Shree H. N. Shukla Institute of Pharmaceutical Education and Research, Rajkot

B. Pharm
Semester-VII

Subject Name: Novel Drug Delivery System
Subject Code: BP704TT

CHAPTER-3- UNIT: 3- NASOPULMONARY DRUG DELIVERY SYSTEM

SYLLABUS:

Nasopulmonary drug delivery system:

Introduction to Nasal and Pulmonary routes of drug delivery, Formulation of Inhalers (dry powder and metered dose), nasal sprays, nebulizers

This subject is designed to impart basic knowledge on the area of novel drug delivery systems.

Learning objectives

Upon completion of the course the student shall be able to

1. To understand various approaches for development of novel drug delivery systems.
2. To understand the criteria for selection of drugs and polymers for the development of Novel drug delivery systems, their formulation and evaluation.

Nasopulmonary Drug Delivery System

What is Nasopulmonary Drug Delivery System (NPDDS)

- It is also a type of muco-adhesive drug delivery system.
- Drugs are administered through nasal cavity by different dosage forms like solutions, emulsions, gels etc.

Nasal pH:

- Adult nasal secretion pH: 5.5-6.5
- Infants & children: 5-6.7.
- It becomes alkaline in conditions rhinitis, acute sinusitis.

Nasal Enzyme

hydrolases, esterases, lactic dehydrogenases, malic enzymes, lysosomal proteinases, steroid hydroxylases etc.

Advantages

- The nasal mucosa has been considered as a potential administration route to achieve faster and higher level of drug absorption.
- This is due to the large surface area & porous endothelial membrane.
- The avoidance of first-pass metabolism, and ready accessibility.
- Route of administration is the poor contact of the formulations with the nasal mucosa.
- Researchers became interested in the nasal route for the systemic delivery of medication due to high degree of vascularization and permeability of the nasal mucosa.

Disadvantages

- Pathologic conditions such as cold or allergies may alter significantly the nasal bioavailability.
- Low bioavailability for proteins and peptides and polar drugs.
- Once administered, rapid removal of the therapeutic agent from the site of absorption is difficult.
- The histological toxicity of absorption enhancers used in nasal drug delivery system is not yet clearly established.

- Relatively inconvenient to patients when compare to oral drug delivery systems since there is a possibility of nasal irritation
- Rapid mucociliary clearance will occurs.
- Chances of immunologic reactions

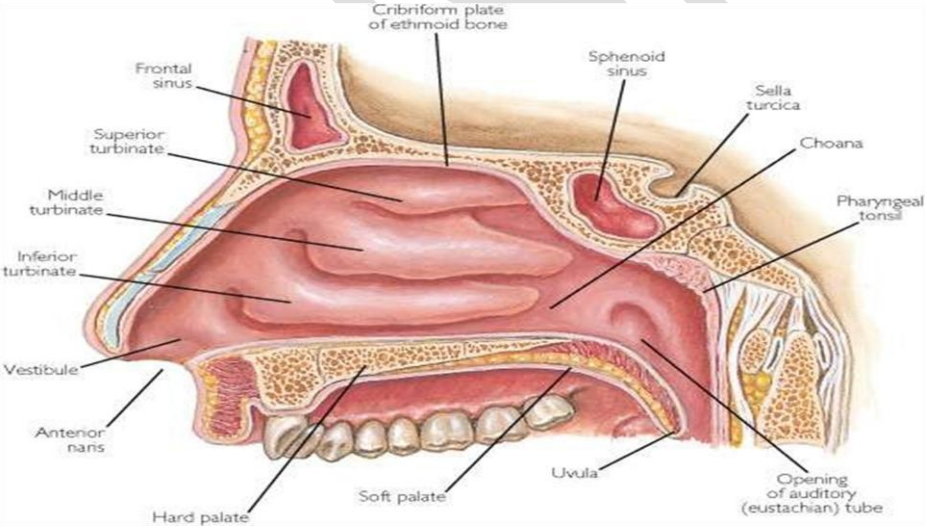
ANATOMY & PHYSIOLOGY OF NOSE

- The nose is an important part of the face; it gives the individual his characteristic appearance.
- The nose is divided into 2 parts:

1. The external nose.
2. The internal nose (nasal cavities)

1. The external nose:

- It is the prominent part of the face, pyramidal in shape.
- The apex is the tip of the nose; the base is the attached area to the forehead. The external nose projecting downwards and is perforated by two apertures called the nostrils separated by the columella.
- The lateral surfaces joined along the dorsum of the nose where it meets the forehead.
- The external nose has a skeleton made up of bony and cartilaginous parts.
- The bony part is the two nasal bones, the nasal processes of the frontal and maxillary bones.



