Section of Laryngology with Section of Otology

COMBINED SUMMER MEETING HELD IN BRISTOL

LARYNGOLOGICAL SESSION

[*July* 2, 1948]

Chairman—A. J. WRIGHT, F.R.C.S. (President of the Section of Laryngology)

Recent Progress in Nasal Physiology

By ARTHUR W. PROETZ, Saint Louis, U.S.A.

AT first thought I had intended to pick up the thread where I had left it in a presentation before this Society in 1938 (*Proc. R. Soc. Med.*, **31**, 1405) and to bring it up to date by reviewing the literature of the decade. It quickly appeared that such a report would be misleading since progress during this time has, in some phases, rested much more upon older investigations than upon current ones. A few titles of articles appearing since 1938 have been appended. From these it will be seen that research on nasal physiology is still restricted and, as usual, highly specialized.

Before our day, interest was sometimes concentrated upon special investigations such as Braune and Clasen's work on nasal air pressures (1876) and Zwaardemaker's practical treatise on the physiology of smell (1895), but all this seemed fairly remote from clinical rhinology and very little effort was made to bring it closer. Probably the germ from which sprang our present interest was an article written by an Englishman in 1924: "Methods of Estimating the Activity of the Ciliated Epithelium Within the Sinuses", by A. Lowndes Yates. It somehow fired the imagination of investigators in this country and in America and led to a recrudescence of interest in the whole subject of nasal physiology. Co-ordination followed and finally the more systematic application of physiological principles to a none too satisfactory therapy.

It has been reiterated in the textbooks, in a detached way, that the nose moistened and heated the air for the lungs and that it was coated with a ciliated columnar epithelium. In practice, however, physiological processes were treated as something academic, which could be disregarded when the problem was one of eradicating infection. Emphasis was laid upon the "vestigial" character of the nasal structures. Since their importance in maintaining nasal health was not understood it cannot be said that they were wilfully disregarded but the unsatisfactory results of radical exenteration finally forced us to examine them more closely.

To-day we have learned to conserve tissues and functions wherever possible.

Whenever this question of conservation is introduced someone invariably cites cases in which conservation would be folly. I also have such cases. However, these are the exception and we have found it practical to suit our procedures to the requirements and not invariably to go the limit on the mere basis of supposed thoroughness.

Among the trends of the past decade the appreciation of ciliary activity in the nose and especially in the accessory sinuses undoubtedly is first in importance. Cilia are primitive structures surviving anything which does not destroy epithelium. They are powerful in their effect and they behave in an orderly manner. They are our best allies in the prevention and removal of infection and they cannot be indiscriminately done away with if nasal health is to be maintained. The fact that in the average adult nose there are areas of altered mucosa without cilia—and this without producing untoward symptoms—may have led us to underestimate them. Patches of pseudo-squamous epithelium result where the air can strike directly and for this reason they are either dry or accessible to blowing. But in the meatuses about the ostia, and certainly in the sinuses where this is impossible, cilia persist and it is desirable to maintain the continuity of streaming from sinus to ostium, to meatus, to nasopharynx as well as may be. Wherever disease or surgery results in a strip of non-ciliated epithelium in the path of the streaming there is a stasis of the mucus and conditions favourable to bacterial growth are set up. This is not always apparent on inspection for the normal mucus blanket is of microscopic thinness. The mucus is of such nature and of such minute quantity that unless it is augmented by exudates and the degenerative products of inflammation it cannot be seen. With a microscope and by other special means it can be demonstrated and in proportion to the size of the bacterial elements picked up it is completely adequate.

We were taught a generation ago, and with seeming logic, that removing a middle turbinate did not reduce the moistening surface of the nose so very much and that it could be sacrificed in the interests of drainage with relative impunity. To a great extent this is true owing to a circumstance not considered at the time, namely, that the middle turbinates are streamlined to the passing air currents. Thus, although the moistening surface is reduced, there is little interference with the distribution of inspired air. Minor changes of another type may be followed by distressing consequences. This occurs when the air stream is so obstructed or deviated as to project it in a concentrated jet against some restricted area or to deflect it away from some part of the nose, leaving an area unventilated.

