

From Inhaled Drugs to Exhaled Viruses:

A Journey of my 45 years in Aerosol-Medicine.

Gerhard Scheuch

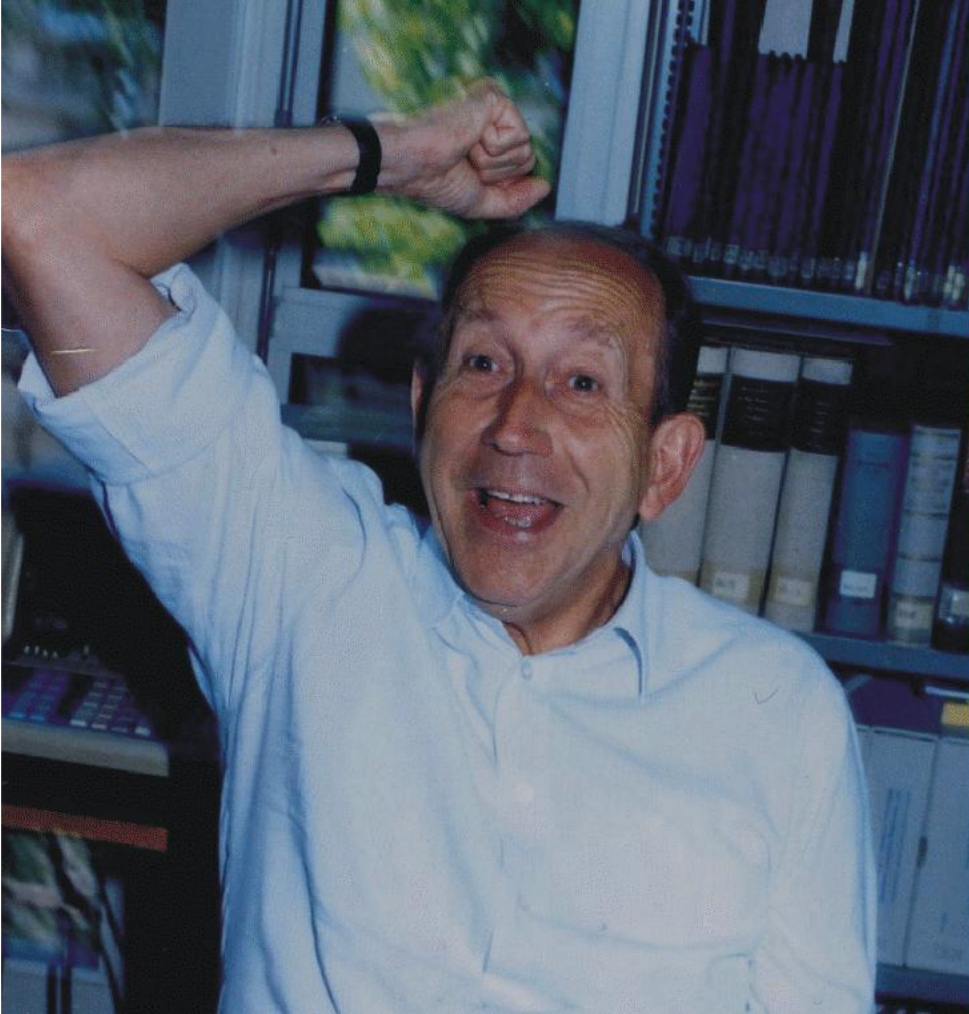
GS Bio-Inhalation GmbH

My start as an Aerosolscientist

- ▶ 1980 Starting at Willi Stahlhofen's lab in Frankfurt/Main
- ▶ 1980 - 1993 Aerosol Deposition, Dispersion and Clearance from inhaled particles
- ▶ ISAM and GAeF member, connection and collaboration with diff. Labs
- ▶ 1993 - 1998 Establish Clinical Cooperation at GSF Munich Aerosolstudies with patients



Willi Stahlhofen



- ▶ Main 2 lessons learned:
- ▶ 1. Be curious
- ▶ 2. Be critical

Clearance of Inhaled Particles

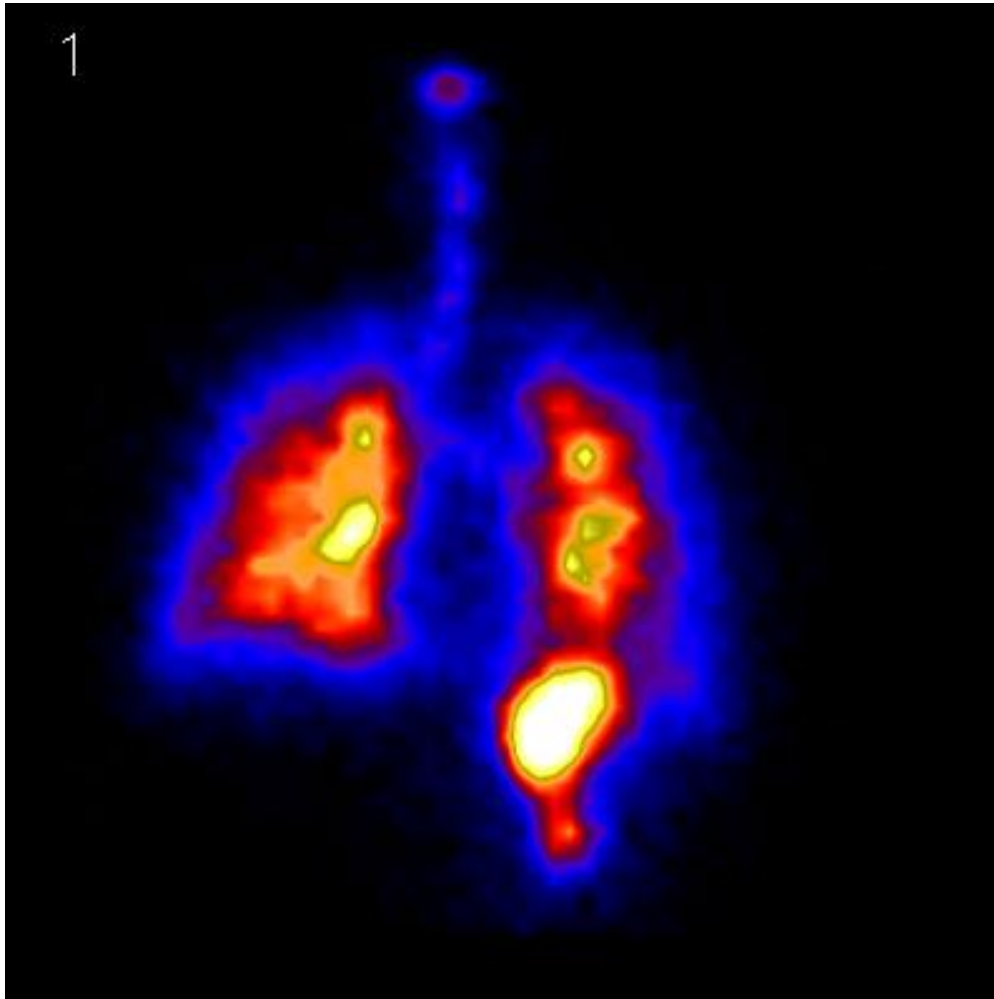


The Doctrine in the 1980s:

