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Austra Redlichs

Dermal Histology of the Latvian „Naked Mouse“.

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Dermal Histology of the Latvian "Naked Mouse".

By
Austra Redlichs.



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(Institute of Comparative Anatomy and Experimental Zoology of the Latvian
University in Riga, Director: N. G. LEBEDINSKY.)

Dermal Histology of the Latvian "Naked Mouse"

By

Austra Redlichs.

11 Text-figures.

(Eingelangt am 23. März 1936.)

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I. Introduction.

Some years ago in the vivarium of the Institute of Comparative Anatomy of the Latvian University there appeared by way of mutation a mouse whose pelage greatly differed from the hair-coat of a normal animal. In the place of the normal thick coat the body of this half-naked mouse was covered only with rare long hairs, the sensory hairs, however, being normally developed. When this mouse was mated with a normal one there appeared beside the normal offspring 4 half-naked ones. By homozygous mating quite naked specimens were obtained. The results of this crossing were described

by N. LEBEDINSKY and A. DAUVARTS in their article „Atrichosis und ihre Vererbung bei der albinotischen Hausmaus“ (1927).

Thus the half-naked mice are bastards of the naked mutants and normally haired animals. When summarising the results of a succession of crossings of the F₁-bastards, the following split was found: 33 normal mice, 74 half-naked, and 38 naked ones. Considering this there can be no doubt that it is a simple Mendelian case. From the genetical point of view this character may be described as recessive atrichosis with a heterozygous dominant hypotrichotic effect.

In their post-natal development these half-naked mice acquired a quite normal pelage, but at the age of about 1½—2 weeks they began to lose their hair-covering. This shedding of the hairs began at the head, spreading over the neck and the thoracic region to the posterior part of the animal. Yet before the wave of shedding had reached the caudal part of the body a new growth of hair began on the anterior part, following in its turn the direction to the posterior part of the body. In this way each wave of hair-shedding was followed by one of hair-growing, and this produced a partical pelage, the body of the animal being at one and the same time covered with hair in some parts and hairless in the others.

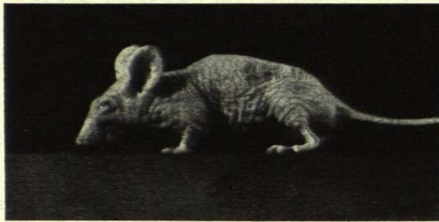


Fig. 1. Adult naked mouse. Side view.



Fig. 2. Adult half-naked mouse. Side view.



Fig. 3. Adult half-naked mouse. Dorsal view.

The entirely naked mice which in general are of a weaker constitution than the normal animals are never normally haired. Their skin remains hairless also in its post-natal development.

Besides the hairless mice there exist hairless dogs as a distinct race and, as results of mutation, hairless rats, rabbits, shrews, moles, goats, bulls, and horses.

The structure and the development of the skin of the Latvian half-naked and naked mice were described in 1932 by L. THIGPEN DAVID in her paper "The External Expression and Comparative Dermal Histology of Hereditary Hairlessness in Mammals". Concerning the structure of the skin of these mice the authoress says: "Heterozygous dominant hairless (Nn) mice" (our half-naked mice) "always show a normal structure of the skin as well as a normal development and structure of the stratum corneum. Homozygous dominant hairless (NN) mice" (our naked mice) "at birth, show no histological abnormality. The most evident early peculiarity is the slow development of the thickness of the skin, chiefly manifested in the subcutis".

DAVID thinks that the slow development of the thickness of the skin does not depend on the potential hairless condition, but that it stands in correlation with the retarded development of the body in general.

At the age of three days it is already possible to distinguish the homozygous from the heterozygous individuals, and this precisely by the thickness of the skin. When comparing the skin of 4 days old homozygous and heterozygous mice it appeared that the stratum corneum, the epidermis, and the skin musculature were of the same thickness in both animals, while the corium and the subcutis of the heterozygous mouse were 2—5 times thicker than those of the homozygous animal.

Homozygous mice with a better structure of the body do not show so great a difference in the thickness of the skin or of the corium, when compared with the corium of heterozygous mice, while on the other hand the difference between the thickness of the skin of a weakened homozygous mouse and that of the skin of a normal mouse is much more perceptible.

Directly after the first depilation a quite normal quantity of stratum corneum is found in the hair-canals; later on, when the hair remains are not eliminated, the stratum corneum augments and appears as "epithelial pearls".

Heterozygous recessive hairless mice are quite normal.

Likewise homozygous recessive hairless animals are quite normal till the shedding of the first pelage. Directly after the depilation stratum corneum is found in the hair canals in normal quantities, and the only hystological abnormality of the skin is the total lack of the pelage. Yet soon after the shedding of the hairs the stratum corneum gradually increases until, in older animals, it entirely obstructs the hair-canals.

During the growth of the second generation of hairs cysts are formed in the different parts of the follicles. These cysts are found either only in the corium or, if they are more numerous, in the subcutis also. It is easily understood that these formations call forth changes in the layers of the skin owing to which the thickness of the skin is much greater than in normal individuals. In the corium and in the subcutis cell-infiltrations are formed which resorb within the skin the remains of the hairs growing in the wrong direction.

The epidermis is normal; there may be a hypertrophy of the stratum granulosum. The stratum corneum in the hair canals is greatly augmented and continuous with the stratum corneum of the epidermis. Thus there is a hyperkeratosis. DAVID thinks that this

hyperkeratosis is of secondary character in the skin in which hairs are developing and that the hypertrophy of the stratum corneum in the hair-canals is the result of an abnormal pressure upon the follicle caused by the hairs growing in a wrong direction.

After this short account of the results of hystological investigation of the hairless skin of the mouse other reports will be examined in chronological order.

