Histological Study on the Innervation, Especially, Sensory Innervation of the Anus of Formosan Macaque.

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YAMAMOTO, one of the present authors, has been engaged for some years past in a series of histological studies on the nerve supply, especially, the sensory nerve supply of the alimentary tract of the Formosan macaque, in collaboration with his coworkers, and has reported on some noticeable findings already. Most lately, the anus of this macaque was given as the material of a link in this chain of our studies.

Now, the sensory nerve supply of the anus, a histologically as well as clinically important and interesting subject as it must be, has been rarely taken up with results in the past. In 1940, however, Prof. H. SETO of this laboratory first succeeded in studying the subject with minute thoroughness, with the anus of human adult and fetus as materials, and described the intraepithelial sensory terminations found in the columnar and the intermediate zones with particular accuracy. IZUMI (1955) succeeded SETO in his study on the subject and besides confirming the latter's observations on the innervation of the adult human anus, reported on many interesting details concerning the non-intraepithelial sensory terminations therein. Besides, SHIMODA (1954) studied the innervation of the anus of dog, NIIZUMA (1955) of that of cat, and KAKAZU (1957) of that of canine fetus, shedding much light on the subject. We will hereunder discuss our findings on our macaque's anus in collaboration with the utterly reliable results obtained by these authors from the viewpoint of comparative histology.

The materials from the adult Formosan macaque were fixed in 10% neutral formal solution for a long time, cut into 40 μ longitudinal frozen sections and very beautifully stained by SETO's impregnation method.

1. Individual Findings.

As elucidated in many works at this laboratory, the distribution of the nerves supplied to any organ shows a very close correlation with its histological construction. This correlation is particularly evident in the anus which forms a transition zone from the skin to the mucous membrane. So, we will preface our description of the innervation with a word on the fine structure of the anus of Formosan macaque.

The anus of Formosan macaque, as in man, comprises the columnar, the intermediate and the cutaneous parts. The zona columnaris lies between the wavy linea
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anorectalis above and the margins of the anal valves below and consists of anal columnae and anal sinus. These anal columnae, however, as already pointed out by MAMAMOTO (1957), extend slightly beyond the anorectal line into the rectum. The columns are covered by a non-cornified stratified flat epithelium, but the valleys between the columns or the sinus are mostly covered by a non-cornified stratified cylindrical epithelium. The epithelium here frequently forms swellings bulging down into the propria mucosae. The surface of these swollen parts often has a shallow depression and the superficial one-rowed epithelial cell layer consists of large clear cylindrical glandular cells having an oval nucleus at their basis, forming the so-called intraepithelial mucous gland (Fig. 1). These glands show morphological resemblance to the proctal glands Type I found by SETO in the human anus.

The propria mucosae of the columnar zone is composed of a fibroreticular connective tissue rich in free cells, especially, lymphocytes, and contains many lymphatic follicles (Fig. 2). As in the part of man and bat, no papillae formed out of it into the epithelium — a finding at variance with that in dog and cat's anus, where the propria mucosae in this part shows a prominent papillary formation. Beneath the propria are seen many smooth muscle fibres running longitudinally, which originate in the muscularis mucosae of the rectal mucosa.

The so-called anal canaliculi found in the human anus (SETO) are found very well developed in the anus of Formosan macaque, too, growing upwards and downwards from the sinus as epithelial canaliculi, as shown in Fig. 2. Those running upwards are formed of several-layered cylindrical epithelium; no papillae grow into it from the propria here either. As already reported by YAMAMOTO (1957), these canaliculi often ramify, some of the branches running into the propria of the rectal mucosa and sometimes further between the intestinal crypts to open out on the surface of the mucous membrane. The canaliculi running downwards are

Fig. 1. Mucous membrane of the sinus columnaris ani of a Formosan macaque. Longitudinal section. d intraepithelial gland (SETO's proctal gland I Type) formed in the stratified cylindrical epithelium, p propria rich in lymphocytes, m longitudinal smooth muscle fibres. SETO's impregnation. Photo × 200.
formed of thicker stratified flat epithelium, of which the superficial layer partially cornify in the downward course while long and slender papillae come into formation out of the propria into the epithelium (Fig. 3). A part of these descending canaliculi run through the cutaneous zone of the anal orifice to open out externally on the bodily surface.

