CILIARY FUNCTION

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The ciliated epithelium has a special and exceptional importance for the function of the nose and paranasal sinuses. Combined with the blanket of mucus the cilia represents a "propulsion organ" (GUSIC), an organ for cleansing and protection.

Some morphological facts

During the last years ENGSTRÖM, WERSÄLL, RHODIN, DALHAMN and others succeeded in clearing up the structure of the ciliated cells and the single cilium by means of electron microscopy. The most important facts of these investigations are the following:

The body of the ciliated cell as well as the cilia and the socalled filiform projections are covered by the same continuous membrane without any interruption or suture (Dia). Between the cells, there are interspaces and indentations of variable dimensions. —

The upper surface of a ciliated cell shows two different prominent structures: The cilia and the filiform projections. These filiform projections have a length of 1 micron and form ridge-like patterns around the cilia; they probably have a metabolic function for ciliary activity; which we shall discuss later.

The cilium itself has a length of about 5 microns. In transverse sections, round-shaped or slightly oval, each cilium contains a ring of 9 peripheral filaments and besides 2 central filaments. There is some suggestion that the 9 peripheral filaments join together in the tip of the cilium. The base of the cilium contains a basal corpuscle surrounded by the peripheral filaments that fuse below the basal corpuscle, forming a netlike structure (Dia). On the other hand, the two central filaments are without contact to each other or another structure — at least in the optical sense —; they cease above the basal corpuscle. —

It would be beyond the scope of this subject to discuss also the morphology of the goblet — and basal cells, though these cells are of no less importance for the ciliary function than the ciliary cell.

The function of the ciliary cell

To accomplish the principal purpose, i.e. the continuous cleansing of the surface of the mucosa, the cilium requires precise cooperation of many factors. Especially the mucous blanket, gliding on the ciliary collective and pushed away by it, requires some particular properties. The secretion, a product of goblet cells and mucous glands, consists of two layers; the upper is highly viscous, elastic and tenacious and forms a continuous, tough and movable protective film, a "tapis roulant". The lower layer is low-viscous and represents the medium of the cilia's activity (Dia) —

One period of the cilium's work comprises two phases: during the **effective stroke** the tip of the straightened cilium touches the high-viscous layer and pushes the blanket away. Finishing the effective stroke, the cilium bends, loses contact with the overlying film and slips off. During the second phase or the **recovery stroke,** the cilium rises up again. One fifth of an entire cycle

covers the effective stroke, four fifths the recovery stroke. While such a cycle reiterates about 200 times/min., the cilia beats metachromically so that the impression of a waving corn-field arises (Dia). — There is some suggestion that the impulse for a ciliary contraction is induced by the basal corpuscle under cooperation of the mitochondria and then transmitted to the peripheral filaments. These structures probably have the function of contractile elements. On the other hand the two central filaments possibly act as nerve-tracts (RHODIN), although a connection between the cilia and the submucosal nervous network could not be found until now.

The monotonous morphological feature of the ciliary cycle is not variable, except by mechanical obstacles, whereas the frequency and the amplitude of a stroke are changeable. Besides, an increased number of beats does not also cause an increase of efficiency — as is demonstrable by the employment of surface-active agents on the mucous membrane.

Many years ago, HILDING, PROETZ, TREMBLE a.o. pointed out that the direction of ciliary beats is fixed for all time; for instance, when an excised fragment of ciliated mucosa is reimplanted under rotation of 180 degrees, these cilia maintain their working direction, that means, they now beat paradoxically to the surrounding areas. Besides, it is very important, that cicatricial spots of the mucosa, not having ciliary activity, represent — circumstances permitting — an invincible obstacle for the continuous transport of the mucous blanket, especially when arranged vertically to the mucous-flow-direction. Therefore, in the case of an intranasal operation, one should carefully consider the direction of the incision!

