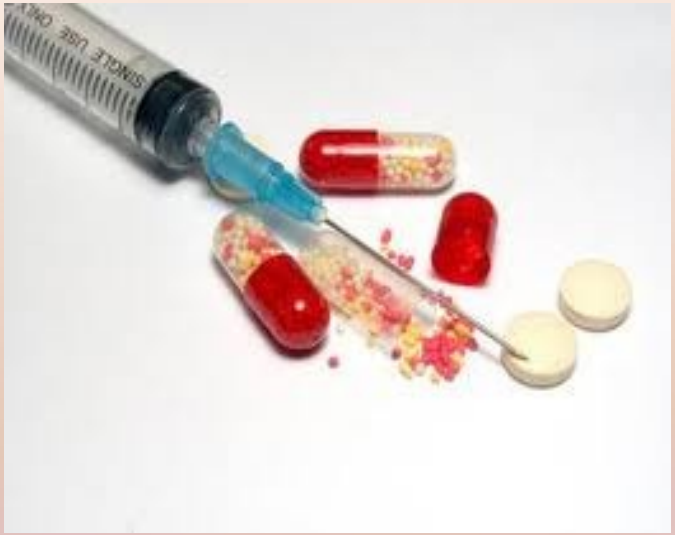


# *Routes of drug administration*

***Prepared by: Shaikh Abusufyan,***
***M. Pharm (Pharmacology)***

- The choice of appropriate route in a given situation depends both on:
  - drugs
  - patient related factors.

**Mostly common considerations are:**

1. Physical and chemical properties of the drug
   - Solid/liquid/ gas
   - Solubility and stability
   - PH and irritancy
2. Site of desired action - localized and aprochable

3. Rate and extent of absorption of the drug from different routes.

4. Effect of digestive juices and first pass metabolism of the drug.

5. Rapidity with which the response is desired (eg. routine treatment or emergency).

6. Accuracy of dosage required (i.v. and inhalation).

7. Condition of the patient (unconscious, vomiting) etc.

Routes can be broadly divided into those for (a) Local action and (b) Systemic action.

- **Local routes:**
  - Topical
  - Deeper tissues
  - Arterial supply
- **Systemic routes:**
  - Oral
  - Sublingual or buccal
  - Rectal
  - Cutaneous
  - Inhalation
  - Nasal
  - Parentral

    -Subcutaneous

    -Intravenous

    -Intramuscular

    -Intradermal

## LOCAL ROUTES

- Only be used for localized lesions at accessible sites and for drugs whose systemic absorption from these sites is minimal or absent.

**Advantages:**

- High concentrations are attained at the desired site without exposing the rest of the body.

- **Systemic side effects** are absent or minimal.

- For drugs (in suitable dosage forms) that are **absorbed** from these routes, the same can serve as systemic route of administration, e.g. glyceryl trinitrate (GTN)

- The local routes are:

  1. Topical
  2. Deeper tissues
  3. Arterial supply

## 1. Topical

- This refers to external application of the drug to the surface for localized action.

**Advantages**:

- More convenient and encouraging to the patient.

- Drugs can be efficiently delivered in the form of
  - lotion, ointment, cream,
  - powder,
  - rinse,
  - paints, drops, spray,
  - lozengens, suppositories or pesseries.

# Other forms of Topical applications

- Non-absorbable drugs given orally for action on g.i. mucosa Eg. sucralfate, vancomycin.
- Inhalation of drugs for action on bronchi (salbutamol, cromolyn sodium)
- Irrigating solutions/ jellys (povidone iodine, lidocaine) applied to urethra