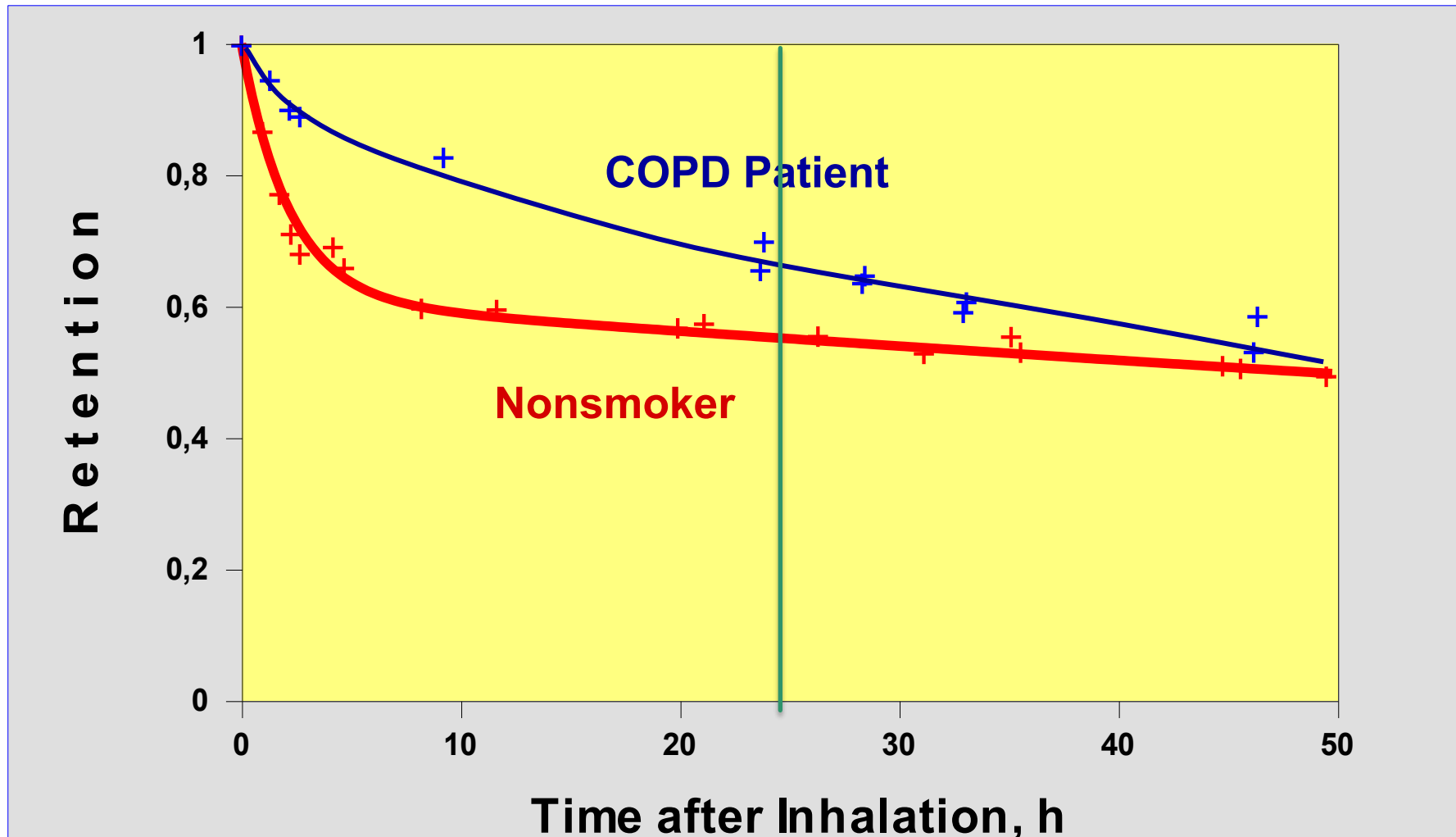
All particles deposited in the conducting airways are cleared within 24 hrs.

