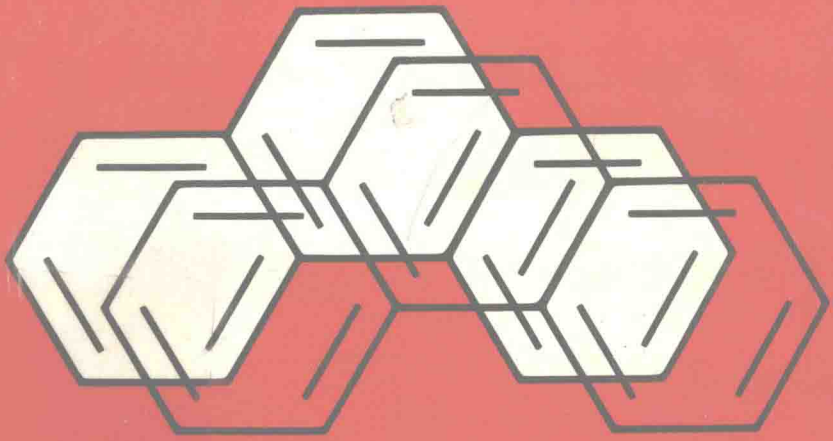
ELEVENTH EDITION

CLINICAL PHARMACOLOGY FOR NURSES

J. R. TROUNCE



Churchill Livingstone

Clinical Pharmacology for Nurses

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Clinical Pharmacology for Nurses

Preface to the eleventh edition

The ever changing practice in the use of drugs has made necessary an extensive revision for the present edition.

Drug dependence has been given a separate chapter and the rest of the text updated. A number of sections have been added and others have been rewritten with new tables and illustrations. Drugs which are no longer important have been eliminated.

We hope this book presents the nurse with a modern account of drugs in current use together with an appropriate amount of basic pharmacology, some indication of how the drugs are used in treating disease and sections on various practical problems.

We would like to thank all those members of the nursing profession and others who have helped with criticism and suggestions and have modified the content accordingly.

Finally, we would like to thank the staff of Churchill Livingstone for their unfailing help.

London, 1985 J.R.T.

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Introduction

Pharmacology may be defined as the study of drugs. This includes their origin, chemical structure, preparation, administration, actions, metabolism and excretion. The application of the action of drugs and other measures in the treatment of disease is called therapeutics.

Drugs have been used in treating disease for thousands of years. The writings of most of the ancient civilizations contain directions for the preparation and administration of drugs. Nearly all the remedies described had little if any effect but it is of interest that among the bizarre prescriptions containing such ingredients as fat of the hippopotamus and pig bile, can be found drugs which are still used today. The ancient Egyptians were familiar with the purging effect of castor oil, the Arabians used both opium and senna, and in more recent times the effects of digitalis on oedema were known to country people with no medical training. Nevertheless, the use of drugs in the treatment of disease remained entirely empirical and usually misdirected until the nineteenth century. This period saw the emergence of rational physiology and pathology and on this foundation it was possible to study the effect of drugs and their use in disease.

At first, investigation was confined to observation of the effect on the whole animal or human patient. With the rise of experimental physiology it became possible to investigate the action of drugs on isolated organs and thus obtain a much clearer picture of their effects and potential uses as therapeutic agents.

Such investigation has brought into use such useful drugs as adrenaline and ergometrine.

While this work was progressing the chemical structure of many drugs was being unravelled and it thus proved practicable to relate the function of drugs to their chemical composition. This was an important advance for it meant that by altering slightly the structure of a drug it might be possible to enhance its useful action and get rid of any troublesome side-effects. This led to the introduction of many synthetic substances which have proved invaluable in the treatment of disease.

Although extensive experiments in animals led to many useful advances, it is now realised that there are important differences between the pharmacology of drugs in animals and man. Even in the relatively early stages of introducing a new drug investigation of its action requires studies in humans. This has led to the emergence of *clinical pharmacology* which is essentially the study of drug action in man.

