THE REGIONAL ANATOMY OF THE HUMAN INTEGUMENT WITH SPECIAL REFERENCE TO THE DISTRIBUTION OF HAIR FOLLICLES, SWEAT GLANDS AND MELANOCYTES

By G. SZABÓ*

Department of Zoology, University College London

(*Communicated by Sir Peter Medawar, F.R.S.—Received* 6 *May* 1964—*Revised* 24 *March* 1966)

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* Present address: Department of Dermatology, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts, 02114, U.S.A.

Vol. 252. B. 779. (Price £1. 1s.; U.S. $3.15) 56 [Published 22 September 1967

The regional anatomy of human skin is discussed in terms of (*a*) the regional variation of the architectural pattern of the basal layer of the epidermis, (*b*) the regional variation in the distribution of hair follicles and eccrine sweat glands, and (*c*) the regional variation in the distribution of melanocytes.

(*a*) The architecture of the basal layer is regionally specific. The epidermis of the cheek is almost flat between the numerous hair follicles. Regions under tension have parallel ridges that end abruptly (neck, breast, abdomen); regions with a thick keratin or mucous layer have deep ridges with circular imprints of tall dermal papillae (sole, palm, knee, heel and oral mucosa). Elsewhere in the epidermis the creases of the skin surface divide the pattern of the basal layer into diamond-shaped areas where the imprints of the dermal papillae are to be seen.

(*b*) There is great individual and regional variation in the distribution of hair follicles and sweat ducts: 700 ± 40 hair follicles per cm^2 were counted on the face, but only 65 ± 5 in the rest of the body. The corresponding density for eccrine sweat glands was 270 ± 25 in the face and 160 ± 15 in the rest of the body. There are altogether about two million hair follicles and three million sweat glands in the integument. The epidermal appendages are symmetrically distributed; there is no significant difference between male and female in the density of hairs or sweat glands. The density of appendages is much higher in the foetus and in the infant than in the adult. Numerical estimates have shown that the differential rate of growth of the body surface may be solely responsible for regional differences in the density of appendages. A uniformly distributed foetal population of appendages would become 'diluted' three times more on the trunk and extremities than on the head during postnatal growth. The numerical ratio of sweat ducts/hair follicles is the same throughout foetal and postnatal life.

(*c*) On the average there are about 1500 epidermal melanocytes/mm^2 of skin surface, excluding those in hair follicles. The total number of epidermal melanocytes in an adult is about 2000 million. They occur consistently in the basal layer of the epidermis of 'white' human skin (including the oral and nasal cavities). Their absolute number and their proportion to the keratinizing basal Malpighian cells are constant and characteristic in given regions.

The distribution of melanocytes is also bilaterally symmetrical and their regional frequency is the same in male and female. The individual and regional variations of melanocyte distribution are, however, great. There are two or three times as many melanocytes per unit area in the epidermis of the cheek or forehead as in the other regions of the integument. Because melanocytes are mostly located on ridges, the numerical ratio of Malpighian cells/melanocytes is lower on than between the ridges.

The cause of the great regional variation of melanocytes is not known. The regional differences are smaller in foetal than in adult skin. Regional differences in the degree of expansion of the body surface by growth cannot, however, explain the regional variation in the adult.

Melanocyte density in the foetus is lower than in the adult, and in old epidermis a decrease in melanocyte density is one of the manifestations of ageing.

Comparisons of the frequency distribution of melanocytes reveal no significant difference between the various human races. The degree of melanization of skin therefore depends not only on the number of melanocytes, but, more particularly, on their physiological activity in melanogenesis.

The absolute number of melanocytes and the ratio of Malpighian cells/melanocytes are high enough to allow melanocytes to make contact with every Malpighian cell and so to disseminate melanin through the entire basal layer of the epidermis.

The salient statistical data are presented in the following table:

	hair follicles (av. no./cm^2 ± S.E.)	sweat ducts (av. no./cm^2 ± S.E.)	melanocytes (av. no./mm^2 ± S.E.)
face	700 ± 40	270 ± 25	2120 ± 90
trunk	70 ± 10	175 ± 20	890 ± 70
arm	65 ± 5	175 ± 15	1160 ± 40
leg	55 ± 5	130 ± 10	1130 ± 60
average	330 ± 20	215 ± 15	1560 ± 110

1. Introduction

No extensive quantitative studies of the regional differences of human skin have been reported in the last fifty years. According to a recent comprehensive treatise (Horstmann 1957) the skin from various body regions can be characterized only in descriptive terms without benefit of numerical data. Modern textbooks (e.g. Rothman 1954) still cite Drosdoff (1879) on the regional variations in the thickness of the epidermis, Krause (1844) on the regional distribution of sweat glands and Meyer-Lierheim (1911) on the distribution of hair in the foetus. The older data are imperfect in various ways. It has been the aim of the present investigation to compensate for some of their shortcomings. The regional anatomy of the human integument will be described by qualitative and quantitative analysis of the occurrence of various components of the epidermis, such as ridges, appendages and melanocytes.

Gross regional differences in the human integument are obvious. For instance, visible hairs are restricted mostly to the scalp, cheeks, axillae, chest and pubic regions (Danforth 1925*a*; Reynolds 1951) where their number and quality vary between the sexes. Hairs are absent on the soles and palms. The regeneration and the rate of growth of hair vary from region to region (Myers & Hamilton 1951); so also does the output of sweat (Kuno 1938; Weiner 1945; Randall 1946) and sebum (Emanuel 1936; Herrmann & Prose 1951). Other attributes that vary from region to region are the distribution of 'pain spots' (Frey & Rein 1929), the pigmentation of the skin (Edwards & Duntley 1939; Edwards 1953) and the number of capillaries (Wetzel & Zotterman 1926). Skin transplants usually behave 'herkunftsweise,' as experiments on the hair slope of transplanted skin have shown (Trotter & Dawson 1931, 1932). It is a well-established concept in plastic surgery that skin regions possess structural 'autonomy' (Danforth 1939; Billingham & Medawar 1950*a*, *b*).

The currently cited statistical data on the distribution of skin appendages, however, are incomplete. The various methods of enumerating eccrine sweat ducts show the number of functioning glands and not the total number of glands. This difficulty has been overcome

by Thomson (1954), who compared the density of functioning glands with their overall number and found some indirect evidence that the counts based on functioning glands are proportional to the total anatomical counts. Past enumeration of hairs on the basis of counts made from photographs (Garn 1951) and counts of hairs longer than 2 mm that had been cut off (Schultz 1931) were inaccurate because, as Danforth (1925*a*, *b*) has pointed out, the number of visible, 'terminal' hairs does not correspond with the number of hair follicles present, since certain follicles produce only the fine, vellus type of hair. The estimates arrived at by counting follicles in sections were usually the result of complicated arithmetical procedures and general conclusions as to the hairiness of the Japanese or 'white' races often were derived from specimens taken from only one individual (Taniguchi & Kurita 1941). Danforth (1921), however, carried out a full histological and statistical study on the digital hair of man.

The present investigation carries Danforth's idea further in a complete histological and statistical survey of all areas of the integument of man.

First (§ 3A), a regional mapping of the architecture of the basal layer of the epidermis is presented. The basal layer will be viewed from beneath after the dermis has been removed. This procedure was originally recommended by Kölliker (1852) and has been successfully employed by Billingham (1948, 1949), Becker, Jr., Fitzpatrick & Montgomery (1952), Billingham & Medawar (1953), and Medawar (1953) in describing the pigmentary system of the mammalian epidermis. The study presented here is a complete scalp-to-sole study of the pattern of the basal layer of the human epidermis which complements the widely scattered studies that have appeared in the German literature (Blaschko 1887; Greb 1939; Wolf 1940; Fleischhauer & Horstmann 1951; Oberste-Lehn 1952; Fleischhauer 1953*a*, *b*; Horstmann 1952*a*, *b*, 1954, 1957).

Secondly (§ 3B), the distribution of hair follicles and sweat ducts is the basis of a statistical analysis of regional differences in human skin at the microscopic level. All follicles were counted individually, whether in groups or singly, or producing coarse or fine hair. All the counts were carried out on preparations which were processed uniformly. The term 'sweat ducts' is used instead of 'eccrine sweat glands' because in my preparations only the straight portions of the duct were included. It is assumed, however, that one duct corresponds to one gland.

Thirdly (§ 3C), the regional microanatomy of the human melanocyte system is presented in detail. Bloch (1917, 1929), Becker, Sr. (1927), Rawles (1940, 1947) and Billingham (1948, 1949) have shown that the epidermis consists of cells belonging to two distinct systems: the Malpighian, or keratinizing, system (keratinocytes) and the melanocyte, or pigmentary, system (see Medawar 1953). Epidermal melanocytes are part of the original system of four envelopes or layers of melanocytes (cutaneous, pericoelomic, perivascular, perineural) (Weidenreich 1912) that exists in lower vertebrates. They are of neural crest origin (Du Shane 1934; Rawles 1940, 1947; Hörstadius 1950). The invasion of the epidermis by melanoblasts has been described by Zimmermann & Becker, Jr. (1959). Epidermal melanocytes are already present in fishes but are of relatively greater importance in mammals, where the 'contractile' dermal melanocytes of lower vertebrates are absent. Epidermal melanocytes are integrated with keratinocytes, for pigment is not retained in the melanocytes, but is transferred into the keratinocytes ('cytocrine' action) (Masson 1948).

Melanocytes are thus true secretory cells and as such are endowed with a well-developed, rough-surfaced, endoplasmic reticulum and a Golgi zone where their product, the 'melanosome' (Baker *et al.* 1960; Seiji, Fitzpatrick, Simpson & Birbeck 1963), can be found. Histochemically, melanocytes can be demonstrated by the well-known dopa reaction of Bloch (1917). Billingham (1948, 1949) was the first to combine the skin-splitting technique of Medawar (1941) with the dopa technique, thus revealing the melanocyte system as a monocellular layer fitted into the basal layer of the keratinocytes. Following this pioneer work, Billingham & Medawar (1953) presented quantitative data on the distribution of epidermal melanocytes in the guinea-pig, and Szabó (1954, 1959*a*) and Staricco & Pinkus (1957) gave data on the distribution of the melanocytes in the human epidermis. For further data the reader is referred to the excellent review of Billingham & Silvers (1960).

2. Materials and methods

Skin specimens were obtained during plastic and gynecological surgery or at biopsy. The age of donors varied from 7 months *in utero* to 77 years. The data reported were obtained from the skin of about 350 donors.

The epidermis was separated from the corium by the skin-splitting technique of Medawar (1941) as modified by Szabó (1955). Thiersch grafts were firmly attached to a coverglass by stopcock grease, dermal side uppermost, and placed in a 0·5% solution of commercial trypsin in physiological saline. The saline was buffered by 0·05% sodium bicarbonate. The trypsin was allowed to act overnight at about 4 °C. The dermis was then removed with fine forceps and the epidermal sheet, still attached to the coverglass, was fixed in 2% formaldehyde-saline solution overnight (Becker, Sr. 1942). While still attached to the coverglass, the epidermal sheet was rinsed in distilled water and incubated twice in buffered dopa solution at pH 7·3: the first incubation took place in a water-bath at 37 °C for 1 to 1½ h until the originally colourless dopa became red or grey; the second at room temperature (60 to 65 °F) overnight. The buffered dopa solution was prepared by adding 3 ml. of Soerensen's phosphate buffer to 7 ml. of stock dopa solution (1:1000 in distilled water). A final fixation in 4% formaldehyde followed. The epidermal sheets, still on the original coverglass, were dehydrated in a graded series of alcohol, cleared in cedarwood oil and xylene and mounted with Canada balsam. Some epidermal preparations were counterstained with Meyer's paracarmine before being mounted in Canada balsam. In these specimens the numerical ratio of Malpighian cells/melanocytes was determined.

The number of melanocytes was estimated per mm^2 of the surface area of the skin in plane projection. The calculations were based on ten readings, corresponding to 0·342 or 0·256 mm^2. The standard error of the mean is included in the following tables and in some cases an estimate of standard deviation (S.D.) is also presented.

The methylene-blue technique described by Billingham & Medawar in 1953 was used also to demonstrate dopa-negative melanocytes.

About 160 specimens were large enough to permit a count of the number of cutaneous appendages. The average number of hair follicles and sweat ducts was estimated per cm^2 of the surface area of fixed skin. To obtain estimates, as many readings were made as size of specimen allowed; no figure reported is based on less than five readings and most

estimates are based on counts from twenty-five fields. Since only skin that had been freshly obtained from living subjects could be used for 'splitting', the size of specimens was limited by the quantity it was permissible to remove. When surface inspection did not permit differentiation between 'fine' hair follicles and sweat ducts, counts were made in terms of 'skin appendages' and are so recorded (table 2, p. 458).

No attempt was made to correct the data for shrinkage during fixation. All figures therefore refer to skin fixed in formalin and treated uniformly throughout the investigation. When compared with counts obtained by various authors from living human skin, the figures obtained in these studies show that pure epidermis shrinks much less than dermis.

3. Results

A-1. *Regional variations in the architecture of the basal layer (age 16 to 70 years)*

(i) *General*

The structural elements of the basal layer are the *epidermal ridges*, which interlock with dermal papillae; the *hair follicles*, and the *sweat ducts*. The configuration and density of these elements vary from region to region, but follow certain basic patterns (plates 21 to 24).

The pattern characteristically found in thigh skin was chosen as the basis of reference (figure 3, plate 21). Here, the basal layer is divided into diamond-shaped areas by a grid of large, shallow grooves. These grooves are the impressions of the macroscopically visible grooves or flexure lines of the skin surface. Within the areas between these flexure lines,

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Description of plate 21

Regional anatomy of the architecture of the dermo-epidermal interface. I

Pure epidermal preparations, dopa and paracarmine, × 40

Figure 1. Thigh, full-term foetus. Hair follicles solitary or grouped in twos or threes. Large numbers of sweat ducts between follicles. Some indication of ridges. Melanocytes not dopa-positive.

Figure 2. Thigh, 18-month-old infant. Well-developed system of ridges. Density of hair follicles and sweat ducts lower than in foetus. Melanocytes dopa-positive.

Figure 3. Thigh, adult. Further reduction in density of hair follicles and sweat ducts. Impressions of the flexure lines of the skin surface more marked than in the child (figure 2).

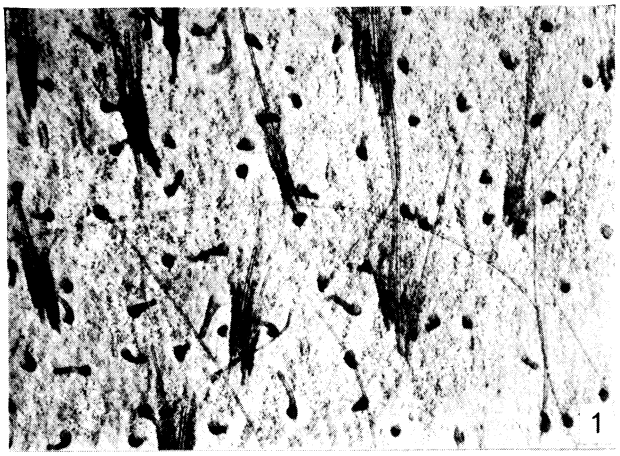
Figure 4. Lower leg, frontal aspect, adult. Basal layer mostly flat. Ridges only around appendages.

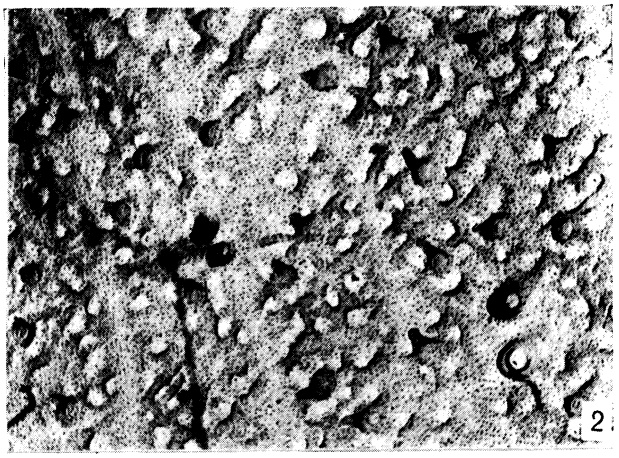
Figure 5. Heel, adult. Almost complete absence of appendages. The dermal papillae (here removed) penetrated the epidermis at an acute angle. Melanocytes dopa-positive.

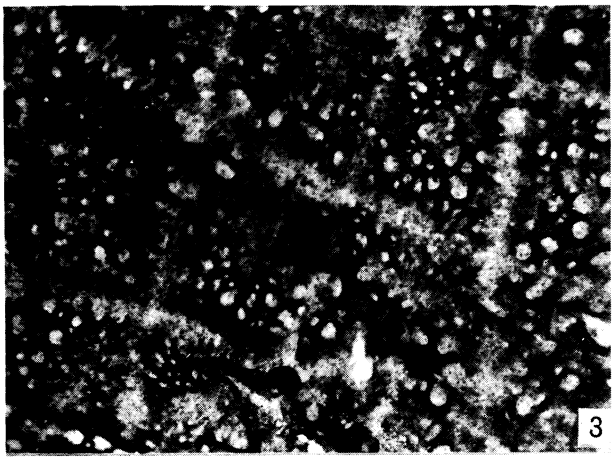
Figure 6. Forearm, frontal aspect, 8-year-old child. Well-developed flexure lines with shallow ridges or flat areas in between. High density of melanocytes.

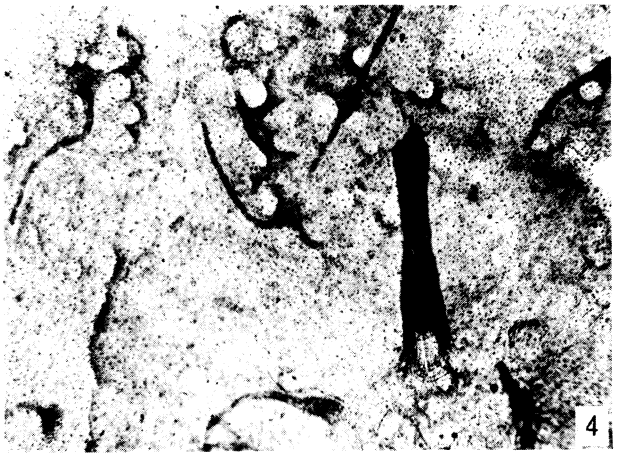
Figure 7. Elbow, adult. Well-developed pattern of deep ridges. The flexure lines of the skin surface (seen as straight lines across the field) are 'bridged over' by cross ridges. Same donor as in figure 5.

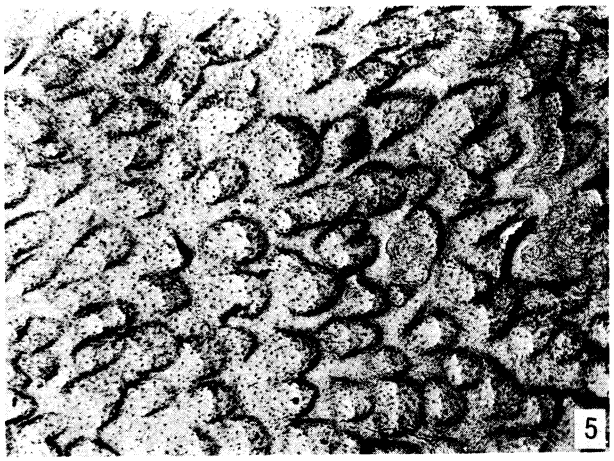
Figure 8. Wrist, adult. Deep ridges with sweat ducts. Vitiliginous epidermis. The right half is normal (dopa-positive melanocytes); the left half is the vitiliginous area without dopa-positive melanocytes.

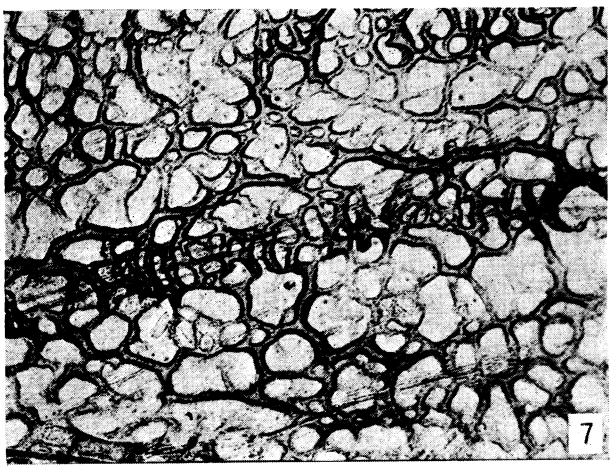


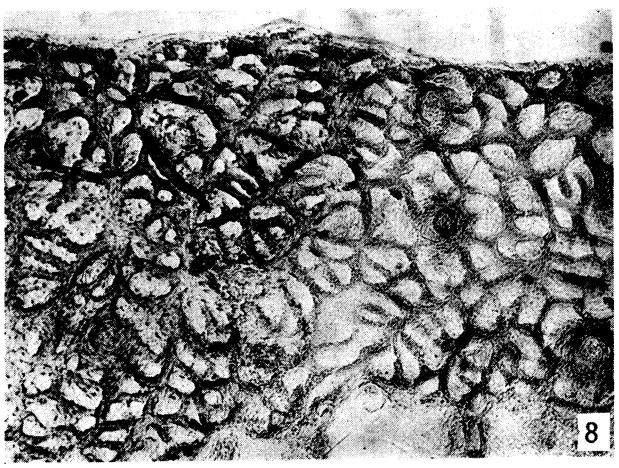












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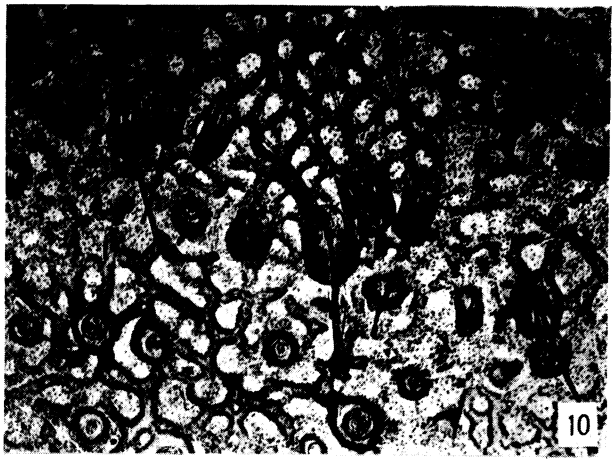
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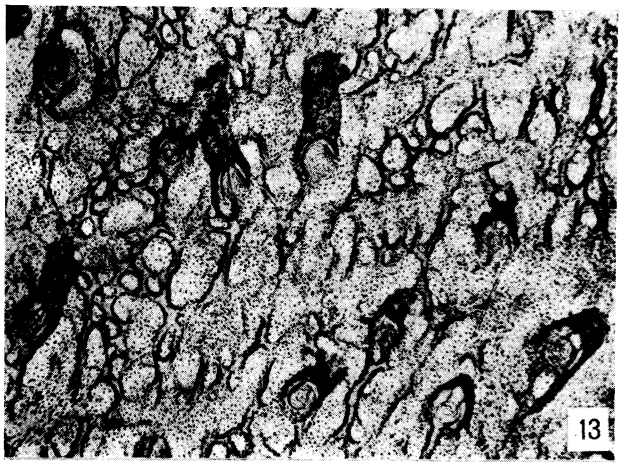
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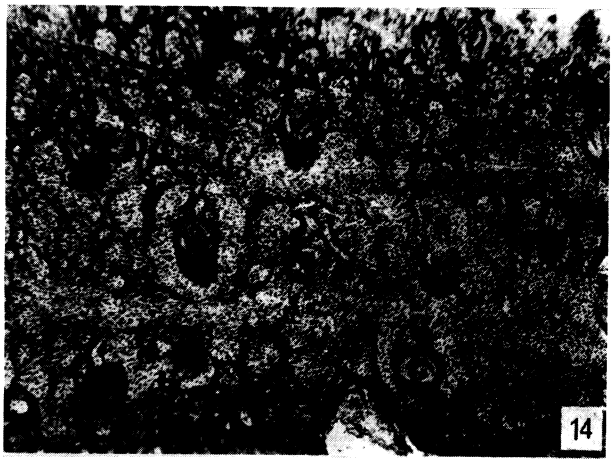
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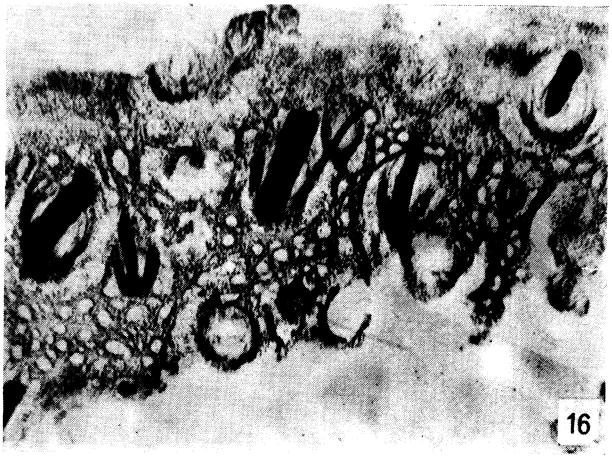
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one finds circular or semicircular epidermal ridges engulfing the finger-like imprints of dermal papillae (removed by tryptic digestion). The height of these ridges varies considerably. Between the ridges there are almost completely flat valleys; these valleys increase in area with age.