= Mucociliary Clearance

Clearance of Inhaled Particles

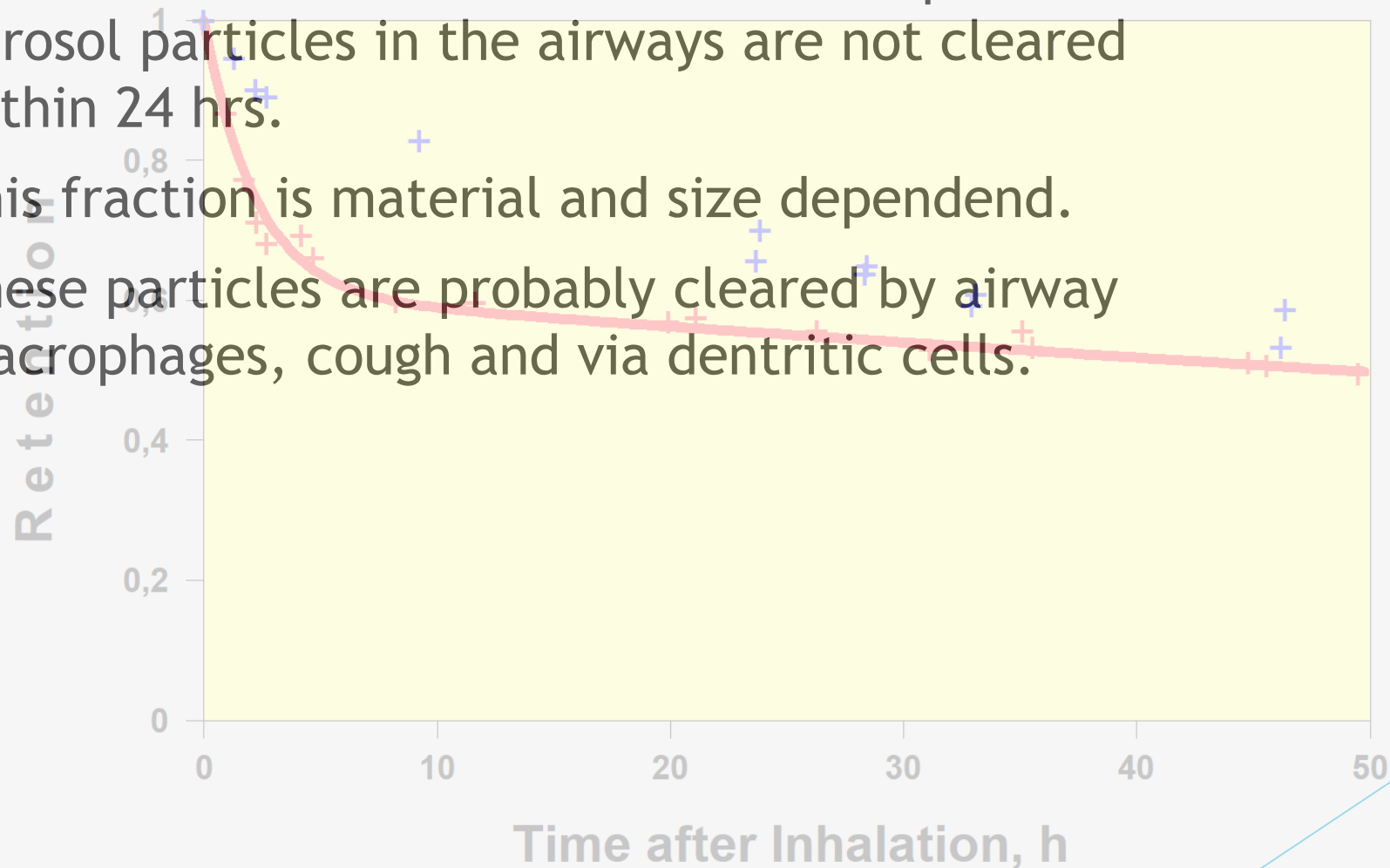


Clearance of Inhaled Particles



Clearance of Inhaled Particles

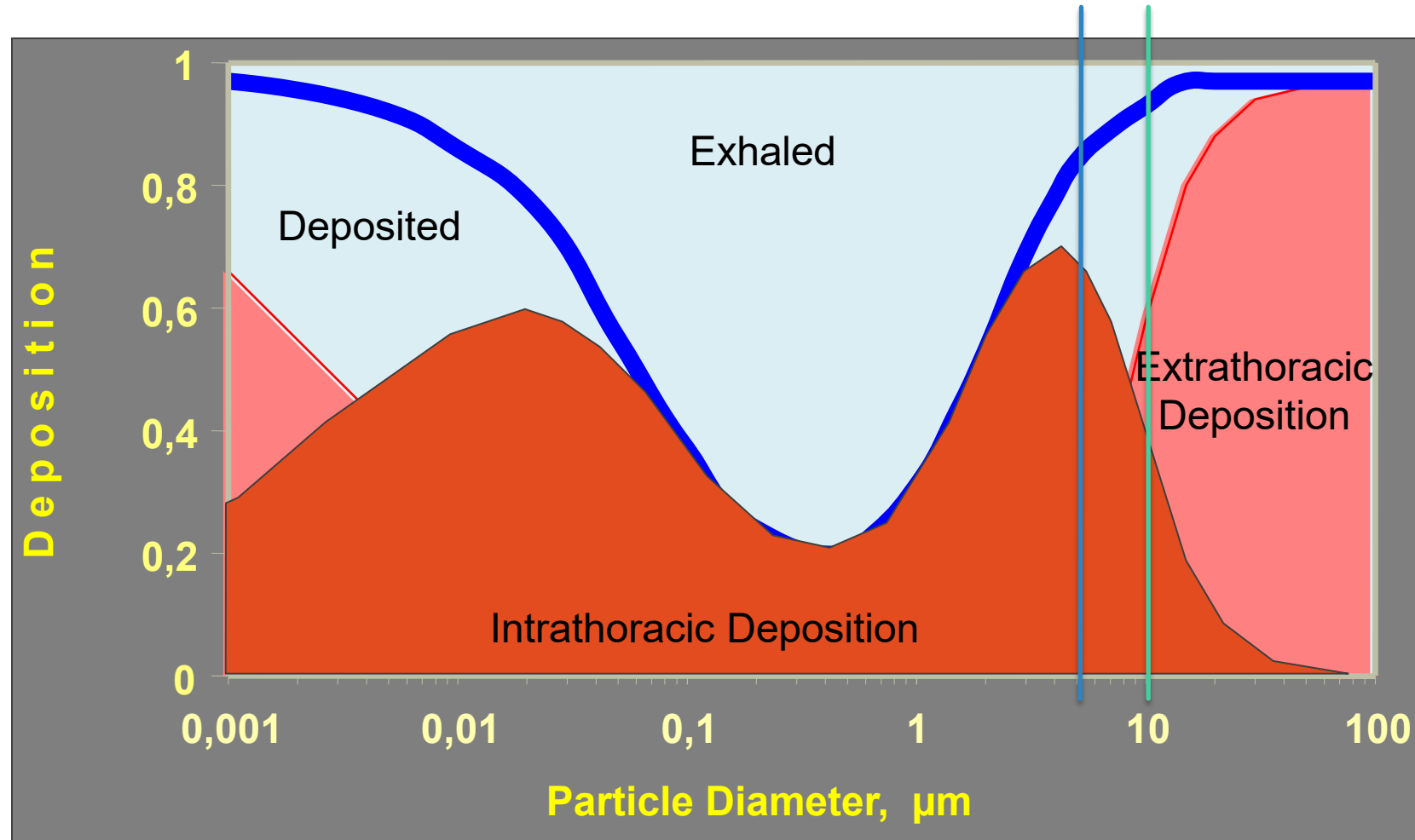
- ▶ A substantial amount of inhaled and deposited aerosol particles in the airways are not cleared within 24 hrs.
- ▶ This fraction is material and size dependend.
- ▶ These particles are probably cleared by airway macrophages, cough and via dendritic cells.



The 5 μm doctrine

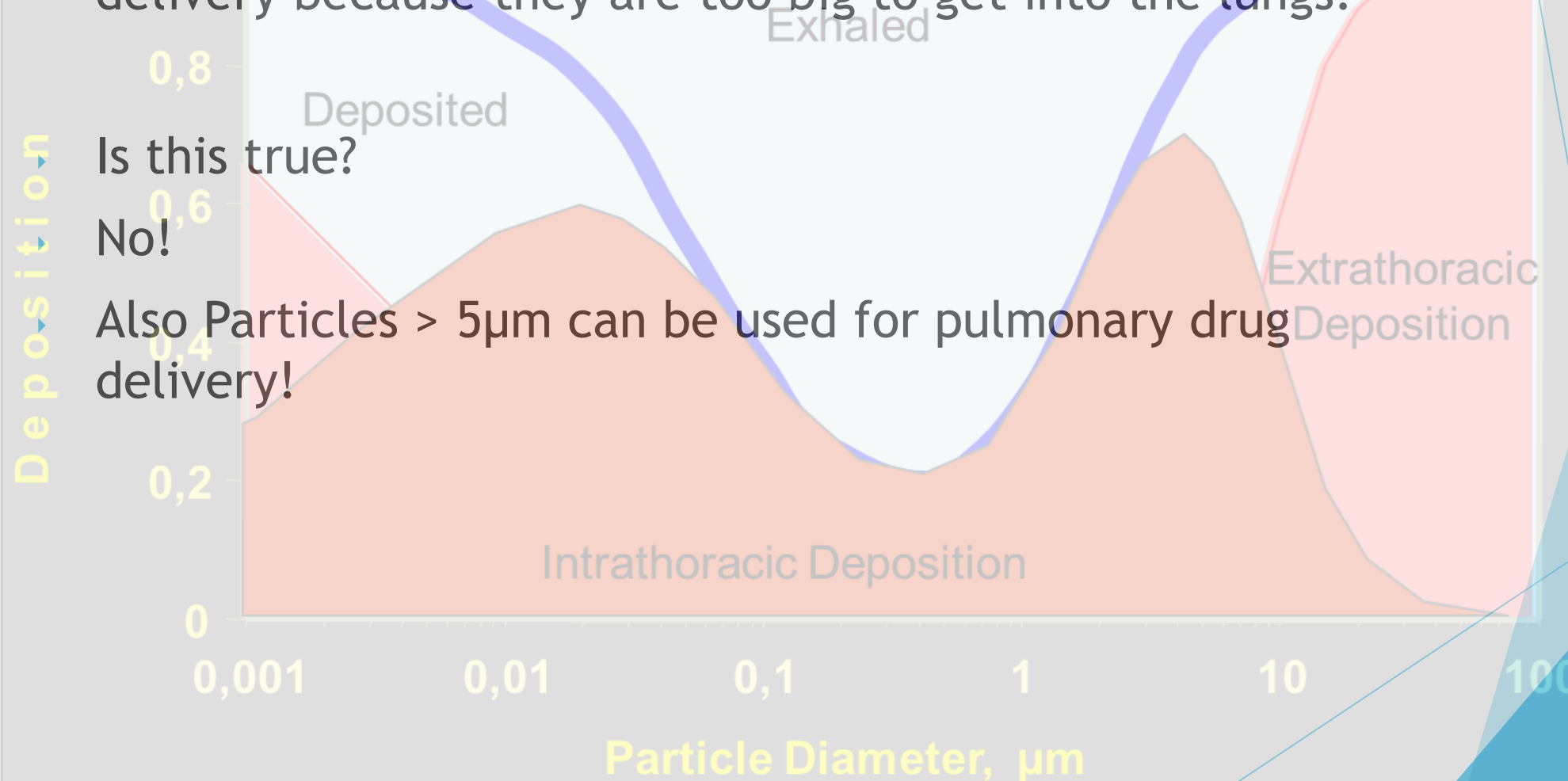
- ▶ Particles $> 5 \mu\text{m}$ cannot be used for pulmonary drug delivery because they are too big to get into the lungs.
- ▶ Is this true?

