Histological Study on the Innervation, especially on the Sensory Innervation of the Lung in Hedgehog.

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Since more than a score of years ago, studies on the nerve supply, especially, the sensory nerve supply of various organs of man and a number of animals have been conducted at this laboratory under the leadership of Prof. SETO. The works on the nerve supply of the lung have been also many and fruitful. In particular, HAYASHI, SAIKO, OMOTO, FUKASE and NUMATA have obtained many interesting results in their studies on the nerve supply of the lungs of man, dog, goat, Formosan macaque and bat, respectively, while MIZUKOSHI and TANAKA published reliable reports on the development of the nerves in the lungs of the human and cat's fetus.

In succession of these illustrious predecessors, the present author was given the opportunity of studying the innervation of the lung of a hedgehog. The materials, after fixing for a long time in 10% neutral formol solution, were cut into 40μ frozen sections and these were stained by SETO's silver impregnation method. The large series of the beautifully stained preparations thus obtained were minutely examined under a microscope, the findings were studied in comparison with the reported findings on the innervation of the lungs of man and the other animals cited above (referred to as the other animals hereunder) and some interesting results have been obtained, as detailed hereunder.

I. Individual Findings.

I will first touch upon the common histology of the lung of the hedgehog, before entering upon my description on the nerve supply of the part, for the fine structure of the lung of this animal has not yet been described in details, and, moreover, very interesting constructions not found in the other animals have been discovered therein.

The largest-sized intrapulmonary bronchial branches of hedgehog have the diameter of only ca. 3 mm, that is, are about one-third as large as those of goat or dog, but are somewhat larger than those of bat. The cartilaginous pieces around the major bronchial branches, similar to those in bat, are very ill developed and are of hyaline nature, but are not ossified as some of those in bat.

The epithelium of such bronchial branches, as shown in Figs. 6 and 7, is generally of 2-rowed ciliated type containing a small number of goblet cells. The mucous membrane has many longitudinal folds on it. for the muscularis lining it is rather
well developed. The muscularis around the propria mucosae of loose connective tissue of comparatively low thickness is composed of a layer of circulasly running smooth muscle bundles. These bundles lose gradually in development in the more distal parts as in bat. The muscle layer is covered by an adventitia of connective tissue more or less rich in connective-tissue cells. The bronchial glands are very retrogressive and are found in an extremely small number in the submucosa. No lymphoeytic gathering has been found here.

The large bronchial branches bifurcate into medium sized bronchial branches of 1—1.5 mm in diameter (Fig. 1). In these, the longitudinal mucous folds become lower, the epithelium is a 1—2-rowed ciliated epithelium and the muscularis is far thinner than in the former. A very small number of bronchial glands are still observable in their adventitia. The small-sized bronchial branches coming next (Figs. 1 and 2) are 0.5—0.7 mm in diameter, their mucous folds are still lower, the epithelium is a one-rowed ciliated epithelium, the circulari muscularis thins further down and bronchial glan's are seen no more.

In the bronchioli of 0.3—0.4 mm diameter, the mucous folds are extremely ill developed. These may be called the bronchioli terminales and have a one-rowed ciliated epithelium and a layer of very thin 2-rowed circular smooth muscle fibres. These ducts take comparatively long courses before passing over into the bronchioli respiratorii, but the boundary of transition is very indefinite, because the epithelium remains to be the same ciliated epithelium in most cases, a cubic epithelium appearing only more rarely, and the walls of the respiratory bronchiolos are devoid of alveoli as those of bat. A very small number of smooth muscle fibres are found

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Fig. 1. 2 medium-sized bronchial branches in the lung of a hedgehog. g ill-developed bronchial gland, s small-sized bronchial branch, p a. pulmonalis, b bronchiolus, d alveolar duct, a alveoli. Details in the text. Same staining. Photo ×40.
The alveolar ducts and the alveolar sacs are formed by chains of successive alveoli (Figs. 2 and 3). The epithelium on the inside of the alveoli consists of flat around the bronchioli.
cells with a single round or oval nucleus and unnucleated flat cells. Many blood capillaries run along the underside of this epithelium.

The interlobular septa are very frequently invisible, as in bat. The media of the v. pulmonalis is not composed of heart muscle fibres as it is in bat, but is of smooth muscle fibres as in man and the other animals. Its development, however, is very poor in hedgehog.