In the centre of figure 3, a group of hair follicles can be seen; sweat ducts are scattered over the whole area. The epidermal ridges usually stop at the junction of the outer root sheath and the basal layer. In some cases, however, especially in the large follicles of coarse hairs, the ridges continue for some distance down the outer root sheath (in figure 11, plate 22, they come 'upwards'). In transverse sections of such follicles the outer root sheath is scalloped because of the presence of these anchoring ridges. No such system was found around the sweat ducts, which are very often located in a bay completely free from ridges (figure 21, plate 23). The ridges may, however, run through the junction of the sweat ducts with the basal layer or terminate at the ducts. Bilateral symmetry in the epidermal pattern of any given donor is readily demonstrable (figures 13 and 14, plate 22).

(ii) *Extremities*

The basal layer of the epidermis of the extremities resembles that of the thigh although it exhibits some slight, localized variations. Over the forearm (figure 6, plate 21) and the frontal aspect of the lower leg (figure 4, plate 21) there are characteristic extensive flat areas. Over the calf of the leg, the knee, the heel (figure 5, plate 21), the wrist (figure 8, plate 21) and the elbow (figure 7, plate 21) there is a very marked deep, circular pattern. In the upper arm, especially on the inner aspect, parallel ridges are combined with the usual circular pattern.

Description of plate 22

Regional anatomy of the architecture of the dermo-epidermal interface. II

Pure epidermal preparations, dopa and paracarmine, ×40

Figure 9. Forehead, 7-month foetus. High density of hair follicles and sweat ducts. Low number of dopa-positive melanocytes. No epidermal ridges.

Figure 10. Forehead, adult. Well-developed pattern of ridges connecting the hair follicles. High density of melanocytes. Density of skin appendages lower than in foetal skin.

Figure 11. Scalp with microscopically visible hairs, adult. Large follicles with anchoring ridges. Relatively smooth epidermis. Same donor as in figure 12.

Figure 12. Scalp from a bald site, adult. Distribution of follicles similar to that in hairy scalp of same donor. See figure 11.

Figure 13. Behind right ear, 9-year-old child. See also figure 14.

Figure 14. Behind left ear, 9-year-old child. Bilateral symmetry of pattern marked. Sweat ducts absent from both right and left sides. See also figure 13.

Figure 15. Helix, outer aspect, adult. Large hair follicles. Pattern similar to that of forehead, but melanocytes less numerous than in forehead.

Figure 16. Eyebrow, adult. Deeply pigmented shaft of large coarse hairs. Usual circular pattern of basal layer.

(iii) *Trunk*

On the trunk the architecture of the basal layer is similar to the basic pattern on the thigh. Deep, well-marked, circular epidermal ridges can be found between the groups of hair follicles or around the sweat ducts (figure 21, back, plate 23). Abdominal skin is characterized by deep impressions of flexure lines bridged over by short, parallel ridges (figure 20, plate 23).

(iv) *Hand and foot*

The epidermal ridges of the hand and foot are very long and deep. Palm and sole differ from their dorsal counterparts by their lack of hair follicles and by the greater thickness of their epidermal ridges. The well-known embryonic pattern of sole (Blaschko 1887) or palm is somewhat obscured in the adult (figure 22, plate 23) by the development of connecting transverse ridges between the original parallel ridges that bear sweat ducts and those that bear none. The pattern on the fingers and toes resembles that in the corresponding aspects of the hand and foot, and the characteristic pattern of the fingerprint is clearly recognizable even at the level of the basal layer (figure 25, plate 24). Very thin, deep, parallel ridges can be found in the nail bed.

(v) *Head*

The architecture of the basal layer of the skin of the head is characterized by its large number of hair follicles. The skin of the cheek (figure 18, plate 23) is unique in that its basal layer is almost flat between the hair follicles and sweat ducts in spite of the fact that the system of rete ridges is well developed in other regions of the head epidermis. The width of the hair follicles varies greatly within any given region and within different regions. The largest hair shaft found was in the eyebrow (figure 16, plate 22). There are very broad hair follicles in the scalp, with well-developed, anchoring ridges (figures 11, 12, plate 22). The width of follicles in the cheek (figure 18, plate 23) and on the forehead (figure 10, plate 22) varies greatly in a given individual. The very broad follicles with large hairs are classified as 'coarse'. The proportion of these to the follicles with 'fine' hairs in the skin from cheek, eyelid and forehead is given in table 2. It is noteworthy that there are no anatomical differences between the patterns of the epidermis of the bald and the hairy scalp (figures 11, 12, plate 22). Statistical estimates also have shown that there may be no significant difference in the distribution of hair follicles on the bald and the hairy scalp (table 2, p. 458).

The eyelid (figure 17, plate 23), like the cheek, has a unique type of epidermis. Here the diamond-shaped epidermal ridges, which resemble plateaux, are arranged in a bizarre pattern similar to that seen in the epidermis covering a naevus. The pattern of the outer aspect of the helix (figure 15, plate 22) resembles that of the forehead (figure 10, plate 22).

(vi) *Neck*

In the epidermis of the neck, flat areas alternate with straight, parallel ridges (figure 19, plate 23) which end very abruptly. The usual, basic, circular pattern of ridges may be combined with the parallel ridges. A similar configuration of parallel ridges has been found in the female breast and in senile abdominal skin.

(vii) *Genitalia*

The architecture of the epidermal covering of the genital organs is unique. In scrotal skin the epidermal pattern consists mainly of wide, parallel, interweaving ridges (Szabó 1957, see figures 5, 6). On the penis a somewhat similar pattern can be found, but the predominant design of this region is the alternation of circular imprints of very large dermal papillae with the intricate, horseshoe-like pattern of epidermal ridges (figure 23, plate 23). A comparable structure has been observed in skin from the clitoris of Rhesus monkeys (Szabó, unpublished). In general, even after the last vestiges of dermis have been removed, sheets of epidermis from the skin of the genital region are very elastic and often curl up.

(viii) *Squamous epithelium of body openings*

The pattern of the squamous epithelia of the nasal and oral cavities is also distinctive. There is an abrupt change from the flat, cheek-like basal layer of the lip to the configuration of anastomosing ridges of the vermilion border (figure 26, plate 24). The hair follicles of the moustache are abundant in the lip and absent in the vermilion border. The anastomosing pattern of the vermilion border continues into the mouth where the dermal papillae are very long and thin. The pattern of the vermilion border is very similar to that found at the perianal junction. The epidermis of the nasal cavity (figure 24, plate 23) is characterized by small, oval or round ridges but hair follicles may be present near the nasal opening.

The squamous epithelia of the inner surface of prepuce and vagina are usually flat, with small, circular casts of dermal papillae.

A-2. *Age changes in the architecture of the basal layer (foetal and senile skin)*

The architectural pattern of the basal layer of the thigh (figures 1 to 3, plate 21) and of the forehead (figures 9, 10, plate 22) changes markedly between foetal and adult life. The foetal pattern is characterized by absence of epidermal ridges and a much higher density of appendages. The epidermis of the thigh of a baby (figure 2, plate 21) has a characteristic structure which occupies a position transitional between that of the foetus and that of the adult, with the pattern of the impressions of the flexure lines already clearly visible.

With increasing age, the extent of the flat areas in the basal layer tends to increase and in obese subjects the epidermal ridges become short and are parallel, as they are in the skin of the adult neck (figure 19, plate 23). A particular type of epidermal ridge (not illustrated) characterizes senile epidermis: the usual circular pattern of ridges (figure 3, plate 21) is broken up into a system of beaded, deep, short ridges.

The sebaceous glands usually enlarge late in adult life.

B. *Regional frequency distribution of hair follicles, sweat ducts and appendages*

In this section the quantitative data on the population of cutaneous appendages are given in table form. As used here, the term 'appendages' includes both hair follicles and sweat ducts, which, strictly speaking, are 'epidermal derivatives' (Odland 1966). Table 1 presents estimates obtained from multiple samples from individual donors and shows regional variations in the distribution of appendages. In table 2, twenty-three body areas are listed in alphabetical order with the average number of hair follicles and sweat ducts in each. In the last column the average number of skin appendages is presented. This is not

a simple total of the number of hairs and sweat ducts; in fifteen instances the total number of skin appendages was estimated without breaking the figure down into hair follicles and sweat ducts. In these fifteen instances the number of donors is not the same for hair follicles, sweat ducts and appendages.

In table 3 the distribution of hairs, sweat ducts and appendages is shown in different body regions which are arranged in order of decreasing density. In table 4 the average number of appendages per unit area is given for the head, trunk, arms and legs (summarized in table 5), while in table 6 the total number of hairs, sweat ducts and appendages is presented. In table 7 it is shown that there is no significant sexual difference in the distribution; in table 8 the numerical ratio of sweat ducts/hair follicles is analysed.

In the next three tables age-differences in the density of skin appendages are shown (table 9, foetal skin; table 10, baby and adolescent skin; table 11, senile skin).

The distribution of appendages is bilaterally symmetrical. To prove this point it was possible to calculate the numerical ratio of skin appendages on the right/left side in specimens from six donors. This ratio proved to be $0{\cdot}9716 \pm 0{\cdot}073$ with a standard deviation of 0·176. The theoretical value of this ratio is 1·00; the calculated value approximates this very closely.

C-1. *Regional anatomy of the melanocyte system*

(i) *General*

Dopa-positive melanocytes were found in the epidermis of all body regions studied from the scalp to the sole of the foot. The domain of melanocytes extends at least as far as the uvula in the buccal cavity; melanocytes are present in the squamous epithelium of the nasal cavity and in the perianal epithelium. Regions beyond these limits were not investigated. No dopa-positive cells were present in the four specimens of vaginal epithelium studied, but when these specimens were stained with methylene blue they were found to contain cells resembling dopa-negative melanocytes. Great individual variation in

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Description of plate 23

Regional anatomy of the architecture of the dermo-epidermal interface. III

Pure epidermal preparations, dopa and paracarmine, ×40

Figure 17. Eyelid, adult. Characteristic pattern of angular epidermal ridges.

Figure 18. Cheek, adult, male. Almost complete absence of epidermal ridges. Great variation in the shape and size of melanocytes and hair follicles.

Figure 19. Neck, frontal aspect, adult. Parallel ridges end abruptly. Sweat ducts clearly visible.

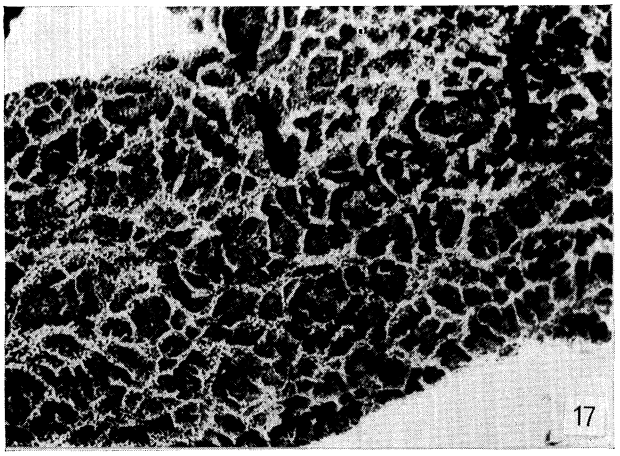
Figure 20. Abdomen, adult. Basic circular pattern combined with parallel ridges. The flexure line of the skin surface (upper half of the photograph) is 'bridged over' by short parallel ridges lying at right angles to the direction of the flexure line. Same donor as figures 5 and 7, plate 21.

Figure 21. Back, 10-year-old child. Group of four hair follicles surrounded by sweat ducts.

Figure 22. Sole of foot, adult. Very pronounced circular pattern with long sweat ducts.

Figure 23. Prepuce, adult. Outer aspect.

Figure 24. Nasal cavity, adult. Longitudinal and circular ridges densely covered by melanocytes. Hair follicles in the lower right corner.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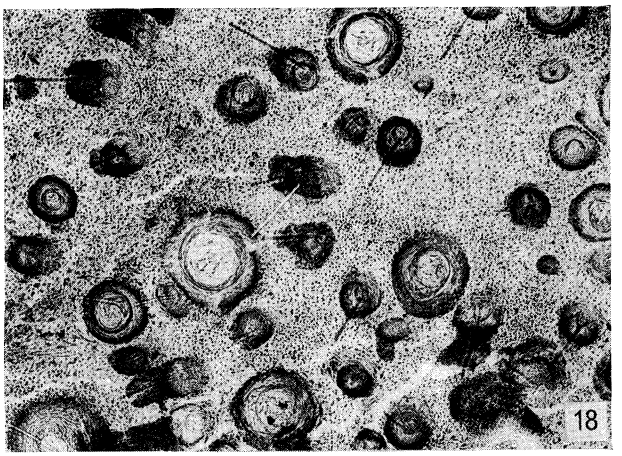
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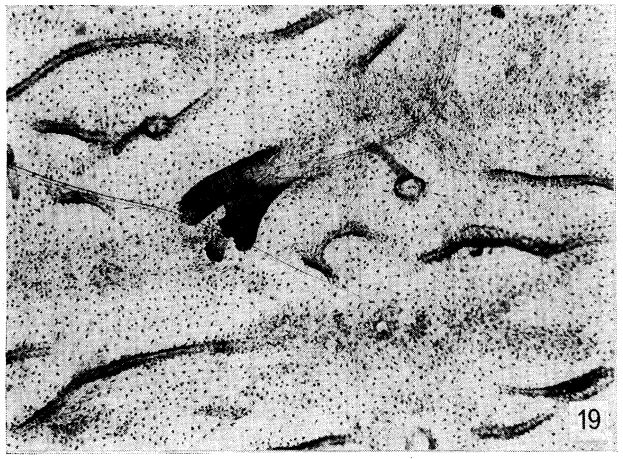
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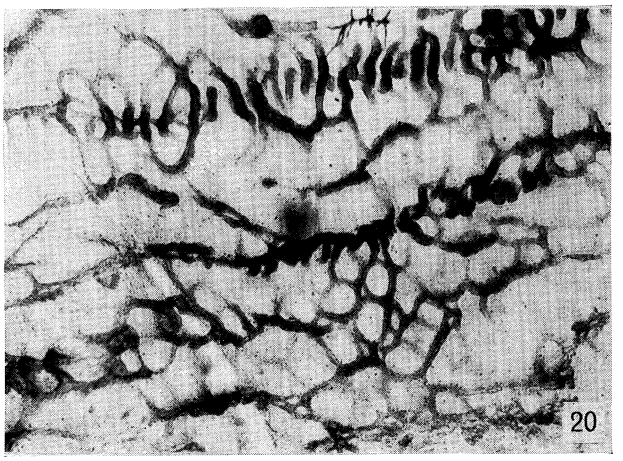
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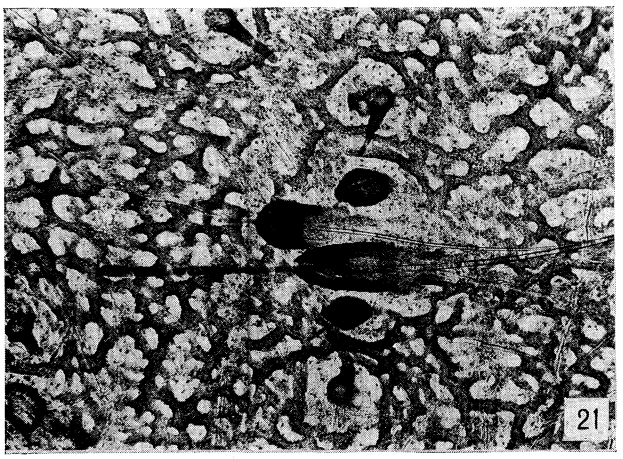
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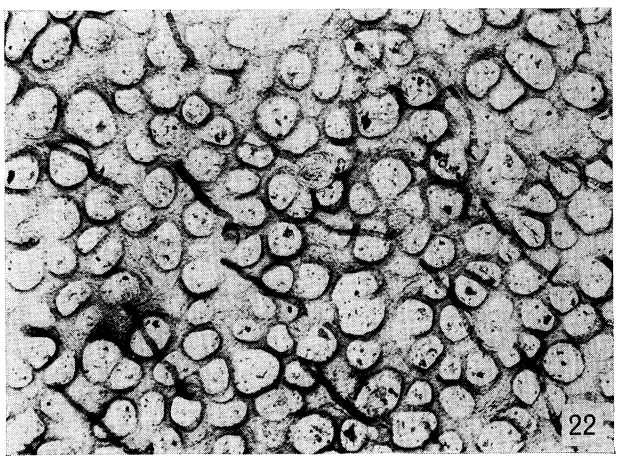
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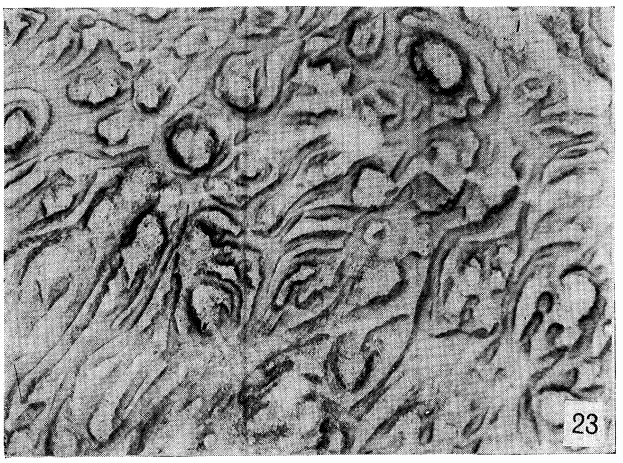
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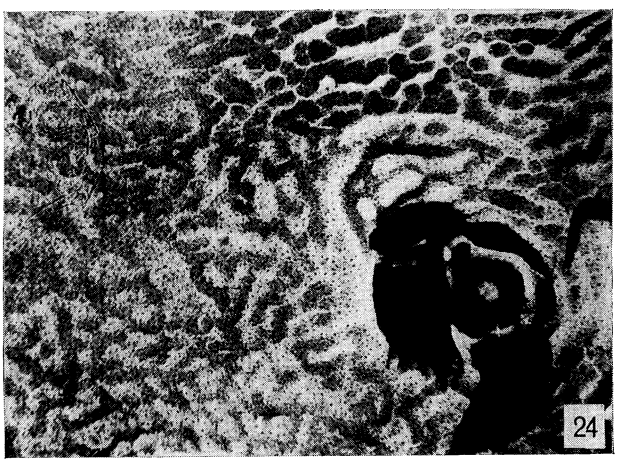
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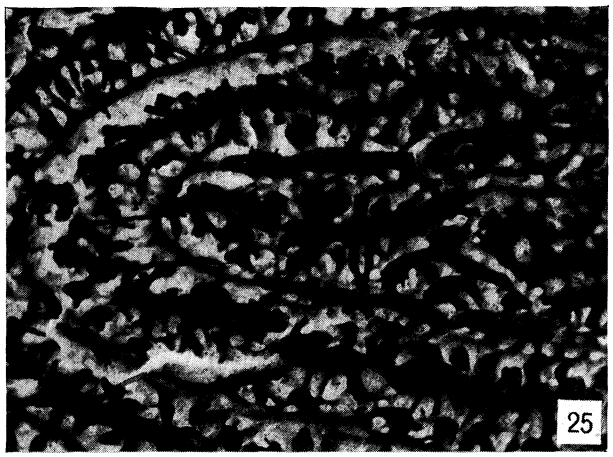
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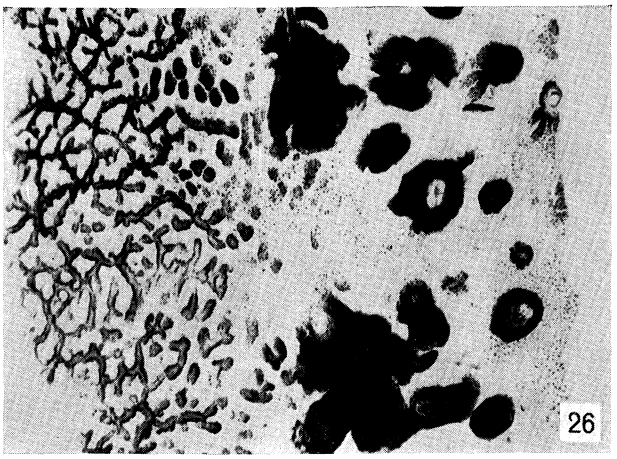
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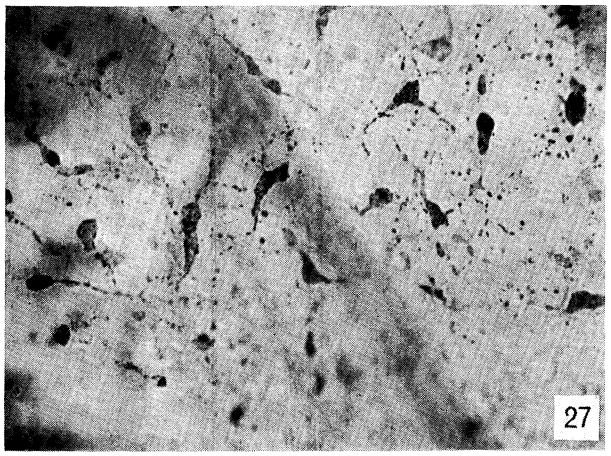
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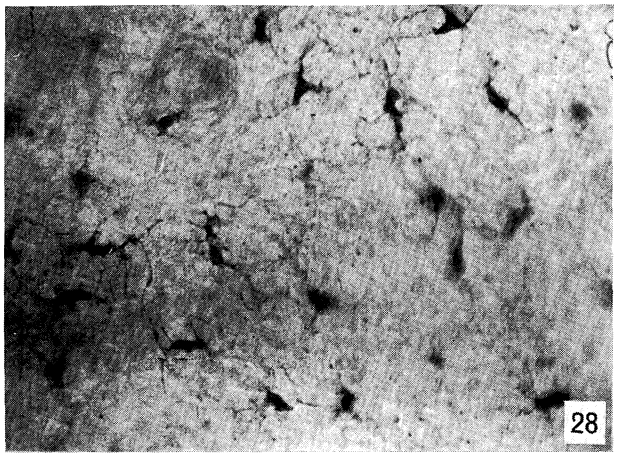
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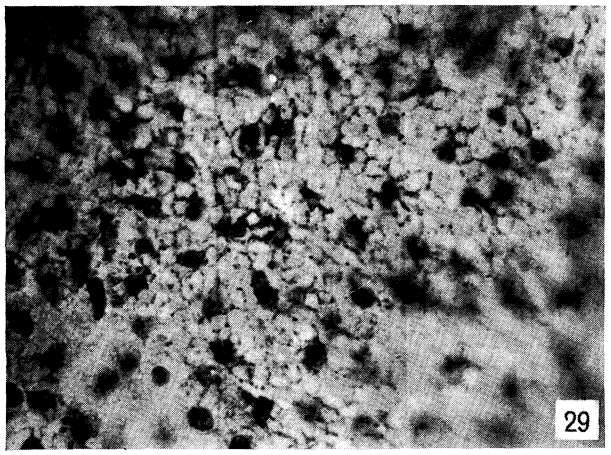
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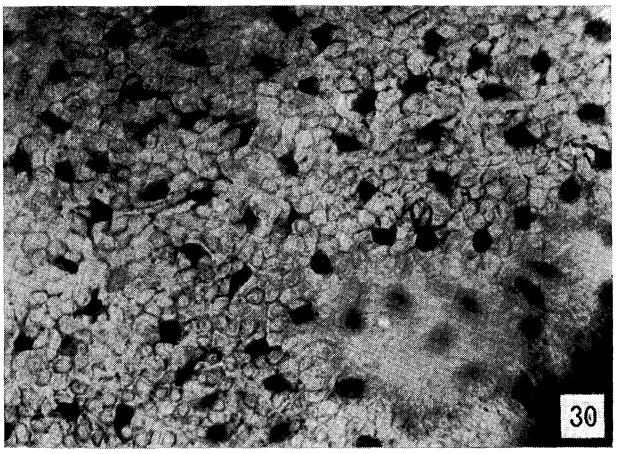
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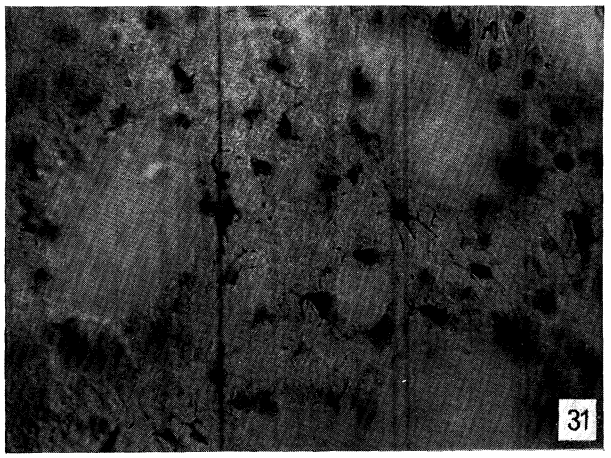
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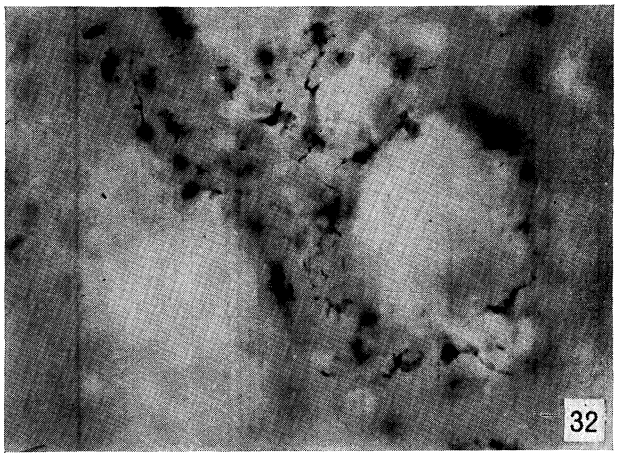
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TABLE 1. ESTIMATES OF THE REGIONAL FREQUENCY DISTRIBUTION OF APPENDAGES IN FOUR DONORS

region	hair follicles (mean no./cm² ± S.E.)	sweat ducts (mean no./cm² ± S.E.)	appendages (mean no./cm² ± S.E.)	sweat ducts/ hair follicles (num. ratio)
		donor I (aged 37 years)		
temporal	420 ± 40	430 ± 140	850 ± 130	1·0
thigh	30 ± 20	160 ± 30	190 ± 30	5·0
		donor II (aged 43 years)		
thigh, frontal	50 ± 20	120 ± 20	170 ± 30	2·2
thigh, dorsal	70 ± 30	110 ± 20	180 ± 40	1·6
lower leg, frontal	50 ± 20	190 ± 20	240 ± 30	3·9
lower leg, dorsal	40 ± 10	130 ± 20	170 ± 20	3·2
sole of foot	—	830 ± 40	830 ± 40	—
dorsum of foot	60 ± 20	250 ± 40	310 ± 60	4·1
		donor III (aged 69 years)		
forehead	870 ± 120	350 ± 50	1210 ± 190	0·4
thigh	40 ± 20	50 ± 20	90 ± 20	1·2
		donor IV (aged 77 years)		
cheek	550 ± 80	120 ± 40	670 ± 90	0·2
helix, dorsal	1220 ± 160	—	1220 ± 160	—
helix, frontal	500 ± 150	—	500 ± 150	—
back	150 ± 40	70 ± 20	220 ± 60	0·4
thigh	60 ± 40	110 ± 20	170 ± 30	1·6

DESCRIPTION OF PLATE 24

REGIONAL ANATOMY OF THE ARCHITECTURE OF THE DERMO-EPIDERMAL INTERFACE. IV

Pure epidermal preparations, dopa and paracarmine, × 40

FIGURE 25. Fingerprint, adult.

