are diseases which are treated more or less successfully at Ems. Skin diseases and scrofula are also in evidence here as at almost every other bath resort. The baths are extensively employed in cases of leucorrhœa, in catarrhal conditions of the uterus and cervix uteri, in nervous cases of dysmenorrhœa and in sterility.

Indeed, one sometimes wonders what chronic diseases that flesh is heir to are not benefited at such popular spas as Ems, according to the advocates of natural hydrotherapy. The comparative ease of access from Paris or England renders Ems very available for Americans; and its attractive situation in the vicinity of the Rhine invites the weary traveller to settle down there for a brief season, improve his metabolism by a course of water-drinking, diet, and rest, and then go on his way rejoicing in his renewed health and vigor.

Edward O. Otis.

ENCEPHALOCELE. See *Brain: Cephalocele.*

ENCHONDROMA. See *Chondroma.*

ENDARTERITIS. See *Blood-Vessels. (Path.)*

ENDOCARDITIS. See *Heart Diseases.*

END-ORGANS, NERVOUS.—While in origin all nervous structures may be said to have been derived from peripheral structures, in so far as the nervous elements are ectodermal rather than otherwise, yet in higher animals the separation of those elements that are aggregated within the body to form a central system from those which retain their primitive connection with epidermal structures is so complete as to warrant the division of nervous elements into central and end-organs.

End-organs fall likewise into two great classes depending on the origin of the stimulus they are designed to receive. Peripheral organs, properly so called, are such as are adapted to receive stimuli from without, as in the case of the sensory cells in the skin and organs of special sense (and this group cannot well be arbitrarily separated from the entirely similar organs of the æsthesodic system within the body) while kinesodic end-organs are such as are intended to deliver to organs like muscles and glands the stimuli elaborated in the central system. In addition, there is the system of somatic or sympathetic organs which serves to modify the function of one organ in accordance with the activities of others—a system of somatic equilibrium probably much more important than even yet supposed.

In this article the somatic or so-called sympathetic system is not included.

PERIPHERAL END-ORGANS.—It would seem from the data of comparative anatomy that the progenitors of the vertebrates had sensory cells scattered among the epidermal elements in the skin, and that in the course of evolution there was exhibited a tendency for these cells to become collected toward the lateral and dorsal parts of the body and especially in the region of the future head.

Probably Van Gehuchten was the first to announce the discovery of scattered sensory cells in the skin of the earthworm, though the observation was made some time earlier in the writer's laboratory. This author and Retzius agree that these cells are directly connected with the central nervous system by nerve fibres having origin in the cells. Such cells would seem to be analogous with sensory ganglia and might be supposed to combine the function of such ganglion cells with those of special sense cells (rod cells and the like).

Lewis Atheston has described (*Anat. Anz.*, xvi., 20) nervous structures in the worm *Tubifex rivulorum*, exhibiting a still higher differentiation. He shows that in worms there are not only scattered nerve cells in the epidermis which have the direct fibrous connection with the central system described by Retzius, but that there are other cells, in no way fundamentally different, which are grouped symmetrically to form sense organs upon the prostomium and first few segments of the body. These sense organs, though there are no specially modified supporting or central glandular cells as in vertebrates, bear an unmistakable resemblance to the lateral-line buds of amphibians, etc. Atheston finds all gradations between the isolated cell and the sense bud, and is inclined to regard the one as a derivative of the other, either in that the sense organ is the result of a closer aggregation of the isolated cells or that the isolated cells are the result of a degeneration of more primitive sense organs, perhaps as a result of the influence of the enclosing tube (see also Miss Langdon's paper on the "Sense Organs of Nereis." *Jour. of Comp. Neurol.*, x., 1.)

In the case of vertebrates the concentration proceeds further and the spinal ganglia are permanently separated from the skin, while the peripheral sensory fibres in most cases seem to arise in the cells of the ganglia and proceed by a process of repeated subdivision and elongation toward the skin, where connections are effected in a secondary manner with sensory cells in the epithelium.

