CHAPTER 11

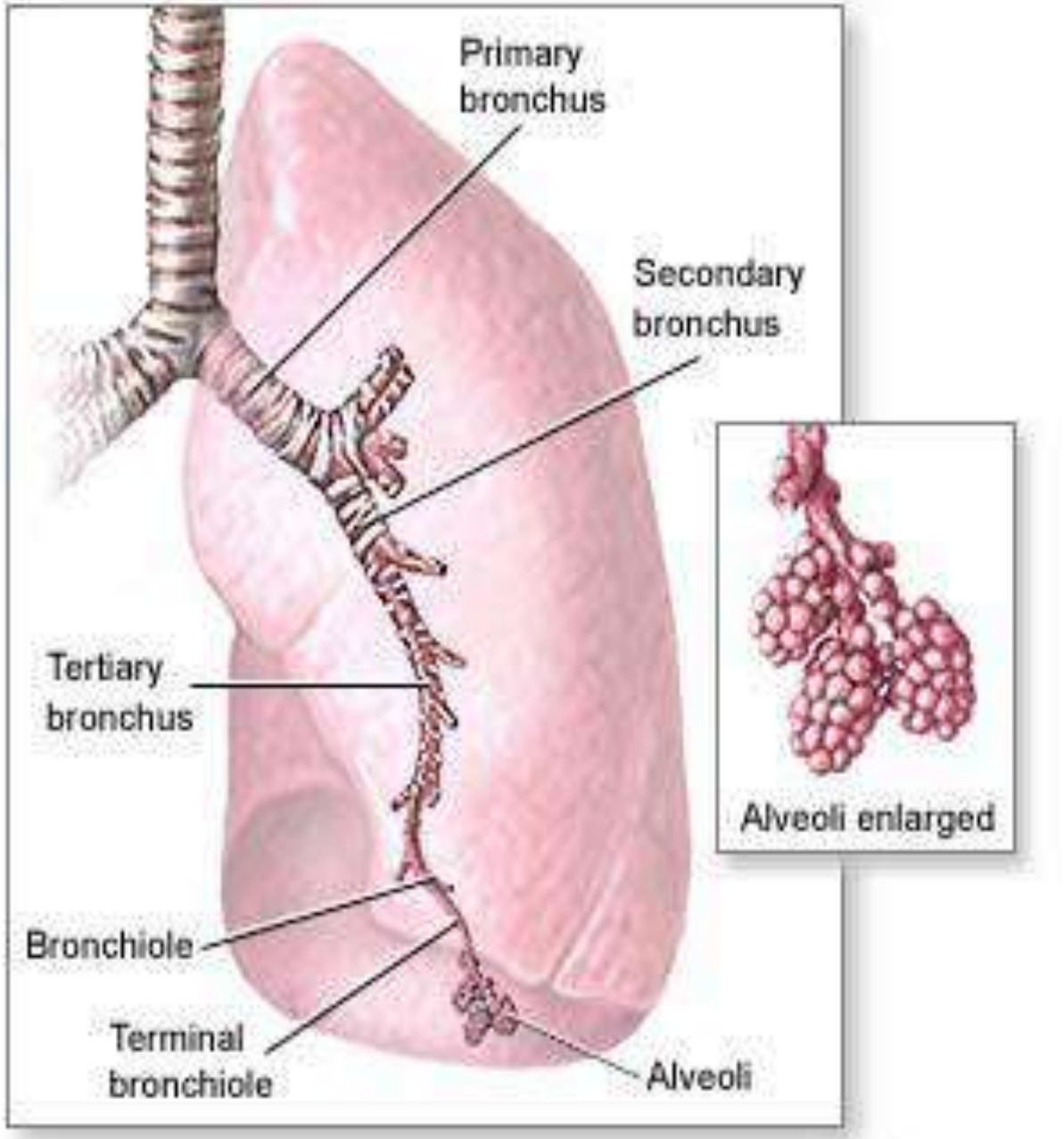
Pulmonary route of Administration. Advantages and disadvantages. Dosage forms. Deposition of aerosols in the Respiratory tract. Factors affecting the deposition. Factors affecting the Pulmonary Absorption.

Pulmonary route of administration

- In 1846 Morton was the first scientist who uses this route of administration for the general anesthesia by using **Diethyl ether**.

- The absorption of the drugs by using of the inhalation route of administration occurs via Alveolar membranes.

- Anesthetics should be used to give local (Antiasthmatic) or systemic (general anesthesia).