The pleura visceralis is a rather thick layer of connective tissue rich in cell nuclei and covered by a one-rowed flat epithelism. It is of interest that, be it so sporadic, some groups of dense-packed smooth muscle fibres should be found in this pleura of hedgehog. Some of these fibre groups consist of a single muscle bundle but some contain half a dozen bundles, which run in random directions, sometimes in X-shape, sometimes in Y-shape and as often in totally irregular arrangement (Figs. 4 and 5). Recently, YAMAMOTO of this laboratory has found similar small smooth muscle groups sporadically situated in the parenchyma of the pancreas of Formosan macaque. Such findings by YAMAMOTO and the present author seem to indicate that such peculiar smooth muscle groups may be found in some visceral organs of some animals at least. What can the existence of these muscle fibre groups in some of the entrails mean? In fine, the location of groups may be possibly some interesting peculiarities specific to some orders, genera or species of animals, but our data are far too meagre for making generalizations.

In short, the most prominent points of note in the histological findings of the lung of hedgehog are as follows. In the largest bronchial branches, the cartilaginous pieces as well as the bronchial glands are very few, but since the smooth muscle layer is well developed, the longitudinal folds on the mucous membrane are also promi-
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... The epithelium is a thin ciliated one.

The medium- and small-sized bronchial branches are similar to the large-sized ones in construction, but with the decrease in size, the smooth muscle layer becomes the worse developed and accordingly the mucous folds lose in height. The epithelium of the bronchioli is of one-rowed ciliated type, except in some distalmost parts where cubic epithelium is observed. The epithelium is lined by a 2-rowed layer of smooth muscle fibres. This part is devoid of alveoli. The alveolar ducts and the alveolar sacs are formed of continuous chains of alveoli, and their inside is covered by a one-rowed epithelium composed of flat cells with or without nucleus. It is of interest that small groups of smooth muscle fibres were found sporadically in the pleura visceralis.

The fundamental bronchial plexus originating in the pulmonary plexus found in the walls of the major bronchial branches is most typically formed in man, is far worse developed in goat and dog, and still lower in development in the lower mammal the bat, as far as the studies at this laboratory have ascertained. In my hedgehog of the lower order of mammals, its development was similar to that of the plexus in bat. The nerve bundles composing the bronchial plexus run periadventitiously and ganglia are formed here and there along their courses (Figs. 6 and 7).

In comparison with those of man, dog or goat, the numbers of both the ganglia and the ganglion cells composing them are far smaller in hedgehog, the largest of the ganglia in the latter containing only 15—20 cells. The nerve cells retain their characteristic multipolarity, but cells with prominent processes are rather very few, most of the cells giving the impression of apolarity. In consequence, nerve cells with prominent processes as might be ascribed to either Type I or Type II of DOGIEL could be hardly detected. In this respect, the hedgehog stands on a similar level as

Fig. 5. 2 smooth muscle bundles found in the pleura visceralis of a hedgehog. e pleural epithelium, a alveolar sac. Same staining. Photo ×200.
the bat and both these animals may be ranked as inferior to goat and monkey in evolution.
The nerve bundles of the bronchial plexus, as shown in Fig. 6, comprise both non-myelinated fine vegetative fibres and myelinated thick sensory fibres, the former occupying the majority in most cases, but in rarer cases, the latter outnumber the former. Some of the minor nerve bundles are almost wholly composed of sheer sensory fibres. Interestingly enough, the ratio of the number of vegetative fibres to that of the sensitive fibres in this plexus is considerably larger in hedgehog than in man, dog or goat. The terminations of the vegetative fibres are always in the form of the STÖHR's terminal reticula in the lung of this animal as everywhere else, and are particularly well developed in the muscle tissue and also typically formed around the blood vessels.

It is undoubtedly a great contribution to the advance of neurology that since the days of SUNDER-PLASSMANN and HAYASHI, and especially, through many studies at this laboratory, the existence of sensory terminations of various types in the lung of man and many other animals has been clearly demonstrated.

Of the sensory terminations found in the human lung, the sensory terminations Type I concerned with the blood-pressure falling reflex found in the muscularis of the major bronchial branches discovered by SUNDER-PLASSMANN must be mentioned first. Terminations seemingly belonging in this type are found in the well-developed muscularis of the large- and medium-sized bronchial branches of hedgehog too (Figs. 8 and 9). These are in the form of complex terminations containing frequent very typical neurofibrillar leaves in the human lung, but in that of hedgehog, they are far poorer in development, terminations with such fibrillar leaves being not found
in my specimens. But since the characteristic of their terminal fibres consisting in thick fibres showing very frequent change in size is maintained intact, it is very probable that they belong to the reflex system concerned with the blood pressure falling.