- The cartilaginous part is made up of 2 pairs of lateral cartilages (upper lateral cartilages and lower lateral cartilages) these cartilages are connected by fibrous tissue.
- The lower lateral cartilages help in shaping the nostrils.
- The outer surface is covered by skin, which is thin, and mobile above and thick and adherent to the subcutaneous structures near the tip.

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	What is adult normal nasal secretion pH?	pH: 5.5-6.5
2	hydrolases, esterases, lactic dehydrogenases are found in?	Nasal secretion
3	In which route, avoidance of first-pass metabolism, and ready accessibility?	Nasal route
4	How many parts the nose is divided?	Two
5	How many layers of cartilages part in nose?	Two
6	Nasal bioavailability majorly affected by?	Cold or allergies

2. The internal nose (the nasal cavity)

- The nasal cavity is divided by midline partition (the nasal septum) into right and left chambers.
- It extends from the nostrils in front into the choanae behind (where it opens into the nasopharynx)
- The entrance to the nasal cavity is called the nasal vestibule which ends at themucocutaneous junction, it is lined by skin and contains skin appendages.
- The vestibule is a common site of boil development because it is hair bearing area
- The rest of nasal cavity lined by respiratory mucosa (pseudo-stratified columnar ciliate epithelium), and small area lined by olfactory epithelium.
- Each cavity has a roof, floor, medial and lateral walls.
- The floor is formed by the palatine process of the maxilla and the horizontal process of palatine bone.
- The roof is narrow and is formed (from behind forward) by the body of the sphenoid,cribriform plate of the ethmoid and the frontal bone.
- *Clinical point (4): cribriform plate is a thin plate of bone and easily to be fractured in head injury and may associated with CSF leak through the nose.*
- The medial wall (the nasal septum) is an osteocartilaginous partition covered by adherent mucoperichondrium and mucoperiostium.
- The upper part is formed by the perpendicular plate of the ethmoid bone, the posterior part by the vomer and the anterior portion is formed by septal cartilage.
- The lateral wall is the most complex, it contains 3 shelf –like projections into the nasal cavity called the turbinates (the superior, middle and the inferior turbinates).
- The groove below each turbinate is referred to as a meatus.
- There are 3 meati called the superior, middle and the inferior meatus) into these meati the paranasal sinuses open and join the nasal cavity.
- The area above the superior turbinate is called the sphenoethmoial recess.

MECHANISM OF DRUG ABSORPTION

- The first step in the absorption of drug from the nasal cavity is passage through the mucus.
- Small, unchanged particles easily pass through this layer.
- However, large or charged particles may find it more difficult to cross.

- Solutes, hindering diffusion.
- Structural changes in the mucus layer are possible as a result of environmental changes (i.e. pH, température, etc.) subsequent to a drug's passage through the mucus.
- There are several mechanisms for absorption through the mucosa.
- These include transcellular or simple diffusion across the membrane, paracellular transport *via movement between* cell and transcytosis by vesicle carriers.
- Drug absorption are potential metabolism before reaching the systemic circulation and limited residence time in the cavity.

Following mechanisms have been proposed:

- The first mechanism involves an aqueous route of transport, which is also known as the paracellular route.
- This route is slow and passive.
- There is an inverse log-log correlation between intranasal absorption and the molecular weight of water-soluble compounds.
- Poor bioavailability was observed for drugs with a molecular weight greater than 1000 Daltons.
- The second mechanism involves transport through a lipoidal route that is also known as the transcellular process and is responsible for the transport of lipophilic drugs that show a rate dependency on their lipophilicity.
- Drugs also cross cell membranes by an active transport route *via* carrier-mediated means or transport through the opening of tight junctions.

FACTORS INFLUENCING NASAL DRUG ABSORPTION

Factors Related to Drug

a) Lipophilicity

- On increasing lipophilicity, the permeation of the compound normally increases through nasal mucosa because of high lipophilicity though it has some hydrophilic character.eg: alprenolol and propranolol.

b) Chemical Form

It's an important factor for absorption.

- Conversion of the drug into a salt or ester form can alter its absorption. eg: *In-situ* nasal absorption of carboxylic acid esters of L-Tyrosine was significantly greater than that of L-Tyrosine.

c) Polymorphism

- Polymorphism is known to affect the dissolution rate and solubility of drugs and as well as their absorption through biological membranes.