- **The respiratory tract consists of:**

➢ Conducting regions(trachea, bronchi, bronchioles, terminal and respiratory bronchioles) and

➢ Respiratory regions (respiratory bronchioles and alveolar regions).

- The upper respiratory tract comprises the nose, throat, pharynx and larynx.
- The lower tract comprises the trachea, bronchi, bronchioles and the alveolar regions.

➢ Advantages of pulmonary drug delivery

1. Rapid onset of action, instantaneous absorption of the drug, (S= 30-100m2) and good blood supply.
2. Avoidance of intestinal and hepatic first-pass metabolism.
3. Avoidance of gastrointestinal upset.
4. No pain.
5. Small particles administration minimize mechanical irritation.
6. In case of pulmonary diseases, the local application of the drug at the desired site of action (β- adrenergic)"reduced dose" → Low conc. in the systemic circulation →reduced systemic side-effects
7. Variability of dosage form administration as nebulizers, micronized powder from active breath device and spray from a pressurized aerosol.
8. High volume of gas can be administered.
9. Pulmonary system contains macrophage → cleaning alveoli.
10. Highly controllable and less enzyme degradation.

➢Disadvantages of pulmonary drug delivery:

1. Poor ability to regulate the dose, only small portion of the drug reaches the site of action.
2. Propellant toxicity (Cancer probability).
3. Hypoxia.
4. Irritation of pulmonary epithelium by gases & volatile drugs.
5. Lethal effect of risk drugs (high conc.).
6. Narrow therapeutic index- drugs can not be administered.
7. Only gases and volatile liquids can be administered (not suitable for all pharmaceutical forms).
8. Special technique for application.
9. Special precaution to patients with pulmonary disease and not suitable for children.

➢ **Dosage forms:**

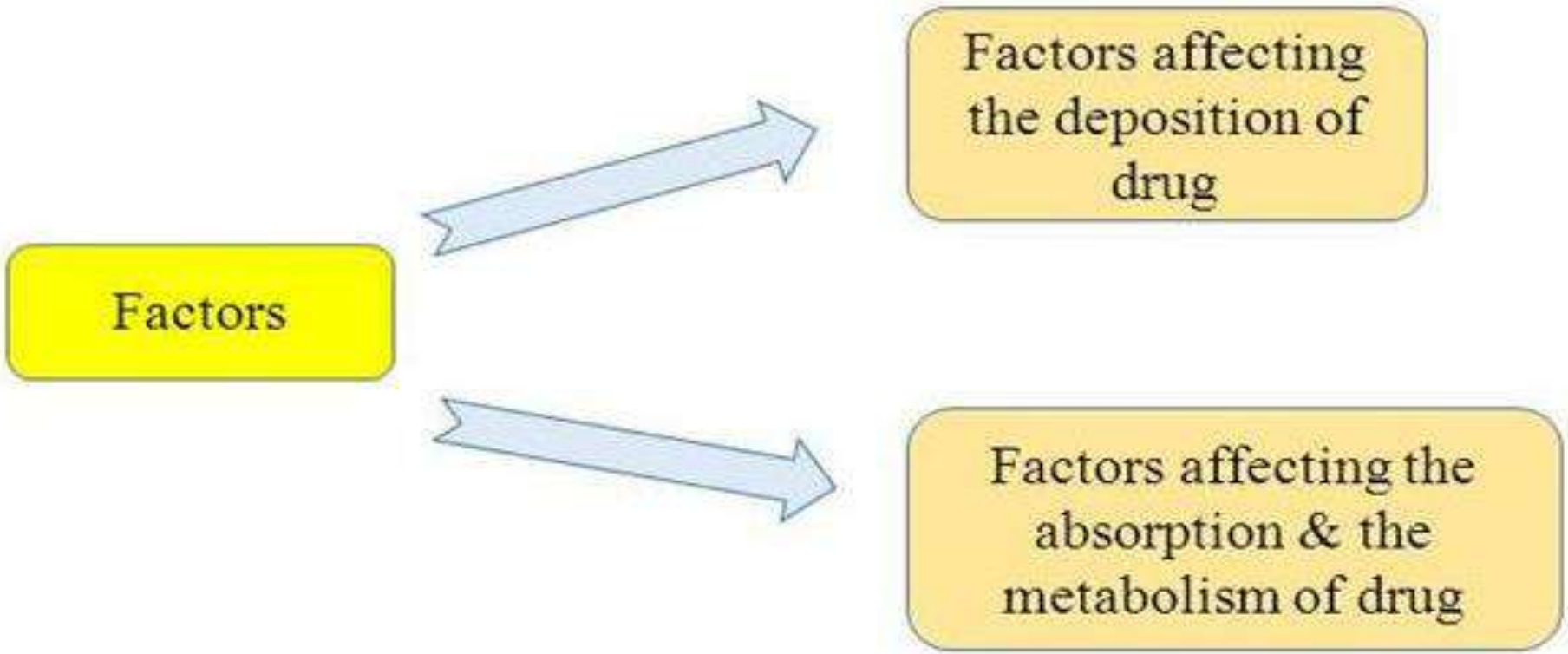
1. Aerosols:

