

- **RF declines with age even in healthy individuals in the absence of renal disease**
- **Both serum creat and CL_{creat} may be used as indicators of impaired RF in the elderly**
- **Serum creat alone not accurate in the elderly:**
 - **↓ lean body mass → lower creatinine production**
 - **↓ glomerular filtration rate**
- **Serum creatinine stays in normal range, masking change in creatinine clearance**

Type A (augmented)	Type B (bizarre)
• Due to extension of pharmacological action	• Immunological/ genetic basis
• Predictable	• Mostly not predictable
• Quantitative (dose dependent)	• Qualitative (dose dependent)
• High incidence but low mortality	• Low incidence but high mortality
• Dose reduction is needed	• Drugs has to be discontinued
• Examples: dryness of mouth & blurring of vision due to atropine; hypoglycemia with glibenclamide	• Anaphylactic reaction due to penicillin G; hemolysis with primaquine

Secondary Effects

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- Examples:
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Toxic Effects

- Result from excessive pharmacological action of the drug due to over dosage (absolute/relative) or prolonged use.
- Manifestations are predictable & dose related

Intolerance

- It is the appearance of characteristic toxic effects of a drug in an individual at therapeutic doses.
- Indicates low threshold of the individual to the action of the drug
 - Chloroquine - Vomiting & abdominal pain
 - Triflupromazine - Muscular dystonias
 - Carbamazepine - Ataxia

Idiosyncrasy

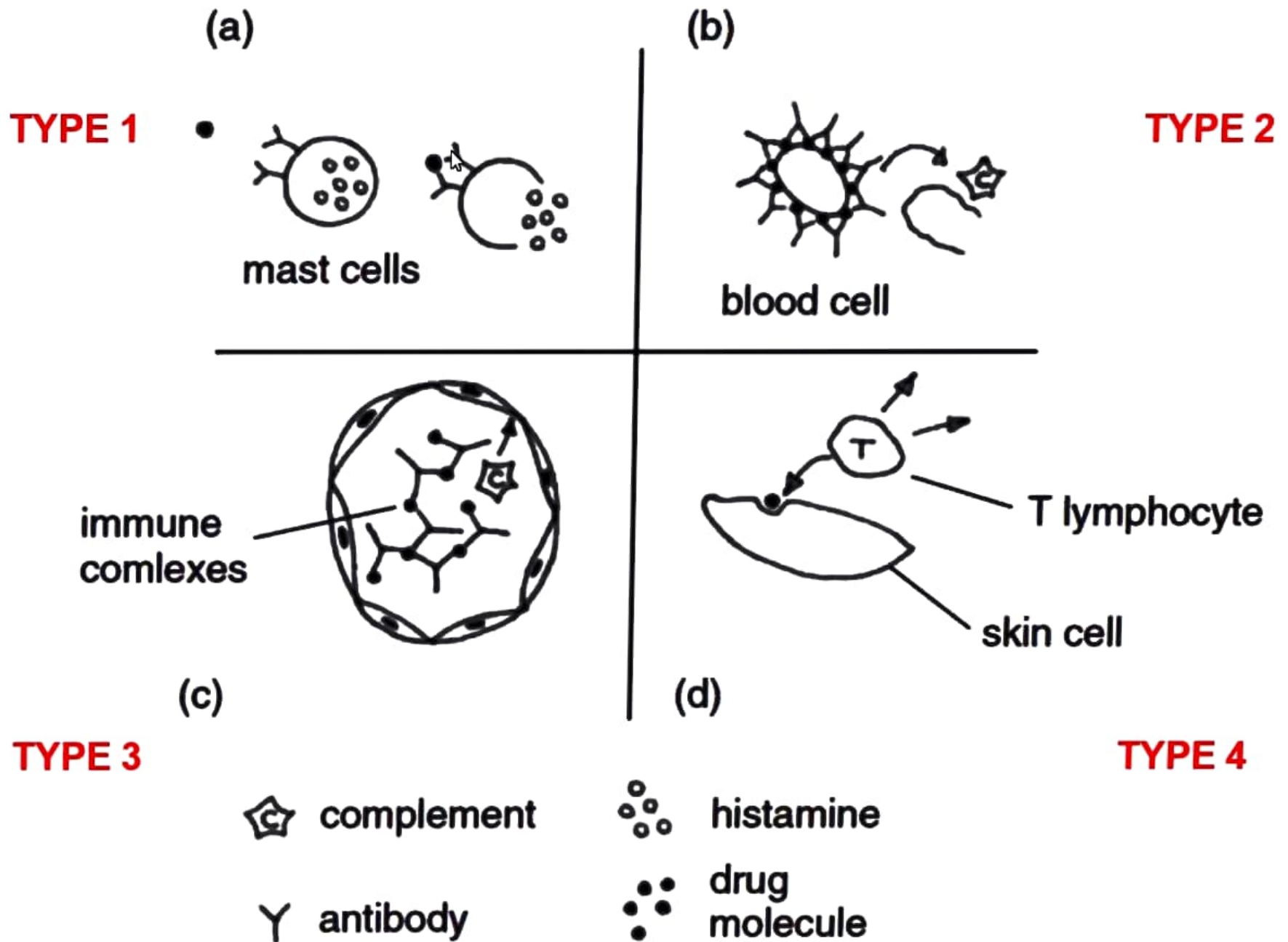
- Genetically determined abnormal reaction to a chemical
- Total absence or reduced activity of some enzyme
 - G6PD deficiency – primaquine, salicylates, sulfonamides leads to hemolysis
- Other examples:
 - Barbiturates - excitement & mental confusion
 - Chloramphenicol - aplastic anemia

