Drug interactions

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- Drug interaction is the modification of the action of one drug by another. There are three kinds of mechanism:
- 1. pharmaceutical;
- 2. pharmacodynamic;
- 3. pharmacokinetic.

- Pharmaceutical interactions occur by chemical reaction or physical interaction when drugs are mixed.
- Pharmacodynamic interactions occur when different drugs each influence the same physiological function (e.g. drugs that influence state of alertness or blood pressure); the result of adding a second such drug during treatment with another may be to increase the effect of the first (e.g. alcohol increases sleepiness caused by benzodiazepines). Conversely, for drugs with opposing actions, the result may be to reduce the effect of the first (e.g. **indometacin increases blood pressure in hypertensive patients** treated with an antihypertensive drug such as **losartan).**
- Pharmacokinetic interactions occur when one drug affects the pharmocokinetics of another (e.g. by reducing its elimin-ation from the body or by inhibiting its metabolism).

Useful interaction

- Drugs can be used in combination to enhance their effectiveness. Disease is often caused by complex processes, and drugs that influence different components of the disease mechanism may have additive effects (e.g. an antiplatelet drug with a fibrinolytic in treating myocardial infarction. Other examples include the use of a β2 agonist with a glucocorticoid in the treatment of asthma (to cause bronchodilation and suppress inflammation, respectively. Combinations of antimicrobial drugs are used to prevent the selection of drug-resistant organisms. Tuberculosis is the best example of a disease whose successful treatment requires this approach. Drug resistance via synthesis of a microbial enzyme that degrades antibiotic (e.g. penicillinaseproducing staphylococci) can be countered by using a combination of the antibiotic with an inhibitor of the enzyme: **co-amoxiclav is a combination of clavulanic acid, an inhibitor** of penicillinase, with **amoxicillin.**
- Increased efficacy can result from pharmacokinetic interaction. **Imipenem is partly inactivated by a**dipeptidase in the kidney. This is overcome by administering **imipenem in combination with cilastin, a specific renal** dipeptidase inhibitor. Another example is the use of the combination of **ritonavir and saquinavir in antiretroviral therapy**. **Saquinavir increases the systemic bioavailability** of **ritonavir by inhibiting its degradation by gastrointestinal** CYP3A and inhibits its faecal elimination by blocking the P-glycoprotein that pumps it back into the intestinal lumen.

Useful interaction

- Some combinations of drugs have a more than additive effect (‘synergy’). Several antibacterial combinations are synergistic, including **sulfamethoxazole with trimethoprim (co-trimoxazole), used in the treatment of *Pneumocystis*** *carinii. Several drugs used in cancer chemotherapy* are also synergistic, e.g. **cisplatin plus paclitaxel**.
- Therapeutic effects of drugs are often limited by the activation of a physiological control loop, particularly in the case of cardiovascular drugs. The use of a low dose of a second drug that interrupts this negative feedback may therefore enhance effectiveness substantially. Examples include the combination of an angiotensin converting enzyme inhibitor (to block the renin-angiotensin system) with a diuretic (the effect of which is limited by activation of the renin-angiotensin system) in treating hypertension.