

High Yield

Adverse drug reactions

- Harmful unwanted drug reactions
- Which is
 - _ Due to a drug
 - _ At normal therapeutic doses
 - _ May requires treatment , decrease in dose , stop the drug or caution in the future use of the same drug .

Adverse drug reactions develop: Immediately, prolonged drug administration or after drug withdrawal

Incidence of ADR more in:

- Polypharmacy, Elderly, Children, Patient with multiple diseases, Pregnancy, Malnourished, Immunosuppression, Drug Abusers and addicts

Note

An effect may be therapeutic in one context but side effect in another context

Examples:

- 1) H1 Anti-histamines: Sedation
- 2) Aspirin: antithrombotic effect

Side effects

- Unwanted (at time of treatment) unavoidable Pharmacological effects of the drug.
- They can be harmful or beneficial depending on time of use
- Occur at therapeutic doses.
- Predictable

CLASSIFICATIONS OF ADR

Predictable

Type A- Augmented

- These are based on the pharmacological actions of the drug so can be predicted.
 - They are common and account for 75% of ADRs
 - Dose-related and preventable mostly reversible.
- Examples:-
- Anticoagulants(e.g., warfarin, heparin)-bleeding
 - Anti-hypertensives(e.g. a1-antagonists: prazosin)-hypotension
 - Anti-diabetics(e.g. insulin)-hypoglycemia

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

Type D - Delayed

Predictable

Un-predictable

Type B- Bizarre

- Have no direct relationship to the dose of the drug or the pharmacological actions of the drug.
- Develop on the basis of:
 - Immunological reaction to the drug (Allergy)
 - Genetic predisposition (Idiosyncrasy): abnormal drug reactions to the usual dose of the drug.
- More serious clinical outcomes with higher mortality and morbidity.
- Mostly require immediate withdrawal of the drug.
- Uncommon

- Drug withdrawal syndromes and rebound phenomenons

Example:

- Sudden withdrawal of long term therapy with B-blockers can induce rebound tachycardia and hypertension

Type E - End Of Use

Predictable

Predictable

TYPE C - CHRONIC (CONTINUOUS) USE

- They are mostly associated with cumulative-long term exposure
- Example:-
- Analgesic (NSAID: aspirin)- interstitial nephritis, papillary sclerosis

- Failure of responsiveness to the usual dose of a drug
- Types: 1- ACQUIRED 2- CONGENITAL: atropine can not cause mydriasis in rabbits due to atropinse
 - Acquired tolerance:
 - It occurs on repeated administration of the drug.
 - More doses are needed to obtain the original effect.
 - It is reversible: it disappears when the drug is stopped for some time.

- Examples of drugs causing tolerance: morphine, nitrates.

Type F- FAILURE OF RESPONSE (TOLERANCE)

Un-predictable

Information to type D (Delayed):



TERATOGENICITY (Teratos- Monster)

- The ability of a drug to cause defects in a developing fetus when it is administered during pregnancy.
- Drugs can affect the foetus at 3 stages:
 - 1- Fertilization and implantation: conception to 17 days: failure of pregnancy which often goes unnoticed.
 - 2- Organogenesis: 18 to 55 days of gestation most vulnerable period, deformities are produced.
 - 3- Growth and development: 56 days onwards: developmental and functional abnormalities can occur

Examples:
ACE inhibitors(growth retardation) , Thalidomide, Warfarin (eye and hand defects), antiepileptic drugs (cleft lip/palate).

Mutagenicity And Carcinogenicity

- Drugs that can Cause genetic defects and cancer respectively.
- Mutagenicity: Reactive intermediate metabolites of the drug can affect genes and may cause structural changes in the chromosomes
- Carcinogenicity: Certain chemicals and drugs can promote malignant change in genetically damaged cells, resulting in carcinogenesis.
- Examples: anticancer drugs, radioisotopes, oestrogens, tobacco

Information to type F (Failure of response) (Tolerance):

Special types of acquired tolerance

1. Tachyphylaxis: Tachyphylaxis (Greek word, tachys, "rapid", and phylaxis "protection")
 - Acute, sudden decrease in response to a drug after its administration (a rapid and short-term onset of drug tolerance).
 - It can occur after an initial dose or after a series of small doses.
 - The original effect can not be obtained by increasing the dose.

- Example: tachyphylaxis to action of salbutamol (beta 2 agonist bronchodilator) used for treatment of bronchial asthma
- single-use bronchodilator response followed by a significant decline in bronchodilator response
- Mechanism: polymorphism of beta 2 receptors leading to receptor downregulation

Tolerance, There is not a biochemical, histological marker, or laboratory test that will predict tolerance or degree of tolerance in an individual.

Drug abuse

- **Tolerance is the basis of drug abuse and addiction: When a person uses a drug repeatedly, the body may develop tolerance to the drug.**
- **Tolerance may lead to drug dependence—the body develops a chemical need for the drug and can't function normally without it.**
- **Drug abuse occurs when people intentionally use any kind of drugs for non-medical purposes.**
- **A mood-altering drug, also called a psychoactive drug, is a chemical that affects brain activity (morphine, cocaine, methamphetamine).**
 - Most abused drugs are psychoactive.
- **Drug abuse (psychoactive drugs) > tolerance > dependence > addiction**

