

Paparella: Volume I: Basic Sciences and Related Principles

Section 2: Physiology

Part 2: Head and Neck

Chapter 12: Physiology of the Nose and Paranasal Sinuses

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The nasal pyramid, as pointed out by Schaefer (1920), is a uniquely human attribute not possessed by any other primate. Since it is large and centrally placed, it is an individual's chief characterizing facial feature and, according to Groner (1963), is of basic importance in the formation and preservation of the body image.

For these reasons questions as to why there is a nose, what it does, and how it does it were among the earliest physiologic interests of the physician.

The first physiologic concepts of the nose, like all early physiologic concepts, were based on intuition. It was eventually realized that intuition is not enough; there must be rigorous scientific validation if the factual is to be separated from the merely fanciful. The rhinologist became the first respiratory physiologist. It is therefore not surprising that Rohrer (according to Mead), the father of respiratory mechanics, was the son of a distinguished rhinologist.

Early primacy was, however, a misfortune to rhinology. The fact that air, below Mach 1, behaves like an incompressible fluid of low viscosity was lost on those engaged in rhinologic research that preceded explanation of the flow of fluid through round pipes, to say nothing of flow through twisting conduits of irregular circumference and varying section. The experiments of the rhinologist were inconclusive and frustrating.

Mathematics and physics are basic for study of driving pressure, resistance, conductance, and flow rate, as Reynolds (1883) demonstrated in deriving the criterion of whether turbulent flow can be sustained by fluid flowing through a round pipe. The mathematics of hydrodynamics, however, proved to be difficult for the rhinologist.

The doctrine developed that intuitive hypothesis, particularly the concept of final purpose, is scientifically inadmissible. This, it was said, is "teleology" or armchair science. This dogma conceals the fact that the roots of nasal physiology, as of any science, lie in intuitive reality. Disregard for application and intuition, as Courant and John (1965) point out, leads to an introverted science, isolation, atrophy of the imagination, and a smug purism.

Rhinologic physiology was undone by the rush of enthusiastic hope for a "scientific" practice of medicine because it did not have the steady and saving grace of a foundation in the basic sciences. The rhinologist was also deprived of a normal impulse toward justification by a profound feeling of guilt, for indeed he had much in his past to regret. Therefore, since the rhinologist could not furnish valid laboratory research support for his claims, physiology and basic science in general began to ignore them and him. Much mention

of the nose or of its possible respiratory activity was cleverly avoided in the formative undergraduate medical years. This resulted in an attrition of respect for rhinology as a discipline, which has extended to otorhinolaryngology as a whole. This bland disregard has even, at times, persuaded the rhinologist himself that such nasal function as is generally conceded to take place is of such minor importance as to scarcely warrant consideration.

The present trend toward early integration of the laboratory and clinic in the teaching of medicine bodes ill for selection of otolaryngology as one of the junior or senior "pathways" by medical students of the future.

Without a properly developed nasal physiology there can be no advances in rhinology. It is high time that the limitation of nasal function to the surface epithelium and ciliary streaming is corrected by the realization that the present attitude of many otorhinolaryngologists must be abandoned for a thorough involvement of otolaryngology in basic rhinologic research.

Anatomic Considerations

Epithelial Lining

The epithelial membranes of the human nose must provide humidification, filtration, temperature regulation, and protection. In this regard, form has followed function, and specific sites within the nose are covered by a particular type of epithelium. As the air stream enters the anterior nose, vibrissae aid in the initial filtration process; while keratinized, stratified squamous epithelium interspersed with sebaceous and sweat glands protects this region from the trauma from the outside world inherent to a portal of the upper respiratory tract (Negus, 1958). Beginning at the posterior aspect of the vestibule, the remaining nasal cavity, with the exception of the 2 cm² of olfactory mucosa, is lined by respiratory epithelium (Fig. 1). (Busuttil and colleagues, 1977). This epithelium varies morphologically depending on its location. The paranasal sinuses are lined by a flattened pseudostratified to simple columnar ciliated epithelium, which may increase their vulnerability to infection. In particular, there is a paucity of seromucinous glands, a thin epithelium with a minimal lamina propria, and the basement membrane is absent, which diminishes the exchange between tissue fluids and the environment (Topozada, 1980). Reflecting the transition from regulation of filtration to conduction of the air stream, the most posterior aspect of the nose is covered by a moist, nonkeratinizing, stratified squamous epithelium (Jafek, 1983).

The nasal respiratory epithelium contains highly specialized cells, the most apparent of which are the ciliated cells. Each cilium is characterized by two central microtubules surrounded by nine outer doublets (the typical pattern of nine plus two) with connecting dynein arms. In the absence of these arms, as in the immobile cilia syndrome, there is mucous stasis and sterility. In contrast, normal cilia move in a metachronal beat toward the nasopharynx propelling a mucus blanket. This beat is facilitated by the stratification of the mucus, which is composed of a thinner, periapical layer and a surface, nasal luminal layer that is thicker (Wolstenholme, 1970). Other important elements of the mucosa are the goblet cells, which synthesize and discharge the glycoprotein containing mucus (Rhodin, 1966). Other cells include the intermediate and basal cells, with as many as 11 different respiratory epithelial types being described in various species. However, as recently noted by Jafek (1983), it is

probably inappropriate to offer as a precise description of the human nasal mucosa the findings in nonhuman and lower respiratory tract observations.

Vasculature

Burnham (1935, 1941) found the arterial supply to the inferior and middle turbinates to be from the sphenopalatine artery (external carotid system) and its branches, which run in the periosteal layer of the mucoperiosteum. The arterial supply divides into (1) a superficial system, which supplies the surface epithelium and the tissue immediately subjacent, and (2) a deep system, which enters canals in the bony skeleton of the turbinates that are lined with periosteum. The periosteum of these bony canals contains venous plexuses carrying blood away from the deep (true) layer of erectile tissue. Dilatation of the canalicular arterial vessel, therefore, tends to produce distention of the erectile tissue. The remainder of the arterial supply comes from the superior labial, descending palatine, and greater palatine arteries (all three of the external carotid system) and the anterior and posterior ethmoid arteries of the internal carotid system.

Certain blocks of cavernous tissue react as physiologic units. The cavernous tissue of the inferior turbinate is divided into three functional areas; the first comprises the anterior two-fifths of the turbinate; the second, the middle one fifth; and the third, the posterior two-fifths. It was found that these areas of cavernous tissue do not contract systematically in an anteroposterior direction. Ephedrine applied to the posterior area causes shrinkage of the anterior region but has very little effect on the middle area. Application of ephedrine to the middle area produces comparatively little effect on the anterior and posterior areas but exerts a powerful constricting effect on the plexus of vessels in the bony canals. Under normal circumstances, reactions in the two anterior segments are carried on without any appreciable influence on the posterior region. The influence of the area of the posterior tip on the anterior tip is called into play only when the first area is subjected to excessive stress. Removal of the anterior tip of the inferior turbinate produces much subsequent discomfort to the patient, the most annoying symptom being watering of the ipsilateral nose. Removal of a mulberry posterior tip of the inferior turbinate has not been found to produce symptoms.

The arterial supply (from the inferior turbinate) to the maxillary sinus gains entrance through the ostium and the bone immediately surrounding it. The veins accompany the arteries. On reaching the sinus interior, the vessels form a collar-like plexus about the ostium a few millimeters in width and then radiate out in straight lines from the plexus "like the setting sun". Negus (1958) found that the arrangement of the vascular supply to the turbinal tissues and nasal mucosa generally allowed four possible modes of reaction of the nasal mucosa and swell bodies: (1) Hyperemia of surface vessels with filling of erectile tissues. This is associated with an increase in mucosal temperature and may be produced by exposure to cold, dry air. (2) Ischemia of superficial vessels, shrinkage of cavernous tissues, and decrease in mucosal temperature, which may be produced by exposure to warm, moist air. (3) Ischemia and constriction of superficial vessels but congestion of cavernous tissues. This reaction may be produced by breathing warm air of average relative humidity. (4) Superficial arterial dilation with increased mucosal surface temperature but without congestion of cavernous tissues. This reaction may be produced by superficial irritation.

Innervation

Common sensation, according to Slome (1966), is carried from skin, mucosa, and subcutaneous and submucosal tissues by the first and second divisions of cranial nerve V. Motor supply to the nasal respiratory muscles (second branchial arch derivatives) is through cranial nerve VII; integration of their contraction with the respiratory rhythm is carried to cranial nerve VII by the vagus.