The 5 μm doctrine

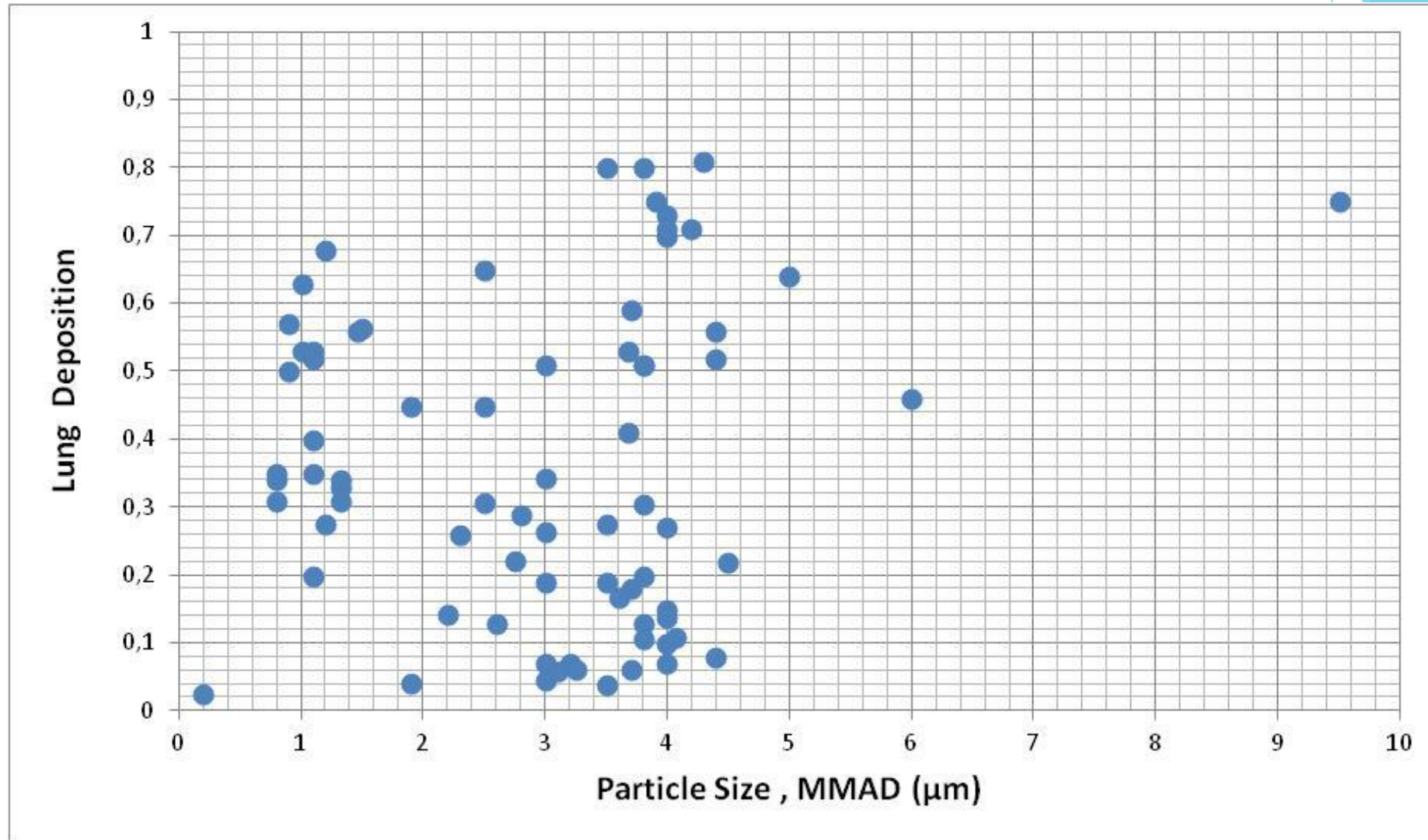


The 5 μm doctrine

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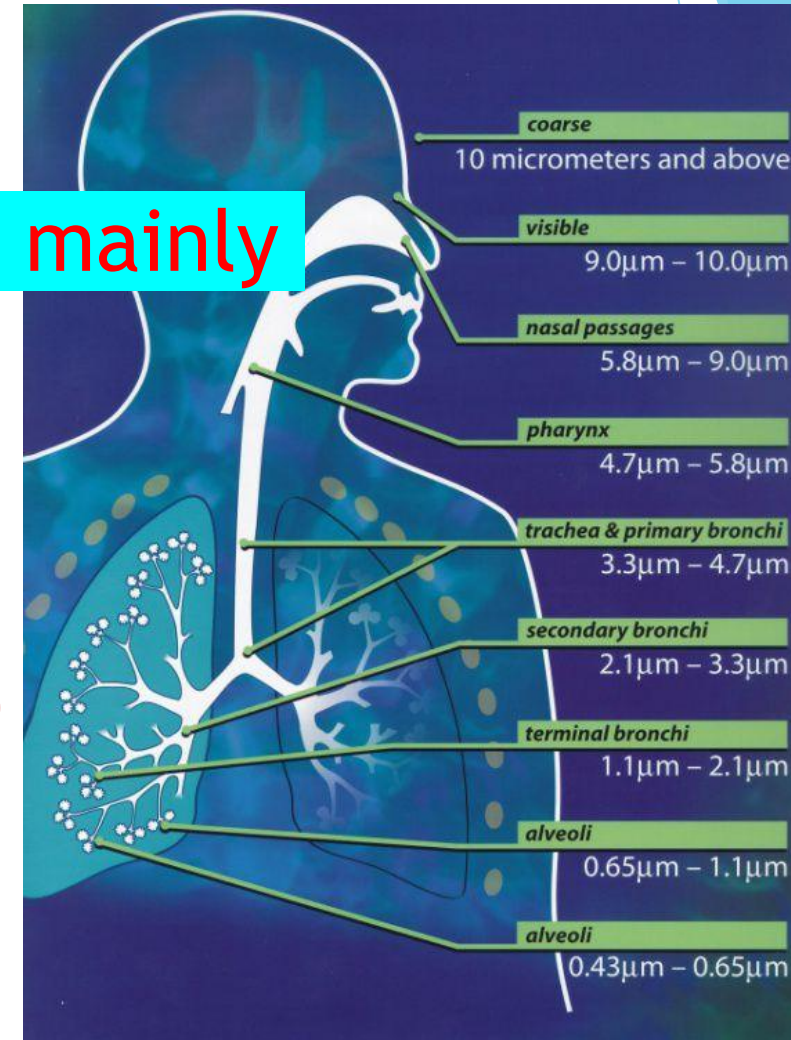
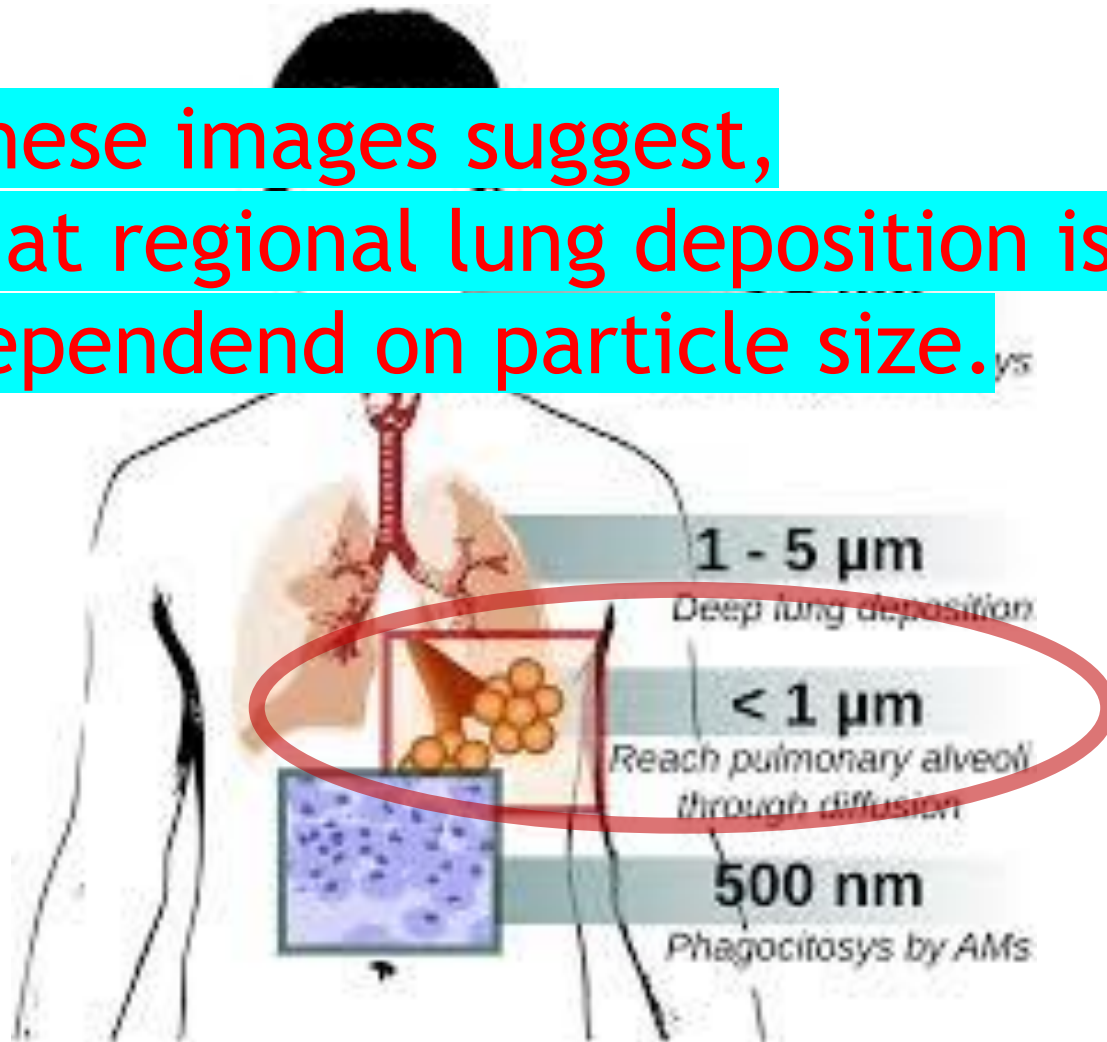


