson disease treatment



← يمكنه منك ويمكنه *
predictable + بين فترة un predictable

Predictable

TYPE E – END OF USE

* الأعراض الإيجابية *

Drug withdrawal syndromes and rebound phenomena

← أنت بتوقف الدواء و يحصل
عكس ال symptoms إيل الدواء بعملها .

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

↓
an abnormally rapid heart rate.



❖ زي دوا الضغط ما ينفعش المريض
يوقفه فجأة ، فتنبه على العيان ما
يوقف الدواء ده من دماغك ❖

Predictable

PREVENTION OF ADVERSE EFFECTS TO DRUGS

Avoid inappropriate use of drugs .

Appropriate drug administration (Rational Therapeutics)

Dose

Dosage form

Duration

Route

Frequency

Technique

الدوا ما نفتيش فيه ما فيهوش هزار ✨

Ask for previous history of drug reactions and allergies

Always suspect ADR when new symptom arises after initiation of treatment.

Ask for laboratory findings like serum creatinine etc.



Categorized into:

classify

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). → (sleep not harmful) → (الردو الصافية side effect مثلاً)

Occur at therapeutic doses.

Predictable

Examples.

بسن حماد
الممثال

-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.



TOXIC EFFECTS (Poisonous effect)

An adverse effect of a drug produced by an exaggeration of the effect that produce the therapeutic response. overstatement

Predictable	Unpredictable
Dose dependent	Allergy Idiosyncrasy

Over dose or prolonged use.

The CNS, CVS, kidney, liver, lung, skin and bone marrow are most commonly involved in drug toxicity.



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

use in HF ←

زبي
الباندر
شوبيل بس اخذو
بكثرة .

- **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:

- 1 **Direct damaging effect to tissue:** Paracetamol overdose leads to hepatotoxicity, Aminoglycoside (Gentamicin) causes nephrotoxicity.

- 2 **Rebound response:** abrupt withdrawal after chronic use. Glucocorticoid withdrawal leads to acute adrenal insufficiency.

- 3 **Excess pharmacological effect:**

- Result of excessive pharmacological action of the drug due to overdosage 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



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.

[4] Tolerance (hyporeactivity):

- It is progressive reduced responsiveness to the drug on repeated administration so that higher doses are needed to produce the same original effect.

أسبابه:

- Acquired tolerance:**
 - Pharmacokinetic tolerance:** is tolerance due to decreased drug level e.g.
 - ↓ Absorption e.g. furosemide in heart failure (gut edema).
 - ↑ Elimination e.g. ↑ metabolism with phenobarbitone
 - Pharmacodynamic tolerance:** is tolerance without decreased drug level e.g.
 - Desensitization of the receptors (conformational changes in receptor shape) e.g. opiates
 - Down regulation of receptors e.g. β_2 -agonists

Special types of acquired tolerance:

Handwritten notes in Arabic:

- هذا ال decrease مع الوقت يزيد تدريجي يعني بين تصير تأخذ جرعات متتالية ببلش ال effect يزيد وعاذ السبب الي بعلي المريض بزيادة الجرعات حتى يحصل على نفس التأثير لما اخذ اول مرة زي المسكن او المنوم اولها ببلش تأثيره فل الفل بعد هيك بعصور بذك تزيد الجرعة حتى تحصل بنفس التأثير زمان وهكذا
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شرح كامل
Lec 11
في

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

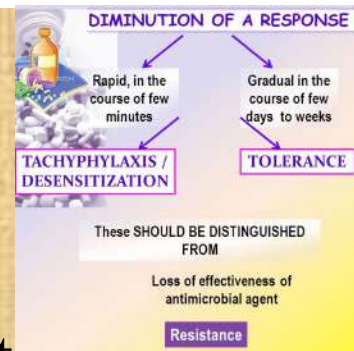
Tachyphylaxis:

- 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(bloodpressure).Repetitive stimulus over a short time causes the depletion of a vasoconstricting substance.



اعرفوها لو سمحتو

اكثر ايشي
common في فترة
الشتا لما منستخدم
الادوية الموسعة
للشعب اولها بتعطي
مفعول قوي وبتروح
القحة تعال/ي بعد كم
يوم بتلاقي القحة
رجعت رغم انك ماخذ
العلاج فصار
tolerance

IDIOSYNCRASY

It is **abnormal reaction to a drug due to genetic abnormality.** →

خلت ردت
الفعل
وختلقة
عن أي
حدثاتي

Example :-

مثال مهم أكثر عن الثاني

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

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

4. Succinylcholine Apnea

- Pseudocholine esterase enzyme is responsible for breakdown of neuromuscular blocker (succinylcholine). In genetic defect of the enzyme, **Succinylcholine** → respiratory muscle paralysis with apnea.