The physiologically important control of the circulation to the nasal airways is mediated by the autonomic system. The adrenergic nonmedullated postganglionic fibers pass through the sphenopalatine ganglion, without synapsing, to the serous and mucous glands of the respiratory epithelium. These sympathetic fibers to the nasal structures originate in the first and second thoracic segments of the spinal cord. One preganglionic adrenergic fiber synapses in the outlying superior and middle cervical ganglia (stellate ganglion) with about 30 postganglionic fibers. Sympathetic (adrenergic) action is, therefore, quite diffuse. Postganglionic fibers travel in a plexus around the internal carotid artery, and then, via the deep petrosal nerve and nerve of the pterygoid canal (vidian nerve), they travel to the sphenopalatine ganglion. The parasympathetic fibers (cholinergic) also pass through the vidian canal to the sphenopalatine ganglion. These fibers have their cell bodies in the superior salivatory nucleus in the brain stem and project fibers via the intermediate nerve to join the facial nerve in the internal auditory canal. They leave the facial nerve at the geniculate ganglion and pass to the middle meningeal artery by way of the greater petrosal nerve. Here, with sympathetic fibers from the middle and superior cervical ganglion, they form the nerve of the vidian canal. When the parasympathetic fibers reach the sphenopalatine ganglion, they synapse and send their postsynaptic fibers to the vessels and glands of the nasal mucosa. The neuroeffector substance for the postganglionic adrenergic fibers is norepinephrine and that for the postganglionic cholinergic fibers is acetylcholine.

In general, the effects of the sympathetic and parasympathetic nervous systems are antagonistic. In some areas, however, both systems cause the same general effect but of a different quality. For example, parasympathetic stimulation causes an abundant, watery, saliva-like flow, whereas sympathetic stimulation causes a mucinous, "enzymatic" secretion in the nose. The non-medullated adrenergic fibers end in relation to the arterioles and do not supply precapillaries or capillaries. Following cervical sympathetic block (producing parasympathetic overaction), nasal hypersecretion, hyperemia, swelling, and obstruction occur. Following section of the greater petrosal nerve, according to Gardner and co-workers (1947), the nasal mucosa becomes pale, dry, and shrunken from the effect of unopposed adrenergic activity.

Disorders of nasal function that are associated with so-called autonomic imbalance can be explained by the hypothesis of Szentivanyi (1968). Interruption of the action of catecholamines on the effector substance adenyl cyclase is responsible for symptoms attributable to allergic hypersensitivity.

Lymphatics

Rouviere (1938) stated that the lymphatics of the maxillary sinus anastomose with one another and converge beneath the mucosa toward the sinal ostium. After coursing through the

ostium, they arrive at the middle meatus and unite with the lymphatics of that region. The lymphatic trunks of the middle meatus join the lymphatic plexus lying above the pharyngeal orifice of the eustachian tube, which is also joined by the "paratubal lymphatics". From this plexus, the lymphatics of the middle meatus drain to the lateral retropharyngeal nodes.

The lymphatics of the inferior meatus do not communicate freely with those of the middle meatus, nor at all with the lymphatic plexus above the torus, but drain to the deep cervical internal jugular nodes. This somewhat unexpected distribution of the lymph vessels has a definite influence on the production of serous otitis media in conjunction with chronic infection of the ipsilateral maxillary sinus. The products of inflammation cause congestion in the lateral retropharyngeal nodes, which also accept lymph from the plexus above the torus. This latter plexus receives tributaries from the paratubal lymphatic trunks from the membranocartilaginous portion of the eustachian tube. The resulting tubal lymphedema causes eustachian tube blockage and subsequent serous otitis media.

The blood and lymph capillaries of the nasal mucosa lie in the superficial stroma, whereas the larger blood and lymph vessels lie in the deep stroma. The mucous membrane as a whole rests on a periosteum of variable thickness. The fact that all the blood and lymph channels entering or leaving a sinus pass through or close to the sinal ostium is of considerable clinical importance. In inflammation, with swelling of the mucosa in the region of the ostium, this anatomic arrangement leads to early edema and congestion of the sinal lining. This relationship also contraindicates instrumentation through the ostium because of the possibility of interference with lymphatic and venous return from the sinus.

Nasal Respiratory Function

Majer (1968) quoted Galen as saying "... the parts of the lung will never be chilled when often time the air surrounding us is very cold, and the particles of dust, ashes, or anything else of the sort very frequently mixed with the air will not penetrate as far as the artery (Trachea)". For both clarity and convenience, although there is considerable overlap, the respiratory functions of the nose have been considered to be (1) an airway; (2) a mechanical, negative feedback control to match the supply of air to the need for alveolar ventilation; (3) a tempering mechanism for inspired air and partial control of body temperature; (4) a humidifier of inspired air; (5) a filter of inspired air for dust and microorganisms; and (6) as a practical consequence of the latter, a device for resistance of the nose and paranasal sinuses to invasion by pathogenic microorganisms.

Airway

Phylogenetically and embryologically, the nose is an essential respiratory organ. Oral respiration is an animal physiologic acquired and learned substitute to be used only in periods of emergency or increased ventilatory demand. Long periods of mouth-breathing are inefficient and lead to increased expenditure of energy for a given alveolar ventilation (Yasa, 1939; Manchioli, 1942; Ogura et al, 1968). Hellman (1927) recognized that the physiologic superiority of nose-breathing to mouth-breathing is based on the slower, deeper respiration he found associated with the former. He suggested that inadequate mixing occurred in mouth-breathing, that mass transfer of inspiratory gas might interfere with maximum diffusion of O₂ in the pulmonary alveoli, and that the slower, deeper respiration associated with nasal

breathing gives more needed time for this process. These opinions received support from Arnott and coworkers (1968). Pattle (1963) and Williams and associates (1966) suggested that deeper breathing dilates the more peripheral alveoli and allows better surfactant distribution, preventing development of microatelectasis. Although arterial pH, pO₂, and PCO₂ apparently control respiration, Haldane and coworkers (1919) found shallow breathing to cause anoxemia and, in turn, anoxemia to cause further shallow breathing, resulting in a vicious circle.

Lüscher (1930) found a decrease in alkali reserve and respiratory acidosis, and Noonan (1965) described reversible cor pulmonale in patients with nasopharyngeal airway obstruction secondary to hypertrophied tonsils and adenoids. Luke and associates (1966) and others have confirmed this phenomenon. Slocum and coworkers (1976) demonstrated decreased PO₂, decreased pulmonary compliance, and increased pulmonary resistance in patients with nasal obstruction, whereas Cavo and associates (1975) found blood gases unchanged in laryngectomized dogs with nasal packing. This latter finding suggests the absence of a nasopulmonary reflex and simple upper airway obstruction as the underlying etiology for observed changes. Although much has been written on this subject, the site responsible for increased airway resistance, if indeed it does exist when the nose and nasopharynx are obstructed, remains obscure.

Resistance

The nose acts as a variable resistor and may account for as much as 40 per cent of total airway resistance. The efficiency of the nose as an airway is dependent upon the downward direction of the nares, the small inlet and large outlet, the shape and size of the nasal cavity, the streamlined nasal turbinates, and the flow velocity. This simple but accurate relationship may be stated:

$$R = K(PLV/D^4).$$

In this equation R = resistance, K = constant, P = gas density, L = tube length, V = velocity of flow, and D = tube diameter.

During normal respiration, pressure changes in the nasal chambers approximate 6 cm of water, and flow rates average 15 liters per minute (Hilding, 1976). Under these conditions, the size of the nasal vault (tube diameter) is the most susceptible parameter to change. This change is influenced by vasomotor response to hormones, emotions, the environment, and a long list of pharmacologic agents. Vasomotor reactions of the nose are partly under the control of acetylcholine mediated by the parasympathetic nervous system fibers that originate in the hypothalamus. Acetylcholine is normally destroyed by acetylcholinesterase within 30 msec. This process is speeded up by the ions calcium and magnesium and slowed by the sex hormones estrogen and, to a lesser degree, testosterone. In liver disease in which the liver fails to metabolize estrogen, this hormone attains increased circulating levels, resulting in nasal congestion (Taylor, 1973).

Fear and terror result in vasoconstriction and mucosal shrinkage (sympathetic response), whereas resentment, humiliation, frustration, and anxiety lead to vascular engorgement with swelling of the erectile tissue and increased volume of nasal secretions (parasympathetic response). Hyperemia, nasal obstruction, hypersecretion, and even pain can

occur with sexual stimulation, menstruation, pregnancy, or inhalation of irritant fumes and dusts. This may be a result of histamine release or a decrease in sympathetic tone.

An additional mechanism for nasal congestion is proposed by Taylor (1973). He suggests that the stimulus of passing air through the nose expands the ipsilateral lung by means of a reflex arch in the hypothalamus. Conversely, lung compression causes ipsilateral nasal congestion. This may well explain the nasal congestion that occurs on the downside while sleeping to be the result of a reflex arch, as opposed to passive gravitational influence.