FIGURE 26. Vermilion border of lip, adult, male. Right half similar to cheek: flat epidermis with coarse-hair follicles (moustache). Left half is vermilion border devoid of follicles but rich in anastomosing epidermal ridges.

MELANOCYTE DISTRIBUTION IN THE FOREHEAD AND THIGH AT VARIOUS AGES

Pure epidermal preparations, dopa, × 400

FIGURE 27. Forehead, 7-month-foetus. Strongly dopa-positive melanocytes with fewer dendrites than in the adult. See figure 29.

FIGURE 28. Thigh, foetal. Melanocytes hardly visible.

FIGURE 29. Forehead, adult. Typical, strongly dopa-positive melanocytes with numerous short processes. Relative density of melanocytes higher than in foetus. *Note*: All Malpighian cells are in contact with more than one melanocyte.

FIGURE 30. Thigh, adult. Melanocyte density lower than in adult forehead but higher than in foetal thigh. Dopa reaction also stronger than in the foetus. See note for figure 29.

FIGURE 31. Forehead, senile. Dopa reaction still strong. Density of melanocytes lower than in the adult.

FIGURE 32. Thigh, senile. Dopa reaction variable, some melanocytes almost dopa-negative. Decrease in melanocyte density. Increase in the size of melanocytes and in the length of their dendrites.

melanocyte density accounts for the large standard error of the regional averages shown in table 12. In addition to variation in melanocyte density from person to person, there is great variation in melanocyte density from area to area in the body of any given individual.

(ii) *Adult skin (age 16 to 70 years)*

The average number of melanocytes in the adult integument is shown in tables 13 to 15, the tables being arranged in order of increasing size of regions studied. The average number of melanocytes in the entire integument of the human body was found to be $1560 \pm 110/mm^2$ (table 15). From the figures obtained for melanocyte density per unit area,

TABLE 2. ADULT SKIN: DISTRIBUTION OF HAIR FOLLICLES, SWEAT DUCTS AND APPENDAGES IN HUMAN SKIN (AGE 16 TO 70 YEARS)

Figures are the averages of means from individual donors. Regions are arranged in alphabetical order.

	hair follicles			sweat ducts			appendages		
region	no. of donors	av. no./cm² ± S.E.	S.D.	no. of donors*	av. no./cm² ± S.E.	S.D.	no. of donors*	av. no./cm² ± S.E.	S.D.
abdomen and groin	5	70 ± 15	30	—	190 ± 5	45	—	255 ± 30	65
arm, lower	5	95 ± 15	30	—	225 ± 25	60	—	320 ± 25	60
arm, upper	10	45 ± 10	30	—	150 ± 20	60	—	195 ± 20	65
axilla	1	65 ± 35	—	—	130 ± 25	—	—	180 ± 20	—
back and buttock	3	65 ± 15	25	—	160 ± 30	65	4	210 ± 5	15
cheek†	7	830 ± 40	100	6	320 ± 60	140	11	1050 ± 70	230
coarse‡	1	240 ± 75	—	—	—	—	—	—	—
fine‡	1	690 ± 95	—	—	—	—	—	—	—
chest	4	75 ± 25	50	—	175 ± 35	70	—	250 ± 15	35
chin	3	520 ± 70	120	—	220 ± 70	125	—	740 ± 25	40
ear	10	600 ± 35	110	—	140 ± 40	130	14	760 ± 30	115
eyelid, upper§	1	145 ± 40	—	—	?	—	—	610 ± 80	—
eyelid, lower	1	455 ± 55	—	—	190 ± 35	—	—	645 ± 60	—
fingerprint	1	—	—	—	345 ± 40	—	—	345 ± 40	—
foot, dorsum	1	60 ± 25	—	3	250 ± 5	10	3	270 ± 20	35
foot, sole	3	—	—	3	620 ± 120	—	3	620 ± 120	—
forehead	4	765 ± 20	40	—	360 ± 50	100	—	1130 ± 60	120
coarse‖	1	370 ± 40	—	—	—	—	—	—	—
	1	400 ± 110	—	—	—	—	—	—	—
fine‖	1	840 ± 80	—	—	—	—	—	—	—
	1	200 ± 140	—	—	—	—	—	—	—
leg, thigh	21	55 ± 5	20	—	120 ± 10	35	—	180 ± 5	15
leg, lower	5	45 ± 10	25	—	150 ± 15	40	—	200 ± 30	65
lip	1	385 ± 70	—	1	190 ± 20	—	5	790 ± 175	350
neck	5	300 ± 15	35	1	375 ± 55	—	5	420 ± 100	220
				1	180 ± 20	—	—	—	—
nose	1	535 ± 55	—	—	155 ± 50	—	—	700 ± 50	—
	1	720 ± 80	—	—	175 ± 45	—	—	1040 ± 80	—
scalp	1	350 ± 50	—	—	—	—	—	350 ± 50	—
bald	1	320 ± 50	—	—	70 ± 30	—	—	390 ± 30	—
hairy		320 ± 60	—	—	100 ± 30	—	—	400 ± 30	—
scrotum	1	60 ± 40	—	—	80 ± 30	—	—	140 ± 30	—
toe	1	—	—	—	540 ± 20	—	—	540 ± 20	—

* If different from previous column.

† In one male there were 6·6% 'coarse, beard follicles'; in 1 female, 10%; for another female the figures are shown.

‡ Female.

§ The figure listed in the hair-follicle column is for coarse-hair follicles. The figure listed in the appendage column includes the coarse-hair follicles.

‖ Males only.

TABLE 3. ADULT SKIN: FREQUENCY DISTRIBUTION OF HAIR FOLLICLES, SWEAT DUCTS AND EPIDERMAL APPENDAGES IN DIFFERENT REGIONS OF THE BODY (AGE 16 TO 70 YEARS)

region	no. of donors	av. no./cm^2 ± S.E.	S.D.
	A. Hair follicles		
cheek	7	830 ± 40	100
forehead	4	765 ± 20	40
forearm	5	95 ± 15	320
chest	4	75 ± 25	50
abdomen and groin	5	70 ± 15	30
back and buttock	3	65 ± 15	25
thigh	21	55 ± 5	20
upper arm	10	45 ± 10	30
lower leg	5	45 ± 10	25
	B. Sweat ducts		
sole of foot	3	620 ± 120	120
forehead	4	360 ± 50	100
cheek	6	320 ± 60	140
dorsum of foot	3	250 ± 5	10
forearm	5	225 ± 25	60
abdomen and groin	5	190 ± 5	45
chest	4	175 ± 35	70
back and buttock	3	160 ± 30	65
lower leg	5	150 ± 15	40
upper arm	10	150 ± 20	60
thigh	21	120 ± 10	35
	C. Appendages (hair follicles and sweat ducts)		
forehead	4	1130 ± 60	120
cheek	11	1050 ± 70	230
lip	5	790 ± 175	350
ear	14	760 ± 30	115
forearm	5	320 ± 25	60
abdomen and groin	5	255 ± 30	65
chest	4	250 ± 15	35
back and buttock	4	210 ± 5	15
lower leg	5	200 ± 30	65
upper arm	10	195 ± 20	65
thigh	21	180 ± 5	15

the total number of epidermal melanocytes in the entire integument of a 24-year-old donor was calculated (table 16). Although melanocyte density is greater in the epidermis of the head than elsewhere, the absolute number of melanocytes is lower in this region than in the rest of the body because the total surface area of the head is relatively small. Altogether there are about 2000 million melanocytes in the epidermis of a normal 24-year-old adult, exclusive of the melanocytes in hair follicles.

If the distribution of melanocytes is bilaterally symmetrical, the numerical ratio of their density on the two sides of the body should be one. As calculated, this ratio was found to be 1·04 ± 0·076 with a standard deviation estimated at 0·27.

Table 17 shows that there is no significant sexual difference in melanocyte distribution.

Figures 29 to 36 in plates 24 and 25 demonstrate the continuity of the melanocyte system at the dermo-epidermal interface, regardless of the great regional variation in melanocyte density. They also show that melanocytes possess several dichotomizing dendritic processes that branch off between the Malpighian cells.

The ratio of Malpighian cells/melanocytes was estimated in 67 donors. Estimates for

individual donors are given in table 18. There is great difference in the ratios on and between the ridges (table 19). The overall averages are presented in table 20.

The ratio is constant on the face, but varies greatly on the trunk and extremities. Since there are more melanocytes on the cheek and forehead than elsewhere, the Malpighian cell/melanocyte ratio is lower in these two regions than elsewhere in the body integument. There is no regional variation in the number of Malpighian cells.

Melanocytes show a preference for epidermal ridges (table 19; figures 35 and 36, plate 25). For this reason the regional difference in melanocyte density is not an optical illusion due to regional differences in the frequency and depth of the epidermal ridges, as is illustrated in figures 37 to 40, plate 25).

(iii) *Foetal, young and senile skin*

Tables 21 and 22 show the frequency distribution of melanocytes in the skin of donors less than 16 years of age. Table 23 contains comparable figures for senile skin (age $>$ 70 years). Table 24 shows the numerical ratio of Malpighian cells/melanocytes in young (ages 0 to 15 years) and senile (age $>$ 70 years) skin. Foetal melanocytes are shown in figures 27 and 28, plate 24).

Description of plate 25

Melanocyte distribution

Figure 33. Nasal cavity, squamous epithelium, adult. Melanocytes chiefly on epidermal ridges. Malpighian cells also visible. Pure epidermal sheet, dopa and paracarmine, × 400.

Figure 34. Sole of foot, adult. Epidermal ridges in focus. High density of small, weakly dopa-positive melanocytes. Dopa reaction variable. Dopa, × 400.

Comparison of figures 35 *and* 36 *shows differences in the distribution of melanocytes within the same preparation of abdominal epidermis*

Figure 35. Abdomen, adult. Epidermal ridge in focus. Melanocytes numerous. Individual cells small. Dopa, × 400.

Figure 36. Abdomen, adult. Circular imprint of a dermal papilla in focus. Fewer melanocytes than in figure 35, those present being larger and having longer dendrites than those shown in figure 35. Dopa, × 400.

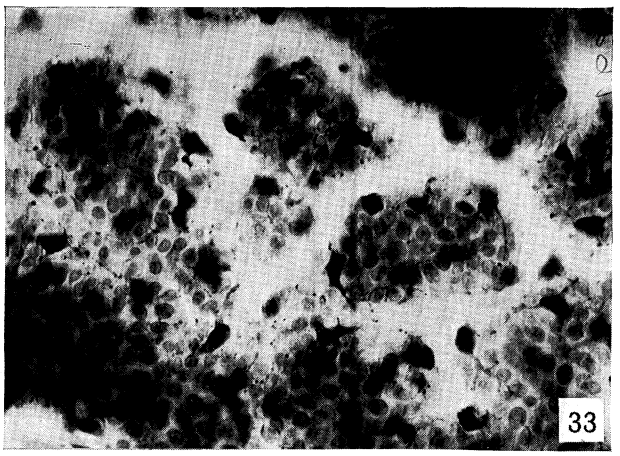
Comparison of figures 37 *and* 38 *with figures* 39 *and* 40 *shows that regional variation in melanocyte density is not an optical illusion*

Figure 37. Epidermis from behind ear, smooth basal layer, adult. Melanocyte density high. Shape and size of melanocytes vary. Dopa, × 95.

Figure 38. Thigh, adult. Melanocyte density lower than in figure 37. Deep undulations in basal layer. Dopa, × 95.

Figure 39. Epidermis from behind ear, adult. Transverse section. Continuous layer of melanocytes at dermo-epidermal junction. Halo around melanocytes ('clear cells'). Decrease in intensity of dopa reaction along outer root sheath of hair follicles. Basal layer almost smooth. Same donor as in figure 37. Dopa, × 330.

Figure 40. Thigh, adult. Transverse section. Deep undulations in basal layer. Most melanocytes at tips of ridges. Dopa and paracarmine, × 330.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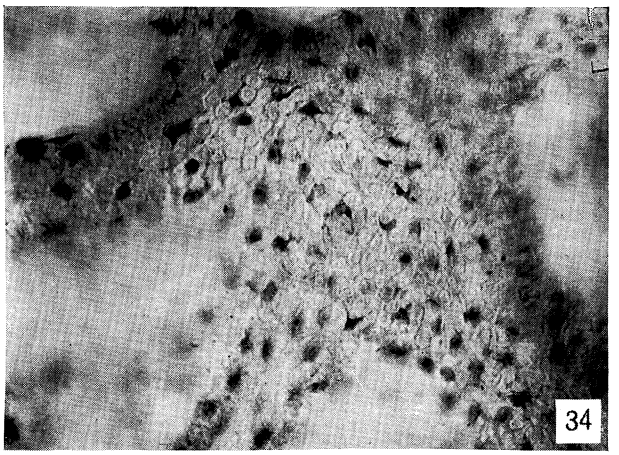
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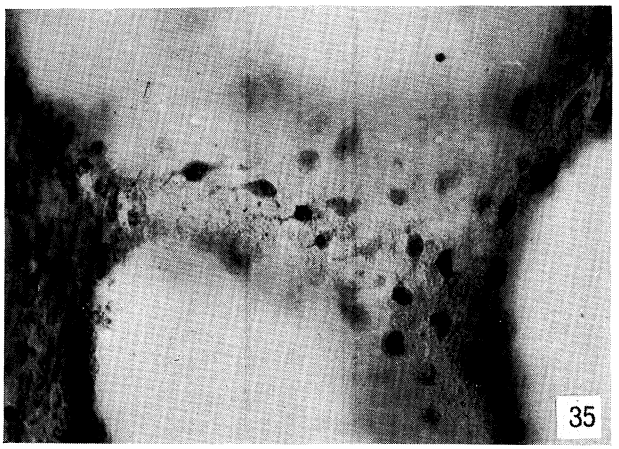
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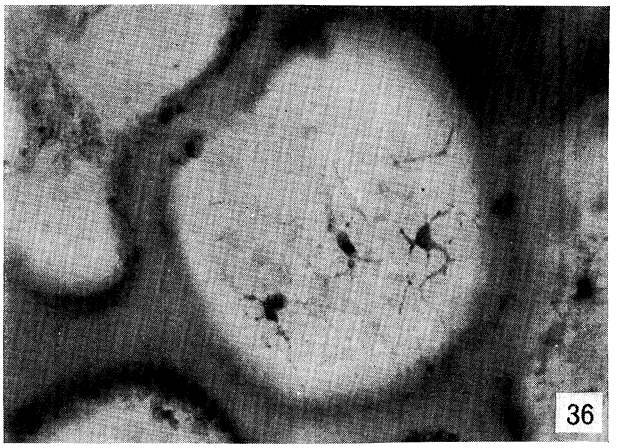
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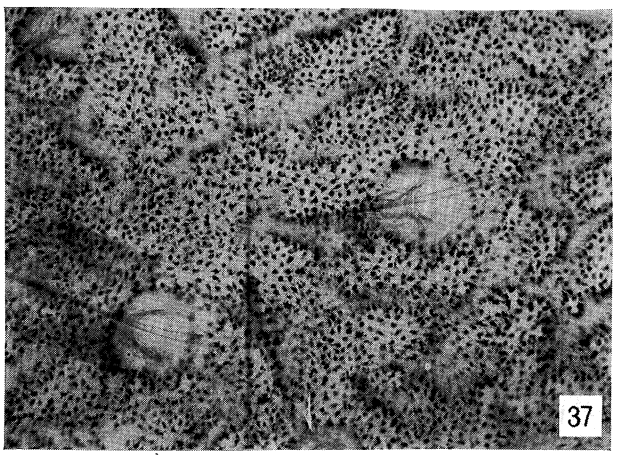
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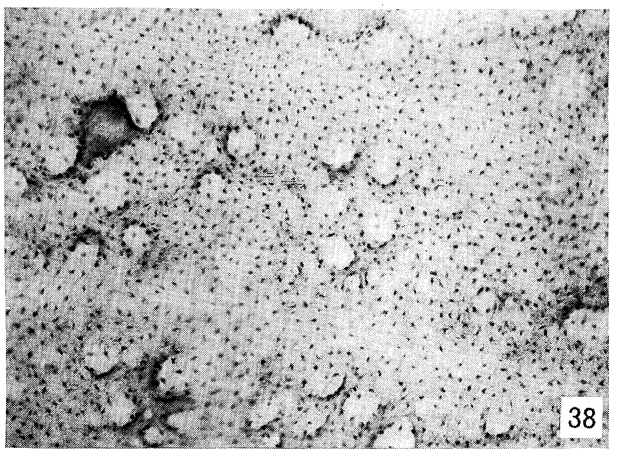
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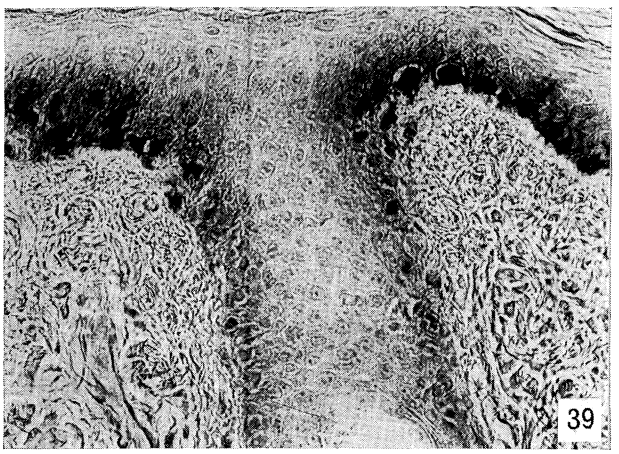
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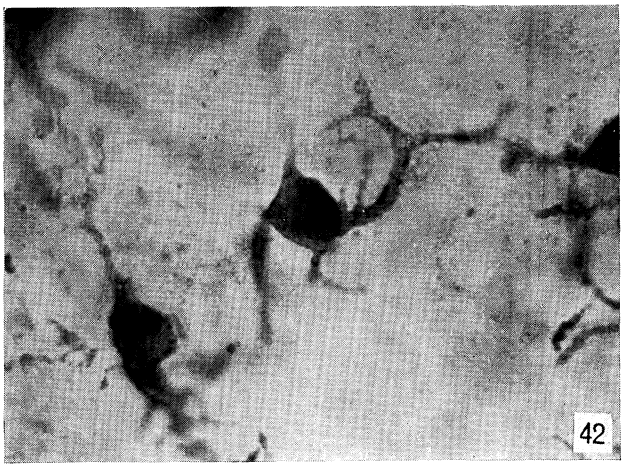

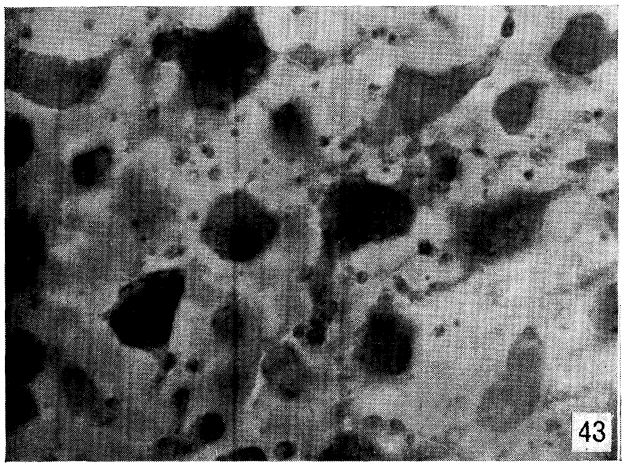

MELANOCYTE CYTOLOGY

FIGURE 41. Lower leg, adult, Negro. Malpighian cells deeply pigmented. Melanocytes dopa-positive. Dopa, × 330.

FIGURE 42. Thigh, adult. Angular melanocyte characteristically present in regions of low melanocyte density. Long dichotomizing processes. Dopa, × 950.

FIGURE 43. Behind ear, 9-year-old child. Round melanocyte from region of high melanocyte density. Short processes with terminal end-buttons. Dopa, × 950.

FIGURE 44. Cheek, adult. Giant melanocytes. Dopa, × 950.

TABLE 4. ADULT SKIN: FREQUENCY DISTRIBUTION OF HAIR FOLLICLES, SWEAT DUCTS AND EPIDERMAL APPENDAGES (AGE 16 TO 70 YEARS) AS CALCULATED FOR THE MAIN REGIONS OF THE BODY

Regions are listed in order of decreasing density.

region	no. of donors	av. no./cm² ± S.E.	S.D.	% of total
		A. Hair follicles		
face (cheek, chin, forehead, lip, nose)	17	705 ± 40	155	79
trunk	12	70 ± 10	35	8
frontal	9	75 ± 15	30	—
dorsal	3	65 ± 15	25	—
arm	15	65 ± 5	30	7
leg	26	55 ± 5	25	6
		B. Sweat ducts		
face (check, chin, forehead, lip, nose)	17	270 ± 25	110	36
trunk	13	175 ± 20	70	23
frontal	9	185 ± 20	55	—
dorsal	3	160 ± 30	65	—
arm	15	175 ± 15	65	23
leg	26	130 ± 10	40	17
		C. Appendages		
face (cheek, chin, forehead, lip, nose)	25	940 ± 60	300	58
head (face with scalp and eyelid)	29	890 ± 40	210	—
ear	14	760 ± 30	113	—
face and ear	41	610 ± 30	180	—
trunk	13	240 ± 15	55	15
frontal	9	255 ± 20	35	—
dorsal	4	210 ± 5	15	—
arm	15	255 ± 15	60	16
leg	26	185 ± 5	15	11

TABLE 5. ADULT SKIN: AVERAGE NUMBER OF APPENDAGES (AGE 16 TO 70 YEARS) AS CALCULATED FOR THE WHOLE BODY

	whole body			head, neck and sole excepted		
	no. of donors	appendages av. no./cm² ± S.E.	S.D.	no. of donors	appendages av. no./cm² ± S.E.	S.D.
hair follicles	94	330 ± 20	160	54	65 ± 5	30
sweat glands	85	215 ± 15	125	57	170 ± 10	60
appendages	110	495 ± 30	320	59	230 ± 10	60

TABLE 6. TOTAL NUMBER OF APPENDAGES IN THE SKIN OF AN AVERAGE 24-YEAR-OLD MAN AS CALCULATED WITH BOYD'S ESTIMATES (1935)*

region	hair follicles	sweat ducts	appendages
head	925000	355000	1230000
trunk	425000	1065000	1460000
arms	220000	595000	870000
legs	370000	880000	1220000
approximate total	2 million	3 million	5 million

* Body size hypothetical.

