

Adverse Drug Reactions

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Adverse Drug Reaction

A response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function

WHO, 1972

Adverse drug reactions



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graph TD; A[Adverse drug reactions] --> B[Type A (80%)]; A --> C[Type B (20%)]; B --> D[On target]; B --> E[Off target]; C --> F[Immunologic]; C --> G[Non-immunologic];
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The diagram is a hierarchical flowchart on a dark blue background. At the top is a white box with a gradient containing the text 'Adverse drug reactions'. A vertical line descends from this box and splits into two horizontal lines. The left horizontal line leads to a white box with a gradient containing 'Type A (80%)', which is highlighted with a red border. The right horizontal line leads to a white box with a gradient containing 'Type B (20%)'. From the 'Type A' box, a vertical line descends and splits into two horizontal lines leading to 'On target' and 'Off target'. From the 'Type B' box, a vertical line descends and splits into two horizontal lines leading to 'Immunologic' and 'Non-immunologic'. All boxes have a white-to-gray gradient and a slight shadow.

Type A
(80%)

On target

Off target

Type B
(20%)

Immunologic

Non-immunologic

Adverse drug reactions

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Type A
(80%)

Type B
(20%)

On target

Off target

Immunologic

Non-immunologic

Case History 1

80 y/o

Hypertension

Hypercholesterolaemia

Stroke

Carotid endarterectomy

Total hip replacement

Osteopaenia

BP 160/80

- **Bisoprolol 5mg**
- **Lercanidipine 10mg**
- **Ramipril 10mg**
- Galfer
- Duphalac
- Atorvastatin 40mg
- Lansoprazole 15mg
- Aspirin 75mg
- Calcichew
- Paracetamol prn
- **Doxasocin XL 4mg added**

Case History 2

50 y/o

Lung Cancer

Crizotinib

Domperidone added

VFib cardiac arrest in the main concourse of the hospital

Factors increasing the likelihood of type-A ADRS

- Age
- Disease states eg liver function, renal function
- Polypharmacy/multi morbidity

Adverse drug reactions



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Type A
(80%)

Type B
(20%)

On target

Off target

Immunologic

Non-immunologic

Immunologic

Type I reaction (IgE-mediated)

Anaphylaxis from β -lactam antibiotic

Type II reaction (cytotoxic)

Hemolytic anemia from penicillin

Type III reaction (immune complex)

Serum sickness from anti-thymocyte globulin

Type IV reaction (delayed, cell-mediated)

Contact dermatitis from topical antihistamine

Specific T-cell activation

Morbilliform rash from sulfonamides

Fas/Fas ligand-induced apoptosis

Stevens-Johnson syndrome

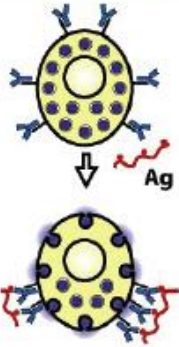
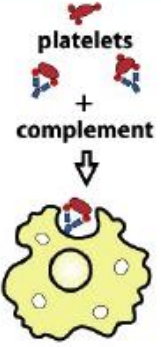
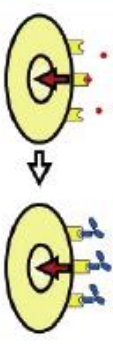
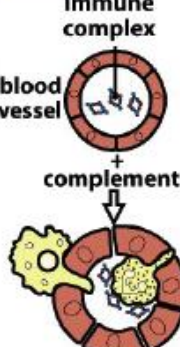
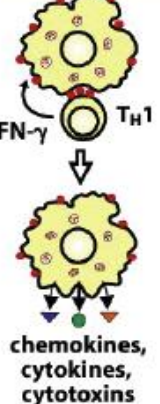
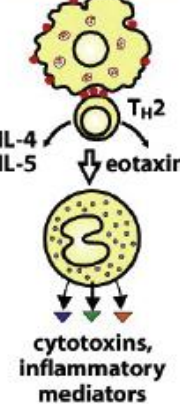

Toxic epidermal necrolysis

Other

Drug-induced, lupus-like syndrome

Anticonvulsant hypersensitivity syndrome

Immunologic

	Type I	Type II		Type III	Type IV		
Immune reactant	IgE	IgG		IgG	T _H 1 cells	T _H 2 cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, FcR ⁺ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, phagocytes	Macrophage activation	IgE production, eosinophil activation, mastocytosis	Cytotoxicity
							

Non-Immunologic

Pseudoallergic

Anaphylactoid reaction after radiocontrast media

Idiosyncratic

Hemolytic anemia in a patient with G6PD deficiency after primaquine therapy

Intolerance

Tinnitus after a single, small dose of aspirin

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Type A
(80%)

On target

Off target

Type B
(20%)

Immunologic

Non-immunologic



- 85 y/o
- Hypertension
- ACEi
- Thiazide
- Gout
- NSAID
- Vomiting



Multiple hits on renal function:

- Age
- Depleted volume status 2° to diuretic
- Decreased glomerular pressure 2° to ACEi (efferent arteriole)
- Further decrease in glomerular pressure 2° to NSAID
- Volume loss compounded by vomiting



- Inpatient stay for ARF & delirium
- Fall during night
- Hip Fracture
- RIP

Summary

- All drugs can cause ADRs to a greater or lesser extent.
- Knowledge of the mode of action of drugs integrated with an understanding of physiology in health and disease is necessary to maximise safe prescribing
- Individual patient factors must always be taken in to account to minimise the risk of prescribing drugs

References

- Riedl MA, Casillas AM, *Adverse drug reactions: types and treatment options*, Am Fam Physician, 2003 Nov 1;68(9):1781-90.
- Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology, *Drug allergy: an updated practice parameter*, Ann Allergy Asthma Immunol, 2010 Oct;105(4):259-273.
- Pirmohamed M, Park BK, *Adverse drug reactions: back to the future* Br J Clin Pharmacol, 2003 May;55(5):486-92.