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SMELL, TASTE, AND ALLIED SENSES IN THE VERTEBRATES

BY

G. H. PARKER, Sc.D.
PROFESSOR OF ZOÖLOGY, HARVARD UNIVERSITY

37 ILLUSTRATIONS

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EDITORS' ANNOUNCEMENT

The rapid increase of specialization makes it impossible for one author to cover satisfactorily the whole field of modern Biology. This situation, which exists in all the sciences, has induced English authors to issue series of monographs in Biochemistry, Physiology, and Physics. A number of American biologists have decided to provide the same opportunity for the study of Experimental Biology.

Biology, which not long ago was purely descriptive and speculative, has begun to adopt the methods of the exact sciences, recognizing that for permanent progress not only experiments are required but quantitative experiments. It will be the purpose of this series of monographs to emphasize and further as much as possible this development of Biology.

Experimental Biology and General Physiology are one and the same science, in method as well as content, since both aim at explaining life from the physico-chemical constitution of living matter. The series of monographs on Experimental Biology will therefore include the field of traditional General Physiology.

Jacques Loeb,
T. H. Morgan,
W. J. V. Osterhout.

AUTHOR'S PREFACE

Sense organs have always excited general interest, for they are the means of approach to the human mind. Without them our intellectual life would be a blank. The deaf and the blind show how serious is the loss of even a single set of these organs.

Although the ear and the eye have commonly received most attention, the other sense organs, such as those of smell and of taste, are in reality equally worthy of consideration. These organs are of first significance in warning us of untoward conditions that may exist about us particularly in relation to our food. But they not only serve us in this protective way, they are also of the utmost importance in initiating that chain of events which culminates in successful nutrition. Through their action the secretion of the digestive juices and other like operations, so essential to the proper treatment of the food, are started and furthered in the alimentary canal. Thus their activities, though less associated with our mental states than are those of the ear and of the eye, are nevertheless so essential to our organic well-being that they are in reality quite as necessary to us as the so-called higher senses.

Smell and taste, together with certain other senses not so well known, form a more or less natural group in which there is a certain amount of functional interrelation and genetic connection, and it is from this standpoint that these senses will be considered in the following pages. They will thus illustrate in a way principles common to other groups of sense organs, and these principles will be found to be of an essentially dynamic character as contrasted with the older conceptions in which function has been brought into relation less intimately with structure.

The author is greatly indebted to the editors of this series of monographs for many suggestions that have led to improvements in the text. He is also under obligations to his wife for a careful revision of the manuscript. He wishes to extend his thanks to numerous persons who have permitted him to copy and use figures contained in their publications. In all such instances the sources of such figures are acknowledged in the text. Where a figure is given without reference, it is an original. The drawings for all figures were made by Mr. E. N. Fisher.

G. H. P.

Harvard University, Cambridge, Mass.
January, 1922.

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SMELL, TASTE, AND ALLIED SENSES IN THE VERTEBRATES

CHAPTER I.

NATURE OF SENSE ORGANS.

Contents.—1. Older Conception of Sense Organs. 2. Modified View due to Theory of Reflex Action. 3. The Genesis of Receptors. 4. Bibliography.

1. Older Conception of Sense Organs. In the conventional text-book, sense organs are commonly looked upon as structures that supply the brain with those nervous impressions from which the mental life of the individual is built. During normal activity these organs are incessantly in operation and flood the central apparatus with a stream of impulses by which are carried to us evidences of the multitudinous alterations of the environment. Through the ear and the eye pass continuous streams of change by which we adjust ourselves not only to the immediate material world about us but to the world of ideas whose elements are spoken and written words.

Sense organs from a structural standpoint are organs whose cells are so specialized that they are subject to stimulation by only a particular category of external changes. As Keith Lucas has expressed it, sense cells approximate a unifunctional state. The changes by which they are brought into action form rather homogeneous groups of environmental alterations. Thus the chemical changes of the surroundings affect the organs of smell and of taste, the pressure changes those of touch and hearing, and alterations in the radiant energy those of sight. These natural groups of environmental changes have been designated as homologous, or, better, adequate stimuli for the sense organ that they activate. Such organs are ordinarily arranged under five heads each with an adequate stimulus and productive of a special sensation; they are the organs of smell, taste, touch, hearing, and sight.

Experience has also shown that when in a given person a sense organ exhibits complete congenital incapacity, such an individual lacks certain mental elements that can never in reality be made good to him by the activity of the remaining parts. A state of this kind implies a certain mental deficiency in the given individual. If a person has been blind from birth, no amount of description can supply to him the sensations of the wealth of color that the external world holds for the normal man. Where blindness is an acquired defect, the rememberance of the former color sensations as compared with the present deprivation, makes the state of deficiency still more pronounced. And in those rare cases where there is a unilateral defect in color vision with sight otherwise unimpaired, the subject can contrast most vividly the state of deficiency with that of normal completeness. Such conditions, which are known to occur not only in sight but in the other senses as well, have had a most profound influence on the interpretations that naturalists have placed upon the states presented by the lower animals.

It has been commonly assumed, and with no small show of reason, that where an animal is found to possess an eye or an ear, for instance, it should be accredited with all the central nervous activities, sensations and the like, that accompany such an organ in man, qualified only by the degree of development to which the particular organ in the given animal has arrived. Conclusions based upon such a course of reasoning were commonly admitted as valid by the workers of a few decades ago (Lubbock, 1882; Graber, 1884) and the text-books of that period in dealing with the sense organs of the lower animals discuss these parts ordinarily under the conventional five heads of the older human physiology (Jourdan, 1889). From this standpoint one of the lower animals is like a defective human being in that its full sensory activity falls short of that of the normal man. Or it may be compared to a person whose sensory development is unsymmetrical and whose relations with the surroundings have come to be predominant through a limited number of sensory channels rather than through all.

It is likewise perfectly clear that a given animal, whose organization in general may be simpler than that of man, may nevertheless excede him in a particular sensory capacity and in this respect at least stand above him. It is commonly admitted that the dog far outruns man in the keeness of his sense of smell and it has long been known that cats hear tones of a pitch much too high for the human ear. These and other like examples show that though the senses of the lower animals are in general less efficient than those of man, the reverse is occasionally true.

Moreover among some of the lower forms, sense organs have been discovered that are not represented in man. Thus fishes possess, in addition to the five classes of human sense organs, the so-called lateral-line organs.

Here then must be a wholly novel set of sensory relations. As to the sensations arising from these organs man can form no direct conception, for they are entirely outside the range of his experience. Hence Leydig, the discoverer of the sensory nature of these parts, wrote of them as organs of a sixth sense. Thus to the older workers the senses of the lower animals were like those of a human being that had suffered either curtailment or expansion even to the extent of excluding or including whole categories of stimuli. But quite aside from the question of the number and variety of these parts, is the opinion held by most of the early workers that the sense organs of the lower animals are primarily concerned with providing the brain or corresponding structure of the given creature with that body of sensation which was supposed to represent all the significant changes in the effective environment.

2. Modified View due to Theory of Reflex Action. The belief that sense organs were chiefly concerned with providing the brain with the elements of which the mental life is composed suffered an important limitation from the work of the physiologist. This limitation arose from the development of the idea of reflex action. Originating about the time of Descartes in the seventeenth century, the conception of the reflex action grew in time into a most important principle for the interpretation of nervous operations. It was at first applied to that form of nervous activity whose outcome is fairly constant and in a way mechanical in that it is unassociated with consciousness, but it was gradually extended to include those performances in which consciousness is involved and at present it commonly refers to any chain of nervous activity in which a sensory stimulation produces an im-

pulse that, after passage through the central nervous organs, results in action.

From the beginning many reflexes were believed to be unassociated with consciousness and though this view was subsequently combated and the idea of the reflex extended to nervous operations that included an obvious sensational element, it nevertheless remained true that a host of reflex operations could be pointed out that were without representation in consciousness. Thus the impulses that flow from the vestibular portion of the human ear and that are of the utmost importance in maintaining equilibrium provoke no obvious sensations and the vast flux of afferent nerve action that moves from the muscle to the spinal cord and that is so essential to the coördination of bodily movements, runs its course without exciting sensation. These and many like instances have made it clear that the reflex, even in the most special application of the term may as often be unassociated with sensation as associated with it.

As the first step in every reflex is the excitation of a sense organ and as many reflexes are unassociated with consciousness, it must be admitted that sense organs, notwithstanding the name, are not always necessarily concerned with sensations. Many certainly have nothing whatever to do with such central nervous states. Thus it is doubtful if the normal activity of the sensory endings in our muscles and tendons is ever productive of sensation. In consequence of this condition a reasonable objection was raised to the term sense organ and it was proposed by Bethe (1897) to use in place of it the word receptor. Although the theoretic force of this objection has not always carried conviction, the term receptor has come into common use and the emphasis that it places on the organs to which it is applied as receivers of environmental change rather than as originators of impulses to sensation is certainly a step in the right direction.

Human receptors belong to one or other of two classes. Either they are concerned purely and simply with the excitation of reflex acts and take no part in the production of sensations, in which case they may be called activators, or they are at the same time effective in arousing sensations, the elements of the intellectual life and hence may be appropriately termed sense organs. All receptors belong to either one or the other of these classes though in some instances a certain degree of temporary vacillation occurs. Hence it may be that these classes exemplify in a way two receptive functions, one of which predominates in one class and the other in the other. How these functions are related can best be gathered from the genetic history of receptors.

3. The Genesis of Receptors. Receptors such as the eye and the ear, the organs of smell and taste, and the more diffuse sensory equipment of the skin, are found in all the more complex animals. They abound in the vertebrates, the mollusks, the arthropods, and to a less extent in the worms. They may be said to occur even in the cœlenterates, as, for instance, among the jelly fishes, though in the majority of these animals the receptors present a diffuse condition more like that seen in the vertebrate skin than in the vertebrate eye or ear. This diffuse state seems to be characteristic of the receptors in the simpler sessile invertebrates. The more complex animals such as are capable of active locomotion exhibit almost invariably specialized types of organs.

So far as the neuromuscular system of the invertebrates is concerned, forms as low in the scale as the annelid worms appear to possess all the elements of the corresponding system in the vertebrates. Such worms may have specialized receptors, eyes and the like, often of a highly complex structure. They possess a well-differentiated central nervous system as represented in their so-called brain and ventral ganglionic chain. Finally, they have an abundant variety of specialized effectors in their various muscles, glands, and luminous organs. Their receptors, central nervous organs, and muscles are so related that reflexes can be demonstrated on them as readily as on vertebrate preparations. In other words, they possess in completeness, though in simple form, a working neuromuscular mechanism essentially like that of the higher animals.

When, however, an examination of such forms as the cœlenterates is made, it is found that the coral animals, the sea-anemones, the hydroids, and the like, possess scarcely any trace of a central nervous apparatus. In these animals fairly well specialized sensory surfaces occur, whose nervous prolongations connect either immediately with the subjacent musculature or give rise to a nerve-net which in turn connects with the contractile elements. Thus the receptor is applied to the muscle very directly and without the intervention of a central organ. Such an arrangement allows of simple reflexes, for, when the receptive surface is stimulated, the animal responds at once by an appropriate muscular movement. Thus if meat juice is discharged on the tentacles of a sea-anemone, these organs carry out vermiculate movements and the gullet opens; or if the pedal edge of the column is touched, the whole animal contracts. The fact that meat juice will not excite the pedal edge of the column and that a touch applied to the tentacles is seldom followed by more than a slight local activity shows that the external surface of the sea-anemone, though generally receptive, is locally specialized. As a matter of fact this surface in degree of differentiation stands between a diffuse receptive surface, such as the vertebrate skin, and a specialized organ like the eye or the ear.

In the literal sense of the word the outer surface of a sea-anemone is not sensory though abundantly receptive. There is no reason to suppose that the receptive areas of these animals are concerned with initiating impulses to sensation. They connect very directly with muscles and serve quite obviously as trigger-like organs by which the muscle is set in action. A careful examination of the activities of sea-anemones has failed to reveal any evidence, such as can be produced from the more complex animals, to show that these simple creatures possess central nervous functions. Such functions apparently have no part in their organized performances. Hence their receptors have nothing whatever to do with initiating impulses to sensation, but are limited in their action to the excitation of the muscles after the type of the most mechanical reflex. The presence in cœlentrates of eye spots, olfactory pits, statocysts and other such special receptors is, therefore, no indication that these animals are endowed with corresponding sensations, as many of the older workers believed, but this condition merely shows that their possessors are especially open to a particular stimulus. An eye spot does not mean that the animal possesses sight, but that it is readily excited to action by light.

Thus of the two functions that have been attributed to receptors, the capacity to excite action and the ability to initiate impulses for sensation, the former is much the more widely distributed of the two and is without question the more primitive.

Since sponges are known to possess muscles but are devoid of nervous tissue, it is probable that they represent a type of organization which in point of time preceded that in which the nervous elements arose. So far as can be judged these elements originated in connection with the previously differentiated muscle and as a special means of exciting it to contraction. This earliest nervous material must have been, therefore, essentially receptive in character and must have served as the source of the more obvious receptors of specialized types. Thus receptors must be regarded as the original form of nervous structure, concerned in the beginning with the simple excitation of muscle (activators) and subsequently involved, after the development of the central organs, with that supply of impulses which yields the elements of the intellectual life (sense organs).

The extent to which a natural group of receptors may undergo differentiation and yet maintain a striking degree of mutual interdependence can nowhere be better illustrated than with the chemical receptors, the organs of smell and of taste. It is from this standpoint that the structure and function of these receptors will be considered in the following chapters.

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CHAPTER II.

ANATOMY OF THE OLFACTORY ORGAN.

Contents.—1. Nasal Cavities in Man. 2. Nasal Membranes. 3. Olfactory Epithelium. 4. Intermediate Zone. 5. Polymorphic Cells. 6. Sense Buds. 7. Free-nerve Endings. 8. Development of Olfactory Nerve. 9. Comparative Anatomy of Olfactory Organs. 10. Bibliography.

1. Nasal Cavities in Man. In man the olfactory organs are paired and are situated one in each nasal cavity. Each of these cavities possesses an external opening, the anterior naris, and an internal one, the posterior naris or choana, which communicates with the pharynx. (Fig. 1). The two nasal cavities are separated by the nasal septum, a partly bony, partly cartilaginous wall, which forms a smooth median partition between them. The lateral walls of these cavities are thrown into a series of more or less horizontal folds, the nasal conchæ. These are commonly three in number for each cavity though in some instances only two are present and in others a fourth, fifth or even a sixth can be discerned. Of the three conchæ usually present the most ventral one, the inferior concha, is the largest and extends through much of the length of the cavity in a direction approximately parallel to its floor. Immediately above the inferior concha is the somewhat smaller middle concha which is followed by the still smaller superior concha. When only two conchæ are present, they are the inferior and the

middle, the superior being absent. When a fourth concha is to be seen, it is found above and behind the superior. It has been designated the first supreme concha and it may be followed by a second or even a third supreme concha. According to Schaeffer(1920), the first supreme concha is to be observed in about 60 per cent of all adult human beings.

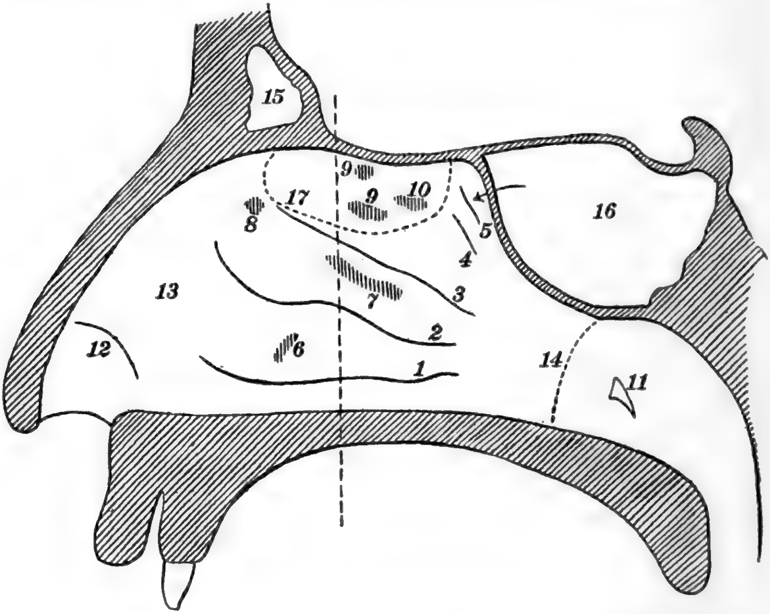

Fig. 1.—Diagram of the lateral wall of the right nasal cavity of man. 1, Inferior concha; 2, middle concha; 3, superior concha; 4, first supreme concha; 5, second supreme concha; the apertures numbered 6 to 10 are covered from sight by the conchæ, but their positions are indicated by vertical lining; 6, aperture of the nasolacrimal duct opening into the inferior meatus; 7, opening of the maxillary sinus (middle meatus); 8, opening of the frontal sinus (middle meatus); 9, and 10, openings of the ethmoid cells, 9, into the middle meatus, 10, into the superior meatus; 11, opening of the Eustachian tube; 12, vesibule; 13, atrium; 14, choana; 15, frontal sinus; 16, sphenoidal sinus whose opening is indicated by an arrow; 17, olfactory region whose limits are marked by the dotted line. The vertical dotted line shows the plane of section from which Fig. 2 was drawn.

The three conchæ ordinarily present project from the lateral wall of each nasal chamber into its cavity and partly divide that cavity into three approximately horizontal passages: the inferior meatus under the inferior concha, the middle meatus under the middle concha and the superior meatus under the superior concha. (Fig. 2). The external naris leads at once to the first chamber of the nose, the vestibule, which connects almost directly with the inferior meatus, less directly with the superior meatus and through the so-called atrium with the middle meatus. Between the median septum of the nose and the laterally situated conchæ is a considerable space known as the common meatus. Dorsally this space is continuous with a narrow slit lying between the superior concha and the septum and called the olfactory cleft. All these passages and spaces communicate more or less directly and freely through the posterior naris or choana with the pharynx.

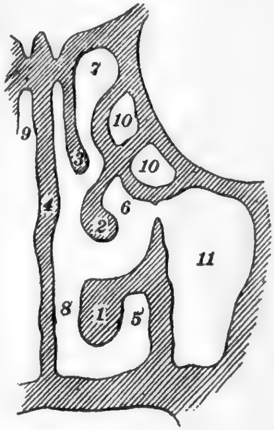

FIG. 2.—Diagram of a transverse section of the right nasal cavity in man made at the plane indicated by the vertical dotted line in Fig. 1. 1, inferior concha; 2, middle concha; 3, superior concha; 4, nasal septum; 5, inferior meatus; 6, middle meatus; 7, superior meatus; 8, common meatus; 9, olfactory cleft (left side); 10, ethmoid cells; 11, maxillary sinus.

In the bones about the nose in man are large paired air-spaces or sinuses that communicate with the exterior through the nasal cavity. These spaces, which have been very fully described by Schaeffer (1916), are of considerable size and are lined with a mucous epithelium continuous with that of the nose. They are somewhat variable in number and connections and yet they fall more or less naturally into four sets, the maxillary, frontal, and sphenoidal sinuses and the ethmoidal cells. Each maxillary sinus is a large space in the maxillary bone above the teeth. It opens by a considerable slit into the anterior part of the middle meatus. (Figs. 1 and 2). The frontal sinus,in the frontal bone also opens into the middle meatus at a point above and anterior to the opening of the maxillary sinus. Each sphenoidal sinus opens into the posterior end of the appropriate olfactory cleft in a region known as the spheno-ethmoidal recess. The remaining accessory nasal spaces, the ethmoid cells, are more or less variable; some of them open into the middle meatus by several apertures well above the slit for the maxillary sinus. Others open, more commonly by a single aperture, into the superior meatus. In addition to these various openings, the naso-lacrimal duct, by which the lacrimal secretions from the eye are carried to the nasal cavity, opens between a pair of lips on the lateral wall of the inferior meatus near its anterior extremity,

2. Nasal Membranes. The nasal vestibule is lined with a delicate continuation of the outer skin. The walls of the deeper part of the nasal cavity are covered with a mucous membrane which is divisible into two regions, the restricted olfactory region in the dorsal part of the cavity and the much more extended respiratory region embracing the remainder of the cavity.

The mucous membrane of the respiratory region is reddish in color and consists of a pseudo-stratified epithelium containing ciliated cells and basal cells backed up by a well developed tunica propria. (Fig. 3.) The cilia of this region lash towards the choana. The secretion covering the surface of the epithelium comes from numerous branched alveolo-tubular glands which contain both mucous and serous cells.

The conchæ of the respiratory region have long been known to be extremely vascular and to be possessed of a structure like that of erectile tissue. This is especially true of their edges. They can be excited through reflex channels to considerable enlargement and the swelling thus produced may be sufficient to close completely the respiratory passages. It is believed that this high vascularity of the respiratory region is concerned with the moistening and warming of the current of respiratory air. The secretions of this portion of the nose are also believed to be inimical to pathogenic germs and thus to afford a protection to the deeper parts against the invasion of disease.

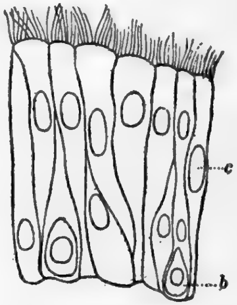

Fig. 3.—Respiratory epithelium from the nasal cavity of a young pig; b, basal cell; c, ciliated cell. After Alcock, 1910, Fig. 2.

The olfactory region in man is yellowish in color as it is in the calf and in the sheep. In the dog and the rabbit it is of a more brownish hue. According to the older anatomists it was supposed to extend in man over the dorsal half or even more of the nasal cavity. Von Brunn (1892), however, claimed by a reconstruction from sections that the olfactory epithelium was much more restricted than had been originally supposed. According to this author only a small portion of the superior concha and a correspondingly small part of the nasal septum represent the unilateral area of distribution of the olfactory nerve. This area in one subject measured 257 sq. mm. and in another 238 sq. mm. The more recent results of Read (1908), however, show that in man the olfactory fibers spread from the dorsal portion of the olfactory cleft ventrally over the superior concha almost to its free edge and correspondingly over the septum to about one third its extent. (Fig. 4). The antero-posterior spread of the nerve, according to this author, is about twice that of its ventral distribution on either the concha or the septum; hence the whole area innervated by each olfactory nerve, if spread out flat, would be approximately square in outline and not far from 25 mm. to a side, somewhat over twice the extent ascribed to it by von Brunn.

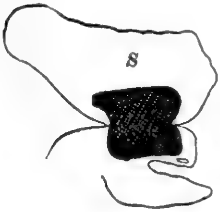

Fig. 4.—Olfactory cleft of man opened by turning the nasal septum (s) upward; the blackened area shows the distribution of the olfactory nerve. After Read, 1908, Plate 11, Fig. 31.

3. Olfactory Epithelium. The olfactory epithelium has been an object of interest to histologists for a long time. As early as 1855 Eckhard stated that in the frog it was composed of two classes of elements, long epithelial cells and nucleated fibers. Which of these served as the endings of the olfactory nerve he was unable to say. In the same year Ecker discovered on the deep face of the olfactory epithelium a third class of cells subsequently called by Krause (1876) basal cells. (Fig. 5.) These three classes of elements were identified in a number of vertebrates and described by Schultze (1856, 1862) who expressed the belief that the nucleated fibers were sense cells and represented the true endings of the olfactory nerve though he was unable to demonstrate a connection between these cells and the nerve.

It is probable that the connection of the so-called olfactory cell with the olfactory nerve-fiber was first seen by Babuchin in 1872 who showed that in a gold-chloride preparation, fibers could be traced from the nerve to the cells that were suspected by Schultze to be sense cells. In 1886 this connection was demonstrated with much greater certainty in methylen-blue preparations by Ehrlich whose results were confirmed the following year by Arnstein.

Because of the transitoriness of methylen-blue preparations, the results of Ehrlich and of Arnstein were looked on with some suspicion till they were reproduced in Golgi preparations by a number of workers, such as Grassi and Castronovo (1889) on the dog, Ramón y Cajal (1890) on mammal embryos, Van Gehuchten (1890) on rabbits, von Brunn (1892) on man, Retzius (1892a, 1892b, 1894) on fishes, amphibians, reptiles, and mammals, and by many other later workers on various vertebrates. (Fig. 6). The results of all recent students in this field of histology support the statement that the olfactory epithelium of vertebrates is composed of at least three classes of cells: basal cells, ordinary epithelial or substentacular cells, and sense cells from which the olfactory fibers take their origin. Thus the opinion of

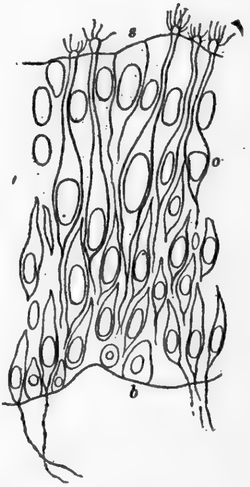

FIG. 5.—Olfactory epithelium from a pig embryo 6½ inches long; b, basal cell; 0, olfactory cell; s, sustentacular cell. After Alcock, 1910, Fig. 10.

Schultze on this subject has been unquestionably and abundantly confirmed.

The sustentacular cells are the chief supporting elements of the olfactory epithelium. Each of these cells has a distal cylindrical portion that contains the yellowish or light brownish pigment so characteristic of the olfactory region. The nuclei of these cells are oval and constitute the outermost zone of nuclei in the epithelium. Their proximal portions are more or less irregularly compressed and branched, hence the outlines of these parts are commonly jagged.

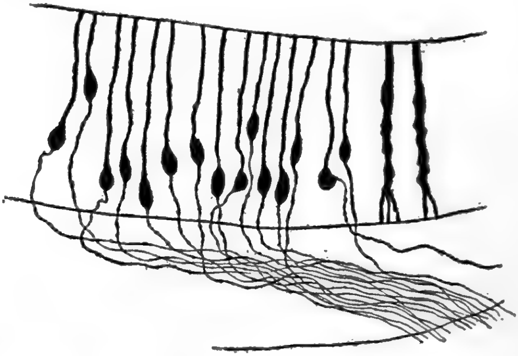

FIG. 6.—Olfactory epithelium of a young mouse showing the olfactory cells and, to the right, two sustentacular cells. Golgi preparation. After Retzius, 1892a, Plate 10, Fig. 2.

The basal cells form a single row of block-like elements on the proximal face of the olfactory epithelium. Their short branching processes extend distally among the other cells of the epithelium.