As long ago as 1830 Bell described the constriction which exists approximately one centimetre proximal to the naris. Only recently was it pointed out that this constriction projected the initial air stream vertically, setting the pattern for its even distribution through the nose and being largely responsible for the prevention of local dry spots. Thus our predecessors, regarding the removal of nasal tissue wholly from the standpoint of its moistening function alone, did not hesitate to remove it extensively. We think of it now as upsetting the even distribution of air with its attendant mucus stasis and nasal infection.

We know also that the total moisture reaching the lung is not too dependent upon the retention of the nasal structures. It has been shown that breathing through the mouth supplies practically the same humidity at the glottis as breathing through the nose, with the important difference that the mouth soon dries while the nasal mucosa continues to supply moisture. There is one mechanical circumstance, however, which is commonly overlooked, namely, that the air channels are not a tube at all and certainly not a chamber but a series of extremely narrow slits by which arrangement all the inspired air is brought into intimate contact with the nasal surfaces. If we alter this condition the mechanics of nasal respiration are greatly upset.

That the nose is a filter has been known as long as anyone has paid attention to such things. "The nares", writes Cicero, "which are always open on account of necessary functions have narrower entrances lest anything which might be injurious should enter them, and they always are supplied with a moisture not useless for arresting dust and many other things." We know that this takes place through sifting, through impingement and through adsorption. It is axiomatic that a filter must be rid of the residue which accumulates upon it if it is to continue to function. This the nose does very well by means of the cilia and their mucus blanket. So long as these remain intact, infection cannot occur, largely for the reason that at the normal rate of progress bacteria which fall on the surface are carried past any given cell in something less than 1/10th second, a time too short for incubation and penetration [12]. What the effect of viruses may be in disrupting this system is as yet not clear.

Nevertheless we are confronted with the fact that all infectious ailments of the nose stem somehow from a single source, namely, the failure of the filter to cleanse itself. That this cleansing mechanism should have first consideration in every plan of treatment and surgery is only an extension of the old principle of maintaining drainage.

It has been shown experimentally that removing strips of mucosa within the sinus is not always followed by complete regeneration and results sometimes in fibrous septa, their extent depending in a general way on the width of the strip removed.

Entering a sinus surgically by enlarging its ostium is comparable to these experiments. It results in a denuded strip of injured bone and the tissue which forms in Nature's attempt to close the opening resembles the experimental fibrous septum and not the normal ostium.

Drainage artificially maintained by displacement over a period of time is preferable to instrumentation of any kind, since it maintains the continuity of ciliary activity.

In 1943 Hilding made a significant contribution to the controversial subject of negative pressure in the sinuses and more especially of its origin [5]. He introduced a needle into each of the frontal sinuses of a dog through the skull and connected them through tubes with separate manometers. A quantity of mucus was injected through another needle into one sinus, the other being used as a control. As the mucus was forced out through the ostium by the cilia the pressure began to fall in the manometer of that side, the other remaining stationary. The experiment was then repeated after killing the dog, to rule out possible air absorption. The results were the same except that the negative pressure was slightly less than in the living animal. The published graphs show a drop of 44 mm. of water in fifteen minutes in the dead animal. This is a negative pressure comparable to that produced by a violent sniff (50 mm. Braune and Clasen).

Ciliary streaming within a sinus does not approach the ostium in a haphazard pattern but assumes a roughly vortical character, the direction of whorl being opposite on the two sides [6]. This is of interest in view of a similar observation regarding the trachea and bronchi by Barclay, Franklin and Macbeth (1937, *J. Physiol.*, **90,** 347).