The zona intermedia (Figs. 2 and 4) begins at the margins of the anal valves, where the boundary between it and the zona columnaris is definite enough, but its lower boundary between the zona cutanea is somewhat less distinct. This zone is covered by a stratified flat epithelium of considerable thickness. The surface is partly cornified but is non-desquamating. The propria mucosae here is a rather dense connective tissue and joins the corium of the cutaneous zone in the distal end. Free cells are not at all abundant in it. The papillae growing out of the propria mucosae into the epithelium here are poorer in development than in the intermediate zone of man, but in the proximal part near the anal valves and the distal part, rather conspicuous papillae are found in formation. As already pointed out by YAMAMOTO (1957), a number of the ascending striated muscle fibres, as found around the anal orifice, are discovered in the propria mucosae of this intermediate zone. It is of interest that a part of these fibres run up into the columnar zone.

The zona cutanea ani, as shown in Fig. 5, is covered by a thick epidermis — far thicker than that of common haired skin in other regions. Here, the papillary formation out of the corium into the epidermis is rather conspicuous. This is suggestive enough of the abundance of sensory fibres in this part. Most of the hair follicles here are entirely surrounded by large sebaceous glands. Besides, there are a small number of eccrine and apocrine glands in the anal skin.

Many works at this laboratory have definitely established that the development of the sensory nerve fibres distributed in the mucous membrane covered by a strati-
fied flat epithelium is proportionate with the development of the papillary formation out of the propria mucosae into the epithelium. Accordingly, in the anus of dog and cat, the sensory nerve supply is better in the columnar zone where the papillary formation is better than in the intermediate zone, while in the anus of man and bat, the papillae are better developed in the intermediate zone than in the columnar zone and accordingly, the sensory fibres and their terminations are better developed in the former than in the latter part.

Now, the histological architecture of the mucous membrane of the anus of Formosan macaque being similar to that in man and bat, the pattern of the sensory nerve distribution belongs to the human type. So, in the columnar zone of this animal with no papillae in formation is very poor in sensory fibres, of which the terminations are nothing more complex than unbranched terminations or very simple branched terminations at most. Their terminal fibres end sharply beneath the surface epithelium and the epithelium of the anal canaliculi, and never enters the epithelium as far as we could ascertain with all our thorough search, though intraepithelial terminations have been found in this part of man and some other animals.

The intermediate zone is far better supplied with sensory fibres than the columnar zone. In particular, the proximal part adjoining the anal valves and the distal part adjoining the cutaneous zone, both containing well-developed papillae, are rich in sensory fibres, which form, besides unbranched and branched terminations, sometimes genital nerve bodies as well. The unbranched and the branched terminations always originate in medium-sized myelinated fibres and are far more densely distributed here than in the columnar zone. Their terminal fibres mostly run into the papillae and end just beneath their epithelium, but none were found to run into the epithelium. Most of the branched terminations are of simple type, but rather complex branched terminations consisting of several branches spread out over a considerable area are not rare either.
The genital nerve bodies are numerous in the vicinity of the anal valves, especially near the origins of the descending anal canaliculi, and the distal part adjoining the cutaneous zone of the intermediate zone where the papillae are in good formation, but in the intermediate part where the papillae are long but lean, such bodies are much fewer. These genital nerve bodies can be classified morphologically into 2 types as described below.

The Type I bodies, as shown in Fig. 6, resemble the genital nerve bodies Type I found in the human anus (IZUMI, 1955) in form but are smaller than these. They are mostly originated in a single, but more rarely in 2 or 3 medium- or large-sized myelinated fibres, and are formed in the papillae. These fibres, after losing their myelin sheaths, run into an inner bulb containing specific cell nuclei and branching out into severl branches, end in a special glomerular arrangement. These terminal bodies are covered by a thin connective tissue capsule.

The genital nerve bodies Type II, as shown in Figs. 7, 8 and 9, are of very peculiar form. These are usually formed within the papillae, are larger in size than those of Type I above and are in the largest majority uncapsulated. The inner bulb containing specific oval cell nuclei are stained more dark-reddish under silver impregnation than that of the Type I bodies. One or two medium- or large-sized stem fibres run into this inner bulb after losing their myelin sheaths and then branch out into several branches, which very frequently change their size and often form swellings during their strongly winding courses and end sometimes sharply but much more often swelling out into club-form points. The swollen parts show conspicuous neurofibrillar expansion.