The 5 μm doctrine

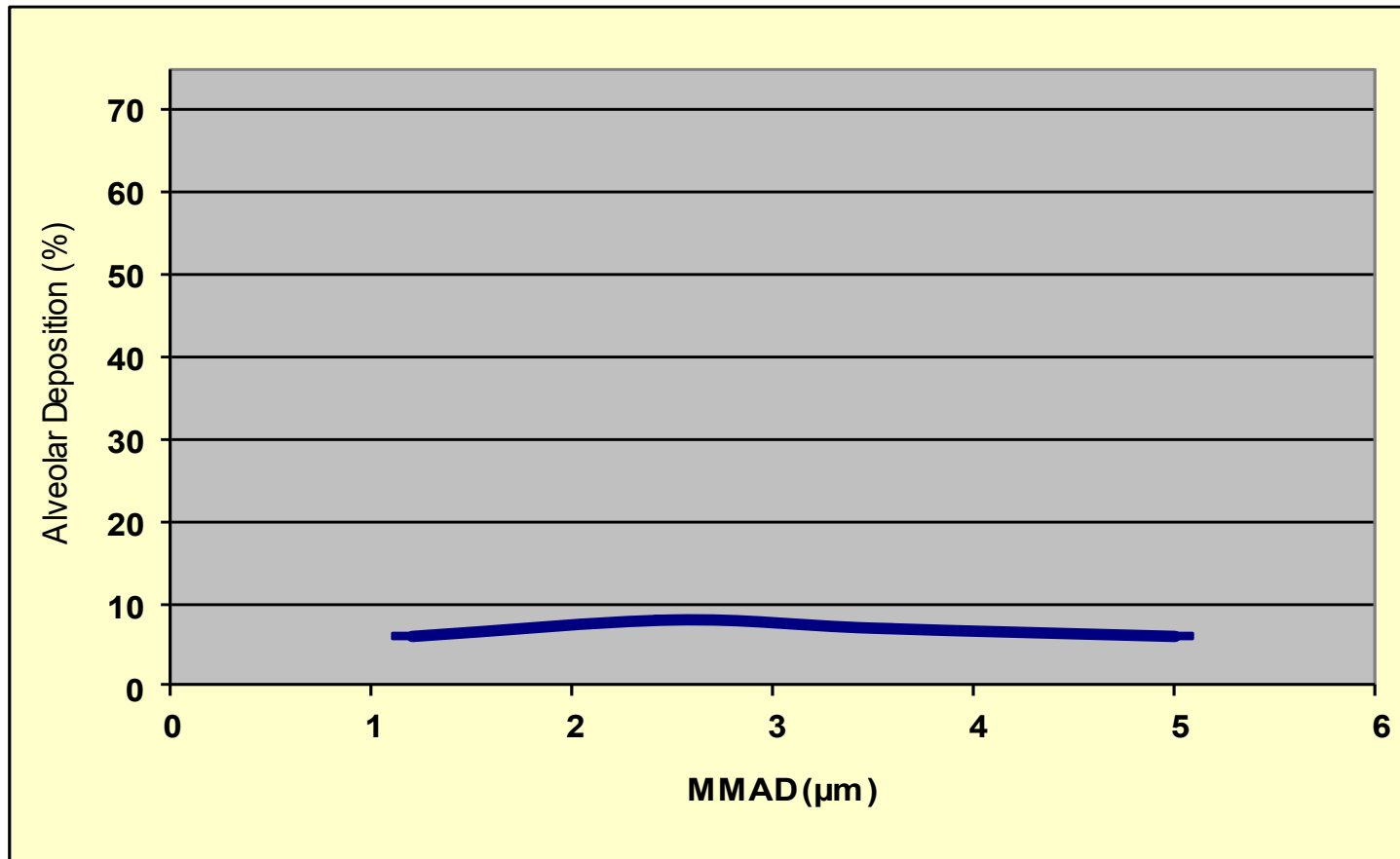


Regional Lung Deposition

These images suggest, that regional lung deposition is mainly dependend on particle size.



Impact of Breathing Pattern (Alveolar Deposition!)



Flow
(ml/s)

Volume
(ml)

