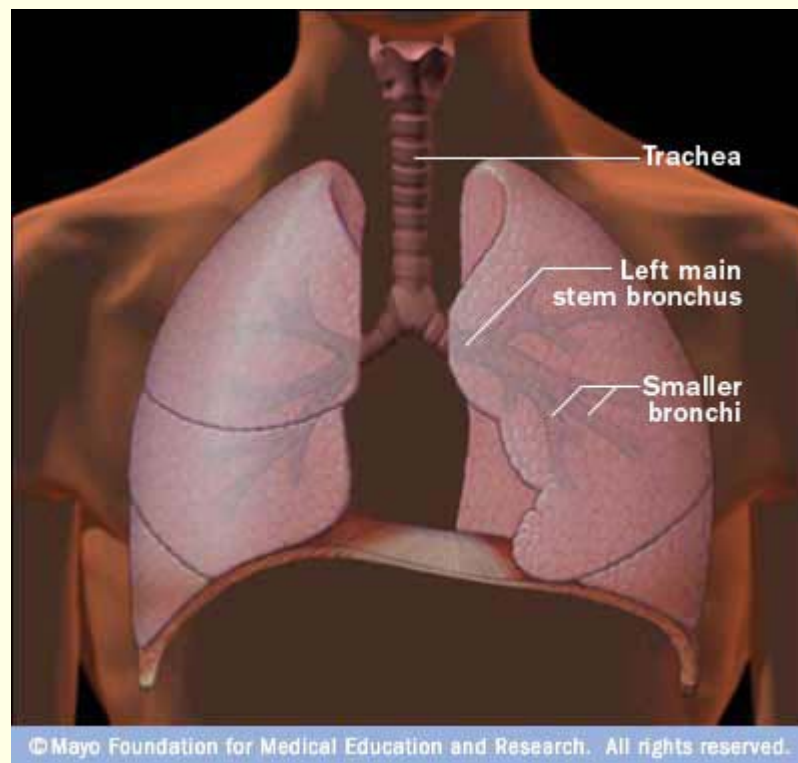


Inhaled Drug Delivery Science and Technology



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What are we going to learn in this presentation?

- Respiratory system and its functioning
- Respiratory Illness: causes and effects
- Ways to deliver medicine/drug to Lungs
- Working of medicine delivery devices
- Role of computer in developing new technology

Let us begin the journey....

What is Inhalation?

How about a movie?

Respiratory System

Oral Cavity – Mouth

Nasal Cavity – Nose

Pharynx

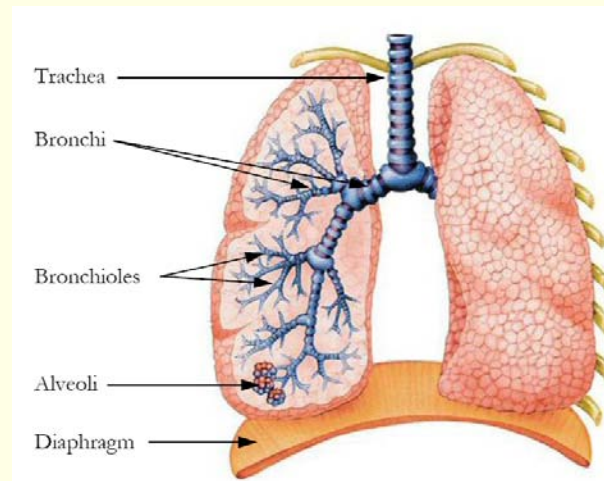
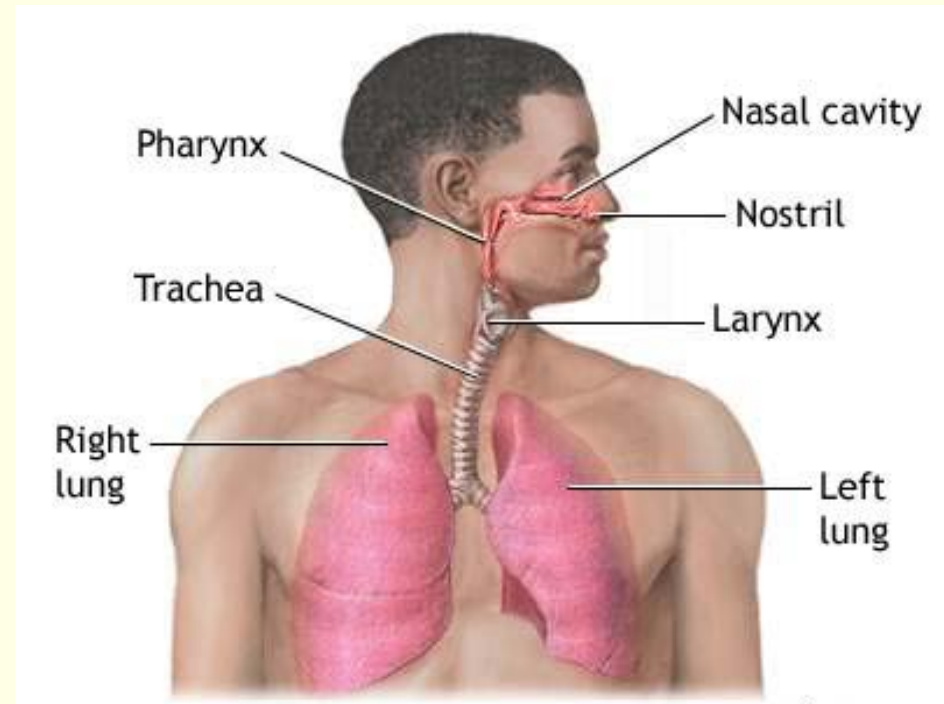
Larynx

