Chapter 2
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Routes of Drug Administration

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2.1 Introduction of Routes of Drug Administration

(Routes or Way/Passes and administration or management).

The routes of administration are depends on drug and as well as patients related factors. The routes can be divided into two classes.

2.2 Factor Affecting Routes of Drug Administration

Note- Factor affecting choice of route:-

- Physical and chemical properties of the drug (solid/liquid/gas, solubility, stability, pH, irritancy).
- Site of desired action-localized and approachable generalized and not approachable.
- Rate and extent of absorption of the drug from different routes.
- Effect of digestive juices and first pass metabolism on the drug.
- Rapidity with which the response is desired (routine treatment or emergency).

Routes are basically two types.

I. Local routes
II. Systemic routes

2.2.1 Local routes

A) Topical route
B) Deeper tissues
C) Arterial supply

A) Topical route:-

This refers to external/(outer surface of body) application of the drug to the surface for localized action. It is often more convenient or suitable as well as encouraging to the patient. These are another two types.

a) Skin
b) Mucus membrane

a) Skin:-

Drug is applied as cream, lotion, ointment, jelly, paste, powder, dressing and spray etc.

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b) Mucus membrane:-

The dosage form depends on the site.

Mouth and pharynx-	Paints, lozenges, mouth washes, gargles.
Eyes, ear and nose-	Drops, ointment, irrigation, nasal spray.
Gastrointestinal tract GIT)-	Non-absorbable drugs given orally e.g. magnesium Hydroxide, sucralfate, neomycin.
Bronchi and lungs-	Volatile liquid, gases and fine powder (Aerosols and salbutamol etc).
Urethra-	Jelly (lidocaine), ointment and irrigating solutions.
Vaginal-	Tablet, inserts, cream, powder, douches.
Anal canal-	Ointment, suppositories.

B) Deeper tissues:-

In this routes, drug is apply for certain deep areas can be approached by using a syringe and needle, but the drug systemic absorption is very slow/minimum or absent, e.g. Intraarticular injection (hydrocortisone acetate), Intrathecal injection (lignocaine, amphotericin B)

C) Arterial supply:-

It is used for close intra-arterial injection, where the drug injected for contrast media in angiography. In this route anticancer drugs can be infused in femoral or brachial artery to localize the effect for limb malignancies.

2.2.2 Systemic routes

The drug administered through systemic routes is intended/reaches to be absorbed into blood and distributed all over the body, including the site of action, through circulation, these are various types.

A) Oral
B) Sublingual (Sl) Buccal
C) Nasal
D) Inhalation
E) Rectal
F) Cutaneous
G) Parenteral

A) Oral:-

Oral route is the oldest and commonest mode of drug administration. It is safer more convenient or suitable, does not need assistance, non-invasive, often painless, the medicament need not be sterile and so is cheaper. Both solid (tablet, capsule, powder etc) and liquid (syrups, emulsion, suspension, elixirs, solution etc) dosage forms can be given orally.

<u>Note</u>- Limitation of oral route of Administration:-

- Action is slower and thus not suitable for emergencies.
- Unpalatable drugs (paraldehyde) are difficult to administer, drug may be filled in capsules to circumvent this.
- May cause nausea and vomiting (emetine).
- Cannot be used for uncooperative/unconscious/vomiting patient.
- Certain drugs are not absorbed (streptomycin).
- Other are destroyed by digestive juices (penicillin, Insulin) or in liver (nitroglycerin, testosterone, lignocaine).
- Easy to intake for administration and no need of any maintenance.

B) Sublingual (Sl) Buccal:-

The tablet or pellet containing the drug is placed under the tongue or crushed in the mouth and spread over the buccal mucosa. Only lipid soluble and non-irritating drugs can be administered in this route. Absorption is relatively rapid and action can be produced in minutes. The chief advantage is that liver is bypassed and drugs with high first pass metabolism with absorbed directly into systemic circulation e.g. nitroglycerine, isoprenaline, clonidine.

C) Nasal:-

The mucus membrane of the nose can readily absorb many drugs, digestive juices and liver are bypassed. However only certain drugs like posterior pituitary powder and desmopressin applied as a snuff or spray or nebulized solution have been used by this route.

D) Inhalation:-

Volatile liquids and gases are given by in this route for systemic action, e. g. general anesthetics, amyl nitrite. Absorption takes place from the vast surface of alveoli and action is very rapid or fast. Thus in this route controlled administration is possible with moment to moment adjustment.

E) Rectal:-

Certain irritant and unpleasant drugs can be put into rectum as suppositories or retention enema for systemic effect. This route can also be used, when the patient is having recurrent vomiting. In this route absorption is slower, irregular and often unpredictable. Rectal inflammation can be cure by best result from irritant drugs in this route, e. g. Indomethacin, paraldehyde, diazepam, aminophylline etc.