The olfactory cells are the most numerous of the three classes of cells in the epithelium. Their nuclei are roundish with well marked nucleoli and form the extensive nucleated band between the distal zone of sustentacular nuclei and the less distinct proximal zone of basal nuclei. Each of the olfactory nuclei is lodged in an oval cell-body. Proximally this tapers rapidly into a fine olfactory nerve-fiber which eventually enters the olfactory bulb of the brain. Distally the body of the cell extends as a somewhat coarser rod-like structure to the outer surface of the olfactory epithelium where it terminates in a small enlargement. This enlargement has been called the olfactory vesicle by Van der Stricht (1909) who ascribed to it a centrosomal origin and believed it to play a significant part in olfactory reception. The olfactory vesicle carries a cluster of protoplasmic filaments, the olfactory hairs. (Fig. 7). These hairs are apparently extremely delicate and are easily destroyed; hence they have escaped observation by many workers. They were probably seen in the frog as early as 1855 by Eckhard, but they were first generally identified and thoroughly studied by Schultze (1856, 1862) in a number of vertebrates. Apparently they are never very numerous; Schultze (1862) found that in the frog there were five to six hairs on each olfactory cell (Fig. 8), and von Brunn (1892) and Kallius (1905) recorded six to eight in man. Retzius (1894) noted two to five hairs on each cell in the snake Tropidonotus. Ballowitz (1904) found ten to twelve or more in Petromyzon, and Alcock (1910) states that in the pig the number varies

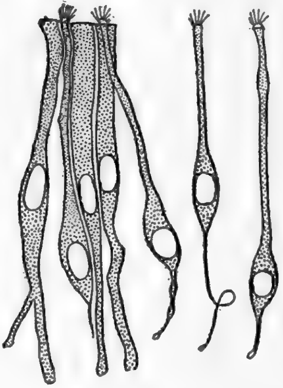

Fig. 7.—Isolated olfactory cells and sustentacular cells from man. After von Brunn, 1892, Plate 30, Fig. 4.

from five to eight. Because of their great delicacy the olfactory hairs are probably seldom observed to their full length. Schultze (1856) described those of the frog as long, but Jagodowski (1901) has shown that in the pike the hair may be twice as long as the olfactory cell itself, (Fig. 9) and may reach from the distal end of the cell through the whole thickness of the superimposed slime. So delicate are the distal portions of these hairs that Jagodowski has proposed for them the name of olfactory flagella or lashes. In the opinion of this author the so-called olfactory hairs are only the proximal ends of these lashes, the distal part having disappeared in the course of preparation. The lashes can be demonstrated by means of the Golgi method or by osmic acid. These lashes are without doubt the true receptive elements of the olfactory cells. The secretion in which they are suspended and whose thickness they probably penetrate is produced by the numerous olfactory or Bowman glands whose ducts open out abundantly through the olfactory epithelium.

Fig. 8.—Isolated olfactory cell and sustentacular cell from a frog. After Schultze, 1862, Plate 1, Fig. 4.

4. Intermediate Zone. In the majority of vertebrates there seems to be a fairly sharp boundary between the respiratory epithelium and the olfactory epithelium. In some mammals, however, these two regions are separated by a considerable intervening area, known as the intermediate zone. This was first described by

Grassi and Castronovo (1889) in the dog, and subsequently was identified by Alcock (1910) in the pig. In this mammal the epithelium of the intermediate zone is thicker than that of the respiratory region and thinner than that of the olfactory region. Besides basal cells it possesses two types of epithelial cells, ciliated cells like those of the respiratory epithelium and non-ciliated sustentacular cells like those of the olfactory region. It also contains many olfactory cells, but these cells are not as numerous in the intermediate zone as they are in the olfactory region where they are said to make up about seventy per cent of the cells present. It is plain from the accounts given that the intermediate zone is a region of transition between the two chief nasal regions, the olfactory and the respiratory.

FIG. 9.—A Golgi preparation of an olfactory cell from a pike (Esox) in which not only the cell body and the basal nerve-fiber process are well shown, but also the long peripheral olfactory flagellum. After Jagodowski, 1901, Fig. 8c.

5. Polymorphic Cells. In most vertebrates the olfactory cells exhibit great uniformity of structure. In the fishes, however, Dogiel (1887) has called attention to a polymorphism among these elements, and he has described in addition to the ordinary type of spindle-shaped olfactory cell, cylindrical olfactory cells and conical olfactory cells. These three types have been identified by Morrill (1898) and by Asai (1913) in a selachian (Mustelus) and by Jagodowski (1901) in the pike (Esox). To what extent this polymorphism occurs in other vertebrates and how important it is for a right understanding of the action of the olfactory organ has not yet been determined.

6. Sense Buds. In 1884 Blaue described what he believed to be sense buds in the olfactory epithelium of certain fishes and amphibians. This observation was not confirmed by later workers and it appears, as Retzius (1892b) has remarked, that the so-called sense buds are not true buds but folds or bands of olfactory epithelium seen in transverse section. The buds subsequently described by Disse (1896b) in the nose of the calf and shown by him to be supplied by free-nerve terminations are believed by this author to be concerned with taste rather than with smell. These structures, however, are claimed by Kamon (1904) not to be true buds but bud-like appearances produced by the mouths of the Bowman glands. If this is so, no sense buds of any kind are known in the olfactory epithelium of vertebrates.

7. Free-nerve Endings. In 1889 Grassi and Castronovo with some uncertainty described from the epithelium of the intermediate zone of the dog what they regarded as free-nerve endings. Whether these were end-organs of the olfactory nerve-fibers or not, they were unable to determine. In 1892 similar endings were observed by von Brunn at the border of the respiratory region in man. Von Brunn believed these endings to be terminals of the trigeminal nerve and, apparently by mistake, mentioned Ramón y Cajal as their discoverer. Free-nerve endings in the olfactory region were subsequently recorded by Retzius (1892b) in the mouse and frog, by von Lenhossék (1892) in the rabbit, by Morrill (1898) in Mustelus, by Jagodowski (1901) in Esox, by Kallius (1905) in the calf, and by Read (1908) in the kitten. Morrill's observation for Mustelus has recently been confirmed by Asai (1913). Hence there seems to be no doubt that in addition

to the olfactory cells, free-nerve endings occur in the olfactory epithelium of vertebrates.

The source of the nerve-fibers from which the free-endings of the olfactory epithelium arise is not definitely settled. The fact that these endings may be very near the outer surface of the olfactory epithelium shows that they are not due to the incomplete impregnation of fibers from the olfactory cells as was suggested by Van Gehuchten (1890). Free-endings like those in the olfactory region also occur in the respiratory region and here the only possible source for them is the trigeminal nerve; hence it is probable that this nerve is also the source of the free-nerve endings of the olfactory region. This opinion is supported by the observations of Rubaschkin (1903) who has shown that in certain portions of the olfactory epithelium of the developing chick the two sets of fibers, those from the olfactory nerve and those from the trigeminal nerve, take somewhat different courses and that the trigeminal fibers are the fibers that give rise to the free-endings. (Fig. 10). Thus such evidence as there is favors the opinion first expressed by von Brunn and subsequently reiterated by a number of investigators, that the free-nerve endings of the olfactory region are from the trigeminal fibers. The vertebrate olfactory epithelium, therefore, has two types of nerve terminations, olfactory cells as the exclusive receptors for the olfactory nerve and free-nerve endings as the probably exclusive endings for the trigeminal nerve.

8. Development of Olfactory Nerve. Since the fibers from the olfactory cells pass as olfactory nerve-fibers to the olfactory bulb and terminate there without direct connections with any other cells, the olfactory cells in the

nasal epithelium must be their cells of origin, as in fact was shown to be the case for the chick by Disse (1896a, 1897). Here the olfactory nerve-fibers have been demonstrated to grow from certain olfactory epithelial cells into the olfactory bulb, the epithelial cells acting in all respects like neuroblasts Bedford (1904). The trigeminal fibers must on the other hand grow from trigeminal ganglion cells into the olfactory epithelium there to terminate as free-nerve endings, but of this there is at present no direct evidence.

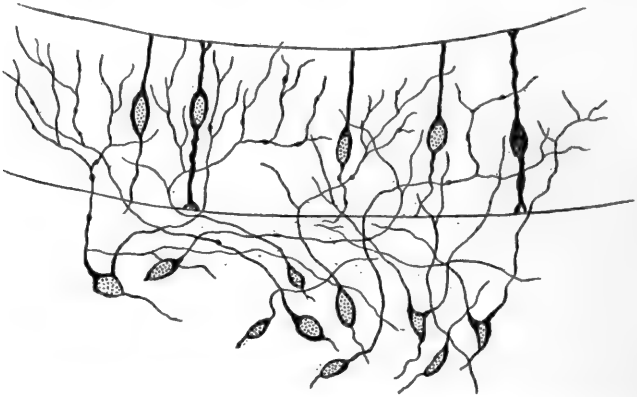

FIG. 10.—Olfactory epithelium of an embryo chick (ninth day) showing olfactory cells, sustentacular cells, and free-nerve endings of fibers from ganglion cells of the trigeminal nerve. After Rubaschkin, 1903, Fig. 3.

9. Comparative Anatomy of Olfactory Organs. The nasal organs in the lower vertebrates are very different from those in man. In Amphioxus a single sensory pit slightly to the left of the median dorsal line of the head and connected with the anterior end of the nerve-tube is assumed to be an olfactory organ. If this is so, it is probable that this pit corresponds to the single median olfac-

tory sac in the cyclostomes notwithstanding the fact that this sac shows evidence in its deeper parts of being a double organ. In consequence of single nasal openings Amphioxus and the cyclostomes are commonly contrasted with other fishes, and in fact with all other vertebrates, and are called monorhine. Those in which the olfactory organs are obviously paired have been designated as amphirhine.

In the sharks and rays the paired olfactory pits are situated usually on the ventral side of the snout. (Fig. 11). The single opening of each pit is more or less divided by a fold of skin into an anterior inlet and a posterior outlet the latter sometimes leading into the mouth. As the fish swims through the water and particularly as it takes water into its mouth in breathing, a current of water is passed through each of its olfactory sacs. In this way the olfactory organs become associated with the respiratory current, a condition that is more pronounced in the lung-fishes than in the sharks and rays, for in the lung-fishes the anterior apertures are external and form true anterior nares, and the posterior openings lie within the mouth and correspond to the choanæ of higher vertebrates. In the highly specialized bony fishes, the paired olfactory pits are almost always on the dorsal aspect of the head and quite distant from the mouth. Each pit has two entirely separate openings, an anterior inlet and a posterior outlet. By means of these two openings a current of water enters and leaves each pit. This current is produced either by ciliary action within the pit (Amiurus) or by the action of the muscles associated with the jaws and gills (Fundulus). In bony fishes, then, the olfactory pits are purely receptive and are in no direct way connected with the respiratory current as they are in the sharks and rays, and in the lung-fishes.

In the air-inhabiting vertebrates each olfactory sac possesses, as in man, an external inlet, the anterior naris, and a posterior outlet, the choana, opening into the mouth or the pharynx. The olfactory sacs are relatively simple in amphibians, but become progressively more complicated in reptiles and birds, and vastly more so in mammals. Here the surface of the sac is enormously extended through the development of lateral folds or conchæ which may be further complicated by the production of secondary folds. In mammals the more ventral of these conchæ, those attached to the maxillary bone, are apparently not concerned with olfaction, but lie in the purely respiratory region of the nasal chamber. The more dorsal conchæ those from the ethmoid bone, serve as olfactory surfaces. It has been shown that in some mammals, as for instance in Orycteropus, there may be upwards of ten olfactory

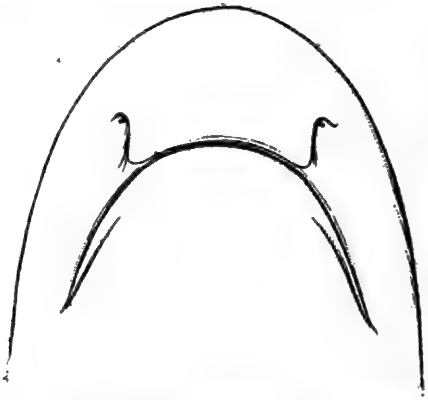

Fig. 11.—Ventral view of the head of a shark (Scyllium) showing the olfactory pits in relation to the mouth.

conchæ. Forms that possess these larger numbers of conchæ are known to be keen-scented and are termed macrosmatic. Those in which the number of olfactory conchæ is small, four or fewer, such as the seals, some whales, monkeys, and man, are known to be less acute of smell and are called microsmatic. Others again, such as the toothed whales, porpoises and the like, in which the olfactory organ has almost completely degenerated, are supposed to be devoid of olfaction and are called anosmatic. In such forms the nasal cavities have lost their original sensory function and have come to be of importance only in connection with respiration, a purely secondary relation.

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CHAPTER III.

PHYSIOLOGY OF OLFACTION.

Contents.—1. Nerves of Olfaction. 2. Passage of Air through the Nasal Cavity. 3. Minimum Stimulus. 4. Physical Condition of Stimulus, Gas or Solution? 5. Olfaction in Fishes. 6. Fatigue and Exhaustion. 7. Qualities of Odors. 8. Chemical Relations of Odors. 9. Inadequate and Adequate Stimuli. 10. Olfactory Reflexes. 11. Bibliography.

1. Nerves of Olfaction. The olfactory region of vertebrates has been shown to possess olfactory cells as terminations of the olfactory nerve and free-nerve endings representing in all probability the trigeminal nerve. It has long been the opinion of investigators that the olfactory sense is mediated by the endings of the olfactory nerve, but this opinion has not been without its opponents. Thus Magendie, in a series of publications beginning in 1824, came to the conclusion that the trigeminal nerve was the nerve of olfaction and that the so-called olfactory nerve was one whose function was wholly unknown. His opinion was based in part upon experiments on the dog. After the olfactory nerves of this animal had been cut, it was found still to respond to acetic ether and to ammonia. Even when blindfolded a dog with severed olfactory nerves would seize cheese or meat but it would not eat meat sprinkled with tobacco. It was pointed out by Magendie's critics that many of the stimulating substances used by him, such as ammonia and the like, not

only possessed odor but were irritants for mucous surfaces generally and thus without reference to olfaction could call forth vigorous responses. Magendie, however, claimed that his results were not dependent upon these substances, but could be demonstrated by the use of non-irritants, such as lavender oil.

Magendie's opinion that the trigeminal nerve was the nerve of olfaction was opposed almost from the beginning. Eschricht in 1825 pointed to numerous cases of persons who were anosmic in consequence of the absence of the olfactory nerve or of its degeneration. Bishop in 1833 described a case of paralysis of the trigeminal nerve in which there was, however, full retention of olfaction. Picht (1829) and Dugès (1838), both of whom were incapable of olfaction in the ordinary sense of the word, were nevertheless easily stimulated through their nasal membranes by the vapor of acetic ether, or of ammonia. Valentin (1839) found that a normal rabbit would sniff the body of a dead one, but that a rabbit whose olfactory nerves had been cut would not thus respond. Schiff (1859) experimented on five pups, in four of which the olfactories were severed, the fifth being retained in a normal condition as a control. After recovery from the operation, the four pups in which the nerves had been cut were unable to find the mother's nipples, and did not distinguish between a man and the mother though they turned their heads away and sneezed when ammonia or ether was administered. Acetic acid stimulated them only when its vapor was very concentrated. These and many other similar results completely overthrew Magendie's contention and showed that, though the trigeminal endings were concerned with the reception of what may be called irritants, true olfaction was accomplished only through the olfactory terminals, which have to do with delicate perfumes, aromas, and the like, many of which were associated with food.

The recognition in nasal stimulation of the two classes of substances, irritants acting on trigeminal terminals, and true odors affecting the olfactory endings, is of fundamental importance, and the failure to appreciate this distinction is responsible in part at least for much of the confusion that exists in what has been written on the olfactory stimulus. As early as 1851 Fröhlich pointed out this distinction and called attention to the fact that irritants or stimuli for the fifth nerve ordinarily induce vigorous reflexes, respiratory and the like, whereas true odors are in nature much milder and seldom call forth strong responses. It is quite possible that some materials are stimuli for both classes of end-organs; thus tobacco smoke not only carries with it an aroma or true odor but also acts as an irritant. These two actions, however, may depend upon different chemical substances in the smoke. Other stimuli such as oil of mustard or possibly ammonia, that are chemically much more homogeneous than tobacco smoke, may affect, nevertheless, both sets of receptors and thus exhibit the characteristics of both irritants and true odors. A revision of the so-called olfactory stimuli from this standpoint is much to be desired.

2. Passage of Air through the Nasal Cavity. In ordinary respiration in man the passage of air through the nasal cavity does not necessarily excite olfaction at once. Sooner or later, however the odor may be slightly sensed after which a few deep breaths or sniffing movements are usually made, whereupon full stimulation ensues.

The course that the current of air takes through the nasal chamber during quiet respiration has been studied in several ways. Paulsen in 1882 published the results of experiments on the human cadaver. He opened the nasal cavity by sawing through the head of a cadaver close to the median plane. Pieces of red litmus-paper were then placed on different parts of the nasal surface and the two halves of the head were brought together again. By means of a bellows attached to the trachea of the cadaver, the current of air that in life passes through the nasal chambers was imitated. This artificial current was charged with ammonia and thus a means was given of indicating the spread of the current by the location of the pieces of litmus-paper that changed from red to blue. As a result of this test it was found that the inspired air took a curved course from the naris to the choana. (Fig. 12). The highest part of this curve was near the middle of the nasal cavity, but this never reached a point as high as the olfactory cleft. When the current was reversed by causing it to enter at the choana and emerge at the external naris, as in expiration, the direction of the current was found to be much the same as in inspiration except that a somewhat lower course was followed. Thus in both inspiration and expiration the current of air is limited to what is more generally regarded as the respiratory region of the nasal cavity, the olfactory region being essentially undisturbed.

Paulsen's results were confirmed in all essential particulars by a number of later investigators including Franke, Zwaardemaker, Danziger, and Rethi, who worked on dead animals and human cadavers by methods not unlike those used by Paulsen. Franke (1893) sawed open the head of a human cadaver in the median plane, replaced the nasal septum with glass and by means of an artificially produced respiratory current showed that smoke in its passage through the nasal cavity remained in the so-called respiratory region. He observed, however, that both inspiration and expiration were accompanied by strong eddies in the moving air. Kayser (1890) aspirated very light magnesia powder into the respiratory current of a quietly breathing normal subject and then inspected the nasal surfaces by means of a rhinoscope. The magnesia particles accumulated on the moist surfaces of the respiratory portions of the nose and not on those of the olfactory region, thus confirming Paulsen's results but by a method that was by no means so artificial as that employed by other workers. It may, therefore, be regarded as

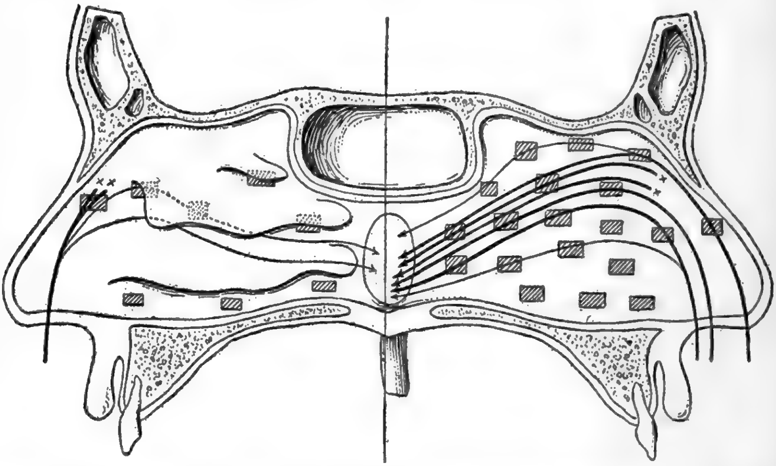


FIG. 12.—Diagram of the right nasal cavity of man laid open and showing by arrows the direction of the inspired current of air over the nasal septum (right half of figure) and over the lateral wall (left half of figure). After Paulsen, 1882.

fairly well established that the current of air that sweeps through the nasal cavity in quiet respiration is limited chiefly to the non-olfactory portion of that cavity. According to Paulsen and to Zwaardemaker this current even in its eddying effect does not rise above the lower edge of the middle concha or at most, according to Franke, the lower edge of the superior concha. This limitation is probably more pronounced in expiration than in inspiration.

Although the experimental evidence does not show that the respiratory current spreads to the olfactory surface of the nose, odorous particles must in some way reach this situation. Zwaardemaker (1895) was led to believe that the diffusion of these particles played an important part in this process, but diffusion is a relatively slow operation and it is very doubtful if it is a significant factor in carrying the odorous material to the olfactory receptor. It seems more probable that the shifting pressures that accompany respiration and the slight eddies that are formed in the general current are responsible for a gradual change of air in the olfactory cleft. The change thus produced is probably too slight to be detected easily by the means heretofore employed in tracing the current and yet it may be sufficient to initiate such olfaction as occurs in quiet respiration. Olfaction thus once begun would naturally excite sniffing and this process seems to be entirely sufficient to account for a rapid change of air in the olfactory cleft whereby olfaction would be brought to full height. Thus air currents are certainly the chief if not the sole factors concerned with transporting the odorous particles to the olfactory membranes.

The accumulation of odorous materials on the olfactory surfaces may be much intensified by the condensation of moisture within the nasal cavity. Zwaardemaker (1917) has called attention to the fact that a fog formed from a vaporized salt solution is very much less stable when it includes odorous substances than when it does not. This condition is believed to depend upon the electric charges carried by the particles concerned, and Durand (1918a, 1918b) recently claimed that olfaction is more or less dependent upon an appropriate hygrometric state in the olfactory atmosphere and that whatever facilitates the condensation of watery vapor there facilitates olfaction.

Among the older physiologists Bidder (1844) maintained that olfaction was possible on inspiration and that expired air could not stimulate the organ of smell. Paulsen's observations show that this opinion is improbable and the direct test of breathing odorous air in through the mouth and out through the nasal cavity has demonstrated that it is quite erroneous. The olfactory sensations produced on expiration are noticeably less than on inspiration and this is probably due partly to the lower course maintained in the nasal cavity by the expired air and partly to the previous elimination of much of the odorous material by attachment to the moist surfaces of the mouth, pharynx, and other parts over which the air passes on its way to the nasal chamber. Nevertheless, as Nagel (1904) has pointed out, the odors of our food during mastication are the results of stimulating material that reaches the olfactory surfaces through the choanæ rather than through the external nares. The importance of these odors in promoting the various kinds of digestive reflexes, muscular, secretory, and so forth, has long been recognized.

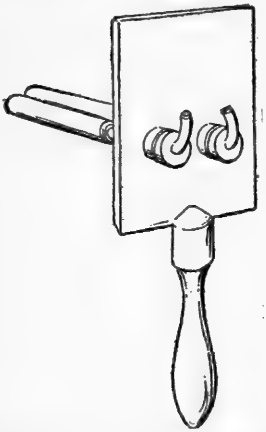
3. Minimum Stimulus. The common belief that the olfactory stimulus consists of minute material particles suspended in the air current of the olfactory organ is supported by the observation that odors may be carried on the wind in a definite direction many miles. Odors do not emanate from a given center and disperse in all directions as sound and light do. Moreover many substances, such as arsenic, that are odorless under ordinary circumstances, give out an odor after they have been heated sufficiently to volatilize. The fact, discovered in 1917 by Woodrow and Karpman, that the adaptation time for olfaction—the time needed for an olfactory sensation to wane completely—is directly proportional to the vapor tension of the odorous material shows that olfactory stimulation is due to the activity of gaseous particles. These and other like observations have led to the conclusion, now generally accepted, that the olfactory organs are normally stimulated by material particles, and not by disturbances of a non-material character.

Some odorous bodies such as musk are well known to give out these material particles for a very considerable time without appreciably changing weight. From the standpoint of the receptor this indicates that olfaction is called forth by an infinitesimally small amount of substance, and measurements directed toward testing this question justify the conclusion. These measurements have been made in a variety of ways.

One method of procedure is that of evaporating a given weight of odorous material in a known volume of air and then testing the air by sniffing it. This method lends itself readily to the determination of absolute measurements but it is not so easily applied to questions involving the comparison of odors. For the measurement of olfactory acuity, but especially for the comparison of odors, Zwaardemaker invented an ingenious piece of apparatus called an olfactometer. (Fig. 13). This consists of two tubes that slide one within the other and so shaped that one end of the inner tube may be applied to the nostril. The odorous material is carried on the inner surface of the outer tube. When the inner tube, which is graduated, is slipped into the outer one so as to cover completely its inner face and air is drawn into the nostril through the tube, the odorous surface being covered gives out no particles and no odor is perceived. If, now, the inner tube is withdrawn a certain distance so that a given surface of odorous material is exposed to the current of air, odorous particles escape into the current and these may be sufficient in amount to call forth olfaction. By adjusting the inner tube in relation to the outer one whereby more or less of the odorous surface is exposed, a point can be found where minimum stimulation occurs. The amount of odorous substance delivered under these circumstances to the air current has been designated by Zwaardemaker as an olfactie, the unit of olfactory stimulation. Having determined for a given substance the area necessary for the delivery of one olfactie, doubling

Fig. 13.—Simple rubber olfactometer. After Zwaardemaker, 1895, Fig. 14.

that surface by an appropriate movement of the inner tube will produce a stimulus of two olfacties and so forth. Thus a graded series of measured olfactory stimuli can easily be obtained. Further, by using outer tubes carrying different odorous substances, various comparisons can be instituted as measured in olfacties. Moreover, a double olfactometer (Fig. 14) may be easily devised in that two single olfactometers may be combined so that one current carrying an odorous material of a given concentration may be introduced into one nostril and another carrying a second odorous substance of known concentration can be introduced into the other nostril, or both currents may be united and the odorous mixture thus produced can be let into one nostril. Thus a variety of comparisons may be easily made.



14.—Double olfactometer. After Zwaardemaker, 1895, Fig. 15.

Van Dam (1917b) has modified Zwaardemaker's apparatus by applying the odorous material in the form of a rod instead of a coating to the inside of a tube. The rod is made of paraffin mixed in a definite proportion with the odorous substance and the extent to which the rod is exposed in the olfactometer tube is a measure of the concentration of the odorous particles in the air current. Rods of metal, platinum, gold, or zinc, have also been used; these have been charged by immersing them in an atmosphere of odorous material for a given length of time and then tested. The odorous particles gather on their surfaces and are subsequently freed. The success of this method makes it clear that in the original evaporation method more or less of the odorous material must become ineffective in that it adheres to the walls of the container in which the evaporation is carried out.