TABLE 7. ADULT SKIN: COMPARISON OF THE FREQUENCY DISTRIBUTION OF SKIN APPENDAGES IN MALES AND FEMALES (AGE 16 TO 70 YEARS)

	hair follicles			sweat ducts		
	no. of donors	av. no./cm² ± S.E.	S.D.	no. of donors	av. no./cm² ± S.E.	S.D.
face						
male	9	690 ± 55	170	8	310 ± 35	100
female	8	715 ± 50	145	8	260 ± 50	140
thigh						
male	7	55 ± 7	20	7	105 ± 10	25
female	14	55 ± 5	20	14	130 ± 10	40

TABLE 8. ADULT SKIN: NUMERICAL RATIO OF SWEAT DUCTS/HAIR FOLLICLES IN DIFFERENT REGIONS OF THE BODY (AGE 16 TO 70 YEARS)

Regions are arranged in order of increasing ratio.

		sweat ducts/hair follicles	
region	no. of donors	num. ratio ± S.E.	S.D.
face	17	0·35 ± 0·08	0·30
cheek	8	0·30 ± 0·13	0·35
forehead	4	0·38 ± 0·03	0·06
trunk	12	3·22 ± 0·64	2·28
chest	4	4·08 ± 1·96	3·90
back and buttock	3	2·33 ± 0·65	1·19
abdomen	5	3·06 ± 0·17	1·20
arm	15	4·50 ± 1·10	4·10
upper arm	7	2·81 ± 0·60	1·59
forearm	5	2·67 ± 0·91	2·04
leg	26	2·70 ± 0·30	1·50
thigh	21	2·40 ± 0·80	3·60
lower leg	5	4·00 ± 1·02	2·24

TABLE 9. FOETAL SKIN: COMPARISON OF THE REGIONAL FREQUENCY DISTRIBUTION OF HAIR FOLLICLES, SWEAT DUCTS AND APPENDAGES IN THE SKIN OF AN INDIVIDUAL FOETUS WITH CORRESPONDING AVERAGE FIGURES FOR ADULT SKIN (AGES 16 TO 70 YEARS)

Adult figures are shown in bold face.

		hair follicles		sweat ducts		appendages		sweat ducts/hair follicles	
region	age of donor	av. no./cm² ± S.E.	S.D.	av. no./cm² ± S.E.	S.D.	av. no./cm² ± S.E.	S.D.	num. ratio ± S.E.	S.D.
forehead	7 months	—	—	—	—	3420 ± 40	—	—	—
	full term	1060 ± 110	—	330 ± 40	—	1390 ± 150	—	0·3	—
	adult	**765 ± 20**	**40**	**360 ± 50**	**100**	**1130 ± 60**	**120**	**0·4 ± 0·03**	**0·06**
cheek	24 weeks	—	—	—	—	4780 ± 110	—	—	—
	full term	—	—	—	—	1670 ± 70	—	—	—
	adult	—	—	—	—	**1050 ± 70**	**230**	—	—
thigh	24 weeks	1010 ± 250	—	2970 ± 610	—	3980 ± 780	—	2·9	—
	7 months	570 ± 70	—	1730 ± 70	—	2300 ± 70	—	3·0	—
	full term	480 ± 40	—	1560 ± 50	—	2040 ± 300	—	3·2	—
	adult	**55 ± 5**	**20**	**120 ± 10**	**35**	**180 ± 5**	**15**	**2·4 ± 0·80**	3·00
sole of foot	24 weeks	—	—	12710 ± 500	—	12710 ± 500	—	—	—
	7 months	—	—	7170 ± 220	—	7170 ± 220	—	—	—
	full term	—	—	5330 ± 190	—	5330 ± 190	—	—	—
	adult	—	—	**620 ± 120**	—	—	—	—	—

In ageing skin, the epidermal ridges tend to flatten. The distribution of melanocytes becomes less dense and more uniform (table 23; figures 31, 32, plate 24). Their dendrites are longer than in younger skin. The dopa reaction is variable, some melanocytes showing a stronger positive reaction than others. The Malpighian cell/melanocyte ratio (table 24) is lower than in adult skin.

TABLE 10. YOUNG SKIN: COMPARISON OF THE REGIONAL FREQUENCY DISTRIBUTION OF HAIR FOLLICLES, SWEAT DUCTS AND APPENDAGES IN THE SKIN OF YOUNG DONORS (11 MONTHS TO 12 YEARS) WITH CORRESPONDING AVERAGE FIGURES FOR ADULT SKIN (AGE 16 TO 70 YEARS)

Adult figures are shown in bold face. Compare tables 2, 3 and 9.

			hair follicles		sweat ducts		appendages		sweat ducts/hair follicles	
region	no. of donors	age of donors	av. no./cm² ± S.E.	S.D.	av. no./cm² ± S.E.	S.D.	av. no./cm² ± S.E.	S.D.	num. ratio ± S.E.	S.D.
ear*	9	7 to 12 years	420 ± 50	144	180 ± 15	35	600 ± 60	130	0·45 ± 0·11	0·25
	10	adult	**600 ± 35**	**110**	**140 ± 40**	**130**	**760 ± 30**	**130**	**0·50 ± 0·08**	**0·20**
thigh	4	11 to 18 months	220 ± 25	155	500 ± 80	155	720 ± 80	155	2·39 ± 0·50	1·01
	21	adult	**55 ± 5**	**20**	**120 ± 10**	**35**	**180 ± 5**	**15**	**2·40 ± 0·80**	**3·60**
groin	1	11 months	140 ± 50	—	400 ± 60	—	540 ± 90	—	2·08 —	—
	1	11 years	80 ± 40	—	270 ± 50	—	350 ± 60	—	3·30 —	—
	5	adult	**70 ± 15**	**30**	**190 ± 5**	**45**	**255 ± 30**	**65**	**3·06 ± 0·17**	**1·20**

* Hair follicles and sweat ducts were counted separately in skin from five donors only.

TABLE 11. SENILE SKIN: COMPARISON OF THE REGIONAL FREQUENCY DISTRIBUTION OF HAIR FOLLICLES, SWEAT DUCTS AND APPENDAGES IN THE SKIN OF INDIVIDUAL DONORS OVER 70 YEARS OF AGE WITH THE CORRESPONDING AVERAGE FIGURES FOR ADULT SKIN (AGE 16 TO 70 YEARS)

Adult figures are shown in bold face. Compare tables 2, 3 and 9.

			hair follicles		sweat ducts		appendages		sweat ducts/hair follicles	
region	no. of donors	age of donors (years)	av. no./cm² ± S.E.	S.D.	av. no./cm² ± S.E.	S.D.	av. no./cm² ± S.E.	S.D.	num. ratio ± S.E.	S.D.
cheek and forehead	4	73 to 74	—	—	—	—	995 ± 60	370	—	—
	23	—	—	—	—	—	**955 ± 50**	**230**	—	—
arm	3	72 to 77	50 ± 5	10	175 ± 20	30	220 ± 15	30	3·40 ± 0·28	0·50
	15	—	**65 ± 5**	**30**	**175 ± 15**	**65**	**255 ± 15**	**60**	**4·50 ± 1·10**	**4·10**
thigh	5	73 to 77	40 ± 5	15	105 ± 20	40	150 ± 20	40	2·60 ± 0·60	1·41
	21	—	**55 ± 5**	**20**	**120 ± 10**	**35**	**180 ± 5**	**15**	**2·40 ± 0·80**	**3·60**
abdomen	1	72	50 ± 40	—	190 ± 40	—	240 ± 40	—	3·70	—
	5	—	**70 ± 15**	**30**	**190 ± 5**	**45**	**255 ± 30**	**65**	**3·06 ± 0·17**	**1·20**
hand	1	73	—	—	370 ± 60	—	390 ± 60	—	—	—
dorsum	—	—	—*	—	370 ± 60	—	390 ± 60	—	—	—
palm	—	—	—	—	390 ± 60	—	390 ± 60	—	—	—
back†	1	77	—	—	—	—	210 ± 60	—	—	—
	4	—	—	—	—	—	**210 ± 5**	**15**	—	—
ear†	1	77	500 ± 150	—	240 ± 40	—	1220 ± 160	—	0·27	—
	10	—	**600 ± 35**	**110**	**140 ± 40**	**130**	**760 ± 30**	**115‡**	—	—

* Below 10%. † Back and ear skin from same donor. ‡ 14 donors.

C-2. *Relation between melanin content and melanocyte density*

Two aspects of the relation between melanin content and melanocyte density were investigated: (*a*) are melanocytes more numerous in the pigmented than in the non-pigmented epidermis of 'white' skin? (*b*) are there more melanocytes in the skin of the coloured races than of the 'white'?

Table 25 shows that macroscopically unpigmented skin may contain as many melanocytes per unit area as the pigmented epidermis of the same individual. The difference between the melanocyte density of the pigmented areola of the nipples and that of the normal skin of the breast is of the same magnitude as the difference in melanocyte density in normal unpigmented breast skin from the two sides of the body.

Table 26 compares averages from individual coloured donors with overall averages from 'white' skin. There is no significant difference between these two sets of data. The high density in the lip of the Indian suggests that, as in 'whites', melanocyte density is higher on the face than elsewhere. It is shown in figure 41 (plate 26) that the melanocytes of coloured donors are similar in shape and size to those of 'white' donors.

C-3. *Cytology of melanocytes*

Four types of melanocytes were observed. The *angular* type (figure 42, plate 26) is a typical stellate cell with long dendritic processes, occurring usually in regions with a melanocyte density of 1600 or less/mm^2. The *round* melanocyte (figure 43, plate 26) has a somewhat larger perikaryon than the angular type and its dendrites are shorter. It occurs in regions with a melanocyte density of 1600 or more/mm^2. The *spindle-shaped* melanocyte (figure 44, plate 26) may have two terminal processes and may be either small or large. The smaller ones are found for the most part on epidermal ridges in the skin of the neck or extensor surface of the forearm. The *giant* melanocytes, which are two to four times larger than the others, usually occur in the epidermis of the cheek around the orifices of hair follicles and sweat ducts; they were found in 23 specimens of skin, 18 of which came from regions that had been exposed to solar radiation. These giant cells have several long flat processes with well-developed, terminal buttons (figure 44, plate 26).

4. Discussion

A. *Regional specificity of the architecture of the epidermis*

(i) *General*

The epidermis, although of binary embryological origin (Medawar 1953), is an organ system in which the pattern of ridges and the distribution of hair follicles, sweat ducts and melanocytes are closely integrated and subject to characteristic regional differentiation. The integument is as varied in structure as other organ systems. The existence of characteristic regional variations in epidermal pattern and in density of appendages explains why in man grafted skin does not blend imperceptibly into the skin of its new site. Besides differences in the vascular supply and other dermal characteristics, the hue of a graft will never exactly match that of the skin which surrounds it; the density of hair follicles and sweat ducts in the graft will always betray the site of origin. When skin from the scalp is transplanted to another area of the body, it retains the characteristics of scalp skin,

including the capacity to grow hair. Orentreich (1959) has shown that hair is lost from transplanted as well as from normal scalp skin *in situ* when alopecia begins.

(ii) *Origin of epidermal pattern and its postnatal changes*

What first induces the development of epidermal ridges in characteristic regional patterns has not yet been determined. Fleischhauer (1953*a*) describes an early orientation

TABLE 12. INDIVIDUAL ESTIMATES OF REGIONAL FREQUENCY DISTRIBUTION OF EPIDERMAL MELANOCYTES IN FIFTEEN DONORS

Specimens from more than one region obtained from each donor.

region	age of donors (years)	mean no./mm² ± S.E.	exposed area / unexposed area (num. ratio)
nose	14	2490 ± 60	0·90
nasal cavity, squamous epithelium		2750 ± 50	
cheek	15	2470 ± 90	1·69
forearm		1460 ± 20	
finger, dorsum	17	800 ± 50	—
fingerprint		790 ± 30	—
periungular region		1020 ± 50	—
upper arm	18	1970 ± 40	—
thigh		1340 ± 30	—
scalp	21	1600 ± 50	—
forehead*		3000 ± 100	2·18
thigh		1370 ± 40	
scrotum		2510 ± 140	
nose	30	1700 ± 80	1·39
nasal cavity, squamous epithelium		1220 ± 60	
upper lip	32	1900 ± 80	1·35
oral epithelium		1400 ± 30	
thigh	36	910 ± 40	—
knee		1490 ± 80	—
heel		1020 ± 150	—
temporal region	38	2380 ± 30	3·01
thigh		790 ± 50	
thigh, frontal	43	1390 ± 240	—
thigh, dorsal		1260 ± 80	—
lower leg, frontal		1290 ± 50	—
lower leg, dorsal		2170 ± 90	—
foot, dorsum		2090 ± 50	—
foot, sole		1120 ± 50	—
cheek	43	3060 ± 260	—
chin		2870 ± 100	—
over mastoid process		3780 ± 120	—
eyelid, lower		2120 ± 90	—
upper arm	43	970 ± 30	—
thigh		670 ± 50	
nose	57	1690 ± 130	
behind ear		1210 ± 140	—
hand, dorsum	73	1320 ± 60	1·14
hand, palm		1150 ± 60	
cheek	77	1290 ± 90	
helix, frontal		750 ± 40	0·49†
helix, dorsal		1530 ± 160	
back		610 ± 20	2·11‡
thigh		650 ± 70	1·98§

* Suntanned. †Ratio, frontal/dorsal. ‡Ratio, cheek/back. § Ratio, cheek/thigh.

of nuclei in the basal layer which he interprets as indication of incipient localization of hair follicles and epidermal ridges. Whether the dermis plays any role in the development of epidermal ridges is not known. That the mesenchyme plays an important special role in the development of ectodermal appendages (Platt 1897, teeth; Lillie & Wang 1941, 1944, feathers; Sengel 1957, feathers; Cohen & 'Espinasse 1961, feathers; Rawles 1963, feathers) is known.

The dermis also exerts a general effect on the induction and later moulding of the architecture of the basal layer of the epidermis. According to Billingham & Silvers (1963, 1965) in adult skin it is the dermis that regulates cytomorphosis of the overlying epidermis, e.g. ear epidermis becomes sole epidermis when grafted over sole dermis. Tongue

TABLE 13. ADULT SKIN: DISTRIBUTION OF EPIDERMAL MELANOCYTES IN HUMAN SKIN (AGE 16 TO 70 YEARS)

Figures are the averages of means from individual donors.

region	no. of donors	melanocytes: av.-no./mm² ± S.E.	melanocytes: S.D.
abdomen	5	800 ± 40	90
arm, foream	9	1100 ± 80	260
arm, upper	11	1210 ± 120	410
axilla	1	1290 ± 50	—
	1	1510 ± 60	—
back and dorsum of neck	6	930 ± 140	350
buttock	1	850 ± 55	—
	1	1670 ± 230	—
cheek	18	2310 ± 150	630
chest	5	890 ± 95	215
chin	5	1880 ± 325	730
ear	12	1400 ± 80	260
eyebrow	1	1910 ± 250	—
eyelid, upper	1	2040 ± 140	—
	1	1370 ± 40	—
eyelid, lower	1	1970 ± 220	—
finger	8	1120 ± 180	500
dorsum	1	800 ± 50	—
	1	2040 ± 150	—
periungular region	1	1020 ± 50	—
fingerprint	1	670 ± 40	—
	1	780 ± 30	—
foot, dorsum	1	610 ± 710	—
foot, sole?*		560 ± 20	—
foot, sole	4	1440 ± 420	840
forehead	8	2010 ± 210	600
leg, lower	11	1510 ± 170	760
leg, thigh	35	1000 ± 70	390
lip, skin	7	1980 ± 180	470
lip, vermilion border	4	1940 ± 200	400
squamous epithelium, oral and nasal	14	1660 ± 130	460
neck, frontal	12	1400 ± 220	770
nose	4	1930 ± 190	380
penis†	2	2380 ± 280	560
scalp	4	1220 ± 80	170
scrotum	3	2300 ± 305	515
toe	1	1190 ± 60	—
	1	1390 ± 30	—

* Necrotic skin. † Average of inner and outer epithelia.

epidermis, however, is an exception to this rule and retains its own characteristics even when 'hybridized' with dermis from the general body integument.

Although the architectural design of the basal layer is genetically determined, it is subject to alteration as the result of growth, increasing age and changes of stress. The pattern of epidermal ridges may be rearranged as stretching of the epidermis is followed by loss of some of the ridges and reorientation of those that persist into parallel rows which

TABLE 14. ADULT SKIN: AVERAGE NUMBER OF EPIDERMAL MELANOCYTES IN VARIOUS BODY REGIONS (AGE 16 TO 70 YEARS)

Figures are arranged in order of decreasing density. Small regions are grouped together.

region	no. of donors	melanocytes: av. no./mm² ± S.E.	melanocytes: S.D.
penis	4	2380 ± 280	560
face (cheek, forehead, lip, nose)	45	2120 ± 90	600
squamous epithelium of nasal and oral mucosa	14	1660 ± 130	460
leg, lower	11	1510 ± 170	760
sole of foot	4	1400 ± 420	840
scalp	4	1220 ± 80	170
arm, upper	11	1210 ± 120	410
arm, forearm	9	1100 ± 80	500
thigh	35	1000 ± 70	390
back	6	930 ± 140	350
chest	5	890 ± 95	215
abdomen	5	800 ± 40	90

TABLE 15. ADULT SKIN: AVERAGE NUMBER OF EPIDERMAL MELANOCYTES IN THE SKIN OF LARGE SEGMENTS OF THE BODY (AGE 16 TO 70 YEARS)

segment	no. of donors	melanocytes: av. no./mm² ± S.E.	melanocytes: S.D.	melanocytes: % of total
whole body	169	1560 ± 110	460	—
head (all regions)	63	1930 ± 60	470	38
head and neck	75	1840 ± 90	750	—
trunk (all regions)	13	890 ± 70	260	17
trunk and neck				
all regions	28	1040 ± 100	530	—
frontal	22	1150 ± 120	570	—
dorsal	6	930 ± 140	350	—
arms (except hand)	20	1160 ± 40	170	23
legs (except foot)	46	1130 ± 60	430	22

TABLE 16. ADULT SKIN: TOTAL NUMBER OF EPIDERMAL MELANOCYTES IN THE SKIN OF A 24-YEAR-OLD DONOR AS CALCULATED WITH BOYD'S ESTIMATES (1935) FOR THE SURFACE AREA OF THE HUMAN BODY (AGE 16 TO 70 YEARS)

region	melanocytes: millions ± S.E.	melanocytes: S.D.	melanocytes: % of total
head	250 ± 10	60	13
trunk	630 ± 60	320	31
arms	390 ± 10	60	19
legs	760 ± 40	290	37
approximate total	2000	—	—

TABLE 17. ADULT SKIN: COMPARISON OF THE FREQUENCY DISTRIBUTION OF EPIDERMAL MELANOCYTES IN MALES AND FEMALES (AGE 16 TO 70 YEARS)

region	no. of donors	melanocytes: av. no./mm² ± S.E.	melanocytes: S.D.
cheek			
male	9	2530 ± 160	490
female	9	2090 ± 230	630
thigh			
male	12	950 ± 120	430
female	23	1030 ± 80	380

TABLE 18. ADULT SKIN: NUMERICAL RATIO OF MALPIGHIAN CELLS/MELANOCYTES IN DIFFERENT REGIONS OF FIVE INDIVIDUAL DONORS OF VARIOUS AGES

Figures are the averages of means from individual donors.

region	age of donor (years)	Malpighian cells/melanocytes (num. ratio ± S.E.)
cheek	15	4·25 ± 0·38
forearm	—	9·05 ± 0·38
nose	21	5·71 ± 0·60
squamous epithelium	—	7·15 ± 0·60
temporal region	38	4·42 ± 0·78
thigh	—	10·40 ± 1·40
hand, border of palm	44	9·50 ± 0·31
upper arm	—	19·90 ± 0·60
thigh, frontal	43	19·19 ± 5·10
lower leg, frontal	—	6·24 ± 0·90

TABLE 19. LOCAL VARIATION IN THE NUMERICAL RATIO OF MALPIGHIAN CELLS/MELANOCYTES WITHIN GIVEN REGIONS OF INDIVIDUAL DONORS

Average figures are in order of decreasing ratio.

region	age of donor (years)	Malpighian cells/melanocytes (num. ratio ± S.E.): ridges	between ridges	average
abdomen	36	3·95 ± 1·14	35·80 ± 3·31	19·87 ± 5·76
back	9	6·70 ± 0·10	23·70 ± 0·40	15·20 ± 3·40
scrotum	32	4·86 ± 0·82	9·36 ± 1·32	7·11 ± 1·07
forehead	22	2·92 ± 0·15	6·99 ± 0·66	4·96 ± 0·72

TABLE 20. ADULT SKIN: AVERAGE RATIO OF MALPIGHIAN CELLS/MELANOCYTES IN DIFFERENT REGIONS OF THE BODY

Regions are listed in order of increasing ratio.

region	no. of donors	Malpighian cells/melanocytes: num. ratio ± S.E.	Malpighian cells/melanocytes: S.D.
cheek	9	4·53 ± 0·29	0·89
face (cheek, forehead, lip, nose)	20	4·63 ± 0·21	0·95
arm	7	10·00 ± 2·10	5·60
ear	5	10·26 ± 1·48	3·33
legs	14	10·82 ± 1·79	6·71
trunk	7	13·39 ± 1·97	5·19

end abruptly (figures 19, neck and 20, abdomen, plate 23). The resulting structure is similar to that normally seen in the skin of the female breast.

Certain changes in the epidermal pattern are characteristically found in ageing skin. In senile skin the epidermal ridges were flattened and there was a statistically insignificant decrease in the density of hair follicles and sweat ducts which might have resulted from general stretching of the skin.

A special role is played by epidermal ridges in the foreskin as they are grouped in such a way as to provide this tissue with a certain degree of 'elasticity' even when all traces of dermis have been removed by digestion with trypsin (figure 23, plate 23).

B. *Distribution of skin appendages*

(i) *Relation between density of hair follicles and visible hairs*

Although man is less furry than some other mammals (Friedenthal 1908), he is by no means hairless. Table 5 shows that approximately 330 hair follicles are present in each

TABLE 21. FOETAL SKIN: COMPARISON OF THE REGIONAL FREQUENCY DISTRIBUTION OF EPIDERMAL MELANOCYTES IN FOETAL SKIN (AGE 7 TO 9 MONTHS *IN UTERO*) WITH CORRESPONDING AVERAGE FIGURES FOR ADULT SKIN (AGE 16 TO 70 YEARS)

Adult figures are shown in bold face.

	no. of donors	age of donor (months *in utero*)	melanocytes	
			av. no./mm² ± s.e.	s.d.
forehead	1	7	450 ± 20	—
	1	9	710 ± 40	—
	8	—	**2010 ± 20**	**600**
thigh	1	7	530 ± 30	—
	1	9	810 ± 30	—
	34	—	**1000 ± 70**	**390**

TABLE 22. YOUNG SKIN: COMPARISON OF THE REGIONAL FREQUENCY DISTRIBUTION OF EPIDERMAL MELANOCYTES IN YOUNG SKIN (AGE 0 TO 15 YEARS) WITH CORRESPONDING AVERAGE FIGURES FOR ADULT SKIN (AGE 16 TO 70 YEARS)

Adult figures are shown in bold face.

region	no. of donors	age of donors	melanocytes	
			av. no./mm² ± s.e.	s.d.
ear	10	7 to 12 years	2580 ± 250	800
	12		**1400 ± 80**	**260**
thigh	4	11 to 18 months	1600 ± 110	200
	34		**1000 ± 70**	**390**
cheek	1	10 years	2140 ± 130	—
	18		**2310 ± 150**	**630**
groin	1	11 months	920 ± 70	—
	1		**780 ± 60**	—
	1	11 months	480 ± 30	—
	1		**760 ± 30**	—
forearm	1	8 years	3540 ± 150	—
	9		**1100 ± 80**	**500**
prepuce	1	5 years	1290 ± 70	—
	4		**2380 ± 280**	**560**
	1	7 years	1590 ± 60	
	4		**2380 ± 280**	**560**

square centimetre of human integument—a total of two million hair follicles on the body as a whole. These follicles are potentially capable of producing either fine or coarse ('terminal') hairs, the type of hair actually produced being determined by the effect of genetic and hormonal factors on the follicle. There are no significant sexual differences

TABLE 23. SENILE SKIN: COMPARISON OF THE REGIONAL FREQUENCY DISTRIBUTION OF EPIDERMAL MELANOCYTES IN SENILE SKIN (AGE > 70 YEARS) WITH CORRESPONDING AVERAGE FIGURES FOR ADULT SKIN (AGE 16 TO 70 YEARS)

Adult figures are shown in bold face.

region	no. of donors	age of donors (years)	melanocytes: av. no./mm² ± S.E.	melanocytes: S.D.
thigh	4	73 to 75	560 ± 70	150
	34		**1000 ± 70**	**390**
arm	4	72 to 77	630 ± 70	400
	20		**1160 ± 40**	**170**
cheek	1	73	2380 ± 90	—
	1	77	1280 ± 90	—
	18		**2310 ± 150**	**630**
forehead	1	73	1010 ± 40	—
	1	75	980 ± 70	—
	8		**2010 ± 210**	**600**
behind ear	1	77	1530 ± 160	—
	12		**1400 ± 80**	**260**
back	1	77	610 ± 20	—
	6		**930 ± 140**	**350**

TABLE 24. YOUNG AND SENILE SKIN: COMPARISON OF THE NUMERICAL RATIO OF MALPIGHIAN CELLS/MELANOCYTES IN YOUNG (AGE 0 TO 15 YEARS) AND SENILE (AGE > 70 YEARS) SKIN WITH CORRESPONDING AVERAGE FIGURES FOR ADULT SKIN (AGE 16 TO 70+ YEARS)

Adult figures are shown in bold face.

region	no. of donors	age of donors	Malpighian cells/melanocytes: num. ratio ± S.E.	Malpighian cells/melanocytes: S.D.
young skin				
cheek	1	10 years	6·26 ± 0·40	—
	9		**4·53 ± 0·29**	**0·89**
ear	8	7 to 12 years	3·51 ± 0·42	—
	5		**10·26 ± 1·48**	**3·33**
thigh	4	11 to 18 months	9·41 ± 2·40	—
	11		**11·21 ± 2·57**	**8·53**
senile skin				
thigh	3	73 to 75 years	16·51 ± 0·44	—
	11		**11·21 ± 2·57**	**8·53**
arm	1	73 years	13·30 ± 1·74	—
	1	77 years	21·00 ± 4·15	—
	7		**10·00 ± 2·10**	**5·60**

TABLE 25. ADULT SKIN: COMPARISON OF MELANOCYTE DISTRIBUTION IN BREAST SKIN AND AREOLA OF NIPPLE FROM ONE DONOR (AGE 42 YEARS)

	melanocytes: av. no./mm² ± S.E.	melanocytes: S.D.		melanocytes: av. no./mm² ± S.E.	melanocytes: S.D.
left breast	710 ± 20	170	right breast	570 ± 30	100
left areola	800 ± 60	190	right areola	850 ± 80	260

in the distribution of hair follicles (Trotter 1921; table 7). The absence of coarse beard hairs in the female is not due to the absence of follicles but to a low level of testosterone. The data reported here statistically confirm the concept advanced by Danforth (1925*a*, *b*) that the total number of hair follicles present in human skin and the number of hairs visible on that skin are not identical. Further evidence that there is no simple correlation between density of hair follicles and degree of hairiness is the fact that the density of follicles on the scalp is less than half that on the cheek and forehead (table 2).