In Amphioxus it would appear that the sensory ganglia are as yet unformed, their elements being scattered in the form of dispersed nerve cells throughout the dorsal or sensory nerve trunk in each segment. In lower vertebrates, notably aquatic amphibia, if our studies are correct, an intermediate condition is found. The peripheral sense organs show an unmistakable tendency to collect into bands along the lateral aspects of the body to form the so-called lateral-line organs which are composite aggregates of nervous and glandular elements. Not all the sensory cells are thus collected, but, especially on the head, there are numerous cells of unmistakably nervous nature that are not collected into buds as are those of the lateral line.

FIG. 1890. — Isolated Sensory Cells from *Tubifex rivulorum*. (After Atheston.)

In the tailless amphibia the curious fact was noticed that after the metamorphosis the sensory or rod cells are liberated from their original association in the "buds," and are scattered on the surface of the head and back in groups in such a way that the free or distal end of all the cells of the group lie in a pore of the skin. It seems scarcely to be doubted that these scattered groups are actually the same cells that in the larva are found in the sense buds.

The greatest diversity of opinion still prevails as to the nervous connections of these peculiar cells.*

The most probable view is that two entirely distinct sets of nerve fibres are associated with the lateral-line buds, one consisting of such a felting of perigemmal fibres as may be demonstrated by methylene blue in the case of skin glands, while in the other, the specific ner-

* The contrast between the results of different methods is nowhere better illustrated than in the different conclusions reached by Fusari and Panasci on the one hand (Arch. italiennes de Biol., xiv., p. 240) and those of Arnstein (Archiv f. mikroskop. Anat., xxxi., 2). The former authors worked with the chrome-silver method and describe a direct communication of the nerve fibre with the rod cells of the taste buds. (This we are able to substantiate from personal observation.) Arnstein, on the other hand, denies such connection most emphatically and claims that teased preparations with methylene blue show with all possible clearness that there is no such connection, but instead that the varicose nerve fibres form a felting of fibres around the axial and outer cells of the bud and end free in the pore. Arnstein finds quite similar nerve endings in the filiform papillæ. He does not find forked cells, but inclines to the view that such cells result from the separation of the true nerve fibre from the peripheral end of the cell to which it is attached. The appearance of continuity between the cell and the nerve fibre is said to be illusory and is explained as due to the blackening of the cell as well as the fibre. Ehrlich (Deutsch. med. Wochenschrift, 1886, 4) described intensely colored cells in the mucous membrane of the olfactory region which pass without interruption into a nerve fibre, but these cases Arnstein also dismisses as illusory. Dr. Niemack has also reached similar conclusions by the use of different material (Anat. Hefte, Merkel und Bonnet, Anat. Anzeiger, viii., p. 20).

vous structures consist of rod cells, not in the centre of the bud as stated by authors but more peripherally situated. The last-mentioned undoubtedly connect with a nerve fibre that seems to be continuous with the cell, though it is possible that there is an interruption of the actual continuity beneath the corium of the skin.

Inasmuch as the epithelial layers of the mouth and

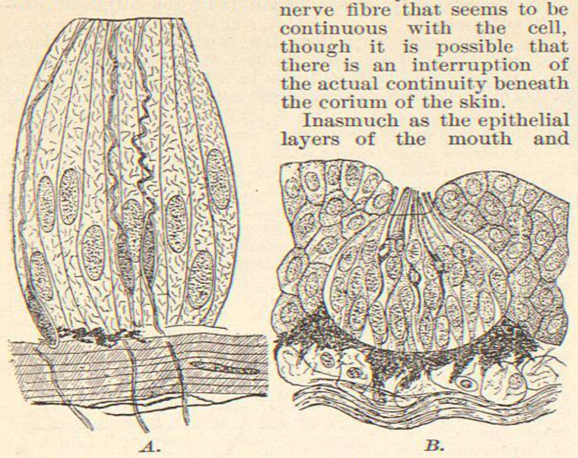

FIG. 1891 *A* AND *B*.—Sense Buds from the Skin of the Axolotl. (Original.)