Nasal Cycle

Another factor that affects the diameter of the nasal vault is the nasal cycle. The upper respiratory tract is a twisting, curving, closed conduit of varying section and irregular circumference stretching from the nares to the glottis. Its nasal portion is divided from nares to choanae by a wall, the nasal septum.

The teleologic explanation for this division is that one nasal chamber may rest while the other carries on the functions of the nose. It is a well-supported observation that in a normal nose one nasal airway opens with secretion of serous and mucous glands while the opposite airway closes with almost complete cessation of such activity and that passage of respiratory air is carried on in nearly its entirety through the open nasal chamber. No convincing explanation has been presented as to why such alternation should be necessary for the well-being of the organism.

The presence of a cyclic change (congestion and decongestion of the cavernous tissues of the nasal conchae) was observed by Kayser (1895) and termed the nasal cycle. He suggested that there is a continual shifting in autonomic balance between the two body halves, which, in turn, causes a continually changing blood balance in the erectile tissues of the turbinate and septum.

Emptying of the turbinal and septal swell bodies by the continuously present recoil of elastic fibers surrounding these structures was described by Wright (1910), and the mechanism of filling of these structures was described by Burnham (1941).

Lillie (1923) related the complaint of alternating nasal obstruction, present in some patients, to the nasal cycle. He was first to associate shrinking of the mucosa of one nasal chamber with throwing off of its serous and mucous secretions while the mucosa of the opposite nasal chamber shows an increasing congestion approaching complete nasal respiratory obstruction with repression of secretions. Lillie's findings were confirmed by Heetderks (1927). The former reported that there was a characteristic individual cycle of reaction in about 80 per cent of his test subjects. He found, in general, that the nasal cycle is most active during adolescence and young adulthood and gradually decreases in activity with age. He also found that damp, cold atmosphere brought about the most marked mucosal congestion and warm, dry air a somewhat less marked reaction, whereas optimum conditions in the ambient atmosphere (humidity 50 to 60 per cent and temperature 15 to 18°C) caused cycles of the least degree. Although the same nose might respond somewhat differently at different times under apparently the same conditions, the cycles, including filling and emptying on the same side, occurred characteristically for a given nose over periods of 30

minutes to 4 hours. Heetderks suggested that activity of the nasal cycle might be related to the activity of secretion of the sex hormones. He believed this view to be supported by the appearance of so-called "honeymoon" coryza of marked edema, swelling, and increased serous secretion under the stress of unusual or excessive sexual arousal.

Heetderks also examined the effect of sleeping posture on filling of erectile tissue swell bodies. He found that the turbinates in the dependent nasal chamber reached a maximum size in 15 to 20 minutes. By turning the test subject to the opposite side, the upside of the nose became open and the downside congested in 10 to 15 minutes. He concluded that changes in turbinate congestion, as influenced by position, must be produced by the effect of gravity.

Stoksted and coworkers (1953, 1976) and Arbour and Kern (1975) also found the nasal cycle present in about 80 per cent of individuals tested. Guillerm and associates (1967) studied the nasal cycle by rhinometry and demonstrated that total nasal resistance (using the formula $R = R1 + R2$ in which R is the combined resistance of both nasal airways, R1 the resistance to passage of air through one airway, and R2 the resistance to passage through the other) remains essentially constant in spite of continual cross-sectional changes caused by congesting and decongesting of turbinal and septal erectile tissues in the separate nasal airways. They stressed the functional importance of steadily maintained total resistance, despite the nasal cycle, in noses in which, because of either trauma or developmental aberration, there is great inequality in effective section of the two sides. This was further emphasized by Spoor's (1963, 1967) and Principato and Ozenberger's (1970) findings that total conductance of the nasal airways tends to remain the same no matter what changes in conductance are found when each nasal airway was measured separately.

Ogura and Stoksted (1958) found that when one nasal cavity is anatomically wide and the other narrow, respiration through the wide side is parallel with and about equal to the total nasal respiration. Because of this, the cyclic changes on the wide side are not compensated for by reciprocal changes on the other. During the congested phase on the wide side, they found that obstruction of the upper airway might produce hypoventilation. When very marked septal deflection was present, they found regular and normal cyclic fluctuations on the wide side, whereas on the narrow side cyclic changes were irregular and appeared to be influenced by premature contact of turbinate with septum during the congested phase. When "vasomotor rhinitis" was present, they found that both nasal cavities reacted synchronously to external irritants to an exaggerated degree, with interruption or disturbance of the normal nasal cycle and decrease of total nasal conductance. In the normal nose, they found that bilateral synchronous turbinal reaction to external irritants took place to a limited degree and required only a short time for adaptation so that cyclic rhythm was not disturbed.

Keuning (1968) made cycle determinations on 17 men in their 20s who were found to have normal noses on rhinoscopic examination and who had no history suggesting hypersensitivity or recurring sinusitis. He found regular cycles in seven subjects that were individually characteristic and ranged from 2 to 7 hours; there were no patency reversals in six members of the group and irregular cycles were found in four. The amplitudes of the curves were remarkably constant in a given individual, whether they had rhythmic cyclic congestion and decongestion, irregular cycles, or no reversals of patency. Total nasal conductance remained essentially constant whether regular or irregular cycles or no reversals

were present.

In 19 children between 4 and 10 years of age, cyclic activity while sitting was investigated by use of Zwardemaker's nasal mirror. From his observations, Keuning concluded, as had Kayser (1895), that the nasal cycle appears to be initiated by a physiologic mechanism in which a sympathetic (adrenergic) predominance exists on one body half, whereas a parasympathetic (cholinergic) predominance exists on the other. These predominances alternate from one side to the other. The cycle is not influenced by anesthetizing the nose or the larynx or by mouth-breathing but is absent after laryngectomy. These factors, he believes, are arguments against the cycle originating in the nose, and yet a direct influence from the larynx seems improbable, as does a reflex from the bronchi.

Based on the observation that the cycle continues after anesthetizing the nasal as well as the laryngeal mucous membranes and also continues during temporary prevention of nose-breathing, it was Keuning's opinion that the initiating mechanism of the nasal cycle has not been identified. He believed, that "receptor" structures in the nasal mucosa described by Temesrakasi (1959), Terracol (1958), Majer (1968), and Jabonaro (1953), which are not affected by topical anesthesia, must be the structures responsible, since some balancing mechanism producing the nasal cycle must exist. From experiments on unilateral adrenergically or cholinergically denervated nasal cavities, it appeared to Keuning that while a nasal cycle may be present in the parasympathetically denervated side, one is not present on the sympathetically denervated side. This seemed to him to imply that an intact sympathetic supply is essential for maintenance of the nasal cycle. He offers the "more or less teleological conclusion" that the nose maintains a constant respiratory resistance.

When sympathetic or parasympathetic denervation has been performed unilaterally, the patient may continue nasal breathing because respiratory resistance remains the same. If the situation is altered artificially, the nose adapts itself so as to again offer the same respiratory resistance. The assumption may be made that the nasal cycle is maintained by peripheral vegetative centers, sphenopalatine and stellate ganglia, with interconnections through which an increase of tonus in one set results in a decrease of tonus in the others. The two peripheral centers must be regulated by a central autonomic "center", possibly located in the hypothalamus. By increasing or decreasing the tonus, this center can produce increased or decreased nasal conductance in keeping with the requirements of the organism for intake of oxygen or discharge of carbon dioxide. The conclusion and suggestions of Keuning seem to receive support from the observations of Connell (1968).

Nasal Valves

During periods of extreme inspiratory effort, the equation for nasal resistance becomes invalid because of the nasal valves causing a Starling resistor effort. The collapse of the upper lateral cartilages and engorgement of erectile tissue on forced inspiration are known as the flow-limiting segment, and occlusion of the nasal vestibule by the lower lateral cartilages is referred to as alar collapse (Kern, 1975). These nasal valves are influenced by ethnic origin and the origin of the muscles of second branchial arch (Bridger, 1970; Sasaki and Mann, 1976).

Although it has been said that the cartilaginous skeleton of the lobule prevents drawing in of the nasal wings except under "extreme conditions", this suggests both inadequate anatomic knowledge and lack of clinical observation.

The effect of the nasal respiratory muscles in maintaining nasal section was demonstrated by van Dischoeck. He called attention to the collapse of the ipsilateral ala on inspiration in Bell's palsy, in which the effect of absence of normal tonus in the nasal respiratory muscles may be plainly seen.

Bilateral alar collapse has been seen as a genetic trait in certain families. In a son, father, and grandfather, although the crura of both lower lateral (lobular) cartilages appeared to be present on both sides, the alae nasi were equally drawn in on inspiration, even during quiet respiration. This produced subjective nasal obstruction and forced mouth-breathing. This type of maldevelopment may be more frequent than has been reported, since the cause of difficulty has so frequently been unrecognized.