Examination of the very sparse data to be found in the literature shows that failure to distinguish between hair count and follicle count may be responsible for certain misconceptions. Schultz (1931), for example, stated that the back is completely hairless and that on the chest there is only 1 hair follicle/cm^2, a conclusion based on tallies of hairshafts which he pulled from the skin of these areas: that is, on the number of visible hairs. My count of hair follicles on the scalp (table 2) corresponds fairly closely to Schultz's finding of 288 to 341 hairs/cm^2 of scalp skin, thus indicating that on the scalp each follicle produces a visible hair. As regards the distribution of visible hair on the head, what is true for man may be true for other primates. Straus's data (1950) show that the relative density of hair is highest in the crown of the gorilla. Data published by Taniguchi & Kurita in 1941, which had been obtained from twenty-two subjects after death, show a hair-follicle distribution similar to that found in our investigation.

(ii) *Differences in density of hair follicles*

There is great individual and regional variation in the density of hair follicles in the adult (tables 1 to 5). In foetal life the density is high in all regions (table 9). After birth there is a progressive overall reduction of follicle density which continues until adult life; this

TABLE 26. 'COLOURED' SKIN: COMPARISON OF EPIDERMAL MELANOCYTE FREQUENCY DISTRIBUTION IN THE SKIN OF INDIVIDUAL 'COLOURED' DONORS WITH COMPARABLE AVERAGES FOR 'WHITE' SKIN (AGE 16 TO 70 YEARS)

region	'coloured' skin melanocytes (av. no./mm^2 ± S.E.)	no. of donors	'white' skin* melanocytes (av. no./mm^2 ± S.E.)	S.D.
	Negro			
back	940 ± 60†	6	930 ± 140	350
lower leg, frontal	1050 ± 60‡	11	1510 ± 170	760
foot, dorsum	1440 ± 70	1	610 ± 70	
		1	2840 ± 40	
	West Indian (mulatto)			
thigh	1350 ± 40	35	1000 ± 70	390
thigh	890 ± 40	35	1000 ± 70	390
scrotum	2690 ± 100	3	2300 ± 305	515
	Indian (native of India)			
thigh	1370 ± 60	35	1000 ± 70	390
neck	830 ± 40	12	1400 ± 220	770
upper arm	910 ± 30	11	1210 ± 120	410
upper lip	1820 ± 50	7	1980 ± 200	400
vermilion border	1410 ± 50	4	1940 ± 200	400

* See table 13. † Sudanese. ‡ African.

reduction is less marked on the head than on the rest of the body (table 10). Regional differentiation of follicle density therefore increases gradually with age until maturity (tables 9 and 10). In the past, postnatal reduction in hair density has been explained by various theories, many of which have been reviewed by Flesch (1954). A new theory based on our statistical findings will be outlined here after the characteristic distribution of sweat ducts has been considered.

(iii) *Differences in density of sweat glands*

In man the vast majority of sweat glands is of the eccrine type. The average density of sweat ducts in adult human skin is 200/cm^2 (table 5). The total number of sweat ducts in the body approximates 3 million, a figure close to that suggested by Kuno (1938). Thomson's (1954) figures, obtained from normal, living, human skin, differ from ours by as much as 48 to 77%. These differences may reflect diverse regional changes of dimension during fixation, or more, probably, as Thomson himself has pointed out, failure to enumerate all existing ducts. There is an even greater difference (38 to 94%) between our figures and the century-old data of Krause (1844).

That the rate of sweat excretion depends not on the number of sweat ducts actually present in the skin, but on nervous and temperature factors that influence the activity of the sweat glands is well known (Kuno 1938). At any given moment, the number of *active sweat glands* may be far from identical with the *total number of sweat glands* present in the skin.

(iv) *Relation of regional differences in the density of skin appendages to growth of body surface*

Several authors (Meyer-Lierheim 1911; Schulz 1931; Kawaji 1934; Taniguchi & Shibayama 1935; Carter & Dowling 1954; Hafez, Badreldin & Shafei 1955; Lyne 1957; Lyne & Heideman 1959) have provided evidence that reduction in the density of hair follicles during postnatal development may be due to expansion of the skin surface; other authors (Taniguchi & Kuriki 1937; Fleischhauer 1953*a*, *b*; Thomson 1954) feel that changes in the density of sweat glands may be explained in the same way.

We found that the validity of this hypothesis can be tested only when the densities of both these types of cutaneous appendages are considered together. This was the reason that we pooled data obtained from the study of hair follicles and sweat ducts under the heading 'cutaneous appendages'.

Table 27 shows how the normal rates of regional growth of the body surface of man would affect the distribution in the adult of cutaneous appendages which had been evenly distributed *at birth* and not formed *de novo* after birth. Using the data of Boyd (1935) it is possible to calculate how this even distribution would be 'diluted' during postnatal growth. The appendages become more widely spaced in the trunk and extremities than in the head, because the surface area of these regions enlarges more than that of the head. The percentage regional distribution of these structures in such a system can be seen to approximate quite closely the percentage distribution estimated from directly observed data.

It is also possible to calculate the percentage distribution of cutaneous appendages in the adult on the assumption that the number of appendages becomes fixed, not at birth,

but at some time between the third and the eighth month *in utero* (table 28). The percentage distribution actually found in our study of adult skin falls between the figures estimated for the fifth and sixth months of development *in utero* (tables 4, 28). It is known that during foetal life the development of hair follicles and sweat glands progresses in a caudo-ventral direction. Therefore, the data shown in table 28, which indicate that skin appendages appear between the fifth and sixth month *in utero*, refer to average age and not to the actual time when these appendages first appear.

It is evident therefore that once the body has developed beyond the stage at which hair follicles and sweat ducts are formed *in utero* the total number of these cutaneous appendages in the individual has been permanently determined. Any increase in the surface area of the body thereafter would produce an *apparent* (not a real) decrease in hairiness because it would increase the space between existing appendages without decreasing the absolute number of these structures. Mere growth, therefore, and the change from lanugo-type hair to fine, adult hair could give rise to mistaken belief in the large-scale destruction of hair follicles after birth.

TABLE 27. GROWING SKIN: REGIONAL DIFFERENCES OF DILUTION BY POSTNATAL GROWTH OF AN ARBITRARILY CHOSEN FIXED NUMBER OF CUTANEOUS APPENDAGES UNIFORMLY DISTRIBUTED AT BIRTH

	full-term foetus appendages		increase in size	full-grown adult appendages	
region	no./cm²	% of total	of region*	no./cm²	% of total
head	1000	25	× 2·98	335	52
trunk	1000	25	× 9·02	111	17
arms	1000	25	× 9·55	104	16
legs	1000	25	× 10·46	95	15

* Boyd's figures (1935).

TABLE 28. FOETAL AND ADULT SKIN: REGIONAL PERCENTAGE DISTRIBUTION OF CUTANEOUS APPENDAGES IN SKIN OVER DIFFERENT SEGMENTS OF THE HUMAN BODY AS CALCULATED FOR THE FOETUS AND THE ADULT

Extension of the data presented in table 27, based on the assumption that the absolute number of skin appendages becomes fixed between the third and the ninth month *in utero*. Adult figures are shown in bold face.

	hypothetical (% of total)			observed in adults	hypothetical (% of total)			
in utero (months)	3	4	5	(% of total)	6	7	8	9
head	68	62	59	**58**	56	54	53	52
trunk	16	17	17	**15**	17	17	17	17
arms	9	12	14	**16**	16	16	16	16
legs	7	9	10	**11**	12	13	14	15

(v) *Numerical ratio of sweat glands/hair follicles. The dermal papilla as indicator of hair development*

The data presented in tables 27 and 28 indicate that appendages are originally spaced at equal distances regardless of whether they are destined to become hair follicles or eccrine sweat glands. Fleischhauer (1953*b*) stressed the similarity of the anlage of hair follicles and sweat glands in a surface view of the basal layer. Japanese investigators (Kato 1936; Taniguchi & Mochizuki 1937) have also expressed the view that distribution of these

appendages should be regarded as governed by the same principle. Horstmann (1957) more recently has proposed that the original density of appendages is uniform over the entire body and that at some stage 'suddenly a command is given to form sweat glands instead of hair follicles'. It seems as though downgrowths develop at regular intervals in the epidermis and that the eventual character of a given downgrowth depends on whether or not it combines with a dermal papilla. Appendages which come into contact with papillae develop into hair follicles, while those which do not come into contact with papillae may develop into sweat ducts. This hypothesis has not yet been substantiated by experimental data. The role of dermal papillae in the formation of hair follicles is still only incompletely understood (Billingham 1958; Pinkus 1958). Developmental studies of similar structures indicate that mesenchymal elements play an inductive role in initiating the development of teeth (Platt 1897; De Beer 1947) and feathers (Lillie & Wang 1941, 1944; Sengel 1957). Evidence that they play a comparable role in the development of mammalian hair has not yet been obtained, although the vital role of dermal papillae in the hair cycle has been widely accepted (Bullough & Laurence 1958).

In discussing the phylogenetic evolution of dermal papillae, one may suggest that in mammals other than primates the density of hair papillae could correspond to the density of all epidermal appendages. Under these conditions all appendages in the general body skin would become hair follicles (some with apocrine sweat glands) and there would be no eccrine sweat glands except in the palms and soles. In primates, including man, the density of hair papillae would decrease in a caudal direction during foetal development, with a proportionate increase in the number of eccrine sweat glands.

The neoformation of hair follicles in experimental wound healing (Breedis 1954, rabbit; Billingham & Russell 1956, rabbit; Kligman & Strauss 1956, man; Kligman 1959, man; Mikhail 1963, rat; Brook, Short & Lyne 1960, lamb; Lyne & Brook 1964, lamb) may indicate that in mammalian epithelium there is an innate tendency to project epidermal ingrowths at regular intervals. New hairs are formed year after year in the regenerating antlers of the deer (Billingham, Mangold & Silvers 1959).

There is also statistical evidence for the existence of a developmental relationship between hair follicles and sweat glands. During foetal life (table 9) the ratio of sweat ducts/hair follicles increases gradually in the caudo-ventral direction and finally becomes established in the newborn with characteristic regional variation (table 10).

(vi) *'Practical' applications of this investigation*

There are between four and five times more pilosebaceous units and sweat glands ('pores') in the skin of the head than in the skin over other parts of the body. This anatomical fact is important for the understanding of skin ailments that affect the orifices of these structures. Any changes arising at random in hair follicles are likely to be about ten times more numerous per unit area on the head than elsewhere (table 3). Changes in the sweat ducts on the head should be about twice as numerous per unit area as on the leg, arm and trunk (table 3). Szabó (1959*a*) has shown that the regional incidence of naevi is similar to the regional density of hair follicles and that the regional incidence of melanomas is similar to the regional density of skin appendages. This may indicate that neoplastic changes of melanocytes originate in the pilosebaceous units and around the orifices of

sweat glands, whereas naevi may be intimately connected with hair follicles only. Data reported in the literature are so varied, however, that interpretation must proceed with extreme caution.

C. *The melanocyte system*

(i) *Distribution of dopa-positive and dopa-negative melanocytes in mammals*

The most important result of our investigation is the finding that dopa-positive melanocytes are ubiquitous in human epidermis and in the epithelia of the nasal and oral cavities. We are corroborating the studies of Billingham (1949) and expanding Szabó's previous findings (Szabó 1954, 1959*a*). The human integument is, thus, an example of that type of mammalian skin in which the epidermal melanocytes contain an active tyrosinase system. This is not true for all mammals (Montagna 1962, p. 77). In some rodents, such as mice, rats and rabbits (Holmes 1953; Reynolds 1954), melanin is present only in the hair matrix and in certain circumscribed body regions (ear, nose, palm, sole and tail). In guinea-pigs, on the other hand, pigment may be present in both the epidermis and the hair follicles according to genotype (Billingham 1948; Billingham & Medawar 1953). The epidermis of carnivores and pinnipedia, such as cats and dogs, and seals contains functioning melanocytes (Szabó 1959*b*). The epidermis of the whale is pigmented and in some primates the epidermis contains an active melanocyte system. In species whose epidermis contains no dopa-positive melanocytes, however, the presence of inactive dopa-negative melanocytes can be demonstrated by means of methylene blue, toluidine blue or brilliant cresyl blue stain. These dopa-negative cells can be activated by a variety of agents, including carcinogens (Szabó 1963). Only the so-called 'white spotted' (Silvers 1956) mammals seem completely to lack epidermal melanocytes. The so-called 'albino' guinea-pigs have scattered, large, pigmentary melanocytes interspersed with much smaller, fusiform, non-pigment-forming melanocytes (Szabó 1965). In human albinos there are melanocytes that produce amelanotic melanosomes (Barnicot & Birbeck 1958).

Melanocytes are not confined to the epidermis and the leptomeninges in mammals. There are pigment cells in the dermis of primates that follow blood vessels much as they do in the lower vertebrates. Furthermore, as has been pointed out (Nichols & Reams 1960; Reams 1963), melanocytes are consistently present in the leg muscles of so-called 'PET' mice. Their occurrence in the pharynx (Becker Sr. 1927; Némai & Kelemen 1928, primates) indicates that pigmentary melanocytes are also associated with entoderm.

(ii) *The integrated, epidermal, pigmentary system*

It is evident from our data that some mechanism regulates the Malpighian cell/melanocyte ratio. There is a general 'attraction' of melanoblasts by the epidermal cells, since the long migration of melanoblasts from the neural crest terminates in the epidermis. The melanoblasts attach themselves first to any epidermal ridges that may be present, e.g. in the sole, and later to the whole basal layer. Thence in hairy skin they are carried down to the hair bulb as the follicle develops from the epidermis (Danneel & Weissenfels 1953). In the adult melanocytes are more abundant in the epidermal ridges than elsewhere.

The average ratio of Malpighian cells/melanocytes varies from 4:1 (cheek) to 14:1 (trunk) in adult skin (table 20). Since each melanocyte has more than one dendrite and can reach at least as far as the second row of Malpighian cells, each Malpighian cell must

be in contact with one or more of the melanocytes in the basal layer. This is circumstantial, anatomical and statistical confirmation of the concept formulated by Masson in 1948 that melanocytes and only melanocytes are responsible for the formation of pigment in the epidermis and that they are true unicellular secretory units disseminating pigment by cytocrine activity through their dendrites.

The close integration of melanocytes and Malpighian cells has led Fitzpatrick & Breathnach (1963) to coin the term 'epidermal melanin unit', which emphasizes the anatomical and physiological union of these two types of cells. Indeed, the melanization of the epidermis depends as much on the propagation of melanin granules by melanocytes as on the incorporation of melanin granules by Malpighian cells. Imperfect donation of melanin granules by melanocytes or failure of Malpighian cells to accept the granules, as well as lack of an active tyrosinase system in the melanocytes, can lead to defects of pigmentation. In the 'dilute' genotypes of mice conveyance of melanin granules within the epidermis seems to be abnormal, with the result that Malpighian cells are sparsely pigmented while the melanocytes are choked with melanin. In the normal black or brown genotypes of mice and in man, on the other hand, the Malpighian cells are well pigmented because the melanocytes are able to donate melanin efficiently. The processes of pigment donation by melanocytes and of acceptance of pigment granules by Malpighian cells are so effective in these mice and in man that the melanocytes are usually *less* pigmented than the cells which accept their product.

(iii) *Skin colour and melanocyte density*

It is obvious that in any tissue intensity of pigmentation must depend on (*a*) the number of pigment-containing cells present and (*b*) the number, colour and location of pigment granules in each of these cells. The pigment-containing cells may be either pigment-forming, pigment-receiving or both. It follows, then, that the colour of a tissue whose only pigment-containing cells are melanocytes (e.g. the dermis or leptomeninges) will be determined by (*a*) the number of melanocytes within that tissue and (*b*) the nature and density of the pigment granules within those melanocytes.

By contrast, in the epidermis of vertebrates, which contains both melanocytes and Malpighian cells, colour is determined by the functional equilibrium of pigmentary units composed of pigment-forming and pigment-donating melanocytes and pigment-accepting Malpighian cells. In 'dilute' genotypes of mice with 'congested' melanocytes (Markert & Silvers 1956), in *Rana pipiens* (Szabó, unpublished) and in carnivores (Montagna 1962, p. 77) and seals (Szabó 1959*b*) melanocytes contain more pigment than do other epidermal cells. In other mouse genotypes and also in man melanocytes 'go underground' and pass unnoticed among the pigmented or unpigmented Malpighian cells unless their presence is revealed by dopa, because they have either acted very efficiently or become dormant. In such epidermis intensity of pigmentation therefore depends more on the function than on the number of melanocytes. Since this concept was still relatively new and unfamiliar a decade ago, most of the published studies of animal colouration have been focused on the pigmentary effector system of lower vertebrates (Hogben 1924; Parker 1948).

A striking illustration of this is the fact that intensity of colour and melanocyte density may be inversely related. There are twice as many epidermal melanocytes in skin from the

cheek of the Caucasian as in epidermis from the thigh of the Negro (tables 14 and 26); the melanocytes in skin from the Negro thigh are more efficient than those in the Caucasian cheek. The sparse population of melanocytes in the Negro thigh produces a dark pigmentation whereas in the Caucasian cheek a population twice as dense colours the skin only slightly.

It is not surprising therefore to find that melanocyte density does not differ significantly in corresponding areas of the epidermis of the various human races (Negro, West Indian and Indian, table 26). Our initial data have been substantiated by Staricco & Pinkus (1957) for the American Negro and by Mitchell (1963) for Australian aborigines. Racial colour is determined by the functional activity of the tyrosinase system.

Certain mammalian skin is coloured because its dermal melanocytes are pigmented, e.g. that of the ear, tail and scrotum of mice (Reynolds 1954) and the general body of primates (Montagna 1962, p. 77). It seems that the four enveloping layers of melanocytes of lower vertebrates described by Weidenreich (1912) (see § 1) are not reduced in the course of evolution as much as has hitherto been assumed.

(iv) *Changes due to age*

Scanty data from foetal skin (table 21) show that the number of melanocytes increases during intra-uterine life. This increase may be due either to continuous migration of melanocytes into the epidermis or to division or maturation of melanocytes manifested as an increase of dopa-positive cells. In young skin (age 0 to 15 years) melanocyte density is significantly higher in most body regions than in adult skin (age 16 to 70 years) (table 22). The observed decline in melanocyte density in the adult continues in old age (age $>$ 70 years) (table 23).

Snell & Bischitz (1963) have substantiated the findings that are presented here in tables 22 and 23. They have shown that after birth melanocyte density decreases approximately 10% per decade.

Cytological changes also take place during ageing, as the cell bodies of melanocytes gradually become larger and in old age their dopa reaction becomes variable. The ratio of Malpighian cells/melanocytes shifts in favour of Malpighian cells (table 24) as age increases. This may indicate that the rate of replacement of Malpighian cells and dopa-positive melanocytes is not the same and that there is a gradual dying out of melanocytes. The concomitant histological changes are similar to those found at the edge of a vitiliginous lesion (Jarrett & Szabó 1956) in which melanocytes are much larger than in normal skin.

It has been proposed in § 4B (tables 27, 28) that developmental factors are responsible for regional differences in the distribution of skin appendages. The same is not true for melanocytes. If one compares the last column in table 15 with that of table 27, it becomes evident that regional differences in the distribution of melanocytes and skin appendages are of different proportions. The causes of regional differences in melanocyte distribution are not known.

(v) *Correlation between epidermal pattern and melanocyte density*

The architectural pattern of the basal layer of the epidermis influences the regional frequency distribution of melanocytes. As has already been mentioned (§ 4C (i); figures 35,

36, plate 25; table 19), in areas where the pattern of ridges is well developed melanocytes are concentrated on the ridges. Regions such as the abdomen, groin and thigh, where the density of melanocytes is lowest, are characterized by very large inter-ridge areas in which the density of melanocytes is low. The inter-ridge areas of infants are less extensive than those of adults, and the overall average of melanocyte density is therefore higher in infants than in adults. Billingham & Medawar (1953) have found that in the guinea-pig melanocytes are more numerous in the ridges than in the valleys between them. Ridges were also found to be more active than valleys in the replacement of epidermis. Snell & Bischitz (1963) found the same to be true of human abdominal skin.

The cheek can be regarded as one continuous ridge, where the density of melanocytes is very high. The skin of the cheek is unique as regards both structure and melanocyte density. The absence of epidermal ridges and the high density of skin appendages and melanocytes distinguish it from skin from other regions of the body.

(vi) *Symmetry of distribution*

The distribution of melanocytes is bilaterally symmetrical (§ 3 C-1 (ii)). In man the ratio of the number of melanocytes in the right/left side is $1{\cdot}04 \pm 0{\cdot}076$ (S.D. = 0·27). The same is true for the guinea-pig. Our calculations from the data of Billingham & Medawar (1953) give the ratio for the right/left side of the ear of the guinea-pig as $0{\cdot}973 \pm 0{\cdot}044$ and for the right/left side of the abdomen as $1{\cdot}066 \pm 0{\cdot}049$.

(vii) *Melanocyte morphology*

Density affects the shape of melanocytes and the length of their dendrites (figures 42 to 44, plate 26). We have found these cells to be angular in areas of low density, round where the density is high. They are spindle-shaped where the epidermis is under tension, e.g. in the skin of the neck, the forearm, in the epidermal ridges of abdominal skin and in scar tissue. Staricco & Pinkus (1957) and Mitchell (1963) also have described different types of melanocytes, i.e. stellate, spindle-shaped and giant.

The origin and significance of the giant melanocytes noted in our study are not fully understood. Solar irradiation favours their occurrence. They are found in pathological specimens, near basal cell carcinomas and in skin subjected to radiotherapy (Szabó 1959*a*). Grand, Chambers & Cameron (1935) have reported finding both large and small melanocytes in tissue cultures of human melanoma. The melanocytes in epidermis taken from the primary lesions of melanoma differ from these giant cells (Szabó 1959*a*). The neo-plastic melanocytes tend to clump together and their dendrites have a moniliform appearance. Giant melanocytes, on the other hand, though hypertrophic, are morphologically normal.

(viii) *The importance of being pigmented (effect of radiation)*

Some years ago it was fashionable to declare that the inability to produce pigment was of little consequence to man (Keller 1930; Blum 1948) and only as an afterthought was it admitted that melanin present in the retina and choroid provides protection for the photoreceptors. The idea that melanin pigment is of no vital importance in the skin and has no role in the development of the integument was seemingly supported by Rawles's (1947)

success in producing perfect hairs *in vitro* without the intervention of any melanocytes and by the fact that in 'white spotted' (Silvers 1956) animals the Malpighian cells produce normal keratin without any help from melanocytes.

Some authors have claimed (Kopac 1948; Helmy & Hack 1965) that melanin performs a vital role in cell metabolism. Further evidence is needed for the validation of such claims. One can state with confidence, however, that the permanent absence of pigmentation can be a source of social maladjustment, physical discomfort or disability in vision and cosmetic problems for albino members of the coloured races (see Barnicot 1957; Keeler & MacKinnon 1963).

Even the keratinized flakes on the surface of Negro skin are pigmented (Thomson 1955) and thus protect the skin from actinic rays. In doing this they reduce the incidence of skin cancer on the exposed parts of the body (Dorn 1944; Mitchell 1963).