As a means of avoiding these and other difficulties Allison and Katz (1919) have recently employed in the testing of stenches a type of odiometer that for accuracy of work bids fair to replace most of the other devices. It consists of a number of Venturi-type flow-meters so arranged that a measured volume of air can be passed at a uniform rate through or over the chemical, and this air is then mixed with another measured volume of pure air also flowing at a uniform rate. The concentration of the chemical is measured by determining its loss in weight after a measured volume of air has passed through or over it. From this loss of weight and the total volume of air with which the chemical has been mixed, the concentration in milligrams per liter of air is determined. The mixture of air and chemical passes finally through a tube with a glass funnel at the open end. The funnel is placed over the nose of the person who by a single inhalation tests the mixture. The odors are rated arbitrarily as detectable, faint, quite noticeable, strong or very strong. By this means extremely accurate quantitative results can be obtained.

In testing olfactory acuity the majority of workers have used the method of evaporating a known weight of substance in a given volume of air. By this method Valentin (1848) found that 1/2,000,000 of a milligram of oil of rose per cubic centimeter of air was odorous. Assuming that 100 cubic centimeters of this mixture were necessary for olfaction, he concluded that the total weight of oil of rose used in this operation was the very small amount of 1/20,000 of a milligram. Valentin also found that water containing 1/2,000,000,000 of its weight of tincture of musk had a perceptible odor whereas water containing only 1/3,300,000,000 of this tincture could not be distinguished from ordinary water. One gram of the odorous mixture called forth the characteristic smell and contained only 1/2,000,000 of a milligram of tincture of musk.

More significant measurements were made by Fischer and Penzoldt (1886) on chlorphenol and mercaptan. One milligram of chlorphenol was evaporated in a room of 230 cubic meters capacity and was thoroughly mixed with the air. This dilution called forth an unquestionable olfactory sensation. It contained 1/230,000,000 of a milligram of chlorphenol per cubic centimeter of air or, if it is assumed that 50 cubic centimeters of air are the minimum needful for olfaction, the total amount of chlorphenol necessary was found to be 1/4,600,000 of a milligram. By a similar method it was shown that mercaptan, a liquid with a penetrating garlic odor, could be recognized at a concentration of 1/23,000,000,000 of a milligram per cubic centimeter, a concentration that would yield 1/460,000,000 of a milligram for every 50 cubic centimeters of air. Notwithstanding this infinitesimally small amount of mercaptan, the quantity, just designated was estimated by von Frey (1904) to contain some 200,000,000,000 molecules of mercaptan.

Passy (1892a, 1892b) has made similar minimum determinations for a number of substances and has shown that artificial musk, probably the most powerful of all known odorous materials, is about a thousand times stronger than natural musk. In his other determinations he found that olfactory acuity ranged in thousandths of a milligram per liter of air from camphor at 5 to vanillin at from 0.005 to 0.0005. The last determination may be expressed as equivalent to 1/2,000,000,000 of a milligram of vanillin in a cubic centimeter of air, a high dilution but still not so extreme as that already recorded by Fischer and Penzoldt for mercaptan.

The details of the more important of Passy's determinations are given in the following table in which olfactory acuity, as measured by the minimum amount of substance that was stimulating to the several persons tested, is expressed in thousandths of a milligram per liter of air.

Table I.

Minimum concentrations for olfaction in thousandths of a milligram of substance per liter of air (Passy, 1892b).

Substances	Thousandths of a milligram
Camphor	5.
Ether	1.
Citral	0.5 to 0.1
Heliotropin	0.1 to 0.05
Cumarin	0.05 to 0.01
Vanillin	0.005 to 0.0005

Passy (1892c) has also determined the minimum concentration necessary for the olfaction of a number of alcohols. These determinations have been recorded in millionths of a gram per liter of air and are given in Table II.

Passy's determinations indicate that the lower alcohols have relatively faint odors, but that the higher members of the series are fairly comparable with, for instance, the essential oils. A determination for ethyl alcohol by Parker and Stabler in 1913 showed that this alcohol could be detected only to a concentration of about 5.75 milligrams of alcohol per liter of air. The smaller amount found by Passy, namely 0.25 milligrams per liter of air, is believed by these authors to be due to odorous impurities that were found by them in certain ethyl alcohols and that may have been present in those tested by Passy.

Table II.

Minimum concentrations for olfaction in millionths of a gram of alcohol per liter of air (Passy, 1892c).

Alcohol	Primary	Secondary	Tertiary
Methyl	1000		
Ethyl	250		
Propyl	10 to 5	40	
Normal Butyl	1		20 to 10
Isobutyl	1		
Normal Amyl			40 to 20
Active sinistral Amyl	0.6		
Inactive Isoamyl	0.1		
Caprylic		0.005	

Some of the more striking determinations by Allison and Katz (1919) are reproduced in Table III.

Here it will be noted that the most active mercaptan tested, propyl mercaptan, is detectable at a concentration of 0.006 milligrams per liter of air which is equal to 6/1,000,000 of a milligram per cubic centimeter. This determination is by no means so extreme as that of Fischer and Penzoldt, 1/23,000,000,000 of a milligram per cubic centimeter. Whether this difference is due to a difference in the compounds used, for Fischer and Penzoldt do not state what mercaptan they tested, or whether it represents a difference in the methods employed cannot be stated. In the table from the work of Allison and Katz, as in all previous sets of determination, artificial musk is shown to be without question the most stimulating substance tested and thus stands at the head of olfactory stimuli.

Table III.

Concentrations in Milligrams of Chemical per liter of air.

Chemical	Intensity of Odor				
	Detectable	Faint	Noticeable	Strong	Very Strong
Ethyl ether	5.833	10.167	14.944	17.667	60.600
Chloroform	3.300	6.800	12.733	28.833	46.666
Ethyl acetate	0.686	1.224	2.219	4.457	6.733
Ethyl mercaptan	0.046	0.088	0.186	0.357	0.501
Pyridine	0.032	0.146	0.301	2.265	5.710
Oil of peppermint	0.024	0.032	0.109	0.332	0.348
Iodoform	0.018				
Methyl isothiocyanate	0.015	0.039	0.067	0.108	0.144
Butyric acid	0.009	0.021	0.066	0.329	0.580
Allyl isothiocyanate	0.008	0.012	0.024	0.030	0.201
Propyl mercaptan	0.006	0.020	0.028	0.043	0.054
Amyl thioether	0.001	0.007	0.011	0.012	0.015
Artificial musk	0.00004				

Notwithstanding the numerous discrepancies between the various sets of determinations for olfactory acuity made by various workers, it must be admitted that olfaction is accomplished through very small, often infinitesimally small, amounts of material, and yet these amounts involve immensely large numbers of molecules of the odorous substance.

4. Physical Condition of Stimulus, Gas or Solution? In olfaction in the air-inhabiting vertebrates the stimulus has been generally assumed to be material particles in a vaporous or gaseous condition and not, for instance, in the form of a solution.

This opinion was long ago supported by the experiments of Tourtual (1827) and especially of Weber (1847) both of whom believed that it could be shown that substances that could be smelled as vapors could not be smelled as solutions when introduced as such into the nose. Thus Weber was unable to recognize cologne water when this liquid, much diluted with ordinary water, was poured into his nasal cavities. He, therefore, concluded that though the vapor from cologne water was easily smelled, a solution of it was not so sensed and that hence the vaporous state of the substance was necessary as a stimulus for the olfactory organ. This conclusion was accepted by a number of investigators including Nagel (1894, 1904), Zwaardemaker (1895), Haycraft (1900) and others.

Aronsohn, in 1884, pointed out the great influence that water and temperature had on the olfactory organ. Ordinary cold water when introduced into the nose will so affect the organ of smell that olfaction is impossible for some time to come. Cold water is known to excite an increased production of mucous whose volume would materially interfere with stimulation by covering up the olfactory surfaces. Moreover if the action of water on the organ of smell in an air-inhabiting vertebrate is continued for some time, it is said to result ultimately in the destruction of the olfactory hairs. Thus Schultze (1862) noted that when the olfactory membrane of an air-inhabiting amphibian is flooded with water, the cilia with which it is provided may continue to beat for hours, but the much longer and heavier olfactory hairs vanish almost at once. To minimize this deleterious effect Aronsohn, therefore, introduced into the nose material dissolved, not in ordinary water, but in physiological salt solution and at an appropriate temperature. With these precautions he claimed that it was very easy to recognize weak solutions of clove oil. Vaschide in 1901 confirmed Aronsohn's results and pointed out that temperature was a more important factor in carrying out conclusive tests than the composition of the solvent.

These results, which were in direct opposition to those of Weber, were criticized by Zwaardemaker (1895) and especially by Veress (1903) who showed that the procedure employed by Aronsohn probably resulted in a failure to fill the olfactory cleft. Veress maintained that unless great care was taken at this step, air was very likely to remain in this cleft and thus the solution that was being tested would never really reach the olfactory terminals. Under such circumstances odorous particles would escape from the solution into the air filling the cleft and thus reach the olfactory organ as in ordinary olfaction. Thus it became necessary in making a conclusive test to take steps to insure the complete filling of the olfactory cleft with the solution to be tested. After some experimentation on the human cadaver, Veress perfected a technique whereby this could be accomplished.

On thus introducing odorous solutions into the nasal chambers of a living subject, he found that these solutions were stimuli for the olfactory organs, but that they did not produce the sensation ordinarily associated with them. A person, however, could soon learn to associate a given sensation with a particular substance and could thus acquire an ability to recognize this substance, but not by what would be called its proper odor. Veress, therefore, concluded that though solutions of odorous materials are stimuli for the olfactory organs, they are inadequate rather than adequate stimuli. It thus appears, contrary to the results obtained by Weber, that the olfactory organs of an air-inhabiting vertebrate can be stimulated by ordinary solutions, though this form of stimulation cannot be looked upon as normal.

To deny that the olfactory organs of man and other like vertebrates are stimulated by solutions, as has been done by a number of workers, implies a certain lack of appreciation of the actual environment of the olfactory terminals. These are the olfactory hairs that project into the coating of mucous that covers the olfactory membrane. These hairs appear to be completely covered by the mucus and should any of their lash-like ends reach to the outer surface of this layer, they are certainly far too delicate to project into the adjacent air; they would unquestionably remain within the limits of the mucous layer. Thus the olfactory hairs are at all times surrounded by watery mucous, which is in contact on its outer face with the air carrying the odorous particles. These particles, as already indicated, must be caught in great numbers on the moist mucous surface, absorbed according to Zwaardemaker (1918b), and, since they are in the form of gaseous or vaporous particles, they probably enter quickly into solution in the watery mucous and in this state come in contact with the olfactory hairs. From the nature of the surroundings, then, it would seem extremely improbable that the stimulating material for the olfactory terminals should be in any other state than that of a solution. This opinion seems to be gaining ground rapidly among the more recent workers, for it has found clear expression within the last few years in papers by Backman (1917a), by Durand (1918b), and in a qualified way by Henning (1916).

As already indicated, the difficulty met with in attempting to stimulate adequately the human olfactory epithelium with solutions of odorous material is due in all probability to the effects of the solvent on the olfactory hairs and not to the incapacity of these terminals to be stimulated by solutions. These hairs are apparently very delicately attuned to a mucous environment that would be very difficult to duplicate experimentally and yet this environment seems to be essential to a wholly successful test. Care as to temperature and salt contents of the solvent, as emphasized by Aronsohn, Vaschide, and Veress, are probably only the first steps in this direction.

The relation of the solubility of a substance to its efficiency as an olfactory stimulus has been discussed recently by Backman (1917a). This investigator has expressed the opinion that not only the aqueous environment of the olfactory hairs must be considered but also the substance of the hairs themselves. This he believes to be lipoid in character, an opinion that is supported by the well known fact that these hairs are best demonstrated by osmic acid. If the embedding mucous layer is watery and the olfactory hairs oily, it follows that any substance that gains entrance into the body of the hair must first have been dissolved in water and then in oil. From this standpoint Backman attempted to determine whether there was any relation between the effectiveness of certain olfactory stimuli and their solubility in water and in oil. Water and olive oil, each at 30 degrees centigrade, were used as the test solvents. Thus methyl alcohol and ethyl alcohol, which are without strong odor, were found to be freely soluble in water, but only very slightly soluble in oil. Hence while they would dissolve abundantly in the olfactory mucous, they would fail to enter the hairs to any great extent in consequence of which their effectiveness as stimuli must be, according to Backman, very slight. On the other hand normal butyl alcohol has a strong odor and its efficiency as a stimulus was believed to depend upon the fact that it is soluble in water to the extent of 8.3 per cent and in oil to an almost indefinite amount. Other substances showed somewhat different relations. Thus chlorbenzol could be detected at a dilution of 6.7 x $10.^{-8}$ gram-molecules per liter of air, and is soluble in water to the extent of 0.25 per cent and in oil indefinitely. Brombenzol could be smelled at the somewhat greater dilution of 1.1 x $10.^{-8}$ gram-molecules per liter of air; yet it is less soluble in water (0.045 per cent) than chlorbenzol though indefinitely soluble in oil. In these instances the degrees of solubility in water are the reverse of the effectiveness of these two substances as olfactory stimuli. Possibly solubility in oil, as intimated by Larguier des Bancels (1912), is of much more significance for olfactory stimulation than solubility in water. If the olfactory hairs in man are provided with flagella, such as have been described by Jagodowski (1901) in the pike, and the distal ends of these flagella reach through the olfactory mucous to the nasal atmosphere, the odorous particles may come directly in contact with them and dissolve in their lipoid substance without passing through an intermediate watery layer. In that case solubility in lipoid would be the only form of solubility necessary for the introduction of an effective stimulus. That a number of odorous substances are more soluble in lipoid than in water has recently been shown by Kremer (1917) who found that larger quantities of citral, guaiacol, pyridine, and even chloroform and ether would dissolve in a saturated aqueous solution of lecithin than in pure water. Of course the varying capacity for reaction of such materials as may thus become dissolved in the substance of the hairs must profoundly influence stimulation and possibly it is in this direction that the difference between such substances as chlorbenzol and brombenzol is to be explained. But however these details may be worked out eventually, the general opinion that olfactory stimulation is dependent upon some form of solution seems to be beyond question.

That the material thus dissolved must act chemically on the olfactory receptors and not by means of any radiation that it may give out seems probable from the fact that olfactory stimuli are substances that are not known to be radio-active. That there is a kind of physiological radio-activity, such as has been claimed recently for potassium by Zwaardemaker (1918a, 1920) and as might be urged for the materials of olfactory stimulation, seems extremely improbable from the recent work of R. F. Loeb (1920) and of J. Loeb (1920). Moreover it would be very difficult to explain the variety of olfactory sensations on the basis of stimulation by radio-activity, but the assumption that the stimuating materials act chemically on the substance of the receptor is in easy accord with the diversity of olfactory experience.

5. Olfaction in Fishes. It has already been pointed out that most fishes possess paired olfactory sacs whose structure and innervation are essentially indentical with the corresponding parts in the air-inhabiting vertebrates. Nevertheless currents of water flow through these sacs and such stimulation as they receive must come from these currents. Nagel (1894), who was one of the most vigorous opponents to the idea that the olfactory organs were stimulated by solutions and believed that gases or vapors were the only real stimuli for these receptors, was led to conclude that the so-called olfactory organs of fishes were fundamentally different from those of the air-inhabiting forms and that they probably more nearly resembled organs of taste than any other receptor possessed by the higher animals. This opinion was based upon theoretic considerations rather than upon any particular observation or test.

But before these views had been expressed by Nagel, a certain amount of experimental evidence concerning olfaction in fishes had been gathered. This was preliminary in character and inconclusive, but it nevertheless paved the way for further advance. Thus the observation of Aronsohn (1884a), that goldfish, which ordinarily will eat ant pupæ with avidity, would not take these pupæ after they had been smeared with a little oil of cloves, is not final evidence that the fish scented the oil, for it is entirely possible that this oil irritated the skin of the fish's snout and did not stimulate the olfactory apparatus at all. Nor was the discovery made by Steiner (1888), that the spontaneous appropriation of food by the shark, Scyllium, ceases on the removal of the cerebral lobes or simply on cutting the connection between these lobes and the olfactory bulbs, satisfactory evidence that the olfactory apparatus in these fishes is an organ of smell rather than a receptor for taste or some closely allied sense. Nagel (1894) noted that the front of the head of the fish, Barbus, was as sensitive to sapid substances after the olfactory tracts had been cut as before that operation, and Sheldon (1909), who studied the dogfish with great fulness, demonstrated that the decided sensitiveness of the nostrils of this fish to weak solutions of oil of cloves, pennyroyal, thyme, and the like, was not influenced by severing the olfactory crura, but disappeared on cutting the combined maxillary and mandibular branches of the trigeminal nerve. Evidently the nasal surfaces of fishes like those of the higher vertebrates, are innervated by fibers from the trigeminal nerve, and it is this nervous mechanism rather than the true olfactory apparatus, that is stimulated by the substances that have ordinarily been applied by experimenters. In 1909, Baglioni showed that blinded fishes were excited by the presence of food. None of these experiments, however, demonstrated conclusively that smell rather than taste or some other allied sense, was concerned as the receptor.

As early as 1895 von Uexküll observed that dogfishes from which the olfactory membranes had been removed did not respond to the presence of food whereas normal dogfishes three to five minutes after food had been introduced into their tank, sought it with great eagerness.

In these experiments no attempts were made to exclude sight or to ascertain the effects of the operation. In experiments carried out by me in 1910 an attempt was made to gain more conclusive evidence. Five normal catfishes (Amiurus) were allowed to swim in an aquarium in which were hung two wads of cheese cloth one containing concealed earthworms, and the other made of cloth only. In the course of an hour the wad containing the worms was seized eleven times by the fishes notwithstanding the fact that from time to time this wad was interchanged in position with the other. During the same period the wad without worms was passed over by the fishes many times and never excited any noticeable reaction.

Ten catfishes were next prepared for further experimentation; in five of these the olfactory tracts were cut and from the remaining five the barbels, the seat of the chief external gustatory organs, were removed. After the fishes had recovered from these operations, they were put in an aquarium into which was introduced a wad of cheescloth containing minced earthworms. During the first hour the wad was seized 34 times by fishes without barbels but with normal olfactory organs and, though often passed over by fishes with cut olfactory tracts, it was never seized by any of these and ''nosed'' only once by one of them. None of these fishes paid any attention to a wad of cloth containing no worms. Repetitions of these tests gave uniformly similar results and led to the conclusion that the olfactory organs of the catfish are serviceable in sensing food at a distance much beyond that at which the organs of taste are capable of acting; in other words, catfishes truly scent their food.

Similar experiments on the killifish (Fundulus) gave like results Parker (1911). Here, however, the olfactory organs were excluded, not by cutting the olfactory tracts, but by stitching up the anterior nares. As a result of this operation the fish no longer responded to hidden food, but quickly reacquired this power after the anterior nares had been reopened. These results were confirmed in work on the dogfish, (Mustelus), by Sheldon (1911) and on the swellfish, (Spheroides), by Copeland (1912). Sheldon closed the nares of the dogfish with cotton plugs and, in 1914, I showed that when only one nostril is thus plugged, the fishes turn persistently toward the side of the open nostril. Such responses indicate that in the seeking of food under normal conditions, dogfishes, and probably other fishes as well, turn

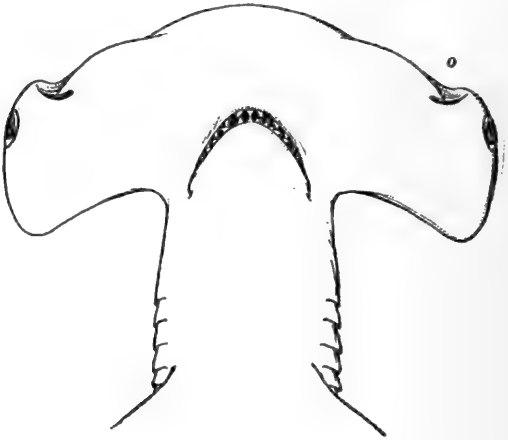


Fig. 15.—Ventral view of the head of a Hammer-head Shark (Cestracion) showing the olfactory pits (o) widely separated. After Garman, 1913, Plate 1, Fig. 2.

toward the side on which the concentration of odorous particles is greater. The certainty of this operation would increase in proportion as the nostrils of a given fish are separated one from the other laterally. A good example of an animal in which this condition reaches its maximum is seen in the hammerhead shark in which the nostrils, as well as the eyes, are carried on the remarkable lateral projections that extend sidewise from its head into the sea (Fig. 15).

Table IV.

Records in per cent. of Turning Movements of three Dogfish under the following successive Conditions: Normal, Left Nostril Occluded, Right Nostril Occluded, Both Nostrils Open Parker, (1914).

States of Fishes	Turning Movements in Per Cents.	
	To left	To right
Normal	50	50
Left nostril occluded	11	89
Right nostril occluded	87	13
Both nostrils open	44	56

The turning response of dogfishes under the conditions mentioned in the preceding paragraph has a striking resemblance to the circus movements in the tropic reactions of many of the lower animals and, were it not that fishes are so highly organized, it might be accepted at once as a response of that kind. The detailed condition of such reactions is well illustrated by the records in Table IV.

As a result of the evidence thus far accumulated, it seems quite clear, contrary to the opinions expressed by Nagel and others, that many fishes scent their food much as air-inhabiting animals do and that they must be regarded as possessing powers of olfaction fairly comparable with those of the higher forms. This opinion is in entire harmony with the well known fact that fishes, especially sharks, can be drawn from a long distance by ill smelling bait or by oily fish carcasses ground up and thrown into the water as in the practice of chumming. The extremely small amount of substance needed in these operations agrees well with what is known of olfaction among air-inhabiting vertebrates and reaches almost infinitesimal proportions as is indicated by the work of Olmsted (1918) on Amiurus.

The water-inhabiting stages of amphibians will doubtless be found to exhibit the same type of olfaction as that seen in fishes. This is already clearly indicated by the work of Copeland (1913) on the newt Diemyctylus and of Risser (1914) on tadpoles.

The opinion that fishes possess powers of olfaction comparable with those of the air-inhabiting vertebrates, though rejected by many of the older writers, has been accepted in recent years by Baglioni (1913) and by Luciani (1917). In fishes there can be no doubt that the stimulating material for the olfactory organs is carried in the current of water that is passing more or less continuously through these parts. Since in air-inhabiting vertebrates the stimulating materials are caught on the watery mucous of the olfactory surfaces, it follows that, as Durand (1918b) has recently declared, the olfactory stimulus throughout the whole range of vertebrates is material in a state of solution and not simply a gas or a vapor. This conclusion is in agreement with the opinion expressed many years ago by Johannes Müller. Henning (1916), some time since called attention to the possibility that odorous material may form with the olfactory mucous an emulsion rather than a true solution, but this suggestion did not seem even to Henning to be of much significance, for in other parts of his work he refers repeatedly to the state of the stimulating material as that of a solution and there appears to be no good ground for assuming that such is not the case.

6. Fatigue and Exhaustion. It is well known that the olfactory organs in man are quickly and easily fatigued by continuous exposure to odorous materials. Persons whose occupations lead them to work among disagreeable odors soon become insensitive to these and it has long been recognized that invalids are not affected by the malodors that may come from their own bodies. Although these conditions of irresponsiveness may be due in part to central nervous states such as lack of attention and the like, they are also dependent in part on peripheral exhaustion. The effects of unpleasant smells on the growth of guinea pigs has been tested very recently by Winslow and Greenberg (1918). These investigators employed a pair of air-proof cages through which were passed 1.5 cubic feet of air per minute amounting to 4 liters of air per minute for each animal in the test. Through one of these cages pure air was circulated; through the other, air that had passed over fresh moist fæces and that in consequence was impregnated with a strong fæcal odor. A total of 15 sets of growing guinea pigs, including 261 animals, were subjected to these conditions. In the first week of the tests the animals supplied with fæcal air did not grow as much as the controls did, but in the second week they caught up in weight with the controls and were thereafter in-

distinguishable from them. Thus the guinea pig, like man, though sensitive to disagreeable odors in the beginning, appears to become in the course of time entirely inert to this form of stimulation.

To test the immediate effects of the continuous action of odorous substance on the olfactory organ of man, Aronsohn (1884a) determined the length of time certain olfactory stimuli at full strength continued to call forth sensation. Thus oil of lemon and oil of orange were smelled by nine persons till the odors of these substances could no longer be perceived The period necessary to bring about this obliteration of sensation varied from 2.5 minutes to 11 minutes with an average of 3 minutes. A 0.2 per cent solution of cumarin in water was smelled for from 1.75 to 2.3 minutes after which it was no longer sensed. Thus olfactory exhaustion under strong stimulation is accomplished in a very few minutes. The recovery of excitability is apparently equally rapid and may be accomplished in as short a time as from 1 to 3 minutes though complete recovery probably requires a longer time.

Zwaardemaker (1895) tested fatigue in another way and determined by means of his olfactometer the increase in minimum stimulation as the olfactory organ gradually approximated exhaustion. During a continuous stimulation of known intensity the minimum stimulus was from time to time determined and was found to increase steadily. Two substances, benzoin and rubber, at two different strengths were tested (Fig. 16). Benzoin induced fatigue more rapidly than rubber and of the two concentrations employed for each substance the stronger in each instance called forth fatigue more quickly than the weaker.

Some persons are absolutely devoid of true olfaction, a condition which, as already pointed out, is attendant upon certain deficiencies in the essentials of the olfactory apparatus and which is designated as anosmia.

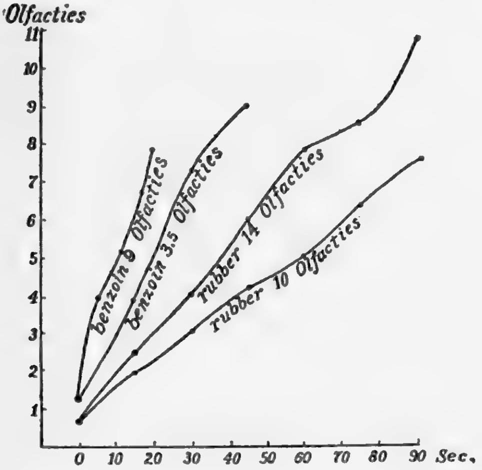


FIG. 16.—Curves of olfactory exhaustion produced by the action of benzoin of 9 and of 3.5 olfacties and by rubber of 14 and of 10 olfacties, acting for different periods. The threshold values in olfacties are marked on the ordinates and the duration of stimulation in seconds on the abscissæ. After Zwaardemaker, 1895, Fig. 22.

This state may be congenital or acquired and acquired anosmia may be either permanent or temporary. Some forms of anosmia, like color-blindness, are probably inheritable Glaser (1918). Of considerable interest from a theoretical standpoint are the cases of partial olfactory defects. Winkler noted a patient who was quite incapable of smelling benzoin though he easily recognized musk and another who was just the reverse of the first one. Blakeslee (1918) has recorded similar cases in relation to the odor of verbena flowers. Probably many persons are defective in this respect though their defects may not have been serious enough to have attracted attention and record.