From Lec 12

Can succinylcholine cause apnea?

Suxamethonium (succinylcholine) apnoea occurs when a patient has been given the muscle relaxant suxamethonium, but does not have the enzymes to metabolise it. Thus they remain paralysed for an increased length of time and cannot breathe adequately at the end of an

Unpredictable

DRUG ALLERGY

rare

It is abnormal reaction to a drug due to antigen-ab 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

Occurs on reexposure

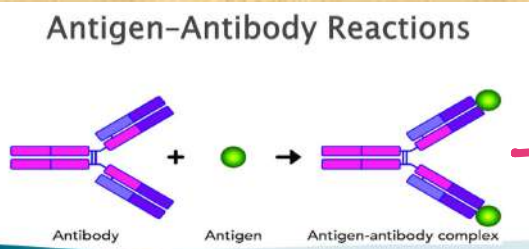
أنا يشوف رد الفعل العيان
عابشوف الغناقة الي حاملة جوا الجسم *

مفروض
نعمل
اختبار
حسابية
قبل كل ابرة

E.g. penicillin → 1st time → stimulate antibody → Ag-
Ab reaction → allergy

الكرة او فتلا واحد بياخذ ابرة البنسلين فتعود عليك كل فترة
ومهل ٣ ابرة عند ابرة (٣١) صبار مع ردت الفعل هاي

Chief organ: Skin, respiratory tract, GIT, Blood & blood vessels



release of (histamine) فتلا

لأنها rare جداً

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.

✨ اقرأوها مش تطنشوها ✨

+الدكتورة ما قرأتهم 🤗🤗🤗



• Grading system for hypersensitivity reactions

• 1-Mild



حکمت تلعت تـصرف

- Cutaneous and subcutaneous only
- Generalized erythema, periorbital edema, urticaria.

• 2-Moderate

- Cardiovascular, respiratory, or gastrointestinal involvement
- Dyspnea, stridor, wheeze, nausea, vomiting, dizziness, diaphoresis, chest or throat tightness, or abdominal pain

• 3-Severe



يا تلعتو
يا ما تلعتوش

- 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:

حصّة الكريم على الوجه
وبعد ما تعرّفت للشمس
→

A) Photo-toxic :- (T-S)

Drug or its metabolite **Accumulates** in the skin, absorbs light and undergoes a **Photochemical** reaction followed by **Photobiological** reaction resulting in Tissue damage (sunburn-like), i.e. erythema, edema, blistering, hyper pigmentation, desquamation.



(B)

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

الدكتورة ما قرأت
شرح الزقطة وحكت "هتتعرّفوها"

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



DRUG DEPENDENCE

الادمان شكل من اشكاله →

Use of drugs for personal satisfaction

- ①
- ② Psychological dependence

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.**

بسرھاي

Drugs producing physical dependence are (opioids,) barbiturates and other depressants including alcohol and benzodiazepines



2

• **Drug abuse :** →

يمكن تحمل
addiction ويمكن
لا
يعني عاري حاجة
يمكن أوقفها

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

3

Drug addiction

الاستخدام القهري للدوا
لأنه الدوا عسيطر على جسكو

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

أول اولوياته



4

2

Drug habituation (Psychological dependence)

حادثة (تعودن)

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

← انت ارتبته فيها ارتباط نفسي



ادوية تسبب تشوهات
في الجنين.

TERATOGENICITY (Teratos- Monster)

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

Drugs can affect the foetus at 3 stages-

فترة قبل ال

الاسبوعين



يعني يا باشا تو مبتكل كعمل
يا عا باشا

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

(ii) Organogenesis-**18 to 55 days**(3-12 weeks) of gestation
most vulnerable period, deformities are produced. → أكثر فترة خطر

(iii) Growth and development-56 days(12-38 weeks) onwards
developmental and functional abnormalities → الخطر موجود لسا ناخذ بالنا

can occur, e.g. ~~ACE inhibitors~~, Thalidomide, Warfarin,
~~Barbiturates~~,.....

لاشو لسا في

organ بتتكون



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

وفناد
حيوي

بتعمل

إلي بالاسنر هون و ال slide آحت
هو إلي قرأتو



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.....



← بتدي الدواء وانت عارف
انو بي عمل ضرر عدين

DRUG INDUCED DISEASES

- 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
- **(Retinal damage by chloroquine)**

جب ستو عمل ؟
بري احاول ارتجيبها
بأي طريقة



INDIVIDUAL VARIATION IN RESPONSE TO DRUG

- A) Alteration in concentration of drug that reaches the receptors
- B) 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



✦✦ حفلة الدكتور

اخر ايدي ← الامثلة والتعاريف تدعفا

THANKS