At the present time the frontiers of pharmacology are still being extended, and much work is now concerned with the actual effect of the drug on the complex chemical reactions which are continually occurring within the living cell. Much of this work is difficult, expensive and time consuming, but it is by such a methodical approach, occasionally illuminated by a flash of empirical genius that pharmacology will advance and the therapeutic armoury of the nurse and doctor be enlarged.

PHARMACOLOGY

ABSORPTION AND METABOLISM OF DRUGS

Drugs may be given to a patient in various ways, they may be injected, absorbed from the gastro-intestinal tract or applied locally.

The term *bioavailability* is used to denote that proportion of the

administered drug which reaches the circulation. If it is given intravenously then the bioavailability is obviously 100 per cent, if it is swallowed then only a proportion may reach the circulation.

Oral administration is the commonest and easiest way to give a drug and the bioavailability by this route depends on several factors.

1. *Absorption.* This will depend on the physical properties of the drug which determines whether it will pass through the wall of the gut, and on the formulation of the drug by the manufacturer. Absorption may also be modified by interaction with other drugs or food.

2. *First pass effect.* When absorbed from the gastrointestinal tract drugs have to pass via the portal vein to the liver before reaching the general circulation (Fig. 1). This may be important

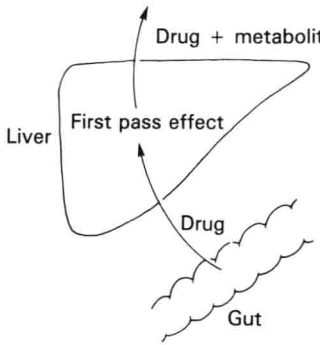

Fig. 1 First pass metabolism of a drug

as many drugs are metabolised (broken down) as they pass through the liver so that only a proportion of the amount absorbed actually reaches the circulation. This removal of the drug as it passes through the liver is called the first pass effect. Drugs which show a very large first pass effect are almost inactive if swallowed, examples being lignocaine and glyceryl trinitrate,

and these have to be injected or, if absorbed from the oral mucosa, can be chewed or sucked thus bypassing the liver.

After absorption, drugs enter the blood stream and are carried round the body. They may be in simple solution in the plasma, but many are poorly soluble and are partially bound to plasma proteins which act as carriers. It is important to realise that the fraction of a drug which is bound to protein is inactive and only the free unbound portion has any pharmacological action.

The concentration of a drug in the bloodstream is a good index of whether the correct dose is being given. Therefore, the nurse should know something of the factors which govern the blood concentration.

1. *The dose.* It is obvious that the larger the dose, the higher the concentration achieved.

2. *The route of administration.* Intravenous injection produces a rapid rise in blood concentration whereas oral administration gives a slower rise and a lower peak concentration. Intramuscular injection rates lie between the two (Fig. 2).

3. *The distribution of the drug.* This is another important factor in determining the plasma concentration and also its activity and therapeutic usefulness (Fig. 3). Some drugs are confined to the bloodstream, and this obviously limits their effect, for instance, an antibiotic which would not enter the tissues would be useless in treating most infections.

Other drugs diffuse out of the circulation into the tissue spaces and some enter the cells and spread through the total water of the body. A few drugs are actually concentrated in cells.

The average volume of the distribution space is:

Plasma	3 litres
Extracellular space	15 litres
Total body water	36 litres

It can be seen, therefore, that the more widely a drug diffuses, the lower will be the concentration produced by a given dose.

4. *The rate of elimination.* The faster the body breaks down or excretes a drug, the more rapidly will the blood level fall.