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	The area above the superior turbinate is called?	sphenoethmoial recess
2	How many meatus are found in nose?	Three
3	In first step nasal drug absorption occurs in?	Nasal cavity through mucous
4	Structure changes in mucus layer due to?	Change in environmental condition
5	The first mechanism involves an aqueous route of transport, which is also known as ?	Paracellular route
6	How much bioavailability was observed for drugs with a molecular weight greater than 1000 Daltons.	Poor bioavailability
7	In nasal mucosa higher lipophilicity shows?	Greater penetration

- It is therefore advisable to study the polymorphic stability and purity of drugs for nasal powders or suspensions.

d) Molecular Weight

- In the case of lipophilic compounds, a direct relationship exists between the Molecular Weight and drug permeation where as water soluble compounds depict an inverse relationship.
- The permeation of drugs less than 300Da is not significantly influenced by the physicochemical properties of the drug, which will mostly permeate through aqueous channels of the membrane.
- By contrast, the rate of permeation is highly sensitive to molecular size for compounds with MW = >300 Da.

e) Partition Coefficient and pKa

- As per the pH partition theory, unionized species are absorbed better compared with ionized species and the same holds true in the case of nasal absorption.
- Quantitative relationship between the physicochemical properties of drugs and their nasal absorption, the results showed that a quantitative relationship existed between the partition coefficient and the nasal absorption constant.
- The nasal absorption of weak electrolytes such as salicylic acid and amino-pyrine was found to be highly dependent on their degree of ionization.
- Although for amino-pyrine, the absorption rate increased with the increase in pH and was found to fit well to the theoretical profile.
- Substantial deviations were observed with salicylic acid.
- The authors concluded that perhaps a different transport pathway, along with the lipoidal pathway, eg:salicylic Acid pathways.

B) Factors Related to Formulation

1) *Physicochemical Properties of the Formulation*

a) *pH and Mucosal Irritancy*

- The pH of the formulation, as well as that of nasal surface, can affect a drug's permeation. To avoid nasal irritation, the pH of the nasal formulation should be adjusted to 4.5–6.5. In addition to avoiding irritation, it results in obtaining efficient drug permeation and prevents the growth of bacteria.

b) Osmolarity

- Because of the effect of osmolarity on the absorption isotonic solutions are usually preferred for administration for shrinkage of the nasal epithelial mucosa.

- This results in increased permeation of the compound resulting from structural changes

c) Viscosity

- A higher viscosity of the formulation increases contact time between the drug and the nasal mucosa there by increasing the time for permeation.
- At the same time, highly viscous formulations interfere with the normal functions like ciliary beating or mucociliary clearance and thus alter the permeability of drugs.

POLYMERS FOR NASAL DDS:

Mucoadhesive polymer	Drug	Dosage form	Reference
CMC	Apomorphine	Powder	Ugwoke MI *et al.*[7]
MCC	Ketorolac acid	Spray	Quadir M *et al.*[44]
MCC/HPC	Leapralide	Powder	Suzuki Y *et al.*[28]
HPC	Dopamine	Liquid	Ikeda K *et al.*[38]
HPC	Metaclopramide	Gel	Zaki NM *et al.*[32]

DOSAGE FORM USED FOR DEVELOPING THE FORMULATION

1.Nasal drop
2.Nasal spray
3.Nasal gel
4.Nasal powder

1. Nasal drop

- Most simple and convenient systems developed for nasal delivery.
- The main disadvantage of this system is the lack of dose precision and therefore nasal drops may not be suitable for prescription products.
- It has been reported that nasal drops deposit human serum albumin in the nostrils more efficiently than nasal sprays

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	Water soluble compounds depict relationship to permeation?	Inverse relationship
2	For osmoloarity principle, which is preferred for administration to avoid nasal mucosal shrinkage?	Isotonic solution
3	Absorption of unionized molecule is ?	Greater as compared to ionized drug
4	Viscosity is increased than increase contact time so that affects on drug release?	Slow drug release
5	Most simple and convenient systems developed for nasal delivery is?	Nasal drops
6	Nasal drops are retained in which type of protein that found in nasal mucosa?	Albumin

2. Nasal Spray

- Both solution and suspension formulations can be formulated into nasal sprays.
- Due to the availability of metered dose pumps and actuators,
- a nasal spray can deliver an exact dose from 25 to 200 L.
- The particle size and morphology (for suspensions) of the drug and viscosity of the formulation determine the choice of pump and actuator assembly.
- Solution and suspension sprays are preferred over powder sprays because powder results in mucosal irritation.

3. Nasal Gels

- Nasal gels are high-viscosity thickened solutions or suspensions.
- Until the recent development of precise dosing devices, there was not much interest in this system.
- The advantages of a nasal gel include the reduction of post-nasal drip due to high viscosity, reduction of taste impact due to reduced swallowing, reduction of anterior leakage of the formulation, reduction of irritation by using soothing/emollient.
- Excipients and target delivery to mucosa for better absorption.

4. Nasal Powders

- This dosage form may be developed if solution and suspension dosage forms cannot be developed e.g., due to lack of drug stability.
- The advantages to the nasal powder dosage forms are the absence of preservative and superior stability of the formulation.
- However, the suitability of the powder formulation is dependent on the solubility, particle size, aerodynamic properties, and nasal irritancy of the active drug and/or excipients.
- Local application of drug is another advantage of this system but nasal mucosa irritancy and metered dose delivery are some of the challenges for formulation.