It has been observed that stimulation of the intact vagus in dogs causes a vigorous constriction in the nose with a drop in nasal air pressures without affecting the general circulation as evidenced by the femoral blood-pressure [8]. Injection of histamine into the circulation causes a dilatation of the nasal vessels, but the effect in this case is general although there seems to be a certain specificity for the nasal vessels. Sympathetic activity is said to predominate following exposure to cold.

The absorptive capacity of the nasal mucosa is variable [10]. Any increase in blood and lymph circulation whether produced by physical or pathological agents increases absorption. The ease with which absorbable drugs are taken up by the sinus mucosa after displacement depends upon the viscosity. The absorption is apparently somewhat selective.

Protracted exposure to toxins of infection stops the activity first of mucous and then of serous glands [1].

The subject of lysozyme in the nasal secretions still appears sporadically in the literature. It is reported [13] that the lysis of test bacteria by nasal mucus is inhibited by acid concentrations which may be present "in the usual pH swings". In acid media adsorption takes place but no lysis. Change to a neutral reaction completes the cycle, but the bacteria may already have been killed by the adsorption, without being dissolved. The same author states that lysozyme disappears on the first or second day of a cold, and that there is none to be found in a "running nose". Secretions from hay-fever sufferers showed a high lysozyme content.

Some controversy still exists regarding the normal pH of the nasal mucosa. It seems likely that the figure closely approximates 7 under varying conditions and that the disparity in findings of various investigators is due to technical errors and the shifting reactions of the secretions on the surface [16, 17].

It has been shown clinically that deficiency of the thyroid hormone may result in changes in the nasal mucosa which can be recognized [25]. These changes may be either exfoliative in nature or resemble the pale, boggy manifestations of allergy. Patients deficient in the thyroid hormone commonly have an increased tendency to nasal infection which can be corrected by the administration of thyroid extract alone. Similarly, allergic individuals are less apt to exhibit nasal symptoms under an adequate thyroid supply.

The use of the extract and the dosage are best determined by the patient's response, the basal metabolic rate is of secondary importance and at times misleading.

This finding is in line with what is known of the general tissue reactions to deficiencies in the thyroid hormone. The symptoms arising in the nose which respond to thyroid administration, namely, extravasation, changes in the nature of the surface fluids, permeability, malnutrition, swelling and œdema, could logically result from these reactions. Any of them would render the mucosa more susceptible to infection and possibly to antigens as well.

This by no means touches upon all the individual observations in nasal physiology during the last ten years but it epitomizes those which are apt to have an influence on our clinical management of nasal disease.

ARTICLES FOR REFERENCE

MUCOSA

1 BRUNNER, H. (1942) Nasal Glands, *Arch. Otolaryng., Chicago*, **35**, 183.
2 BURCH, G. E. (1945) Study of Water and Heat Loss from Respiratory Tract of Man: Gravimetric Method for Measurement of Rate of Water Loss, Quantitative Method for Measurement of Rate of Heat Loss, *Arch. intern. Med.*, **76**, 308.
3 DAVIES, C. N. (1946) Filtration of Droplets in Nose of Rabbits, *Proc. roy. Soc., London*, s.B., **133**, 282.
4 FRENCKNER, P., and RICHTNER, N. G. (1940) Ciliary Movement in Upper Respiratory Tract in Man and Animals under Normal and Pathologic Conditions, *Acta oto-laryng., Stockh.*, **28**, 215.
5 HILDING, A. C. (1943) Role of Ciliary Action in the Production of Pulmonary Atelectasis, Vacuum in Paranasal Sinuses and in Otitis Media, *Ann. Otol. Rhin. Laryng.*, **52**, 816.
6 —— (1944) Drainage of Mucus in Man, *Ann. Otol. Rhin. Laryng.*, **53**, 35.
7 —— (1945) Production of Negative Pressure in Trachea and Frontal Sinus by Ciliary Action. Further Experiments, *Ann. Otol. Rhin. Laryng.*, **54**, 725.
8 JACKSON, D. E. (1942) Experimental and Clinical Observations Regarding Physiology and Pharmacology, *Ann. Otol. Rhin. Laryng.*, **51**, 973.
9 LEASURE, J. K. (1941) Mucus Sheet on Membrane, *Arch. Otolaryng., Chicago*, **33**, 66.
10 SALTZMAN, M. (1944) Absorptive Capacity of Nasal Mucous Membrane, *Arch. Otolaryng., Chicago.*, **40**, 44.
11 PROETZ, A. W., and PFINGSTEN, M. (1939) Tissue Culture of Nasal Ciliated Epithelium, *Arch. Otolaryng., Chicago*, **29**, 252.
12 —— (1946) Nasal Physiology in Relation to the Common Cold, *Ann. Otol. Rhin. Laryng.*, **55**, 306.