Temporary partial anosmia may accompany certain diseases or may be induced by the application to the olfactory surfaces of anesthetizing drugs. Cocaine has been used in this way by a number of investigators, including Zwaardemaker, but without very clearly defined results. Zwaardemaker observed that temporary anosmia induced in this way was preceded by a brief period of increased sensibility or hyperosmia. Subsequently Reuter (1900) found that cocaine was also followed by hyperosmia. Rollett (1899) produced a complete anosmia by the use of gymnemic acid after which different olfactory sensations returned at different intervals.

7. Qualities of Odors. The qualities of odors appear to be almost innumerable. When we attempt to name on odor, we almost always designate it by the body from which the odorous material emanates like the smell of heliotrope, of onion, of rubber, and so forth. With tastes, as we shall see later, there are at least four clearly marked qualities, sweet, sour, bitter, and salty. The first three of these are general terms connected in no necessary way with the substances associated with them as stimuli, and we are continually finding new substances whose tastes are some one of these three. The odors of new substances, on the other hand, are almost certain to be individual and novel and to agree with odors already known only in a most general way. Thus odors have a certain historical value and get their names after the introduction of the substances with which they are

associated; the smell of illuminating gas was not a generally known odor till this material was brought into common use. Should it be abandoned commercially, its odor would cease to be a part of common human sensation. In consequence of economic changes many odors of trade articles, of kitchen products, and the like have disappeared from the list of human sensations and many new ones have come in. Yet notwithstanding this relatively rapid evolution in the field of olfaction, the organ of smell seems to remain the same; it gives up old forms of stimulation and takes on new ones in a way that is almost incredible. As a result of these peculiarities of the olfactory organ the classification of odors has proved to be a most perplexing problem and has resulted in most instances in what seem to be extremely artificial schemes.

Haller and particularly Linnaeus proposed systems of odors that have formed the bases for many of the modern classifications such as the one given by Zwaardemaker (1895). In this odors are arranged in nine general classes each of which may contain two or more subdivisions. These nine classes are briefly as follows:

1. Etherial odors; three subdivisions: odors of fruits, beeswax, ethers.
2. Aromatic odors; five subdivisions: odors of camphor, cloves, lavender, lemon, bitter almond.
3. Balsamic odors; three subdivisions: odors of flowers, violet, vanilla, cumarin.
4. Ambrosial odors; two subdivisions: odors of amber, musk.
5. Alliaceous odors; three subdivisions: odors of hydrogen sulphide, hydrogen arsenide, chlorine.

6. Empyreumatic odors; two subdivisions: odors of roast coffee, benzole.
7. Caprilic odors; two subdivisions: odors of cheese, rancid fat.
8. Repulsive odors; two subdivisions: odors of deadly nightshade, bedbug.
9. Nauseating odors; two subdivisions: odors of carrion, fæces.

A survey of this classification shows at once that more or less of it is associative and subjective and hence artificial, for what may be repulsive to one person may be just the reverse to another. It is, therefore, not surprising that some of the recent students of this subject, as for instance Henning (1916), have advised the complete abandonment of such arrangements and have sought to establish by a thorough re-testing of odors an impersonal and reasonable classification. As the result of an extended and judicious re-examination of odors Henning has come to the conclusion that they fell into six fundamental classes as follows:

1. Spicy odors, such as those of fennel, sassafras oil, anise, and cloves.
2. Flowery odors, such as those of heliotrope, cumarin, and geranium oil.
3. Fruity odors, such as those of oil of orange, citronella, oil of bergamot, and acetic ether.
4. Resinous or balsamic odors, such as those of turpentine, of Canada balsam, and of eucalyptus oil.
5. Burnt odors, such as those of tar and pyridine.
6. Foul odors, such as those of carbon bisulphide and of hydrogen sulphide.

Although each of these six classes, according to

Henning, is represented by a number of odors, it is not absolutely separated from the others, but between any pair of them there are numerous odors that assume intermediate positions. The six classes, however, are the striking predominant elements in this complex and are in no sense submerged in the general array of odors.

Henning has tried to make clear his idea of the relations of these six classes by imagining them located one at each corner of a three-sided prism which he calls the olfactory prism (Fig. 17). From each corner of this prism lines may be imagined to pass out to the other corners; these lines traverse either the edges of the prism or pass over its faces and mark the positions of all intermediate odors. Thus all odors, be they fundamental or intermediate, find places on the surface of the prism. Relations indicated by lines within the prism and connecting any two points on its surface indicate only mixed odors. Thus by means of a figure of three dimensions Henning brings into clear view the relations he conceives to exist between the six fundamental odors,

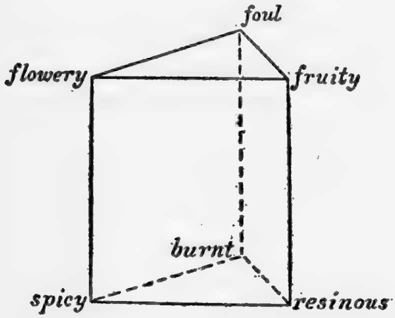


Fig. 17.—Olfactory prism. After Henning, 1916, Fig. 4.

their intermediates and mixtures. So far as an arrangement of odors is concerned the clarity of Henning's scheme is at once its most attractive and most suspicious feature.

8. Chemical Relations of Odors. The scientific value of any classification of odors will depend upon the success with which such a classification brings the odorous substances as stimuli into relation with the receptor. A satisfactory classification ought to make evident the number of elements or components concerned in olfaction. That olfaction is made up of a number of components is far from established, but what may be called the component theory of olfacton is generally assumed by the majority of writers on this subject Zwaardemaker (1895). That the classification outlined by Zwaardemaker shows very little of this feature is readily admitted even by this author himself. Quite aside from the fact that it may include irritants as well as true odorous substances, its classes do not stand up well under experimental test. Nagel (1897) tested this question in an investigation of the odors of vanillin and cumarin. These two substances, according to Zwaardemaker's classification, belong not only to the same class of balsamic odors but to the same subdivision, the vanilla odor. They ought, therefore, to show considerable olfactory similarity. Nagel attempted to test this relationship by ascertaining whether the temporary exhaustion of the olfactory organ by one of these substances would influence its receptive capacity for the other. To carry out this he prepared an aqueous solution of the two substances in such proportions that the smell of only vanillin could be recognized. He then exhausted the olfactory organ

for vanillin by smelling for a long time a pure solution of this material. On testing now the solution containing the mixture of substances, it was found to smell only of cumarin. Thus the exhaustion of the olfactory surface for vanillin did not prevent stimulation by cumarin. The placing of these two substances in the same subdivison is, therefore, obviously artificial.

Similar evidence as to the artificiality of Zwaardemaker's classifications had also been obtained from the study of persons suffering from partial anosmia and from neither this line of investigation nor from that dealing with partial exhaustion has there come any special justification of the conventional olfactory groupings.

Yet it is admitted on all sides that olfaction is essentially a chemical process. And, as a matter of fact, some progress has been made in discovering relations between chemical structure and olfactory sensation. This is not necessarily of a general nature, but seems usually to be limited to narrow ranges. Thus among the alcohols Passy (1892c) has discovered that the olfactory potency increases progressively in passing over this series from methyl to amyl as shown in Table V.

Backman (1917c) has likewise determined that in the methylbenzene series olfactory acuity for benzene, toluene, xylene, cumene, and durene increases as the substitute methyl group increases.

Changes in the quality of odors also follow some natural series of organic compounds as has been pointed out by Haycraft (1900) in the following etherial salts.
Ethyl acetate with acetic etherial odor.
Propyl acetate with acetic odor and slight flavor.
Butyl acetate with slight acetic odor and pineapple flavor.

Amyl acetate with no acetic odor but well marked pineapple flavor.

Ethyl acetate and amyl acetate have entirely distinct odors, but when propyl acetate and butyl acetate are taken into consideration the four compounds form a series in which there is a transition in odors corresponding to the changes in chemical structure. Other series of homologues, however, such as the one tested by Huyer (1917), analine, o-, m-, and p-toluidine, xylidine, and cumioline, show no such relations.

Table V.

Estimated potencies of alcohols, Passy (1892c).

Alcohol	Estimated Potency
Methyl	1
Ethyl	4
Propyl	100
Butyl	1000
Amyl	10000

Not a few investigators have suggested that the odors of many substances depend upon the number and arrangement of certain chemical radicals contained within the odorous molecule. Such radicals are commonly called osmophoric groups. Perhaps one of the most considerable studies of this kind was that carried out by Cohn (1904), but without commensurate results. The most recent and ambitious of these attempts is by Henning (1916) whose classification of odors has already been referred to.

Henning's studies on the relations of odors to chemical constitution have to do almost entirely with the aromatic compounds, though there is no reason to believe that his generalizations, if true, may not be extended eventually to the aliphatic series. He abandons the idea that special odors are to be associated with particular osmophoric groups. In odors these groups are significant, not because of the structure they themselves possess, but because of the positions they may occupy on the benzene ring. Osmophoric groups are such as the hydroxyl, aldehyde, keton, ester, nitro, and nitril groups. None of these, however, is associated with a particular odor, but any one may be the occasion of odor, if it occupies an appropriate place on a benzene ring. The position on the ring not the particular radical, according to Henning, is the determining factor so far as odor is concerned.

Henning is further convinced that in a general way types of chemical constitution can be indicated for the six groups of odors that he was able to distinguish (Fig. 18). Thus the class of spicy odors is represented by compounds in which the osmophoric groups are in para-position (Fig. 18a), as in anisaldehyde. In the flowery odors the osmophoric groups are in the meta- or the ortho-positions (Fig. 18b), as in tuberon. In the fruity odors the groups are forked (Fig. 18c) as in citral. In the resinous odors the groups are within the ring (Fig. 18d) as in pinene. In the burnt odors the ring is smooth (Fig. 18e) as in pyridin, and in the foul odors the ring is fragmentary (Fig. 18f) as in cacodyl. In this way each class of odors is associated with a special feature in the constitution of the molecule though not necessarily with a particular osmophoric group. Intermediate odors are due to combinations of groupings which partake of the nature of the two classes between which the intermediate lies. Thus vanillin has an odor between spicy and flowery and its three osmophoric groups (Fig. 18g) are attached so as to represent both the para-position (spicy) and the ortho-position (flowery). By this ingenious system Henning has attempted to connect odor with chemical constitution and though the attempt is avowedly fragmentary and may be open to much subsequent modification, it gives promise of the solution of a problem that heretofore has been most baffling.

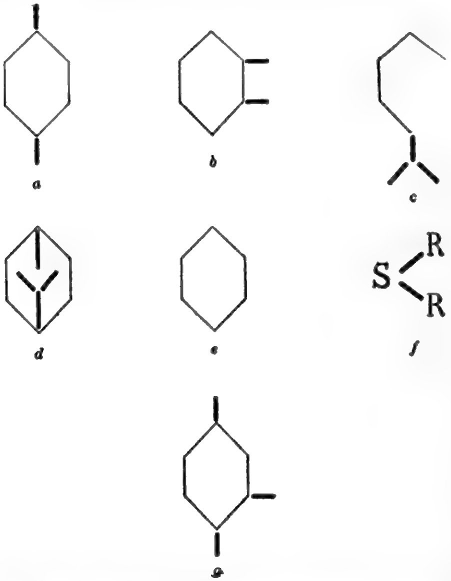


FIG. 18.—Generalized diagrams of the molecular structure of the six classes of aromatic bodies that serve as olfactory stimuli according to Henning (1916); a, for spicy odors; b, for flowery odors; c, for fruity odors; d, for resinous odors; e, for burnt odors; f, for foul odors; and g, for an intermediate odor between spicy and flowery.

9. Inadequate and Adequate Stimuli. Inadequate olfactory stimuli are apparently very few in number and not well known. Thermal stimuli when applied to the

olfactory organs are said to call forth no sensations of smell, and Valentin's statement that mechanical stimuli will produce unpleasant olfactory sensations has not been confirmed. Aronsohn (1884b), after filling the nasal cavity with warm physiological salt solution led a direct electric current through this cavity with the result that certain obscure sensations were produced depending upon whether the anode or the cathode was within the nose. With the anode in the nose a sensation was called forth on opening the circuit; with the cathode in the nose on closing it. There was, however, no evidence to show that these effects were not due to a stimuation of trigeminal endings instead of olfactory endings. Althaus in 1869 recorded as the outcome of electrical stimulation a phosphorous-like smell in a patient suffering from double trigeminal paralysis. Apparently the electric current is a true inadequate stimulus for the olfactory organ, but its peculiarities are very incompletely understood. Aside from this and the effects from solutions as described by Veress, inadequate olfactory stimulation seems not to exist.

The adequate olfactory stimulus for both water-inhabiting and air-inhabiting vertebrates is a solution in contact with the olfactory hairs and perhaps formed in part within these bodies. The solvent is probably first the olfactory mucous which receives the solute from the current of water or of air that passes over its outer surface. This watery solvent, which from its nature must be almost universal in its dissolving power, passes the solute on to the olfactory hairs whose capacity as receptors is probably limited by their lipoid composition. Only those substances that are soluble in lipoids can be taken up by the hairs, a process that must precede the initiation of the olfactory nerve-impulse. The solute may be any one of an immense variety of substances whose primary characteristics are that they are not only soluble in water but also in oil. The amount of these substances necessary for olfaction even in the case of the least odorous of them is very small and in that of the most odorous incredibly small. The amounts that are usually estimated for olfaction are those contained in what is believed to be the minimum volume of water or of air necessary for stimulation, but of the very minute amount of odorous substance contained in this volume only a very small fraction of it can reach the olfactory hairs. Much must be carried away in the general current or left stranded on non-olfactory portions of the nasal surfaces. Whether the olfactory hairs can concentrate this material or not remains to be ascertained, but even assuming that they can, the effective concentration must be of an extremely low order.

The substances thus brought in solution into the olfactory hairs must initiate those nervous changes that eventually produce the olfactory sensations. There ought, therefore, to be some relation between these substances and the resulting sensations. It is generally assumed that the substances that act as olfactory stimuli fall into classes associated with corresponding classes of sensations. As already indicated this conception may be called the component theory of olfaction, and if we assume, for instance, that the six classes of odors distinguished by Henning are separate classes, a view that Henning, however, opposes, then these classes would represent the olfactory components that physiologists have sought for so long.

The very existence of partial anosmia implies olfactory components the inactivity of one of which is accountable for the partial defect. But such cases are too little known to admit of clear interpretation. Thus Aronsohn's observation (1886) that partial anosmia produced by the exhaustion of the nose through ammonium sulphide leaves that organ sensitive to etherial oils but insensitive to hydrogen sulphide, hydrochloric acid and bromine, may be a differential effect between true odors (olfactory endings) and irritants (trigeminal endings), and not between groups of true odors. Nevertheless it must be in this direction that an experimental analysis of the general problem of olfaction will eventually proceed.

From this standpoint the condition presented by mixed odors is of significance. At least two classes of odor mixtures are to be distinguished, one spurious and the other real. Spurious mixed odors are those in which the gases or vapors act chemically on each other and thus produce a third substance which may or may not have an odor of its own. Thus ammonia and acetic acid both stimulate the nose, but when mixed they possess no odor for they combine to form odorless ammonium acetate. Obviously such instances are not, accurately speaking, instances of mixed odors. On the other hand there are many pairs of odorous substances in which one member does not act upon the other chemically and consequently in which the two are left to act independently on the olfactory receptors. Such double stimuli, from the standpoint of the component theory might be expected to excite two sensations, but apparently this is not always the case. If in a pair of such odors one is much stronger than the other, its smell dominates completely. If, however, the two odors are closely balanced a true odor may result which in quality is said to be unlike that of either component. Novel odors of this kind may be produced, according to Aronsohn (1886), by such combinations as cologne water and oil of orange, cologne water and oil of lemon, oil of bergamot and oil of orange, and so forth. The condition that thus produces a noval odor is one of considerable delicacy and may be easily upset by the greater exhausting effect of one or other of the components thus allowing the less exhausted member to assert itself and to call forth its own peculiar sensation. The presence of a sensation different from those of the pair of stimuli producing that sensation might seem to be a condition adverse to the component theory, but it must be remembered that in vision, in which the component conception is fundamental, an exact parallel occurs. Thus when a pure orange light is mixed with a pure green light, there may result a sensation of yellow that is wholly unlike that appropriate to either member of the combination, and that, as a matter of fact, may be indistinguishable from a sensation of yellow produced by a pure yellow light. Thus in accepting the component theory of sensory activity it must be admitted that two stimuli together may excite a receptor in precisely the same way as a third and entirely different stimulus may do. The existence of a novel olfactory sensation due to the simultaneous activity of two independent stimuli is therefore, no serious obstacle to this theory.

The condition of double olfactory stimulation that has just been described must not be confused with a kind of double stimulation that has been much studied. Valentin observed that when ether and balsam of Peru were smelled at the same time one by one nostril and the other by the other nostril, the odors are perceived not together but alternately and Valentin believed that there was a sensory conflict here as in vision, when one eye is directed to a field of one color and the other eye to one of another color. Aronsohn (1886) noted a similar conflict between the smell of camphor and that of oil of lemon. He also discovered that under similar circumstances one smell could overcome another. Thus the smell of camphor was neutralized by the smell of petroleum, cologne water, oil of juniper and so forth. This question was investigated much more fully by Zwaardemaker (1895) who employed for this purpose his double olfactometer. By this means it was comparatively easy to balance odors and then lead one into one nasal cavity and the other into the other cavity. In this way complete neutralization could be attained with great accuracy. Table VI gives a list of neutralizing pairs of odors and the intensity in olfacties at which Zwaardemaker found neutralization to occur.

Table VI.

Pairs of neutralizing odors (Zwaardemaker, 1895, p. 168).

Pairs of odorous bodies	Neutralizing Strength in olfacties
Cedarwood and rubber	2.75 : 14
Benzoin and rubber	3.5 : 10
Paraffin and rubber	8.5 : 14
Rubber and wax	14 : 28
Rubber and balsam of Tolu	14 : 70
Wax and balsam of Tolu	40 : 90
Paraffin and wax	10 : 20

It is needless to say that since in this form of double stimulation one stimulus is applied to one olfactory organ and the other to the other organ, the phenomenon of neutralization cannot depend upon the chemical action of one odor upon the other, for the odorous materials are not allowed to mingle. The fact that they are separately applied to different receptors shows that this type of conflict and of neutralization must have a central origin.

10. Olfactory Reflexes. In discussing the relations of the two categories of nasal stimuli, irritants and true odors, Fröhlich attributed reflex action to the first but not to the second, and it is true that nasal irritants almost invariably call forth vigorous respiratory responses, such as sneezing, whereas true odors are seldom followed by reactions of a marked kind. Pawlow, however, has pointed out the great importance of true odors in exciting and, in a way, in controlling the whole chain of digestive secretions, a process just as significantly reflex as sneezing but not so easily observed. Both classes of stimuli, then, are followed by abundant and important reflexes, but in one class these are of a kind easily noticed, in the other they are more hidden.

Although the olfactory organs in man are unquestionably concerned with the odors of the food that is being masticated, they are much more concerned with the odors of the environment. From this standpoint the olfactory organs are properly classed as distance-receptors or receptors affected by stimuli that emanate from more remote points in the surroundings. In consequence our olfactory sensations are in a way projected into the exterior and we seek, avoid, or recognize the distant body by its odor. The smell of a skunk is unquestionably a protective odor in that it implies that it can be sensed by other animals that will thereupon avoid its source. The great delicacy of olfaction among the higher animals by which they can scent the hunter is well known. Other odors have much to do with sexual activities whereby one sex is led to find the other or is otherwise excited to activity. But the prime service of olfaction is in the quest of food. From the fishes to the mammals olfaction serves as a means of discovering hidden or remote food and in this respect it is a highly significant sense for the direction of locomotion. In man and other microsmatic forms much of the keenness of olfaction has disappeared and yet the high development of this sense in our ancestry has left such a profound impression on the organization of our central nervous apparatus that we are often surprised by the power of our olfactory associations.

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CHAPTER IV.

VOMERO-NASAL ORGAN OR ORGAN OF JACOBSON.

Contents.—1. Vomero-nasal Organ in Man. 2. Comparative Anatony. 3. Histology. 4. Adjacent Parts. 5. Function. 6. Bibliography.

Vomero-nasal Organ in Man. In early infancy all human beings show traces of a pair of organs that are without doubt homologues of the vomero-nasal organs of the lower vertebrates. Each vomero-nasal organ in the new-born babe is a short tubular structure from a half to two and a half millimeters long and lodged in the lower anterior portion of the nasal septum. The organ opens into the nasal cavity by a minute pore on the free surface of the septum not far from its ventral border and only a short distance inward from the external naris. The tubular part of the organ extends posteriorly from this minute pore and ends blindly at a point somewhat higher than the level of the pore itself.

In early human embryos the pore of the vomero-nasal organ can be easily identified on the median face of the nasal chamber just within the anterior naris (Fig. 19). In adults the organ, though commonly present, may disappear completely. When present it occurs near the ventral margin of the nasal septum (Fig. 20). Kölliker (1877) states that it may vary in length from two to seven millimeters and Anton (1895) gives as the extremes 2.2 millimeters and 8.4 millimeters. As seen in transverse section it has the appearance of a tube flattened in the plane of the nasal septum. Its lateral wall is covered with an epithelium that resembles histologically the respiratory epithelium of the nasal cavity. This lateral epithelium may even be ciliated. The median wall is covered with an epithelium much like the olfactory epithelium of the nose except that differentiated olfactory cells are apparently not present. The cavity of the organ is sometimes obliterated by excessive epithelial growth and calcareous concretions may occur in its walls. As it appears to be without nervous connections, the vomero-nasal organ in man is probably entirely rudimentary.

2. Comparative Anatomy. A vomero-nasal organ has been recognized for some time past in all classes of vertebrates except the fishes, but, according to Gawrilenko (1910), this group too must be admitted to have at least the foreshadowings of such an organ. Even in such primitive forms as the sharks and rays each olfactory sac is divided into two compartments with separate innervation and these two compartments may be supposed to correspond one to the vomero-nasal organ and the other to the olfactory organ proper. This double character of the olfactory apparatus is also seen in other fishes. Thus in the development of the olfactory sac of the salmon Gawrilenko has shown that this organ includes two sensory thickenings or placodes, a median one and a lateral one. These two placodes can be traced into the adult where they are said to give rise to a median olfactory area and a lateral area. The median

FIG. 19.—Lateral view of the head of a human embryo showing the pore (v) of the vomero-nasal organ. After His, 1885, Fig. 29.

area is believed to correspond to the vomero-nasal organ of the higher vertebrates and the lateral area to the true olfactory receptor of these forms.

In some amphibians the distinction between a lateral and a median organ is much more evident than in fishes (Fig. 21). The lateral organ is the one that conducts the newly established air current from the external naris to the choana and hence corresponds to the olfactory organ proper. The median cavity is less involved in this current and is believed to represent the vomero-nasal organ.

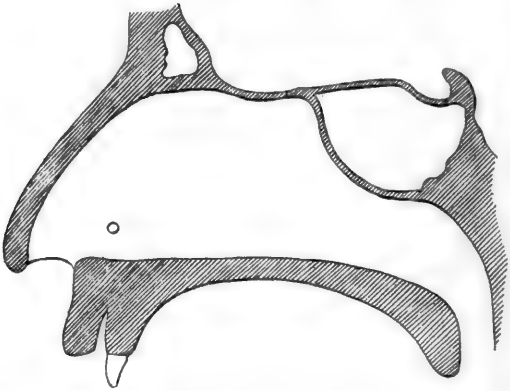

FIG. 20.—Diagram of the median face of the left nasal cavity of man; the small circle marks the position of the vomero-nasal organ in the nasal septum.

In certain sauropsida such as the alligators and turtles the vomero-nasal organ has been said to be at best only poorly developed, though so far as turtles are concerned this opinion is not shared by one of the most recent workers, McCotter (1917). In birds the organ is claimed to be entirely absent, but in lizards and in snakes it is highly differentiated (Fig. 22). Here the olfactory apparatus consists of a well-developed organ of smell located in the respiratory passage and an entirely independent vomero-nasal organ. The latter, in the form of a blind sac, opens into the cavity of the mouth. This peculiarity is probably dependent upon the growth of the hard palate in reptiles whereby a new adjustment between the nasal cavity and the mouth is brought about.

In mammals the vomero-nasal organ also shows much diversity. It is apparently best developed in the lower forms, such as the Australian duckbill Ornithorhynchus, and it is rudimentary in such groups as the primates including man. In general it has the form of a blind sac that opens usually by means of the naso-palatine duct (Stenson's duct) into the mouth, a relation that is probably reminiscent of its original connection with the primitive choana of which the naso-palatine duct may be regarded as a trace. Less commonly it opens directly by its own duct into the nasal cavity. This condition obtains in certain rodents such as the rabbit, guinea pig, rat, and mouse, and in certain primates including man.

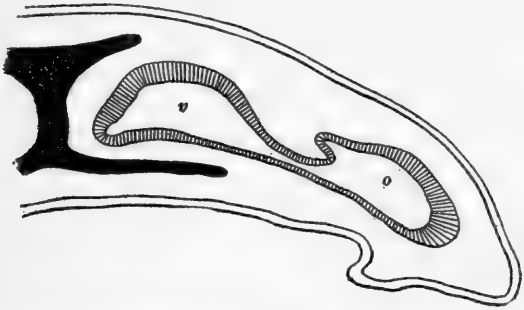

Fig. 21.—Transverse section of the snout of a young frog showing the partial division of the nasal cavity into a lateral or olfactory portion (o) and a median or vomero-nasal portion (v).

In all these higher vertebrates the olfactory organ proper corresponds to the lateral component of the pair of organs in the lower forms and the vomero-nasal organ to the median member of this group (Fig. 23).

3. Histology. The vomero-nasal organ of the dog and the cat, as described by Read (1908), is a tubular organ whose transverse section is circular in outline near its opening and crescentic or kidney-shaped throughout its greater extent. Its median wall may be two to three times as thick as its lateral wall. This thickened portion, which has been observed by numerous workers in a variety of mammals, is similar in cellular composition to the olfactory epithelium of the nose and is in strong contrast with the lateral thin wall which resembles respiratory nasal epithelium. Read has shown that the vomero-nasal organ of the cat and the dog is like the olfactory region of the nose in that it receives nerve fibers from two sources, the olfactory nerve and the trigeminal nerve.

Fig. 22.—Transverse section of the head of a snake embryo (Agkistrodon) showing the nasal canal proper (n) and the large vomero-nasal (v) organ opening on the roof of the mouth. Preparation by Mr. F. B. Manning.