BONNET (1892), in a description of the skin of a hairless goat, indicates the abnormally strong development of the epidermis, the keratosis, associated with the retarded shedding of the hairs. In the areas where the hairs had not yet erupted the continuous horny layer of the epidermis was from 2—4 times thicker than in normal goats of the same age and in the same parts of the body. Plugs of stratum corneum entered deeply into the hair-follicle openings and sometimes even reached the region of the sebacious glands. The Malpighi layer was of normal thickness. The single basal layer was followed by a three- or fourfold layer of fibred (KÖLLIKER) cells. The eleidin layer was of unequal thickness. All over the head there were areas with especially thick epidermis, the basal cell-layer and the Malpighi layer consisting of 3—5 rows of cells were followed by a three-to sixfold layer of eleidin granules and then by a compact or a spongy layer which was at least as thick as the layer of fibred cells and the eleidin layer together. The horny layer peeled off the skin either directly over the layer of eleidin, in which case the plane of exfoliation was in the region of the stratum lucidum, or even higher; in this case the place of separation was marked by cracks in the horny layer at various heights. In some places where the eleidin layer was interrupted, the horny layer was thickened. BONNET regards the abnormal thickness of the horny layer as an application of LEYDIG'S law that the density of the stratum corneum is the reciprocal of the thickness of the hair cover.

KRAUS (1903) studied histologically atrichosis of the skin of a girl aged 3 years and one-half and of a boy aged one year and one-half. The different dermal layers showed a normal structure, but there was a complete lack of hairs, hair-sheaths, and hair-papillae. Hair primordia however, were found, though fewer than in normal individuals.

A. FURLOTTI (1910) investigated the skin of a mole *Talpa europaea* which was entirely hairless with the exception of the

sensory hairs of the snout and the feet and also the hairs of the end of the tail. Within the skin the follicles had developed so abundantly that the interfollicular connective tissue was quite absent. The overdeveloped stratum corneum extended into the hair-follicles. FURLOTTI thinks that the hypertrophy of the stratum corneum had retarded the development of the hair cover.

F. PRINZHORN (1921) examined three young hairless dogs. The puppies had a very thin skin, at later stages the skin became of normal thickness. The epidermal layer with the stratum corneum was well developed and normal, and so was the structure of the corium, only the strands of connective tissue were difficult to distinguish from the subcutis. With age the structure of the skin changed, the number of the nuclei of the corium as well as that of the blood-vessels diminished. The stratum cylindricum was not distinguishable in some places. The stratum germinativum also showed a poor development in some areas, while the stratum granulosum was either hardly visible or even entirely lacking. The stratum corneum showed peripheral exfoliation in some places and hypertrophy in others.

BERGLUND (1927) in a description of the reduced hair-cover of an adult man's skin states that the skin from the head showed a very thin epidermis with a spongy stratum corneum. The skin of one of the daughters of this individual showed a similar structure.

MOHR and WRIEDT (1928) studied histologically the atrichotical skin of a calf. The animal was entirely hairless, excepting the head, the feet, the tail, the umbilical and the pubic region. The follicles, however, were developed in the hairless areas of the skin. The development of the skin was at the stage of the hair "Anlagen" for only in very few cases rudiments of hair papillae were discernible. The epidermis was less developed than in normal individuals, while the sebaceous glands were larger than normal, and showed a cystical development. The hairy areas of the skin were quite normal histologically.

Besides the above-indicated works on the hystology of atrichosis (hypotrichosis) a special interest to us is presented by ZIEHEN's work (1926) on the dermal hystology of the normally haired grey and the albino house mice and by the investigation of the skin of the reindeer by BRAUN and OSTROVSKAJA (1933).

ZIEHEN writes: The thickness of the corium varies according to the stage of development of the hair. At the stage of the hair club the thickness of the corium is considerably reduced in winter as well as in summer, when compared with the stage of the hair-papillae in spring and in autumn, the downward growth of the epithelial projections progresses conjointly with the increase in thickness of the corium.

According to BRAUN and OSTROVSKAJA the skin of the reindeer is characterised by perceptible seasonal variations. In November the corium is much thicker and contains especially many collagen fibres, in March its thickness decreases. In November the corium shows little fat which, however, is abundant in the subcutis. In March fat is no longer found in the corium, and even the subcutis contains but a small quantity.

In conclusion to this short survey of the literature pertaining to the question I take the opportunity of expressing my deep gratitude to my teacher Prof. Dr. N. G. LEBEDINSKY for the problem he gave me to deal with and for his kind advice during my work on the same.

II. Materials and Methods.

Materials for investigation — normally-haired, half-naked, and naked albino mice were obtained from the vivarium of the Institute of Comparative Anatomy. In all, 36 animals were examined, among these 11 normal non-adult individuals, beginning with newly-born ones, and 7 normal adult specimens, 10 half-naked non-adult individuals, beginning with newly-born ones, and 6 half-naked adult ones, and finally 2 naked adult individuals.

The skins were fixed in ZENKER's fluid. The skins of the non-adult specimens were embedded in $52^{\circ} + 54^{\circ} + 58^{\circ}$ paraffin, those of adult mice, in celloidin-paraffin, $56^{\circ} + 58^{\circ}$ paraffin being used at this occasion.

For embedding the skin was usually taken from the middle of the dorsum, from the half-naked specimens, haired and hairless portions. From several normal and half-naked adult mice the skin was taken from the anterior, the middle, and the posterior part of the dorsum. The $6\ \mu$ thick sections were stained with haematoxylin and eosin, and according to MALLORY's three colours method.

The skins and the thickness of their different layers were measured with an micrometre eyepiece.