Generally, the absorption enhancers act via one of the following mechanisms:

- Inhibit enzyme activity;
- Reduce mucus viscosity or elasticity;
- Decrease muco-ciliary clearance;
- Open tight junctions;
- Solubilize or stabilize the drug.
- Absorption enhancers are generally classified as physical and chemical enhancers. Chemical enhancers act by destroying.

Applications

1. ***Delivery of non-peptide*** pharmaceuticals Drugs with extensive pre-systemic metabolism, such as progesterone, estradiol, propranolol, nitroglycerin, sodium chromoglyate can be rapidly absorbed through the nasal mucosa with a systemic bioavailability of approximately 100%.
2. ***Delivery of peptide-based pharmaceuticals***
   Peptides & proteins have a generally low oral bioavailability because of their physico-chemical instability and susceptibility to hepato-gastrointestinal first-pass elimination. E.g. Insulin, Calcitonin, Pituitary hormones etc. Nasal route is proving to be the best route for such biotechnological products.
3. ***Delivery of diagnostic drugs***
   Diagnostic agents such as Phenolsulfonphthalein – kidney function Secretin – pancreatic disorders. Pentagastrin – secretory function of gastric acid are administered through the nasal route.

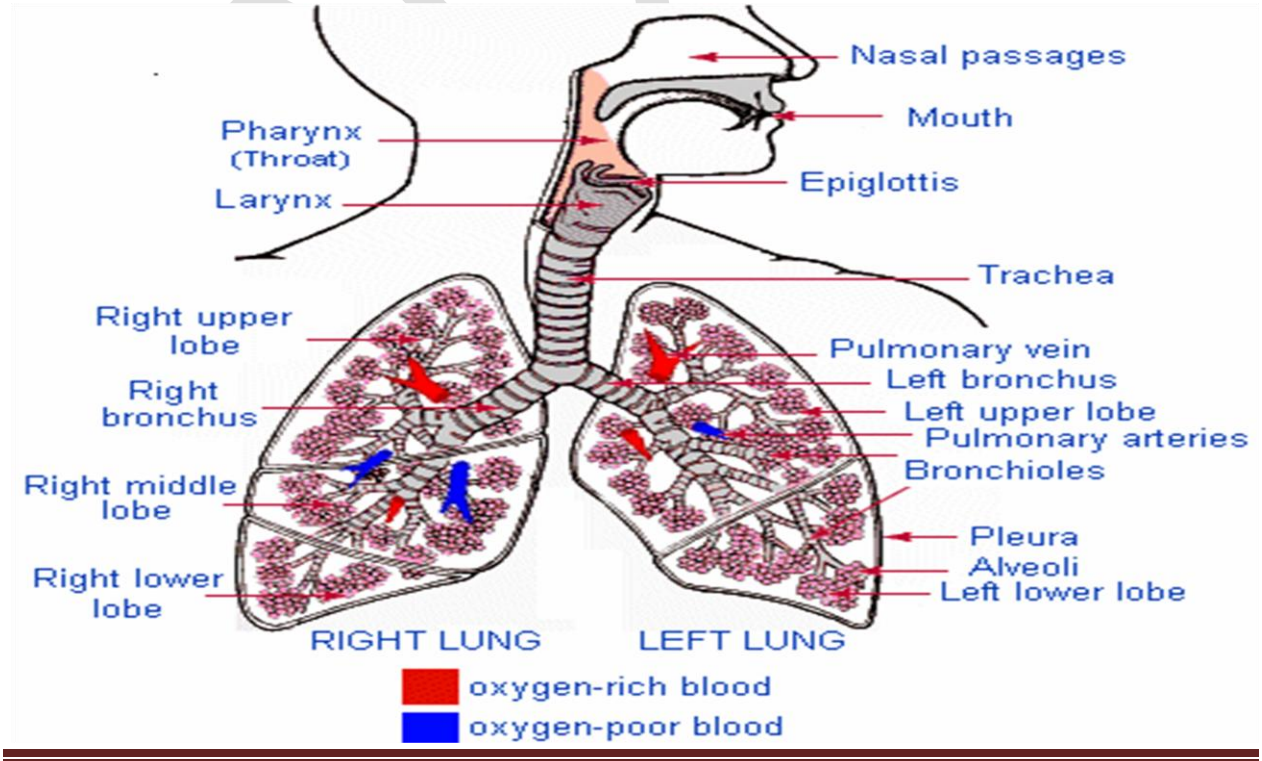
PULMONARY DRUG DELIVERY SYSTEM

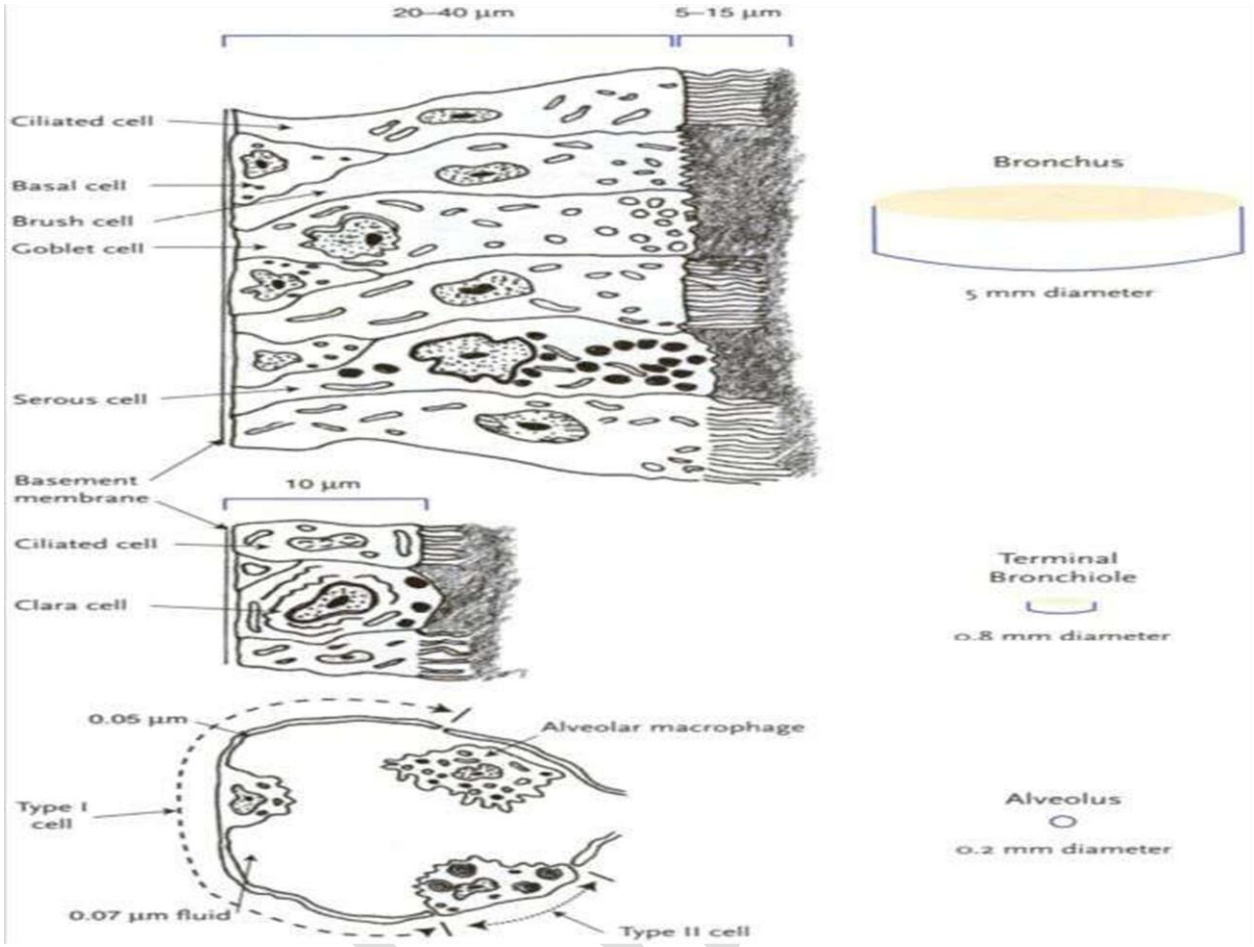
- Pulmonary route was use to treatment of different respiratory diseases from the last decade.
- The inhalation therapies involved the use of leaves from plants, vapors from aromatic plants like balsams, and myhrr.
- In the 1920 s adrenaline can introduce as a nebulizer solution, in 1925 nebulizer porcine insulin was use in investigational studies in diabetes, and in 1945 pulmonary delivery of the newly revealed penicillin was investigated.
- Steroids had been introduced in between 1950s for the treatment of asthma and nebulizers were enjoy widely use.
- In 1956 the pressured metered dose inhaler (pMDI) was placed.
- Lung associated bigger protein molecules may degrade into the gastrointestinal situation and are excreted through the first pass metabolism into the liver, which can be transferred through the pulmonary route if deposited in the respiratory passage of the lungs.