BIOCHEMISTRY

13 CAHN-BRONNER, C. E. (1942) Presence and Action of Lysozyme in Nasal Mucosa, *Ann. Otol. Rhin. Laryng.*, **51**, 250.
14 CICARDO, V. H. (1943) Release of Potassium by Excited Mucosa, *Publ. Centro Invest. tisiol*, **7**, 279.
15 DIETZ, A. A. (1944) pH of Mucosa of Some Animals, *Proc. Soc. exp. Biol. Med., N.Y.*, **57**, 339.
16 NUNGESTER, W. J., and ATKINSON, A. K. (1944) pH of Nasal Mucosa Measured in Situ, *Arch. Otolaryng., Chicago*, **39**, 342.
17 PARKINSON, S. N. (1945) Determination of Intranasal pH—Discussion and Criticism, *Arch. Otolaryng., Chicago*, **41**, 68.

NEUROVASCULAR SYSTEM

18 ALLEN, W. F. (1943) Distribution of Cortical Potentials Resulting from Insufflation of Vapors into the Nostrils and from Stimulation of Olfactory Bulbs and Pyriform Lobe, *Amer. J. Physiol.*, **139**, 553.
19 HYNDMAN, O. R., and WOLKIN, J. (1942) Autonomic Mechanism of Heat Conservation; Effects of Cooling the Body: Comparison of Peripheral and Central Vasomotor Responses to Cold, *Amer. Heart J.*, **23**, 43.
20 RALSTON, H. J., and KERR, W. J. (1945) Vascular Responses of the Mucosa to Thermal Stimuli with Some Observations on Skin Temperature, *Amer. J. Physiol.*, **144**, 305.
21 VAN DISHOECK, H. A. E. (1942) Inspiratory Resistance, *Acta oto-laryng., Stockh.*, **30**, 431.

ENDOCRINES

22 EGGSTON, A. A. (1940) Experimental Evidence of Gonadotropic Hormone in Mucous Membranes, *Laryngoscope, St. Louis*, **50**, 191.
23 MELCHIOR, R. (1945) Relation of Nasal Mucosa to Sex Hormones, *Ann. Oto-laryng.*, **12**, 220.
24 MORTIMER, H. (1940) Genitonasal and Genitoaural Relationships, *Laryngoscope, St. Louis*, **50**, 349.
25 PROETZ, A. W. (1947) The Thyroid and the Nose, *Ann. Otol. Rhin. Laryng.*, **56**, 328.

GENERAL

26 PROETZ, A. W. (1941) Applied Physiology of the Nose. St. Louis.

Gösta Dohlman (Lund, Sweden) asked whether the experiments with soluble dye were made on the living animal or on the preparation. He had put fluorescent particles in the nose and had not been able to observe that these soluble particles dyed the mucous membrane. This could be seen under ultra-violet light. He used fluorescent solution, which was carried away with the mucous blanket. He had tried to observe the same thing with pollen in hay fever, but he had not been able to trace what happened to the pollen. He wondered whether Dr. Proetz, working on these lines, had thought of the mechanism of action of the pollen as comparable with a soluble dye or a virus. Or was there some activity in the pollen particles themselves? Was there something in the action of the pollen, working itself down to the cell, which was likely to cause the allergic reaction or could the activity be compared with that of a virus or infectious agent in a watery solution?