- For local effect, local anesthetic and for asthma.
- For systemic effect: Ergotamine tartrate → Migraine.

2. Anesthetic machines:

- Vapor of the volatile anesthetic liquids to the gas stream.
- The mixture of the O2 + the anesthetic agent is then delivered to a breathing circuit for administration by inhalation.

Factors affecting pulmonary drug delivery system



Deposition of the aerosols to the respiratory tract

- Before absorption, the particles must be deposited at the site of absorption and after deposition the dissolution must occur.
- The deposition of the aerosols in head and tracheobronchial portion is for local effect, and in the pulmonary region(alveoli) is for systemic effect.

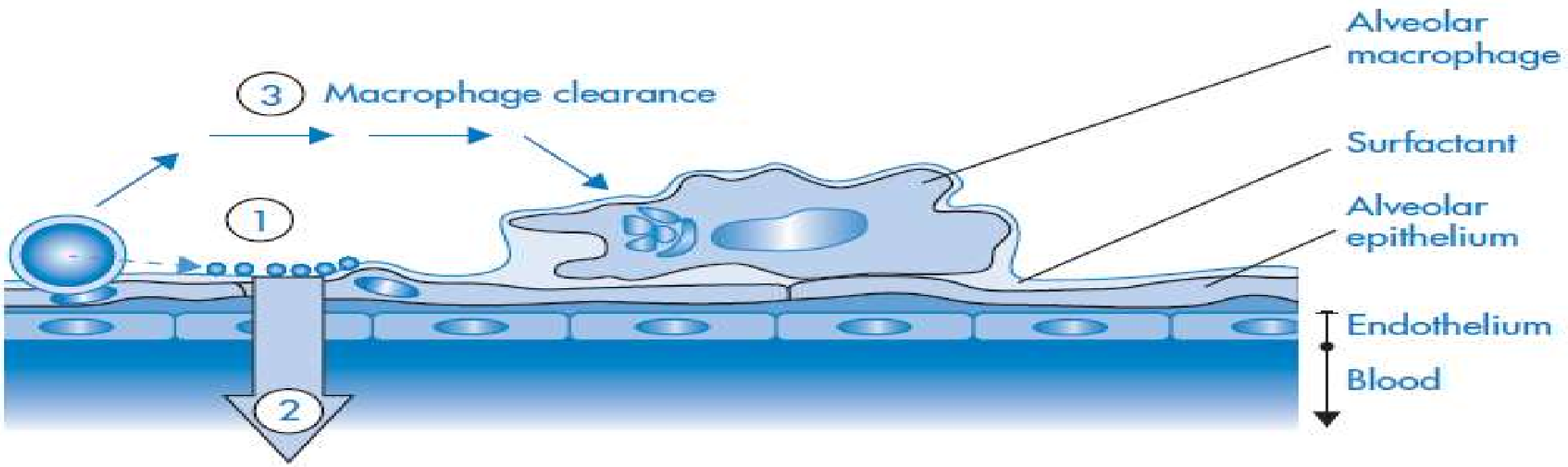


Figure: Diagram of the fate of an aerosol particle in a surfactant-coated alveolar sac. The particle dissolves after landing (1) and is taken up into the alveolar epithelial cell layer (2), transported by transcytotic vesicles into the pulmonary lymph and then into the blood via the capillary endothelium. Alveolar macrophages remove residues.

- Effectiveness of medical aerosols depends on amount of aerosol particles deposition to the lower respiratory tract and deposition of aerosol influenced by many other factors.
- FACTORS INFLUENCING DEPOSITION:

1. The shape of the particles.
2. The density of the particles.
3. The particle size.
4. The charge of particles.
5. The pathology of the respiratory tract.
6. The degree of inhalation.
7. The sedimentation of the particles along the respiratory tract according Stokes' law.