Rhinomanometry

Without hydrodynamics, the rhinologist cannot subject his hypothesis of a relationship between nasal conductance and cellular metabolism to rigorous scientific tests for support or invalidation by use of rhinomanometry. Without such testing, there can be no valid nasal respiratory physiology. Without clear understanding of nasal respiratory function, it is extremely difficult, if not impossible, to soundly establish either medical or surgical treatment for those nasal diseases or disorders that seem to be associated with problems of air flow.

Is it possible that lack of interest in understanding the physics of nasal respiration may have been a major factor in the decline of the relative position of rhinology in the former "triumvirate" of otology, rhinology, and laryngology? Can patient care be inadequate because of this information gap? Yet, at present, rhinomanometry is an investigative rather than a clinical tool (Wenzel and Sieck, 1966).

Since the last edition of this text, there have been further clinical applications of rhinomanometry. These measurements must include both nasal airflow and nasopharyngeal pressure through the nose. Given this understanding of nasal physics, current clinical rhinomanometers now utilize a manometer that is coupled via the nose (ie anterior rhinomanometry) or the oropharynx (ie posterior rhinomanometry) with the nasopharynx, and a pneumotachometer attached or covering the anterior nose (Goode, 1977).

Mechanical Negative Feedback

After his study of respiration, Goodale (1896) concluded that inasmuch as the manner of breathing of each individual is dependent upon a natural or acquired habit peculiar to that person, absolute figures of nasal pressure indicating that nasal respiratory function is normal or abnormal are out of question even under totally physiologic conditions. Goodale stated, "Experiments instituted, therefore, for the purpose of comparing abnormal with normal pressure changes, must inevitably include considerable error, owing to the fallacy involved in attempting to obtain absolute results from relative and variable factors". This statements was true in 1896 and remains true today. No progress was made toward the assessment of the

hypothesis of nasal respiratory control function until Ogura and Stoksted (1958) realized that, to have any meaning, measurements of nasal pressure, flow, and conductance must be correlated in some manner with respiratory function as a whole.

For more than 100 years, the rhinologist has based many therapeutic guidelines on the hypothesis that valvular structures of the nose, pharynx, and glottis composed an inlet valve for a central effector mechanism in a "fail safe" series. The rhinologist has been frustrated, however, in getting "scientific proof" on this idea because of inadequate understanding of fundamental physical facts. As a result, he has quailed before the icy statement of an occasional academician: "I am aware of no data that support the theory that the nasal chambers can have a significant influence on alveolar ventilation and on oxygenation of the cells of the body".

Nasal respiratory physiology has also suffered from an overeagerness on the part of some rhinologists to devise a "scientific" method of measuring isolated nasal function that not only would support the hypothesis of the nose as a control mechanism for respiration but also would tell them what sort of surgical manipulation should be done and on what part of the nasal chamber it should be practiced.

Humidity and Temperature Regulation

From the standpoint of physics, the alveolar membrane may be considered a water film for diffusion of respiratory gases. Preservation of this water film is necessary for respiration and for life. Therefore, air that reaches the alveolus must be saturated with water vapor. As was mentioned previously, this need is evidence of our marine origin and from a teleologic viewpoint can be considered a major factor in the development of the human nose. As was also said before, the primate nose appears to have regressed to a point at which it cannot supply sufficient water for saturation of inspired air even under average conditions.

Goodale (1896) pointed out, however, that many estimations of the humidifying power of the nose were made without regard to conditions of temperature and humidity of the ambient air, "although it will readily be seen that the consideration of these two factors is important". He found, in general, that while the nose nearly saturates the inspiratory stream that passes through it, owing to the intranasal temperature being cooler than body temperature, it contributes only about two-thirds of the water necessary to maintain the alveolar water film intact.

On computing the energy expended by the nose, he found that about 11.5 gm/cal were used during each respiratory cycle in raising the temperature of inspired air from 1 to 27°C. He also drew attention to the antipyretic effect of breathing cold, dry air. Goodale stated that not only is heat continuously drawn off without disturbing the patient but also that it is primarily drawn from the part of the body that it is particularly desirable to cool in febrile conditions. He believed that the relation of pathologic conditions within the nose to changes in heat and moisture of the respiratory current were important in those conditions in which the nose performs *less* than its customary share of work. Atrophy of luminal mucosa because of disease or surgical manipulation and nasal disorders that produce mouth-breathing are unfortunate in setting "the normal functions of the nose in abeyance".

The findings of Goodale have been repeatedly confirmed, although there has been some disagreement as to the relative importance of the nose in supplying moisture to the inspired air. Cramer (1957) stated that his experiments indicated that under ordinary conditions of relative humidity in ambient air, a laryngectomized patient can humidify inspired air as efficiently as a person breathing through a normal nose. This was not true, however, when central heating, which had not been corrected, had created an atmosphere detrimental to the respiratory tract.

Because of the obvious inability of these structures to cope with the added stress of dry air, Cramer proffered the generalization that the nasal mucosa functions chiefly as a regulator of body heat, humidification being a local factor of minor importance to the airway as a whole. Scott (1954) suggested that regression of the primate nose, as mentioned by Negus, might be explained by substitution of sweat gland and subepithelial capillaries of the primate skin for the nasal structures in temperature control.

Ballenger (1925) observed that the nose reacts to environmental insult of dry air by decrease of conductance because of bilateral engorgement of turbinal erectile tissues. This may result in mouth-breathing. Consequently, the increased demand on tissues of the mouth, pharynx, larynx, and trachea produces chronic irritation and inflammation.

Holmes (1914) stated that when, for any reason, the middle turbinate and lower wall of the ethmoid are sacrificed "there results a deformity that practically produces all the ill effects of mouth-breathing. The inspired air is not sufficiently warmed or moistened and there almost always follows a chronic dry pharyngitis and a chronic laryngitis". Koch and associates (1958) stated that most pulmonary complications relating to tracheostomy appear during the postoperative period and are favored by exclusion of the nasal airway. This results in impaired ciliary activity, increased viscosity of secretion, and decreased resistance to bacterial invasion. Adequate saturation of inspired air with water vapor is also essential for maintenance of pulmonary surfactant. The supply of moisture for this humidification is also provided mainly by the physical process of transudation and to a lesser extent by the secretion of goblet cells in the nasal mucous membrane. Inspired air becomes 75 to 95 per cent saturated during its passage through the nose. The volume of water necessary to saturate the total pulmonary ventilation depends on the ambient temperature and relative humidity. In the average individual, on an average day, this ranges from 700 to 1000 mL of water.

Temperature control is regulated by the autonomic nervous system, with the end-organ being the mucous membrane of the septum and scroll-like turbinates with its cavernous, vascular plexus. During its brief passage through the nose (quiet respiratory flow rates approximate 15 liters per minute), inspired air of 25°C is heated to 37°C. Variations in external air temperatures if greater than 25°C cause less than 1°C change in the temperature of the inspired laryngeal air.

Brown (1951) advocated that a relative humidity of 35 to 45 per cent be maintained in the homes of asthmatic children. He mentioned that the state of health is a very subtle evaluation and that a person is usually unaware of not being in full health unless a derangement or alteration of considerable magnitude or degree occurs. He also suggested we tend to forget or ignore differences in the adaptive capacities of different individuals or different groups of people whose bodies cannot take the punishment of a hostile, arid

environment. Some must either leave a frigid, severe environment, or control it adequately, or suffer from disease and a shortened life span.

It seems evident, therefore, that even if the nose is not totally competent to saturate the inspired air at room temperature, its role is still an important one. It should not, however, be asked to perform beyond its capabilities. Humidification of dry, centrally heated air should not only aid the recovery of those with infections of the respiratory tract but should also be considered a prophylactic health measure.

Cleansing and Protection

Anatomic and Biochemical Consideration

Factors involved in the deposition of particulate matter are size, shape, and density of the particles plus air resistance, velocity, inertia, gravity, diffusion, and electric charge. As air is inspired, it expands in the nasal vestibule and also encounters the hairs of this vestibule (vibrissae). The air stream then constricts in the area of the limen nasi, only to reexpand in the preturbinal area. Here the air stream encounters the anterior end of the inferior and middle turbinates, and it is here, in the anterior one-third of the nose, that the majority of suspended material is deposited. Seventy to 80 per cent of all particles 3 to 5 microns in diameter, 60 per cent of all particles 2 micron in diameter, and almost 0 per cent of particles less than 1 micron in size are retained in the nose (Hilding, 1976).