The intensity of ciliary transport is not the same in all areas of the nose and sinuses (Dia). As HILDING a.o. could show, there are fixed and unchangeable courses, partly "highspeed-routes" and partly low-speed-ways. In the sinuses, the direction of the flow has an almost spiral motion centering at the ostium (HILDING). A new window of the sinus, created by an operation, does not influence the direction of the mucousflow in a sinus, so that the ciliary transport remains directed toward the normal ostium. Another interesting and important point of view: Without a normal working ciliary border of the ostium the drainage of the entire sinus is very poor! One should keep it in mind planning and performing operations, probings etc. near an ostium! — In general we have to assume that the secretion-blanket in the nose is renewed within 10 (to 20) Min., except the region of the vestibulum nasi and the foremost part of the lower turbinates, because these regions are inactive no I having a ciliary epithelium (FLOTTES and colleaques, v. REE and v. DISHOECK, a.o.). — The duration of the renewal of the secretion-film in the sinuses is estimated as 10—15 Min. (PROETZ). — Loaded with medicaments (emulsions, suspensions, ointments etc.) the blanket becomes heavier and the transportation-speed lower; and sometimes that phenomenon is favourable from the therapeutical standpoint, especially in cases where the employed drugs are poorly soluble in water or nasal mucous.

Regeneration

On principle — a regeneration of the ciliated epithelium is possible, although the restitution of the ciliary function depends on the extent and the

severity of the antecedent defect. In general the restitution develops over one-layered and then multi-layered pavement — or transitional epithelium.

The differentiation into the typical ciliary cells occurs within weeks or month (STOCKINGER AND BURIAN).

Pathophysiology

a) **Viscosity of the secretion**

Exsiccation, according to PROETZ, is the only natural enemy of the ciliary function. Experiments show that excessive fluid does not cause any harm to the cilia — when the fluid has physiological properties, naturally. On the other hand, just a slight deficiency of fluid causes danger to or death of the cilia almost immediately.

DALHAMN stated that in the trachea of the rat the ciliary movement ceased at about 30 per cent relative humidity only after 3—5 Min. and at 50 per cent after 8—10 Min. At 70% humidity, there was no discernible reduction of ciliary activity. A desiccation over 15 Min. and more causes an irreversible ciliary stop (PROETZ).

b) **Temperature**

The optimum temperature for ciliary activity is between 18 and 37° Celsius, that means, of course, the temperature of the cilium itself, not of the passing air or fluid. Below 18° the frequency of the ciliary beats decreases and between 7 and 12° the ciliary activity ceases (PROETZ).

However, that phenomenon is reversible if the cold is not too prolonged. — At a temperature of 40° there is a decrease in ciliary efficiency and at about 45° ciliary stop sets in. — v. REE and v. DISHOECK found a remarkable weakened ciliary power when the inhaled air was cooled at about minus 6—8° for 10 Min. The cooling of other parts of the body (skin etc.) did not influence the ciliary activity.

c) **Hydrogen ion concentration**

According to NEGUS, PROETZ, FABRICANT and others the ciliary movement ceases at a pH below 6,4 an above 9,0. Since the covering blanket has a remarkable buffer-effect, high-acid or high-alkaline solutions do not impair the ciliary function as long as the secretion can neutralize the deviating pH.

Only a direct and long-acting contact of the cilia themselves with solutions below pH 5,0 or above 9,0 usually causes a stoppage. For practical work therefore we have to insist that locally applicable nasal medicaments have a pH near the neutral point, at least not exceeding over pH 8,0 and below 6,0.

d) **Gases**

The application of pure oxygen intensifies the ciliary activity for 30—50 per cent, a lack of oxygen causes a slowing down of the cliliary beat. The latter phenomenon has a special theoretical interest, since it is demonstrable also under the condition of a totally normal blood- and oxygen-supply of the underlying mucosa. There is some suggestion that the cilia perform their metabolism not only by means of the mucous membrane but also in a direct manner by means of the surrounding atmosphere. FLOTTES and Colleaques

suppose that the filiform projections play an important role for the gas-exchange of the cilia. —