Trachea

Bronchi

Bronchiole

Alveoli



<http://health.allrefer.com>

Respiratory System : Main Function

The primary function of the respiratory system is to supply the blood with oxygen in order for the blood to deliver oxygen to all parts of the body.

The respiratory system does this through breathing. When we breathe, we inhale oxygen and exhale carbon dioxide.

This exchange of gases is the respiratory system's means of getting oxygen to the blood.

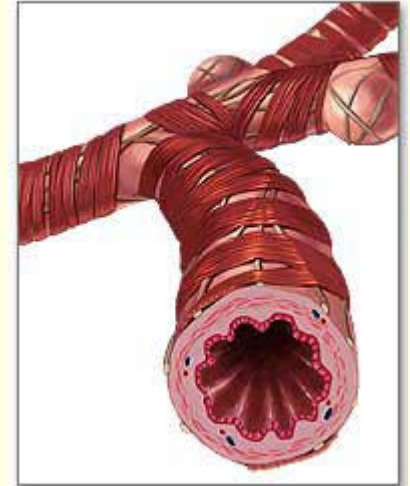
Chronic Respiratory Illness

Asthma

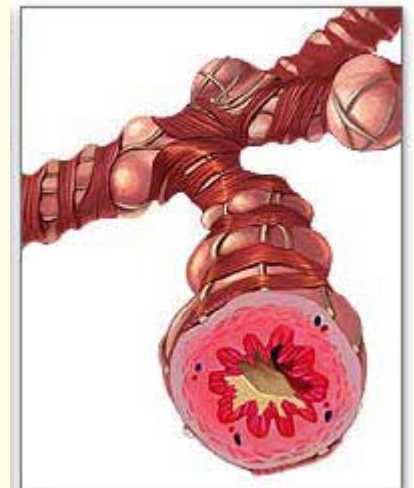
What is Asthma?

- Causes reversible inflammation and narrowing of lung airways.
- During Asthma attack patient experiences wheezing, chest tightness and shortness of breath, and coughing
- It affects over 30 Crore (30,000,0000) people in the world

Normal bronchiole



Asthmatic bronchiole

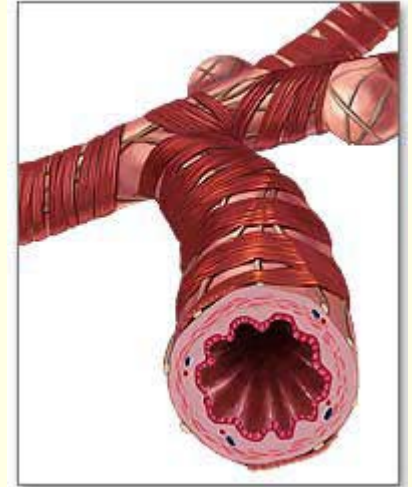


Asthma

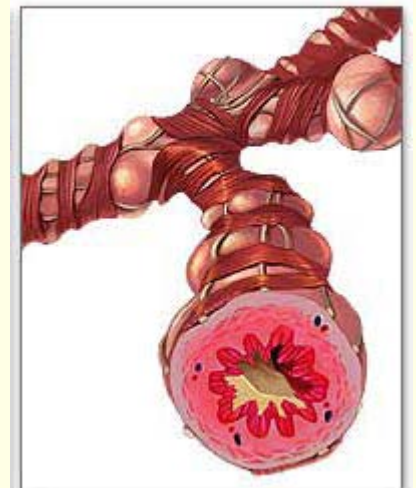
What triggers Asthma attack?

- Allergens found in dust, animal fur, cockroaches, pollens
- Irritants such as cigarette smoke, air pollution, dust
- Sulfites in foods and drinks
- Viral upper respiratory infections due cold
- Exercise (physical activity)

Normal bronchiole



Asthmatic bronchiole



Chronic Obstructive Pulmonary Disease- COPD

What is COPD?