As early as 1892 von Brunn showed that the sense cells of the vomero-nasal organ of the sheep were connected with nerve fibers in exactly the way they were in the olfactory region proper and he assumed, probably with correctness, that these fibers belonged to the olfactory nerve (Fig. 24). These observations were confirmed by all subsequent workers including von Lenhossék (1892) in the rabbit, Retzius (1894) in the snake, Ramón y Cajal (1895) in the rat, and Read (1908) in the kitten. Retzius showed that in the snake those nerve-fibers that were connected with the sense cells in the vomero-nasal organ mingled with the bundle of fibers from the olfactory region of the nose and thus confirmed von Brunn's suspicion that vomero-nasal fibers were true olfactory fibers.

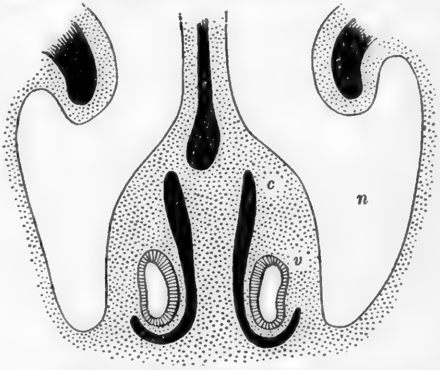

Fig. 23.—Transverse section of the nasal septum of a young cat showing the vomero-nasal organ (v), its cartilage (c), and the nasal cavity (n).

Von Lenhossék pointed out that at least in the rabbit the sense cells were not limited to the thickened face of the vomero-nasal organ, as had been maintained heretofore, but were found upon the opposite thin face of the organ as well This observation was confirmed on the rat a few years later by Ramón y Cajal. Hairlike terminations on the vomero-nasal sense cells, such as those that had been found in the olfactory cells, were sought for by a number of investigators but only traces of these structures could be found (von Brunn, Retzius, Read), probably because of the ease with which they are destroyed in the preparation of the tissue.

Von Lenhossék in 1892 not only confirmed von

Brunn's observation that the vomero-nasal sense cells were directly connected with nerve fibers, but he also pointed out that in the Jacobson organ of the fœtal rabbit free-nerve terminations occurred. These free terminals in some instances reached the receptive surface of the epithelium where they ended in slight knobs. Similar endings were recorded for the rat by Ramón y Cajal (1895). Von Lenhossék was unable to decide definitely whether these terminals belonged to the olfactory or to the trigeminal nerve. Nor is this question definitely settled now, though, judging from the conditions met with in the olfactory organ of the nose, it is highly probable, as Read concludes, that they belong to the trigeminal nerve. Admitting this to be the case, the innervation of the vomero-nasal organ would agree in all particulars with that of the olfactory organ proper. It is quite clear from the studies of Brookover (1917) on the nervus terminalis as well as from those of Larsell (1918) that the relations of this nerve to the vomero-nasal organ are merely incidental; the terminal nerve is in no sense especially connected with the organ of Jacobson.

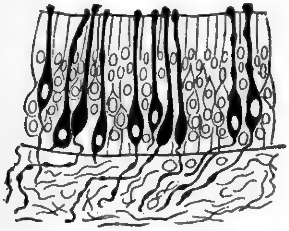

FIG. 24.—Epithelium from the vomero-nasal organ of the sheep showing the receptive cells impregnated by the Golgi method. After von Brunn, 1892, Plate 30, Fig. 12.

4. Adjacent Parts. In many of the higher vertebrates the vomero-nasal organ is contained within a more or less complete capsule of cartilage, the Jacobson cartilage (See Fig. 23). In the cat this capsule, according to Read, is complete anteriorly and incomplete posteriorly; in the dog it is incomplete throughout its whole

length. The vomero-nasal organ of these forms has commonly associated with it a considerable amount of cavernous tissue. This tissue, which was long ago identified in nasal organs by Klein (1881a, 1881b), is so disposed that in connection with the surrounding cartillage and other parts, it may serve as a means of changing in no small degree the volume of the organ.

5. Function. Concerning the function of the vomero-nasal organ almost nothing is known. Von Mihalkovics (1898) found that after burning out the naso-palatine duct and more or less of the vomero-nasal organ in the cat and in the rabbit, the appropriation of food by these animals was not interfered with, but it is hardly to be expected that so crude an experiment as this would yield significant results. Kölliker emphasized the fact that, at least in mammals, the connection between the vomero-nasal organ and the exterior is so narrow and indirect that it seems almost impossible that there should be any transfer of material from the exterior to the interior of the organ as, for instance, is implied in olfaction. He, therefore, suggested that the vomero-nasal organ was concerned with testing the animal's own juices as represented by the secretions from this organ. But the vomero-nasal organ, particularly in mammals, is intimately associated with much cavernous tissue whose change in volume may be concerned with its filling and emptying. Thus it is quite possible that oral or nasal juices may be sucked into the vomero-nasal organ and discharged from it as has recently been maintained by Broman (1918). Henning (1916) has suggested that the organ is concerned with water olfaction as contrasted with air olfaction, but according to an unpublished obser-

vation of Mr. H. E. Hamlin air is often found in the vomero-nasal organs of freshly killed mammals, and this observation when taken in connection with the work of Broman supports the hypothesis already advanced by many investigators (P. and F. Sarasin, 1890; Seydel, 1895; Gaupp, 1900) that these organs are subsidiary olfactory receptors, an opinion that, while it lacks complete experimental proof, is abundantly supported by the finer structure of the parts concerned.

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CHAPTER V.

THE COMMON CHEMICAL SENSE.

Contents.—1. Common Chemical Sense in Man. 2. In Lower Vertebrates. 3. Nerve Terminals. 4. Relation to Other Senses. 5. Bibliography.

1. Common Chemical Sense in Man. It was long ago made clear by Fröhlich that on the nasal surfaces of man there were two systems of receptors that could be stimulated by gaseous or vaporous materials: olfactory cells representing the olfactory nerve, whose stimuli, delicate perfumes and odors, call forth few observable responses, and free-nerve terminals probably representing the trigeminal nerve, whose stimuli, irritants for the most part, are usually followed by vigorous reactions such as sneezing. This distinction has been generally accepted among physiologists, but it has not been so clearly seen that the receptors for irritants are found in other parts of the body than the nose and that they represent a fairly well defined category of sense organs which, if not so sharply marked off as those of taste and of smell, are fairly comparable in distinctness with the receptors for heat, cold, or pain. The extent of their occurrence is easily recognized. Thus the vapor of ammonia not only irritates the nose, but also the eye, causing watering, as well as the mouth and the upper respiratory region whence arise impulses that lead to coughing and choking. Irritants of this kind also stimulate the anus and the genital apertures and in fact any

part of the body where a mucous surface is in contact more or less with the exterior. In man, then, the receptors for irritants have a much wider distribution over the body than the olfactory receptors have in that they are found on almost every exposed or partly exposed mucous surface.

2. In Lower Vertebrates. In other mammals than man, in birds, and in reptiles the receptors for irritating substances are probably distributed in much the same way as in man and are confined to the exposed or semi-exposed mucous surfaces. In the amphibians and the fishes, however, this system of receptors shows a prodigious expansion in that in these animals it is found covering their whole exteriors. The well known experiment of stimulating the frog's foot with solutions of acids and other such substances is based upon this peculiarity and the sensitiveness of the skin of this and other amphibians and of fishes as worked out by Nagel (1894), Parker (1908a, 1908b, 1912), Sheldon (1909), Cole (1910), Crozier (1915, 1916), and others show quite clearly that sensitiveness to solutions of chemicals is a common property of the skin in all these aquatic vertebrates.

As early as 1894 Nagel discovered that the integument of the dogfish Scyllium was extremely sensitive to a great variety of chemical substances. He likewise found that the skin of the goosefish Lophius and of the lancetfish Amphioxus were also generally open to chemical stimulation.

Nagel's observations on Amphioxus were confirmed in 1908 when it was shown that the skin of this fish was sensitive to solutions of acids, alkalis, alcohol, ether, chloroform, turpentine, oil of bergamot and oil of rosemary but not to solutions of sugar. It was also demonstrated that the skin of the catfish Amiurus was sensitive to sour, saline, and alkaline solutions, a condition that was subsequently found to be true for the young of the lamprey eel Ammocoetes Parker (1908b, 1912). In 1909 Sheldon published an account of the chemical stimulation of the skin of the dogfish Mustelus, the most extensive study of this kind thus far made. Sheldon found that the whole outer surface of this fish was very sensitive to acids and alkalis, less so to salts and bitter substances and not at all to sugar solutions, a condition that in general confirmed the results of earlier workers. Crozier (1915) studied the mutual relations of salts of sodium, potassium, and calcium as applied to the frog's skin and was able to demonstrate ionic antagonism which led him to conclude that in normal stimulation the surface of the receptor must be penetrated by the stimulant.

These observations warrant the general conclusion that the outer surfaces of most fishes and amphibians are open to stimulation by chemical substances of a mildly irritating kind. It is probable that this capacity has been retained by the air-inhabiting vertebrates in only a very circumscribed and local way, namely on those exposed or partly exposed mucous surfaces that reproduce in their delicacy and moistness the characteristics of the general outer surface of aquatic forms. From this standpoint the restriction of the chemical sensibility of the air-inhabiting vertebrates is the result of the drying of their skins in consequence of an ancestral migration from an environment of water to one of air.

3. Nerve Terminals. The form of nerve terminal that is concerned with the reception of chemical irritants in the skin of vertebrates is well indicated in the catfish

Amiurus. If a bait in the form of a piece of meat or the like is held close to the flank of one of these fishes, the animal is very likely to turn suddenly and snap it up. This is not a surprising response, for the sides of these animals are well provided with taste-buds. They are also supplied with lateral-line organs. Both these sets of receptors may be eliminated by cutting on the one hand, the branch of the facial nerve that is supplied to the taste-buds of the side of the body and, on the other, the lateral-line nerve that is distributed to the lateral-line organs of the same region. After the fish has recovered from such an operation, it will no longer respond to a bait held near its flank, but the skin of this region is still perfectly open to stimulation by sour, saline and alkaline solutions. As the only receptors left after the operation just described are the free-nerve terminals of the spinal nerves, these terminals must be the receptors for chemical irritants. This conclusion is in accord with the fact that this type of ending is the only one that occurs in many portions of the skin of the dogfish, of the foot of the frog, and of the partly exposed mucous surfaces of the higher vertebrates such as those of the mouth and the nose. Moreover when these endings are rendered inoperative by cutting their nerve trunks, as Sheldon did on the dogfish and as has often been done on the nasal cavities of mammals, irritating substances are no longer effective. Free-nerve endings of spinal or cranial nerves are, therefore, quite certainly the type of nerve-terminal concerned with the reception of chemical irritants.

4. Relation to Other Senses. In discussing the relation of the receptors for chemical irritants to other sense organs some of the earlier workers suggested a compari-

son of these receptors with those for taste Parker (1908a); Herrick (1908). More recently Coghill (1914) has declared that since tactile and chemical irritability develop simultaneously in certain amphibian larvæ, chemical irritability is in reality tactile in nature. It must also be perfectly evident that the receptors under consideration have striking resemblances to those concerned with pain.

The fact that organs of taste always involve specialized end-organs, such as taste-buds, whereas receptive surfaces for chemical irritants may contain only free-nerve endings, shows that the relation of these two classes of receptors is at best only distant. This conclusion is supported by an observation by Parker and Stabler (1913) that the minimum concentration of ethyl alcohol necessary for the stimulation of the irritant receptors in man, 5 to 10 molar, is decidedly stronger than that which will stimulate the human gustatory organs, 3 molar.

The relation of the receptors for irritants to those for touch and for pain seems to be clearly indicated in the results of experiments in which exhaustion and narcotics have been used. If the tail of an amphioxus is subjected to about twenty applications of weak nitric acid, 0.025 molar, in fairly rapid succession, the fish will cease to respond to this kind of stimulus. After the exhaustion of the mechanism for this type of reception, the tail of the fish will be found fully sensitive to the touch of a camel's hair brush. If, now, the tail of a fresh individual is vigorously stroked some thirty times in succession, the fish will cease to respond to this form of mechanical stimulation but it will still be found very sensitive in the exhausted part of the skin to weak acid. Thus mechanical stimulation and chemical stimulation seem to apply to different sets of terminals and the exhaustion of one set does not involve that of the other.

On treating a portion of the surface of a dogfish with 2 per cent cocaine, Sheldon found that tactile stimulation ceased in from ten to twenty minutes whereas chemical stimulation was effective for a somewhat longer period. By continuing the treatment with cocaine receptivity for chemical irritants was also eventually abolished. In a similar way Cole (1910) found that if the hind foot of a spinal frog was treated with 1 per cent cocaine till the animal no longer responded to pricking or scratching with a needle or to pinching with forceps, it would nevertheless respond vigorously to a salt solution. These results were confirmed by Crozier in 1916 who used a half per cent solution of cocaine hydrochloride on a frog's foot. After about 20 minutes' immersion in this solution, the reaction time of the cocained foot to formic acid 0.05 molar, was about twice that of the normal foot. After about an hour to an hour and a half of this treatment the cocained foot no longer reacted to pinching but gave good responses to acid with reaction times of from ten to fifteen seconds, about twice that of the non-cocained foot. These observations show beyond a doubt that the effect of chemical irritants on the naturally moist skin of vertebrates is not to be ascribed to the stimulation of organs of touch or of pain but to some other form of receptor, the terminals of what has been called the common chemical sense.

As Crozier has pointed out, there can be no question of the distinctness of the human sensations attributed to the common chemical sense as contrasted with our sensations of smell, taste, touch, or pain. The curious feeling that comes from vapors that irritate the eyes, nose, or even the mouth has not the remotest relation to touch, smell, or taste and is only distantly suggestive of pain. Pain, however, is easily separated from the common chemical sense by the use of cocaine, and we are, therefore, entirely justified in concluding that the common chemical sense is a true sense with an independent set of receptors and a sensation quality entirely its own. In the fishes and amphibians it pervades the whole integument but in the reptiles, birds and mammals it is restricted to the partly exposed mucous membranes of the natural apertures, a restriction that doubtless arose as the vertebrate changed from an aquatic to an air-inhabiting form.

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CHAPTER VI.

ANATOMY OF THE GUSTATORY ORGAN.

Contents.—1. Distribution of Taste-buds in the Oral Cavity of Man. 2. Comparative Distribution of Taste-buds. 3. General Form of Taste-buds. 4. Cellular Composition of Taste-buds. 5. Intragemmal and Other Spaces. 6. Innervation of Taste-buds. 7. Gustatory Nerves. 8. Relation of Gustatory Nerve Fibers and Taste-buds. 9. Bibliography.

1. Distribution of Taste-buds in the Oral Cavity of Man. In man the organs of taste are located in the mouth. These are the so-called taste-buds discovered independently by Lovén (1867) and by Schwalbe (1867). In the adult human being they have been identified on the dorsal surface of the tongue except the mid-dorsal region, on both the anterior and posterior surfaces of the epiglottis, on the inner surface of the arytenoid process of the larynx, on the soft palate above the uvula, on the anterior pillars of the fauces, and on the posterior wall of the pharynx. All other oral surface in the adult, such as the lips, the gums, the cheeks, the inferior surface of the tongue, the hard palate, the uvula, and the tonsils are devoid of these organs.

In young individuals, babes, and human embryos taste-buds are more widely distributed than they are in the adult. According to Tuckerman (1890a, 1890b) and Gräberg (1898) taste-buds appear in man at about the beginning of the third month of foetal life. Stahr (1902) found them in human embryos in the middle of the dorsum of the tongue and Ponzo (1905) identified them on the palatine tonsils, the hard palate, and the cervical part of the esophagus, regions from which they are absent in the adult. As early as 1875 Hoffmann called attention to the fact that in human embryos and newly born babes taste-buds were commonly found on the free surfaces of the vallate papillæ, situations from which they disappear in later life. This observation was confirmed by Tuckerman (1889) as well as by Hermann (1885), who, however, worked upon the rabbit. Thus the gustatory apparatus of man and of other mammals is by no means constant, but suffers reduction from the late embryonic period to the adult state. On the tongue of man the reduction is chiefly in the middle region of the distal two-thirds so that, as Stahr (1902) has pointed out, the center of taste in this organ shifts with growth from a position near the tip of the tongue to one in the neighborhood of the vallate papillæ. This opinion is in agreement with the observation of Heiderich (1906) that after birth the taste-buds of the vallate papillæ show almost no change.

Wherever taste-buds occur in man, except on the tongue, they are found simply imbedded in the epithelium of the mucous membrane of the region concerned. On the tongue, however, they are almost invariably associated with certain kinds of papillæ. The human tongue possesses several classes of these structures, which from their forms have been designated as conical, filiform, fungiform, foliate, and vallate. The plush surface of the dorsum of the tongue is produced by innumerable fine conical and filiform papillæ. These, however, almost never have taste-buds associated with them. The other types of papillæ, the fungiform, foliate, and vallate, very generally carry taste-buds (Fig. 25).

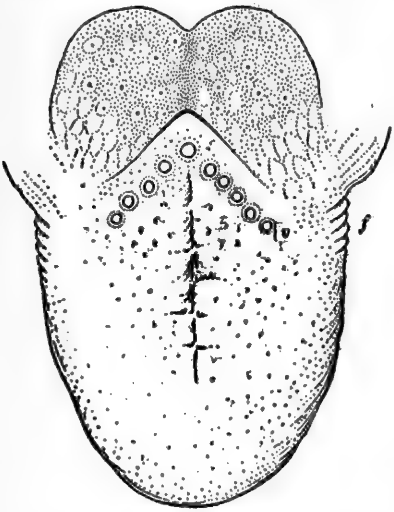

FIG. 25.—Dorsal view of the human tongue showing foliate papillæ (f) and vallate papillæ (v).

The fungiform papillæ are relatively large knob-like elevations scattered over the dorsum of the tongue. They can be easily seen with the unaided eye and may be readily located and identified. They commonly carry a few taste-buds embedded in the epithelium of their free outer surfaces. In sections of the crowns of these papillæ parallel to the surface of the tongue three or four or more, rarely six to eight, taste-buds may be identified. In vertical section it can be seen that the taste-buds are not indiscriminately scattered over the free surface of the papilla, but are perched on the secondary dermal papillæ contained within the papilla proper and that they always reach through the full thickness of the epidermis from the dermal core of the secondary papilla to the free outer surface of the primary papilla itself (Fig. 26). This extension through the whole thickness of the epidermis seems to be a common characteristic of taste-buds, for it is to be noted in them from fishes to man. It is an easy means of distinguishing them from other bud-like receptors such as the lateral-line organs whose cells extend only part way through the epithelium in which they are imbedded.

The foliate papillæ lie on either side of the edge of the human tongue and close to its root. They form a series of from three to eight vertical parallel ridges. Each ridge is abundantly supplied with taste-buds which, however, do not occur on its free outer surface but on its sides. Here the buds open into the ditch between the ridge on which they are located and the next one. In sections transverse to the axis of the ridge the numbers of taste-buds seen on the two sides of a given ditch may vary from three to twenty. In the rabbit the foliate papillæ are especially well developed and are abundantly supplied with taste-buds. These have been very fully studied recently by Heidenhain (1914) who has shown that the buds are arranged in more or less vertical rows on each papillar fold and that they probably increase in numbers by a process of fission.

FIG. 26.—Vertical section of a fungiform papilla showing two taste-buds.

The vallate papillæ, which in man are usually six to twelve in number, form on the posterior part of the tongue a V-shaped row whose angle points toward the esophagus (See Fig. 25). Each papilla is a low circular elevation surrounded by a relatively deep, narrow ditch. The taste-buds are located on the walls of this ditch and chiefly on that wall which forms part of the papilla. In a vertical section through a vallate papilla, it is usual to see on the side of the ditch formed by the papilla from ten to a dozen taste-buds and on the side away from that structure four to six such bodies (Fig. 27). However, as Schwalbe (1868) long ago pointed out, much individual variation occurs and it is, therefore, very difficult even to estimate with any degree of accuracy the total number of taste-buds on a single papilla. W. Krause (1876) believed the number for a single papilla in man to be as high as 2500, but von Wyss (1870) placed it much lower, namely, at about 400. Even these figures seemed too high to Gråberg (1899) who gave the maximum at 100 to 150 and the minimum at 40 to 50. Heiderich (1906) made a close count on 92 papillæ from human beings ranging in age from the first to the twentieth year and found the extreme numbers of buds to a

FIG. 27.—Vertical section of a vallate papilla showing taste-buds.

papilla to be 508 and 33 with an average not far from 250.

2. Comparative Distribution of Taste-buds. Taste-buds, like the olfactory receptors, require a moist surface. It is, therefore, not surprising to find that in all air-inhabiting vertebrates they are limited to the oral cavity. Their distribution in mammals has been very fully studied by Tuckerman (1892), Münch (1896), and Haller (1909).

Taste-buds also appear to be limited to the oral region in amphibians notwithstanding the fact that many of these animals possess a permanently moist skin. In fishes they were apparently first seen by Leydig in 1851 and were subsequently described by Schulze (1863). In these forms they are not restricted to the oral region. According to Johnston (1906) they are present on the heads of cyclostomes as well as on those of ganoids where they were studied by Dogiel (1897). Herrick (1918) states that in some bony fishes, such as the catfishes, the carps, and the suckers they are to be found over the entire outer surface of the body and this investigator (1903) has further shown that in the catfish Amiurus the taste-buds on the flank of the fish are as significant in the detection of bait as are those about the mouth (Fig. 28).

3. General Form of Taste-buds. Taste-buds vary in form from that of a flask to that of a spindle. Commonly they are single bud-shaped bodies opening to the exterior by a small pore (Fig. 29). Compound buds in which the body of the bud appears double and two pores are present have long been known and Heidenhain (1914) has recently shown that this condition may reach an extreme degree of complexity in the foliate papillæ of the rabbit

where compound buds with as many as six pores have been identified. The frequency with which types of buds with different numbers of pores occur may be gathered from the enumeration by Heidenhain who found that in 509 taste-buds from the foliate papillæ of the rabbit 368 had one pore, 100 two pores, 29 three pores, 7 four pores, 1 five pores, and 4 six pores. In the compound buds the pores usually form a more or less linear series and as each pore represents a single element in the complex the whole gives the impression of a row of fused buds (Fig. 30.) These compound buds are believed to result from a process of imperfect division.

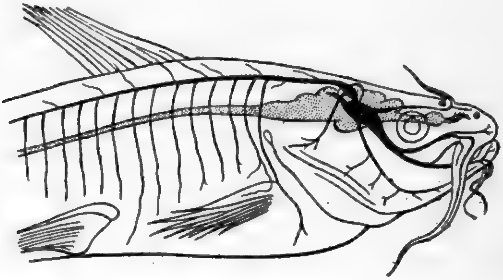

FIG. 28.—Lateral view of the catfish, Amiurus melas, showing in black the gustatory branches of the facial nerve. After Herrick, 1903, Fig. 3.

Some taste-buds open directly on the oral surface where they are located; others are marked by a pore, the outer taste-pore, which leads into a short canal and this in turn ends at the inner taste-pore formed by the distal end of the bud itself. Von Ebner (1897) noted that in some instances the canal expanded into a small chamber or ampulla over the tip of the bud and, though Gråberg (1899) could not confirm this statement for man, the condition has been observed anew by Kallius (1905) in human material and by Heidenhain (1914) in the rabbit.

5. Cellular Composition of Taste-buds. The cells composing the taste-buds are so arranged as to give each bud somewhat the appearance of a flower bud or of a leaf bud not yet unfolded. As has been stated already, these end-organs were described in the skin of fishes as early as 1851 by Leydig and were subsequently simultaneously and independently discovered in the mouths of the higher vertebrates by Lovén (1867) and by Schwalbe (1867). The older workers usually distinguished in the taste-buds two classes of cells, taste-cells, which were supposed to be chiefly central in position, and supporting cells mainly on the exterior of the bud.

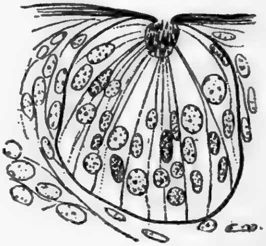

Fig. 29.—A simple taste-bud from a foliate papilla of the rabbit. After Heidenhain, 1914, Plate 19, Fig. 5.

Each taste-cell is an attenuated delicate structure whose elongate nucleus forms a slight enlargement near the middle of the cell-body (See Fig. 31a). Distal to it narrows to a delicate process, the taste hair. This hair either projects out of the pore into the exterior or into the canal when that is present. Proximal to the nucleus the taste-cell extends into the deeper part of the bud there to terminate usually in a small rounded knob. The number of taste-cells in a bud varies from two or three to as many as the contained supporting cells, perhaps ten or more.

Beside the taste-cells proper Schwalbe (1867) described what he believed to be a second form of receptive cell to which he gave the name of "Stabzelle" or rod cell. This type of cell was said to differ from the ordinary taste cell in that it was without a taste hair. It has not been identified with certainty by subsequent investigators.

The supporting cells of the taste-buds have been the occasion of much difference of opinion. The older workers believed that these cells were limited to the exterior of the buds, but Merkel (1880) showed that they also occurred in the interior and Ranvier (1888) definitely described both inner and outer supporting cells. Hermann (1889) concluded that these two classes of supporting cells differed not only in position but also in structure. The outer cells, which he called pier cells (Pfeilerzellen), were relatively large pyramidal elements whose nuclei were proximal in location and whose distal ends terminated in a zone marked with fine vertical stripings. For the inner supporting cells Hermann used Schwalbe's term of rod cells (Stabzellen) without, however, wishing thereby to imply that they were of a sensory nature. They were said to differ from the pier cells in that they were devoid of the peripheral striped zone. Hermann also described basal supporting cells which to the number of two to four were found in the proximal part of the taste-buds. Von Lenhossék (1893b) doubted the existence of basal cells and described four not very sharply separate types of supporting cells. Gråberg (1899) reidentified in human material the basal cells dis-

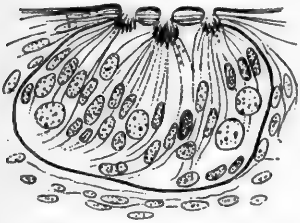

FIG. 30.—A compound taste-bud from a foliate papilla of the rabbit. After Heidenhain 1914, Plate 23, Fig. 27.

covered by Hermann. The other supporting cells were described by this author as either central or peripheral and were to be distinguished from each other rather by location than by differences of structure.