Carbon-dioxyde slows the ciliaty activity down: 7,5% carbonic acid diminishes the ciliary movement by 1/4, 9% by 1/3, 20% by half. At 80% carbonic acid the beat ceases after 15 Min. (DALHAMN).

e) **Mechanical influences**

A slight touching of the mucosal surface by a cotton-pad — as it is used for surface-anaesthesia — already injures the ciliary epithelium remarkably. Such a manipulation usually causes a long or even irreversible ciliary stop and strips off the ciliary epithelium over smaller or larger areas — as histological preparations prove. We admit that the mucous blanket also works in such a situation as a protecting layer, but one should handle the cotton-pas as little and as cautiously as possible!

f) **Allergy**

For several years we have known, that pollens and other inhalant-allergens not only penetrate into the — sensibilised — mucous membrane but also cause a more or less extended ciliary stoppage (STRÖMME, CHEVANCE, NAUMANN). Recently v. REE and v. DISHOECK found out that also in the human mucosa the ciliary activity is remarkably lengthened by allergens. That happens not only by continuously acting allergens like house-dust, but also by periodically acting allergens like pollens and in the same manner **also out of season!** The question now arises whether this phenomenon is a consequence of the sensibilisation or an original and primary peculiarity of the individual mucosa which allowes the allergens to contact and to enter the mucous membrane.

Pharmacological view-points

Many details concerning the influence of drugs upon the cilia are known today. This is neither the place to list them, nor the time to deal with the importance of osmosis, concentration, locality and manner of application and other physical factors for ciliary activity. Only the few facts being of interest for the therapeutical procedure shall be discussed.

Most of the now available **aqueous nose-drugs** apparently do not hurt ciliary activity — as far as they have a pH between 6,0 and 8,0 and as far as they are not used for a long time. But, **chronic** application of such vaso — active drugs not only injures the cilia but also the mucosa and its vascular and nervous systems.

On the other hand, **oily preparations** sometimes cause effects on the cilia, already after a single application. There is a clear explanation: The nasal secretion is emulsifiable with oils, emulsions, some ointments etc. (BREUNINGER).

Therefore the mucus is able to bind oily medicaments to a certain extent. While the blanket becomes heavier, its transportation is thus prolonged. Furthermore mineral-oils sometimes cause clotting and mechanical obstacles to the cilia. The same observation can be made after the application of some ointment-preparations for the nose.

It is not wise to apply **powdery medicaments** in large amounts to the nose.

Undergreater quantities of powder the mucous blanket, the cilia and the mucosa itself come to harm, especially when the substance is only poorly soluble in water.

Penicillin in higher concentration causes a ciliary stoppage; **Tetracycline** has the same effect, while **Streptomycine, Bacitracin** and **Tyrothricin** as well as most **sulfonamides** and most **corticosteroid**-preparations do not influence the ciliary activity. 2 per cent **Pantocain** as well as 10 per cent **Cocain** stop or slow down the ciliary function at least for a certain time.

Furthermore we could show that some **surface-acting agents** cave a deterioration of the ciliary effect. Causing a remarkable reduction of the viscosity of the mucous, these substances loosen the continuous blanket. Under such a condition the number of the ciliary beats increases but the efficiency of the beats diminishes because there are no more sufficient working-points for the cilia.

In conclusion I have to report that many industrial gases as well as tobacco-smoke impair the ciliary function considerably.

In the given time I could furnish you only with a very fragmentary survey of the ciliar function. As this important protective system of high efficiency is so delicate and liable to all kinds of injuries we have during our daily work, to pay attention to two points:

1) For intranasal medication we should use only drugs whose harmlessness for the cilia is proved experimentally, and

2) Planning and performing rhinological operations we should always keep in mind how we can preserve the ciliary function.

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