A progressive disease that makes it hard to breathe. "Progressive" means the disease gets worse over time.

In COPD, less air flows in and out of the airways because of one or more of the following:

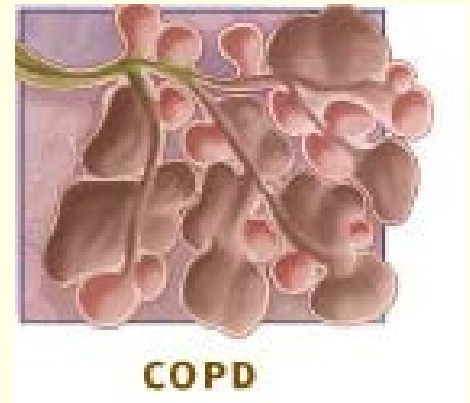
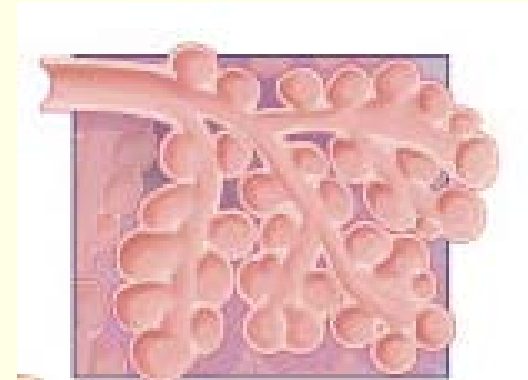
The airways and air sacs lose their elastic quality.

The walls between many of the air sacs are destroyed.

The walls of the airways become thick and inflamed (swollen).

The airways make more mucus than usual, which tends to clog the airways.

It affects over 1 Crore (1,000,0000) people in the world.

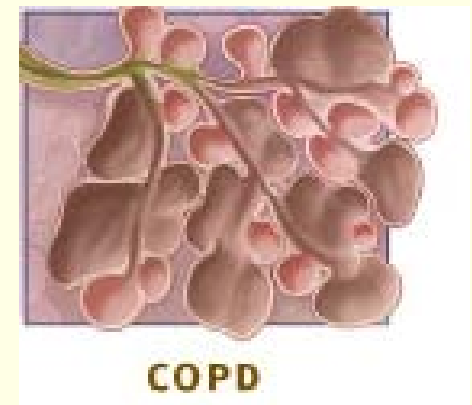
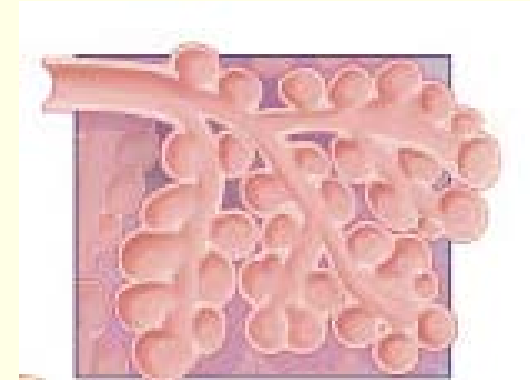


Chronic Obstructive Pulmonary Disease- COPD

- What causes COPD?

Cigarette smoking is the leading cause of COPD

Long-term exposure to other lung irritants, such as air pollution, chemical fumes, or dust.



Inhaled Medicine for the treatment of Chronic Respiratory Illness

Inhaled Medicine

Bronchodilator

Short-Acting beta Agonist

Given to patient for quick relief of bronchospasm in conditions such as asthma and chronic obstructive pulmonary disease.

Example: Salbutamol, Ventolin, Aerolin etc.

Long-Acting Beta Agonist

Usually prescribed for severe persistent asthma following previous treatment with a short-acting beta agonist. These medicine causes broncho-dilation by relaxing the smooth muscle in the airway so as to treat the exacerbation of asthma. The duration of action last for 12 hours.

Example: Salmeterol, Formoterol, Bambuterol etc.

Anti-Inflammation Inhaled Corticosteroid

All forms of corticosteroids reduce inflammation in the airways that carry air to the lungs (bronchial tubes) and decrease the mucus made by the bronchial tubes. This makes it easier to breathe. The duration of action last for 12 hours.

Example: Beclomethasone, Fluticasone, Ciclesonide

**Delivery Device for Inhaled Medicine
for the treatment of Chronic
Respiratory Illness**

Metered Dose Inhaler (MDI)

Metered dose inhalers (MDIs) are pressurised, hand-held devices that use propellants to deliver doses of medication to the lungs of a patient.

This sends a measured dose of medicine into your mouth using a small amount of pressurized gas. Sometimes a "spacer" is placed between the drug reservoir and your mouth to control the amount you inhale.

Medicine is forced into the spacer, which you then squeeze as you inhale the medicine quickly.