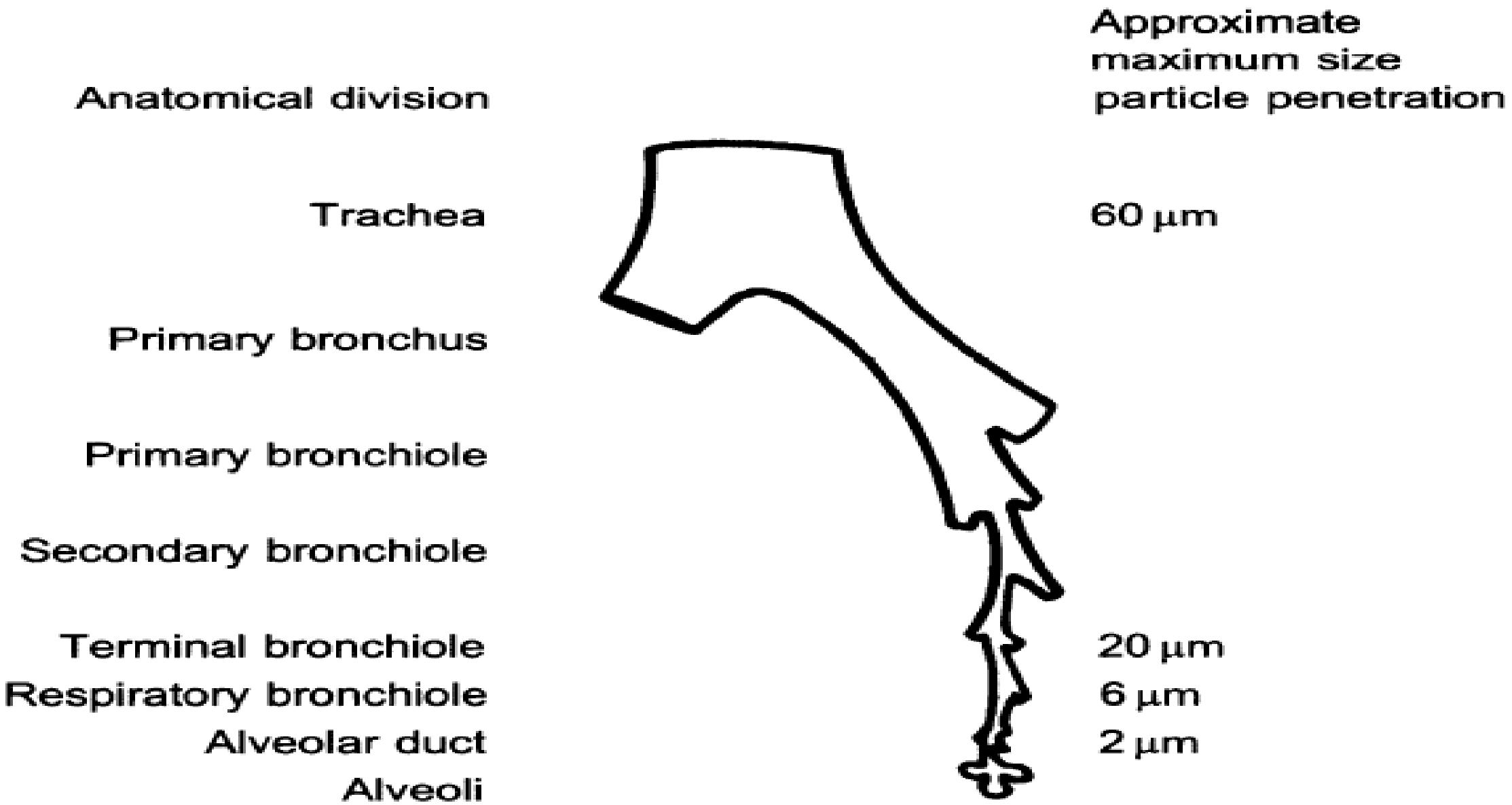
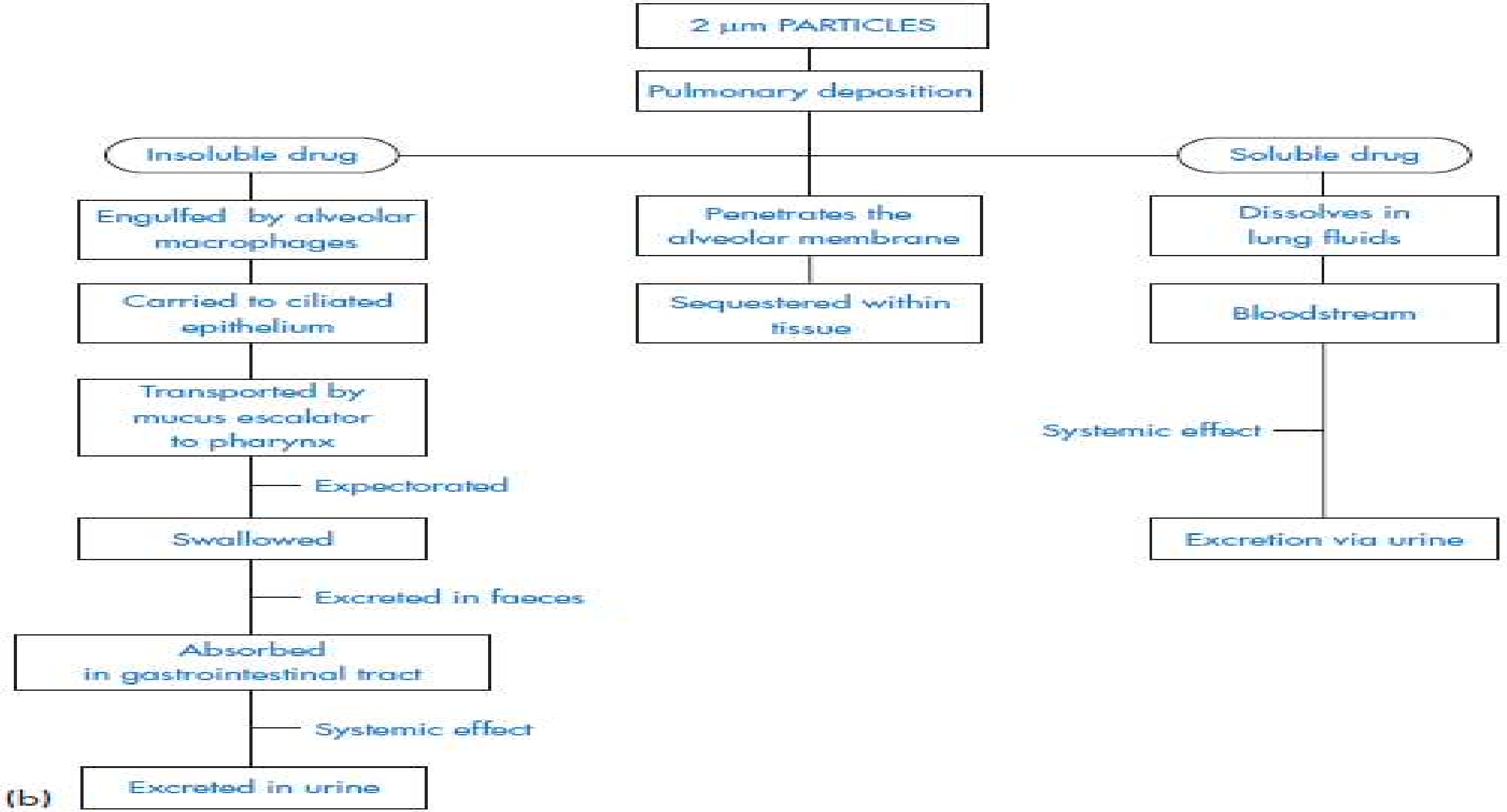