III. Dermal Histology of Adult Animals.

1. The Skin of the Normally-haired Mouse.

When examining macroscopically the hair-cover of the back of a normal mouse it appears quite equal in all parts. But if after cutting with a razor the hairs we examine against the light the prepared skin of the back, it appears that the skin is not of equal thickness all over, but that it is thicker and thinner in different regions. In order to be able to compare the thicker and the thinner portions of the skin microscopical preparations of both kinds of skin were made.

The Thick Skin of the Normal Mouse No. 1.

The maximum thickness of the skin is 526.6 μ .

The epidermis, the surface of which is somewhat wrinkled, is 22.6 μ to 36.7 μ thick. The thickness of the stratum corneum varies from 7 μ to 16 μ and the unequal thickness of this layer is due to the fact that the stratum corneum easily peels off the skin in single scales. The stratum granulosum, the stratum intermedium, and the stratum cylindricum are greatly reduced in some places. In the thinner portions of the epidermis the stratum granulosum is wholly absent and the epidermis consists only of 1—2 rows of cells with oval or elongated nuclei placed parallel to the surface of the epidermis. In the thicker portions of the epidermis the nuclei form 4—7 rows, those of the deeper rows being round or somewhat oval with 1—2 nucleoles and with chromatin granules, in these rows the direction of the nuclei is perpendicular to the surface of the epidermis. In the upper rows the nuclei assume a more and more oval, and even an elongated, form and are placed parallel to the surface of the epidermis. In the thicker portions of the epidermis the stratum granulosum consists of 3—4 rows of dark-staining granules. These rows consist of separate about 12 μ long aggregations of granules stretching parallel to the surface of the epidermis.

The corium is made up of two layers: the upper very dense layer which consists of rough fibres of connective tissue placed very near to one another and the lower spongy layer — the stratum reticulare. The latter is built up of very fine fibres of connective

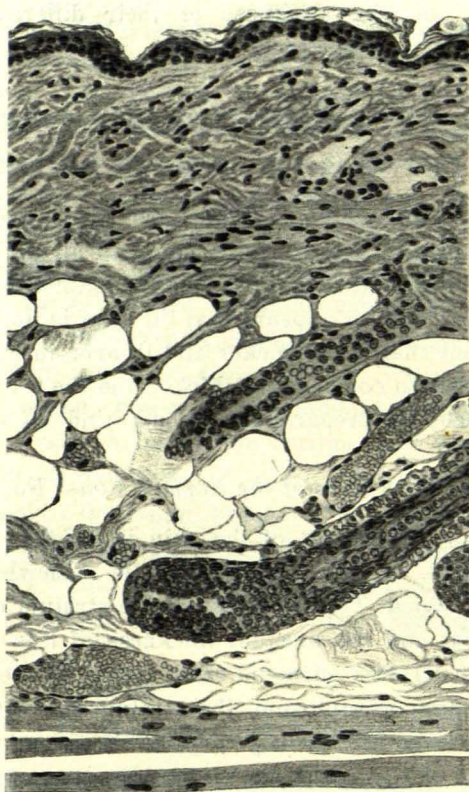


Fig. 4. Normally haired adult mouse. Thick skin. Sagittal section, 240 \times .
The hair-root has reached its maximum length.

tissue joined to one another in the form of a net. The dense layer contains a much greater number of nuclei than the porous, the form of the nuclei being round, oval, elongated, and spindle-like. Cross-sections of blood-vessels are discernible in the spongy layer. While the upper layer is only 167,5 μ thick the lower layer attains 279,1 μ in thickness. The maximum thickness of the skin-musculature is 52,7 μ . About 895,7 μ long hair-roots are found in the skin, they extend through the whole corium and to the skin musculature. At the ends of these roots are seen well developed hair-bulbs and papillae. Along with these roots there are others which from their proximal, *i. e.* bulbshaped, end begin to narrow. They no longer possess hair-papillae.

There are also to be seen hairs in pairs. These pairs consist either of one long and one short hair-root, or of two short ones. Complexes of one long and two short hair-roots have also been observed.

The Thin Skin of the Normal Mouse No. 1.

The maximum thickness of this skin is only 225,2 μ . Thus it is about half as thick as the thick skin of the same animal. This astonishing difference in the thickness of the skin in one and the same individual depends only on the deeper layer of the corium, the stratum reticulare, for if we compare the epidermis and the upper layer of the corium no noticeable difference as to thickness can be found, but the stratum reticulare which constitutes about half the thickness of the thick skin is quite absent in the thin skin.

The thickness of the epidermis varies from 26,7 μ — 37,3 μ , differences being found not only in the stratum corneum but in the other layers of the epidermis as well.

The maximum thickness of the stratum corneum is 21,4 μ .

The stratum granulosum is quite absent in the thinner portions of the epidermis, the latter being made up only of 1—2 rows of cells with elongated nuclei. In the thicker part of the epidermis the granules of the stratum granulosum are placed in 2—3 rows, the stratum cylindricum together with the stratum intermedium consist of 5—7 rows of cells with big oval nuclei in which nucleoli and chromatin granules are well discernible.

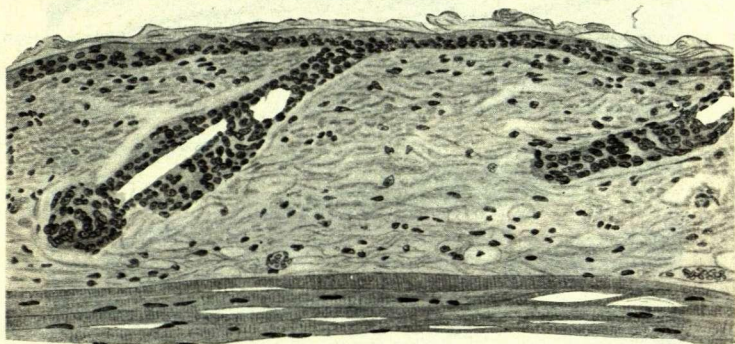


Fig. 5. Normally haired adult mouse. Same specimen as in fig. 1. Thin skin. Sagittal section, 240 \times . The corium consists only of a compact layer. Shortened hair-root with "Anlagen" of the new hair at its end.