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	Which type of formulations can be formulated into nasal sprays.	Solution and suspension
2	nasal spray can deliver how much dose?	25-500 microliter
3	Which formulation reduce post-nasal drip due to high viscosity, reduction of taste impact due to reduced swallowing, reduction of anterior leakage of the formulation, reduction of irritation by using soothing/emollient.	Nasal gel
4	The advantages of nasal powder dosage forms over nasal drop is?	absence of preservative and superior stability
5	Which route was use to treatment of different respiratory diseases from the last decade?	Pulmonary route
6	Delivery of peptide based drug is easily carried out by?	Nasal route
7	Pressurized meter dose inhaler was established in?	1956

DIFFERENT REGIONS OF THE HUMAN RESPIRATORY TRACT





ANATOMY AND PHYSIOLOGY OF LUNGS

1) Lung regions:-

- The respiratory tract starts at the nose and terminates deep in the lung at an alveolar sac.
- There are a number of schemes for categorizing the various regions of the respiratory tract.

2) Nasopharyngeal region:-

- This is also referred to as the “upper airways”, which involves the respiratory airways from the nose down to the larynx.

3) Tracheo-bronchial region:-

- This is also referred to as the “central” or “conducting airways”, which starts at the larynx and extends via the trachea, bronchi, and bronchioles and ends at the terminal bronchioles.

4) Alveolar region:-

- This is also referred to as the “respiratory airways”, “Peripheral airways” or “pulmonary region”, Comprising the respiratory bronchioles, alveolar ducts and alveoli.
- The term “pulmonary” can be used to the alveolar region.

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	The term “pulmonary” can be used for?	Alveolar region
2	Which region is started at the larynx and extends via the trachea, bronchi, and bronchioles and ends at the terminal bronchioles?	Tracheo-bronchial
3	Which region starts at the nose and terminates deep in the lung at an alveolar sac?	Lung region
4	What is referred as upper airways?	Nasopharyngeal region
5	Dry powder and Nebulizer are example of?	Dry Inhalation

- The use of "upper respiratory tract"

Pulmonary epithelium:-

- The lung contains more than 40 different cell types, of which more than six line the airways.
- The diversity of pulmonary epithelia can be illustrated by examining its structure at three principal levels.

The bronchi:-

- These are lined predominantly with ciliated and goblet cells.
- Some serous cells, brush cells and Clara cells are also present with few Kulchitsky cells.

The bronchioles:-

- These are primarily lined with ciliated cuboidal cells.
- The frequency of goblet and serous cells decreases with progression along the airways while the number of Clara cells increases.

The alveolar region:-

- This is devoid of mucus and has a much flatter epithelium, which becomes the simple squamous type, 0.1–0.5 μm thick.

Two principal epithelial cell types are present:

Type-I pneumocytes:

- Thin cells offering a very short airways- blood path length for the diffusion of gasesand drug molecules.
- Type-I pneumocytes occupy about 93% of the surface area of the alveolar sacs.

Type-II pneumocytes:

- Cuboidal cells that store and secrete pulmonary surfactant.
- Alveolar macrophages account for ~ 3% of cells in the alveolar region.
- These phagocytic cells scavenge and transport particulate matter to the lymph nodes and the mucociliary escalator.

Ciliated cells:-

- In the trachea bronchial region, a high proportion of the epithelial cells are ciliated such that there is a near complete covering of the central airways by cilia.
- Towards the periphery of the tracheobronchial region, the cilia are less abundant and are absent in the alveolar region.
- The ciliated cells each have about 200 cilia with numerous interspersed microvilli, of about 1–2 μm in length.
- The cilia are hair-like projections about 0.25 μm in diameter and 5 μm in length.

- Cilias are submersed in an epithelial lining fluid, secreted mainly from the serous cells in the sub-mucosal glands.
- The tips of the cilia project through the epithelial lining fluid into a layer of mucus secreted from goblet cells.
- The cilia beat in an planned fashion to propel mucus along the airways to the throat.

Mechanism of particle deposition airways

- Effective resistance mechanisms may have involved may reduces the burden of external particles enter the airways, and clearing those it may achieve something in being stored.
- Therapeutic aerosols are two-phase colloidal systems in that the Drug is contained in a dispersed phase they may have a solid,
- Liquid or combination of the two, based on the method and formulation of aerosol generation.
- Evidently, for effective therapy, the drug must have obtain able to the lung in aerosol droplets or particles that deposit in the specific lung region and insufficient quantity to be effective.
- The respiratory resistance mechanisms of mucociliary clearance and phagocytosis by macrophages may act upon insoluble particles.
- Aerosol particle dissolution they may slow and the drug may then subsequently to be subject to enzymatic deprivation before it reaches to its specific site of pharmacological action.
- Aerosols for pulmonary drug delivery are transported from the mouth.