The indefiniteness and uncertainty that surrounded the question of the classes of supporting cells in taste-buds has been dissipated in large part by the declaration of Kolmer (1910) that between the taste-cells on one hand and the so-called supporting cells on the other there are all possible transitions and that it is, therefore, a mistake to attempt to draw distinctions not only between various kinds of supporting cells but between supporting cells and taste-cells. Kolmer believed that all the elongated cells in taste-buds are really taste-cells and that their differences are due to the stage of growth at which they are for the moment. This opinion, which is supported by what is known of the innervation of the taste-buds, has gained the acceptance of the more important recent workers in this field, such as Retzius (1912) and Heidenhain (1914). If true, it shows the taste-bud to be a much more unified structure than has heretofore been supposed and it does away at once with the confusion over the classes of cells that were believed to enter into its composition.

The basal cells apparently do not fall into this general category of more or less differentiated receptor cells, but, according to Heidenhain at least, they are elements that only under certain conditions are regularly present and are concerned with the division of the buds.

The epidermal cells immediately next the taste-bud are often flattened against this structure and conform more or less to its outline. These cells have been called by Gråberg (1899) extrabulbar cells and though they are not to be classed as part of the bulb proper they are nevertheless sufficiently related to that structure to be appropriately mentioned in this connection.

As Hermann (1889) long ago pointed out, the cells of the taste-buds are probably undergoing continual change. Old cells are degenerating and disappearing and new ones are forming to take the places of those that have broken down. The degenerating process is indicated by the presence in the taste-buds of cells in all stages of growth and of considerable numbers of leucocytes, as pointed out by Ranvier (1888), von Lenhossék (1893b), and others. The regenerative process is shown in the occasional occurrence of mitotic figures in the base of the bud thus giving evidence of cell division in that region Hermann (1889).

5. Intragemmal and other Spaces. Graberg (1899) has called attention to the fact that taste-buds are not solid structures but that their cells are separated one from another by considerable intervening space, and that much free space occurs in the tissue immediately around the buds. This intra-, peri-, and subgemmal space is believed by Graberg not to be an artifact, for it can be identified by almost all methods of preparation. According to this investigator these various spaces communicate with one another and connect with the exterior through the taste pore. They may be the means of irrigating and thereby cleaning the taste-bud, for it is possible that fluid may flow slowly through them from the interior to the exterior.

6. Innervation of Taste-buds. Among the older investigators the innervation of the taste-buds was a ques-

tion of much uncertainty. Some claimed that the gustatory nerve-fibers connected directly with the cells of the taste-buds; others that they did not so connect. The first to employ special neurological methods for the solution of this question were Fusari and Panasci (1890). These workers claimed that by means of Golgi preparations it could be shown that the gustatory cells were directly connected with nerve-fibers. Two years later Retzius (1892a) published an account of the innervation of the taste-buds of mammals and of amphibians in which he showed in preparations stained by methylenblue as well as by the Golgi process that the nerve-fibers were not directly connected with the taste-cells but ended in close proximity to them (Fig. 31). These results were confirmed in 1893 by von Lenhossék, Arnstein, and Jacques as well as by the subsequent work of Retzius himself (1893) and there seems to be no ground for doubting the correctness of the general conclusion arrived at more or less independently by these four investigators.

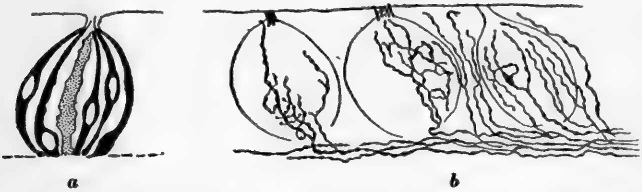

FIG. 31.—Golgi preparations of the taste-buds of the rabbit, *a* showing cells (after von Lenhossék, 1893a, Fig. 1a) and *b* showing nerve-terminations (after Retzius, 1892a, Plate 8, Fig. 4).

The anatomical relations shown by these workers are relatively simple. From the subepithelial nerve plexus in the neighborhood of taste-buds fibers pass outward into the epidermis. These fibers either form systems of branches ending in free terminations around a taste-bud, in which case they are called perigemmal or

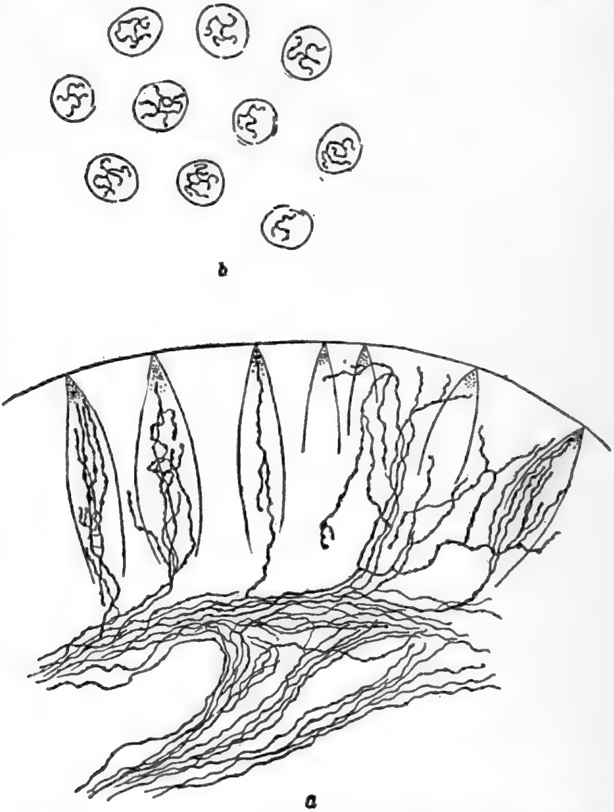

FIG. 32.—Golgi preparations of the taste-buds of the cat, *a*, in longitudinal section showing nerve terminations, and *b*, in transverse section showing intragemmal nerve-fibers. After Retzius, 1892a, Plate 7, Figs. 1 and 4.

peribulbar fibers, or they enter the bud and end freely among its cells being designated then as intragemmal or intrabulbar fibers (Fig. 32). As the figures given by Retzius, Arnstein, and others show, the nerve-fibers in the buds are as intimately applied to the so-called supporting cells as to the taste-cells, showing, as has already been stated, that the distinction between what has been assumed to be two classes of cells is probably quite erroneous.

In addition to intergemmal and perigemmal fibers, which in consequence of their close relations with the taste-buds may be designated as gemmal or bulbar fibers, there are also fibers that pass into the undifferentiated epithelium between the buds and end close to the external surface as free-nerve terminations. These have been called intergemmal fibers, but it is doubtful whether they have anything to do with taste and it is not improbable that they are concerned with other sensory functions such as the common chemical sense, pain, and the like, in which case a designation implying relations to a taste-bud is in no sense appropriate.

Taste-buds such as have already been described have been found in a wide range of vertebrates. They not only occur in mammals, where their relation with the nerve-fibers was first correctly described by Retzius (1892a), but also in fishes as seen by Retzius (1892a, 1893), von Lenhossék (1893a), Dogiel (1897) and others (Fig. 33). It is, therefore, probable that so far as essentials are concerned the innervation of the taste-buds of all vertebrates presents a relatively uniform plan.

7. Gustatory Nerves. There are no separate gustatory nerves in the vertebrates as there are olfactory nerves or optic nerves. Gustatory fibers occur in several cranial nerves and it is by means of these that the taste-buds of various regions are provided with those nervous connections that have been described in the preceding section.

In the fishes the nerves chiefly concerned are the vagus, the glossopharyngeal and the facial. The taste-buds of the gill region are supplied by the vagus and the glossopharyngeal. Those that are in the mouth proper or are on the exterior of the body are innervated by the facial nerve. Consequently in the catfish (See Fig. 28), in which the whole outer skin is provided with taste-buds, this nerve is enormously developed and sends large branches to the barbels and an extensive recurrent branch to the flanks of the body (Herrick, 1903).

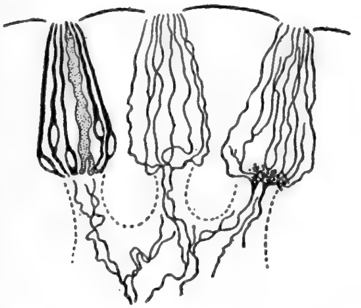
FIG. 33.—Golgi preparations of the taste-buds of the common European barbel showing cells and nerve-fibers. After von Lenhossék, 1893 a, Fig. 2.

In mammals, including man, the innervation of the taste-buds is not upon so simple a plan as in fishes. In these higher vertebrates gustatory fibers may possibly be contained in four of the cranial nerves, the vagus, the glossopharyngeal, the facial, and the trigeminal. The distribution of these nerves in the human tongue has been worked out by Zander (1897). Certain parts of the vagus are distributed to the larynx and to the epiglottis as well as to the most posterior part of the tongue itself and innervate very probably the taste-buds of these regions (Fig. 34). The glossopharyngeal supplies the posterior third of the tongue including the foliate and vallate papillæ, for, as was first shown by von Vintschgau and Hönigschmied (1876), when the ninth nerve is cut the taste-buds of these parts soon degenerate and disappear. Although the correctness of this observation was denied by Baginsky (1894), it has been confirmed by such a number of observers, including Drasch (1887), Ranvier (1888), Sandmeyer (1895), Meyer (1897) and others, that it is now generally accepted. Both the right and the left branches of this nerve innervate the median vallate papilla in mammals and form at the base of this organ, as Vastarini-Cresi (1915) has shown, more or less of a gustatory chiasma. The anterior two-thirds of the tongue in man are innervated by the lingual nerve which is made up of a union of the lingual branch of the trigeminal nerve with the chorda tympani of the facial. It has been an open question whether the gustatory fibers for this part of the tongue belong to the trigeminal, to the facial, or possibly even to the glossopharyngeal, for all these nerves intercommunicate through a plexus of fine branches near their roots. F. Krause (1895) noted the effect on taste of the complete extirpation of the ganglion of the trigeminal nerve, and found that in some instances taste was entirely obliterated from the appropriate part of the tongue, but that in others it was only somewhat reduced. These differences do not appear in the later and more conclusive work of Cushing (1903) who found that, when time enough was given, all subjects from whom the ganglion of the trigeminal nerve had been removed, recovered taste completely. He attributed

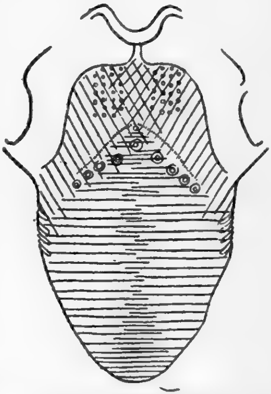

FIG. 34.—Diagram of the human tongue showing the parts innervated by the lingual nerve (horizontal lines), by the glosso pharyngeal nerve (oblique lines), and by the vagus nerve (small circles). After Zander, 1897.

the temporary disturbance in taste, a condition that was supposed to be permanent by Krause, to the effect of the degenerating trigeminal fibers on the adjacent gustatory fibers, an effect that disappeared when the degeneration was complete. Consequently Cushing concluded that the gustatory fibers from the anterior part of the tongue are not part of the trigeminal nerve. If this is so, they must belong to the facial or possibly to the glossopharyngeal nerve (Fig. 35). That they are abundantly present in the chorda tympani of the facial nerve is well known from the fact that direct stimulation of the chorda in the neighborhood of the ear drum is commonly accompanied by sensations of taste, but whether these gustatory fibers on reaching the facial nerve pass into the brain through its root or make their way to the root of the glossopharyngeal is not yet definitely settled. It is, therefore, probable that in mammals the trigeminal nerve, though

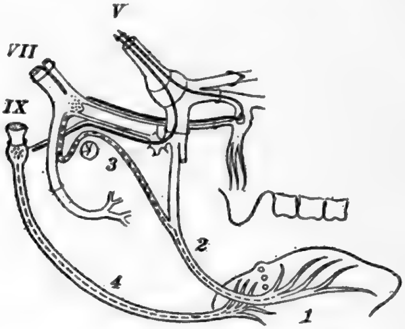

FIG. 35.—Diagram to illustrate the possible paths of the gustatory nerve-fibers from the tongue to the brain in man. The distal part of the tongue (1) is innervated by the lingual nerve (2) whose gustatory fibers pass to the brain by way of the chorda tympani (3), a branch of the facial nerve (VII). The proximal part of the tongue is innervated by the glossopharyngeal nerve (4). The undoubted gustatory paths over the facial nerve (VII) and the glossopharyngeal nerve (IX) are indicated by dotted lines. The commonly assumed paths by way of the trigeminal nerve (V) are shown in heavy black lines with arrows. Modified from Cushing, 1903.

suspected of including gustatory fibers, is really devoid of them. These fibers at most occur in the facial, glossopharyngeal and vagus nerves, but none of these nerves is exclusively gustatory.

8. Relation of Gustatory Nerve-fibers to Taste-buds. It is an interesting and significant fact that on the degeneration of the gustatory nerve-fibers the taste-buds associated with them should disappear. This state of affairs, long ago demonstrated for mammals, has recently been shown by Olmsted (1920a, 1920b) to occur also in fishes. Meyer (1897) showed that thirty hours after cutting the glossopharyngeal nerve in the rabbit the taste-buds began to show a change and that by the end of seven days most of them had disappeared. In the catfish Amiurus, according to Olmsted, the taste-buds on the oral barbels begin to degenerate in a little over ten days after the nerve to these organs has been cut and they completely disappear by the end of the thirteenth day. Ranvier (1888) believed that in mammals the taste-buds were destroyed by wandering cells, but Sandmeyer (1895) and Meyer (1897) held the view that the gustatory cells suffered dedifferentiation and changed into ordinary epithelial cells. In Amiurus Olmsted has found strong evidence in favor of the destruction of the cells of the taste-buds by phagocytes thus supporting Ranvier's original opinion.

Olmsted has shown, further, that on the regeneration of a nerve in a denervated Amiurus barbel from which all the taste-buds had disappeared, new buds reappear coincident with the arrival of the nerve. With the degeneration of the nerve and the loss of the taste-buds the barbels lose their receptivity for sapid materials, nor does this return till the buds regenerate. Since the taste-buds disintegrate with the loss of the nerve and new ones form only with the regeneration of this structure, it is clear that the bud is dependent upon the nerve. As Olmsted has suggested, it is probable that when a twig of the nerve reaches a given spot in the epidermis, it gives out a substance, hormone-like in character, that excites the epithelial cells of that spot to form a bud much as the embryonic eye cup of the vertebrate excites in the superimposed ectoderm the formation of a lens. In this way at least the intimate dependence of the taste-bud on the regenerating nerve-fiber can be explained and, judging from the account given by Landacre (1907) of the ontogeny of these organs, a similar explanation may also apply in development.

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CHAPTER VII.

PHYSIOLOGY OF GUSTATION.

Contents.—1. Location of Taste. 2. Gustatory stimulus. 3. Qualities of Taste. 4. The Sour Taste. 5. The Saline Taste. 6. The Bitter Taste. 7. The Sweet Taste. 8. Inadequate Stimuli. 9. Distribution of Tastes on the Tongue. 10. Action of Drugs on Taste. 11. Substances with two Tastes. 12. Latency of Taste Sensations. 13. Taste Alterations; After-tastes. 14. Gustatory Contrasts. 15. Taste Compensations and Mixtures. 16. The Gustatory Senses. 17. Comparative. 18. Bibliography.

1. Location of Taste. Although in man taste is not strictly limited to the mouth, for it spreads into some of the adjacent cavities, it is primarily located in the buccal space and is especially a function of the tongue. When the mouth of a normal adult is explored with solutions of sapid substances, many parts such as the lips, the gums, the floor, the lower surface of the tongue, the inner surfaces of the cheeks, and the hard palate are found to be insensitive to taste. Even the uvula which, according to many of the older workers, was regarded as having a gustatory function, has been shown by Kiesow and Hahn (1901) not to be concerned with taste. All these regions are well known to be devoid of taste-buds. Whether the pillars of the fauces and the tonsils have to do with taste is a matter of dispute. Hänig (1901) believed that these parts have a gustatory function, but Kiesow and Hahn (1901) regarded them as usually insensitive. The mucous membranes of the following parts

are concerned with taste; the beginning of the gullet, the region of the arytenoid cartilages within the larynx, the epiglottis, the soft palate, and particularly the tongue. In all these regions taste-buds have been identified. On the tongue of adult human beings taste is limited to the tip, the lateral margins and the dorsal surface of the root, the large central area on the upper surface of this organ being devoid of taste. In children, as contrasted with adults, the whole upper surface of the tongue including the central area is said to be sensitive to taste as is also the inner surfaces of the cheeks.

2. Gustatory stimuli. The stimulus for taste is an aqueous solution of a great variety of substances. Materials insoluble in water are tasteless, but not all substances that form aqueous solutions have taste. Thus oxygen, hydrogen, and nitrogen, though freely soluble in water, are without taste. Piutti (1886) long ago showed that lævo-asparagine is tasteless, although its stereoisomer dextro-asparagine is sweet. Other organic compounds, such as the carbohydrates raffinose and alpha-galaoctite are said to be almost, if not quite, tasteless.

When solids or semi-solids are chewed in the mouth, they not only become mixed with the saliva whereby many of their components become dissolved, but they are spread over the surface of the tongue and are thus brought into intimate contact with its taste-buds. In fact it is not improbable that the movement of the tongue facilitates the entrance of these solutions into the pores of the taste-buds. At least solutions placed upon the tongue, particularly near its root, are tasted with greater certainty, when this organ is moved about than when it is held still.

3. Qualities of Taste. Tastes, unlike odors, fall into a limited number of well-circumscribed groups, which have received distinctive names such as sour, saline, bitter, sweet, and the like. The multitude of flavors and other sensations associated with our food are undoubtedly mixed in character and include touch, heat, cold, the common chemical sensation, and especially odor. By applying materials in weak solution, at the temperature of the mouth and with the nostrils closed, extraneous sensations may be eliminated and there remains a certain irreducible residue, the tastes. Zenneck (1839), Valentin (1848), Duval (1872) and later Sternberg (1898) admitted only two classes of tastes, sweet and bitter. Stich (1857), however, long ago showed that sour was a sensation produced by stimulating only a limited part of the buccal surface, and Schiff (1867) made the important observation that a solution of acid too weak to stimulate the general mucous surface would nevertheless call forth a sour sensation when it was applied to the gustatory region. Von Vintschgau (1880) made similar observations concerning the saline taste; solutions of sodium chloride, potassium iodide, and ammonium chloride, if sufficiently weak, will stimulate the organs of taste, but if strong they will stimulate not only these organs but the nerve endings of the general buccal cavity also. In consequence of such observations sour and saline are now universally included with bitter and sweet as true tastes.

In addition to these four tastes there are a number of questionable ones such as metallic and alkaline, tastes that were originally accepted by Wundt (1887) among others. The so-called metallic taste is excited by solutions of salts of the heavy metals, silver, mercury, and the like (Kahlenberg, 1898). The metallic taste of a 0.0005 molar solution of silver nitrate is very pronounced and is discernible even at the greater dilution, 0.0002. Since the nitrate ions are incapable of exciting taste at such slight concentrations, it follows that stimulation must depend upon the silver ions. In a similar way mercury ions in normal solutions of 0.001 to 0.0005 of mercuric chloride have been shown to excite the so-called metallic taste. This taste, however, has been declared to be a complex of other tastes such as sour and sweet, and Herlitzka (1808) has gone so far as to maintain that it is not a true taste but an olfactory phenomenon.

The alkaline tastes so-called are excited by the application to the tongue of dilute solutions of such caustic alkalis as sodium or potassium hydrate. Kahlenberg (1898) has shown that the stimulating material in such mixtures is the hydroxylion which is effective in solutions as weak as 0.0025 molar. In the alkaline taste, as in the metallic taste, the results have been variously explained. Oehrwall (1891) regarded the so-called alkaline taste as a mixture of sensations due to a simultaneous combination of several tastes and touch. Höber and Kiesow (1898) pointed out that weak alkalis produce a sweetish taste, but von Frey (1910) showed that these reagents act on the tongue in such a way as to produce odorous materials that he believed to be the occasion of the so-called alkaline taste. He, therefore, relegated these assumed tastes to olfaction.

Insipidity, such as is characteristic of distilled water, is probably real tastelessness. Oehrwall (1891) attributed it to the absence of small amounts of carbon dioxide from such waters and this is probably true, for tastelessness disappears on the addition of some of this gas to insipid water. Henle (1880) showed that insipidity was characteristic of fluids that contained less salt than the saliva. Insipidity is probably a deficiency phenomenon and may be produced by the absence of several classes of substances. Nevertheless it must not be forgotten that a condition of staleness or flatness in water, practically indistinguishable from insipidity, can be produced by introducing into the water very small amounts of caustic alkali whereby hydroxyl ions are liberated (Kiesow, 1894-1896).

4. The Sour Taste. Sour taste has long been associated with acid substances. In fact it seems very probable that the sour taste is excited only by acids, acid salts, or materials that produce acids. All these substances on going into aqueous solution give rise to hydrogen ions by the dissociation of acid molecules. If the solutions are strong they will also contain a certain number of undissociated acid molecules. It was pointed out by Richards (1898) that, since all such solutions have the sour taste and since the one component that they all have in common is the hydrogen ion, this ion must be the occasion of their common taste. This conclusion was independently arrived at in another way by Kahlenberg (1898). A 0.0025 molar solution of hydrochloric acid has a pronounced sour taste and its dissociation into hydrogen and chlorine ions is practically complete. A corresponding solution of sodium chloride is also about completely dissociated into sodium and chlorine ions but is without taste. It follows, therefore, since there are as many chlorine ions in the salt solution as in the acid solution per unit volume and the salt solution is without

taste, that the sour taste of the acid solution cannot be due to its chlorine ions but must be occasioned by its only other constituent, the hydrogen ions. Kahlenberg, therefore, concluded that these ions are accountable for the sour taste.

This view is supported by the fact that the sourness of all acid solutions is the same, for instance, it is impossible to distinguish by taste hydrochloric acid from nitric or sulphuric acid. So far as the sensations are concerned all these reagents produce identical results, the one quality of sourness. There has been some tendency to separate astringency from sourness, but it is generally conceded that astringency is merely sourness near the vanishing point. With hydrochloric and other mineral acids this occurs in molar solutions at about 0.00125 to 0.001 below which the acid solutions cannot be distinguished from pure water.

From this standpoint sour taste might be regarded as due directly to hydrogen ions and the intensity of this taste to depend upon the concentration of such ions. But the question is not so simple as this. Although solutions of most mineral acids agree well among themselves so far as sourness and hydrogen ion concentration are concerned, organic acids are not necessarily so related. Most organic acids are much less dissociated in aqueous solution than are inorganic acids and contain, therefore, in normal solution, fewer hydrogen ions per unit volume, than inorganic acids do. Nevertheless Richards (1898) found that tartaric, citric, and especially acetic acids were more sour than would have been expected from the hydrogen ion concentration of their solutions. According to Richards acetic acid is about as sour as a solution of hydrochloric acid one-third as concentrated. Nevertheless the acetic acid is dissociated only about one-fourteenth as much as the hydrochloric. Hence ion for ion the acetic acid solution is the more sour of the two. This result was also arrived at by Kahlenberg (1898) who estimated the sourness of acetic acid at a concentration of 0.005 molar to be about four times what should be expected from its hydrogen ion content. These differences were subsequently reaffirmed by Becker and Hertzog (1907).

It is by no means easy to explain the excess of sourness on the part of acetic and other like acids. Richards has suggested, without putting great stress on the idea, that the additional sourness of acetic acid may be due to the undissociated molecules, which, serving as a reserve, producing additional hydrogen ions as those present are used up in the reaction between the acid solution and the surface of the receptor, an opinion supported by the recent work of Harvey (1920). Crozier (1916, 1918a, 1918b), on the other hand, has pointed out the probability that the question is double, one part having to do with penetration and the other with the production of the sour taste. By taking advantage of natural indicators, such as the blue pigment in the integument of Chromodoris, it can be easily shown that acids penetrate living cells. This may be assumed to be the first step in sour gustation. But penetration observed in this way is a much slower process than gustation, hence the penetration concerned with taste can have to do only with the most superficial layer of the taste cells. It is the ease of combination with this layer that may make the difference between acetic acid and other acids. Different acids having penetrated the surfaces of gustatory cells at different rates, their uniform sour taste may then be ascribed to their common dissociation product, the hydrogen ion. How this is accomplished is, according to Crozier, the second problem in gustation. That the sour taste is in some way dependent upon hydrogen ions seems true beyond reasonable doubt. How these ions become effective is still a problem.

5. The Saline Taste. The saline taste is typified by that of common salt. Sodium chloride, however, is not the only substance that possesses this taste, for there is a whole range of compounds that have the same property. The chlorides of potassium, lithium, ammonium, and magnesium, the hydrochlorides of monomethylamine and of diethylamine, the bromides and iodides of sodium and of potassium as well as their sulphates and nitrates are all more or less saline in taste.

Aqueous solutions of most of these salts show a high degree of dissociation so that, beside undissociated molecules, cations and anions are present in these solutions as possible stimuli for the saline taste. Höber and Kiesow (1898) have worked on this question and have declared in favor of ions as the stimulating agents in contrast with undissociated molecules. Kahlenberg (1898) arrived at the same conclusion. He found that a solution of sodium chloride, 0.02 molar, was scarcely to be distinguished by taste from pure water. At 0.04 molar it was a trifle saline. Corresponding solutions of sodium acetate were almost tasteless and certainly not in the least saline. Hence it is evident that the salty taste of sodium chloride is due to chlorine ions and not to sodium ions. This conclusion is supported by the fact that 0.04 molar solutions of potassium chloride and of lithium chloride are also salty. Other chlorides, such as those of ammonium and magnesium, have a saline taste.

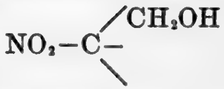
This taste, however, is not due exclusively to chlorine ions. Sodium bromide at 0.02 molar has a faint saline taste and is unquestionably salty at 0.04. Hence the bromine ion must also be a stimulus for the salty taste. Kahlenberg (1898) reported it as not quite so effective in this respect as the chlorine ion. Although solutions of sodium iodide at 0.04 or even at 0.02 molar could be distinguished from water, they did not give an unquestionable taste till a concentration of 0.16 was reached. At this concentration the taste was markedly saline. A corresponding solution of potassium iodide was found also to be salty though in this instance the taste was accompanied by a slightly bitter flavor. From these considerations it is evident that iodine ions are saline stimuli though they are not so effective in this respect as chlorine or bromine ions are. The sulphates of sodium and of potassium as well as their nitrates also have a saltiness in their tastes and it has been shown in these instances that the sulphate and nitrate ions are the effective agents. Thus all saline tastes depend upon ionic stimuli, and, as Kahlenberg (1898) and Höber and Kiesow (1898) have maintained, these ions are always anions, a conclusion supported by the more recent work of Herlitzka (1908).

6. The Bitter Taste. The bitter taste is characteristic of almost all alkaloids, and of certain unrelated substances such as dextro-mannose, the glucosides, picric acid, ether, and certain inorganic salts such as magnesium sulphate or Epsom salt.