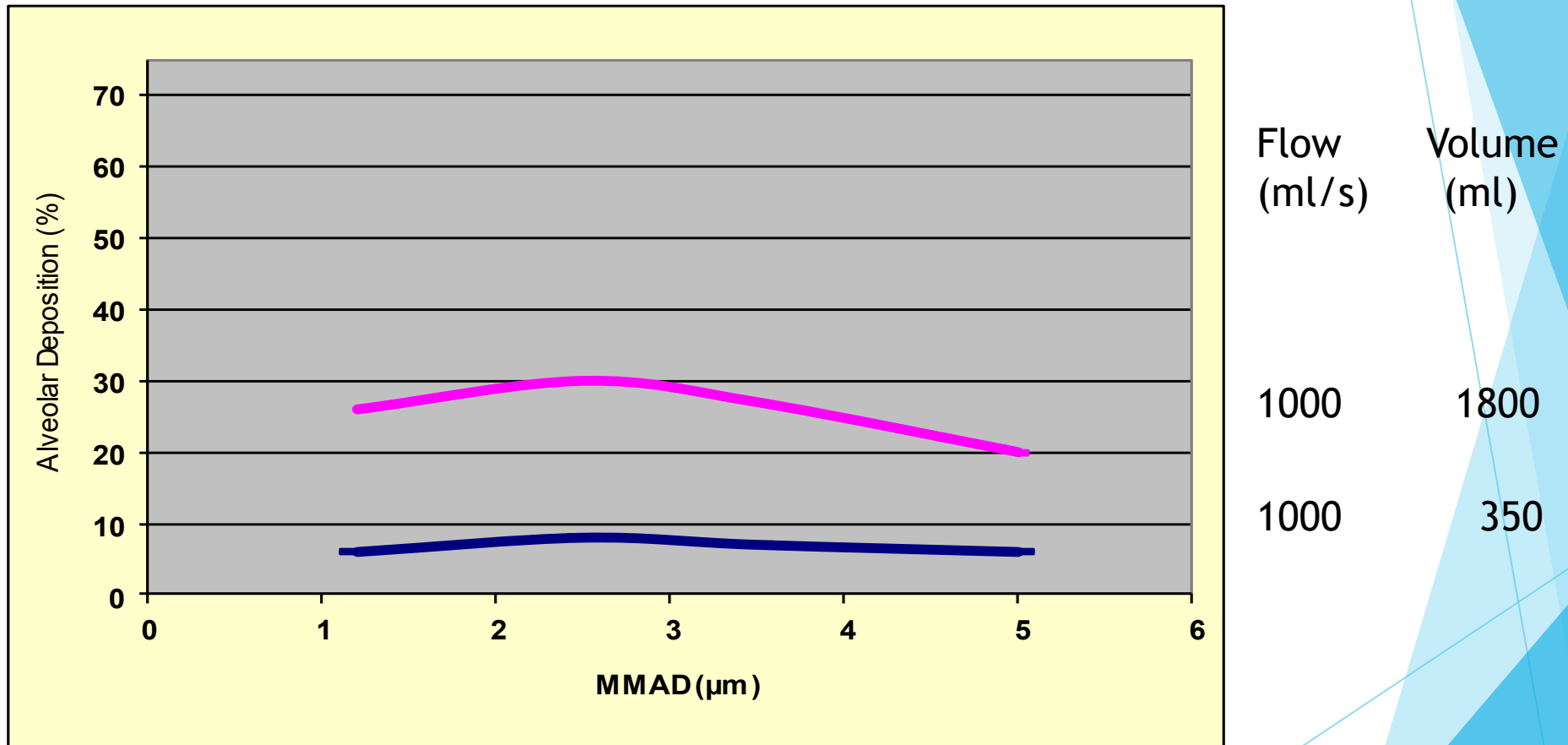
1000

300

350

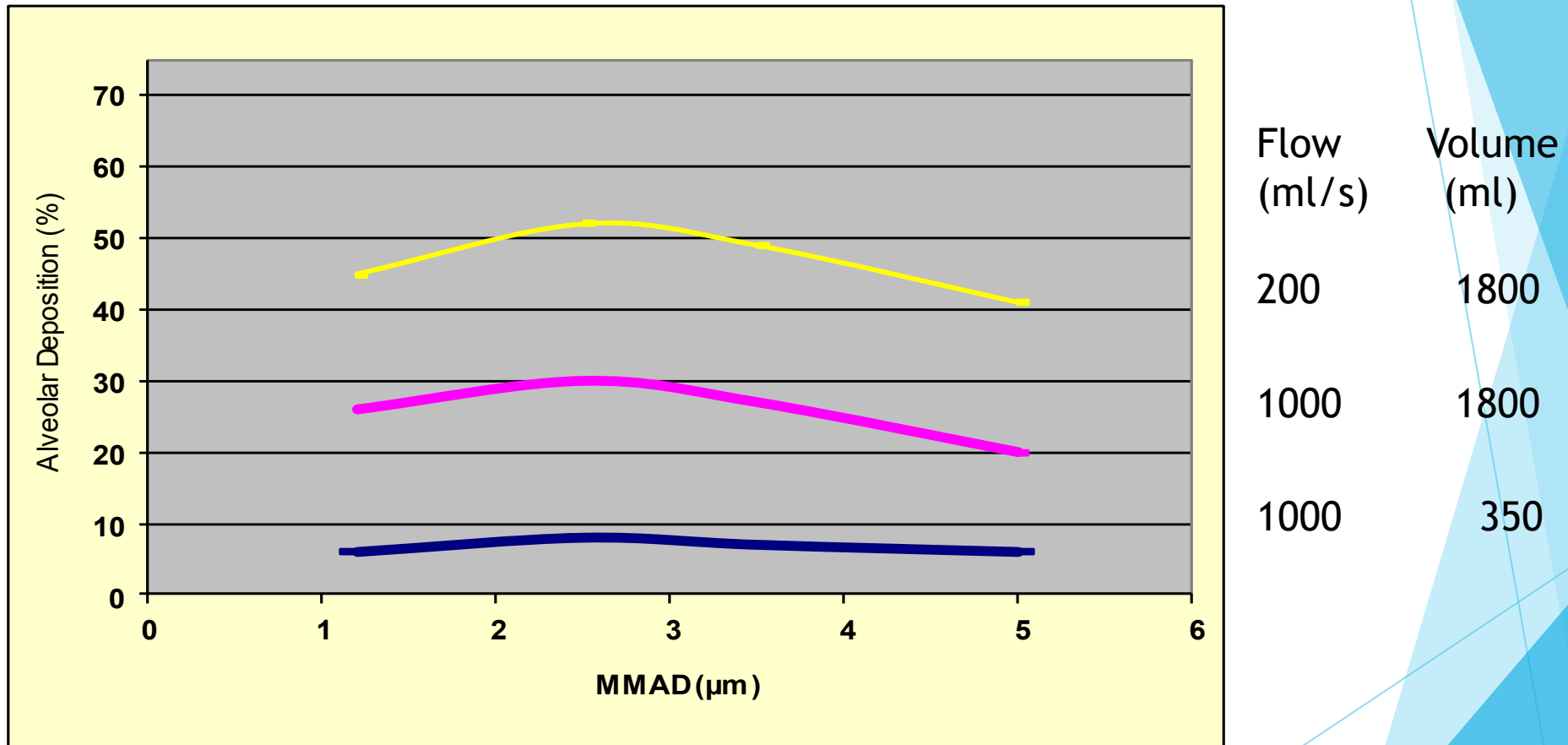
Source : ICRP66; 1994 International Commission of Radiological Protection

Impact of Breathing Pattern (Alveolar Deposition!)



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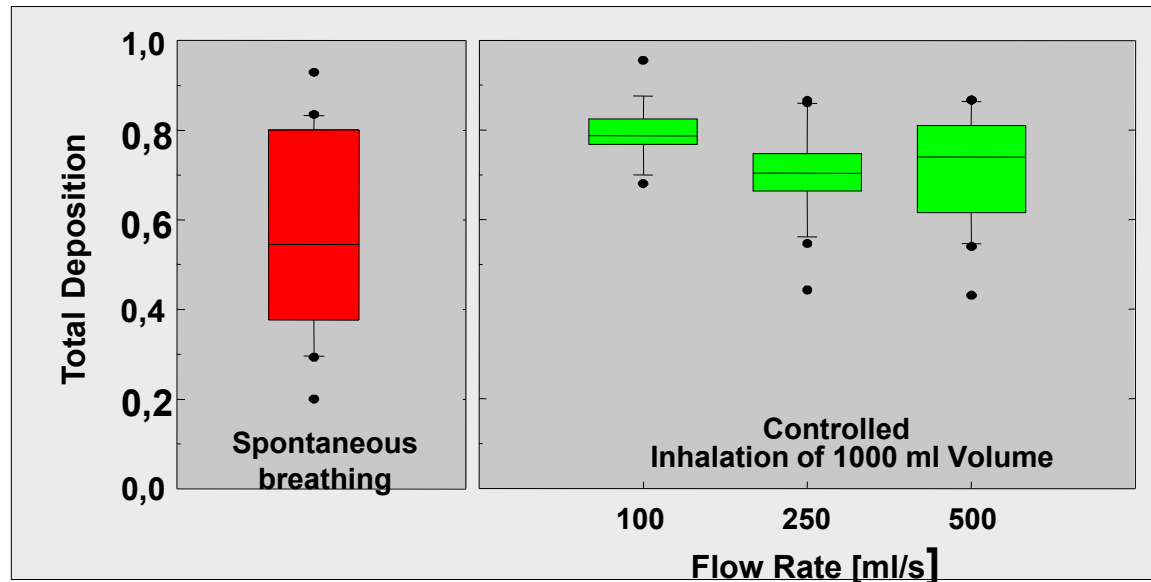
Impact of Breathing Pattern (Alveolar Deposition!)



Source : ICRP66; 1994 International Commission of Radiological Protection

Regional Lung Deposition

- ▶ Inhaled flow rate will determine lung deposition and
 - ▶ Slow flow rate allows particles to penetrate through the larynx
 - ▶ Slower flow rates increase the residence time of the aerosol in the lungs and increase drug deposition