Aerosols fell out of favour a few years ago when the common propellant chlorofluorocarbon (CFC), a gas that depletes the atmosphere's ozone layer, was banned throughout the world

<http://medicine.org.uk>

Dry Powder Inhaler (DPI)

Dry Powder Inhaler delivers medicine in powder form.

The medication is commonly held either in a capsule for manual loading or a proprietary form from inside the inhaler

The dose that can be delivered is typically less than a few tens of milligrams in a single breath since larger powder doses may lead to provocation of cough.

Most DPIs rely on the force of patient inhalation to entrain powder from the device and subsequently break-up the powder into aerosol particles that are small enough to reach the lungs.

www.youtube.com

Insufficient patient inhalation flow rates may lead to reduced dose delivery and incomplete de-aggregation of the powder, leading to unsatisfactory device performance.

In-vitro testing of DPI

Simulation of Human Respiratory System

Preseparator
(10 μm and above)

Stage 1 5.8-9.0

Stage 2 4.7-5.8

Mouth, throat

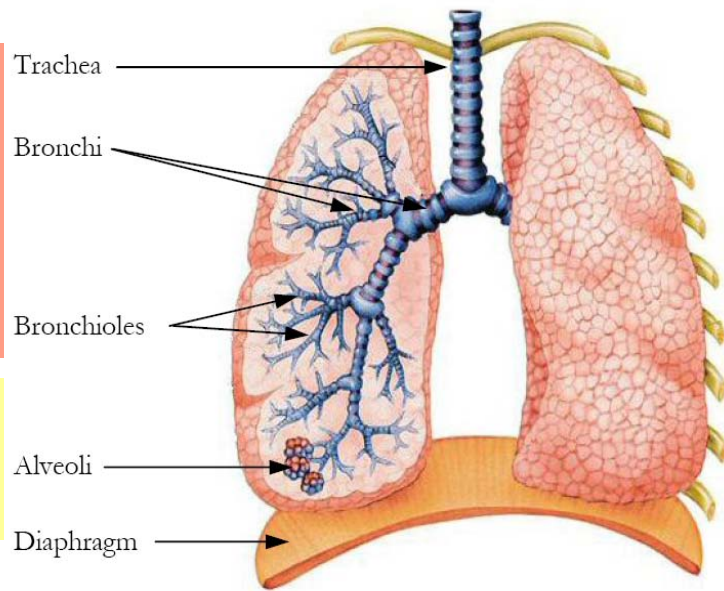
Stage 3 3.3-4.7

Stage 4 2.1-3.3

Stage 5 1.1-2.1

Stage 6 0.65-1.1

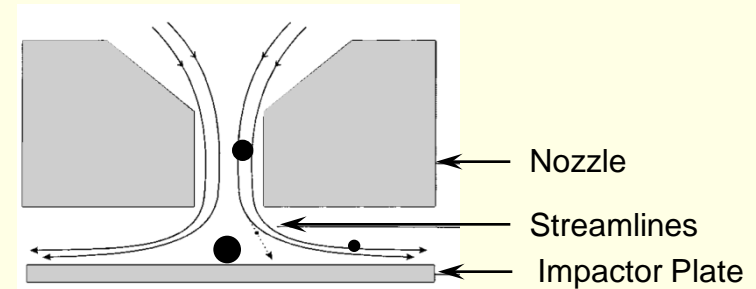
Stage 7 0.43-0.65



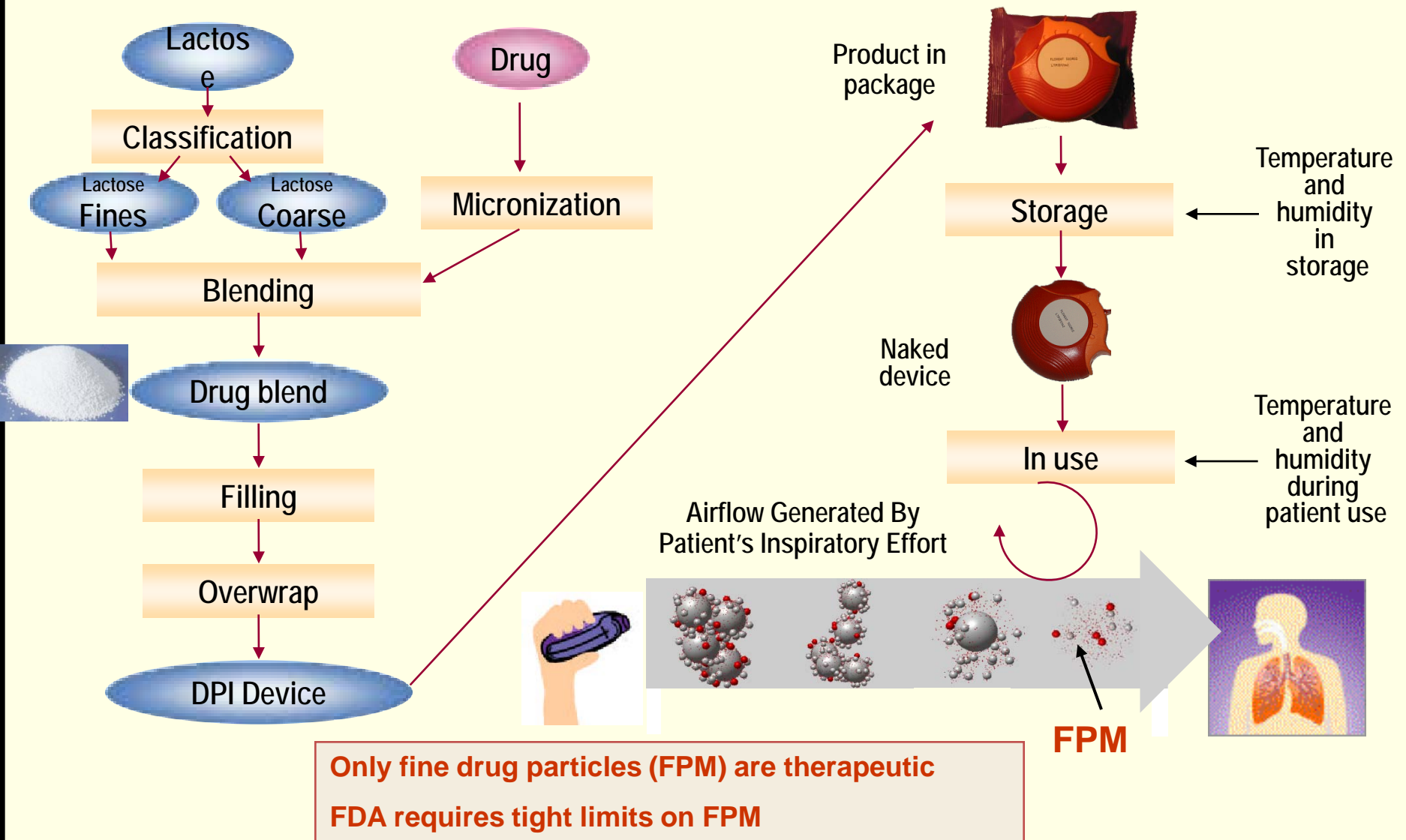
Anderson Impactor



Single stage cross-section

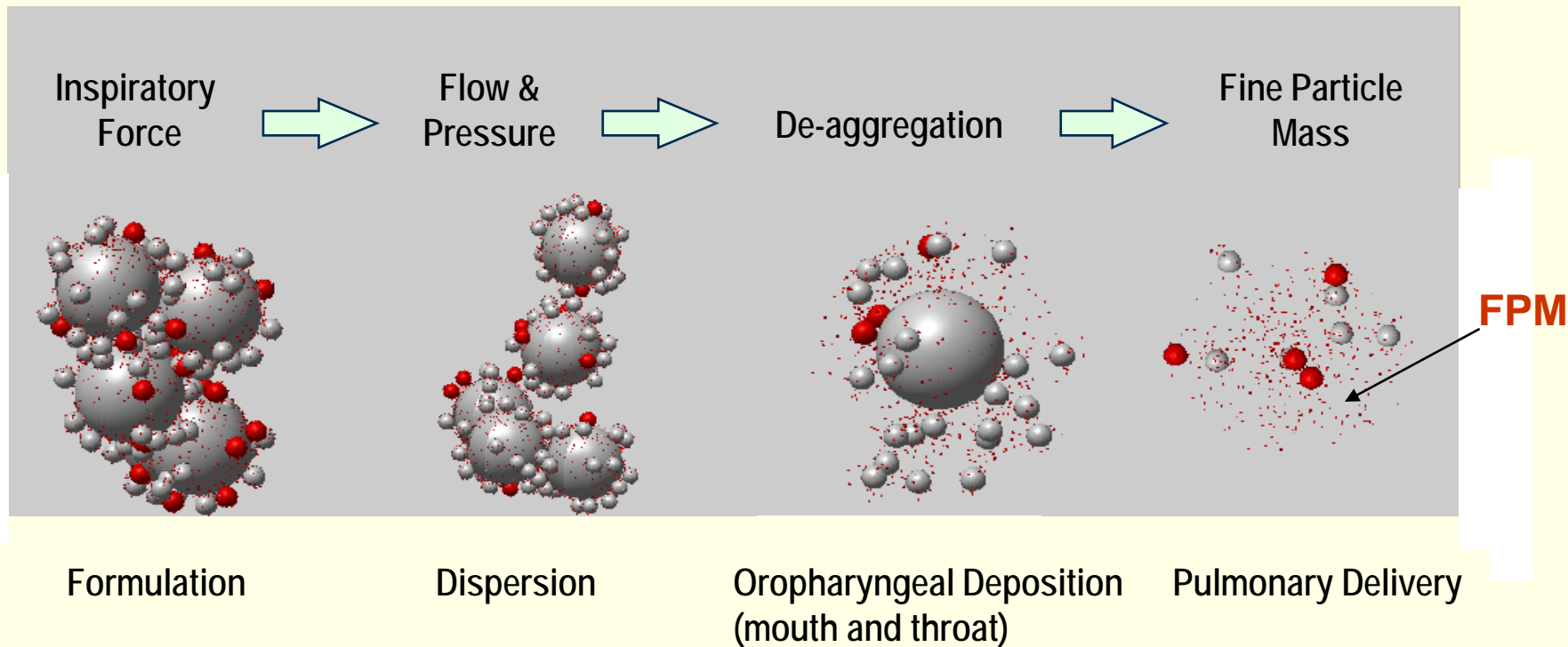


Inhaled drug lifecycle: formulation to usage



Research and Development in developing new Inhaler Technology