Inertial impaction

- This is the main deposition mechanism for particles >1 µm in the upper tracheo-bronchial regions.
- A particle having a large momentum it may not able to follow the altering direction of the inspired air as it transferred the bifurcations and it will show result to collide with the airway walls as it continues on its original course.
- Description of particle deposition mechanisms at an airway branching site
- Impaction it mainly occurs near the bifurcations, certainly the impaction of particles from tobacco smoke on the bifurcations may be one cause why these sites are often the foci for lung tumors.
- The prospect of inertial impaction will be dependents upon particle momentum, thus particles with higher densities or larger diameter and those travelling in airstreams of higher velocity will show superior impaction.

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	Which region is devoid of mucus and has a much flatter epithelium?	Alveolar region
2	Dimension of cilia is?	0.25 µm in diameter and 5 µm in length.
3	In which region, the cilia are less abundant and are absent.	alveolar region
4	What is the function of cilia beat?	to propel mucus along the airways to the throat
5	What are two-phase colloidal systems in that the Drug is contained in a dispersed phase?	Therapeutic aerosols
6	How much size of particles are retained in the upper tracheo-bronchial regions?	>1 µm

Sedimentation:-

- By the settling under gravity the particles may deposited.
- It becomes highly important for particles that reach airways where the airstream velocity is relatively low, e.g. the bronchioles and alveolar region.
- The fraction of particles depositing by this mechanism it may dependent upon the time the articles use in these regions.

Brownian diffusion:-

- This is of minor significance for particles >1 µm.
- Particles smaller than this size are displaced by a sequentially bombardment of gas molecules, which may results in particle collision with the airway walls.
- The chances of particle deposition by diffusion increases with the particle size decreases.
- Brownian diffusion is also more common in regions where airflow is very low or absent, e.g. in the alveoli.
- **Deposition:** ie interception is of important for fibers but it may not for drug delivery.
- Generally Particles bigger than 10 µm will have impact in the upper airways and are rapidly removed by swallowing, coughing, and mucociliary processes.
- The particles in the size range 0.5–5 µm may break away from impaction in the upper airways and may deposit by sedimentation and impaction in the lower TB and A regions.
- If the aerosol particle size is between the 3 and 5 µm then deposition it mainly occur in the TB region.
- If the particles are smaller than the 3 µm then appreciable deposition in the A region is likely to occur.

PHYSIOLOGICAL FACTORS AFFECTING PARTICLE DEPOSITION IN THE AIRWAYS:

Lung morphology:-

- Each successful production of the tracheobronchial tree produces airways of falling diameter and length.
- Every bifurcation results in an increase possibility for impaction and the decrease in airway diameter is associated with a smaller displacement necessary a particle to make contact with a surface.

Inspiratory flow rate:-

- When the inspiratory flow rate increases, they enhance deposition by impaction in the first few generations of the TB region.

- The increase in flow not only increase particle momentum but also result in an increase in turbulence, mostly in the larynx and trachea, which itself will enhance impaction in theproximal tracheo-bronchial region.

Advantages

1. It is needle free pulmonary delivery.
2. It requires small and fraction of oral dose.
3. Low concentration in the systemic circulation are associated with reduced systemic side effects.
4. Rapid Onset of action
5. Avoidance of gastrointestinal upset
6. Degradation of drug by liver is avoided in pulmonary drug delivery.

Disadvantages

1. Oropharyngeal deposition gives local side effect.
2. Patient may have difficulty using the pulmonary drug devices correctly

APPLICATIONS

1) In Asthma and COPD:

- Asthma is a chronic lung that disease is characterized by inflammation and narrowing of airways & it causes recurring period so wheezing, shortness of breath, chest tightness, and coughing.
- For treatment of asthma for ex-levosalbutamol inhalers which show greater efficacy as compare to salbutamol.
- COPD means chronic obstructive pulmonary diseases.
- For the treatment of COPD titropium inhalers are present in market.

2) Pulmonary delivery inpatients on ventilators:

- Now a day's Baby mask is used as patient device & is attached to spacer for small tidal volumes and low inspiratory flow rates infant and young Childers.
- We can easily give medication to child up to 2 years by using baby mask.

3) In cystic fibrosis

- Now a days cystic fibrosis is very common disease pulmonary delivery played an important role in the treatment of CF for decades.
- The main aim of aerosol system is to deliver drugs to infants and children's.
- Ex: N-Acetylcysteine, Tobramycin-spray dried.

4) In Diabetes

- Diabetes is deficiency of insulin secretion or resistance. Insulin inhalers would work much like asthma inhalers.

The products fall into two main groups the dry powder formulations and solution, which are delivered through different patented inhaler systems.

