

Drug Interactions

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Introduction to Drug Interactions I

Drug interactions occur whenever the effect of a drug is modified by the presence of another agent.

Modifying agents: drugs, diet, smoking, drinking, etc.

Most drug interactions involve changes in the absorption, distribution, metabolism and excretion of drugs.

Introduction to Drug Interactions II

Drug interactions are common in the elderly due to age-associated changes in pharmacokinetics, pharmacodynamics and high use of prescription drugs.

Drug interactions rank at least 6th among U.S. causes of death.

Terminology of Drug Interactions

Drug	Response	
A	5	
B	5	
A + B	10	[Summation]
A + B	50	[Synergism]
A + B	2	[Antagonism]

Drug Antagonism

Physiologic :	Alcohol	+	Caffeine
Biochemical :	Phenobarbital	+	Cimetidine
Chemical:	Cholestyramine	+	Dicumarol
Pharmacological :	Acetylcholine	+	Atropine

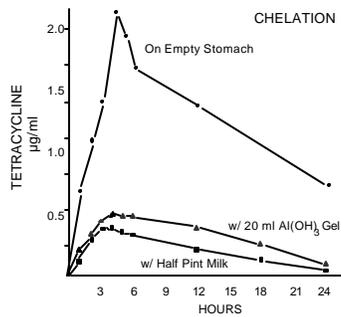
Drug Absorption Interactions I

Chelation is the interaction of metals (Mg²⁺, Ca²⁺, Fe²⁺, Al³⁺, Zn²⁺, etc.) with drugs.

EDTA chelates toxic metals such as lead and reduces toxicity.

Tetracyclines and Quinolones chelate metals and form an insoluble complex that reduces their absorption.

Tetracycline Interaction



Drug Absorption Interactions II

Adsorption is the nonspecific binding of a drug to another agent.

Cholestyramine adsorbs many drugs such as dicumarol, methotrexate and digitoxin and decreases their absorption.

Antacids decrease digoxin and iron absorption by adsorption.

Drug Absorption Interactions III

pH changes can alter the absorption of drugs.

Antacids (increased pH) will decrease the absorption of weak acids and increase the absorption of weak bases.

Infections (decreased pH) will increase the absorption of weak acids and decrease the absorption of weak bases.

Drug Absorption Interactions IV

Gastric emptying time (GET) is the time required to empty the stomach.

GET is increased by food and morphine (reduced absorption).

GET is decreased by fasting and antacids (increased absorption).

Drug Absorption Interactions V

Intestinal peristalsis regulates the passage of drugs through the intestine.

Laxatives will cause drugs to move through the intestine so rapidly that they are poorly absorbed.

Drug Absorption Interactions VI

Increases in blood flow will increase drug absorption whereas a decrease in blood flow will decrease drug absorption.

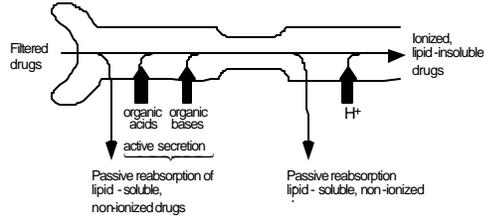
Epinephrine reduces blood flow and is used in combination with local anesthetics [lidocaine and procaine] to decrease their absorption into the blood (rapidly hydrolyzed) and to prolong their duration of action.

Drug Excretion Interactions I

Reabsorption of drugs

Bases: antihistamines and amphetamines increased by sodium bicarbonate and decreased by ammonium chloride.

Acids: aspirin and phenobarbital increased by ammonium chloride and decreased by sodium bicarbonate.

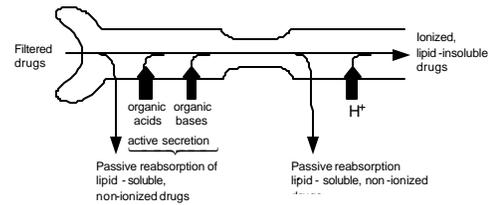


Drug Excretion Interactions II

Acid Secretion: Penicillin, methotrexate, salicylates, probenecid

Base Secretion: acetylcholine, histamine, morphine, atropine

Competition within groups for carriers.



Drug Metabolism Interactions I

Inhibition of drug metabolism occurs rapidly.

The $t_{1/2}$ of drugs increase.

Drug clearance decreases.

Drug dose must be decreased.

Drug Metabolism Interactions II

Chronic alcohol intake induces drug metabolism.

Acute alcohol intake inhibits drug metabolism.

Disulfiram is an effective deterrent to alcohol consumption

since this agent increases acetaldehyde levels (toxic) by

inhibiting acetaldehyde dehydrogenase.

Drug Metabolism Interactions III

Pargyline inhibits monoamine oxidase.

Amphetamine, ephedrine, etc. levels increase.

Levels of tyramine from foods also increase.

These agents produce hypertension.

Drug Metabolism Interactions IV

Imipramine inhibits the clearance of epinephrine.

Local anesthetics containing epinephrine can markedly increase blood pressure.

Patients have died in dentist office.

Drug Metabolism Interactions V

A number of drugs inhibit drug metabolism.
 Chloramphenicol, Cimetidine, Allopurinol & Disulfiram
 are a few of the inhibitors of drug metabolism.
 The inhibition of metabolism occurs rapidly.
 Reduce drug dose because drug levels will increase.

Drug Metabolism Interactions VI

Induction of drug metabolism is slow.
 Drug clearance is increased.
 The $t_{1/2}$ of drugs is decreased.
 The dose of drugs must be increased.

Drug Metabolism Interactions VII

A number of drugs induce drug metabolism.
 Phenobarbital, Rifampin, and Phenytoin are a few
 of the drugs that induce drug metabolism.
 Smoking and chronic alcohol intake induce metabolism.
 There is only one induction period (increase drug dose).
 Drug metabolism levels return to normal when inducer
 is not present.

Drug Distribution Interactions

Albumin binds various drugs.
 Free drug is active.
 Highly bound drugs (>90%) can be displaced.
 Highly bound agents: bilirubin [kernicterus], dicumarol
 [anticoagulant], tolbutamide (reduces blood sugar).
 Displacing agents: aspirin, sulfonamides and phenylbutazone.

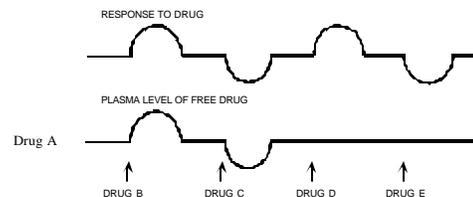
Receptor Interactions

Agonist	Antagonist	Action
Acetylcholine	Atropine	Salivation
Norepinephrine	Prazosin	Capillary
Isoproterenol	Propranolol	Heart
Phenobarbital	Amphetamine	Brain

Combinations of CNS depressants (PB, alcohol & antihistamines)
 cause potentiation of CNS depression.

Drug Interaction Problem I

Drug A is given iv (no absorption problems)
 Drug A is: a weak acid, highly protein bound, metabolized
 by the liver and secreted by the kidney. All other drugs are
 administered at the indicated arrows.



Drug Interaction Problem II

Drug B : inhibit metabolism, protein displacement, block secretion increase reabsorption. **Drug C**:decrease reabsorption. **D**: potentiation. **E**: antagonism.