Functioning of DPI Device



Drug Formulation Challenge

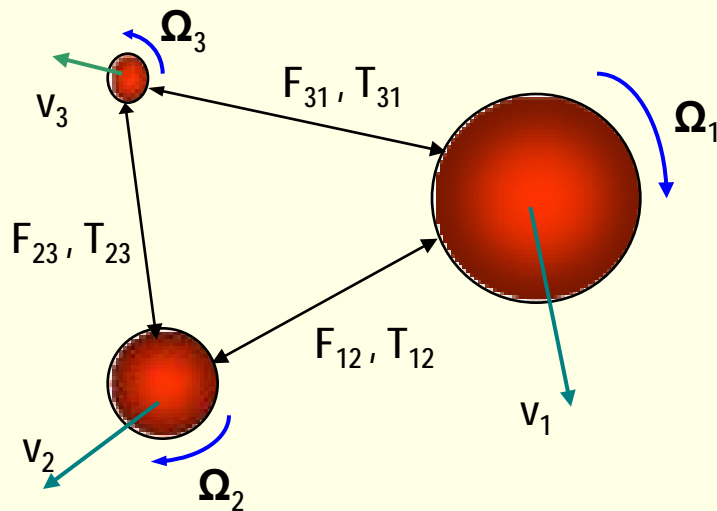
- Only drug that reaches the deep lung has therapeutic effect
- Only small ($\sim 1\text{-}5\ \mu\text{m}$) drug particles reaches deep lung
- Drug only formulations are too cohesive to aerosolize
- Solution: use large ($\sim 100\ \mu\text{m}$) carrier particles

Constrained Design Space:

- Drug must stick to carrier to aerosolize together but...
- Drug must detach in the air stream to reach the lungs
- Tight limit on fine particle during shelf life

How to model particle agglomerates ?

- Treat powder as a large collection of particles
- Discrete Element Method (DEM) involves tracking the trajectory and rotation of each individual particle



