Rhinology, 21, 197-202, 1983

The mucociliary apparatus

Nils Gunnar Toremalm, Malmö, Sweden

The mucociliary function is one of the principle defence mechanisms of the respiratory tract. The cilium constitutes one of the most primitive biological structures and can be traced phylogenitically from single cell organisms to highly developed organ systems. A normal cilium consists of nine microtubular doublets arranged in a ring around two central doublets. They have protrusions extending towards the neighbouring doublet, the so called outer and inner dynein arms. They are also connected to each other by nexin links. The doublets are connected radially to the central tubuli by the stabilizing spokes. This complex constitutes the functional axoneme. Human respiratory cilia are 0.2 µ thick and about 6 µ long. Each cell is provided with about 200–300 cilia.

The cilia work in the periciliary fluid below a carpet of mucus. This two-phase layer of fluids can be looked upon as a passive breaking force, and might therefore appear less interesting than the active propulsive ciliary movements. The periciliary fluid and the floating carpet of mucus on the top must be balanced both quantitatively and qualitatively. It is often easier to improve the mucociliary activity by modifying the viscoelasticity of the mucus than try to speed up the ciliary motion per se. The production of fluid is regulated by a form of "chloride pump". Chlorine and Sodium ions are more concentrated in the fluid than in the plasma. The ion/water transport across the epithelium and the mechanism of transudation are still a matter of controversy. Mucus is produced by the goblet cells and sub- mucosal glands. The former can be activated by local stimulation, for example mechanical irritation. The submucosal glands have neural regulation. A morphologically distinguishable boundary between the two layers is of great interest for the outflux and influx of ions, oxygen, pharmaca etc. and merits further experimental investigations (Figure 1). The depth of the mucus blanket, above the tips of the cilia, does not exceed 20 µ but the mucus coat is not uniform and in some areas it is not even detectable.

Ciliary movements – effective propulsive stroke and recovery stroke – take place about 20 times per second. The tops of the cilia are provided with a brush of claw-like projections which grasp the inner surface of the mucus layer. The cilia can move vigorously in an abnormal amount of periciliary fluid and yet not produce

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Paper presented at the 9th Congress of the European Rhinologic Society and 3rd ISIAN, Stockholm (Sweden), September, 1982.

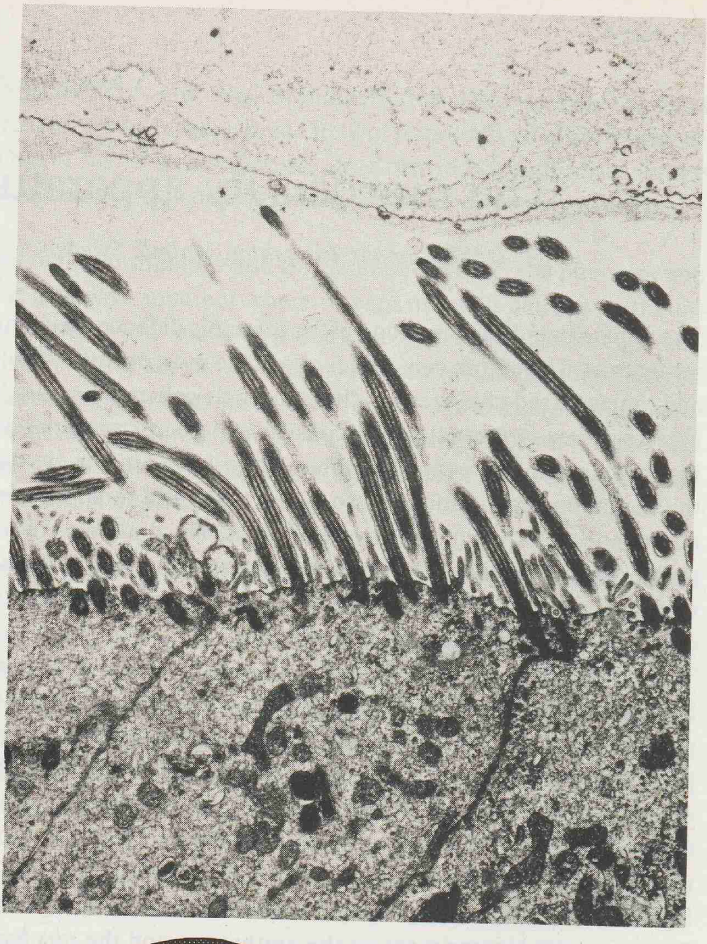

Figure 1. Membrane-like boundary between the mucus layer and the periciliary fluid. (From: Yoneda, Am. Rev. Respir Dis. 114, 1976).