In structure and thickness the thick layer of the corium does not differ from that of the thick layer of the corium of the thick skin. The maximum thickness of the skin musculature is 47 μ .

The hair-roots are short, their length being 200 μ . The hairs are placed in pairs, these erupting through one pore of the skin. A round grouping of nuclei, rich in chromatin, can be observed at the end of the outer sheath of one of these pairs of hairs, and precisely of that one which forms an acute angle with the surface of the epidermis. This is the germ of the new hair which is to replace the hair that will fall out. It continues growing in length and resembles the hair "Anlagen" of a newly-born mouse with only the difference that in this instance it does not form in the stratum cylindricum of the epidermis, but much deeper, in the corium, from the cells of the end of the outer sheath of the short hairs which will later fall out.

The Thick Skin of the Normal Mouse No. 2.

The maximum thickness of the skin is 355,7 μ .

The epidermis is very thin, its maximum thickness being 23 μ , of which 16 μ are occupied by the stratum corneum. The other layers of the epidermis are strongly reduced, and in some places the epidermis consists of one single row of very elongated nuclei. The thickness of the upper compact layer of the corium is 71,4 μ , that

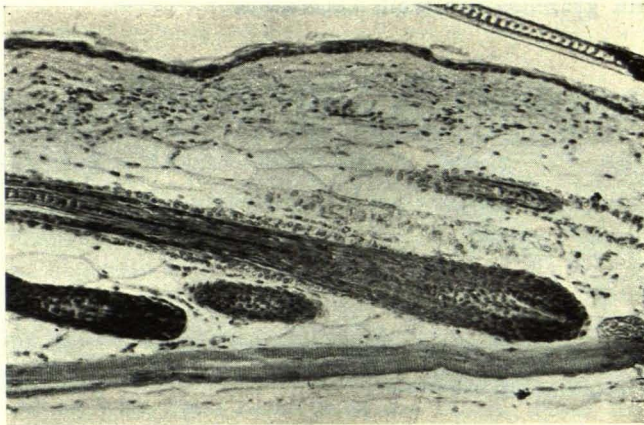


Fig. 6. Normally haired adult mouse. Thick skin. The hair-root has attained its maximal length. Figures 6—11 show sagittal sections, 128 \times .

of the deeper spongy layer $235,3 \mu$. Thus the latter forms $\frac{2}{3}$ and in some places even $\frac{3}{4}$ of the entire corium. Within the skin pairs of hair-roots are found, these consist of a) one long and one short hair-root, and b) of 2 short hair-roots. The long hair-roots show different stages of shortening.

The Thin Skin of the Normal Mouse Nr. 2.

Maximum thickness of this skin is $264,9 \mu$.

When compared with the thick skin no particular difference is found in the epidermis.

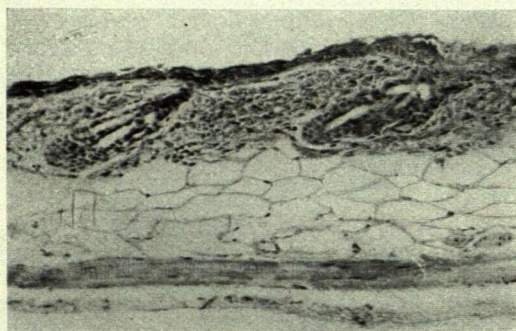


Fig. 7. Normally haired adult mouse. Same specimen as in fig. 6. Thin skin. The porous layer of the corium is only half as thick as in the thick skin. Shortened hair-roots.

The thickness of the compact layer of the corium is equal to that of the thin skin, while the spongy layer is half as thick, its thickness being only 121μ . As to structure both layers of the corium of the thin skin do not differ from those of the thick skin.

All the hair-roots are short, and lie in pairs in the upper layer of the corium.

2. The Skin of the "Half-naked" Mouse.

The Haired Skin of the Mouse No. 3.

Maximum thickness of the skin is $510,8 \mu$.

The epidermis, the surface of which is wrinkled to a certain extent, is $8,6 \mu$ — $25,7 \mu$ thick, the stratum corneum, as well as the other layers of the epidermis varying in thickness. The stratum

corneum is mostly $4\ \mu$ — $6\ \mu$ thick, in some places only its thickness reaches $17\ \mu$. The stratum granulosum is feebly developed, and for the greater part consists of one interrupted row of small nuclei, in some places it cannot be detected.

In the areas of the wrinkles the stratum intermedium together with the stratum cylindricum of the epidermis consist of 3—4 cell rows with oval nuclei, in the portions between the wrinkles there are only 1—2 rows, the nuclei of these cells are elongated. The

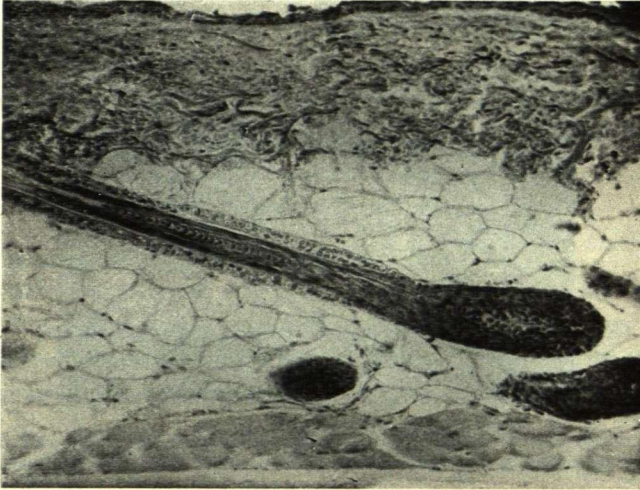


Fig. 8. Adult half-naked mouse. Haired. *i. e.* thick, skin. The hair-root has attained its maximal length.

corium shows very clearly the division into the upper compact layer of connective tissue and the lower spongy layer. The maximum thickness of these layers is $152,1\ \mu$ and $321,4\ \mu$ respectively.