The mucus blanket normally contains mast cells, polymorphonuclear leukocytes, and eosinophils (Bickmore and Marshall, 1976). It is 95 per cent water with a slightly acid pH and contains salt and glycoprotein mucin. The protein moiety comes from the endoplasmic reticulum near the cell base, whereas the carbohydrate comes from the Golgi apparatus (Abramson and Harker, 1973). Several unusual properties are ascribed to the mucus blanket. In association with ciliary streaming, it is said to form a protective barrier over the underlying mucosa of the nose and paranasal sinuses. Lysozyme (muramidase), an enzyme that disrupts some bacteria, was described by Fleming (1921-1922) as being present in the mucus blanket. Francis (1940) demonstrated the presence of antiviral substance in nasal mucus from adults following infection with influenza virus. It is now the consensus, according to Tomasi and coworkers (1965), that lysozyme is probably identical to immunoglobulin A (IgA) but has an additional factor (immunologic piece) added by the secreting cells, as occurs at all body orifices. Some individuals, according to Bellanti (1968), may inherit or develop a deficiency in IgA or a defect in the mechanism by which the immunologic piece is added. It is the addition of the immunologic piece that activates the immunizing power of the globulin. Either of these deficiencies may make an individual more susceptible to invasion of the upper respiratory tract by potentially pathogenic microorganisms. In addition, immunoglobulin G and interferon have been found in nasal and nasopharyngeal secretions during viral infections (Abramson and Harker, 1973; Ogra and Karzon, 1970).

Proetz (1953) estimated the secretion of mucus and serous fluid from the nasal epithelium to be about 1 liter in 24 hours. According to Lucas and Douglas (1934), there tends to be a viscosity gradient from the surface of the mucus blanket in contact with respiratory air and the surface in contact with the epithelium. Thus, the upper layer is highly viscous, elastic, and tenacious and normally forms a continuous, tough, and movable

protective film. The lower layer is of lower viscosity and forms the medium for the recovery stroke of the cilium.

Hilding (1967) found that the speed of flow of the mucus blanket is not the same in all parts of the nose. The line between ciliated and nonciliated epithelium is not a definite boundary and differs among individuals and between the nasal chambers of the same individual. In the sinuses, the direction of flow is spiral, centering at the natural ostium. If the continuity of cilia through a natural ostium is impeded by scar formation, natural drainage of the sinus through the ostium may be very impaired.

Hilding estimated that the mucus blanket in the nose is renewed every 10 to 20 minutes and in the sinuses every 10 to 15 minutes. Grossman (1975), using saccharin and radioactive resin, described three types of mucociliary flow: (1) smooth, moving 0.84 cm per minute; (2) jerky, 0.3 cm per minute; and (3) mucostasis, less than 0.3 cm per minute.

According to Proetz (1956), dryness is the natural enemy of a cilium. At 70 per cent relative humidity of inspired air (body temperature), there is no discernible effect on ciliary activity, but at 50 per cent relative humidity, ciliary action stops after 8 to 10 minutes and at 30 per cent relative humidity, it stops after 3 to 5 minutes. The optimum temperature for ciliary activity is between 18 and 37°C; ciliary action ceases at between 7 and 12°C.

When considering the resistance of the airways to invasion by pathogenic microorganisms, questions may be raised concerning the abstractive term "rhinosinusitis". Is it a term that validly includes the nasal airways with the paranasal sinuses as a unit in this function? Or is it one in which some confusion may be produced by ignoring differences and favoring similarities for increased taxonomic simplicity? There seems to be some evidence that the latter may be the case.

As Negus (1958) pointed out, many bacteria that strike the mucus blanket become caught in its viscous surface and are transported to the pharynx and swallowed. Hilding (1967) assumes that most of them are destroyed in the stomach and intestines. Davison (1944, 1963, 1967) has found that deficiency in immunoglobulin G (IgG) may favor recurring infection. Recurring infection is also found in the lethal granulomatous disease of children in which there is a defect in the immunologic mechanism of the bursal-derived polymorphonuclear leukocyte. Recently this disorder has been described in the adult. These serious developmental deficiencies may also be associated with chronic disease in the airway.

Virologists point out, as Green (1968) stated, that a viral disease is a disease of cellular necrosis. Necrotic cells form excellent culture media for bacteria. Viruses also appear to stimulate the virulence of dormant or commensal bacteria that may be present. Therefore, in a viral rhinosinusitis, a bacterial factor is usually evident in 24 to 48 hours. even so, acute coryza (generally conceded to be viral in origin) usually has an acute course and rarely is a chronic disease, either in the nasal chambers, the paranasal sinuses, or elsewhere in the respiratory tract. In those patients in whom coryza becomes subacute, the use of antibiotics should be considered.

Neural Reflexes

Two other factors important in the protection of the respiratory tract are reflex apnea and the sneeze. Nasal chemoreception is mediated by three main neural pathways: the olfactory nerve, the trigeminal nerve, and the vomer-nasal complex (lacking in humans)(Doty, 1975). These afferent limbs have a capability of reacting to inspired irritants, and by a reflex pathway, probably involving the vagus nerve, this reaction may result in apnea, bronchial dilatation, laryngeal constriction, bradycardia, and hypertension (Widdicombe, 1973).

The sneeze is a primitive neuromuscular physiologic response to irritation (usually allergic) and autonomic alteration, central nervous system seizure, or paroxysmal psychologic response. The sneeze, or sternutatory reflex, is inborn in most animals. When an irritant contacts the nasal mucosa, the trigeminal nerve provides the afferent limb for impulses to the pons and medulla. Preganglionic efferent fibers leave these latter two structures via the intermediate nerve, course through the geniculate ganglion to the greater petrosal nerve, and then, via the vidian nerve, pass to the sphenopalatine ganglion where they synapse. Postganglionic fibers are distributed to the nasal mucosal blood vessels and glands, causing copious amounts of clear secretions and nasal congestion. Fibers from the pons and medulla also stimulate the respiratory center at the floor of the fourth ventricle. The phrenic nerve then activates the inspiratory mechanism (which may come from the nose and not by way of vagal pathways), which is followed by an expiratory phase. The force of the expiratory phase is determined by the Hering-Breuer reflex and reciprocal innervation of the inspiratory neurons. The palate is raised, and the superior constrictor muscle is contracted so that the lower respiratory passages are separated from the nose. The diaphragm and abdominal muscles contract, causing increased intra-abdominal and intra-thoracic pressure. The nasopharynx is forced open, and air is driven out.

Two connections in this reflex pathway are less understood: (1) The temporal lobe, which, if stimulated during surgery, may result in a sneeze, and (2) the photic sneeze, which occurs when an individual is exposed to bright light. Taylor (1973) suggests that bright lights stimulate the optic parasympathetic fibers via the hypothalamus and also the nasal parasympathetic fibers, occasionally resulting in a sneeze.

Olfaction

In discussing the function of the nose, Negus (1958) stated that the observer has become confused as to what its primary function is because of the secondary functions added to that for which the nose was originally designed. Alberts (1974) states, "the concept of an olfactory organ system emphasizes the functional unity of an integrated complex of neural structures and pathways which, in the normal intact animal, mediates sensitivity to both general and specific chemical cues from the external environment". He continues by saying that olfactory stimuli exert influences on feeding and reproduction and on parental and other behaviors.

In fish, the olfactory organ has uses other than finding and recognizing food and procreation. Various stages in olfactory elaboration can be observed in amphibians and reptiles and in various mammals. A multiplication of specialized turbinal bodies with great complexity exists in macrosmatic carnivores, in which the olfactory turbinates extend into

frontal and sphenoid sinuses. In the arboreal apes and in man, reliance is placed on sight rather than smell, and a regression of the olfactory area is observed.

It has been noted by Orlandi and coworkers (1973) that following the application of an electrical stimulus to the olfactory mucosa, there is a 100 per cent elevation of plasmic cortisol (11-OHCS) within 20 minutes, which returns to normal within 60 minutes of stimulation. They noted that this does not occur in anosmics or when the inferior turbinate is stimulated. This may suggest a phylogenetic importance of the olfactory organ as a mechanism in flight-or-fight arousal.

Anatomy

The organ of smell, according to Morrison (unpublished data), is one of the first special sense organs to develop. Olfactory placodes are apparent as early as the fourth week of embryonic development. Bipolar olfactory cells send axons to the primitive brain as early as the fifth week, and this area later elongates to form the olfactory bulb and tract. In conformity with the path of the main air stream through the nasal chambers and the histologic differences in the nasal mucous membranes Negus (1958) stated that the nasal fossae are considered to have olfactory and respiratory portions. He noted that in a nasal fossa the mucous membrane is unequally divided into two types, the olfactory and the respiratory, in conformity with its multiple functions.