## 2. Deeper tissues:

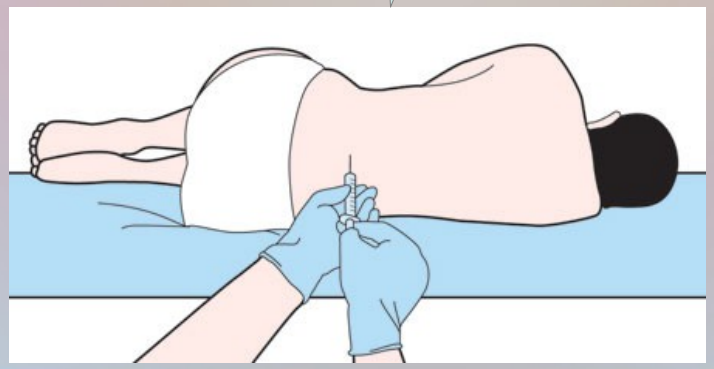
- Deep areas can be approached by using a syringe and needle
- But the drug should be such that systemic absorption is slow.

Eg.

- A. intra-articular injection (hydrocortisone acetate)
- B. intrathecal injection (lidocaine),
- C. retrobulbar injection (hydrocortisone acetate).


A

B

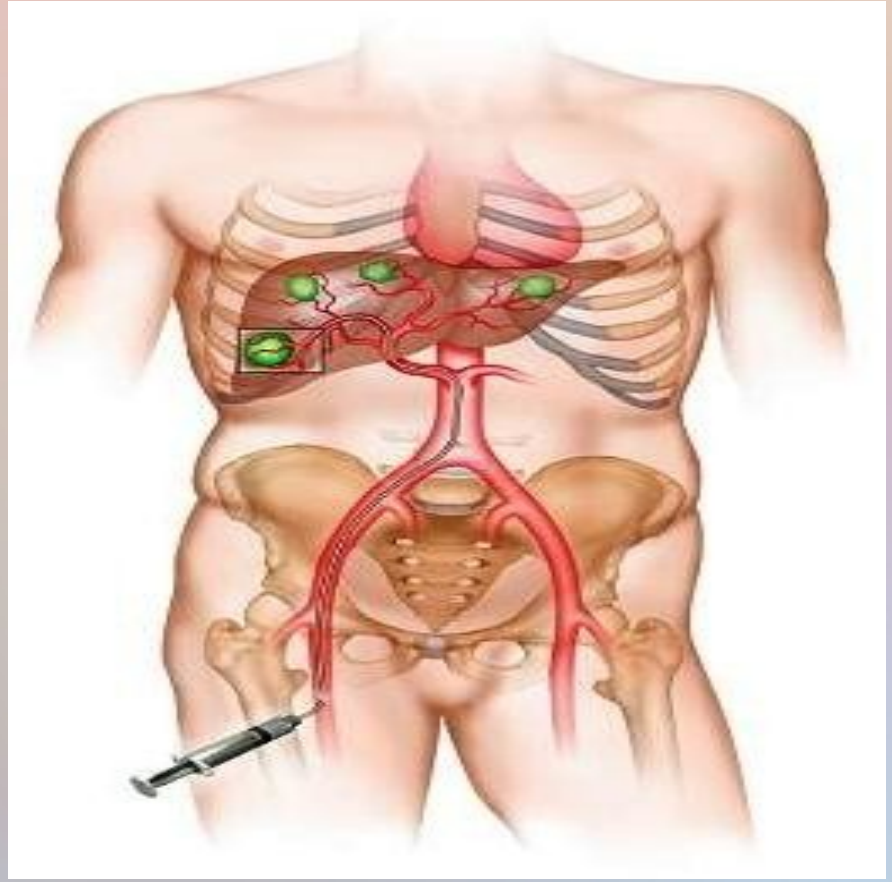


C

## 3. **Arterial supply**:

Eg:

- Close intra-arterial injection is used for contrast media in angiography
- Anticancer drugs can be infused in femoral or brachial artery



# SYSTEMIC ROUTES

- It is intended to be absorbed

Into the blood stream and distributed all over

## 1. Oral

- oldest and commonest mode

**Advantages:**

- It is safer
- more convenient
- does not need assistance
- noninvasive
- often painless
- need not be sterile -- cheaper.
- Both solid dosage forms and liquid dosage forms can be given orally.