E.g. Novel pMDI formulations for pulmonary delivery of proteins

- **One Word Question Answer**

SR NO.	QUESTION	ANSWER
1	the settling under gravity the particles may deposited is called?	Sedimentation
2	The chances of particle deposition by diffusion increases with?	Particle size increase
3	Where Brownian motion is found in common?	where airflow is very low or absent, e.g. in the alveoli.
4	Which technique is needle free, and avoidance of GI degradation by?	Aerosol
5	What is short name of chronic obstructive pulmonary diseases?	COPD
6	Which size of particles impact in the upper airways and are rapidly removed by swallowing, coughing, and mucociliary processes.	Particles bigger than 10 µm
7	For treatment of asthma, which inhalers show greater efficacy as compare to salbutamol.	Levosalbutamol

5) In Migraine:

- Ergotamine is the drug of choice of migraine & earlier it has been used through inhalation (pulmonary route).

6) In Angina Pectoris:

- Nitroglycerine is drug of choice for angina pectoris has been given generally by sublingual route .
- Isosorbide aerosol has also been reported useful in hypertensive crisis.
- In United States inhalation therapy for angina-pectoris is very well accepted .

7) Role in vaccination :

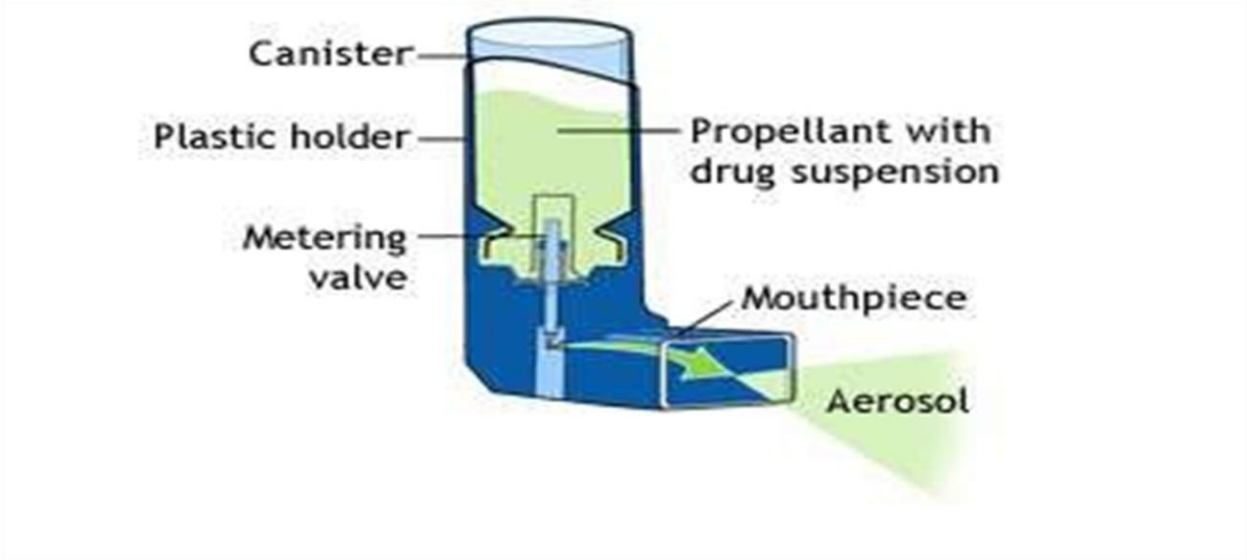
- Nearly 100 vaccines are approved in the U. S. About half of these prevent respiratory infections, yet all are currently injected
- Recently inhaled measles vaccine given by nebulizer.
- As far back as the 1960, influenza experts tested aerosol flu vaccines.

RECENT TECHNOLOGIES OF PULMONARY DRUG DELIVERY:

Nebulizer:

- In jet nebulizers, an aerosol is prepared by a high velocity air stream from a pressurized source directed against a thin layer of liquid solution.
- Ultrasonic nebulizers include the vibration of a piezoelectric crystal aerosolizing the solution.
- The nebulizer can transport more drugs to the lungs than MDI or DPI.
- The most common disadvantage of nebulizer are lack of possibility, higher costs of drug delivery as a result of the larger need for assistance from healthcare professionals.

Meterdose inhaler



- These are the most common device for administration of aerosolized drugs.
- In this technique, a medication is mixed in a canister with a propellant, and the preformed mixture is expelled in exact measured amounts upon actuation of the device.
- EX: Drugs which are administered through this device

One Word Question Answer

SR NO.	QUESTION	ANSWER
1	inhaled measles vaccine given by?	Nebulizer
2	Which inhaler has lack of possibility, higher costs of drug delivery as a result of the larger need for assistance from healthcare professionals is found in?	Nebulizer
3	The vibration of a piezoelectric crystal aerosolizing the solution is found in?	Ultrasonic nebulizers
4	Which type of aerosol is prepared by a high velocity air stream from a pressurized source directed against a thin layer of liquid solution?	Jet nebulizer
5	Which is the drug of choice of migraine?	Ergotamine
6	In which technique medication is mixed in a canister with a propellant, and the preformed mixture is expelled in exact measured amounts upon actuation of the device.	Meter dose inhaler