Previously, NUMATA has found similar terminations, sometimes even rather complex branched ones, in the muscularis of the bronchial walls of bat. In my specimens of hedgehog, however, these terminations are very simply formed in most cases, including only unbranched and simple branched terminations, and such examples of somewhat complex type in which a thick stem fibre ends in the muscularis after branching out into a few branch fibres, as shown in Fig. 10, are very rare. As the terminations of the same type found in the lungs of Formosan macaque (FUKASE) and goat (OMOTO) are reported as rather simply formed, it seems unjustifiable to speak on the phylogenetic ranking of the animal relying on the complexity of such terminations.

Besides the above, subepithelial and intraepithelial sensory terminations have been discovered in the bronchial walls of man and the other animals. Such terminations were found in the bronchial walls of my hedgehog too. In number, construction and density of distribution, however, they were markedly different from those in the other animals.

These sensory terminations usually consist in unbranched and simple branched subepithelial terminations, with large- or medium-sized terminal fibres and not rarely with enormous thick fibres showing conspicuous change in size during their winding courses and ending sharply or bluntly just beneath the epithelium. Intraepithelial fibres are as extremely rare here as in the goat's lung. In particular, such intra-
epithelial sensory terminations have been found in the small-sized bronchial branches only but never in any of the larger branches. This is in high contrast to the case of such terminations in the human, the canine or the chiropterian lung.

The subepithelial sensory terminations are found only rather sporadically in the large- and medium-sized bronchial branches but are more abundant and more or less complex in formation in the small-sized branches. In Fig. 11 are illustrated a medium-sized and 2 large-sized sensory fibres running into the propria mucosae passing between the muscle bundles of the muscularis of a large-sized bronchial branch. It is very rare to find 2 or 3 sensory fibres thus running in company subepithelialwards. In most cases such fibres are found solitarily.

In Fig. 12 is illustrated another sensory termination found also in a large bronchial branch, a bifurcated one. Here, a thick sensory fibre with frequent change in size forms a small loop just before branching out into 2 terminal fibres which end bluntly close to the underside of the epithelium. An unbranched termination of sim-
ple glomerular type found also in a large sized bronchial branch is illustrated in Fig. 13. Here, we see a medium-sized sensory fibre running closely along the underside
of the epithelium while showing some change in size and tapering off into a very simple glomerular tip, which is, however, not clearly visualized in this picture.

Fig. 13. A subepithelial unbranched sensory termination of simple glomerular type found in a large bronchial branch of a hedgehog. \( g \) simple glomerular tip of the fibre not so clearly visualized. Same staining. Photo \( \times400 \).

Fig. 14. A higher magnified drawing of the glomerular tip of the terminal fibre in Fig. 13. \( u \) unbranched sensory termination originated in a somewhat thin fibre and ending in a sharp point. \( \times800 \).
Therefore, a drawing of the part very distinctly illustrating the glomerular arrangement is appended (Fig. 14). Some such extremely simply formed glomerular terminations have been found, though quite rarely.

Subepithelial sensory terminations are found in the medium-sized bronchial branches also, in a number somewhat smaller than in the above. In Fig. 15 is shown an example of such terminations — a bifurcated termination formed by a medium-sized sensory fibre showing somewhat frequent change in size. One of the terminal fibres runs a markedly winding course before ending sharply just beneath the epithelium, but the other comes very soon to a sharp end.

In the small-sized bronchial branches are found subepithelial terminations in a larger number and in more complex form than in the larger branches. Some of these are formed by enormously thick fibres and some rare specimens of intraepithelial terminations are found besides the large number of subepithelial terminations in these small bronchial branches.

In Fig. 16, we see a thick and a thin sensory fibres running through the muscularis into the thin propria with some fine vegetative fibres and ending in sharp points as unbranched sensory terminations. In Fig. 17 is shown an unbranched intraepithelial termination found in a small sized bronchial branch. Its stem fibre, while running through the muscularis into the propria mucosae in company with a few fine vegetative fibres shows very perceptible change in size and a wavy course, then
Fig. 16. A thick and a thin unbranched sensory terminal fibres ending in sharp ends just beneath the epithelium of a small bronchial branch of a hedgehog. Thin fibres are vegetative nerve fibres, m muscularis, p a. pulmonalis. Same staining. ×300.

Fig. 17. An unbranched intraepithelial sensory termination found in a small bronchial branch of a hedgehog. a alveolar epithelium. Details in the text. Same staining. ×330.
parting from the vegetative fibres penetrates into the epithelium and after a rather long course therein, ends sharply in the basis of the epithelium. This intraepithelial portion of the fibre also shows conspicuous change in size during its lightly winding course.