The investigations of Babak (1913) and Green (1964) have shown that the pigment cells of fishes and crustacea may decrease or increase in number according to the conditions of exposure to light. It is well known that non-ionizing radiation (ultraviolet and visible light) induces changes in mammalian melanocytes also. Exposure to such radiation is followed, first, by darkening of pre-existing melanin ('pigment darkening') the mechanism of which is not yet understood. The melanocytes then undergo cytologic changes, which, according to some authors (Peck 1930; Laidlaw 1932; Becker Jr. *et al.* 1952), are manifested by an increase in the intensity of the dopa reaction and in some instances by an increase in the number of dopa-positive cells in the basal layer (Quevedo & Smith 1963). Melanocytes are more readily demonstrated in irradiated than in unirradiated skin. The post-irradiation increase in pigmentation usually starts around the orifices of hair follicles (Miescher 1927).

More detailed information is needed about the response of melanocytes to non-ionizing radiation, especially about the causal relationship between the increased pigmentation and (*a*) *DNA* synthesis in melanocytes, (*b*) rate of synthesis of tyrosinase in melanocytes, (*c*) changes in the tyrosine-tyrosinase reaction, (*d*) changes in the rate of melanosome formation, and (*e*) changes in the rate at which melanosomes are donated to Malpighian cells. Our preliminary experiments have shown that the increase of pigment in the epidermis that follows a single dose of radiation (300 nm) to the skin is not caused by an increase in the number of melanocytes (Pathak, Sinesi & Szabó 1965). Repeated exposure to radiation from a sunlamp, however, is followed by an increase in the number of dopa-positive cells in the epidermis (Snell 1963; Quevedo, Szabó, Virkes & Sinesi 1965).

Finally, a few words must be said about claims that melanocytes may have functions other than the production of melanin. The fact that their distribution differs from that of pain spots (Frey & Rein 1929) and tactile sensory endings (Cornbleet 1953) may refute Langerhans' (1868) assumption that they have a nervous function. According to Weddell and his colleagues (Weddell, Pallie & Palmer 1954; Weddell, Palmer & Pallie 1955) there may be a close but variable anatomical relationship between the nerve endings of the skin and the dendrites of melanocytes.

The role of melanocytes as amphoceptors (Masson 1948) has recently been discussed by Mitchell (1963). Clear-cut histological evidence, especially at the level of electronmicroscopy, is still lacking.

Since the earliest stages of animal evolution, melanocytes have played a very important role in the protection of photoreceptors. That they also provide much needed general protection to the whole body cannot be denied. The absence of pigmentation is often a good indication of general malformations due to an early error in embryonic development. Furthermore, in man melanocytes are not mere phylogenetic remnants but play an essential role in the protection of the individual against the harmful influence of non-ionizing radiation.

This work was supported by a research grant of the Medical Research Council.

The author is greatly indebted to Dr P. B. Medawar, F.R.S., for his continuing interest and great assistance during all stages of this investigation. Grateful thanks are also due to the late Mr Rainsford Mowlem, F.R.C.S., whose generous co-operation made the collection of skin samples possible. The careful work of Mr W. Brackenbury in taking the microphotographs is also thankfully acknowledged.

The editorial assistance of Miss Taylor of the Department of Dermatology, Harvard Medical School, is much appreciated. Thanks are due to Miss Stanganelli for her careful typing of the manuscript and to Miss Butterworth for her work on the final draft.

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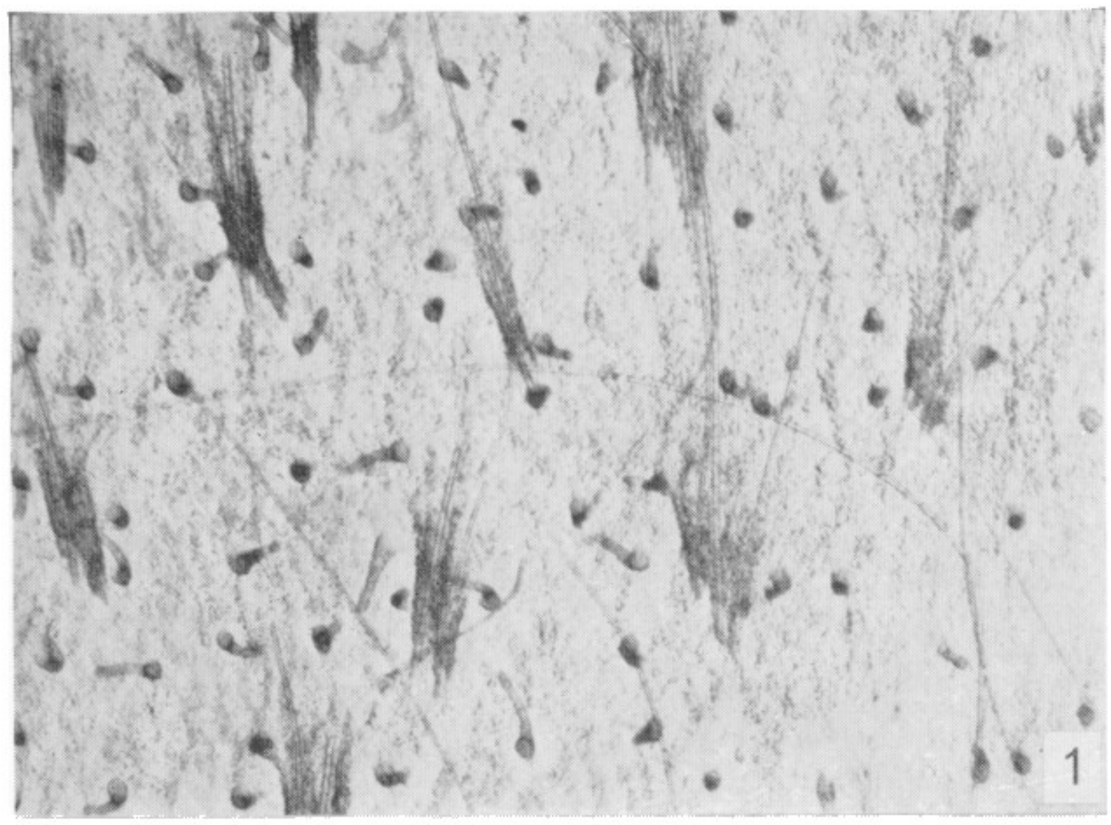