R. G. Macbeth referred to the spiral movement of particles in the trachea. What did Dr. Proetz think was the explanation of this movement? If the particles did not go up in a spiral a certain number of them would reach the carinæ at every bifurcation in the bronchial tree and tend to stick or to fall back again; but, in a spiral movement, there was greater likelihood that they would dodge the carinæ and so reach the pharynx.

F. A. Pickworth asked what was the proportion of surface to blood-stream and lymphatic infections of the nasal sinus membrane. Professor Proetz had confined his remarks to surface infection, and the literature was vague on this question, except that it was established that in the specific infectious fevers the sinus membrane is always involved.

A point of interest concerning the cilia was their collective force. Sir Leonard Hill had shown that small brass weights were propelled along an excised strip of mucosa by cilial activity. In numerous cases of histological sections of pus or mucopus in situ in a nasal sinus taken at autopsies on mental hospital patients, the mass had formed a ball which evidently had been turned round many times, so that there were layers—as indicated by the polymorphonuclear leucocytes—sometimes amounting to twelve or more.

A. W. Proetz, in reply to several questions, said that regeneration of the mucosa did take place in the right milieu. It was necessary to keep the surface as free as possible from the infectious material which accumulated in the viscous secretions. He used the displacement method in order to get the required vasoconstriction in the cells. This, since the solutions were retained for twelve or fifteen hours, got rid of the irritating substances on the surface. The next thing was to get the surroundings as moist as possible, especially during the hours of sleep. It was arranged that the nose should be in as nearly a physiological condition as possible by maintaining normal moisture and heat and keeping it perfectly free. If sticky mucus were left on the surface its presence was always an irritation.

The other thing which he used was a simple solution which he had found very useful—4% alcohol and 4% glycerin in normal saline. It was found a few years ago that the membrane could tolerate about 18% alcohol, so one was within very comfortable limits in using 4%. What he wanted to do was to have something which would stimulate the flow of mucus and then promptly get itself out of the way so that it would not be a constant source of irritation. Therefore they started with 4% alcohol. It stung mildly and then evaporated and disappeared, and the glycerin left behind held the moisture. If the patient were laid down and his head placed back it was slightly painful; he should be allowed to sit up and the solution be put over his turbinates. The action of this solution is the opposite to that of ephedrine. It was used every four hours for two or three days, and the nose was then given a chance to take care of itself. The blood came from small vessels into the mucosa, and he did not see why that should not be the path of the bacteria as well. He illustrated how the converging streams of mucus came along and the appearance of the section layer on layer.

On the question of spirals, he thought the theory of the Archimedean screw would be all right if the column of air were always upright, but in fact it was horizontal during sleep for eight hours of the night, and, moreover, it varied in different positions, being sometimes more uphill than at others. The drainage of the sphenoid was not entirely uphill; some of it was and some of it was downhill. He had the feeling that this was a developmental matter. In the trachea, considering the adjustment of the whole thing, he imagined that it would be better if the fibres were spiral than if they were longitudinal. He did not know about the accumulation of mucus at the carinæ.

Apparently a small amount of injury of the nasal mucosa did not appear to make much difference. Numbers of people had considerable areas in the nose which were devoid of cilia altogether, and they got along just as well as other people. If the mucosa was anything like normal the cilia around the edge of an inactive area could pull the stream along for quite a distance, so that the inactive area did not really signify. There were no cilia in the pre-turbinate area, and yet the cilia at the margin were strong enough to carry the whole mucus right across the surface. If therefore the ciliated area were destroyed here and there it did not seem to make much difference, though if the destruction was at an important spot, of course, there was trouble.