Subepithelial sensory terminations formed by enormously thick fibres are also frequent in the small-sized bronchial branches. A bifurcated termination formed by such a overthick fibre is illustrated in Fig. 18. The thick stem fibre, after losing its myelin sheath, passes over into an exceedingly thick terminal fibre which further gains in size during its course showing frequent and conspicuous change in size, then bifurcates into somewhat thinner short branches which thin down abruptly into sharp points just beneath the epithelium.

Some such terminations of enormously thick fibres are found also within the walls of the small-sized bronchial branches on rare occasions. In Fig. 19 is shown an example of such terminations. Here, a rather complex branched termination formed by enormously thick branch fibres showing frequent change in size and running peculiar winding coursea, coming from a large-sized sensory stem fibre, is found intra-adventitially in the vicinity of the wall of of a small pulmonary artery running between 2 small bronchial branches. One of its terminal branches runs further into the subepithelial propria of the right bronchial branch and there branches out into finer rami, which end in a sharp or blunt subepithelial termination each after running winding courses. It is of interest that intraadventitial and subepithelial branched terminations formed more complexly than those in the larger bronchial branches and formed by enormously thick fibres should be found in the smaller bronchial branches.
The bronchioli also contain subepithelial terminations, which are, however, simpler in construction than those in the small-sized bronchial branches above, being limited to unbranched and simple branched terminations only. Intraepithelial fibres are not rare here either.

Very simple sensory terminations are sporadically found in the vicinity of the alveolar ducts and sacs, that is, in the interalveolar connective tissue, as in the case of bat or goat. For example, in Fig. 20 is shown an unbranched termination found in a connective tissue layer between 2 alveolar ducts and in Fig. 21 another found in the interalveolar tissue, both formed by a rather thick fibre running a wavy course while showing frequent change in size.

NUMATA has succeeded in blamelessly demonstrating the existence of unbranched sensory terminations in the pleura visceralis of bat. Prior to him, TANAKA reported on the unbranched and bifurcated sensory terminations he found in the pleura visceralis of a bovine fetus. In the visceral pleura of my hedgehog too, very typical unbranched and simple branched terminations of medium- or large-sized fibres frequently changing size were found present beyond all doubt. In hedgehog, the number of such terminations is even larger than in bat or fetal cattle.
Fig. 20. An unbranched sensory terminal fibre showing somewhat change in size found in a connective tissue layer between 2 alveolar ducts in the lung of a hedgehog. Same staining. ×400.

Fig. 21. Ditto, found in the interalveolar connective tissue in the lung of a hedgehog. p pleura visceralis. Details in the text. Same staining. ×280.
The sensory fibres coming into the visceral pleura, as clearly illustrated in Figs. 22 and 23, consist in medium- and large-sized and sometimes in very thick fibres, which form small nerve bundles containing also some vegetative fibres and pass through the parenchyma of the lung into the pleura visceralis. These bundles run further to the pleural periphery and the sensory fibres in them, upon reaching their terminal area, branch out into 2 or 3 terminal fibres each, which run short or long wavy courses to end sharply near the epithelium of the pleura. In some cases, however, sharp-tipped unbranched terminations are formed beneath the epithelium (Fig. 24).

Thus, I found in the pleura visceralis of hedgehog quite a large number of sensory fibres, which end subepithelially in unbranched or simple branched terminations.

I did not succeed to clarify the biological significance of the small groups of smooth muscle fibres found in the visceral pleura of hedgehog, but taking into consideration the fact that sensory fibres are very often seen running through or around these groups (Fig. 24) and ending in the nearby pleural connective tissue, we may...
deem it possible that these peculiar muscle tissue groups constitute so many receptors of some specific sensation in the pleura.

II. Summary.

The bronchial plexus found in the bronchial branches of hedgehog is far poorer
in development than those in dog and goat and the nerve bundles run periadventi
tially, accompanying small ganglia frequently along their courses. The ganglion
cells in them are provided with only indistinct nerve processes and barely show their
multipolarity. The nerve bundles, interestingly enough, contain a larger relative
number of thick sensory fibres than in goat and dog. These sensory fibres end in
various types of terminations.

In the first place, I must mention the sensory terminations Type I concerned
with the blood-pressure falling reflex found in a rather large number in the well-
developed muscularis of the large and medium-sized bronchial branches. In hedgehog,
these are in the form of unbranched and simple branched terminations formed by
thick terminal fibres showing frequent and conspicuous change in size but devoid of
such neurofibrillar leaves as found in such terminations in man. Sometimes, these
terminations are of large complex branched type.