tongue are morphologically only portions of the skin, it is necessary to examine these regions for light on the nerve endings as they may be modified under the special conditions here existing. In the frog, which has been the subject of the most elaborate investigation, the sense of taste cannot be at all highly developed, for the animal is accustomed to swallow its food, chiefly horny-coated

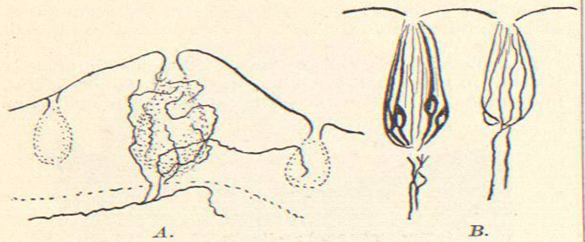

FIG. 1892.—*A*, Pericellular Endings from Sensory Bud of Conger Eel. *B*, Intrabulbar endings in barbus. (Lenhóssek.)

insects, without mastication; and experiments (Bethe) prove a very sluggish response to chemical irritants. In the tongue of the frog, as well as in the palate, there are numerous scattered specific sense organs, those of the tongue being flat end-plates, while those of the palate are protuberant sensory papillæ. Although these organs were described by Leydig in 1858 they have frequently been the objects of special study since then, and even now authors are not wholly in agreement as to the details of the structure. The cellular elements in these sense organs consist of the cylinder of flask cells forming the protection for the sensory rod cells, a subordinate variety of which has been termed forked cells by reason of the divided peripheral projection. Alate, or winged cells, around the cup or flask have also been noticed by some authors. Bethe, who has recently studied these buds by means of the modification of the methylene-blue method which bears his name, finds two sorts of nervous termini in them: first, free termini lying between the cylinder cells and reaching the surface; second, termini with bulb-like expansions on various cells (Fig. 1894). One type of such endings is three-lobed and such endings are affixed to the sides of the cylinder cells; the other variety has simple circular end-plates and these endings are found on the rod cells, fork cells, and possibly also on cylinder cells. In no case did Bethe succeed in finding actual continuity between the rod-cells and the nerve. He in fact seems to find greater intimacy of connection between the cylinder cells, which are not supposed to have a nervous function, than with the rod cells, and in no case is there more than a contact with the ceil wall. He explains the continuity detected by Arnstein and others as the result of faulty observation and imperfect methods. In the ordinary pavement epithelium of the palate Bethe finds termini on gland cells and ciliated cells, as well as deeper elements.

FIG. 1893.—*A*, Nerve Endings in Jacobson's Organ. (Lenhóssek.) *B*, Nerve endings in taste bulbs. (Arnstein.)

Our own studies of the gustatory epithelium of the axolotl are in accord with the results of Bethe upon the frog so far as the diffuse endings are concerned, though the methylene blue does not give adequate insight into the connections between fibres and cells. The taste buds, on the other hand, afford results similar to those obtained from the sensory buds of the skin. The source of many of the erroneous conclusions reached is, as mentioned beyond, the fact that in successful methylene-blue preparations it often happens that fibrous elements stain when the cells of origin for the same fibres do not.

Diffuse Peripheral Connections.—Various early writers have reported the existence of a dense network or felting of nervous material among the epithelial and even the corneum cells of the skin. This structure was first made out by the use of gold chloride, and there was always left open the possibility that the appearance was due to the disposition of metallic salts in the interstices between the cells. Dogiel, in his paper on the nerve endings of the genitalia, figures a very extensive meshwork of this kind with here and there a free knob-like termination, and he traces the lower part of the reticulum to a direct communication with a set of nerve fibres passing perpendicular to the skin (Fig. 1895). Strong, in his paper on the cranial nerves of the frog, figures a similarly minute meshwork. In all of the above cases there is the element of uncertainty growing out of the fact that the methods are impregnation rather than staining processes and are histologically uncertain. In the skin of the Amphibia there exists, at the base or ental aspect of the layer of Malpighi, a layer or stratum