The thickness of the skin musculature is $20\ \mu$ — $37,3\ \mu$. Within the skin are found: 1. long hair-roots extending as far as the skin musculature and which are even up to $1000\ \mu$ long, 2. short hair-roots which are located only in the thick layer of the corium and are $150\ \mu$ — $180\ \mu$ long, 3. hair-roots at different stages of shortening and the length of which varies between that of the long and the short roots. There are also pairs of hairs consisting of one long and one short hair-root. The hair-roots that have begun to shorten are slightly bent at their proximal end. Within the skin

there are also some hypokeratinized hairs, such as have been described by DAVID. These hairs are bent to such an extent as to deform all the hair-follicle. Cysts filled with stratum corneum substance are also found in the hair canals, the stratum corneum substance in the cysts being a direct continuation of the stratum corneum of the epidermis.

The canals contain also tangled hairs.

The Hairless Skin of the Mouse No. 3.

Its maximum thickness is 204,9 μ , this skin being thus less than half as thick as the haired skin of the same animal.

The maximum thickness of the epidermis is 18,8 μ , the epidermis consisting of 1—3 rows of round or oval nuclei. In some places

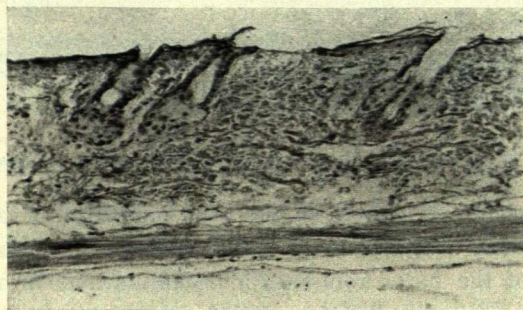


Fig. 9. Adult half-naked mouse. Same specimen as in fig. 8. Hairless, *i. e.* thin, skin. Shortened hair-roots.

the oval nuclei are situated in a direction parallel to the surface of the skin, and in a perpendicular direction in other places. The stratum corneum is 13,4 μ thick and mostly peels off the skin. The stratum granulosum is poorly developed. The upper layer of the corium is 143,5 μ thick. It is only a little thinner than that of the haired skin, while the deep spongy layer, the maximum thickness of which is only 39,3 μ equals but $\frac{1}{8}$ of the thickness of the spongy layer of the haired skin. As to structure the corium does not differ from that of the thick haired skin.

The maximum thickness of the skin musculature is 31,8 μ . Within the skin there are only short hair-roots. The hair-canals are much enlarged.

The Skin with Sparse Hair Growth of the Mouse No. 4.

The maximum thickness of this skin is 190,5 μ .

The epidermis with a moderately wrinkled surface is 12,3 μ to 23 μ thick. In some places the stratum corneum is quite peeled off. In the regions where it is still present it is 4 μ — 16 μ thick. No stratum granulosum is found. The stratum intermedium and the stratum cylindricum are also much reduced, and consist of only 1—3 rows of cells with round and oval nuclei. The thickness of the upper layer of the corium is 76 μ , that of the lower 66,4 μ .

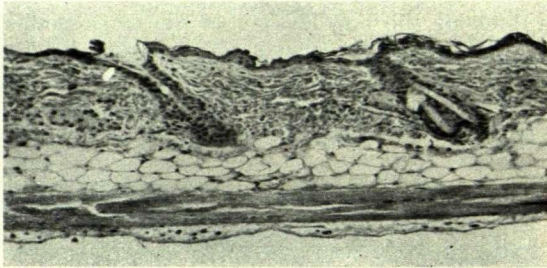


Fig. 10. Adult half-naked mouse. Skin with sparse hair-growth.

The maximum thickness of the skin musculature is 53 μ . Only short hair-roots, single and in pairs, are found within the skin. At the end of the outer root-sheath accumulations of round nuclei rich in chromatin granules are visible. These are the germs of the next hair-growth. The upper layer of the corium contains egg-shaped hair-canal cysts, at the end of which there are also hair "Anlagen" in process of formation. In the region of the sebaceous glands cysts-atheromata as described by DAVID are found.

3. The Skin of the "Naked" Mouse.

The maximum thickness of the skin is 197,9 μ .

The epidermis, the surface of which is slightly undulated, is 23 μ — 26 μ thick. The greater part of this layer is occupied by the stratum corneum which may attain a thickness of 16 μ .

The stratum granulosum is very poorly developed and is visible only in some places where it is seen to consist of rows of granules almost fused together. The stratum intermedium and the stratum cylindricum consist of 1—3 cell rows. The nuclei are irregularly distributed within the epidermis and vary as to their form from

round to oval, in the thinner portions of the epidermis they are much elongated. No lower spongy layer of connective tissue is found in the corium which is quite compact.

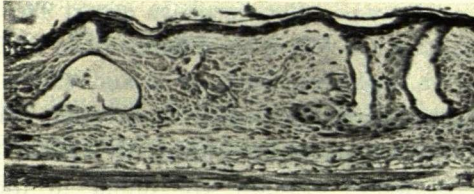


Fig. 11. Adult naked mouse.