# Innovative dosage forms:

## Dragées

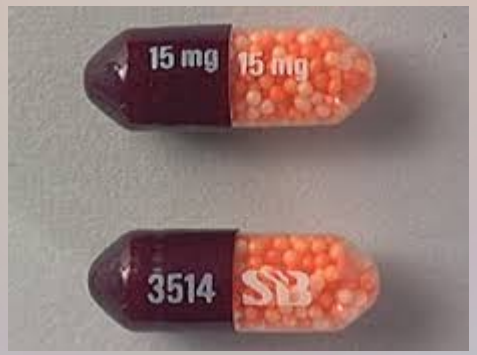
- Medicated candies or sugar coated pills can be referred to as dragées (A).

## spansules

- A capsule that when swallowed releases one or more medicinal drugs over a set period is called as spansules.

A

B



**Disadvantages:**

- Action of drugs is slower - **not for emergencies**.
- **Unpalatable drugs** (chloramphenicol) - 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.
- Absorption of drugs may be variable and certain drugs are not absorbed (streptomycin)
- Some are destroyed by digestive juices (Penicillin G, insulin) or in liver (testostrone, lidocaine).

## 2. Sublingual (s.i.) or buccal

- 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.
- Absorption is relatively rapid- action can be produced in minutes.

**Advantages**

- Liver is bypassed and drugs with high first pass metabolism can be absorbed directly into systemic circulation.

Eg

- buprenorphine,
- desamino-oxytocin.

## 3. Rectal

- Certain irritant and unpleasant drugs can be put into rectum (suppositories or retention enema) for systemic effect.

**Advantages:**

- Used when the patient is having recurrent vomiting or is unconscious.

**Disadvantages:**

- Inconvenient and embarrassing;
- absorption is slower, irregular and often unpredictable
- Drug absorbed into external haemorrhoidal veins.
- Rectal inflammation can result from irritant drugs.

Eg. Diazepam, indomethacin, paraldehyde, ergotamine

## 3. Cutaneous (Over skin)

- Highly lipid soluble drugs can be applied for slow and prolonged absorption.

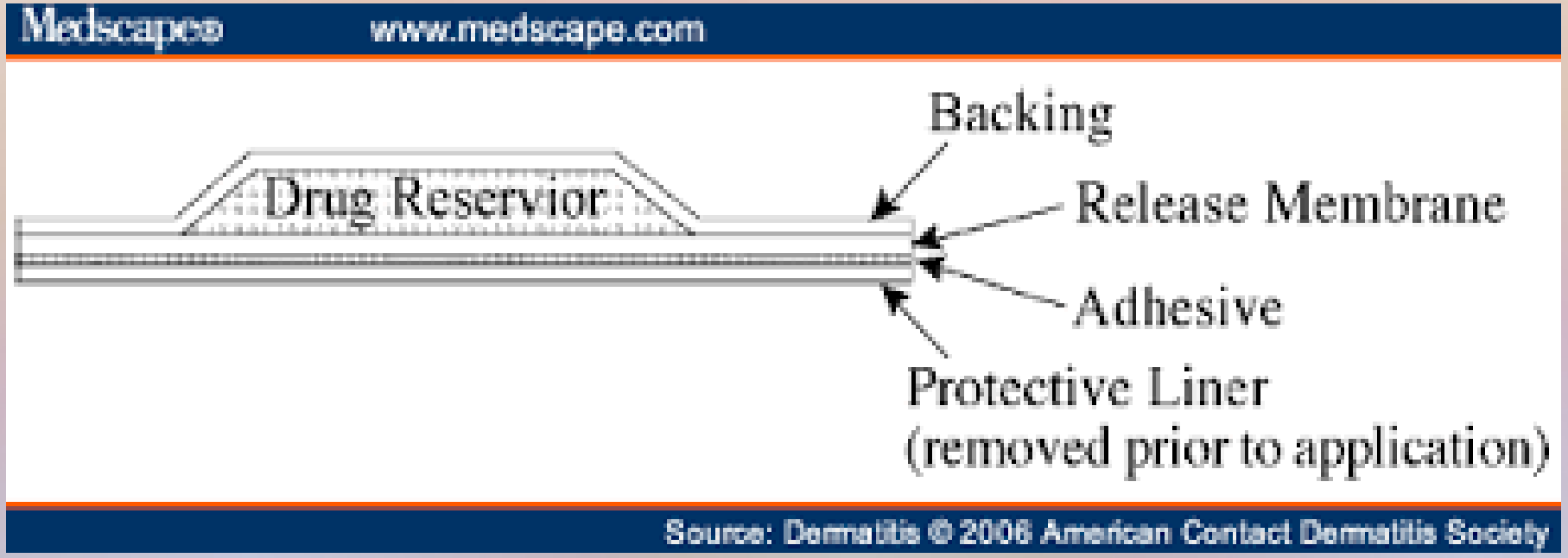
**Advantages**:

- The liver is also bypassed.
- The drug can be incorporated in an ointment and applied over specified area of skin.
- Absorption of the drug can be enhanced by
  - rubbing the preparation,
  - by using an oily base
  - and by an occlusive dressing.

# Transdermal therapeutic systems:

- These are **devices** in the form of adhesive patches of various shapes and sizes (5-20 cm)

- It deliver the drug at a **constant rate** into systemic circulation via the stratum corneum.




- The drug (in solution or bound to a polymer) is **held in a reservoir**

- The drug is delivered at the skin surface by diffusion
- The drug is delivered at a constant and predictable rate
- site of application:
  - usually chest,
  - abdomen/ upper arm,
  - lower back, buttock ect.

- Transdermal patches of GTN, Fentanyl, nicotine and estradiol are available in India

- These have been designed to last the effect for 1-7 days.

- They are increasingly popular, because they provide
  - Smooth plasma concentrations of the drug without fluctuations;
  - Minimize inter individual variations and SE.
  - More convenient
  - Patient compliance is better.

**Disadvantage:**

- Local irritation and erythema occurs in some, but is generally mild;
- Can be minimized by changing the site of application each time by rotation.
- Discontinuation has been necessary in 2-7 %.

## 5. Inhalation

- Volatile liquids & gases are given by inhalation e.g. general anaesthetics.

- **Absorption** :Take place from the vast surface of alveoli: action is very rapid.

- **Elimination**: When administration is **discontinued**

↓

the drug diffuses back

↓

rapidly eliminated in expired air.

↓

controlled administration is possible with moment to moment adjustment.

**Disadvantage:**

- **Irritant vapours (ether):**

  cause inflammation of respiratory tract and **increase secretion.**

## 6. Nasal

- The **mucous membrane of the nose** - readily absorb many drugs

**Advantage:**

- Digestive juices and liver are bypassed.

**Disadvantage**:

- Only certain drugs are used by this route.