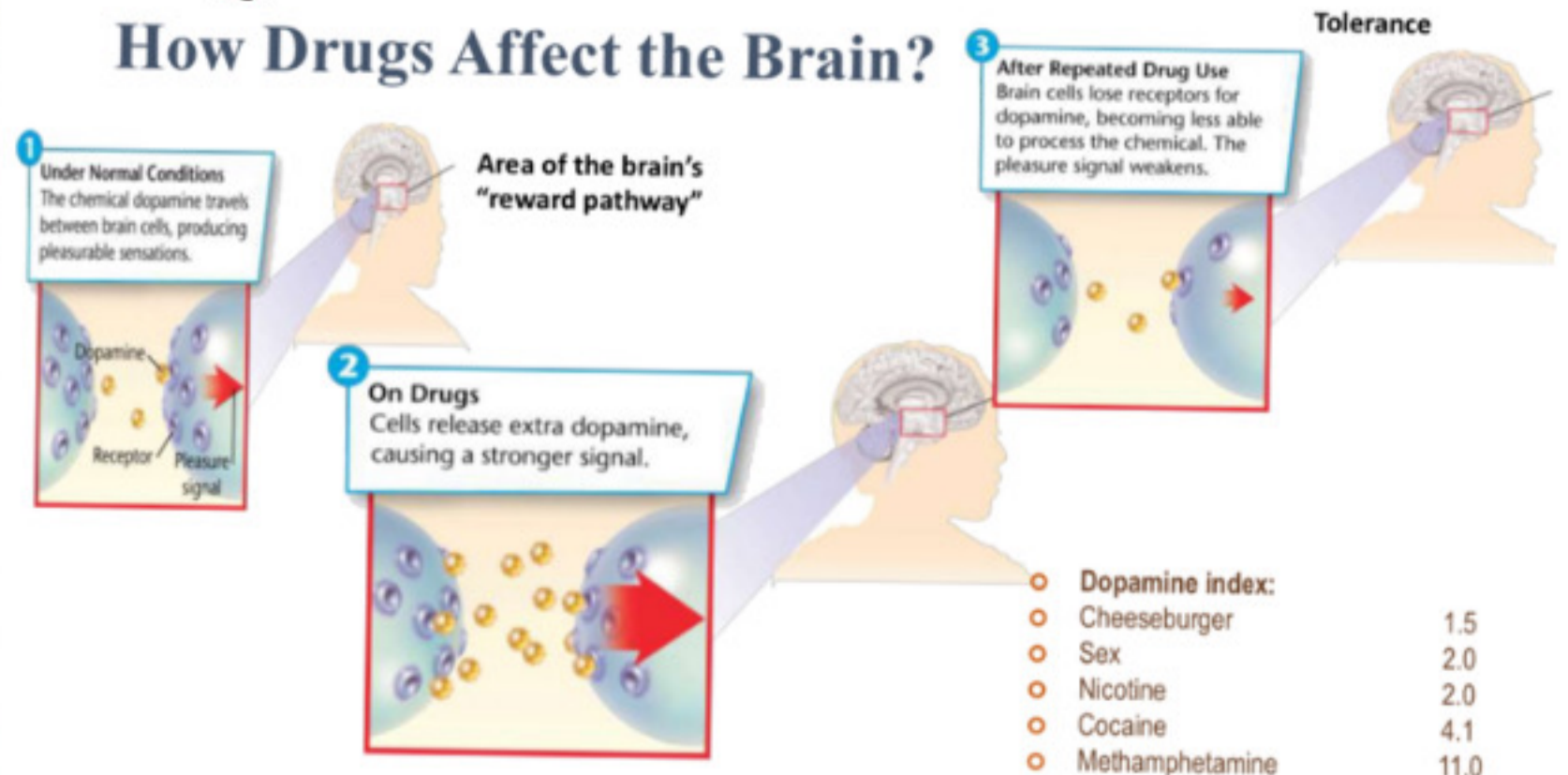
The Reward (system) Pathway

- **Many psychoactive drugs trigger activity along a pathway of cells in the brain called the "reward pathway."**
- **Brain cells along the activated reward pathway release a chemical called dopamine.**
- **The extra dopamine released during drug use can cause the user to ignore the harmful effects of the drug and want to continue using it.**
- **Flooding the reward pathway with dopamine may lead to intense cravings for the drug.**

Addiction

- **Abuse of psychoactive drugs may result in addiction.**
- **Addiction is the compulsive use of a drug, despite any cost to health, family, or social standing.**
- **Addiction is a disease that changes the structure and chemistry of the brain.**
- **Withdrawal symptoms: If a person who is dependent on a psychoactive drug stops taking the drug, that person will experience withdrawal symptoms including:**
- **Nausea, vomiting, headache, indigestion, paranoia or panic**
- **Tremors, seizures or death**

How Drugs Affect the Brain?



DRUG-INDUCED DISEASES

• These are also called iatrogenic (physician-induced) diseases, and are disease caused by drugs .

• Examples:

- Hepatitis induced by isoniazid and Rifampicin
- Peptic ulcer induced by salicylates and corticosteroids
- Ototoxicity of streptomycin



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وقت المذاكرة لله،
وتأكد أن الله لا يضيعُ تعبك.

PHARMACOVIGILANCE (DAUP)

- The science and activities related to the detection, assessment, understanding and prevention of adverse reactions
- The information generated is useful in educating doctors and in the official regulation of drug use.
- Significance:
 - 1- Rational use of medicines
 - 2- Assessment of safety of medicines



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PREVENTION OF ADVERSE EFFECTS TO DRUGS

- Avoid inappropriate use of drugs .
- Appropriate drug administration (Rational Therapeutics)
- Dose
- Dosage form
- Duration
- Route
- Frequency
- Technique
- 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.

Various activities involved in pharmacovigilance

- Post marketing surveillance and other methods of ADR monitoring such as voluntary reporting by doctors.
- Dissemination of ADR data through 'drug alerts', 'medical letters,' sent to doctors by pharmaceuticals and regulatory agencies.
- Changes in the labelling of medicines indicating restrictions in use or warnings, precautions, or even withdrawal of the drug.