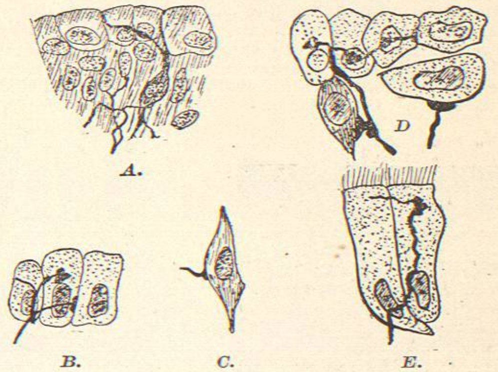

FIG. 1894.—Nerve Endings in the Epithelium of the Frog. (According to Bethe.) *A*, "Gabelzelle," from sensory papillæ of the tongue; *B*, cylinder cells; *C*, isolated rod cell; *D*, upper part of papilla; *E*, ciliate cell of palate.

which is in a peculiarly nascent state. These cells are devoid of the thick and rigid walls characteristic of the superficial cells and are protoblasts rather than complete

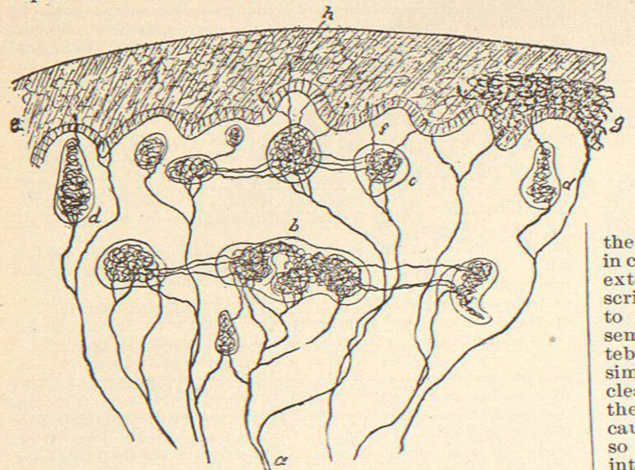

FIG. 1895.—Diagram of the Skin of the Sexual Organs. (After Dogiel.)

cells. In this layer we may find, at all stages, the evidences of mitotic division. In fact there is a permanent proliferating zone in this region. Comparison of this stratum with that of higher vertebrates shows that the latter form no exception, though it is not always easy to detect the protoblastic elements. A single theoretical consideration is sufficient to convince one that this is what should be expected, for it is of course recognized that every type of vertebrate has some provision for the constant or occasional removal of the skin. In some cases the process of removal of the corneum is intermittent, while in others it is gradual. In either case it is obvious that there must be a proton of undifferentiated material—of cells that have not passed beyond the plastic stage. In those parts of the skin where there is little differentiation between the various layers the difference between the corneum and deeper cells is not readily detected in preparations by the usual processes, but in the thicker portions where the so-called Leydig cells appear the basal protoblasts are crowded into the interspaces and pried apart. One effect of this process has been to stretch

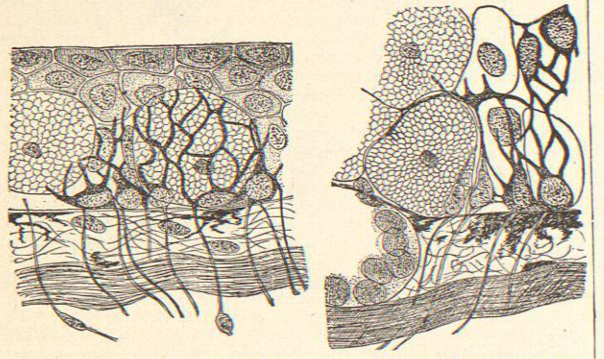

FIG. 1896.—Skin of Axolotl, showing Pericellular Network and the Nerve Fibres Entering from Below. (Original.)

the connecting protoplasm into an excessively thin layer or film enveloping the Leydig cell either completely or as a coarse meshwork of naked protoplasm. In all the preparations we have seen, the appearance is that of a broad reticulum arising in the intercalary or basal protoblasts and enveloping the cell in such a way as to wrap it completely in the products of the adjacent protoblasts.