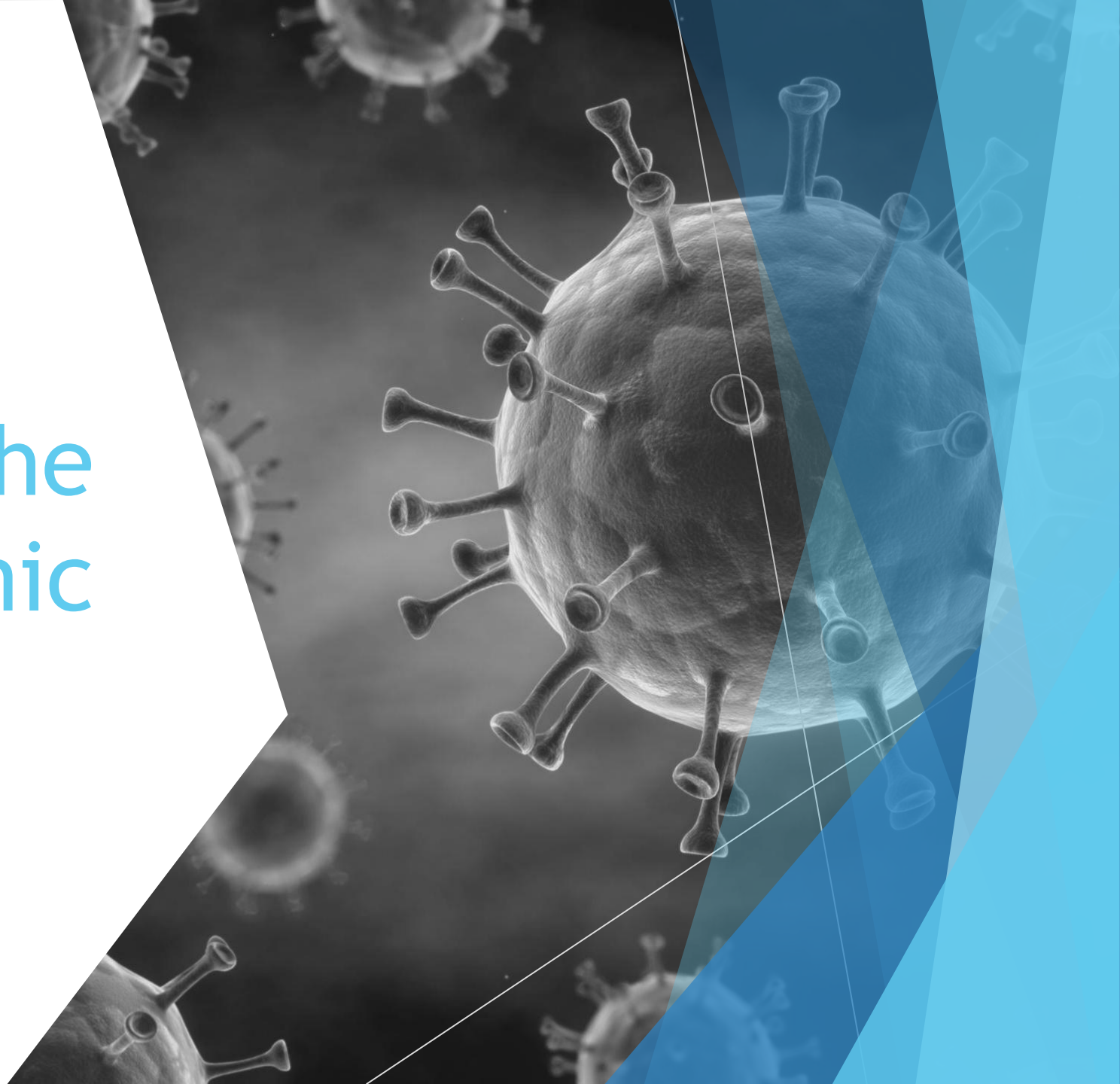


- ▶ Slow breathing also enables passage of air and aerosol past physical obstructions in the lungs and airways

ACTIVAERO



2020: The Corona Pandmic



The Corona Pandemic

- ▶ Statements of WHO in 2020:
- ▶
 1. SARS CoV 2 is not transmitted via ‚Aerosols‘
 2. An ‚Aerosol‘ is a droplet nuclei $< 5 \mu\text{m}$

The Corona Pandemic

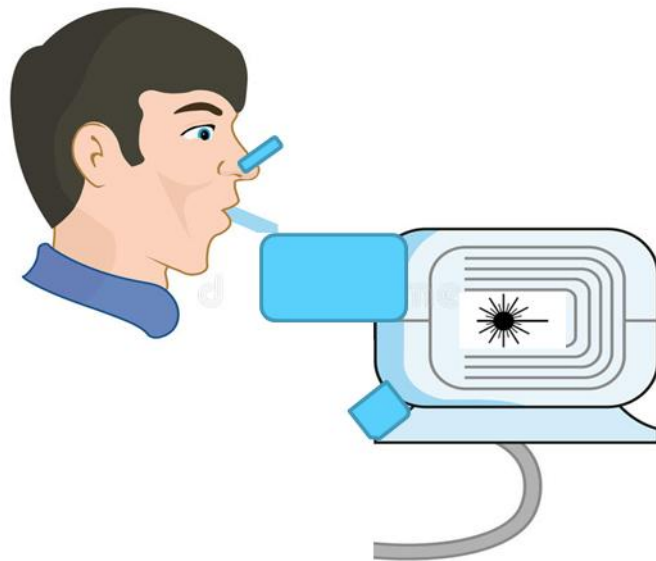
- ▶ Statement 2 is obviously incorrect
- ▶ An Aerosol is a suspension of a gas and non-gaseous particles.

The Origin of Aerosols by Breathing

Coughing, Sneezing, Speaking, Shouting; Singing ... → produce small droplets in different size ranges → Aerosol

But normal breathing?

Experimental setup: strong and very sensitive laser photometer; healthy volunteers breath normally



The Origin of Aerosols by Breathing

Result: The lung generates aerosolparticles!

- 1.) Size 0.2 - 0.4 μm .
- 2.) Increasing breathing flow rate had no significant effect.
- 3.) Increasing breathhold reduce the number of exhaled particles significantly.
- 4.) With an RV (residual volume) breathing manoeuvre the concentration increased significantly.
- 5.) Intersubject variability was high: concentration between one and several thousand particles per liter of exhaled air.
- 6.) Particles were not detected in the first 200-300 ml of exhaled air
- 7.) In ~15% of people with airway infection: the concentration went up by several orders of magnitude.

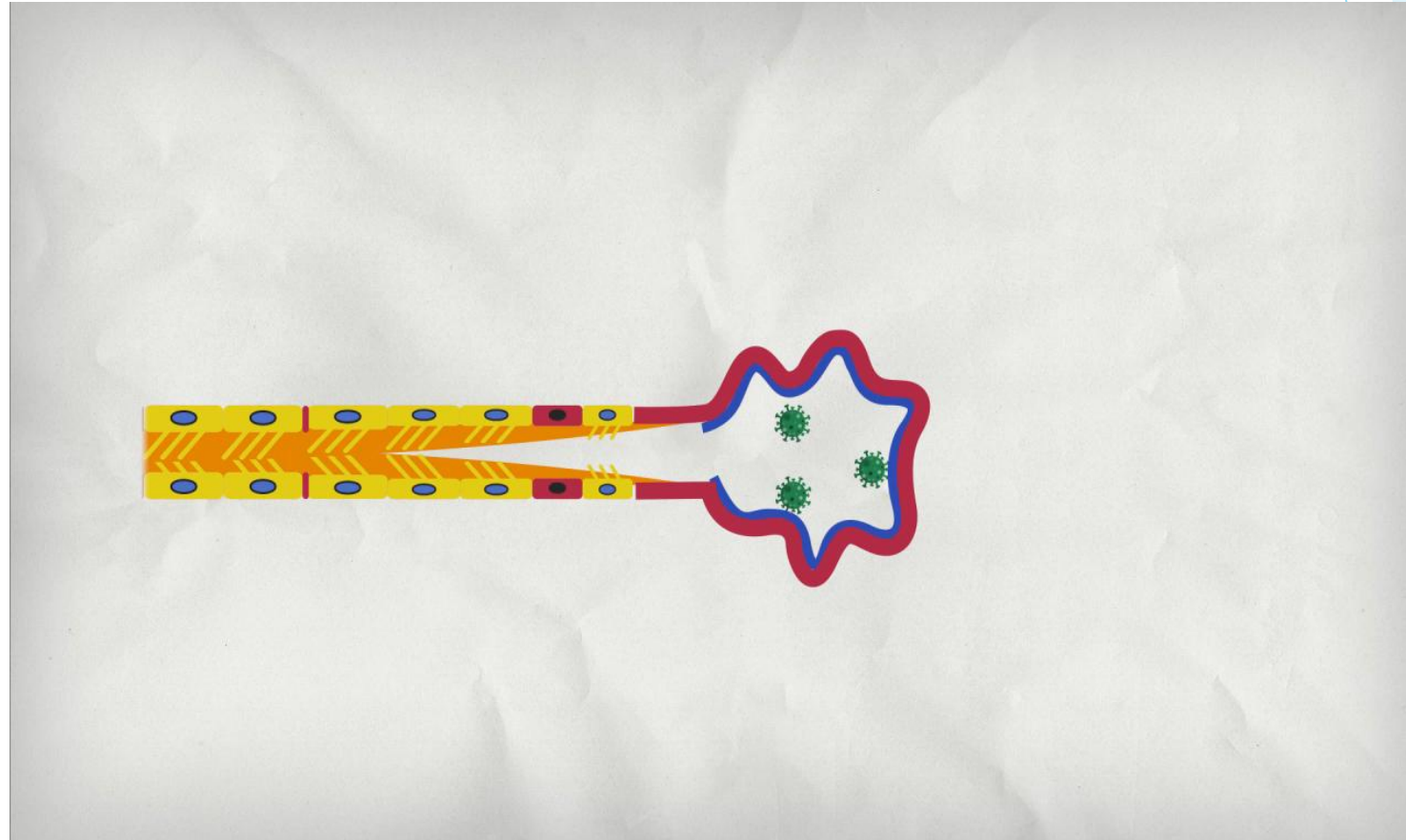
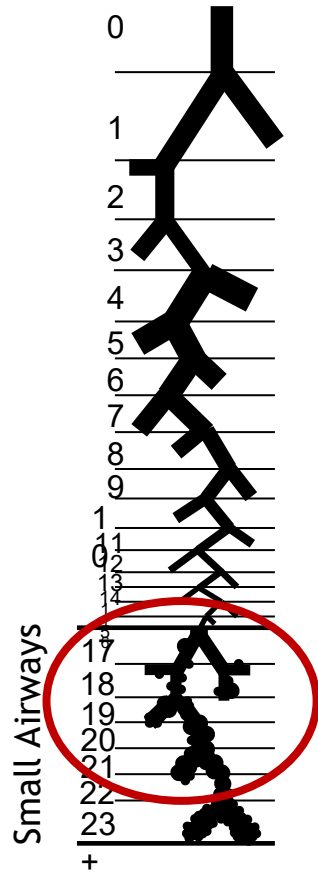
The Origin of Aerosols by Breathing

Our Conclusions:

- ▶ 1.) The particles were not generated by shear forces.
- ▶ 2.) These particles are generated during inhalation.
- ▶ 3.) These particles are exhaled from the deep lung
- ▶ 4.) The effect could be reopening of collapsed small airways.