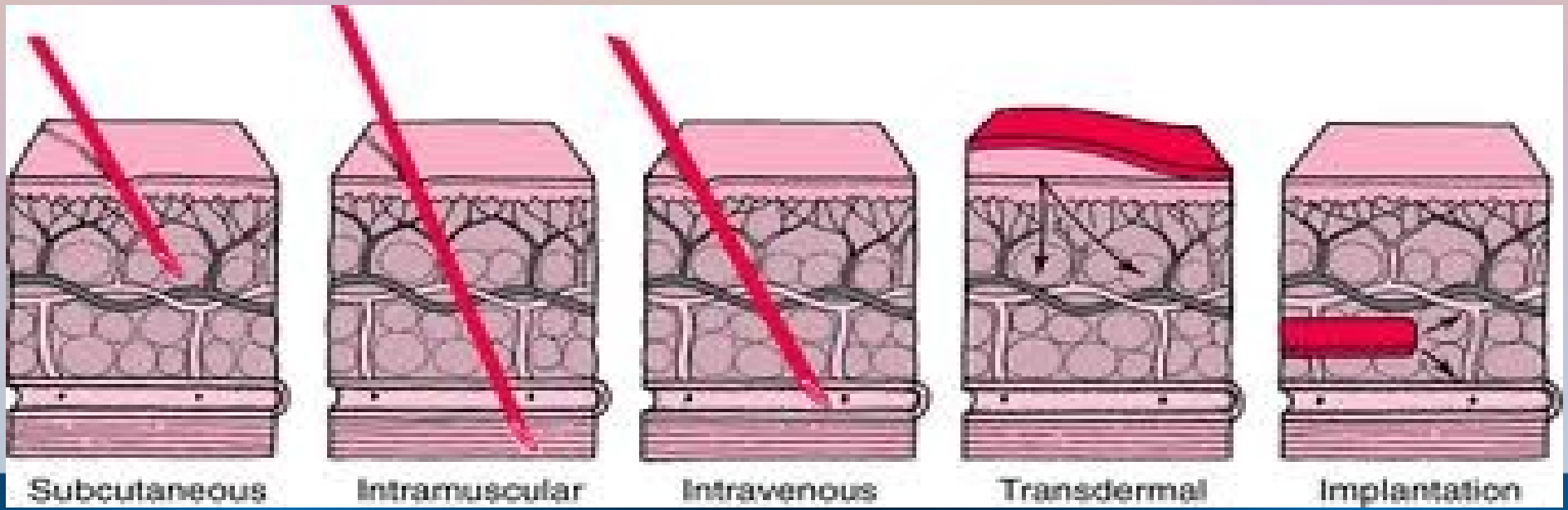
Eg. desmopressin as a spray or nebulized solution.

**Parenteral:** (**Par-**beyond, **enteral**-intestinal)

- Administration by injection which takes the drug directly into the tissue fluid or blood without crossing the intestinal mucosa.

**ADVANTAGES**:

- The limitations of oral administration are circumvented.



- Drug action is faster and surer (valuable in emergencies).
- Gastric irritation & vomiting are not provoked.
- Can be employed even in
  - unconscious,
  - uncooperative or vomiting patient.
- There are **no chances of interference** by food or digestive juices.
- Liver is bypassed.

**Disadvantages:**

- The preparation has to be sterilized --- costlier.
- More risky than oral
- The technique is
  - invasive and painful,
  - assistance of another person is mostly needed
- There are chances of local tissue injury

**The important parenteral routes are:**

**(i) Subcutaneous (s.c.)**: The drug is deposited in the loose subcutaneous tissue

**Disadvantages:**

- It is richly supplied by nerves (irritant drugs cannot be injected)
- It is **less vascular** (absorption is slower than IM).
- Only small volumes can be injected s.c.
- Self-injection is possible because deep penetration is not needed.

- **Precaution**: Should be avoided in shock patients who are vasoconstricted: **absorption will be delayed.**

- Repository (depot) preparations - **prolonged action**.

- Some special forms of this route are:

  (a) Dermojet

  (b) Pellet implantation

  (c) Sialistic (nonbiodegradable) and biodegradable implants etc.

**(a) Dermojet:**

- A high velocity jet of drug solution is projected from a microfine orifice using a gun like implement.

- The solution passes through the superficial layers and gets deposited in the subcutaneous tissue.

**Advantages:**

- It is essentially painless & suited for mass inoculations.

**(b) Pellet implantation:**

- The drug in the form of a solid pellet is introduced with a trochar and cannula.

- This provides sustained release of the drug over weeks and months e.g. DOCA, testosterone.