The nerve supply to the reticulum is abundant, and the fibres can be traced without difficulty through the corium layer in all preparations. The sheaths seem to cease after passing the corium and the subsequent course is less easy to make out. In a considerable number of cases it has been possible to trace such fibres with all desirable clearness to actual connection with the bases of the lower protoblasts above-mentioned. The fibre is red, as is the protoplasm, so that it remains possible that the exact nature of the union is not obvious, yet from the fact that two masses of naked protoplasm thus come in contact, the range for possible modes of union cannot be extensive. It is believed that the condition above described in so striking an example is by no means limited to the aquatic or semi-aquatic vertebrates. It has simply been most clearly seen in these cases because the cells are so large and the intracellular reticulum is so evident (Fig. 1896). It is evident that many of the endings to be described beyond as free nerve endings receive a new interpretation when it is understood that these may be in immediate contact with protoplasmic material lying between the mature cells and forming a stroma in which they are in a sense embedded. It has been suggested that to some such reticulum as that indicated the organs may owe the remarkable solidarity and co-ordination of their activities.

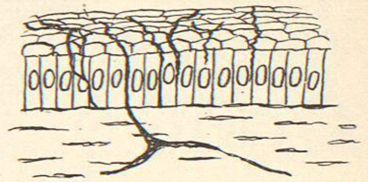

FIG. 1897.—Vertical Section through the Outer Part of the Cornea of a Rabbit. (After Kölliker.)

Free Nerve Endings of the Skin.—It seems abundantly proven, in spite of the doubts of Krause, Goldscheider, and others, that free nerve endings exist in the epidermal

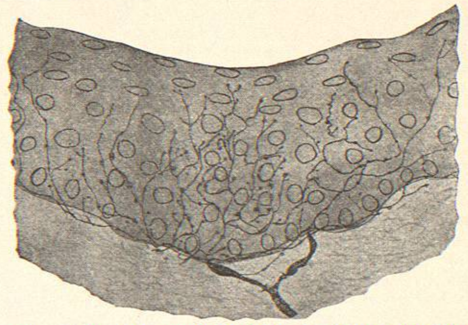

FIG. 1898.—Section through Epithelium and Part of the Mucosa of the Œsophagus of a Cat. End-ball with terminal arborizations.

layer of the skin. These are among the most difficult objects to prepare suitably for study and, as suggested above, it is probable that these fibres have relations primarily with an intercellular reticulum derived from protoblasts of the Malpighian layer. The cornea is a favorite part of the skin in which to demonstrate these fibres, but they seem to be distributed over the whole body surface.

Belonging to the same category apparently are the so-called tactile menisques identified by Ranvier. In this case also the fibres communicate with ill-defined flattened intercellular bodies in the superficial and deep layers of the skin.

It is as yet impossible to determine what the relation of the fine arborizations of these free endings may be to the so-called hot and cold spots. It appears, however, that the perception of heat and pain is intimately associated with circulatory changes and that the nerve supply to the capillaries must not be overlooked.

FIG. 1899.—Tangential Section of Mucosa of Œsophagus of Cat.

Miss DeWitt has described with much skill the terminations of free fibres in the mucous membrane of the œsophagus.

"The large, medullated, sensory fibres, found in the nerve trunks of both the intermuscular and the submucous plexus, pass through the muscularis mucosæ and form, with frequent branching, a finer-meshed plexus in the deeper parts of the mucosa. From this plexus branches, still medullated, are given off, which pass, repeatedly dividing at the nodes of Ranvier, toward the epithelium. Under the epithelium, these nerve fibres lose their medullary sheaths and form a fine-meshed subepithelial plexus, whose fibres extend for considerable