F) Cutaneous:-

Highly lipid soluble drugs can be applied over the skin for slow and prolonged absorption and the liver is also bypassed. The drug can be applied over specified area of skin.
Transdermal therapeutic system- these are recently developed devices in the form of adhesive patches of various shapes and sizes (5-20 cm^2). Which deliver the contained drug at a constant rate into systemic circulation via the stratum corneum. The drug is delivered at the skin surface by diffusion for percutaneous absorption into circulation. Transdermal patches of nitroglycerine, nicotine and estradiol are available in India, while those of isosorbide dinitrate, hyoscine and clonidine are available in other countries.

G) Parenteral:- (Par-beyond, Enteral-intestinal)

This doses form refers to administration by injection directly into the tissue, fluid or blood without having to cross the intestinal mucosa. In this route action is faster and surer (valuable in emergencies). Gastric irritation and vomiting are not provoked.

a) Intradermal
b) Subcutaneous (S.C)
c) Intramuscular
d) Intravenous
e) Intraarticular
f) Intra-arterial
g) Intrathecal
h) Intracisternal
i) Intracardiac
j) Intracameral
k) Intrasynovial

a) Intradermal:-

The drug is injected/projected into the skin dermis and epidermis layer. The volume of injection usually between 0.1-0.2 ml. this route used for skin raising a bleb (e. g BCG vaccine, sensitivity tests) or scarring/multiple puncture of the epidermis through a drop of the drug is done. This route is employed for specific purposes only.

b) Hypodermic/Subcutaneous:-

The drugs is deposited in the loose subcutaneous tissue, which is richly supplied by nerves (irritant drugs can't be injected this route) but is less vascular (absorption is slower than intramuscular). Only small volumes can be injected s.c. Self injection is possible in this route because deep penetration is not needed. The route should be avoided in shock patients who are vasoconstricted absorption will be delayed. The volume of injected drugs usually between 0.5-1.0 ml. some special forms of this route are:

1) **Dermojet**

In this method needle is not used and a high velocity jet of drug solution is projected/injected from a microfine orifice using a gun like implement. It is essentially painless and suited for high amount of mass inoculation.

2) **Pellet implantation**

The drug in the form of a solid pellet is introduced with a trochar and cannula. This drug provides sustained release of the drug over weeks and month's e.g DOCA, testosterone.

3) **Sialistic/Non-degradable/Biodegradable**

In this route crystalline drug is packed in tubes or capsules made of suitable materials and implanted under the skin. This drug provides sustained release of the drug over one year to three years. This has been tried for contraceptives, hormones and microbial infection.

c) Intramuscular:-

The drug is injected in one of the large skeletal muscles deltoid, triceps, gluteus maximus, rectus femoris etc. It is less painful, but self injection is often impracticable because deep penetration is needed. Intramuscular injections should be avoided in anticoagulant treated patients, because it can produce local haematoma. The volume rarely exceeds 2.0 ml.

d) Intravenous:-

The drug is injected as a bolus (Greek: - bolos-lump) or infused slowly over hours in one of the superficial veins. The drug reaches directly into the blood stream and effects are produced immediately (suitable for emergency). Only aqueous solutions are to be injected i. v and there are no depot preparations for this route. The dose of the drug required is smallest (bioavailability is 100%) and even large volumes can be infused. The volumes of such injection can vary from 1.0 -500ml. some time it is more than 500ml also.

e) Intraarticular:-

The drug is injected in certain deep areas, where the systemic absorption is slow. The drug is used in this route into knee, elbow and solder joint.

f) Intra-arterial:-

The close intra-arterial injection is used for contrast media in angiography, anticancer drugs can be infused/used in femoral or brachial artery to localize the effect for limb malignancies. The drug is injected into artery terminating in target area.

g) Intrathecal:-

Into the subarachnoid space surrounding spinal cord which contains cerebro-spinal cord, which contains cerebro-spinal fluid. Injection are generally made in the filum terminale area. Volumes up to 10 ml can be injected.

h) Intracisternal:-

Into the cistern containing cerebro-spinal fluid.

i) Intracardiac:-

Into the heart chamber.

j) Intracameral:-

Into the eye ball.

k) Intrasynovial:-

Into a joint fluid area.

2.3 Bioavailability

(Biological- all living organism, Availability-available/Present).

The rate and amount of unchanged drug absorption into body, through different site of administration (oral, IV, IM & subcutaneous) into systemic circulation/target organ (blood, tissue, fluid & organ) is called bioavailability.

Measurement of bioavailability:-

A) Pharmacokinetics
B) Pharmacodynamics

A) Pharmacokinetics:-

This refers to movement of the drug in and alteration of the drug by the body; includes absorption, distribution, binding/localization/storage, biotransformation and excretion of the drug.

B) Pharmacodynamics:-

This includes physiological and biochemical effects of drugs and their mechanism of action at organ system/sub cellular/macromolecular levels,