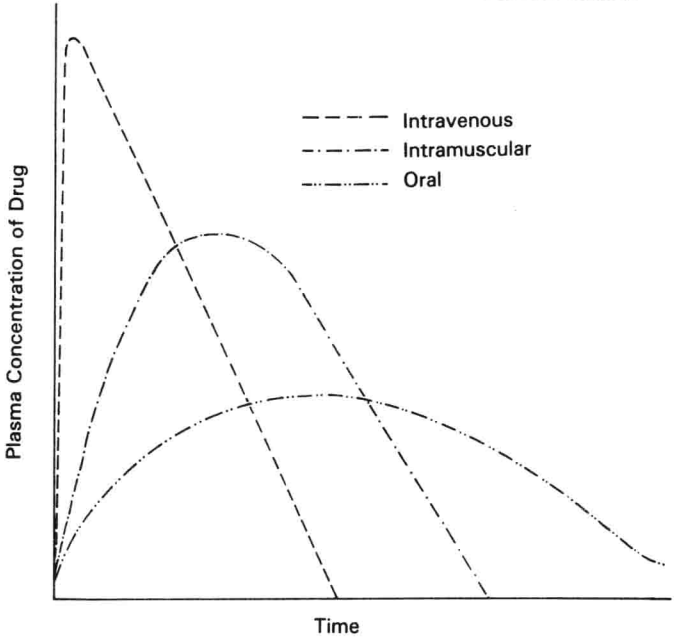

Fig. 2 The effect of the route of administration of a drug on the plasma concentrations

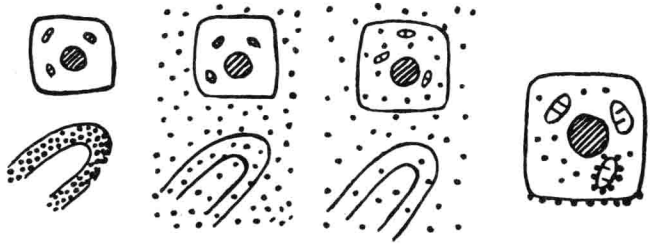

Fig. 3 Distribution of drugs in the body

Drugs are usually eliminated in one of two ways (Fig. 4):

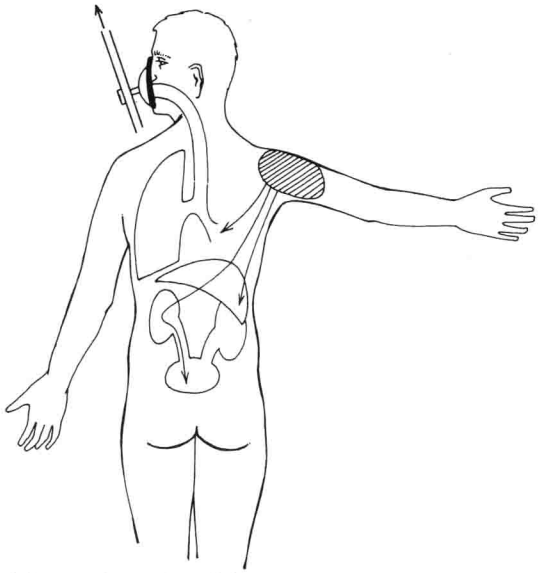

Fig. 4 Breakdown and excretion of drugs

a. They may be broken down or combined with some other chemical so that they are no longer pharmacologically active. This usually occurs in the liver and is brought about by substances called enzymes. Enzymes have the property of promoting certain chemical reactions, and some of these are concerned with the inactivation of drugs. Therefore, if the liver cells are damaged by disease the inactivation process may be slower than normal. The activity of the liver enzymes can be increased or decreased by drugs and this has important implications in treating patients (see Drug Interactions p. 381).

With certain types of drug, if given repeatedly, the breakdown process becomes more effective. Therefore, larger and larger doses are required to produce the same effect and this is known as *drug tolerance.*

It is of interest that there are genetically determined differences in the rate at which some drugs can be broken down by the body. Suxamethonium normally produces a transient paralysis of voluntary muscle, as it is broken down by an enzyme, but in certain families this enzyme is lacking and suxamethonium causes a prolonged paralysis.

b. Drugs or their breakdown products may be excreted through the kidneys, and if these are damaged by disease excretion will be delayed and accumulation can occur. Rarely, drugs are excreted through the lungs and this route is important in the case of volatile anaesthetics.

The speed of elimination is the main factor in deciding the duration of action of a drug and is referred to as the *plasma half-life* ($t\frac{1}{2}$) of that drug. This figure is obtained experimentally by giving a single dose, usually intravenously, and measuring the plasma concentration at intervals. The time taken for this concentration to halve is the plasma or biological half-life (Fig. 5).