In the noses of mammals, Negus (1958) found a correspondence between the olfactory and the respiratory areas. Both areas are small in species with feeble powers of scent and are extensive in keen-scented animals. The primate microsmatic nose shows a regression from the nose of furred macrosmatic vertebrates. Olfactory epithelium covers the superior turbinate and adjacent septum and is yellow because of the phospholipid pigment it contains. Although Negus postulated that this pigment was important in olfaction, this may not be true, since it is not found within the olfactory cells. The pseudo-stratified epithelium has ciliated olfactory cells, supporting cells (sustentacular cells), microvillar and basal cells, and Bowman's glands (Fig. 2). Approximately 1.25 per cent of the human nasal mucosa is covered by this epithelium, which contains an estimated 1×10^6 to 6×10^6 receptor cells (Brian, 1970; Jafek, 1983). These cells have a centrally placed, euchromatic nucleus with both a distal and a proximal process. The distal rod is approximately 20 to 90 microm in length and ends in a knob that projects 2 microm beyond the mucosal surface. It contains 10 to 30 olfactory surface cilia and a few microvilli (the olfactory vesicle). The central end of the olfactory cell tapers to a process of approximately 1 micron in diameter that penetrates the basement membrane as an unmyelinated axon. After leaving the olfactory cell, the axon is sheathed by central projections, both from a sustentacular cell and from a basal cell. Many axons are then gathered into a bundle that is sheathed by a Schwann cell (Doek, 1976). The fascicles are assembled in the small nerve bundles (approximately 20 on each side) called fila olfactoria that pass through the cribriform plate of the ethmoid bone to the dura. The dura is continuous with the nasal periosteum and encases the nerve to the olfactory bulb. Here, the first-order afferent neurons, both crossed and uncrossed, synapse with the second-order neurons or mitral cells. There are approximately 1000 receptor cells for each mitral cell. It has been suggested that the tightly packed state of the unmyelinated axons in the olfactory fascicle may result in synchronization of discharge in the olfactory nerve.

Although not clearly elucidated, the site of olfactory transduction is probably at the cilia and olfactory vesicle (Menco, 1980). The supporting cells are tall, columnar cells that are closely associated with the other cells of the olfactory epithelium. The function of these cells is unknown in man; however, they appear to separate their adjacent olfactory cells and ensheath dendrite/axon projections within the deeper epithelium (Jafek, 1983). Within the upper olfactory lamina propria lies a polygonal or conical cell known as the basal cell. These cells are stem cells and differentiate into the bipolar olfactory and supporting cells. Recently, a new cell, the microvillar cell, has been described by Jafek in humans (Jafek, 1983). These are tadpole-shaped cells with a tuft of microvilli arising from the apical membrane, which project into the mucous layer of the nasal cavity. The most visible elements of the lamina propria are the pyramidal, tubuloalveolar Bowman's glands. Based on their frequency, proximity to olfactory cells, and occurrence in other species, these glands are assumed to be part of the olfactory process.

Incoming impulses to the bulb retain their strength despite repetitive stimulation, suggesting that olfactory adaptation occurs within the bulb itself. The afferent connections from the olfactory bulb appear to be extremely varied and complex and indicate integration of olfaction with a great many other sensory stimuli that reach higher centers, particularly vegetative centers in the hypothalamus and brain stem. The second-order neurons form the olfactory tract, which goes to the center of the piriform cortex, anterior commissure, caudate nucleus, olfactory tubercle, and anterior limb of the internal capsule. Connections to the centres of the limbic system, or visceral brain, have to do with autonomic function (eg dorsal longitudinal fascicle to the superior and inferior salivatory nuclei). Central connections from the olfactory system also go to the uncus and hippocampus of the temporal lobe, thalamus, hypothalamus, and frontal lobe. Connections to the reticular formation in the brain stem are for odor-alerting response (Park, 1973).

Olfactory Perception

Amplitude of the electro-olfactogram increases logarithmically with the intensity of the odor. The just noticeable difference in odor requires approximately a 30 per cent change in intensity. Configuration and duration of the electro-olfactogram vary with each odorant, and different groups of cells have varied thresholds for different stimuli. Adaptation is characteristic for the olfactory system and overlaps with similar odors. As suggested earlier, the site of adaptation is at or central to the olfactory bulb. The nature of stimulation of odor molecules is also unknown. Several theories exist, including specific molecule receptor sites, inhibition of enzyme systems, maintenance of cell membrane potential, selected absorption, electronic polarization, hydrogen binding, and the undulation theory, which suggests that olfactory cells act as a radiation-sensitive or photosensitive membrane. Getchell and Getchell (1974) suggest that odorant molecules interact with one or more specific receptor proteins located in the receptor cell membrane, resulting in the electrical signals recorded from the olfactory receptor. They feel that different receptors have different thresholds to a given stimulus and that by this interaction each cell apparently has the ability to give specific information regarding the identity of the stimulus.

The olfactory glands (Bowman's glands) secrete a lipolipid material that is spread evenly over the surface of the olfactory epithelium. This material is dissimilar to the secretion of other glands of the respiratory epithelium. It gives no reaction for mucin, nor is it typically

serous. In addition, lipase and esterase are found, and the ducts, but not the acini, are positive for alkaline glycerophosphatase. These same enzyme systems are found in the taste buds, which emphasizes the similarity and the association of these two systems for special sensation.

Association of Olfaction and Other Biologic Functions

The extensive interconnections between the primary olfactory centers and many other portions of the brain suggest that the sense of smell may influence several aspects of biologic function.

The role of olfaction in the reproductive process has been emphasized in observations ranging from the ability of many insects to locate mates by means of odor to the psychologic importance of odors in influencing the emotional life of humans (Zanjanian, 1975). In humans, hormones and their metabolites have profound effects on the mutual relations of the sexes. The incorporation of musk as a base in the more expensive perfumes may be pointed out as a practical application of such observations. The effect of odors on appetite, and thus on eating and drinking, has been mentioned previously. Interesting observations have been made concerning the alterations of water metabolism caused by lesions of the olfactory bulb in rats and also their arousal by low-dosage roentgen rays directed at the same area, but these phenomena are not understood as yet.

During experiments on human subjects in whom the nasal vestibular mechanism was stimulated, Bazarov (as quoted by Wenzel and Sieck) found that vestibular and visceral reactions are increased by some odors but inhibited by others. The excitation of visceral reactions by certain odors is an everyday experience, but an inhibiting effect has not been previously recognized; the mechanism of neither reaction has been satisfactorily explained.

Olfactometry

Morrison (unpublished data) has devised a clinical olfactometer somewhat similar to the diffusion olfactometer used by Zwaardemaker. Both observers point out that there is marked deviation in the olfactory end-point in normal individuals from minute to minute and from day to day. Morrison suggests that this difference may depend on many factors, but he especially mentioned the nasal cycle. Owing to this variability, Morrison concludes that the usefulness of olfactometry in a clinical situation is almost always confined to testing for the presence or absence of anosmia, particularly when a medicolegal question is involved.

Morrison found it impractical to make quantitative tests for olfaction for all the odors as classified by Amoore (1962). He observed that few of his patients could identify by name any of the familiar odors such as cinamon, vanilla, coffee, or castor oil, even though they perceived the odor of the test substance. His findings did not agree with those of van Dishoeck concerning "partial anosmia". Morrison found that if a patient could not smell one of the test odors, he could not smell any of them, and if he could smell one odor, he could smell them all. It, therefore, seemed reasonable to him to reduce the test substance to a single odor. After extensive testing, he selected either oil of clove or oil of orange as the odorous substance to be used. Morrison stated:

The procedure is designed to test olfaction at the threshold of minimum perceptible odor. The test is dependent on the cooperation of the patient just as visual testing and audiometric testing are dependent upon patient responses. A single drop of an oily extract of an odorous substance (either oil of clove or oil of orange) is dropped into an ordinary 10 cc syringe barrel. The plunger is inserted and twisted about so as to get an even distribution of the oil over the inside of the barrel and the surface of the plunger. Any excess of oil is expelled from the tip of the syringe and the outside is carefully cleaned with alcohol or ether. After storage of the syringe with the plunger in place at 0°C no odor can be detected about it. The instrument is now capable of delivering a measured amount of odorized air at a reasonably constant concentration. To use this device the plunger is slowly withdrawn to the number of cubic centimeters of odorized air it is desired to deliver. The nozzle of the syringe is then placed under the nostril to be tested, pointing it away from the other nostril to avoid minor bilateral cross stimulation. The patient is instructed to inhale and as he does so the dose of odorized air is delivered by pushing in the plunger at a constant rate. The patient indicates whether or not he has smelled an odor and identifies it if he can. Responses are recorded as positive or negative: a positive answer is regarded as the slightest acknowledgment that olfaction has taken place. Questionable responses are repeated until a definite answer is obtained.

The normal minimum identifiable odor was determined by delivering a smaller and smaller volume of odorized air until the patient's response became negative. It was determined that a patient should normally detect a dose of 0.1 cc of odorized air (oil of clove). This is utilized as the standard normal. A dose of 10 cc or larger that is not smelled is considered to classify the patient as anosmic.