Drug Allergy – Hypersensitivity Reactions

- Immunologically mediated reaction producing symptoms which are unrelated to the pharmacodynamic profile of the drug

Types of Hypersensitivity Reactions

- Type 1: IG_E mediated - Anaphylactic reactions
- Type 2: Complement mediated (cytolytic reactions)
- Type 3: Immune Complex mediated (arthus reaction)
- Type 4: Delayed hypersensitivity reaction



Drug Dependence

- Drugs for personal satisfaction is accorded a higher priority than other basic needs, often in the face of known risks to health.
 - Psychological reinforcement
 - Physical dependence
 - Drug abuse, addiction & habituation

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Drug Dependence

- Psychological dependence – Individual believes that optimal state of well being is achieved only through action of drug
 - Emotionally distressed if drug is not taken – compulsive drug use

Drug Dependence

- Physical dependence – altered physiological state produced by repeated administration of a drug, necessitates continuous presence of drug to maintain physiological equilibrium
 - Discontinuation of drug leads to withdrawal symptoms

Mutagenicity and Carcinogenicity

- Drug cause genetic defects and cancer respectively.
- Oxidation of drug produce reactive intermediates which affect genes and cause structural changes in chromosomes, inducing mutations.

Teratogenecity

- Fetal abnormalities when given to pregnant mothers
- Affect fetus at 3 stages:
 - Fertilization & implantation (conception to 17days) – failure
 - Organogenesis (18 to 55 days) – most vulnerable (deformities)
 - Growth & development (56 days onwards) – developmental & functional abnormalities.

Thalidomide

Phocomelia, heart defects, gut atresia

Warfarin

Saddle nose, retarded growth, defects of limbs, eyes and CNS

Corticosteroids

Cleft palate and congenital cataract

Androgens

Masculinisation in female

Oestrogens

Testicular atrophy in males

Ethanol

Fetal alcohol syndrome

Valproate

Neural tube defects

Phenytoin

Cleft lip/palate, microcephaly, mental retardation

Aminoglycosides

Deafness

B No evidence of risk in humans	Adequate human studies are lacking, but animal studies have failed to demonstrate a risk to the fetus	Penicillin, amoxicillin, erythromycin, paracetamol
C Risk cannot be ruled out	No adequate studies in preg women, & animal studies are lacking or have shown an adverse effect on fetus, but potential benefit may warrant use of drug in preg women despite potential risk	Morphine, atropine, corticosteroids, thiopentone, bupivacaine
D Benefit may outweigh potential risk	There is evidence of human fetal risk, but the potential benefits from use of drug may be acceptable despite the potential risk	Aspirin, phenytoin, carbamazepine, valproate, lorazepam
X Contraindicated	Studies in humans or animals have demonstrated fetal abnormalities, and potential risk outweighs possible benefit	Estrogens, isotretinoin, ergometrine

Pharmacovigilance

- “Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems.”
- Usefulness:
 - Educate doctors
 - Official regulation of drug use
 - Reduction in drug-related harm to patients
 - Rationale use of medicines.



Activities involved in Pharmacovigilance

- Post marketing surveillance & other methods of ADR monitoring
- Dissemination of ADR data – drug alerts, medical letters, advisories
- Changes in labelling of medications

Prevention of Adverse Drug Reactions

- Avoid inappropriate use of drugs
- Use appropriate dose, route & frequency of drug administration
- Previous history of drug interactions, allergic diseases
- Rule out drug interactions
- Adopt correct administration technique
- Carry out appropriate laboratory monitoring