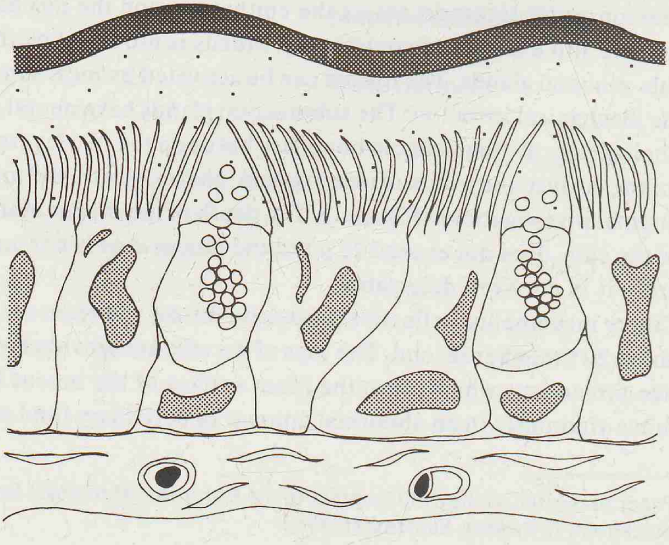

Figure 2. Abnormal amount of periciliary fluid. Normal ciliary movements but reduced transportation.

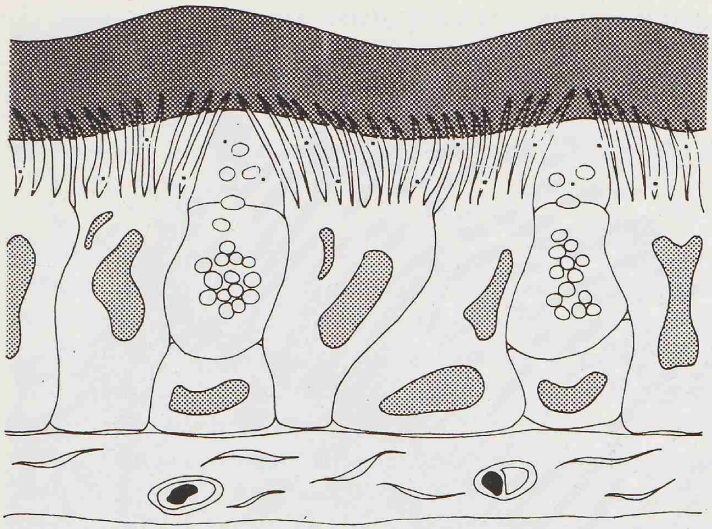

Figure 3. An increased amount of viscous mucus interfering with ciliary movements.

any transportation (Figure 2). This is because they cannot reach up to the mucus blanket. On the other hand if the periciliary fluid is reduced or if there is an increased amount of mucus the cilia are at least temporarely immobilized (Figure 3). This is a reversible situation. The ciliary function is reestablished after suction or dilution of mucus. A thin almost unbroken carpet of mucus immediately on the tops of the cilia is necessary for an effective clearance of secretions (Figure 4). Some biochemical events within the cilia are still obscure but the hypothetic sliding theory proposed by Afzelius in 1959 has subsequently been supported by other authors. Two biochemical components of the sliding mechanism are of special interest. One is tubulin, which makes up the microtubules. The other is dynein, an ATP-ase, which is the effective substance in the dynein arms. Dynein decomposes ATP to ADP and phosphoric acid and is the motor force responsible for the sliding manoeuvre of the microtubules. As long as ATP is available the cilia work autonomously without any need for neural regulation. They are therefore excellent for use in in vitro experiments for up to 12–24 hours. In contrast, in vivo experiments may be influenced by mechanical disturbances, neurotransmitter substances, anaesthetics etc. Recently some interesting in vivo studies have been published by Mercke and Hybinette. They have nicely supplemented earlier investigations by Iravani, Melville and others. Parasympathomimetic drugs like methacoline and sympathomimetics such as Salbutamol and Isophrenaline given intra-arterially were found to stimulate the cilia, while phenylephedrine and oxymetazoline decreased the ciliary function. There is still disagreement as to whether or not there is direct efferent innervation of the individual ciliated cells.