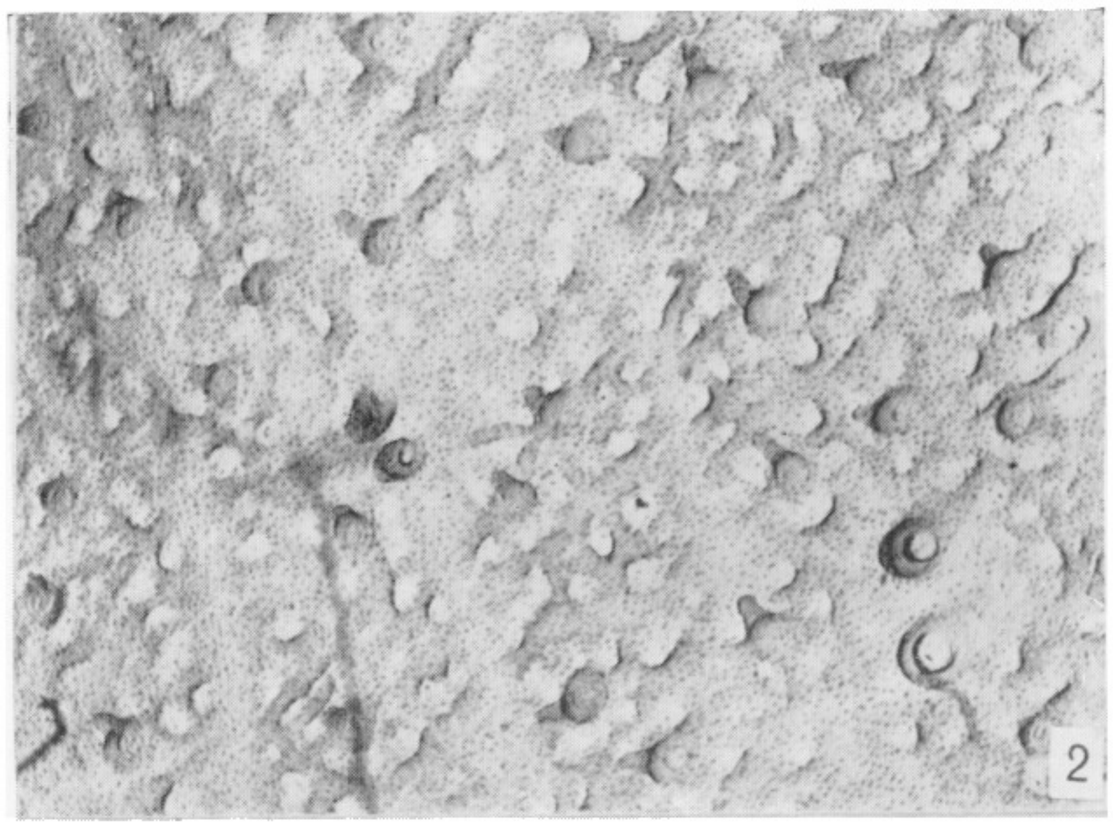

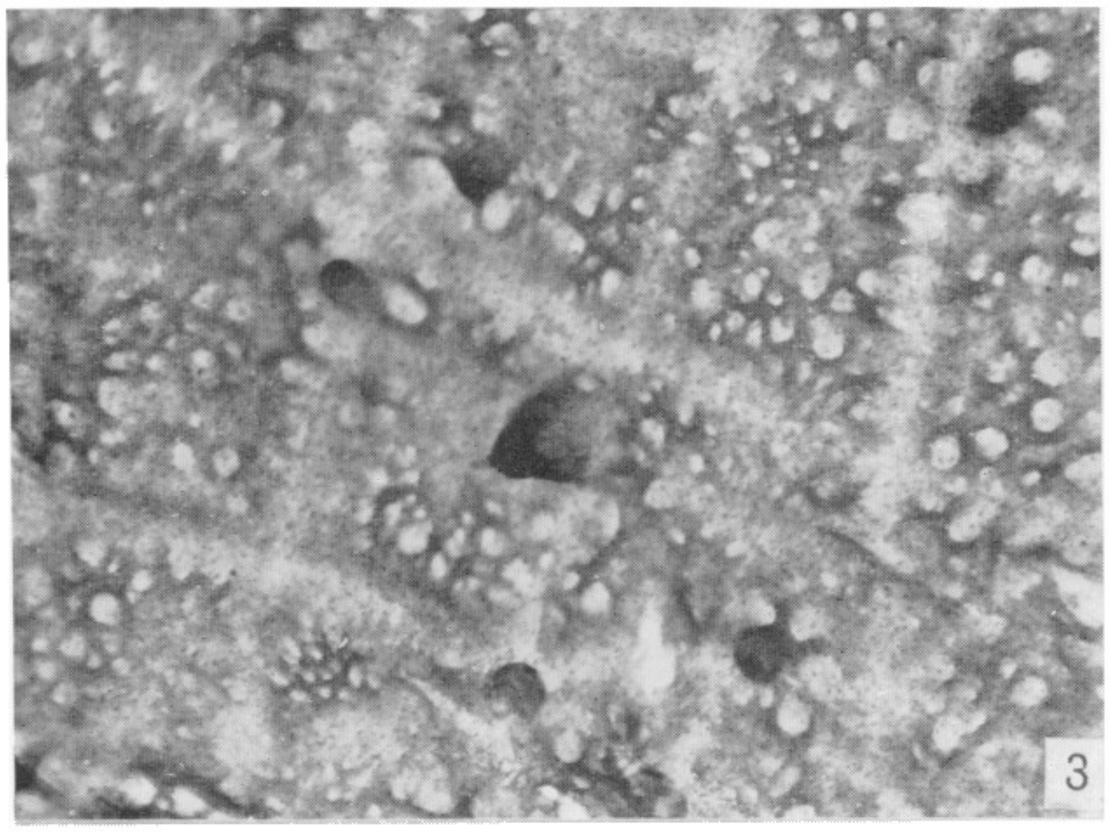

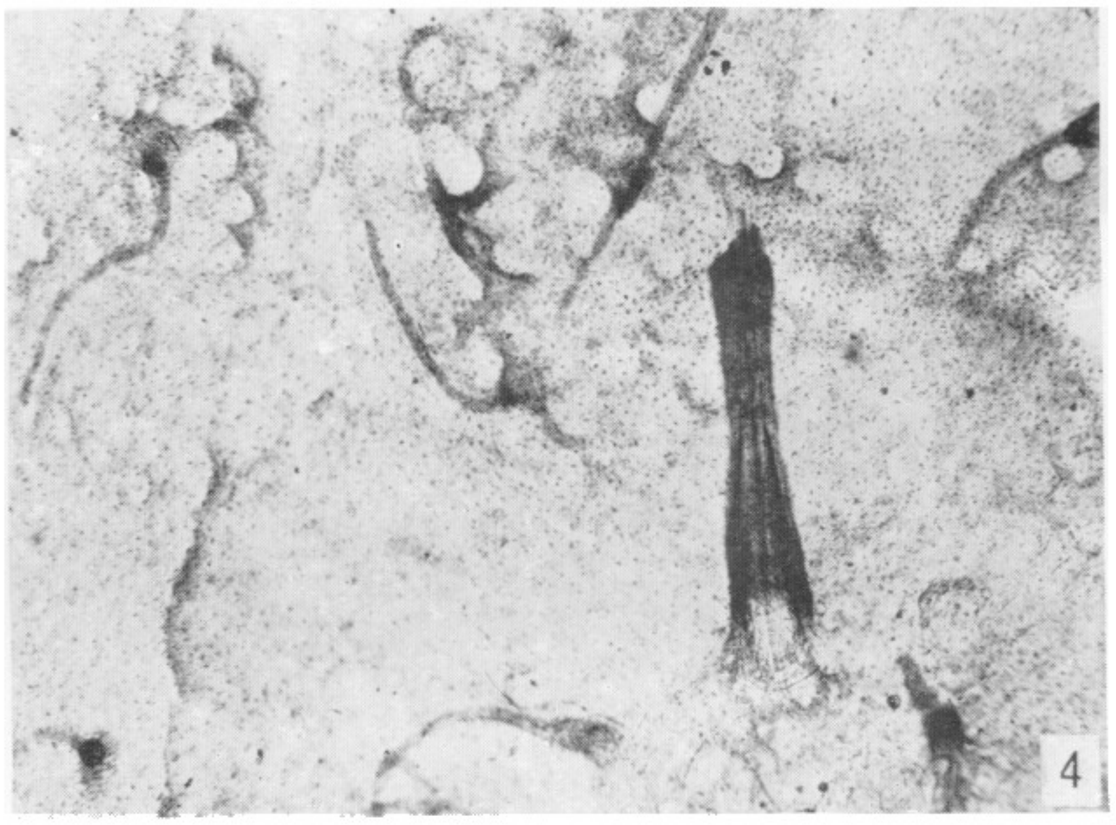

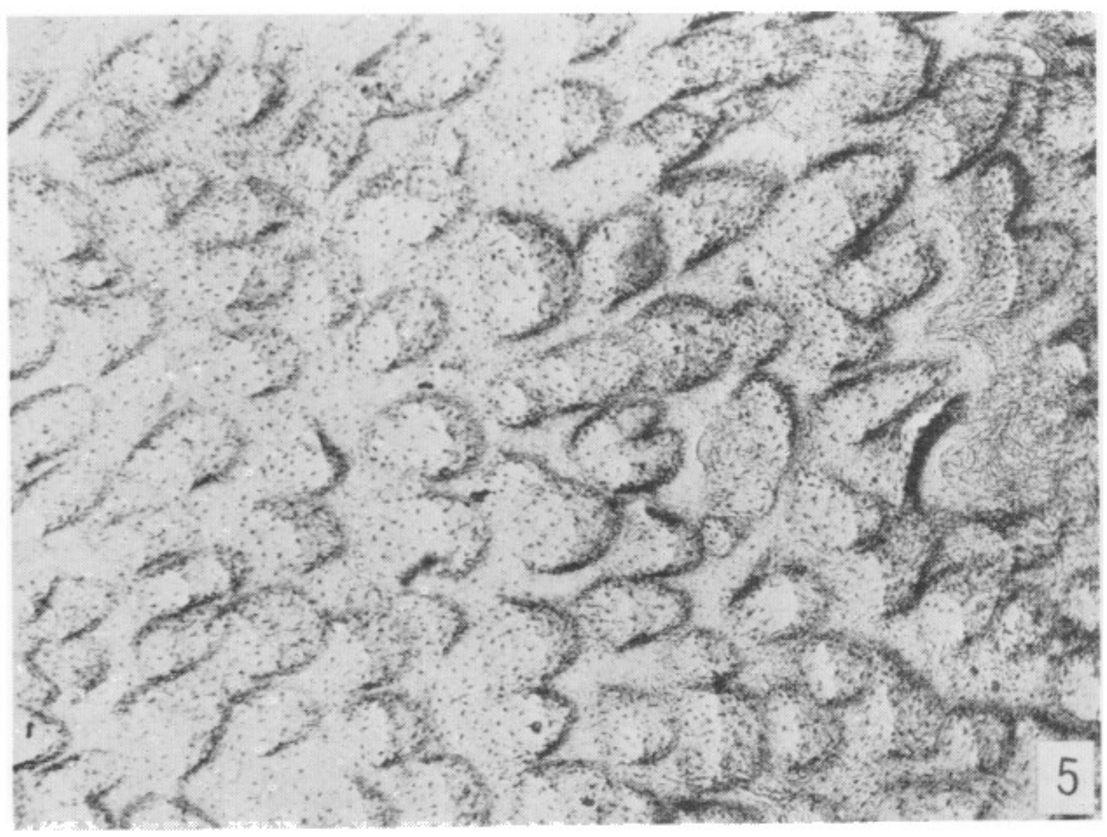

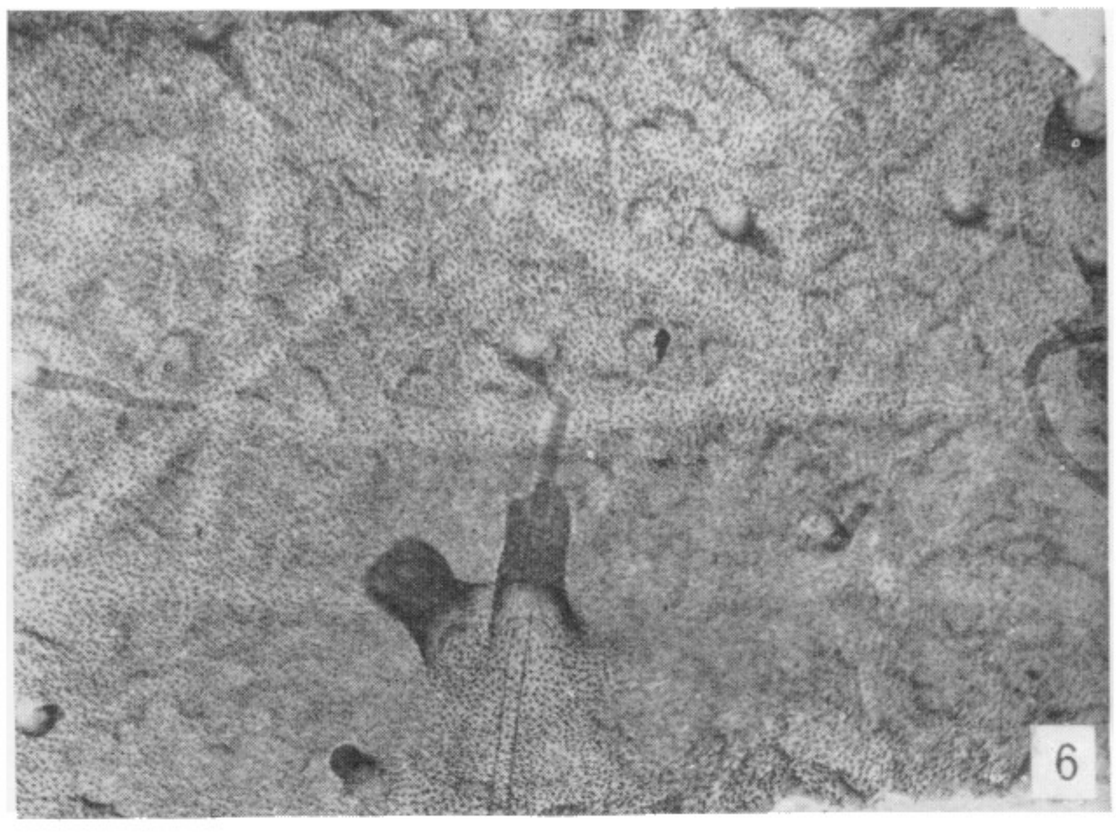

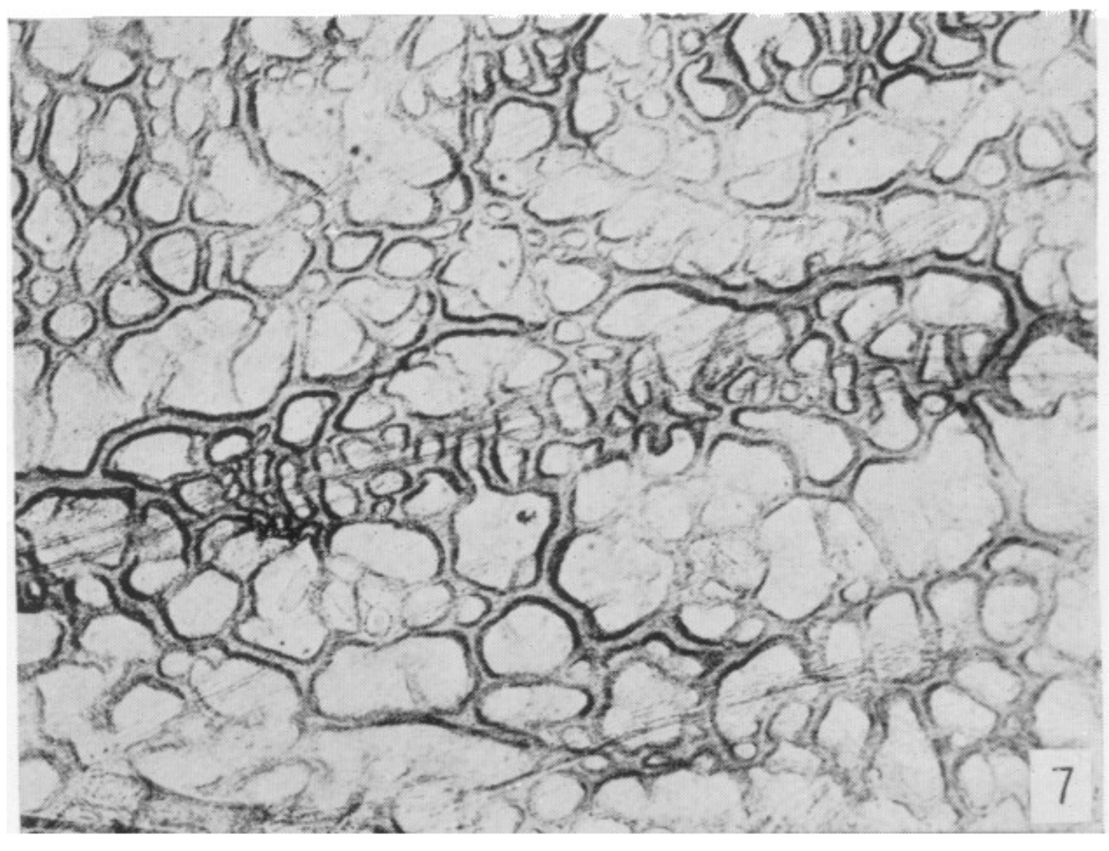

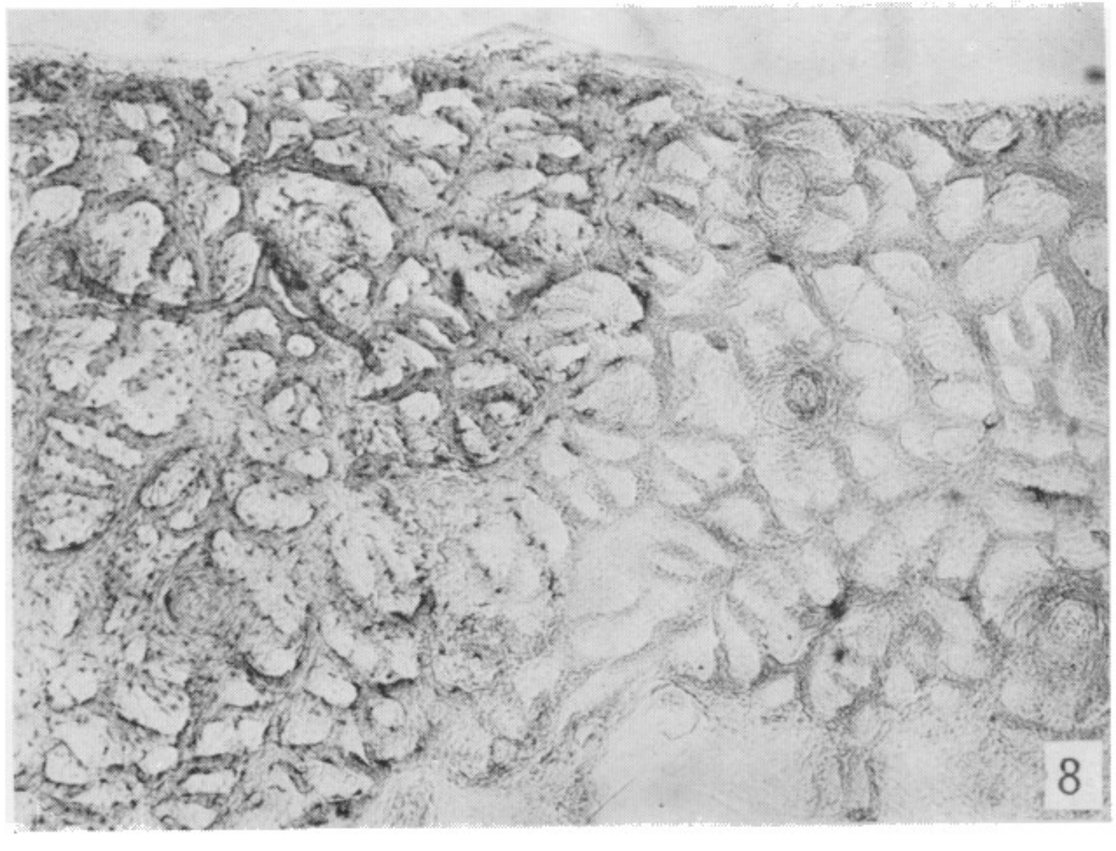

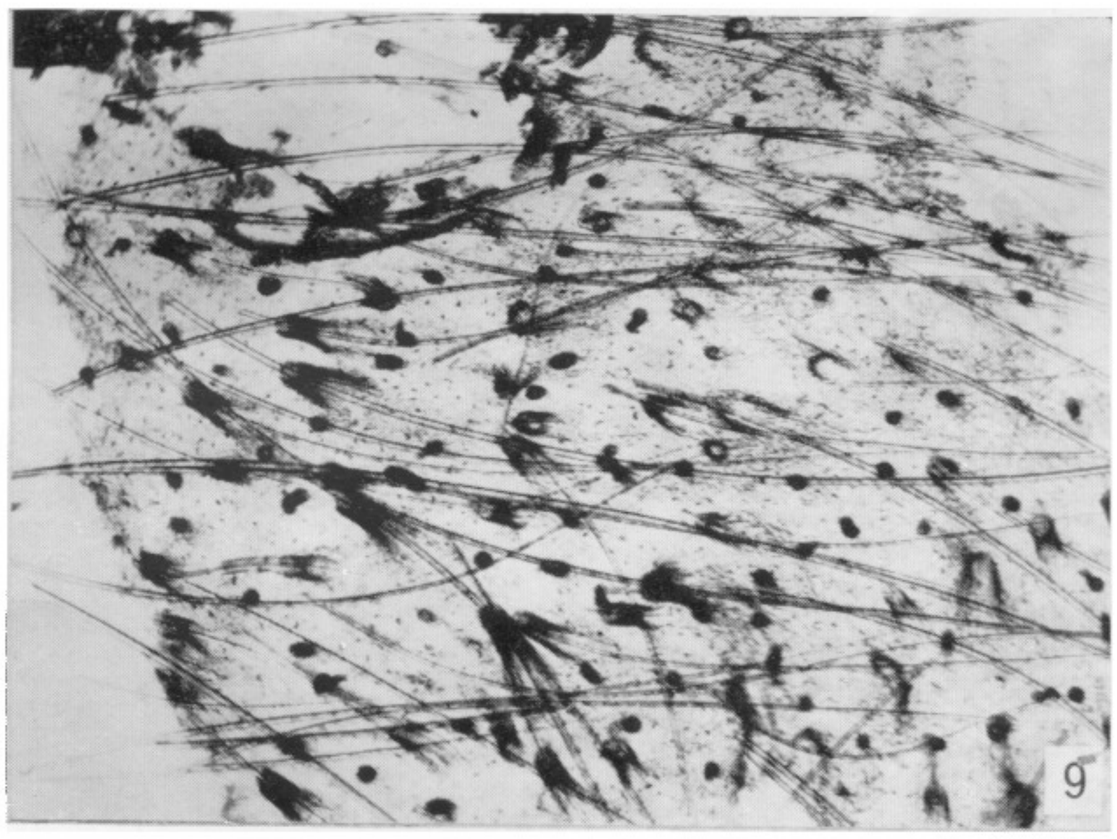
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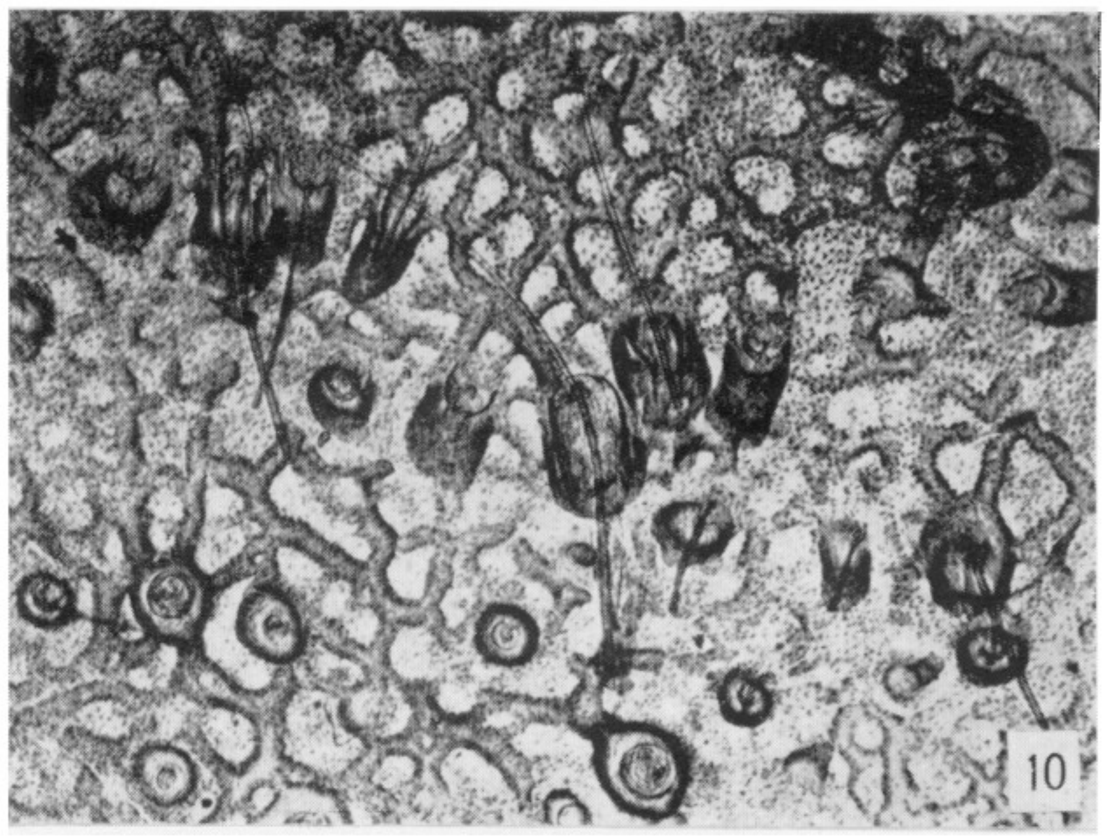
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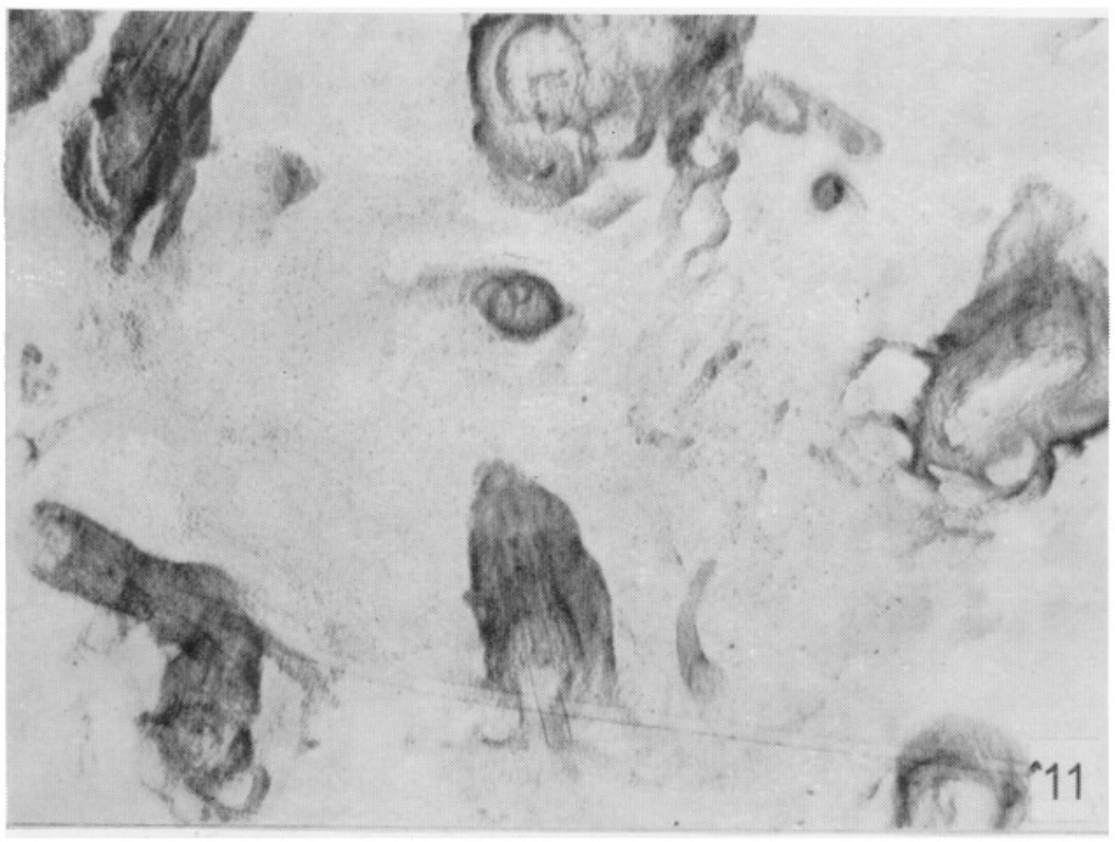
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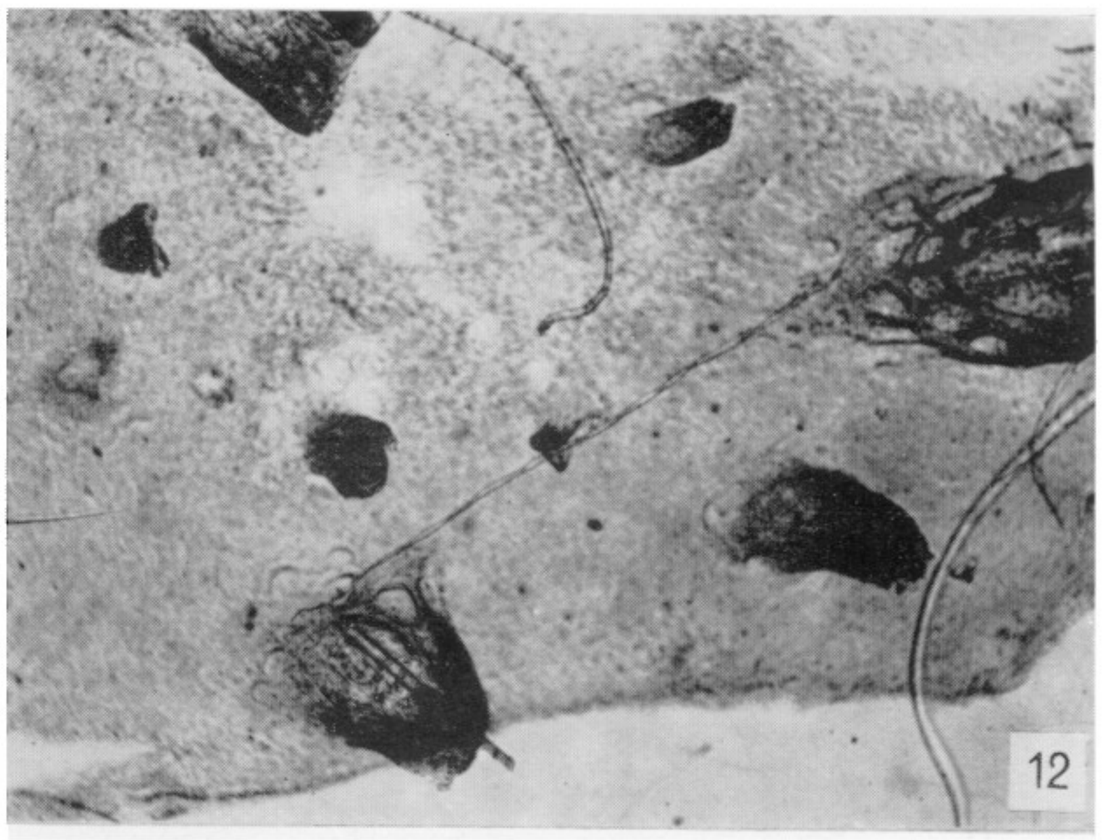
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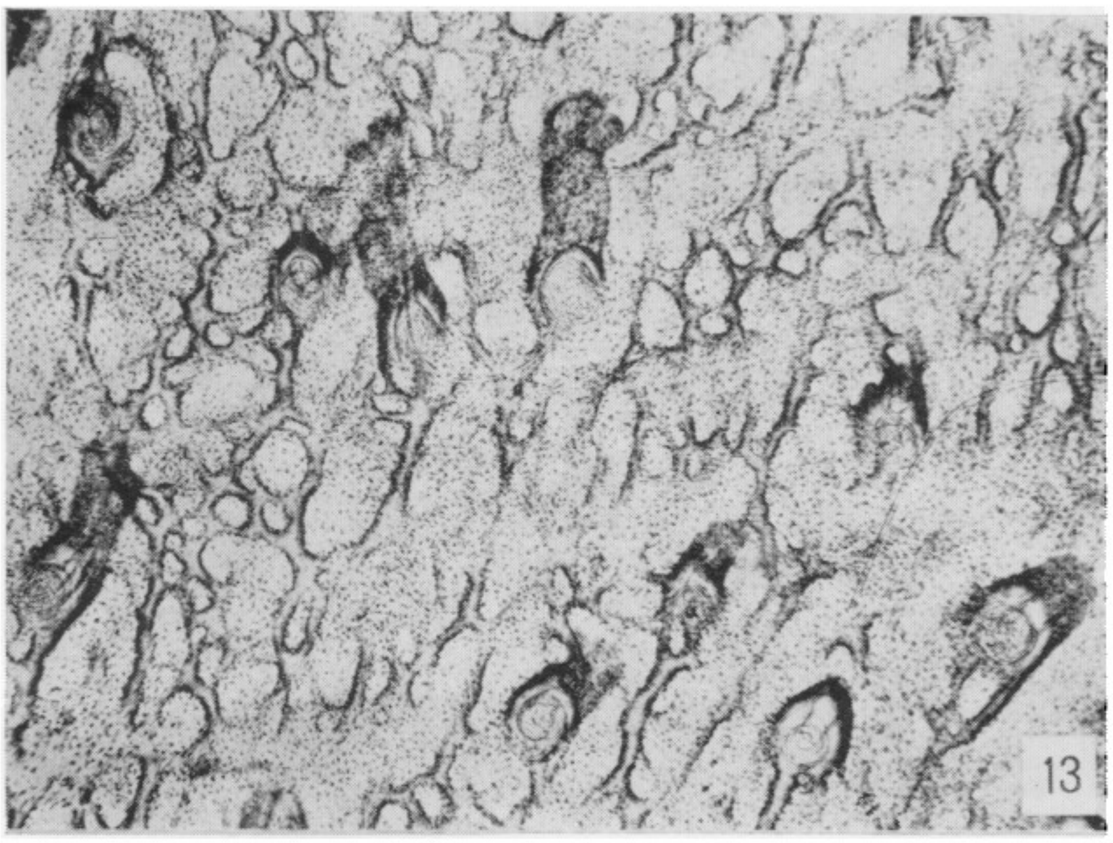
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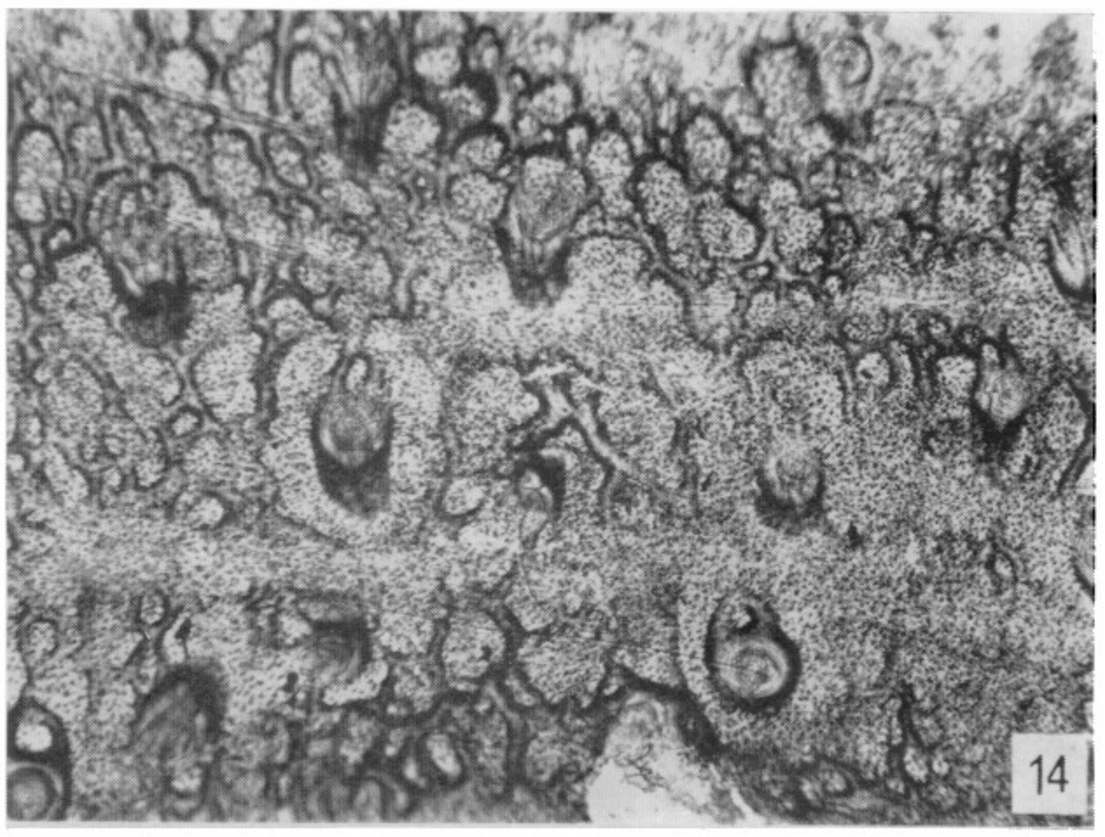
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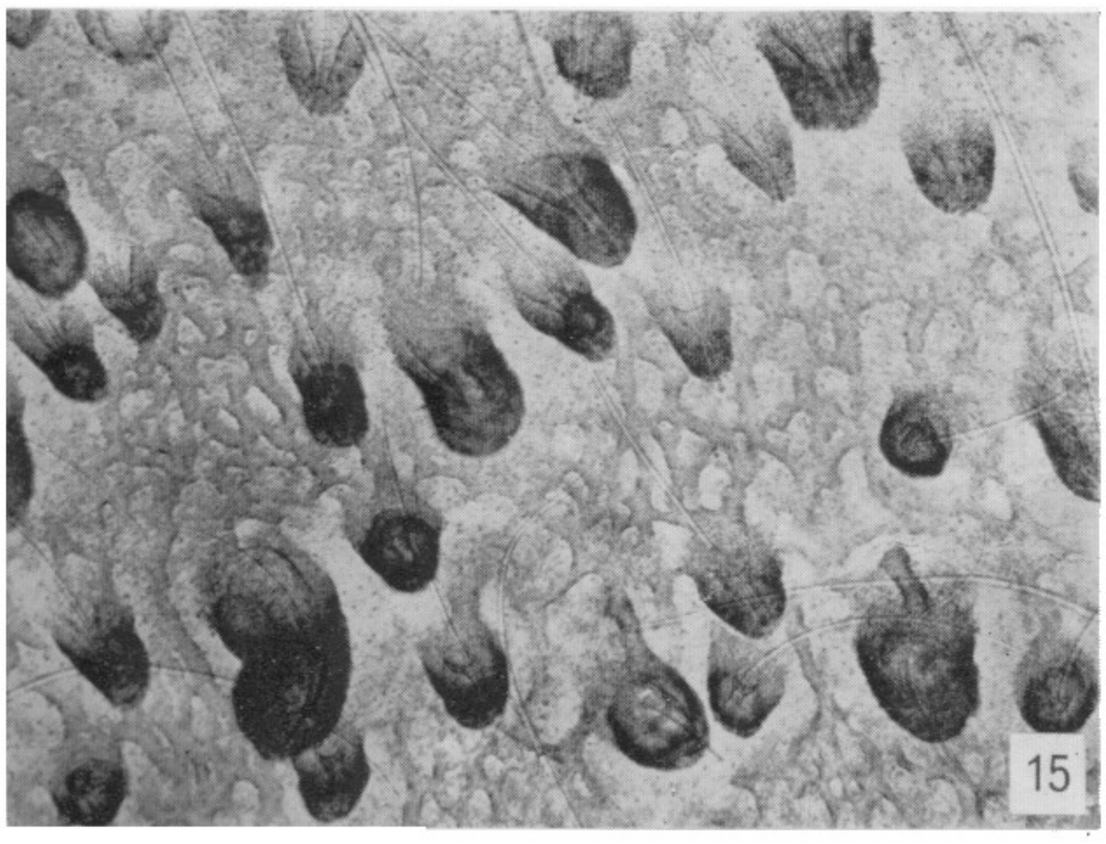