The zona cutanea ani is covered by an epidermis far thicker than that of the common haired skin, and the papillae in it are very powerfully developed, so that the sensory nerve supply must be also much more abundant than in any other part.
Fig. 5. Anal skin zone of a Formosan macaque provided with thick epidermis and well developed papillae. A hair follicle surrounded by large sebaceous glands. Details in the text. Same staining. Photo $\times 50$.

Fig. 6. A genital nerve body Type I formed in a papilla in the zona intermedia ani of a Formosan macaque. Details in the text. Same staining. Photo $\times 800$. 
of the common skin. In fact numerous sensory fibres run hard up to the underside of the epidermis and form unbranched and branched terminations and sometimes also genital nerve bodies there.

In Fig. 10 are shown some unbranched and branched terminations found in a large papilla in the cutaneous zone. The medium-sized myelinated stem fibres, upon reaching their terminal areas, lose their myelin sheaths, and sometimes without branching and sometimes branching out into 2–3 run more or less winding courses before ending sharply beneath the epidermis. These terminal fibres are usually fine
fibres. Such a dense thronging of terminations as shown in this figure is not rare in this part. Fig. 11 shows a branched termination composed of several terminal fibres formed by a large-sized stem fibre. The terminal fibres show considerable

Fig. 9. A genital nerve body Type II formed in a large papilla in the distal part of the zona intermedia ani of a Formosan macaque. e epithelium, t terminal fibres showing conspicuous change in size. Details in the text. Same staining. Photo ×800.

Fig. 10. Some unbranched and simple branched sensory terminations originated in medium-sized myelinated fibres formed beneath the thick epidermis of the pars cutanea ani of a Formosan macaque. Finer fibres (f) are vegetative fibres. Details in the text. Same staining. ×350.
change in size and end just beneath the epidermis spread out over a rather wide area: Branched terminations of large-sized sensory fibres are not rare in this zone.

Genital nerve bodies often come forth in the parts nearer the intermediate zone but much less frequently in the peripheral parts of the cutaneous zone. These bodies show little morphological difference from those in the intermediate zone and belong to Type I in the largest majority, those of Type II being comparatively rare. In Fig. 12 is shown a genital nerve body Type I formed in a conspicuous papilla in the anal orifice. The branch fibres rather frequently change their size and show a very typical glomerular arrangement. This body is devoid of any connective tissue capsule.

The sebaceous glands accompanying the hair follicles in the zona cutanea ani are very well developed, the larger of them completely enclosing the hair follicles on their whole circumference. So, the specific connective tissue area formed between the follicle neck and the surrounding sebaceous glands is rarely in the form of SETO's so-called hair-nerve shield but usually of his hair-nerve tube. The development of the sensory hair-nerve fibres ending in such tubes was found very powerful, as might be anticipated.

Many sensory fibres run into a hair-nerve tube. Their terminations are either of fence-like type or of plexus-like type. In a fence-like termination, as shown in Fig. 13, the sensory stem fibres, upon running into the hair-nerve tube, branch out into a few branches each, which ascend nearly parallel to the longer axis of the hair follicle, some of them bifurcating a few times on their courses, and always end in club-like fibrillar expansions. Sometimes anastomoses between two of such expansions are observable. In general appearance, the terminal fibres show a characteristic fence-like arrangement enclosing the epithelial hair follicles on all sides. The sensory hair-nerve terminations in the anal skin are mostly of such a fence-like type. It is of interest that the prevalence of such fence-like termination differentiates anal skin.
Fig. 12. A genital nerve body Type I Formed in a papilla in the zona cutanea ani of a Formosan macaque. Details in the text. Same staining. Photo \( \times 800 \).

Fig. 13. A fence-like sensory termination formed in a hair-nerve tube in the anal skin of a Formosan macaque. A sebaceous gland. Details in the text. Same staining. Photo \( \times 600 \).
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from the lip skin of the Formosan macaque where such terminations were found only rarely (YAMAMOTO et al. 1958).