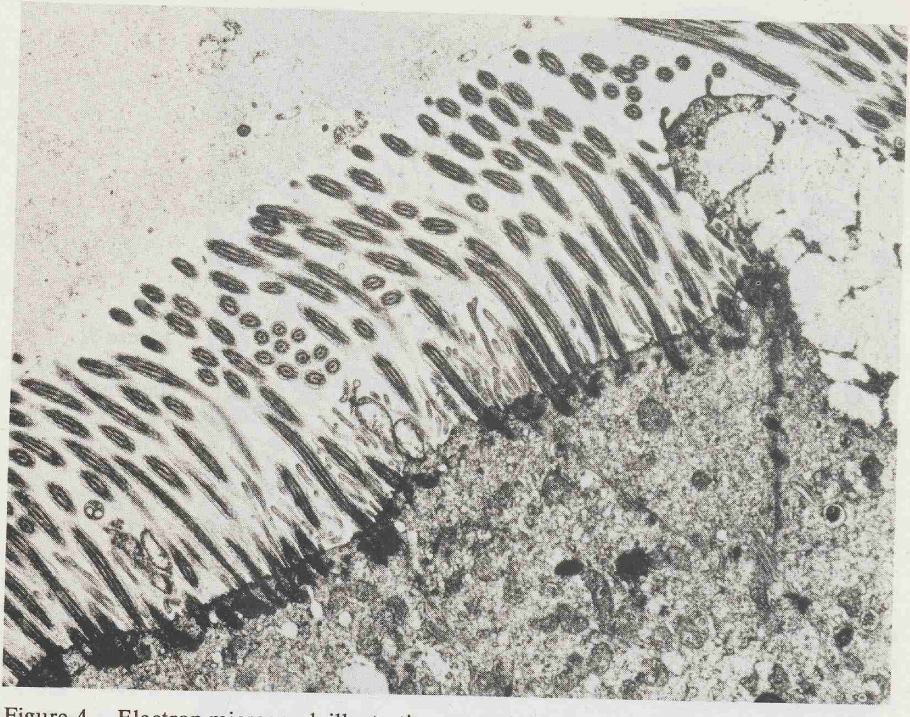

Figure 4. Electron micrograph illustrating normal cilia just reaching the undersurface of the mucus layer.

Neurotransmitter substances like VIP do not seem to have any direct influence on cilia in vivo, but others, like substance P, may perhaps increase the ciliary activity. The intracellular biochemical processes give rise to electrical activities, i.e. voltage changes over the cell membrane. This was shown in mammals by Håkansson and Toremalm (1966). By simultaneously recording the light reflected by surface wave movements on the mucus, it has been possible to distinguish the intracellular electrical activity from the extra-cellular mechanical activity brought about by cilia. In other words, the driving effect of the beating cilia and the retarding effect of the secretion layer could be separated. This finding made it important to introduce the designation "mucociliary wave frequency" to replace the previous term "ciliary beat frequency".

The prerequisites for effective mucociliary function are:

1. A satisfactory aerodynamic shape of the nasal passage.
2. Unpolluted air.
3. Well developed ciliated cells with complete axonemes.
4. A two-phase secretion layer with optimal fluid and a continuous carpet of mucus.

5. Adequate temperature preferably equal to body temperature.
6. Adequate humidity, at least 70 percent.
7. Continuous oxygen supply either from the capillary bed or from the surrounding air.
8. Energy supply because the stored energy in the cell is only sufficient for about 12–24 hours.

Transportation patterns and rates

Already in 1931 Hilding described the course of secretion currents in the nose. New methods using radioactively tagged particles and a gamma camera, or simple methods like the saccharine-blue dye technique, have been used for studying the nasal clearance of secretions. The transportation pattern in the paranasal sinuses has been shown nicely by Messerklinger (1966). The total elimination of substances or particles is called "mucociliary clearance". However, this function is quite individual in normal cases and results are therefore not easy to reproduce. For example, Proctor has found a transportation rate varying from 3 to 25 mm/min in 80% of normal subjects and 20% were "slow clearers" with a rate of only 0.5 mm/min or less. Clearance studies can therefore sometimes be difficult to evaluate. Therefore studies intended to mirror only one experimental parameter at a time need to be checked against standardized in vitro models.

Practical consequences

It is known that patients with the so called "immotile cilia syndrome" can live for many years without any mucociliary defence mechanism. But right from their first day of life these patients have permanent problems with more or less continuous coughing, sneezing and mucus membrane infections. The cilia can also be temporarily immobilised by thick, heavy secretions. This condition, which I would like to call the "immobile cilia syndrome" will be discussed further in the symposium on chronic infections during this congress.

Finally, what can we do for our patients in order to strengthen the mucociliary defence activities?

1. Make surgical corrections in nasal cavities for adequate air passage and nasal ventilation.
2. Provide an anatomical shape of the nasal cavities to allow maximal air conditions capacity, which means anterior and posterior openings giving an adequate degree of turbulent air streams.
3. Avoid local application of ciliatoxic substances and prolonged use of nose drops and other ciliatoxic pharmaca.
4. Help patients with repeated mucosal problems to reduce, as far as possible, their active and passive exposure to tobacco smoke and industrial gases.

5. Bring about early and adequate treatment of acute infections in the nose and sinuses, for example early drainage of maxillary sinuses rather than a second or third course of antibiotics.
6. Improve the mucociliary activity by modifying the viscoelasticity of the mucus, which is easier than trying to speed up the ciliary motion per se. Sodium-chloride lavage, adequate room air humidity and exercise are recommended.
7. In chronic infections and allergic rhinitis it is recommended to test the mucociliary transport capacity by saccharine or some other simple screening methods and perhaps take a biopsy for morphological and functional in vitro studies.

A properly functioning mucociliary apparatus is of great importance not only for maintaining healthy conditions in the nose and paranasal sinuses but also for preventing chronic diseases in the lower airways and lungs. Chevalier Jackson has called the larynx "the watchdog of the lungs", but it would seem even more appropriate to start barking, whenever the different defence mechanisms of the nose are in trouble.

Prof. Nils Gunnar Toremalm
ENT-Dept., General Hospital
S-21401 Malmö
Sweden