

# Diagnosis and management of adverse drug reactions

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# Adverse drug reactions 1 (ADRs)

## Definition

- An ADR is '*a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man*'.

# Adverse drug reactions 2 (ADRs)

## Side effect

*A side effect is 'any unintended effect of a pharmaceutical product occurring at doses normally used by a patient which is related to the pharmacological properties of the drug'.*

- eg constipation with codeine phosphate

# Adverse drug reactions 3 (ADRs)

## Adverse event (experience)

- An AE is *‘any untoward medical occurrence that may present during treatment with a medicine, but which does not necessarily have a causal relationship with this treatment’*.

# The monitoring problem

How do we know if a health event is a reaction to a medicine?

Headache

Fever

Vomiting

Rash

# The process of diagnosis 1

Consider all drugs / medicines

- OTC
- contraceptives
- herbal / traditional
- abused drugs / alcohol
- long term treatment

Check

# The process of diagnosis 2

- Was the event present before the patient began the medicine?
- Did the event occur within a plausible time period of starting the medicine?
  - headache a few hours after - *Yes*
  - liver failure on the first day - *No*

# The process of diagnosis 3

- Allergic type - *previous exposure*
- Foetal abnormality - *stage of pregnancy*
- Consider withdrawal reactions
- Neoplasms - *several years*
- Background frequency
  - agranulocytosis
  - exfoliative dermatitis



# The process of diagnosis 4

Is an event pharmacologically plausible?

- Is it a side effect (class A reaction) of -
  - the drug(s) in question
  - the class?
- Is it a known allergic (class B) reaction
  - the drug(s)
  - the class?

# The process of diagnosis 5

- Trial withdrawal
  - is the time to recovery consistent with the action of the drug?
- Rechallenge
  - same pattern?
  - No effect?

# The process of diagnosis 6

## Investigations

- Blood patterns compared with baseline
- Allergy testing
- Skin biopsy
- Blood levels

# The process of diagnosis 7

- Is there the possibility of an *interaction*?
- Remember
  - OTCs
  - contraceptives
  - herbals / traditional
  - drugs of abuse / alcohol
  - long term medicines

# The process of diagnosis 8

## Interaction?

- OK on first drug
- Problems when a second drug is commenced
- Is it the 2nd drug or is it an interaction?
  - had the 2nd drug before?
  - OK when 1st drug withdrawn?
  - knowledge of metabolism

# The process of diagnosis 9

## Interactions and hepatic metabolism

- Cytochrome P450 enzyme system
  - eg CYP2D6 or CYP2C19
  - inhibition -*increased blood levels*
  - induction -*decreased blood levels*  
(therapeutic effect decreased)

# The process of diagnosis 10

## Interactions and hepatic metabolism

- Mefloquine metabolised by CYP3A4
  - artemesinin, diazepam, diltiazem, erythromycin, fluoxetine, nifedipine, quinine
- Artemesinin -CYP2B6 & CYP3A4

# The process of diagnosis 10

## Which drug?

- Timing of drug and reaction
- Difficult when more than one drug is introduced at the same time
- Pharmacology
- Withdrawal
- Rechallenge



# Management of ADRs 1

Decisions are made by considering

- Seriousness / severity of ADR
- Seriousness of disease
- Benefit / harm assessment

# Management of ADRs 2

If the reaction is serious

- Withdraw suspected (all?) drugs
- Treat urgently

# Management of ADRs 3

If the disease is serious

- Consider the effect of not having treatment
- Continue treatment and treat symptoms of reaction if necessary
- Consider an alternative drug
- Stop unnecessary drugs

# Management of ADRs 4

If the reaction is mild

- Continue treatment if necessary
- Stop unnecessary drugs
- Consider dose reduction
- Reassure and do nothing
- Symptomatic treatment if warranted

# Management of ADRs 5