A plexus-like termination of hair-nerve fibres, as shown in Fig. 14, is formed by the many branch fibres of some stem fibres in the hair-nerve tube running quite irregular courses, sometimes showing mutual fibrous anastomoses and ending in a plexus-like arrangement in general appearance. Terminations of such a type, however, are comparatively rare in the anal skin. The hairs in the skin part of the lip of this monkey most commonly have nerve-fibre basket terminations around their follicles (YAMAMOTO et al. 1958), but such basket terminations could not be found in its anal skin. From the above findings, we learn the very interesting fact that the terminal mode of sensory hair-nerve fibres in the haired skin is considerably dissimilar in different parts of the body.

In man and some other mammals, small-sized PACINian bodies have been discovered within and along the m. sphincter ani internus, but in our Formosan macaque specimens, no such bodies could be found. So, such bodies, if present in the macaque’s anus, must be of very rare occurrence.

II. Summary.

The anus of Formosan macaque, as that of man, consists of the columnar, the intermediate and the cutaneous zones.

In the columnar zone lacking in papillae growing out of the propria mucosae into the epithelium, the distribution of sensory nerve fibres is very scant, only a very small number of subepithelial unbranched or very simple branched terminations being found here. No intraepithelial fibres, as found in man and some other animals, could be found in this part of Formosan macaque.
In the intermediate zone, the papillae being rather conspicuously developed, many sensory fibres are found coming in, their terminations comprising some unbranched and branched terminations as well as some genital nerve bodies. No intraepithelial fibres are to be found in this zone either.

The genital nerve bodies may be classified into Type I and Type II. In a Type I genital body, 1 or 2 stem fibres running into the inner bulb rich in specific cell nuclei divide into several branches, sometimes coming into mutual anastomosis, and end in glomerular arrangement as a whole; most of these are capsulated and resemble the genital nerve bodies Type I found in the human anus (IZUMI) in form, but are smaller in size than the latter. The genital nerve bodies Type II are rather peculiar in form. The 1 or 2 sensory fibres running into the usually uncapsulated and dark-staining inner bulb end in a rather complex branched termination. The terminal fibres are thick, show frequent fibrillar expansions and change in size during their strongly winding courses and very often end swollen out into club-like tips.

The zona cutanea ani is covered by a thick epidermis and well-developed papillae grow out of the corium into it. So, the papillary layer here is far better supplied with sensory fibres than in the common haired skin in other parts. These sensory fibres form, as in the intermediate zone above, unbranched and branched terminations as well as genital nerve bodies, mostly of Type I.

The hair follicle necks of the zona cutanea ani are in a large majority completely hedged in by large-sized sebaceous glands and hair-nerve tubes inside them. Thus, the distribution of the sensory hair-nerve fibres here is plenty. Their terminations in most cases are of the fence-like type and only much less frequently of the plexus Type, no basket terminations as found in the pars cutanea of the lip of this animal being found in its anal skin. No PACINIan bodies could be found here either.

内容自抄

台湾猿の肛門も人の場合と略同様、柱帯、中間帯及び外皮帯に分けられるが、先ず柱帯では上皮に対する固有膜からの乳頭形成が見られないから、知覚神経分布も甚だ劣勢で、極く少量の非分岐性及び単純性分岐性終末を上皮直下に見ると過ぎない。

中間帯には稀々著明な乳頭形成が見られるから、ここでは多数の知覚線維の進入を見、その終末には非分岐性及び分岐性終末の他、陰部神経小体も発見される。尚上皮内神経は人及び他の動物の場合と異って、柱帯にも中間帯にも証明されなかった。

陰部神経小体はI型及びII型に分けられる。I型に於ては1-2条の知覚線維が特殊細胞核所有の内根に進入し、この中で結球状配列を示す数条の分枝に分れて終る。本小体は人の肛門に見られる陰部神経小体第I型（樋）に類似するが、但し規模の点ではより劣勢を示す。II型小体は可なり特有な形態を示す。1-2条の知覚線維は浸染性の内根内に進み、多少複雑な分岐性終末に移行する。終末枝は随時に原線維を拡散を示す太さの変化に富んだそして強い迂曲走行をとる太い
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References.