Magnesium salts when sufficiently concentrated have a bitter taste and this taste is due to the magnesium ion. This is in strong contrast with the ions of sodium and of lithium, which are apparently almost tasteless. Ammonium and calcium ions are also bitter in taste. In picric acid the sour taste of the hydrogen ion is probably completely masked by the bitter taste of the picric anion though the taste of this substance as well as that of ether, dextro-mannose, the glucosides and other such substances appears never to have been fully investigated.

But the substances that are especially characterized by bitter tastes are the alkaloids. These include such compounds as morphine, cocaine, pilocarpine, quinine, nicotine, and strychnine, the bitterest of all substances. In aqueous solution these substances are the most effective agents in exciting the bitter taste. Gley and Richet (1885) determined that strychnine monochloride could be tasted at 0.0006 gram per liter of water. Of such a solution 5 cubic centimeters, which was the volume used by these investigators in their individual tests, contains only 0.000005 gram of the bitter material and yet this very small amount produces a pronounced taste. Quinine hydrochloride can be tasted in a solution as dilute as 0.00004 molar (Parker and Stabler, 1913). Thus bitter substances far exceed hydrogen ions in their capacity to stimulate at high dilution.

What peculiar chemical feature is characteristic of bitter organic substances whereby they excite this taste is at best, poorly understood. Henry (1895) pointed out that the bitter compounds often included the group



$$NO_2-\overset{\diagup CH_2OH}{\underset{\diagdown}{C}}-$$

and this was confirmed by Cohn (1914) whose extensive study of the sapid organic compounds led him to the conclusion that there were several such groups, the presence of any one of which in a given compound would give it a bitter taste. In dyes color-radicals have long been called chromophores; by analogy radicals concerned with taste have been designated saprophores. Among these are hydroxyl and the amine group. The nitro group NO_2 is often associated, especially in aromatic compounds, with a bitter taste. When three NO_2 groups are included in a given compound, it always has a bitter taste; when two are at hand, the taste is commonly bitter but not invariably so; when only one such group is present, the taste is not bitter. Thus the number of NO_2 groups appears to be significant in the production of a bitter taste.

The bitter taste, then, is excited by several classes of substances; by ions that, with the possible exception of the anion of picric acid, are apparently always cations Herlitzka (1908), magnesium, ammonium, and calcium; and by organic substances, especially the alkaloids, which may act either through their molecules or through certain atomic groups, the so-called saprophores.

7. The Sweet Taste. The sweet taste is excited by the diatomic and polyatomic alcohols of the aliphatic series, by the aldehydes and ketons derived from these alcohols, and especially by the hexoses whose polymerization products, the disaccharides and polysaccharides, are in this respect particularly important. Besides these carbohydrates other organic compounds, such as chloroform, dextro-asparagine, and saccharine, have sweet tastes. Among inorganic substances neutral acetate of lead, often called sugar of lead, and the salts of glucinum are known to be sweet. Solutions of the alkalis, if they are of appropriate dilution, are said likewise to excite this taste.

What occasions the sweet taste of lead acetate seems never to have been ascertained. On the other hand glucinum chloride and glucinum sulphate, both of which break into ions in water, have been shown by Höber and Kiesow (1898) to owe their sweet taste to their common constituent, the glucinum ion. Thus ions are one means of exciting this taste.

But the sweet taste, like the bitter one, is primarily associated with organic compounds. It centers about the alcohols and especially the sugars in much the same way that the bitter taste does about the alkaloids. Although the halogenated hydrocarbon chloroform and the aromatic compound saccharine are both sweet, the latter about 500 times as much so as cane sugar, the great majority of sweet substances are aliphatic alcohols and their derivatives. Ethyl alcohol is sweetish in taste as well as the trihydric alcohol glycerol, but the type of sweet substances is cane sugar or sucrose. This can be tasted in aqueous solution to about 0.02 molar; in weaker concentrations it is difficult to distinguish it from pure water. Ethyl alcohol cannot be tasted in solutions much weaker than 3 molar, a relatively high concentration (Parker and Stabler, 1913).

What determines the sweet taste in carbohydrates is by no means settled. It apparently turns upon very slight differences. These are sometimes sterioisomeric in character. Thus, as already stated, dextro-asparagine is sweet and lævo-asparagine is tasteless. Dextro-mannose is sweet and its stereoisomer dextro-glucose is bitter. Other such examples are known. In some instances slight changes in composition are accompanied by considerable changes in taste. Thus, according to Thoms and Nettesheim (1920), dulcin loses its sweetening power when acidic or basic substitutes are introduced into its benzene nucleus. The introduction into a sweet molecule of any considerable radical, especially an aromatic one, is very likely to be followed by a change from sweet to bitter.

Cohn (1914) made an elaborate comparison of the constitution of the sweet substances, as he did that of the bitter compounds, and came to the conclusion that these substances like the bitter ones contained particular groups of atoms that determined their taste and that he designated as glucogenes. Thus among alcohols one hydroxyl is accompanied with slight sweetness and four or five with intense sweetness. But notwithstanding the extent of Cohn's comparisons, Oertly and Myers (1919) found his generalizations inadequate, and proposed in place of his hypothesis one in which two groups were assumed to be present in every sweet molecule. Following by analogy the terminology used for dyes, one of these groups was called a glucophore and the other an auxogluc. By a close comparison of the sugars, amino acids, and halogen derivatives of the hydrocarbons, they believed they could identify at least six glucophores and nine auxoglucs. The glucophores are (1) $CH_2OH\text{-}CHOH\text{-}$, (2) $\text{-}CO\text{-}CHOH\text{-}(H)$, (3) $CO_2H\text{-}CHNH_2\text{-}$, (4) $\text{-}CH_2ONO_2$, (5) $C^{H_{3-x}}_{Hl_x}\text{-}$, and (6) $C^{H_{3-x}}_{Hl_x}\text{-}C^{H_{2-y}}_{Hl_y}\text{-}$. The auxoglucs are (1) $H\text{-}$, (2) $CH_3\text{-}$, (3) $CH_3CH_2\text{-}$, (4) $CH_3\text{-}CH_2\text{-}CH_2\text{-}$, (5) $(CH_3)_2CH\text{-}$, (6) $CH_2OH\text{-}$, (7) $CH_3CHOH\text{-}$, (8) $CH_2OH\text{-}CH_2\text{-}$, and (9) radicals $C_nH_{2n+1}O_n$ of normal polyhedric alcohols.

An illustration of the way in which Oertly and Myers' theory may be made to apply to sweet substances is given in the following table in which the resolution of a number of sweet compounds into glucophores and auxoglucs is indicated.

Table VII.

A table of sweet organic compounds (aliphatic series) showing the constitution of the compound and its resolution into a glucophore and an auxogluc, from Oertly and Myers (1919).

Name of Compound	Constitution	Glucophore	Auxogluc
Glycol	$CH_2OH\text{-}CH_2OH$	$CH_2OH\text{-}CHOH$	$H\text{-}$
Glycerol	$CH_2OH\text{-}CHOH\text{-}CH_2OH$	$CH_2OH\text{-}CHOH$	$CH_2OH\text{-}$
Fructose	$CH_2OHCO(CHOH)_3CH_2OH$	$\text{-}COCHOH\text{-}(H)$	$C_nH_{2n+1}O_n\text{-}$
Glycine	$CH_2NH_2\text{-}COOH$	$\text{-}CHNH_2\text{-}COOH$	$H\text{-}$
Ethyl nitrate	$C_2H_5ONO_2$	$\text{-}CH_2ONO_2$	$CH_3\text{-}$

Notwithstanding the elaborate attempts of Cohn and of Oertly and Myers to elucidate the chemoreception of sweet substances, the subject must be admitted to be one that is far from settled. What may be said with certainty is that the sweet taste, like the bitter taste, is excited both by ions and by organic molecules the details of whose activity, however, are by no means fully worked out.

8. Inadequate Stimuli. Taste is somewhat remarkable for its paucity of inadequate stimuli. Although the tongue is very sensitive to temperature differences, these changes do not seem to excite the gustatory receptors. It is questionable whether mechanical stimulation, such as tapping the tongue as practised by the older physiologists, will call forth sensations of taste. The only really effective form of inadequate stimulus for the gustatory organs seems to be the electric current. As early as 1752 Sulzer noted the peculiar sensations when two dif-

ferent metals are placed simultaneously on the tongue. This observation was independently made by Volta in 1792 who believed these sensations to be produced by the electrical stimulation of the organs of taste, for he obtained the same effects by passing an electric current through the tongue. Five years later, however, Humboldt pointed out that the real stimulating agent in the so-called electric taste might be the substances produced by electrolysis at the region where the current passes from the electrode into the tongue rather than the electric current itself. Thus was established the two opposing views concerning electrical taste.

If an electric current is passed through the human body in such a way that the anode is applied to the tongue and the cathode to some other part, a sour taste develops around the anode. If the electrodes are reversed in position, an alkaline taste appears at the cathode. This conforms with what takes place when an electric current is passed through an alkaline solution, such as the saliva; hydrogen ions appear at the anode and hydroxyl ions at the cathode. Why then are not these two substances, the hydrogen and the hydroxyl, the stimuli for the characteristic tastes?

But Rosenthal (1860) and, before him, Volta, found that if the anode is a weak alkaline solution into which the tip of the tongue is dipped, a sour taste nevertheless arises, though the hydrogen ions under such a combination might be expected to be neutralized immediately by the hydroxyl present. Rosenthal also showed that if an electric current is passed through the bodies of two persons and is completed by bringing the tip of the tongue of one of these individuals into contact with that of the other, the two persons experience different sensations, one sour and the other alkaline. These and other like experiments led Rosenthal to conclude that the electric current itself was the stimulating agent and not the materials produced by electrolysis.

But it must not be forgotten that the electrical stimulation of organs of taste is productive of a variety of sensations. Thus in 1798 Ritter showed that after a current had been passing for some time through the tongue the sour taste of the anode changed first to bitter and then to alkaline while the cathodic alkaline taste changed to sour. Hofmann and Bunzel (1897) demonstrated that during the passage of a current there is at the cathode a burning bitter sensation which changes to a sour metallic taste on breaking the current. The initial taste they believed to be due to the products of electrolysis. Von Zeynek (1898) also accepted this explanation for the electric taste. Gertz (1919), however, pointed out that the alternating current is really more effective in exciting taste than the direct current and that hence the electric taste may be aroused by other means than the products of electrolysis. It is not at all impossible that the gustatory organs may be excited in both ways: by the materials of electrolytic decomposition and directly by the electric current. But how an electric current can stimulate gustation without in some way bringing about a chemical change, at least within the gustatory cell, is difficult to imagine.

The extreme sensitiveness of the organs of taste to electrical stimulation is not only characteristic of man, but is probably found throughout the vertebrates. Among fishes the catfish or horned pout, Amiurus, is apparently easily stimulated in this way. The head and especially the eight barbels about the mouth of Amiurus are richly supplied with taste-buds. These organs, like those on the human tongue, are apparently extremely sensitive to metals probably because of the slight electric currents produced by these bodies, for, the fishes respond with great readiness to a weak constant current from a dry cell. If such a current is led into an aquarium through a water-filled glass tube and out again by a similar tube, the water acting as a conductor, catfishes can be readily stimulated by bringing such tubes close to them. If the current is sufficiently reduced (a little less than a microampere) the fishes will approach the open ends of the tubes and nibble at the current as though it were a bait, thus giving evidence that the organs stimulated are the gustatory receptors (Parker and Van Heusen, 1917). Hence the electric stimulus seems in every way to duplicate the stimulus normal for the organ of taste, a solution of a sapid substance.

9. Distribution of Tastes on the Tongue. The four well-recognized tastes, as the preceding sections show, are normally excited by very different stimuli. The sour taste is dependent upon the cation, hydrogen. The saline taste is called forth by a number of anions: chlorine, bromine, iodine, and the sulphate and nitrate ions. The bitter taste has as stimuli the alkaloids, such cations as magnesium, ammonium, and calcium, and possibly the anion of picric acid. The sweet taste depends upon such organic compounds as the sugars and alcohols, and on saccharine, on lead acetate, and on hydroxyl and glucinum ions. The four tastes, therefore, are excited by entirely independent groups of stimuli and it is a matter

of importance to ascertain in what other respects they are independent. This question can be well approached from the standpoint of their distribution on the tongue.

As already mentioned, the tongue of the normal adult human being is only in part gustatory, its lower surface and the central portion of its upper surface being devoid of taste. This sense is resident only on the tip, the edges and the dorsal part of the root of the tongue. The distribution of the several tastes over the gustatory portion of the tongue has been a matter of investigation for physiologists during more than a century, and the results, particularly among the recent workers, have been remarkably consistent and harmonious. Shore (1892), Kiesow (1894-1896), and Hänig (1901) have been the most important recent contributors

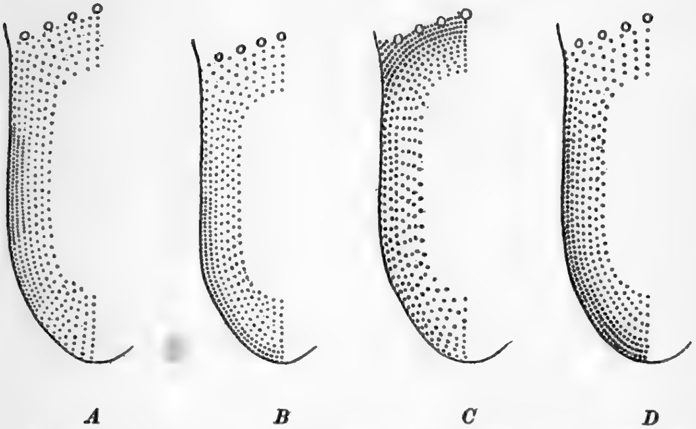


Fig. 36.—Diagrams of the right half of the human tongue illustrating the distribution of the four tastes; the dots represent the area and concentration of a given taste: A, the sour taste, concentrated on the edge; B, the saline taste, concentrated at the tip and on the edge; C, the bitter taste, concentrated at the base; D, the sweet taste, concentrated at the tip. Modified from Hänig, 1901.

to this subject. Their work shows that the four tastes have decidedly individual distributions on the tongue. The sour taste is best developed on the lateral edges of the tongue and diminishes from these regions toward the tip, the base, and the central anæsthetic area (Fig. 36, A). The saline taste is most pronounced at the tip and on the lateral margins of the tongue and diminishes at the base; toward the central area it ends rather abruptly (Fig. 36, B). The bitter taste is most characteristic of the base of the tongue especially in the region of the vallate papillæ whence it diminishes rapidly toward the central area and over the lateral edges to the tip (Fig. 36,C). The sweet taste is at its maximum at the tip of the tongue and diminishes thence along the lateral margins to the base (Fig. 36, D). Thus sour is represented by two marginal regions, saline by a horse-shoe shaped area at the tip, bitter by a single center at the base, and sweet by one at the tip. It is difficult to explain these differences in the distribution of the tastes except on the assumption of an independent sensory mechanism for each taste.

This interpretation of taste is strengthened by what has been learned from the local stimulation of the tongue. Oehrwall (1891) mapped out a group of fungiform papillæ near the tip of the tongue in such a way that the individual papillæ could be reidentified and studied. Each papilla was stimulated by applying to it the point of a very fine brush loaded with a strong solution of a given substance. The substances used were tartaric acid 2 per cent, common salt 20 per cent, quinine hydrochloride 2 per cent, and sugar 40 per cent. The salt was finally abandoned because of the indistinctness of the sensation. In all 125 easily identifiable papillæ were tested. All of these were found to be sensitive to touch, warmth, and cold, but only 98 were stimulated by the solutions used. The results of these tests so far as they relate to taste are given in the following tabulation.

Test Substances	Acid	Quinine	Sugar
Number of papillæ sensitive..........	91	71	79
Number exclusively sensitive...........	12	0	3

The fact that 12 papillæ were stimulated by tartaric acid but not by quinine or sugar and that 3 were stimulated by sugar but not by tartaric acid or quinine is strong evidence in favor of the independence of at least the sour and sweet tastes. Oehrwall also discovered by his method of local stimulation that the surface of the tongue between the papillæ was insensitive to taste.

This result confirmed the earlier work of Goldscheider and Schmidt (1890) who had also shown that when papillæ were tested with a mixed solution of sugar and quinine sometimes a sweet taste was evoked and at other times a bitter one.

This whole subject was thoroughly re-investigated by Kiesow (1898), who used as stimuli solutions of hydrochloric acid, of sodium chloride, of quinine sulphate and of sugar. Of the 39 papillæ tested 4 were found to be insensitive. The conditions presented by the remaining 35 are summarized in the following tabulation.

Test Substances	Acid	Salt	Quinine	Sugar
Number of papillæ sensitive.........	18	18	13	26
Number exclusively sensitive........	3	3	0	7
Failed of stimulation................	17	17	22	9

These results confirm and extend the original findings of Oehrwall in that they show the independence of the sour, saline, and sweet tastes. The fact that the region tested was near the tip of the tongue is probably the occasion of the absence in the records of any papillæ stimulated exclusively by quinine, for this region is one in which the bitter taste is least developed. Kiesow also observed that the papillæ presented a great variety of combinations in taste; some were open to stimulation by two of the four reagents used, others by three and still others by all four. It is known that each gustatory papilla carries a number of taste-buds but whether in those papillæ that are open to stimulation by two or more sapid solutions there is a corresponding number of kinds of buds, one for acid, another for salt reception and so forth, cannot be stated, for it is possible that this differentiation may reach to the gustatory cells of each bud. What can be affirmed, however, is that in those papillæ that respond exclusively to one taste all taste-buds with their contained cells must be so constituted as to be open to stimulation by one class of sapid substances and to be closed to all other classes. Thus in a papilla that is stimulated exclusively by acid the protoplasm of the receptive cells in all its taste-buds must be organized to receive acid stimuli and not to react to those for the saline, bitter and sweet tastes. This conclusion amounts to a very complete confirmation of Müller's theory of the specific energy of sensory nerves as it is interpreted in modern physiology and to the component theory as applied to taste.

10. Action of Drugs on Taste. Certain drugs have the remarkable property of temporarily diminishing or even obliterating taste. Edgeworth discovered that after a person had masticated the leaves of the Indian asclepiad Gymnema sylvestre, he was unable to taste

sugar. Hooper (1887) extracted from the leaves of this plant a compound that he named gymnemic acid and that he showed to be the substance that affected taste. According to him gymnemic acid tends to obliterate the sweet and bitter tastes but has no effect on the saline and sour tastes. Shore (1892) studied the influence of gymnema decoctions on the tongue and found that they obliterated the sweet taste of glycerine very easily and the bitter taste of quinine almost as readily. They had very little effect on the taste of sulphuric acid or of common salt. These results were confirmed in the main by Kiesow (1894). Thus gymnemic acid divides the tastes into at least two distinct classes, one including sweet and bitter, and the other sour and saline.

Stovaine is also known to abolish sweet and bitter without obliterating saline and sour (Ponzo, 1909) and eucaine-B especially reduces bitter (Fontana, 1902). Saline and sweet tastes and in less degree bitter are reduced by a 0.02 normal solution of chromium nitrate (Herlitzka, 1909).

The effect of cocaine on taste is very profound. Von Anrep (1880) and Knapp (1884) observed that this narcotic was capable of abolishing completely all taste. Aducco and Mosso (1886) showed, however, that it acted more energetically on the bitter taste than on the others. Shore (1892) found that on treatment with cocaine the buccal sensations were extinguished in a definite order as follows: pain, bitter, sweet, saline, sour, and touch, a sequence confirmed by Kiesow (1894). Thus cocaine is more selective in its effect on taste than gymnemic acid and leads to a separation of all four tastes.

11. Substances with two Tastes. A number of sub-

stances are known that possess different tastes depending upon the part of the tongue to which they are applied. Many salts have this peculiarity Herlitzka (1908). Potassium nitrate and magnesium sulphate are both said to be saline in taste when applied at the tip of the tongue and bitter at its base. This action, however, is probably due not to the molecules of the salts but to their ions. At the tip of the tongue the anions stimulate the organs of the saline taste, which in this location are in the ascendency, and at the base of the tongue the cations stimulate the organs of the bitter taste which is here better developed. There is thus a kind of competition between the two sets of ions, as Herlitzka has expressed it, and in one locality the anions win out, in the other the cations.

Such an explanation, however, does not apply to substances like parabrombenzoic sulphinide. This material, according to Howell and Kastle (1887) has a distinctly sweet taste when applied to the tip of the tongue and an intensely bitter one at the back. Dulcamarin, the glucoside from bittersweet, is another case of the same kind; a list of these is given by Sternberg (1898). In these instances ions are probably not involved, but each substance is a stimulus for both the organs of the sweet taste and of the bitter taste. It seems impossible to explain double tastes such as those just mentioned except on the assumption of independent receptor systems for the tastes concerned. Thus far no substance is known that excites three categories of tastes though I know of no reason why such a substance might not exist.

12. Latency of Taste Sensations. Von Wittich (1868) appears to have been the first to attempt to measure the interval of time between the application of a

stimulus to a gustatory portion of the tongue and the response of the subject. He used an electric current as a stimulus and found the average time to be 0.167 seconds. Von Vintschgau and Hönigschmied (1875-1877), who used solutions of various substances as stimuli, found that the times were different for the different tastes, being shortest for saline, longer for sweet, still longer for sour and longest for bitter. They also discovered that the times were different for the tip of the tongue and its base. Their results were confirmed in general by the later investigations of Beaunis (1884), of Henry (1895) and of Kiesow (1903) who recorded the following periods for the tip of the tongue:

Sodium chloride	0.308 second
Sugar	0.446 second
Hydrochloric acid	0.536 second
Quinine	1.082 second

These records agree with Schirmer's observation (1859) that when a solution containing all four sapid substances is placed on the tongue, the subject experiences the sensations in the order saline, sweet, sour, and bitter. They also confirm the opinion that the four tastes are separate entities.

One aspect of the problem of gustatory latency turns on temperature. If the stimulation of a taste receptor is a chemical operation, this process should exhibit a considerable temperature co-efficient that might make itself felt in a change in the latent period. But so far as I am aware no studies with this point in view have been carried out.

13. Taste Alterations; After-tastes. A number of

substances are known whose solutions so affect the tongue that its powers of taste become temporarily changed. Thus these substances give rise to what have been called after-tastes. In almost every instance the taste that suffers change is the sweet taste and this is increased in efficiency. Thus Aducco and Mosso (1886) found that after the tongue had been held in dilute sulphuric acid for five to ten minutes, distilled water was then capable of exciting a very sweet taste. A solution of quinine was also sweet to the taste at the tip of the tongue, but it remained normally bitter at the base. This change was not brought about by other acids such as acetic, citric, and formic. Frentzel (1896) also noticed that after washing out the mouth with a weak solution of copper sulphate, smoking a cigar was accompanied by a sweet taste. According to Zuntz (1892) a solution of sodium chloride of one per cent strength will increase the sweetness of sugar, an observation confirmed by Heymans (1899). A mouth wash of potassium chlorate is well known to leave the tongue so that distilled water tastes sweet (Nagel, 1896). In all these instances it is probable that the constitution of the receptor for the sweet taste is so changed by the first solution applied to it that it becomes hypersensitive to its normal stimuli such as sugar or even open to novel stimuli such as distilled water.

Complete loss of taste or ageusia is known to accompany hysterical and other abnormal nervous states. It may be temporary or, in the case of certain lesions, permanent in character.

14. Gustatory Contrasts. Although some acids increase the sensitiveness of the sweet taste and thus give ground for a gustatory contrast, it is questionable whether

such contrasts exist as extensively as was believed by the older workers. It is a common opinion that after a sweet drink a sour taste is more intense, but Oehrwall (1891) was unable to confirm this experimentally nor could he show that bitter increased the sensibility to sweet. Haycraft (1900) noted that when one border of the tongue is rubbed with salt, the other border becomes hypersensitive to sugar, but such a contrast is clearly not peripheral but central in origin, and possibly other contrasts may be thus explained.

15. Taste Compensations and Mixtures. Mixtures of sapid solutions do not as a rule give rise to tastes other than those of their components. Lemonade has both the sweet taste of the sugar and the sour taste of the citric acid it contains. Sugar adds a pleasant element to coffee, but does not destroy its bitter taste. In ordinary food the flavor is the mixture of true tastes and odors accompanied by the multitude of other buccal sensitivities due to the variety of substances in the mouth and accepted in a rather unanalyzed form by the central apparatus. Yet in all this complexity the elements remain essentially distinct. Competition rather than compensation seems to be the rule. Kiesow (1894-1896), however, has claimed that a very weak solution of sugar and salt gives a taste that is neither sweet nor saline but distinctly flat, and Kremer (1918) has recently shown that a solution of sodium chloride too weak to stimulate the saline taste will, nevertheless, considerably increase the sweetness of a cane-sugar solution. Quinine hydrochloride on the other hand will, according to Kremer, reduce sweetness. These instances may be evidence of gustatory compensation, but it seems much more probable, as was indicated

in a preceding section, that they result from a sensitizing or a desensitizing of the sweet receptors by the sodium chloride or the quinine, for it is extremely doubtful, as Oehrwall (1891) has stated, whether true gustatory compensation ever occurs. Ionic antagonism such as Crozier (1915) has discovered in the reaction of the frog's foot to salt solution has thus far not been identified in taste.

16. The Gustatory Senses. When a general survey of the so-called sense of taste is made, the most striking feature that appears is the remarkable independence of the four categories, sour, saline, bitter, and sweet. These are excited by groups of different stimuli, they give remarkable evidence of having separate receptors, they are differently acted upon by various drugs, and they show numerous other peculiarities that are interpretable only from the standpoint of organic separateness. So impressed was Oehrwall (1891, 1901) with these peculiarities that he declared them to be in all essentials four separate senses, a declaration entirely in accord with the component theory as applied to taste. Although this view has a certain radical element in it and has not been favorably received by such workers as Kiesow, Nagel, Luciani, and Henning, who have declared for the unitary nature of taste, it is difficult to say why it should not prevail. It has been urged that gustatory compensation is inconsistent with Oehrwall's hypothesis and possibly this may be true. But gustatory compensation is so uncertain a phenomenon that when compared with the substantial body of evidence in favor of the hypothesis, this objection lacks force. Henning (1916) has declared that the tastes of different substances, members of one category, are not necessarily alike; thus the saline tastes of

sodium chloride, sodium iodide, and sodium bromide, though much the same are still characteristically different. And he has further maintained that the mixed tastes so-called cannot be imitated by real mixtures; thus the bitter-saline taste of magnesium chloride cannot be reproduced, he believes, by a mixture of sodium chloride and bitter aloes. But all such statements imply that the conception of the receptive independence of tastes necessarily involves the further view that a gustatory stimulus is limited to one category of receptors. That some substances, such as parabrombenzoic sulphinide, stimulate two categories of receptors has already been made clear and though most stimulating materials influence in a vigorous way only one set of end-organs, it is more than probable that they all affect at least to a slight degree other such sets. The taste of any substance then is not necessarily one of the four tastes and this alone, but one of these qualified by traces of other tastes excited slightly and simultaneously by the same stimulating agent. Hence any substance such as sodium chloride, or sodium bromide, may perfectly well have a somewhat individual taste without doing violence to the hypothesis that there are four separate tastes, and the success with which mixed tastes so-called may be imitated is rather a matter of skill than despair.