Newton's law for linear and angular motion

$$\frac{dx}{dt} = v$$

position of each particle

$$\frac{dv}{dt} = F / m$$

velocity of each particle

Total force

particle mass

$$\frac{d\theta}{dt} = \Omega$$

orientation of each particle

$$\frac{d\Omega}{dt} = T / I$$

angular velocity of each particle

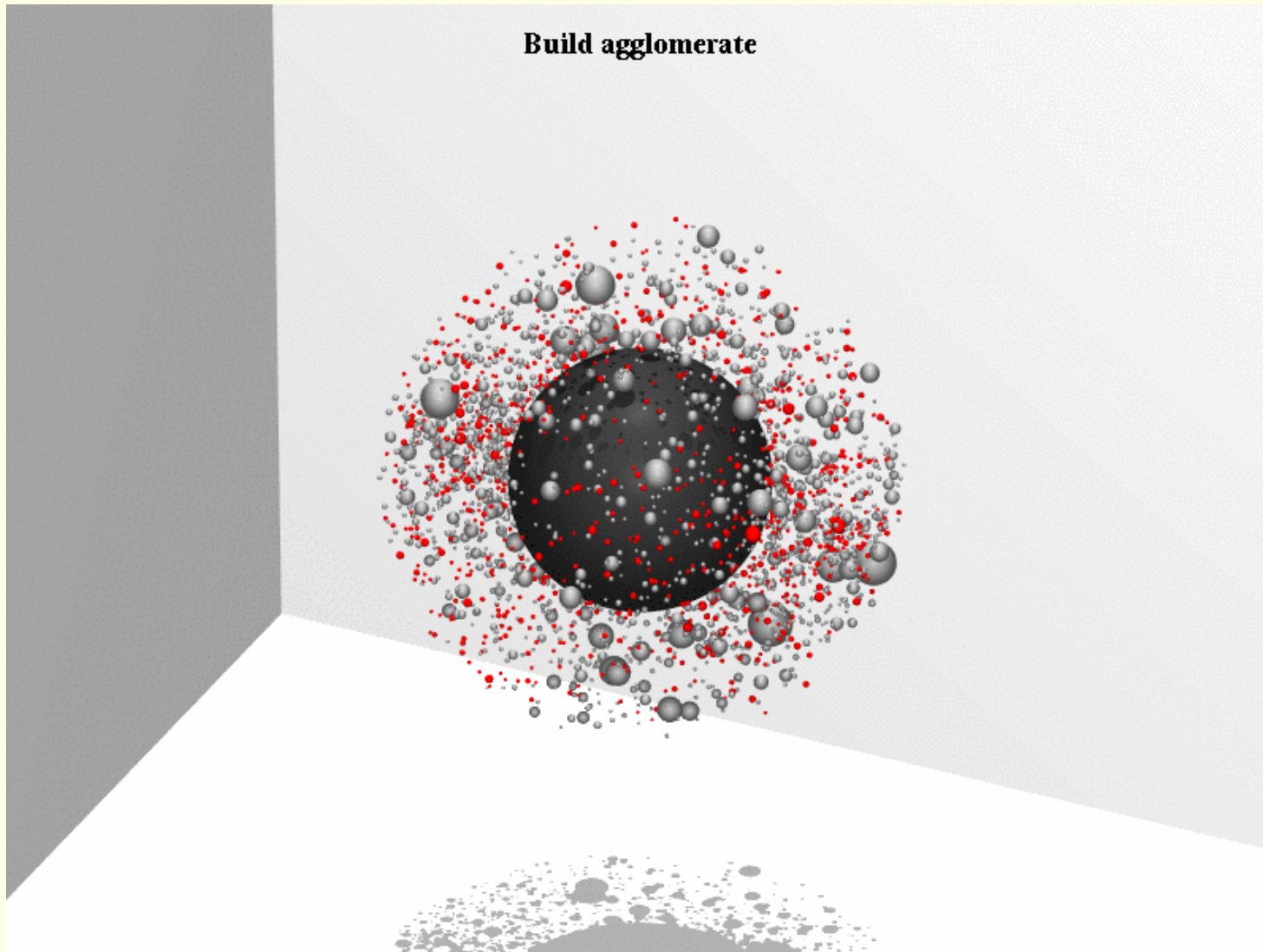
Total Torque

particle moment of inertia

DEM solves the Newton's equation of Motion for each particle in the system

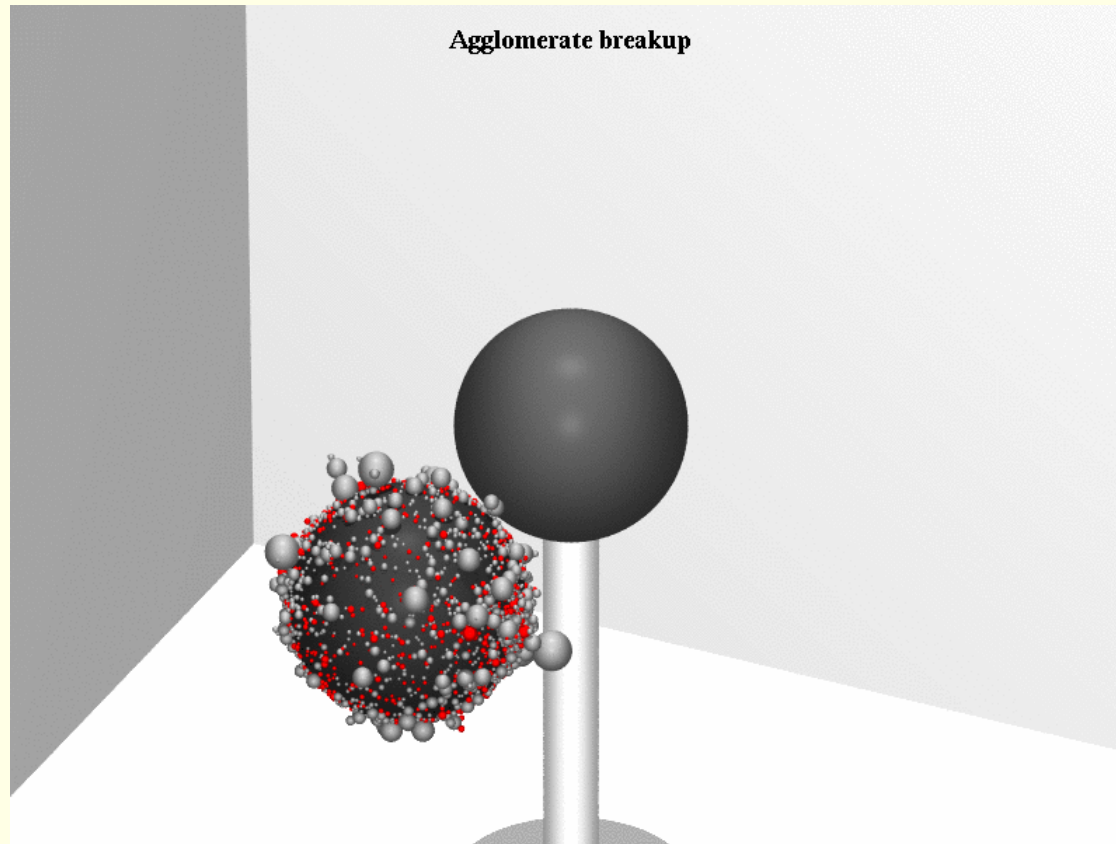