Subepithelial and intraepithelial sensory terminations are found in the bron-
chial branches of hedgehog as in those of man, Formosan macaque, dog, goat and
bat, but in different construction and distribution density from those in the other ani-
mals. Very few of these terminations are found within the epithelium of the small-
sized bronchial branches only, the greatest majority of them consisting of unbranched
and simple branched terminations formed beneath the epithelium. The terminal fibres
of these terminations are large or medium in size and show conspicuous change in
size during their winding courses and usually end just beneath the epithelium in
sharp or blunt points. Such subepithelial terminations are found only sporadically
in the large- and the medium-sized bronchial branches but more abundantly and
somewhat more complex in form in the small-sized branches. Some very simple glo-
merular terminations were also discovered.

Some of the sensory terminations are formed by exceptionally stout fibres, chief-
ly in the adventitia or beneath the epithelium of some small-sized bronchial branches
only. In such terminations, a thick stem fibre after losing its myelin sheath further
thickens into an enormously thick fibre which shows conspicuous change in size,
and often divides into 2 or 3 terminal fibres which end either sharply or bluntly.

Subepithelial sensory fibres are not rare either in the bronchioli, but these are
simpler in construction than those in the small-sized bronchial branches above, being
limited to the simplest types of unbranched and simple branched terminations. In-
traepithelial sensory fibres are also not rarely found here.

Very simply formed sensory terminations are found sporadically around the
alveolar ducts and the alveolar sacs that is in the interalveolar connective tissue as
in bat and goat.

A rather large number of sensory fibres are found running into the pleura vis-
ceralis of hedgehog. They terminate in unbranched and simple branched termina-
tions formed of thick terminal fibres, which show frequent change in size and end
sharply beneath the epithelium. Terminations formed of very thick fibres are not
rare either in the pleura.

Small groups of smooth muscle fibres are sporadically found in the visceral
pleura and sensory fibres are very often found running through or around them.
These formations may possibly represent so many special receptors of some kind of
内容自抄

針鼠の気管支枝神経窩は大きな動物の支に発達遙かに劣勢し、然しその神経末は尚お所々に小型神経窓を有する。神経細胞は不明瞭な神経突起を有し僅かに多極性を暗示する。然し神経末は大動物の支に於けるよりも多くの知覚線維を含んでいて興味深い。その終末は種々の型に分けられる。

先ず血圧下降反射に関する知覚終末Ⅰ型が大型の気管支枝の良好発達の筋層内に証明される。然し人の場合に比すれば甚だ小規模であり、神経線維枝の形成も見られない。但し稀ならず複雑な分岐型終末も認められる。

針鼠の気管支枝にも人や他動物に於けると同様上皮下及び上皮内知覚終末が明かにされる。但し上皮内線維は専ら小型気管支枝に稀に見られるに過ぎない。上皮下終末は非分岐性及び単純性分岐性終末として表われる。その終末枝は特有な迂曲走行と著明な太さの変化を示す太い又は中等大線維から成るが、又稀ならず極めて太い線維で表われ、その多くは上皮の直下に尖锐状又は短状に終る。尚この上皮下終末は大型及び中型気管支枝では散在性に見られるに過ぎないが、小型気管支枝ではより多数に発見される。その他極めて単純な糸球状終末も稀ならず証明される。

極めて太い終末枝で構成される分岐性終末が専ら小型気管支枝の外膜又は固有膜内に形成される事は興味深い。尚この線維は著明な太さの変化を示し、その先端は尖銳状又は短状に終る。

細気管枝に於ても複々上皮下知覚終末の形成を見るが、之等は小型気管支枝に於けるよりもより単純に構成される。その他上皮内線維も複々発見され興味深い。

肺胞間結合繊内にも細小や山羊の場合と同様甚だ単純に構成される知覚終末が散在性に発見される。

針鼠の内臓胸膜には可なり多くの知覚線維が存在する。その終末は太さの変化に富んだ太い終末枝から成る非分岐性及単純性分岐性終末で表われ、終末枝の先端は上皮下に稀少状に終る。

この内臓胸膜内には平滑筋小群が散在性に発見されされる。且知覚線維はこの中をうすその周辺を走り、その附近に終る場合が甚だ多い。そこでこの特殊筋束は胸膜内に於ける或種特殊感受器官を表わすに非ずやと考えられる。

References.