As to the distribution of the nuclei in the corium, these are mostly found in the lower side of the corium, near the skin musculature. Immediately under the epidermis the corium contains very few nuclei. These vary as to size and shape being round, oval, elongated and spindle-shaped. Directly over the skin musculature, which is $6\ \mu$ — $14\ \mu$ thick, cross-cuttings of the blood-vessels with the red blood corpuscles are found. Normal hairs and hair-follicles do not develop in the skin, but there are hair-follicle cysts, follicle-end cysts, and cysts formed in the region of the sebaceous glands, as described by DAVID. Another naked individual presents a somewhat more peculiar structure of the skin:

Thickness of the skin — $175\ \mu$, of which about $37\ \mu$ is occupied by the skin musculature.

The epidermis is very thin, being at its maximum only $14.3\ \mu$, the stratum corneum occupies half of the thickness of the epidermis. The other layers are much reduced, so that the epidermis is mostly made up of one single cell layer with oval or very elongated nuclei.

The corium consists almost only of a compact layer of connective tissue. Its nuclei are of different shapes, but their distribution in the corium is uniform. There are also hair-follicle cysts.

IV. The Post-natal Development of the Skin.

1. Development of the Skin of the Normally-haired Mouse.

The maximum thickness of the skin of the newly-born mouse is $138.5\ \mu$.

The epidermis is wrinkled, at the outer surface to a higher degree than at the boundary of the epidermis and the corium. In consequence of this wrinkling, the skin is thicker in some portions and thinner in others. The thinness of the skin is chiefly due to the thinness of the epidermis in the respective areas. Two adjacent portions of the skin show the following differences in thickness: 133,4 μ and 119,7 μ , — the epidermis being 53 μ and 42,1 μ thick respectively. In the deepest epidermal layer, the stratum cylindricum, are found big, round and oval, nuclei with easily visible 1—2 nucleoles and chromatin granules. Mitoses are found in the nuclei. The nuclei of the stratum intermedium are also oval or round, with 1—2 nucleoles, but they do not contain so many chromatin granules as the nuclei of the stratum cylindricum and therefore appear much lighter than the latter. In the stratum intermedium the nuclei are not directly surrounded by the protoplasm, it seems as though the protoplasm had receded from them, and round each nucleus there is a light space. The stratum granulosum is very well developed and consists of 3—4 rows of granules parallel to the surface of the skin. In the lower rows these granules are very small, in the upper rows they are bigger and not always round, they may assume the shape of a cube with rounded edges. The stratum corneum is built up in rows. The structure of the corium is not homogeneous throughout: a much greater amount of connective tissue fibres and of nuclei is found in the upper layer than in the lower. The shape of the nuclei varies much, they are round, oval, elongated, and spindle-shaped.

Hair germs at various stages of development are found in the skin of the newly-born mouse. Some of them only begin to form, and consist of aggregations of stratum cylindricum slightly sunk into the corium, whereas others have attained a length of 140 μ , and extend obliquely about 77 μ deep into the corium. The diameter of such follicles is 40 μ and the papilla is already forming.

The maximum thickness of the skin of the 1 day old mouse is 168 μ the epidermis being 56,1 μ thick. When compared with the skin of the newly-born specimen we observe that the epidermis has become thicker and that the stratum corneum has reached 34,7 μ . As to structure the epidermis shows no difference when compared with that of the newly-born mouse.

The division of the corium into an upper and a lower layer has become more definite, and is especially conspicuous in preparations stained according to the method of MALLORY.

In the upper layer the nuclei stained with haematoxylin are dark blue, the nuclei of the deep layer are bigger, and appear of a reddish violet. The thickness of the upper layer is 55 μ , that of the lower- 43,1 μ .

The hair-follicles show a quite developed hair cone, rudiments of the sebaceous glands, and the elevation of the outer hair-sheath.

Depressions appear in the layers of the stratum granulosum of the epidermis, they mark the places where the hairs will erupt.

The maximum thickness of the skin of the 2 days old mouse is 206,3 μ , that of the epidermis 60,4 μ .

The stratum corneum is very well developed and 36,1 μ thick, it is twice, and in some places even three times, thicker than all the other layers of the epidermis together. The thickness of the upper layer of the corium is 56,7 μ , the already typically reticular lower layer being 68,8 μ and in some places 86,1 μ thick. The hairs have reached the upper part of the stratum corneum, but have not yet emerged from the skin.

The thickness of the skin of the 3 days old mouse is 317,4 μ , that of the epidermis, 66 μ . In thickness and structure the epidermis does not show any difference from that of the 2 days old animal. Neither does the upper layer of the corium present any noticeable difference, but the lower porous layer is more than twice as thick as the porous layer of the 2 days old mouse, its thickness being 182 μ .

The hair-roots extend through the whole corium reaching the skin musculature, the hairs have already found their exit through the stratum corneum and rise about 280 μ above the skin.

The skin of the 4 days old mouse is not, as one might suppose, thicker than the skin of the 3 days old mouse, it is thinner, its maximum thickness being 271 μ . This is an individual variation of the thickness of the skin and very likely to depend on the weaker constitution of the animal. The maximum thickness of the epidermis is 68,8 μ . The stratum corneum is especially well developed being 51,6 μ thick, while in its other layers the epidermis has become somewhat thinner.

The thickness of the upper layer of the corium equals 66,5 μ , the lower layer being 133,9 μ .

The skin of the 5 days old mouse shows again an increase in thickness. Its maximum thickness is 393,1 μ , that of the epidermis 63,1 μ .

The lower layer of the corium has become much thicker, reaching 229 μ , it is thus twice as thick as that of the 4 days old mouse. The upper layer of the corium is 103,2 μ thick.