In reply to a question on air circulation in the nose and the nasopharynx, this was checked by taking a section of a specimen head, not too emaciated, and pinching it between two plates of glass, then passing a current of smoke-laden air through the nose and taking motion pictures. It was found that a vertical rush of air was an invariable result; the air then spread out in various forms of eddies. A point which worried him was that he was not sure that the eddies were not to be considered in relation to the distribution of air in the back of the nose. There was a certain fallacy attaching to a model viewed through a glass plate. The septum was not the equivalent of a straight glass plate. His anatomist and he were trying to work out some nasal reconstruction by means of plastic in such a way that they could get a true representation of the nose, but they had to admit that noses, like other parts of the anatomy, varied, and this was a long job, and he did not yet know the answer. Comparative anatomy could be studied to any extent. The functions of the sinuses, for example, differed very greatly. In some lower animals, such as the seal, there were no sinuses. He had an idea that the sinuses might be insulatory in their nature. The giraffe, for instance, had a brain about as big as one's fist, and all the rest was sinuses—an air jacket.

He had no particular experience of the phase of the subject which Dr. Dohlman had developed. He had wanted to make it clear that he was not so much concerned with the infection of the cells and whether they could be stained as he was to try to work out some means by which an invading mechanism could stay in contact with one cell surface long enough to infect. If the substance was soluble it could spread over enough of the surface as it moved along to affect the viscosity of the mucous blanket and so make it ineffective. A slight variation in the mucus content had a great effect on the viscosity. If a soluble substance could bring that viscosity down to a point where the mucous blanket could no longer be pulled over the surface, like a tablecloth over a table, an opening was afforded for infection. This was admittedly theoretical.

As to the nature of the ciliary movement, nobody knew why it took that particular pattern nor what caused it. He had tried ways of getting enough magnification of the cilia to see whether they had any structure that would give an indication as to what made them move. The cilia were difficult to study and to photograph; they were packed closely and were highly refractile. It was like taking a photograph of a plastic hair-brush while the bristles were moving at 10 or 15 cycles a second. Sodium light had been used, also polarization; the stroboscope and the high-speed flash had been employed, but no structure could be seen in the cilium. It was the deduction of Seo (1931, *Jap. J. med. Sc. Tr. III*, Biophys., **2,** 47) that the movement was nervous. Various experiments had been made, but the result was hard to evaluate. It might be a chemical stimulation due to potassium secreted at the end of a nerve. The subject was an open one.

The Nasal Mucous Membrane in Relation to the Lymph Stream and Cerebrospinal Fluid

By J. M. Yoffey

The nose in mammals possesses a rich submucous lymphatic plexus, which drains finally into the deep cervical duct or jugular lymph trunk. The deep cervical duct descends alongside the internal jugular vein to enter the thoracic duct on the left side, and the right lymph duct on the right. The deep cervical duct passes in most mammals through one large lymph node, but in monkeys and man the single large node is replaced by several smaller ones, strung along the course of the duct to give a characteristic appearance. Submucous lymphatic plexus, collecting vessels, cervical lymph node or nodes, and deep cervical duct together constitute a single functional pathway for the flow of lymph, mainly from the nose, but to a lesser extent from the mouth, pharynx and deep structures of the neck. We have called this the deep cervical pathway.

The deep cervical pathway can be clearly demonstrated as a functioning unit by the nasal instillation of a vital dye, as shown by Yoffey and Drinker (1938, *J. Exp. Med.*, **68,** 629). The dye passes through the intact mucous membrane, enters the submucous lymphatics, and passes through the lymph node or nodes and the cervical duct to reach the blood. On subsequent dissection the pathway stands out very sharply—almost diagrammatically—and is deeply coloured by the dye. The more functional aspect of the pathway can best be shown if the cervical duct is first cannulated, and clear lymph obtained, and then dye introduced into the nose. It is only a matter of minutes before dye begins to appear in the cannula in gradually increasing concentration.

Not only dyes, but also proteins of low molecular weight, such as egg albumin with a weight of about 34,000, can readily pass through the living and intact nasal