Droplet formation (slow motion)

Droplet particles (an aerosol) are formed through rupture of RLF film during airway re-opening



The Origin of Aerosols by Breathing

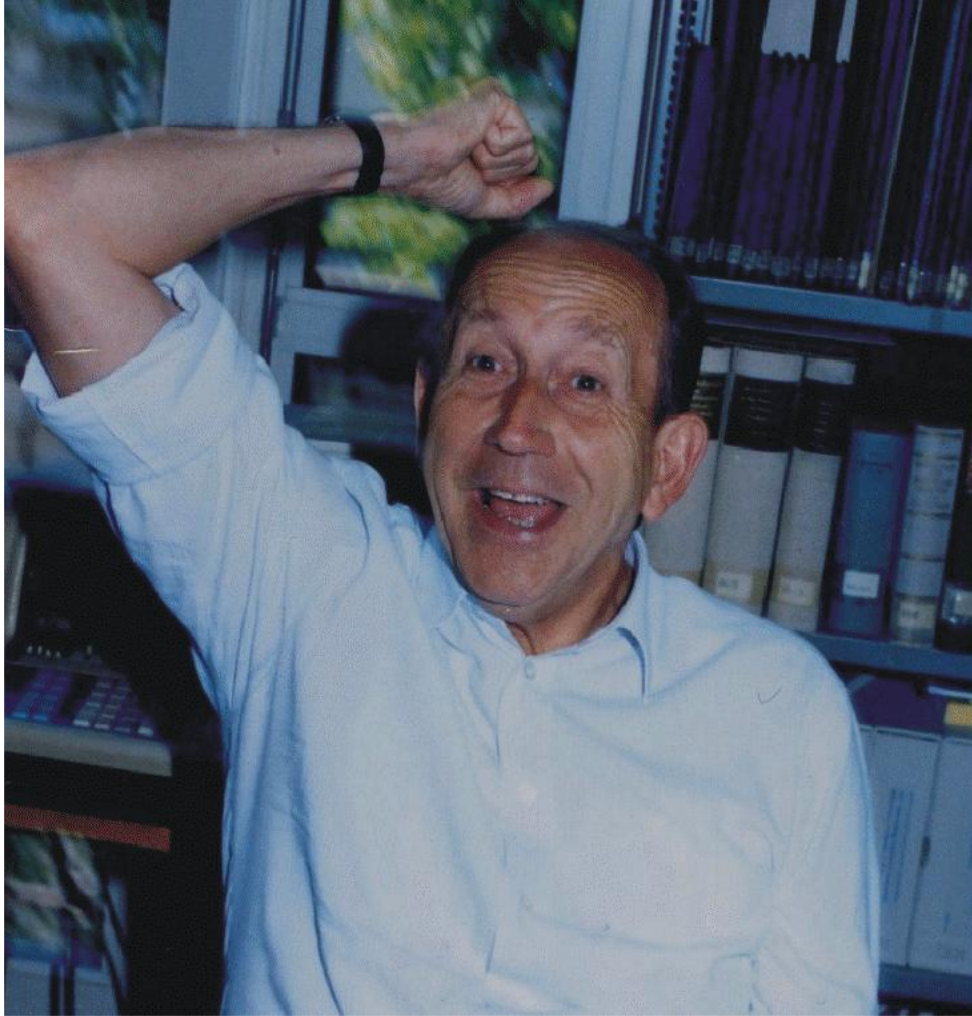
	Median age	Exhaled Particle/Liter		N(%) > 5000
		Healthy	SARS CoV 2	
Adults	53	252	1491	15,60%

- ▶ Gutmann D, Scheuch G, Lehmkuhler T, et al. Aerosol measurement identifies SARS-CoV 2 PCR positive adults compared with healthy controls. Environ Res. 2022 Sep 24;216(Pt 1)
- ▶ Gutmann D, Donath H, Herrlich L, Lehmkuhler T, Landeis A, Ume ER, Hutter M, Goßmann AK, Weis F, Weiß M, Rabenau HF, Zielen S. Exhaled Aerosols in SARS-CoV-2 Polymerase Chain Reaction-Positive Children and Age-Matched-Negative Controls. Front Pediatr. 2022 Jul 18;10

Transmission of SARS-COV 2 as exhaled aerosol?

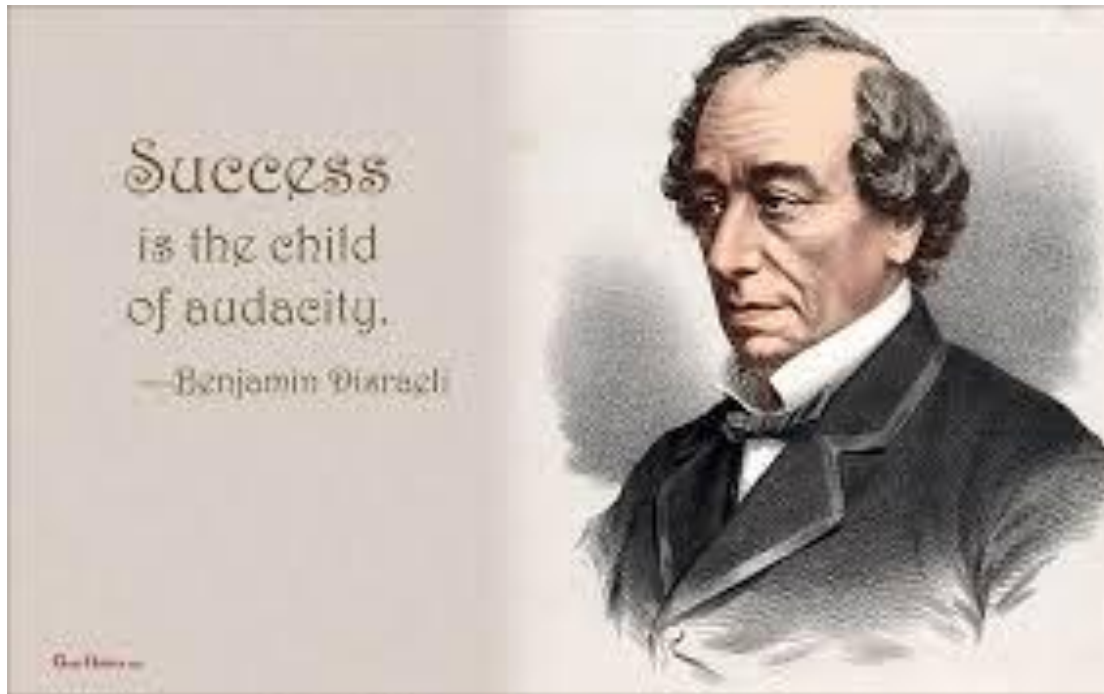
- Yes, there is sufficient evidence.
- My feeling: There are two ports of entry for SARS-CoV-2:
 - Nose
 - If this is the main infection site, the disease will be mild (OMICRON?).
 - Alveolar Region
 - If infected via tiny aerosol particles in this region, disease can be severe
- Aerosol particles can be generated by breathing (speaking, singing, coughing, sneezing).
- Not every infected person is infectious.
- Adults exhale significantly more particles than children.

After 45 years in Aerosol Medicine



- ▶ Main 3 lessons learned:
- ▶ 1. Be curious
- ▶ 2. Be critical
- ▶ 3. Be brave and take your chance

After 45 years in Aerosol Medicine



Thank You for your attention. DANKE.