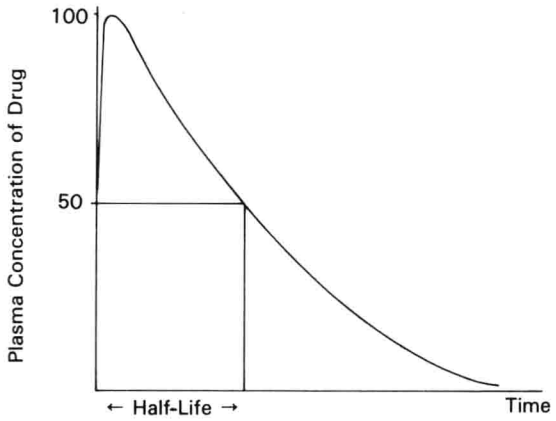

Fig. 5 Plasma levels and half-life of a drug after a single intravenous injection

FACTORS INFLUENCING THE DOSAGE RÉGIME

Several factors must be considered when a drug is given to a patient. The time it takes to act is largely determined by the route of administration. The blood level and therapeutic effectiveness depend on the dose, distribution within the body and to some degree on the mode of administration and speed of elimination.

Rapidly excreted drugs with short half-lives require frequent dosage to maintain a fairly constant concentration in the body, while those which are eliminated slowly can be given less often. With repeated dosing, the concentration in the plasma climbs until a more or less steady level is obtained. This is termed *steady state* (Fig. 6). The time taken to reach steady state is approximately five times the half life of the drug. For example,

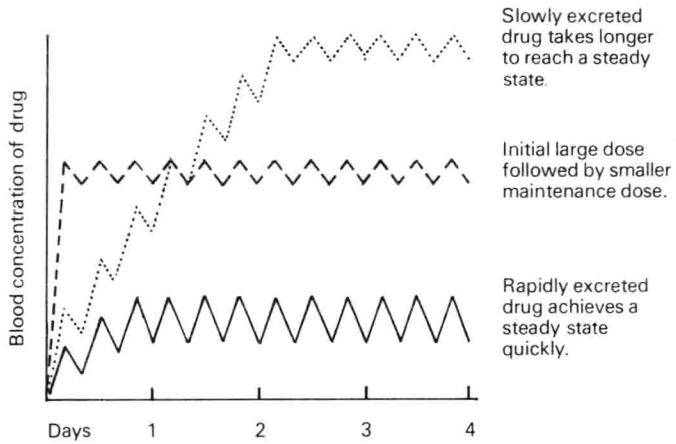

Fig. 6 Steady state concentrations of drugs

the half-life of digoxin is 36 hours so steady state for digoxin given regularly will be reached in 36 × 5 = 180 hours.

It can be seen that the shorter the half-life (i.e. the quicker the elimination) of a drug, the more rapidly will it reach steady state.

In order to hasten the achievement of steady state and full therapeutic effect with more slowly excreted drugs, a large loading dose may be given followed by smaller maintenance doses (see Fig. 6).

HOW DO DRUGS WORK?

In spite of a great deal of research it is still not known how some drugs produce their effect but it is possible to describe the way in which some of them act.

1. *The receptor theory.* It is believed that the cells in certain tissues contain structures called receptors. These combine with substances which are produced naturally in the body and the cells are stimulated, the contraction of muscle fibres produced by acetylcholine being an example. The drug is thought to fit onto a receptor rather as a key fits a lock. It may then either stimulate the receptor and produce an effect similar to that of the naturally occurring substance or it may occupy the receptor without producing any effect but preventing any naturally occurring stimulation. The blocking of acetylcholine by atropine is a good example (Fig. 7).

2. *Antimetabolites.* These drugs closely resemble substances which are used by the cells for nutrition and when absorbed, the cells cannot use them and so fail to multiply. The sulphonamides which are used to stop the multiplication of bacteria are a good example. They are very similar in structure to para-aminobenzoic acid and certain bacteria cannot distinguish between them, and absorb the sulphonamides and stop regenerating.

3. *Enzyme inhibitors.* Enzymes are substances which speed up many chemical processes within the body. Some of these enzyme-activated processes are concerned with the transport of chemicals in and out of the cells. Certain drugs have the property of inhibiting their action and thus interfere with some of these