## (c) Sialistic (nonbiodegradable) and biodegradable implants

- Crystalline drug is packed in tubes or capsules made of suitable materials and implanted under the skin.
- Slow and uniform leaching of the drug occurs over months providing constant blood levels.
- The nonbiodegradable implant has to be removed later on but not the biodegradable one.
- Eg. for hormones and contraceptives

  (e.g. NoRPLANT).

**(ii) Intramuscular (i.m.):**

- The drug is injected in one of the large skeletal muscles-- triceps, rectus femoris etc.
- Muscle is less richly supplied with sensory nerves (mild irritants can be injected).
- It is more vascular (absorption is **faster**).
- It is less painful - self injection is often impracticable.
- Depot preparations (oily solutions/ aqueous suspensions) can be injected by this route.

- Intramuscular injections should be **avoided** in anticoagulant treated patients

because it can produce local haematoma.

**(iii) Intravenous (i.v.):**

- The drug is injected as a bolus or infused slowly over hours in the superficial veins.

- The drug reaches directly into the blood stream

  ↓

  Effects are produced immediately

  ↓

  Great value in emergency

- The intima of veins is insensitive and drug gets diluted with blood

even highly irritant drugs can be injected

But may produces thrombophlebitis of the injected vein & necrosis of adjoining tissues if extravasation occurs.

- These complications can be minimized by diluting the drug or injecting it into a running i.v. line.

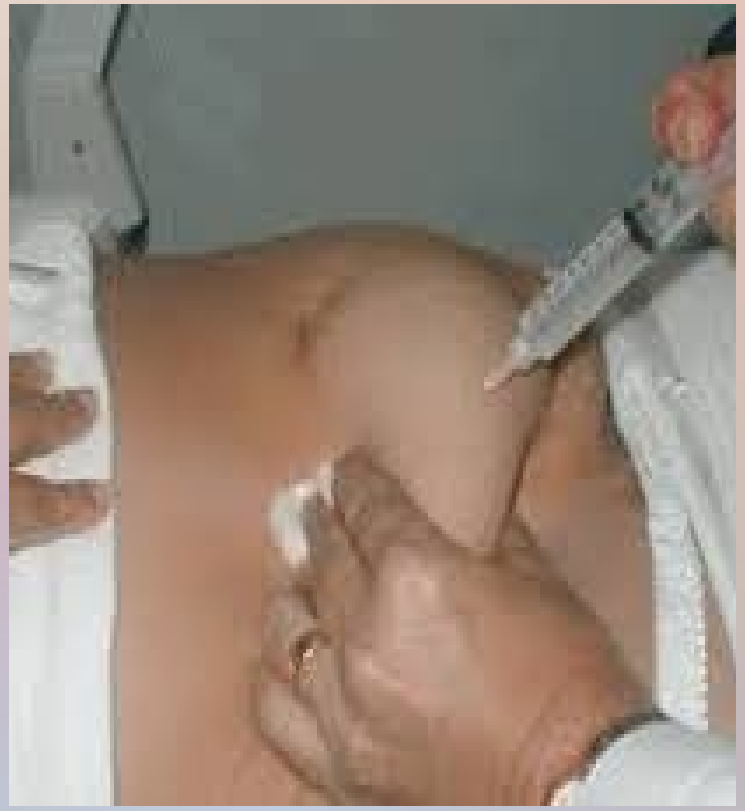
- The dose of the drug required is smallest (bioavailability is 100%)
- And even large volumes can be infused.
- The response is accurately measurable (e.g. BP) & titration of the dose with the response is possible.

**Disadvantages:**

- **Most risky route**
- Vital organs like heart, brain etc get exposed to high concentrations of the drug.
- Only aqueous solutions (not suspensions) can be injected and there are **no depot preparations.**

## (iv) Intradermal iniection:

- The drug is injected into the skin raising a bleb (e.g. BCG vaccine, sensitivity testing) or making puncture of the epidermis.



THANK YOU