It is true that gustation is a strikingly unified operation, but when this unity is looked into, it is seen to depend upon simultaneousness of action rather than on interdependence of activities. Smell is related to taste in much the same way that one taste is related to another. On the whole it would seem more consistent with fact to speak of the sour sense, the saline, the sweet, and the bitter sense than of the sense of taste. Just as the sense of feeling in the skin has been shown to consist of at least four senses, touch, pain, heat, and cold, so taste must be regarded as composed of at least four senses. That these act together and in everyday experience produce a unified effect upon us is no more reason for classing them as one sense than in the case of the integumentary senses. The sense of taste must, therefore, be regarded as a generic term under which at least four true senses are gathered: sour, saline, bitter, and sweet (Oehrwall, 1891, 1901).

Although the sense of taste thus loses a certain amount of its reality, the senses classed under it probably possess a kind of genetic unity that is not without significance. It is very probable that these four senses represent four lines of differentiation that have evolved from a single ancestral sense. The remarkable uniformity of their structure is suggestive of this view. If the four senses under discussion have had some such origin as that just indicated, the term sense of taste might well apply to that primitive state, perhaps represented in some of the lower vertebrates today, from which the four gustatory senses of man have been derived.

17. Comparative. The comparative physiology of taste in vertebrates is almost an untouched field. The distribution of taste-buds in the vertebrate classes indicates the presence of this sense in the mouth regions in forms as low as the amphibians. In fishes Herrick (1903) lists over thirty-five species in which taste-buds are known to occur on the outer surface of the animal as well as in the mouth. The catfish Amiurus is remarkable in this respect in that its whole outer surface is provided with these organs which are most abundantly present on the

barbels. When a piece of meat is brought into contact with the barbel of one of these fishes, the animal will immediately seize and swallow the morsel. The same is true when the meat is brought in contact with the side of the fish. This quick seizure and swallowing of the food has been called by Herrick the gustatory response. If a barbel or the flank of Amiurus is touched with a pledget of cotton instead of the meat, the fish will turn toward the object, but, as a rule, will not snap at it. This Herrick has designated the tactile response. If, now, the cotton is soaked with meat juice and brought to the side of the fish, the quick gustatory response follows. The same form of response is made to meat juice discharged from a pipette on the side of the fish. From this and other tests Herrick concluded that the gustatory response in Amiurus could be called forth by purely gustatory stimuli unaccompanied by touch and that for this fish taste is accompanied by a local sign as touch is. That these responses are really gustatory is shown by the fact that when the branch of the seventh nerve that innervates the taste-buds on the flank of Amiurus is cut, the responses no longer occur (Parker, 1912).

Conditions similar to those in Amiurus were recorded by Herrick in a number of gadoid fishes and it is thus clear that taste is a general integumentary function in many of these animals. To what extent the taste-buds of the fish skin are differentiated for the several senses of sour, saline, bitter, and sweet cannot be stated. It is remarkable, however, that in almost all the fishes tested no response to sugar has been found not only on the surface of the body but also in the mouth (Parker, 1912).

The sweet sense may, therefore, be an exclusive possession of the higher vertebrates.

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CHAPTER VIII.

INTERRELATION OF THE CHEMICAL SENSES.

Contents.—1. Common Features in the Stimulation of Chemoreceptors. 2. Differences among Chemoreceptors. 3. Groups of Chemoreceptors. 4. Classification of Receptors in General. 5. Genetic Relations of Chemoreceptors. 6. Bibliography.

1. Common Features in the Stimulation of Chemoreceptors. The sense organs that have been discussed in this volume, the olfactory organs, the vomero-nasal organs, the common chemical receptors, and the organs of taste, form a more or less natural group of organs under the general title of chemical receptors or chemoreceptors. This designation is justified by the fact that in stimulation these several types of receptors present certain important features in common. In all instances they are activated by solutions. This is most obvious in the sense of taste whose stimuli from fishes to mammals consist of materials in solution either in the water that enters the mouth or in the saliva that is mingled with the crushed food. An aqueous solution is also the stimulus for the common chemical receptors. The nasal cavities of fishes are likewise bathed by a continuous stream of water that carries the stimulating substances to the olfactory surfaces. And in the air-inhabiting vertebrates, as already pointed out, the olfactory terminals are probably not exposed in any direct way to the air that carries the stimulating material but are immersed in mucous through

which this material must make its way before it becomes effective. In olfaction, moreover, it is probably not simply a question of aqueous solution but, as already explained, one of solution in oil as well, for the olfactory stimulus seems to be a material that must reach its receptors through an aqueous medium that covers them and then enter them through their lipoid components. What has been said of the stimulation of the olfactory organ is probably true of the vomero-nasal organ also. Thus in one way or another all appropriate stimuli of the so-called chemoreceptors are materials in solution.

But not all soluble materials stimulate the chemoreceptors. Thus such elementary gases as hydrogen, oxygen, and nitrogen are odorless and tasteless, and a number of organic substances have no stimulating capacity for these organs. Those substances that do stimulate, as was pointed out especially in the case of taste, fall into groups whose characteristics are chemical and not physical and, though such an analysis cannot at present be made with certainty for smell, it has already been pointed out that the variety of smells can be explained only on a chemical basis. Thus chemoreceptors are stimulated not simply by material in solution, but by the chemical activity of dissolved material. On this assumption it is natural to expect that there would be a certain number of substances, chemically inert toward the given receptors, that would, therefore, be incapable of acting as stimuli for them. Such substances as the gases already mentioned probably represent this group.

The stimulus for the chemoreceptor, however, is not only a solution of a chemically active material, but it is such a solution applied directly to the terminal organ.

This peculiarity of the chemoreceptors is in strong contrast with that which occurs in the so-called mechanicoreceptors, the organs of touch, pressure, and hearing. In these organs the appropriate stimulus is a deforming pressure which may be exerted by an impinging or vibrating material that does not necessarily touch the terminal organ itself, but may act through a considerable amount of intervening tissue. Hence the mechanicoreceptors are not necessarily exposed directly to what is ordinarily called the stimulus as chemoreceptors are, but they may be excited more or less indirectly. Our organs of touch and of hearing, therefore, may be lodged in the deeper part of the skin or the head without interfering in any serious way with their efficiency. All chemoreceptors on the other hand are necessarily either upon the exposed surfaces of the body or are provided with pores that lead from these surfaces directly to the receptors themselves. This condition is in a way merely a corollary of what has already been stated about chemical stimulation, for if the organs of smell, taste and the like are acted on chemically by their appropriate stimuli, these stimuli must of necessity come into direct contact with the given terminals.

2. Differences among Chemoreceptors. The chemoreceptors agree then in the general character of their stimuli. Such stimuli are certain chemically active materials in solution applied directly to the receptors themselves. The variety that these organs exhibit ought, therefore, to turn more or less on the extent of their differentiation in relation to the chemical diversity of the environment. The degree of this organic differentiation, however, has been very inadequately worked out. Almost nothing is

known of the stimuli for the vomero-nasal organ, and very little has been done on those for the common chemical sense. The senses of smell and of taste are naturally much better known. When their stimuli are compared they are found in general to belong to different categories of material; what is smelled is generally not tasted and what is tasted is not smelled.

These two categories of substances afford an important basis for comparing taste and smell. This can be done from the standpoint of the minimum concentrations of materials that serve as stimuli for the two sets of receptors. Bitter substances are apparently the most effective stimuli for the sense of taste. Quinine hydrochloride can be tasted in a solution as weak as 0.00004 molar, but this threshold is exceeded by that of what is probably the most bitter of all substances strychnine. According to Gley and Richet (1885) the weakest solution in which the bitter taste of strychnine hydrochloride can be distinguished contains only 0.0004 gram of this substance in one liter of water. This is approximately equivalent to one and a half millionths of a molar solution (1.48×10^{-6} molar), and much exceeds in this respect the efficiency of quinine. One of the strongest odors known is that of mercaptan of which according to Fischer and Penzoldt (1886), 0.01 milligram evaporated in 230 cubic meters of air gives a perceptible smell. Assuming the substance used by these investigators to have been methyl mercaptan, such a dilution would be represented by about a million-millionths molar solution (9×10^{-13}) or approximately one and a half million times more dilute than the weakest solution of strychnine that can be tasted. Thus the olfactory receptor is open to stimulation by a very much weaker concentration than the gustatory one is.

It might be maintained, however, that the line of argument used in the last paragraph is invalid because it is based upon measurements of one substance for taste and another for smell, and that, therefore, the two sets of figures are not fairly comparable. But the conclusion just reached is also supported by determinations made with a single substance. Ethyl alcohol is soluble in both water and oil and is one of the relatively few substances that has at once both taste and smell. As a matter of fact it is also a stimulus for the common chemical sense. Hence it may be conveniently employed for comparing all three classes of receptors. When such a test is made, it is found that the weakest concentration of alcohol vapor that can be smelled is about 0.000125 molar and that the weakest aqueous solution of this substance that can be tasted is 3 molar. To stimulate the common chemical sense with ethyl alcohol requires an aqueous solution of strength 5 to 10 molar. Hence so far as ethyl alcohol is concerned smell may be said to be about 24,000 times more delicate than taste and about 60,000 times more delicate than the common chemical sense. From the standpoint of a single substance then, smell must be admitted to be vastly more efficient than either taste or the common chemical sense both of which lie in this respect close together (Parker and Stabler, 1913). Unfortunately the stimulation of the vomero-nasal organ has not yet been studied so that its capability from this standpoint is not known, but, judged from its structure, it probably has a receptive efficiency not far from that of the olfactory organ. In that case the chemoreceptors of vertebrates would fall into two groups, the olfactory and vomero-nasal organs with high efficiency and the common chemical receptors and organs of taste with relatively low efficiency. These two sets of organs might in this respect be compared with scales, the organs of taste and of the common chemical sense resembling ordinary scales on which only gross amounts are weighed and the organs of smell and the vomero-nasal organs resembling chemical balances on which small weights may be determined.

As olfaction deals effectively with very minute amounts of substance and gustation only with much greater amounts, it follows that materials that have become highly attenuated by being broadly spread from their sources either in water or in air may nevertheless still be concentrated enough to stimulate the organs of smell though they can have no possible effect upon those of taste. Such faint odors are the means whereby animals scent their food, find their mates, or avoid their enemies. Hence the olfactory organ has been appropriately classed as a distance receptor or exteroceptor, to use a convenient term from Sherrington (1906), in that the impulses to which it gives rise commonly direct the animal toward distant points or away from them.

Taste and, in the higher vertebrates at least, the common chemical sense are stimulated only by relatively concentrated solutions such as occur in connection with the food. Hence the responses that these organs call forth are concerned with the swallowing of food, with the rejection of material taken into the mouth, with mastication and saliva and the like. These receptors are, therefore, rightly classed as interoceptors though it must be remembered, as Herrick (1918) has pointed out, that in some fishes, such as the catfishes, taste-buds serve in the discovery of food as well as in its appropriation, and partake, therefore, more or less of the nature of exteroceptors. Although olfaction has a function independent and separate from that of gustation in scenting mates or enemies and gustation has a function independent of olfaction initiates the feeding reflexes both muscular and noxious material, both senses are intimately associated in feeding. Food is found and the digestive secretions are started through smell; it is swallowed and these secretions are intensified ordinarily through taste. Thus olfaction initiates the feeding reflexes both muscular and secretory and gustation reinforces and completes them. It is remarkable that in some fishes like the catfishes (Amiurus) and especially the dogfishes (Mustelus; Parker, 1914) feeding scarcely ever occurs, even when the fishes are starving and food is present, unless the process is initiated through olfactory reflexes. These seem to be essential for that chain of events that result in the final swallowing of the food, a condition that shows how intimately smell and taste are interwoven in the vertebrate organization.

Smell and taste, though thus most closely involved in the feeding reflexes, are nevertheless perfectly distinct. As long ago as 1821 Cloquet (Larguier des Bancels, 1912) showed that on closing the nose by pinching the nostrils smell can be eliminated and only taste remains. Under such circumstances it is surprising to those who have not previously tried the experiment to discover how small a proportion of our food sensations are due to taste and how large a one to smell. A cold in the head commonly eliminates smell and leaves taste. It reduces a person to a state in which food is often described as without flavor, for only sour, saline, sweet, and bitter tastes can be sensed and onion produces the same sweetish taste that apple does. The separateness of smell and taste depends doubtless upon the conditions already described. Smell is excited in general by one set of substances; taste by another. Smell calls for only very weak solutions; taste requires relatively strong ones. It may also be that these two senses differ in the nature of the solutions that activate them; taste is attuned to substances that form aqueous solutions, smell to those that dissolve in oil. Cell surfaces are commonly believed to be diphasic in that they are composed of a mixture of two materials one oily and the other aqueous. The gustatory hairs may be so constituted that the aqueous constituent is the avenue of entrance for the stimulating substance and the olfactory hairs so that the oily one is the inlet. If such is the case, this feature may also be an important difference between smell and taste.

3. Groups of Chemical Receptors. Taste and smell are two of the five senses ordinarily attributed to man. But in the detailed study of the human senses not one has escaped a kind of functional subdivision whereby it has been shown to be more than a single sense. Thus the internal ear originally regarded by physiologists as purely an organ of hearing, was shown by Flourens in 1828 to be concerned in a most important way with bodily equilibrium. From this standpoint the ear takes on the character of a double sense organ. This duplicity is especially well marked in certain fishes in which the membranous labyrinth is completely divided in two corresponding to the functional differentiation already indicated; one of these parts consists of the utriculus with

its three semicircular canals and has to do with equilibrium and the other of the sacculus and its appended lagena and is concerned with hearing. Even so unified an organ as the human eye is made up of an intermingling of two receptive fields, for, as originally suggested by Schultze (1866) and as elaborated by von Kries (1904), the retinal rods are concerned with colorless vision in dim light and the cones with color vision in bright light. Thus the eye is differentiated for two kinds of sight, one by night and the other by day. The integumentary sense originally supposed to be unitary, was shown by Blix in 1884 to consist of at least three senses, cold, warm, and pressure. To these were added in 1896 by von Frey a fourth, pain. Thus it is clear that the conception of five senses for man is wholly inadequate and though numbers are perhaps not the best way of indicating the sensory equipment of human beings or in fact of any other animal, it is not without interest to record the opinion of Herrick (1918) that the classes of human receptors are now known to be more than twenty.

The chemoreceptors, represented in the older accounts by the organs of taste and smell, have no more escaped this process of increase than have the other sense organs. The vomero-nasal organ appears to be a kind of accessory receptor for smell and the common chemical sense is apparently a primitive form of gustatory organ. But in addition to these subsidiary receptors, the true olfactory surfaces as well as the gustatory areas are not homogeneous, but are marked by local receptive differentiation. This is especially well illustrated by the so-called sense of taste. This, as has already been shown in the preceding chapter, is in reality not a single sense, but, in accordance with Oehrwall's opinion (1901), must be regarded as generic and to consist of at least three and probably four senses, namely the sense of sour, of saline, of bitter, and of sweet. These senses are really distinct and separate. They have independent receptors and give rise to sensations that do not intergrade. Their association under one head as members of the sense of taste is in a way a misconception due doubtless to the fact that in ordinary activity all four senses are commonly in operation at once, and hence acquire a certain degree of functional association. Taste then is not the name for a single sense but for a group of senses and it is likely that smell is of the same nature, but until olfaction is better understood, it is impossible to indicate the elements of which it is composed. Thus the chemical senses, like the others already briefly enumerated, show the same tendency to increase in number as they become better known.

4. Classification of Receptors in General. A detailed investigation of the chemoreceptors leads to an increasing multiplicity of elements as in the other receptor systems, and raises the question of what constitutes a unitary sense and how such units are related. When one or more similarly organized receptors are excited to activity by a single category of stimuli and give rise to the same kind of sensation we think of the aggregate as a sense. Thus when a deforming pressure impinges upon any part of the skin, touch receptors are stimulated and we receive a uniform impression characteristic of the sense of touch. Or when one of a variety of sounds falls upon the ear, we experience hearing. In the second instance the stimulus, different sounds, is open to much greater variety than in the first where the stimulus is, a deform-

ing pressure, and in a corresponding way the sensations in hearing are much more diverse than those in touch. But it is still reasonable to regard hearing as one sense, for its various stimuli grade into one another as its sensations do. With taste on the other hand such is not the case. The acid stimulus as an external agent is entirely distinct from the stimuli for the other tastes and the sour sensation as an internal state does not grade into other gustatory sensations. This separateness in stimuli and in sensations is characteristic of the four kinds of tastes and justifies their acceptance as separate senses, a division that is not permissible in hearing. To constitute a single sense implies a reasonable similarity in stimulus, receptive mechanism, and sensation.

But, as previously pointed out, the initiation of sensations is a function of only a limited number of the human receptors. Many of these organs are concerned with activities entirely unassociated with sensation; hence to speak of them as representing a sense seems somewhat inconsistent. If the term receptor is an improvement over that of sense organ because of its freedom from implications concerning sensation, it might be well for the same reason to substitute some other term for sense, such, for instance, as recept.[1] In that case a recept is that aggregate of action that occurs where the receptive arm of any reflex arc goes into normal activity irrespective of whether this activity is productive of a sensation or not. The recept then includes all the oper-

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[1] I am fully aware that this term has already been appropriated by the psychologists for a very different purpose, but as they have taken almost all the terms in the language for their own use, I do not hesitate to reappropriate this one to fill the present need.

ations from the reception of the stimulus to those central changes that mark the entrance of the impulse into the central organ including the production of a sensation, if such occurs.

Where a recept is concerned with sensation, the production of this state may be regarded as its final step. A sensation, then, is an activity in a particular region or spot of the central nervous organ marking the central end of the receptive portion in a reflex arc. Experience has shown that, irrespective of the means by which this central region is stimulated, it calls forth only one kind of sensation. This in a way is a restatement of the modern view of Müller's specific energy of the nerves, for, according to this principle, however a particular sense organ, or conducting trunk, or nerve center may be stimulated, only one kind of sensation results. In other words the character of a sensation is not determined by peripheral organs but is strictly a central affair and sensations are different not because of the different sources of the incoming impulses, but because of the different central spots excited. Since the anatomical connections are such that a particular receptor always leads to a special central region, it follows that such a receptor becomes thus associated with a given sensation. Hence where sensations occur they may be used in distinguishing receptors, but in the many recepts that are unassociated with sensation this feature naturally cannot be called upon as a means of discrimination.

Although numerous receptors are in no way concerned with sensations, there are no receptors that are not actuated by stimuli. Hence the stimulus affords a more general basis for discriminating between receptors than the sensation does. The two groups of chemoreceptors and of mechanicoreceptors, already frequently alluded to, show how fundamental this method of classification is, for these two groups represent the two well-recognized activities of our material surroundings and together may be put in strong contrast with radioreceptors such as the organs for heat and for cold and the eye, all of which are stimulated by radiant energy.

These three classes constitute the fundamental groups of receptors and under some one of these heads every such organ should find its place. To the chemoreceptors discussed in this volume may possibly be added those on the wall of the stomach that according to Carlson (1916) have to do with appetite. The receptors for pain are possibly stimulated by the chemical action of abnormal tissue juices and the endings for thirst may also depend upon some such form of activation (Cannon, 1918), though both of these organs may belong to the group of the mechanicoreceptors (Müller, 1920). To the mechanicoreceptors belong unquestionably those terminals that are excited by a deforming pressure such as the receptors for touch, for pressure, including the organs for equilibrium, and for hearing. Very probably pressure is the stimulus for muscle, tendon, and joint receptivity and the sense of fullness in cavities. Pressure produced by the contraction of the muscular walls of the stomach appears to be the stimulus for the hunger pang (Cannon and Washburn, 1912). The lateral-line organs of fishes and amphibians give every evidence of being mechanicoreceptors. Finally radioreceptors are those organs that are stimulated by radiant energy such as the heat organs, the cold organs, and the eye.

To ascertain into which of these three groups a receptor falls it is necessary to know how it is stimulated after which its classification is simple and immediate.

Although a grouping of receptors based upon their stimuli will of necessity always be complete, this plan of arrangement is not entirely devoid of difficulties. Chief among these is the fact that the same stimulus may activate what we know from other standpoints to be different receptors. Thus, as already stated, parabrombenzoic sulphinide excites sweet receptors as well as bitter ones, and strong material vibrations will stimulate the organs of touch as well as the ear. But such instances apparently occur only between closely related receptors, for the organs for sweet and for bitter are so closely related as to be regarded by many as belonging to one category and hearing is certainly very near akin to touch. Herrick (1918) has discussed the definition and classification of receptors and has urged for this purpose the use of four criteria: the sensation, the stimulus, the sensory mechanism, and the type of response. In his opinion, however, none of these affords a wholly satisfactory basis for discrimination and grouping, operations that can be successfully carried out only when sufficient information is at hand. But experience scarcely warrants such a conclusion, for it is much more difficult now to discover the interrelation of the twenty or more human receptors with all that is known about them than it was to make a corresponding statement about the original five. The real difficulty lies in the fact that the numerous receptors that we now recognize have undergone varying degrees of differentiation and hence their mutual affinities are extremely diverse. This brings us at once face to face with one of the problems of this inquiry, namely, the genetic relations of receptors.

5. Genetic Relations of Chemoreceptors. The three sets of receptors mentioned in the last section, the chemoreceptors, the mechanicoreceptors, and the radioreceptors, are more than mere convenient assemblages; they represent natural groups of organs whose relations within each group have a certain genetic character. This can be illustrated by the chemoreceptors.

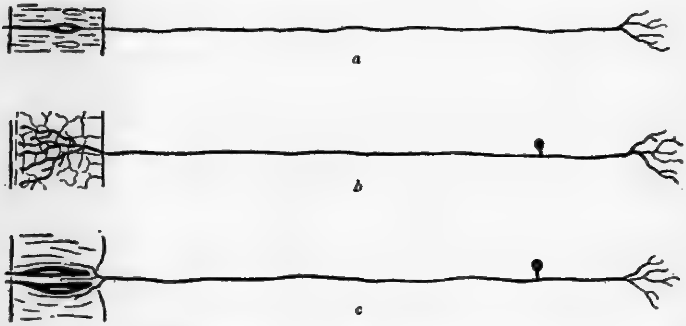

FIG. 37.—Diagrams illustrating the receptor systems of the following vertebrate chemoreceptors: a, olfactory organ and vomero-nasal organ; b, organ of the common chemical sense; c, gustatory organ. After Parker, 1912.

If the structure of the several vertebrate chemoreceptors is compared, it will be found that they present three types of organization (Fig.37). These types can be best appreciated from the standpoint of their constituent neurones. In the olfactory and vomero-nasal organs the neurones have cell bodies in the receptive epithelium and their axons extend as nerve-fibers from these bodies into the central organ. In the common chemical organs the receptors are free-nerve terminations in the mucous epithelium of the mouth, the nose, the eye and other such apertures, from which axons provided with deep-seated cell-bodies extend into the central organs. Finally, in the gustatory organs the taste-buds are composed of receptive epithelial cells that are in synaptic relations with nerve terminals essentially like free endings from which axons with deep-seated cell-bodies pass into the central organs. These three types of structure include, so far as is known, all the vertebrate chemoreceptors. To a common stimulus, like ethyl alcohol, the olfactory type has been shown to have by far the lowest threshold followed in order by the gustatory and the common chemical types both of which are near together in this respect.

When these three types are compared with the receptors of other animals, it is seen that the olfactory type reproduces almost exactly that found in the skins of many invertebrates, and that the other two types are characteristically vertebrates. The integument of animals even as simply organized as sea-anemones is rich in receptive cells that reproduce in almost every detail the conditions of the vertebrate olfactory neurones. Not only do these lowly organized forms show this structural similarity in their integumentary cells, but they are known to be so responsive to minute amounts of material wafted from distant food through the water to them that they have been for a long time past credited with olfaction (Pollock, 1883). Thus the vertebrates olfactory epithelium and the integument of aquatic invertebrates are strikingly alike.

It is more than probable that the vertebrates have descended from ancestors whose skin was an epithelium like that on the exterior of a sea-anemone and that, as this skin thickened over most of the body to give the necessary protection to the slowly metamorphosing animal, the future olfactory region remained unchanged and thus retained its original invertebrate character. This region became the olfactory epithelium of the developing vertebrate, the most primitive chemoreceptor in this group of animals.

The organs next in this series were the common chemical receptors. The neurones for these organs were differentiated from the neurones of the primitive invertebrate skin by a central migration of their cell-bodies till they became part of the spinal ganglia and thus left in the integument free-nerve terminations as receptors. This type of chemoreceptor is found generally in the skin of fishes and amphibians and in the mouths, nasal chambers and other moist cavities of the air-inhabiting vertebrates.

The third and last type of the vertebrate chemoreceptor is the gustatory organ. In this type the conducting neurone presents exactly the condition met with in the common chemical receptor excepting that its nerve terminals, instead of being free in the integument, are associated with epithelial taste-buds. This type of receptor was probably derived from the second type by the appropriation of taste-cells from the integumentary epithelium. Thus the three types of vertebrate chemoreceptors appear to be genetically related in that the olfactory organs represent what may be called the first generation, the common chemical the second, and the gustatory the third (Parker, 1912).

But within each type much detailed differentiation has taken place. It seems to be quite impossible to explain the variety of olfactory sensations without assuming a differentiation among the receptors of the olfactory field. In the common chemical sense the receptors on the moist surfaces of the eye, judged by the sensations they give rise to, are distinguishable from those in the epithelium of the mouth and of the nose. But this special differentiation is best seen in the gustatory organs. Here three and probably four well defined senses can be distinguished, namely, sour, saline, sweet, and bitter. And though separate receptors for these four senses have not as yet been distinguished structurally, their functional separation is beyond doubt.

It is because of the repeated differentiations that characterize the evolution not only of the chemoreceptors but of the other groups of like organs that a classification of them or even a simple enumeration proves to be so unsatisfactory. For they are not unitary elements that can be counted like the fingers on the hand nor are they sufficiently co-ordinated to make classifications easy and natural. They are like the whole organism itself in that they exibit that kind of diversity that characterizes evolutionary flux.

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