Movie of impact

Illustrative of Modeling Approach



Movie of impact

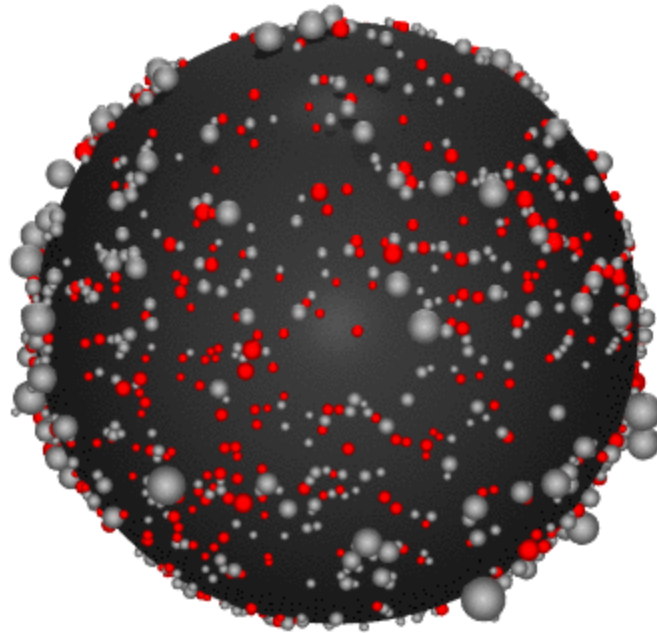
Illustrative of Modeling Approach



Movie of impact

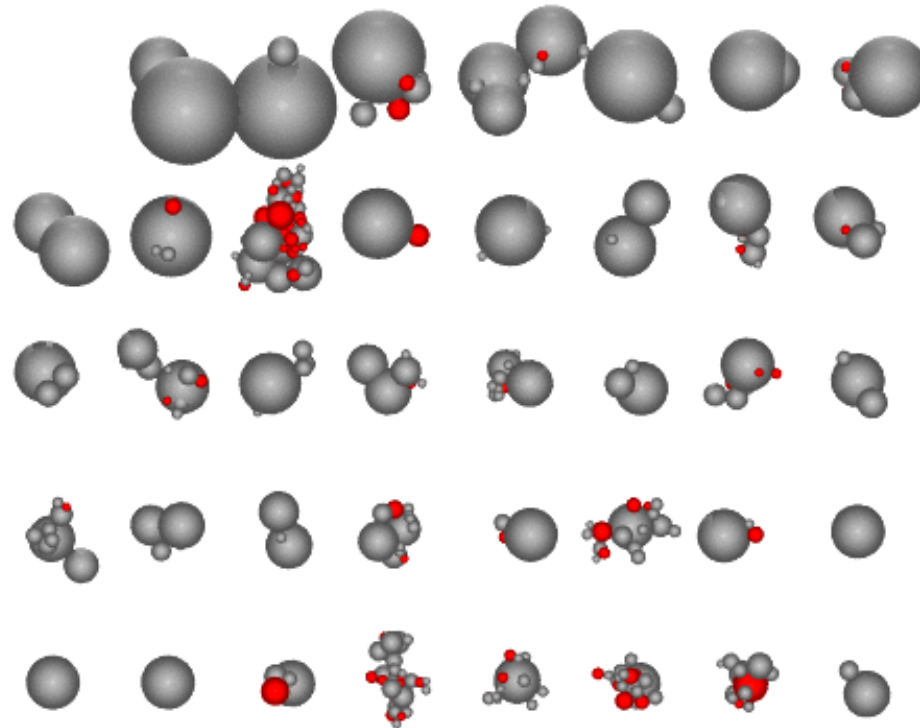
Illustrative of Modeling Approach

Examine coarse lactose cluster



Examining resulting particle clusters

Examine non FPM particle clusters



So did learn we the following in this presentation?

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Thank you for the attention