The skin of the 6 days old mouse is thinner than that of the 5 days old one. It is 313 μ thick, the epidermis being 51,8 μ . Compared with the epidermis of the 5 days old mouse it is thinner in the stratum corneum as well as in the stratum cylindricum and the stratum intermedium, the layer of the stratum granulosum being thicker.

The lower layer of the corium is 199,1 μ thick, and forms $\frac{2}{3}$ and in some places even $\frac{3}{4}$ of the whole corium.

The maximum thickness of the skin of the 7 days old mouse is 368,4 μ , that of the epidermis 51,3 μ .

With the exception of the stratum corneum the epidermal layers are thin and poor in nuclei. In some areas 2—3 rows of oval or much elongated nuclei are visible while in others the epidermis is made up of one row. The nuclei are mostly located parallel to the upper surface of the epidermis.

The reduced stratum granulosum consists of 1—2 rows of granules. In the upper row the single granules cannot be distinguished as they are blended together.

The lower layer is 255 μ thick and forms $\frac{4}{5}$ of the whole corium.

The skin of the 8 days old mouse has a maximum thickness of 416,9 μ , the epidermis 60 μ . The structure of the epidermis and of the corium does not differ from that of the 7 days old animal.

The maximum thickness of the skin of the 12 days old mouse is 379,4 μ , that of the epidermis varies from 25,7 μ to 41,3 μ and this variation depends on the thickness of the stratum corneum as well as of the other layers of the epidermis.

The stratum corneum is 29,7 μ thick, the stratum granulosum is weakly developed and only in some places can it be distinguished as a row of small nuclei.

The stratum cylindricum and the stratum intermedium are made up of 1—4 rows of nuclei which in the thick parts of the epidermis are round or oval and rich in chromatin, in the thinner parts they are elongated.

The lower layer of the corium is 265,2 μ thick, being 3 times and in some places even 4 times thicker than the upper layer. The hair-roots that extend even to the skin musculature begin to shorten from their proximal end.

The skin of the 14 days old mouse has a maximum thickness of 311,3 μ , the epidermis, 27,4 μ . The stratum corneum is 14,3 μ thick and easily peels off the skin.

The stratum granulosum is almost entirely lacking, the stratum cylindricum and the stratum intermedium are also poorly developed. The epidermis consists in some places of one single row of elongated nuclei.

The lower layer of the corium is 201,9 μ thick, being thus thinner than that of the 12 days old individual. This depends on the shortening of the hair-roots.

2. The Development of the Skin of the "Half-naked" Mouse.

The skin of the newly-born half-naked mouse differs neither in thickness nor in structure from that of a newly-born normal animal.

The maximum thickness of the skin is 154,9 μ , that of the epidermis 50,4 μ . All the layers of the epidermis are well developed.

The stratum corneum is 30,7 μ thick.

The corium is 101,5 μ thick and its division into the upper and the lower layer is already indicated.

The hair germs are at different stages of development, while the greater part consists of an aggregation of nuclei of stratum cylindricum which extend more or less into the corium, some show already a well developed hair-papilla, the hair cone, and the elevation of the outer hair-sheath.

In the epidermis depressions of the stratum corneum and of the stratum granulosum are observed, these are the places where the hairs will erupt.

The thickness of the skin of the 1 day old mouse varies from 142,2 μ to 221,8 μ , the surface of the skin being much wrinkled. The epidermis, 36,4 μ — 64,4 μ , and the corium, 91,8 μ — 146,9 μ , both show variations in thickness.

In some places the division of the corium into the upper and the lower layer is yet very indistinct.

Some hairs have already reached the deep surface of the epidermis and their follicles show sebaceous gland cells.

The skin of the 2 days old mouse is not thicker at its maximum than that of the one-day old, it is thinner, reaching only 196,2 μ in thickness. This is again an individual variation depending on the general constitution of the animal.

The epidermis is 58,7 μ thick. Comparing the epidermis with that of the 1 day old animal we see that it is the stratum corneum which has become thinner. Its thickness varies from 10 μ — 35,8 μ , and this variation is a sequel of the partial exfoliation of the stratum corneum. The other epidermal layers are quite well developed, especially the stratum granulosum which in some places is even 10 μ thick and consists of 4—6 very clearly visible rows of granules.

The upper layer of the corium is 58,8 μ thick, the lower 67,4 μ . The latter already shows a reticular structure.

When passing through the epidermis the hairs bend, such bending is also observed in the middle part of the hair-roots. As has already been indicated by DAVID in her above-mentioned paper, the hairs bend because they grow, but being insufficiently keratinized cannot break at once through the stratum corneum.

The skin of the 3 days old mouse is much wrinkled and therefore its thickness varies from 292,7 μ — 397,4 μ . When compared with that of the 2 days old animal this skin shows a much greater thickness in all its layers.

The epidermis attains 77,4 μ , all its layers are particularly well developed, the stratum corneum being 43,6 μ the stratum granulosum 14,6 μ , and the stratum intermedium together with the stratum cylindricum, 19,1 μ , thick.

The upper layer of the corium varies from 90,4 μ — 141,7 μ , the deeper, from 124,8 μ — 170,1 μ .

The hairs have not yet erupted, their bent tips are in the stratum corneum.

The skin of the 4 days old mouse is not much wrinkled at its surface. Its maximum thickness is 371,4 μ , that of the epidermis 68,8 μ . The layers of the epidermis are well developed.

When compared with that of the 3 days old mouse the upper layer of the corium is thinner, attaining only 83 μ , whereas the lower layer is thicker, its maximum thickness is 220,9 μ and it forms almost $\frac{3}{4}$ of the entire corium.

In some instances the hairs do not pass through the epidermis in the place where the stratum granulosum and the stratum corneum have formed depressions, but force another exit through the epidermis.