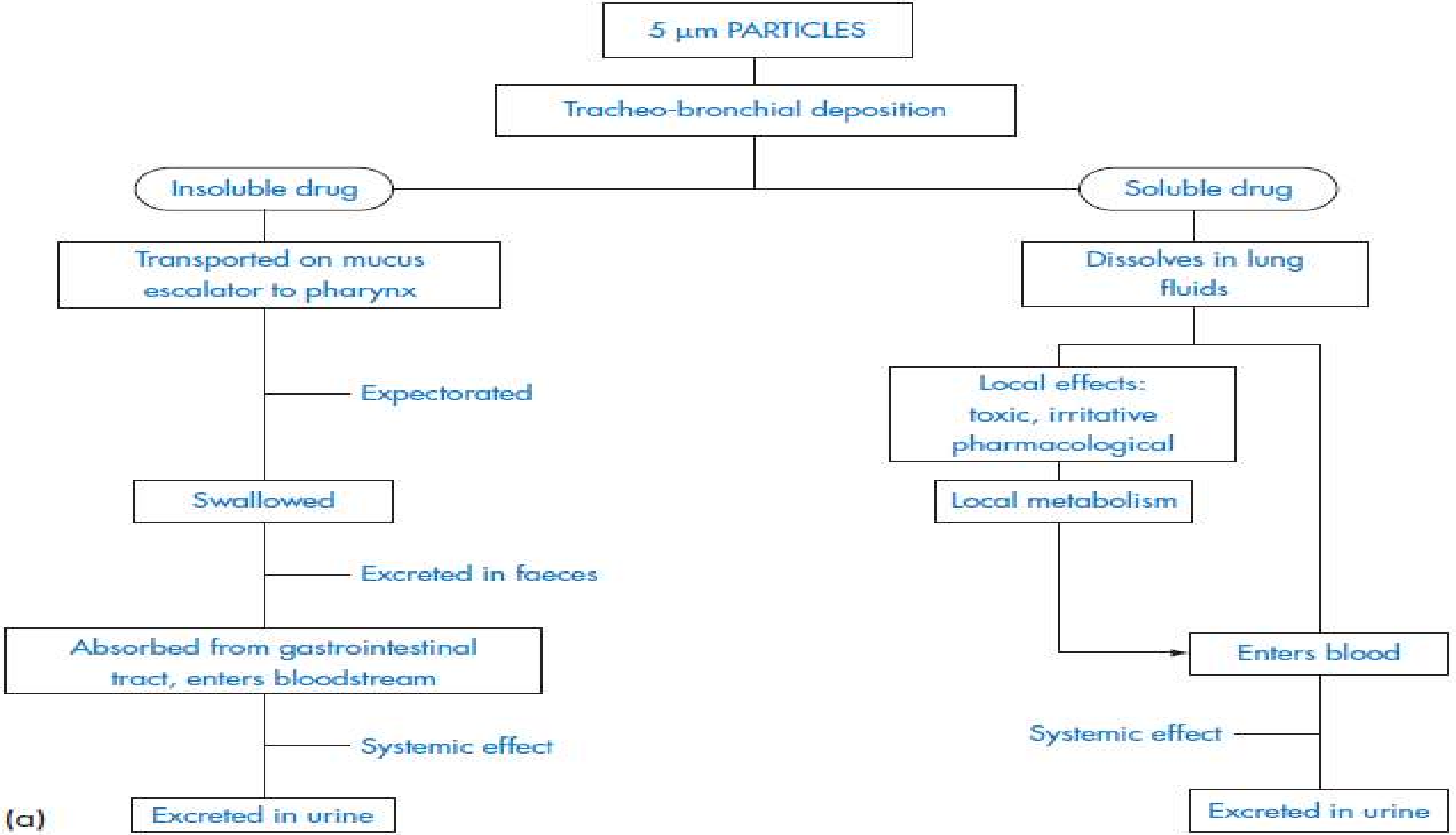