This appears to be a simple and reasonably accurate clinical method of testing for anosmia. More sophisticated tests of olfaction await development.

Anosmia

The interest of rhinologist in olfaction has been stimulated recently by the fact that in some states anosmia has become a compensable disability under Workmen's Compensation laws. Therefore, most clinicians are more interested in tests that will demonstrate the presence or absence of olfaction than in research as to its physiologic mechanism.

To be smelled, a substance must not only be volatile but must also be soluble in water and lipids. It seems probable that the need for enough moisture to preserve the lipoliquid film over the surface of the olfactory epithelium is a factor in the development of the multiple purpose mammalian nose.

Uncomplicated perceptual anosmia is rare. Congenital anosmia is very unusual and appears to be the result of agenesis of the olfactory bulb. Van Dishoeck (1972) classified anosmia as "conductive" when anatomic obstruction keeps inspired air from reaching the olfactory membrane and "perceptive" when there is dysfunction of the olfactory receptive or transmissive apparatus. He found that "conductive" anosmia is relative and, in reality, is nearly always hyposmia, since odor-bearing air usually reaches the olfactory mucosa to some degree. It has been found that, probably because of their close relationship, taste and smell are readily confused by some patients. Using the stereochemical classification of odors of Amoore

(1962), which will be described later, van Dishoeck determined that some patients may be anosmic to certain primary odors but perceive other scents normally. He classified this as partial perceptive anosmia. The most common cause of temporary obstructive anosmia is the common cold. A more persistent "conductive" anosmia may be produced by marked bilateral nasal polyposis. This is usually, but not always, relieved by medical or surgical eradication of the polyps.

Long-continuing or permanent anosmia may follow viral invasion of the olfactory epithelium or possibly result from the effects of viral or bacterial "toxins" by direct contact with the olfactory cells or through the circulation. Such loss may return rather quickly after the infection subsides, may persist for months or years (return of smell after 5.5 years has been reported by Morrison), or may be permanent.

Neurotoxic effects of some airborne agents may also produce either long-continued or permanent primary anosmia. Thus, anosmia may become a medicolegal problem. Control of odor and potentially damaging fumes is important in industries, particularly in regard to air conditioning and ventilation. The perfume industry illustrates the many subtle ways in which odor, by appealing to one of our most primitive senses, may affect our lives without our awareness.

Severe trauma to the skull with fracture of the cribriform plate of the ethmoid and interruption of the olfactory fibers in becoming the most common cause of perceptive anosmia. In trauma, anosmia may be unilateral or bilateral but is nearly always complete and permanent.

The Guide to Evaluation of Permanent Impairment, published by the Journal of the American Medical Association (JAMA), recommends a 3 per cent disability rating for permanent bilateral anosmia. Man is a microsmatic animal, a group that includes the primates, and the whalebone whales. Except for the toothed whales, which are anosmic, all other mammals are macrosmatic, and in them the sense of smell has survival value. Microsmatic man, however, can exist comfortably without the sense of smell, even though anosmia interferes with the enjoyment of food and some social relationships. It has been found on testing thresholds of odor of "domiciled male veterans" from 49 to more than 70 years of age that the veterans showed an increased in absolute thresholds for odor until about the age of 60 years, after which there appeared to be a constancy in thresholds. It was also found that some senile individuals have normal olfactory function.

Speech

There are three groups of sounds that use the nose as a resonator. These sounds include the nasal consonants, nasal vowels, and nasalized vowels. Nasal vowels are not found in the English language but are used frequently in the French, Polish, and Portuguese languages.

Nasal consonants (*m*, *n*, and *ng*) are produced by the nasal and pharyngeal cavities acting together as a resonator. The oral cavity acts a secondary resonator, the size of which varies in different nasal sounds. When producing nasal consonants, the tongue occludes the oral cavity just as it does with plosives. However, for nasal consonants the velum is lowered,

opening the nasal pharynx and nose to the escape of air. Obstruction to the nose or nasal pharynx results in substitution of the letter *b* for the letter *m*, the letter *d* for the letter *n*, and the letter *g* for the letters *ng*.

Nasalized vowels are characterized by a growing intensity in the range of 250 Hz, a weakening of the intensity in the range of about 500 Hz, and the appearance of weak and diffused components between the vowel formants in the range of 1000 to 2500 Hz. The effect of the nasal resonator on the acoustic quality of vowels is dependent on the comparative impedance of the nasal and oral cavities. If the impedance of the nasal cavity is higher than that of the oral cavity, the effect of the nose as a resonator is relatively small. However, the nasal resonator has a considerable effect on the formation of nasalized vowels if the impedance of the oral cavity is higher than that of the nasal cavity (Kytta, 1976). Nasalization of vowels is more complete in American English than it is in most other languages, allowing nasality a better chance to act as a distinctive feature of speech. This supports the assertion that American English is a "carelessly articulated tongue".

The Paranasal Air Sinuses

The maxillary sinus, according to Schaefer (1932), is usually the largest and is always the most precocious of the paranasal sinuses. Both the maxillary antrum and some portions of the ethmoid labyrinth are usually present at birth. The ethmoid cells, from their beginning in the fetus, are divided into two primary groups by the attached border and lamina of the middle nasal (ethmoid) concha. In Caucasians, the expansion of the maxillary sinus into the alveolar process of the maxilla is often carried to an extreme degree, the roots of the molars and premolars all mounding into the antral floor.

From infancy to adult life, the frontal sinuses vary greatly in size and shape, not only in different individuals but also in the same individual, and supernumerary frontal sinuses are common.

The anterior ethmoid cells also empty into the infundibulum, which is usually described as being continuous with the nasofrontal duct. Weille (1946) stated, however, that the classically described nasofrontal duct is frequently not found at operation, the frontal sinus presenting a simple, round opening into the anterior aspect of the superior meatus.

The sphenoid sinus develops after birth. In the adult, the sphenoid sinuses are usually asymmetric, and their walls are often very irregular and may be indented by the hypophysis, pons, optic nerve, carotid artery, or any or all of these structures.

The maxillary sinus is described as communicating with the middle meatus by an oval opening and as being from 1 to 2 mm in size; accessory ostia are often present (Aust and Drettner, 1974, 1975).

Ballenger (1925) and Myerson (1932) found that the maxillary ostium is sometimes supplemented by a tubular formation of the sinusal mucosa having valvelike activity. This observation was confirmed by Drettner (1965), who found that such a structure is capable of maintaining peak expiratory pressures for considerable periods of time; as a rule, there is a lag between changes in intranasal and intra-antral pressures. Although Drettner did not find

correlations between the presence of obstructed sinal ostia and sinal infection, or even correlations between obstruction and subjective symptoms of infection, it has been inferred from similar findings that subjective symptoms varying from vague discomfort to aching pain have been produced by blockage of the sinal ostial valve. Drettner found that partial or complete block of the sinal ostium is usually present in either acute or chronic disease, but he expressed no opinion as to whether such a block is causative or resultant.

Function

The "reason" for existence of the paranasal air sinuses has never been satisfactorily explained. After an extensive review of the literature and experiments on animal models, Mink (1915) concluded that there is no convincing evidence to suggest that the paranasal sinuses serve any purpose whatsoever. This was also the opinion of Negus (1958). Possibly the most interesting hypothesis as to sinal function is that of Semenov (1950). He suggested that since the paranasal air sinuses seem to bear a similar physical relationship to the nasal airway as the "surge tanks" do to the hydraulic braking system of an automobile, they also may serve to dampen the surge of pressure caused, in the case of the nose, by bringing the air stream to a sudden stop twice during each respiratory cycle.

In sudden deceleration of flow, according to Streeter (1958), a sudden surge of pressure occurs known as the "water hammer". In a surge tank, although surge occurs, the development of a high pressure intensity along the conduit is prevented. In an orifice tank (such as a paranasal sinus), the opening or orifice between tank and conduit is restricted and therefore allows more rapid pressure changes in the conduit than would be permitted by an unrestricted orifice. The more rapid pressure change causes a more rapid adjustment of flow through the conduit and dissipation of excess energy resulting from sudden stoppage of flow.

Abruptly stopping and reversing the flow of respiratory air might well be a stimulus sufficient for the development of the paranasal air sinuses.

Relationship of Sinal Infection and Bronchopulmonary Infection

After a series of experiments on dogs, supplemented by observations on chronic disease of the paranasal sinuses in humans, Wilson (1915) stated that there are three elementary facts in regard to chronic bacterial inflammation of a sinus that should be so generally accepted that they become axiomatic: (1) no chronic bacterial inflammation can occur in a sinus unless its physiologic defense mechanisms are disturbed or destroyed; (2) the physical presence of bacteria in the sinal lumen or even in its lymph or blood vascular system does not induce chronic infection; rather it is the functional condition of the tissue on which the bacteria are implanted that influences the future course of disease; and (3) the mucous membranes of the nasal chambers and sinuses are associated in their reaction to stress by a common mechanism, the nervous control of which is through the sphenopalatine ganglion.