The maximum thickness of the skin of the 5 days old mouse is 419,5 μ and, when compared with that of a 4 days old mouse, this skin shows an increase in thickness, less in the epidermis, but to a greater extent in the deep layers of the corium. The maximum thickness of the stratum corneum is 49 μ .

The upper layer of the corium is 82,3 μ thick, the lower 264 μ .

The hair has already erupted through the stratum corneum.

The maximum thickness of the skin of the 8 days old mouse is 657,7 μ , that of the epidermis 84,8 μ , 68 μ being occupied by the stratum corneum.

The stratum granulosum is feebly developed and in some places consists only of one single row of very small granules. The stratum intermedium together with the stratum cylindricum vary from 10,3 μ to 14 μ .

The upper layer of the corium is 111,8 μ thick, the lower, 474,9 μ . There are many long hair-roots within the skin.

The skin of the 12 days old mouse is 476,9 μ thick at its maximum, thus showing a decrease in thickness.

The maximum thickness of the epidermis is 40,1 μ , that of the stratum corneum 30,7 μ . The stratum granulosum is almost entirely lacking and can be detected only in some places as a row of small granules.

Excepting the stratum corneum the epidermis is altogether very thin and consists only of 1—2 rows of oval or elongated nuclei located parallel to the surface of the skin.

The corium shows also a reduced thickness in both layers. The maximum thickness of the upper layer is 94,4 μ , that of the lower 35,5 μ .

The hair-roots begin to shorten from the proximal end. In several follicles coiled hairs are found.

The thickness of the haired skin of the 14 days old mouse is 389,4 μ , that of the epidermis 29,3 μ .

The stratum corneum shows much exfoliation, in the isolated areas where it still remains it is 22,3 μ thick. The other layers of the epidermis are greatly reduced, and the epidermis consists for the most part of one single row of elongated nuclei.

The upper layer of the corium is 72,3 μ , the lower 286,3 μ thick, thus both layers of the corium are thinner than in the 12 days old animal.

The long hair-roots found in the skin begin to shorten from the proximal end. Some are already quite shortened and lie only in the upper row of the corium.

The thickness of the hairless skin of the 14 days old mouse is 339,4 μ , that of the epidermis 24,6 μ . The stratum corneum is 15,1 μ thick, the other layers of the epidermis are much reduced.

The lower layer of the corium is 250 μ thick. There are very few long hair-roots in the skin, most of the hair-roots are reduced by half or quite short.

The haired skin of the 15 days old mouse shows a maximum thickness of 288,4 μ , the epidermis 22,6 μ .

The stratum corneum is 10,3 μ thick, the stratum granulosum is feebly developed and is to be seen only in some places. The stratum intermedium together with the stratum cylindricum consist of 2—4 rows of cells.

The upper layer of the corium is 82,8 μ , the lower — 165,5 μ , the corium being much thinner than that of the hairless skin of the 14 days old mouse.

The hair-roots show different stages of shortening.

The maximum thickness of the hairless skin of the 15 days old mouse is 241,9 μ , that of the epidermis being 19,4 μ . The stratum corneum is 15,1 μ thick. The layers of the epidermis are much reduced.

The upper layer of the corium is 63,1 μ thick, the lower 159,2 μ .

The hair-roots are very much shortened.

V. Summary.

Comparing the skins of the normally-haired, the half-naked, and the naked mouse I have found:

1. The thickness of the skin depends entirely on the length of the hair-roots contained therein, the thickness of the skin being in direct proportion to the length of the roots.

2. The unequal length of the hair-roots is associated with the shedding and regrowth of the hairs on the skin of the mouse for, as is well known, during this change the hairs that are to fall out begin to shorten from their proximal, *i. e.*, bulbshaped, end.

3. The variations in the thickness of the skin in adult mice chiefly depend on the variations in the lower layer of the corium, the stratum reticulare, for when the hair-roots shorten, this layer may be reduced in thickness 2—8 times, and may even disappear entirely.

4. The structure of the skin of the half-naked mouse is normal, the haired skin of the half-naked mouse being like the thick skin of the normal mouse, for in both long hair-roots are found. The naked skin of the half-naked mouse is like the thin skin of the normal mouse, as both contain short hair-roots.

That the skin of the half-naked mouse is hairless in such places where short hair-roots are found, while the skin of a normal mouse is haired in the corresponding places, depends on the fact that when the hair-roots shorten the insufficiently keratinized hairs of the half-naked mouse break off at the surface of the skin. The short-rooted hairs of the normal mouse do not break, but cover the body until the new hair-generation is fully developed and appears above the surface of the skin, after which the short-rooted hairs are gradually shed.

5. The thinness of the skin of the naked mouse depends on the fact that long hair-roots never develop in it.

6. The post-natal development of the skin of the normal and of the half-naked mouse follow in general the same course. The structure and the different layers of the skin of a newly-born normal mouse and of a newly-born half-naked mouse are identical.

With the progressing age of the young animal the skin gradually augments in thickness, in the epidermis as well as in the corium. Of the epidermal layers it is especially the stratum corneum which increases while in the corium it is the stratum reticulare which in an 8 days old mouse may be even 10 times as thick as in a newly-born one. The skin thickens until the hair-roots have reached their maximum length. On the 12th day after birth, when the hair-roots begin to shorten at their proximal ends, the thickness of the skin begins to decrease.

7. Basing on the results of these histological investigations of the skin we come to the following theoretical conclusion: as the thickness of the skin of the naked mouse is not less than that of the normal mouse in the period of the hair change, the thinness of the

skin of the naked mice is not to be considered as a newly acquired character, but only as a sequel of the lack of hair.

8. A further inference from this conclusion is that the thinness of the skin of the hairless varieties of domestic animals is also only a correlative feature.

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