Figure: Deposition of particles in various regions of the respiratory tract according to particle size.


2 μm PARTICLES
Pulmonary deposition
Insoluble drug
Soluble drug
Engulfed by alveolar macrophages
Penetrates the alveolar membrane
Dissolves in lung fluids
Carried to ciliated epithelium
Sequestered within tissue
Bloodstream
Transported by mucus escalator to pharynx
Systemic effect
Expectorated
Swallowed
Excretion via urine
Excreted in faeces
Absorbed in gastrointestinal tract
Systemic effect
Excreted in urine
(b)


5 μm PARTICLES
Tracheo-bronchial deposition
Insoluble drug
Soluble drug
Transported on mucus escalator to pharynx
Dissolves in lung fluids
Expectorated
Local effects: toxic, irritative pharmacological
Swallowed
Local metabolism
Excreted in faeces
Enters blood
Absorbed from gastrointestinal tract, enters bloodstream
Systemic effect
Systemic effect
Excreted in urine
Excreted in urine

(a)

➢Factors affecting the pulmonary absorption:

1. Biological Factors:

A. The thickness of the respiratory tract.

B. The surface area of the alveoli membrane.

C. Blood flow.

D. Pulmonary ventilation.

E. Conc. Gradient.

2. physicochemical Factors:

A. The particle size.

B. Blood/ Gas partition coefficient.

C. The drug conc. In the inspired air.

D. The partial pressure of the drug.

E. Density of the gas.

F. Absolute T of the gases.

3. Dosage form Factors

A. Additives:

1. Surfactant.
2. Propellant and its effect on the vapor pressure.

B. Dosage form type:

1. Solution system→ more available.
2. Suspension system→ orally inhalation aerosols.

GOOD LUCK