The typical attitude of earlier rhinologists concerning the relationship of infections in the paranasal sinuses to those in the lung was expressed by Schenck (1941) in a paper on the etiology of bronchiectasis. He stated that the concept that sinal infection is primary and bronchial infection is secondary is supported by experimental evidence that shows that infectious material is readily carried from the upper to the lower respiratory tract. He

concluded that treatment of chronic suppurative disease of the lower respiratory tract is doomed to failure if it does not include thorough treatment of sinusal infection. However, he added that cure of the diseased sinuses is not always followed by the arrest of the pulmonary lesions, and once the bronchial disease is well established, eradication of the sinusitis does not arrest the disease.

There were many other similar and equally ambiguous statements made that, on the one hand, seemed to promise amazingly good results from sinusal surgery when chronic sinusitis and chronic bronchitis are associated, while, on the other, warned that not too much therapeutic effect on the pulmonary disease should be expected from such surgery. This dichotomy in the opinions expressed resulted from the incomplete understanding of the rhinologist as to both the chronic "hyperplastic" type of sinusitis usually present and the semantics of pulmonary disease. The latter fault usually resulted in the opinion that bronchiectasis and chronic bronchitis are in no respect synonymous and that bronchiectasis is a localized and never a diffuse condition. Neither of these ideas appears to be consistent with the present thinking of most of those specializing in the diseases of the chest.

The matter was brought to a head when Dixon and Hoerr (1944a, b) performed a series of experiments that they said demonstrated the invalidity of the experiments of Mullin (1919, 1926) and of Fenton and Larsell (1937), which Schenck had mentioned in support of his opinions. When the results of Dixon and Hoerr's experiments were added to the fact that, in many patients with "bronchiectasis", chronic suppuration in the paranasal sinuses was apparently not present, grave doubts as to any relationship whatever were raised.

It was Davison's (1944) opinion that when bronchiectasis and chronic sinusitis coexist, the sinusitis and the bronchiectasis both developed at the time of the initial combined upper and lower respiratory tract infection in infancy or childhood. In 45 patients with "bronchiectasis" whom he studied, Davison made a diagnosis of chronic sinusitis in 23. In 20 patients with extensive sinusitis of dental origin of from 1 to 10 years' duration, none had any bronchopulmonary symptoms despite the fact that they had purulent discharge in the nasopharynx both day and night. It seemed apparent to Davison that some mechanism other than the mere presence of bacteria is required to produce bronchiectasis, and he thought this factor might well be mucosal edema on the basis of allergic hypersensitivity with obstruction of bronchi by gummy exudate from hyperplasia and hypersecretion of the mucus-secreting glands. Clerf (1934) noted that although sinusal infection was infrequent in patients with unilateral bronchiectasis whom he studied, 82 per cent of his patients with bilateral bronchiectasis also had chronic sinusitis.

It would seem that more progress might be made in considering the relationship of sinusal disease to bronchopulmonary disease if both the term and concept of bronchiectasis were excluded, since both seem to obscure the point at issue by distracting debate as to the definition, anatomic background, and pathology of this disorder. If we substitute the term chronic suppurative bronchopulmonary disease, the focus becomes clearer and the resolution more definite. Feingold (1959) pointed out the role of infection in bronchial allergic disease in children. Diamond and Van Loon (1942) found chronic sinusal disease in 64 per cent of children with bronchiectasis and in 61 per cent of children with chronic tracheobronchitis. Voorhorst (1962) believed that chronic bronchopulmonary infection developed on the basis of lowered resistance produced by perennial atopies to house dust, mold spores, and human

ander. The "allergic" edema so disturbed the resistance mechanism that it allowed the establishment of *Haemophilus influenzae* as the "resident flora" in an attenuated or commensal form. Van Dishoeck confirmed the relationship of allergic hypersensitivity and infection in sinuses in which, eventually, the "hyperplastic" sinusitis of Uffenorde was established.

The upper and lower respiratory tracts are a continuum, and debate as to which is first in showing evidence of the combination of chronic infection and hypersensitivity is as unrewarding as the debate about the priority of the chicken or the egg. There can be little doubt that infection in one influences infection in the other. Of equal certainty is that both "hyperplastic" sinusitis and chronic suppurative bronchitis, in most instances, constitute a so-called spectrum disorder or disease sui generis termed "bronchosinusitis infection" by Wasson (1929). In this disorder, hypersensitivity and infection, and probably endocrine factors also, are present in different degrees in different patients.

Sasaki and Kirchner (1967) repeated the experiments of Mullin (1926), Fenton and Larsell (1937), and Dixon and Hoerr (1944a, b). They supported the conclusions of Mullin and of Fenton and Larsell and added an additional pathway of infection from sinuses to lung. Sasaki and Kirchner concluded that the probable routes of infection involved in the sinobronchal syndrome are (1) tracheal aspiration, (2) the lymphatic-hematogenous route of Mullin, and (3) a purely lymphatic pathway.

Cowen (1968) stated: "Symptomatic relief of a patient with both paranasal sinus pathology and associated bronchopulmonary change can become almost complete with detailed, diligent, and strict allergic management alone. However, this symptomatic relief is *not* attended by a reversal of chronic mucous membrane disease of the sinuses. Exacerbations recur and the persistent, latent, paranasal sinus pathology can and does continue to produce antigenic stimulation and the ultimate return of some relatively major bronchosinusitis problems, whether it be some type of chronic bronchitis, bronchospastic disease, obstructive emphysema, or frank bronchiectasis".

From this available evidence, an interrelation between hyperplastic sinusitis and chronic bronchopulmonary infections seems not only reasonable but obvious. Dissatisfaction has resulted from overenthusiasm for some single therapeutic approach, such as the idea that surgery alone can accomplish the impossible task of "curing" both the infection and the allergy. Dogged insistence that medical treatment alone will restore full health has also caused unnecessary invalidism. The facts seem to be that in some instances medical treatment will attain an essential cure. Too often, however, a dormant infection is present that will be repeatedly reactivated. A hypersensitivity, probably to breakdown products of the bacterial wall, is set up, which gradually replaces the initial perennial atopies. Surgical intervention may then be needed. Surgery, however, is not curative in itself. It merely affords an improved opportunity for success from a combined specific and nonspecific treatment for both the hypersensitivity and the infection.

Conclusions

Our knowledge of the physiology of the nose and the upper respiratory tract as a whole is slowly approaching a closer approximation to reality, but there are still wide areas of challenge to rhinologic research. Progress was hobbled for a time by fashionable adoption

of the doctrinaire position that clinical observation and experience are unacceptable bases for laboratory research and that intuitive appreciation must by necessity be incorrect. The changing attitude of science, in general, toward this position is permeating research in rhinology, so that a healthier, less restrictive outlook has developed.

The doctrine that so gladdens the indolent skeptic, ie that only the proponent of an idea needs to find support for it, whereas an antagonist need only present a smug nonacceptance, is becoming suspect as a mere intellectual stratagem. It is now incumbent on an opponent to produce nullifying data if he or she is to justify active opposition as something more than a "ploy" or fixation of thought in a well-worn rut.

From the data now available, however, a number of reasonable assumptions and justified conclusions seem possible:

1. Because of its position at the entrance to the airway system and because of its valvular structure, the hypothesis that the human nose plays an important role in the control of respiration seems not without merit. Although some supporting data are at hand, more rigorous experimental validation is needed. Measurements of driving pressure, resistance, flow, and conductance, to have significance, must be correlated with alveolar ventilation and respiration of the entire organism.

2. It has been shown that the most important factor in resistance to nasal air flow is turbulence. Therefore, increased resistance to nasal air flow depends much more on interference with the stream lines in the nasal lumina than on the nasal cross section. Testing the airway conductance before and after the use of nasal vasoconstrictors adds surprisingly little to the ability of a rhinologist to relieve a patient's nasal complaints.

3. The factors of resistance and conductance in the nasal airways have not received proper consideration in planning surgical and semisurgical procedures designed to improve the passage of air through the nasal chambers.

4. Undue emphasis has been placed on the air conditioning function of the nasal chambers and on the activity of the cilia. Although these functions are important, they are probably secondary.

5. It is important for the well-being of the specialty of otology-rhinology-laryngology that nasal physiology be recognized and developed. With new curricula in the medical schools, the relationship of the specialty to the basic subject of respiration must be emphasized if the undergraduate medical student is to become aware that there is a "pathway" such as ours.