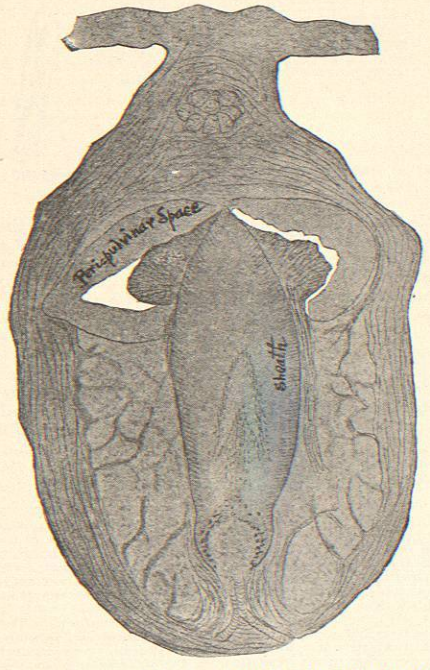

FIG. 1900.—Longitudinal Section of Vibrissa, showing the Pulvinus or Erectile Organ and the Path of the Nerve to the Annular Ring.

distances under the epithelium. Before losing their medullary sheaths, many of the medullated fibres give off at the nodes of Ranvier non-medullated fibres, which also pass up toward the epithelium and assist in the formation of the subepithelial plexus. From this plexus, as well as from non-medullated fibres which come up directly from the mucosa and seem to take no part in the formation of the plexus, fine, varicose nerves pass up into the epithelium, wind between the epithelial cells, occasionally giving off longer or shorter branches, which terminate in varicosities of different forms and sizes; the terminal fibres also finally end in ball-like thickenings on or between the epithelial cells, either near the surface or at a greater depth.

"That the terminal and lateral arborizations surround the epithelial cells, ending on or between the cells in small varicose thickenings, sometimes on the surface cells and sometimes on the deeper ones, may be seen in Fig. 1898, taken from a cross section of the œsopha-

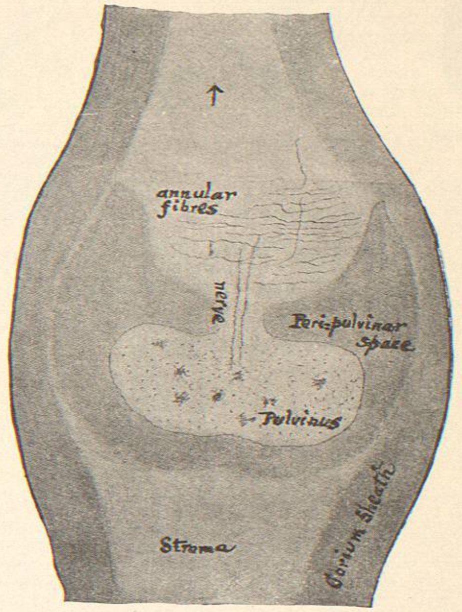

FIG. 1901.—Longitudinal Section of Sheath of Vibrissa at the Pulvinus, showing Part of Annular Nerve Ring as seen by Golgi Method. (From Messinger, after Herrick.)

geal mucosa of a young cat. In the greater part of the œsophagus, these terminal arborizations seem to be puite evenly distributed, and it has seemed to me probable that nearly all of the epithelial cells come in contact with one or more of the terminal nerve fibres. In the upper part of the œsophagus, however, near its junction with the pharynx, there are, in addition to these uniformly distributed telodendria, certain peculiar ball-like masses, consisting of the telodendria of several nerve fibres, whose branches are very short and soon become non-medullated. The non-medullated fibres soon break up into long, slender, varicose end-branches, forming end-brushes which meet and intermingle with the end-brushes of other nerve fibres, making a dense and compact mass of terminal nerve fibres, which, on superficial examination, resembles a special sensory end-organ. Closer study, however, fails to reveal the presence of a connective-tissue capsule, and, in cross sections, we find that the ending is in the epithelium and does not differ from the end-arborizations in other parts of the mucosa except for the fact that here they are more closely crowded together, more richly branched and beset with larger and more abundant varicosities."

A modification of the free endings is found in connection with certain modified hairs. The vibrissæ of car-