PHA3021: Drugs in Health and Disease – EXAM NOTES

*This unit provides an overview of the **use of drugs,** with an emphasis on the **principles underlying the safe and effective current use of drugs** for the maintenance of health and the **treatment of disease**.*

*The importance of **evidence-based drug therapy** is highlighted with an introduction to **statistical and epidemiological concepts**. The pharmacological properties of **drug classes** used to treat specific **respiratory, cardiovascular and gastrointestinal disorders** are studied, concentrating on the **rationale for their use**. **Pharmacological approaches to the study of existing and novel compounds will be reinforced in laboratory sessions.***

Theme 1: Principles of Therapeutics (POT)

This theme provides an introduction to the safe and effective use of drugs, with an emphasis on the design and interpretation of clinical trials and their importance in evidence-based medicine.

The key principle of selective toxicity and its relevance in therapeutics is also described, using antimicrobial therapy as an example.

Theme Learning Outcomes:

- Describe what evidence-based medicine is, and identify/explain different levels of evidence
- Gain an understanding of epidemiology including the differences between observational studies and clinical trials
- Understand the therapeutic principles underlying the safe and effective prescribing of drugs
- Describe the principles of selective toxicity, as well as the processes which can be targeted to achieve selective toxicity in antimicrobial chemotherapy

POT-1: Evidence-Based Medicine

Systematic review

Cochrane review – used to develop clinical guidlines

What is EBM?

- EBM is the integration of:
- Individual clinical expertise (knowledge of clinician)
- Best available exteranl clinical evidence from systematic research (evidence)
- Patients values and expectations, preferences
- Can be categorised into different types/levels of clinical evidence and can be ranked according to their strength of evidence.

The 5A's

Assess patient – what is the problem with patient?

Ask question – construct a clinical question derived from the case

Acquire evidence – gather evidence by searching from appropriate resource

Appraise evidence – decide whether evidence is valid (close to truth) and if its applicable to patient (useful)

Apply evidence – talk with patient, apply clinical expertise and listen to patients preferences.

What is not EBM

- EBM is the opposite of opinion-based medicine, which relies on memory and past experience of drug to treat something.
- EBM is not cook-book medicine: evidence needs extrapolation to patients unique biology and values
- EBM is expensive

4 levels of evidence

- Meta analysis: cochrane review of combined systematic review – strongest evidence becos analytical EBM
- Randomised control trial - strong
- Case series – weakest evidence becos descriptive EBM

Level 1: systematic reviews of multiple relavent RCT's, cochrane reviews (best)

Level 2: evidence from at least one RCT

- Randomised
- Controlled
- Blinded, double blinded
- Info of withdrawal and dropouts provided

Level 3: evidence from

- Non-randomised control trial, or
- Well designed cohort study, or
- Case-controlled study

Level 4: evidence from case series (weakest)

- Descriptive obervational study where looking for patients that have had the treatment or similar treatment.

- Examine their medical records for exposure to treatment and outcome.
- No control group – that's why it's a weak level of evidence.
- Do not test a hypothesis b/n treatment and outcome.
- May generate hypothesis for a clinical trial (levels 2,3): important.

Major issues involved in practise of EBM

- Positive results more likely to be published, don't report negative outcomes.
- Use only easily measurable surrogate parameters
- Narrow queation posed
- Hard to find answers to simple questions.

Surrogate vs clinial trials

- ***Surrogate***
- Measuring things that are not the final outcome. Eg of surrogate measures: blood pressure, cholesterol levels, and angina attacks.
- Biomarker associated w/ condition.
- Surrogate is an indirect measure.
- Indicator of benefit of a drug.
- ***Clinical***
- all or none response/outcome
- eg: surival rate, incidence of stroke, heart attack, mortality

Jadad score

- used to assess quality of a clinical trial according to several criteria
- score ranges from 0 (poor) to max of 5 (very good).
- ***Randomisation (max 2pt)***
- 1 point if study is described as randomised.
- 1 point if method of randomisation is specified (they have said the method of randomisation) and appropriate (eg: using a table of random numbers, computer generated allocation)
- If specified but NOT appropriate, deduct 1 pt (eg: allocated by birth date – not random).
- ***Double blinding (max 2pt)***
- 1 point if study is described as double blind
- 1 point for if method of blinding is appropriate (eg: identical placebo and treatment that can't be distinguished).
- If specified but NOT appropriate: deduct 1 pt.
- ***Withdrawals/dropouts mentioned (max 1pt)***

Forest plot

- Summary of multiple trials used for chochrane review.
- ***Horizontal bar*** = a trial – the more ppl in trial, the narrowe the CI (shorter line). 95% CI
- ***Vertical line*** = no difference
- Bar crosses vertical line – means no difference b/n treatment and control gp. Trial did not show significant effect of drug
- ***Diamond –*** summary of all trials, consolidating all evidence to help clinician make decision. If it crosses line -> there was no overall benefit.

Clinical trial

- Involves human subjects
- Drug/remedy tested against placebo and/or esisting treatment
- Outcome(s) may be surrogate (measured outcome) and/or clinical (endpoint)