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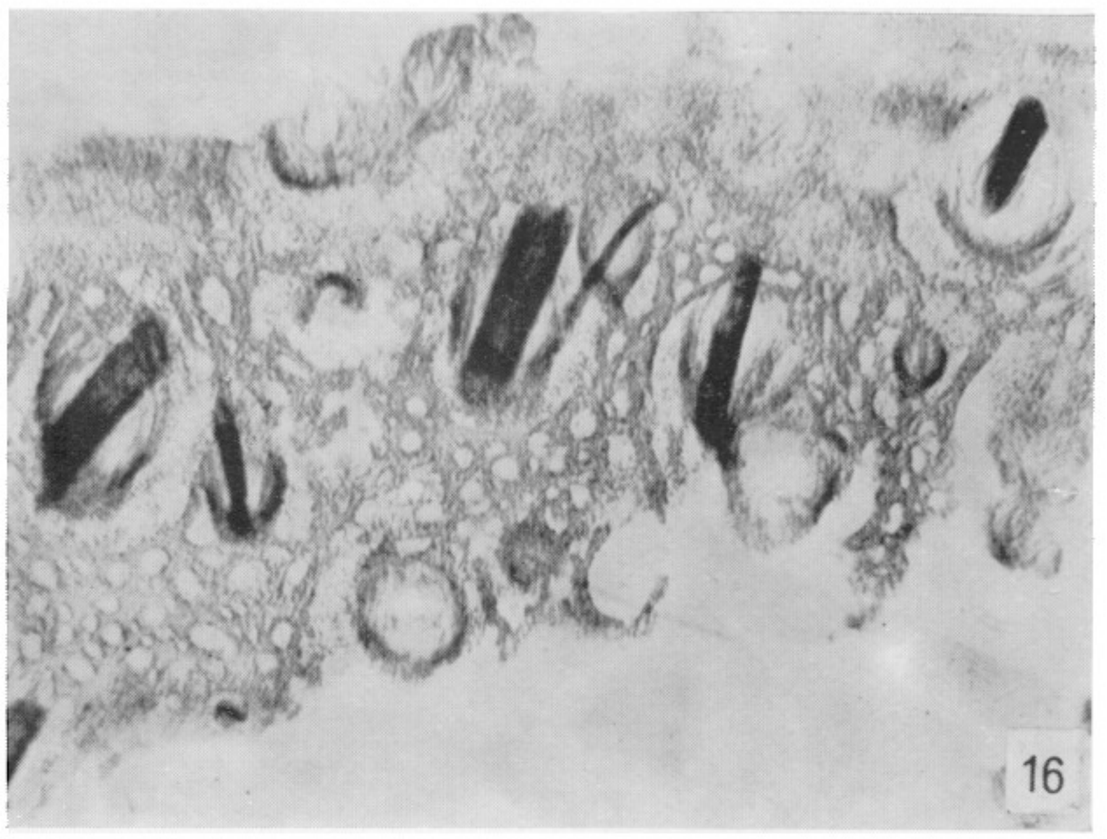
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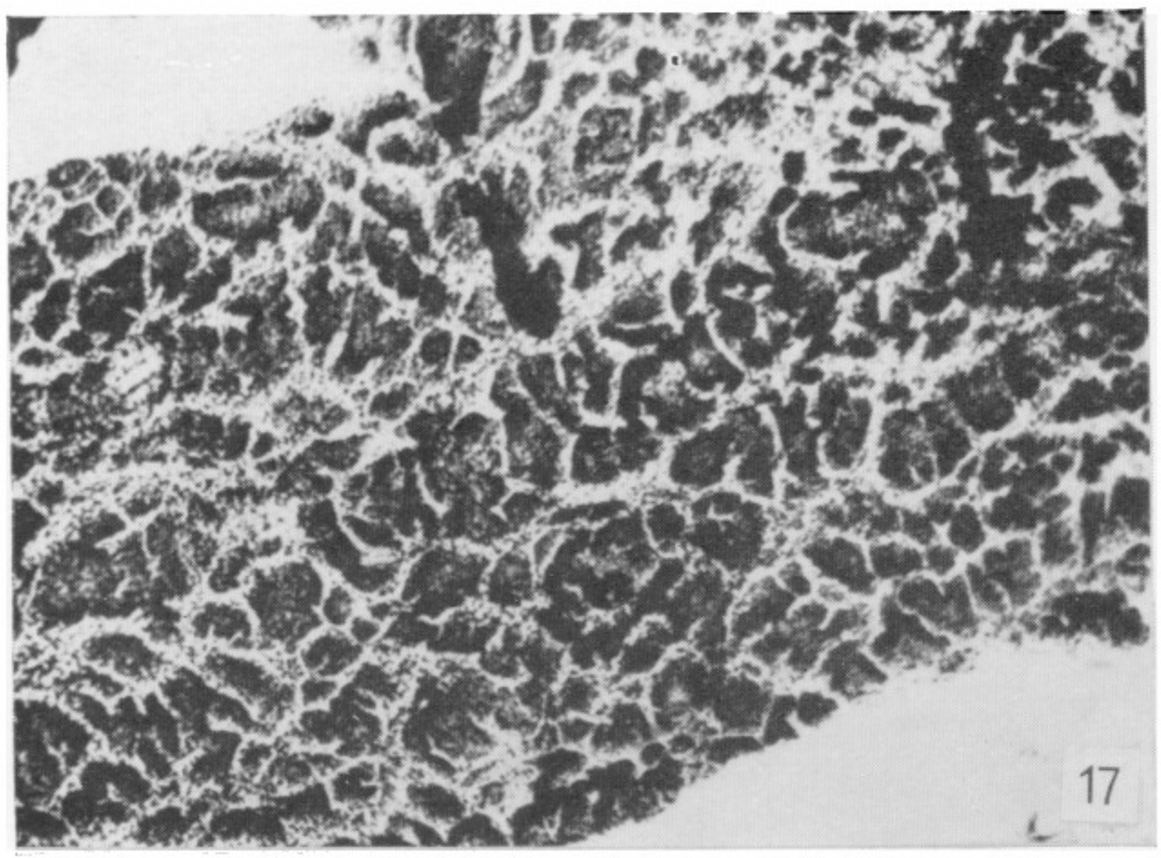
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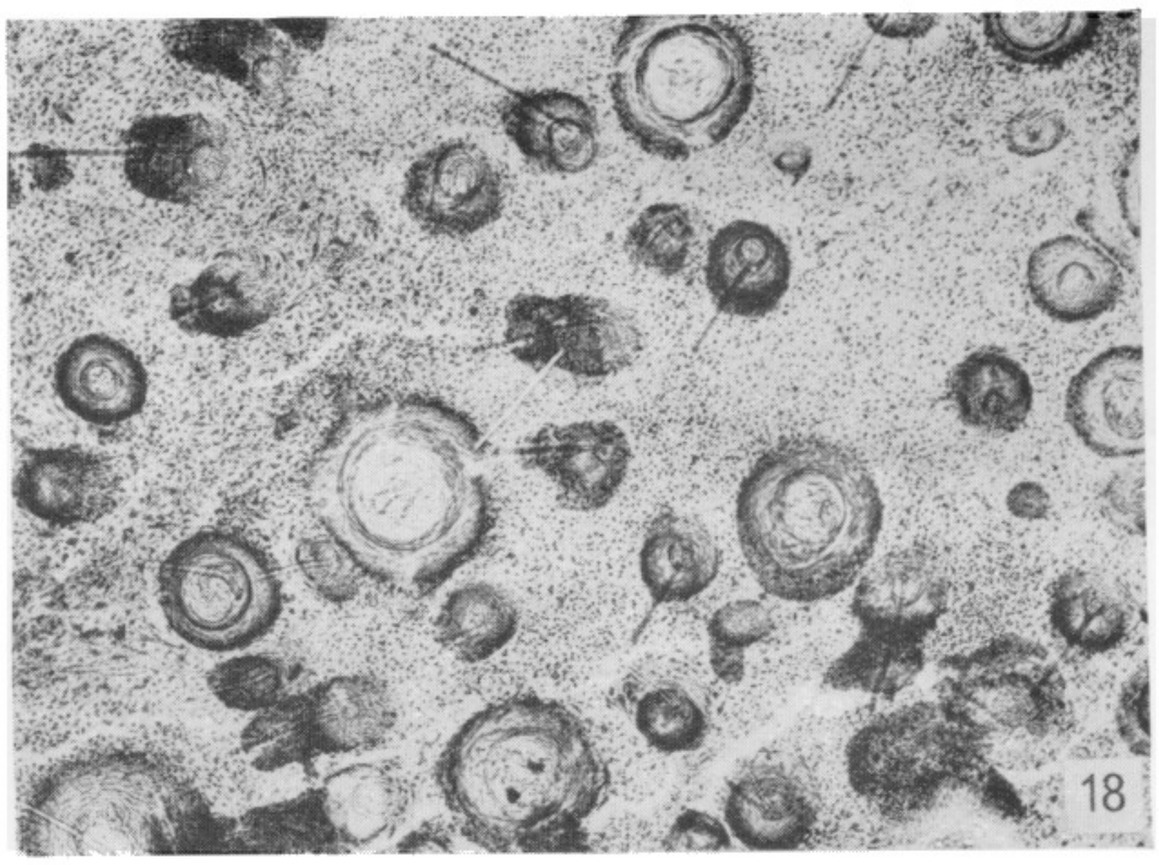
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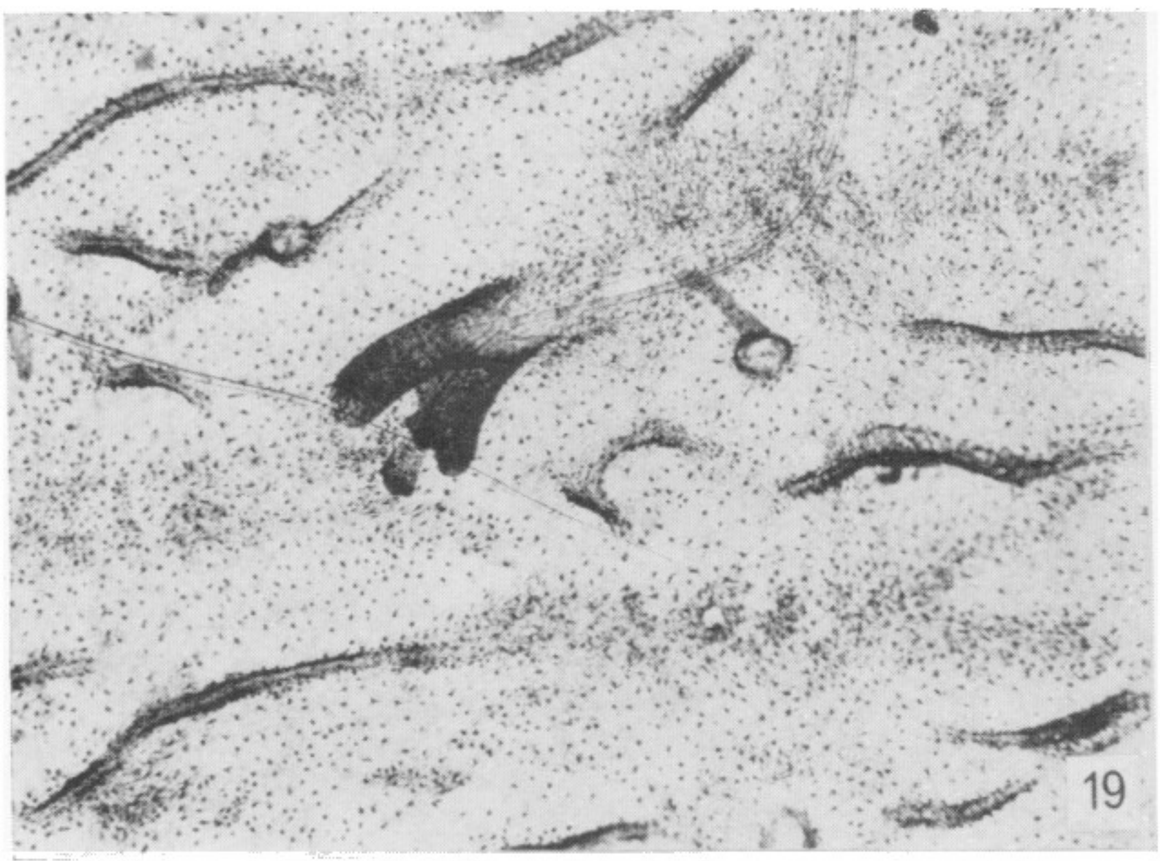
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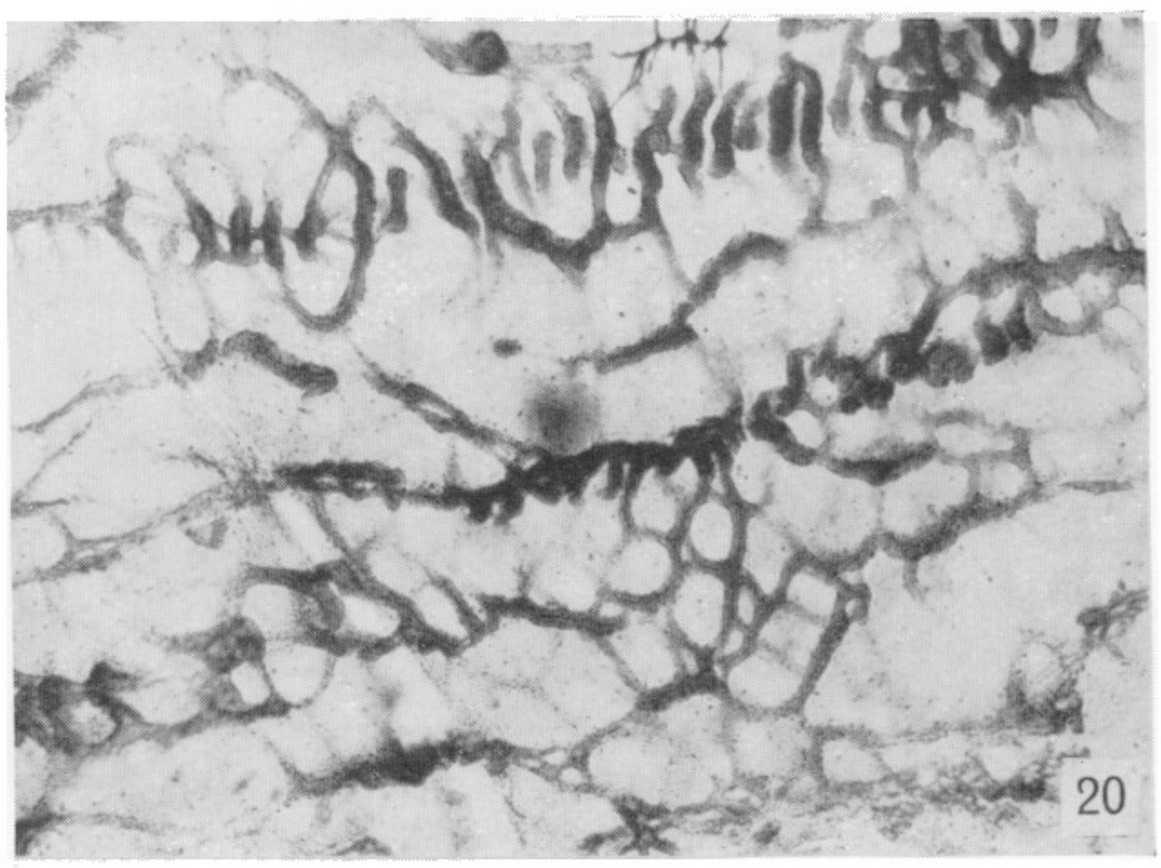
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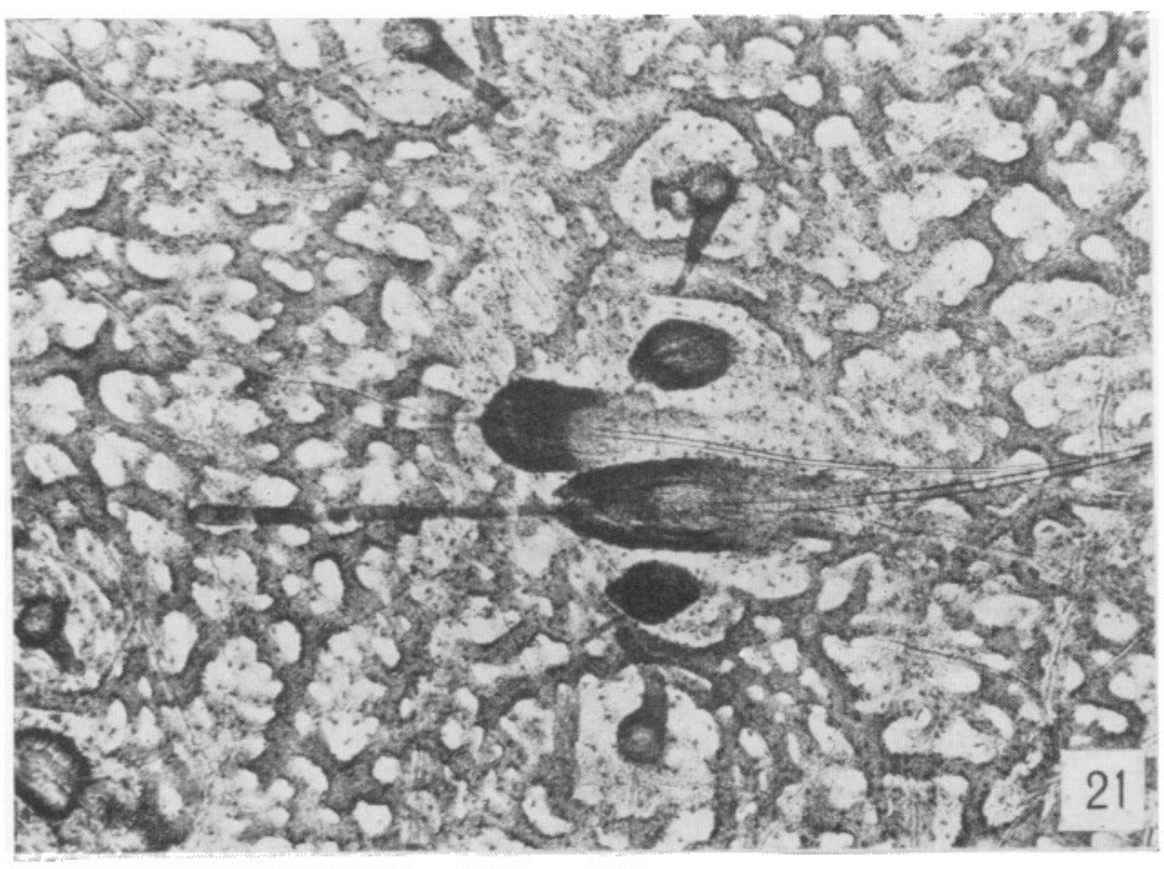
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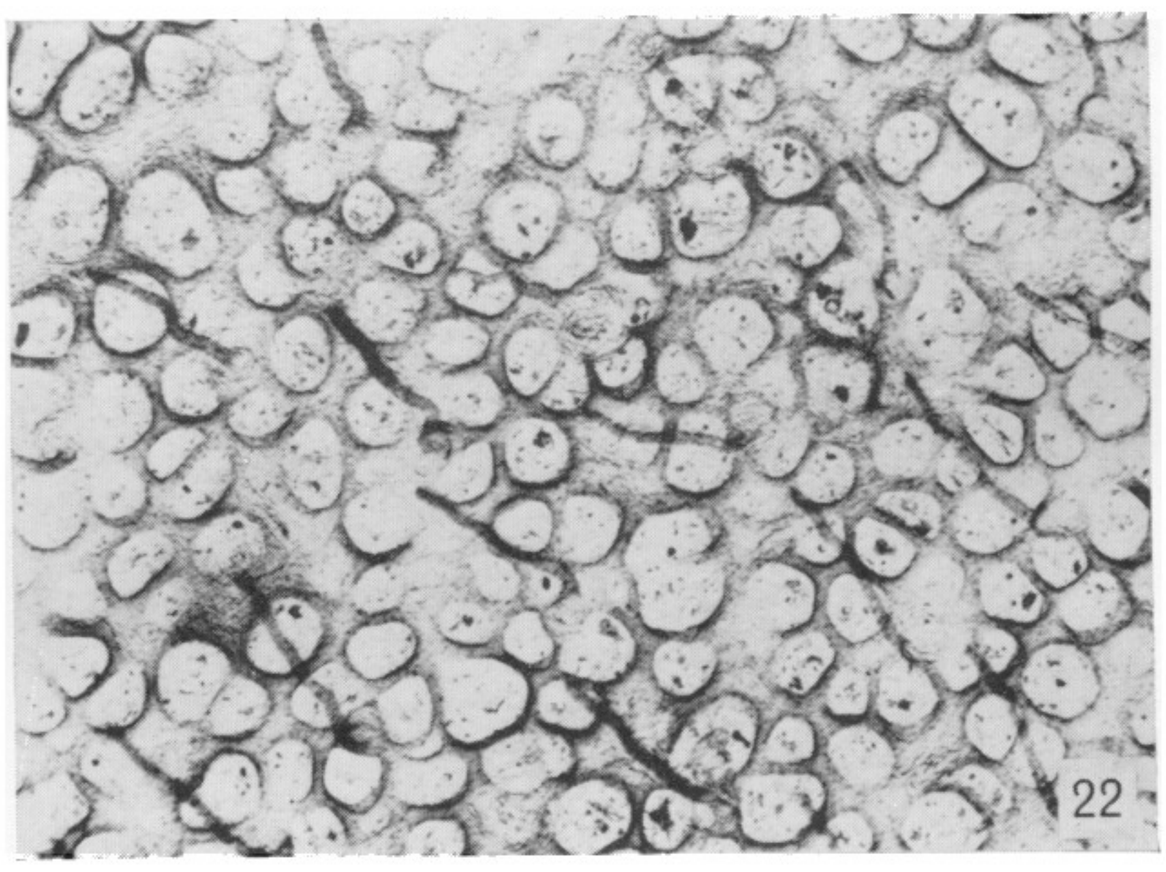
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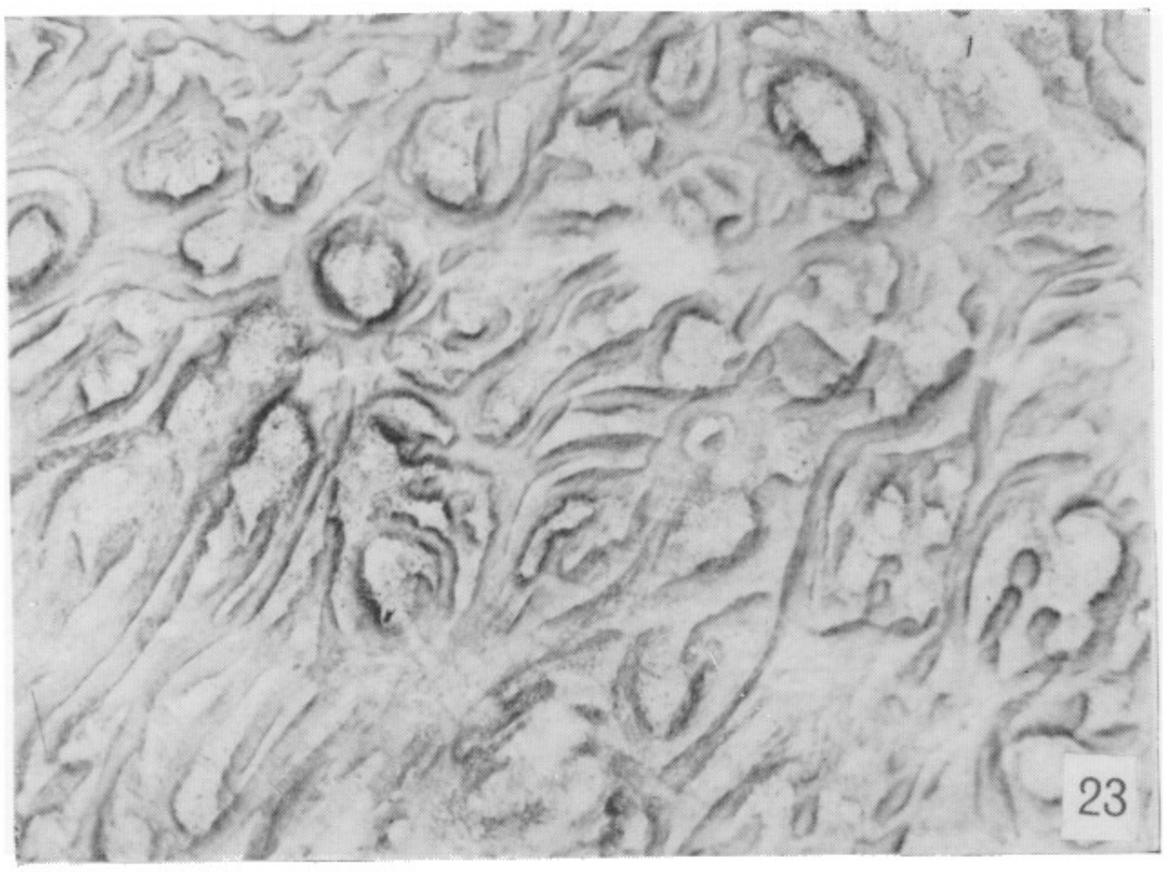
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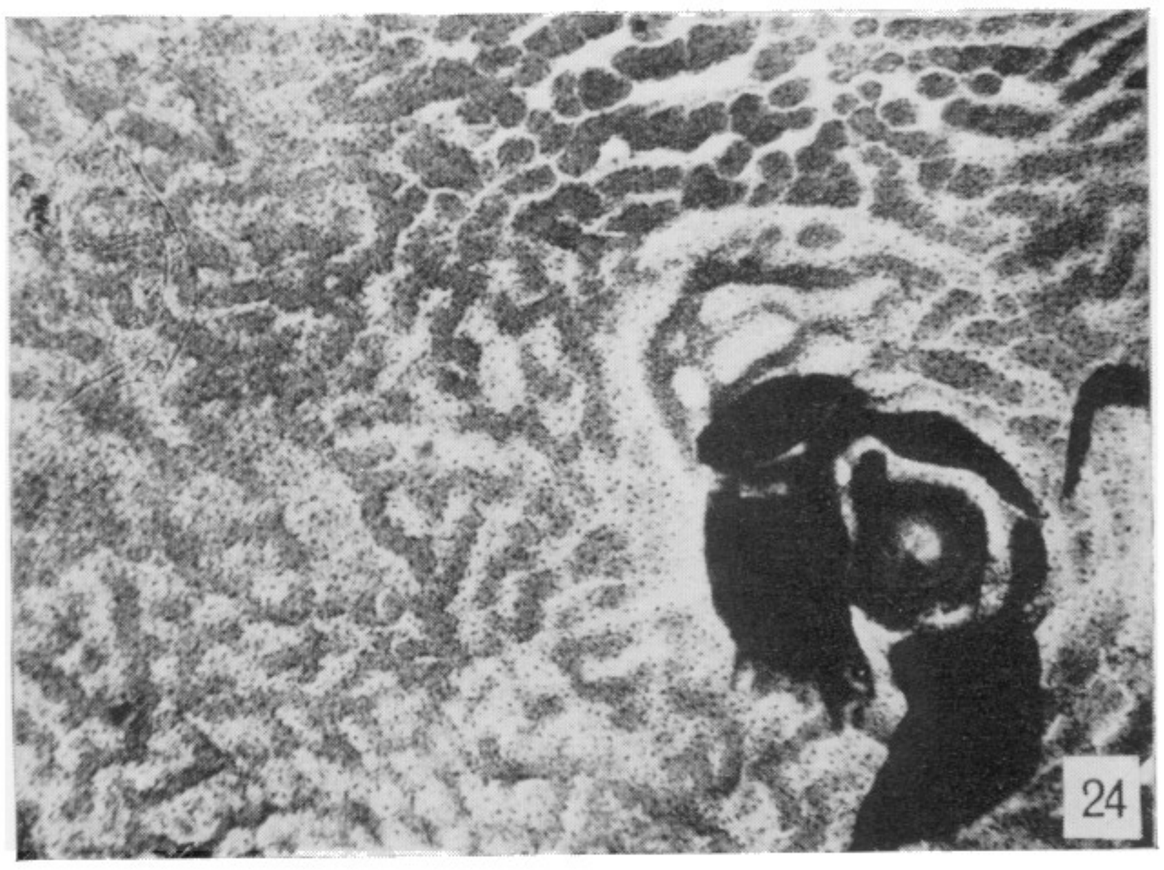
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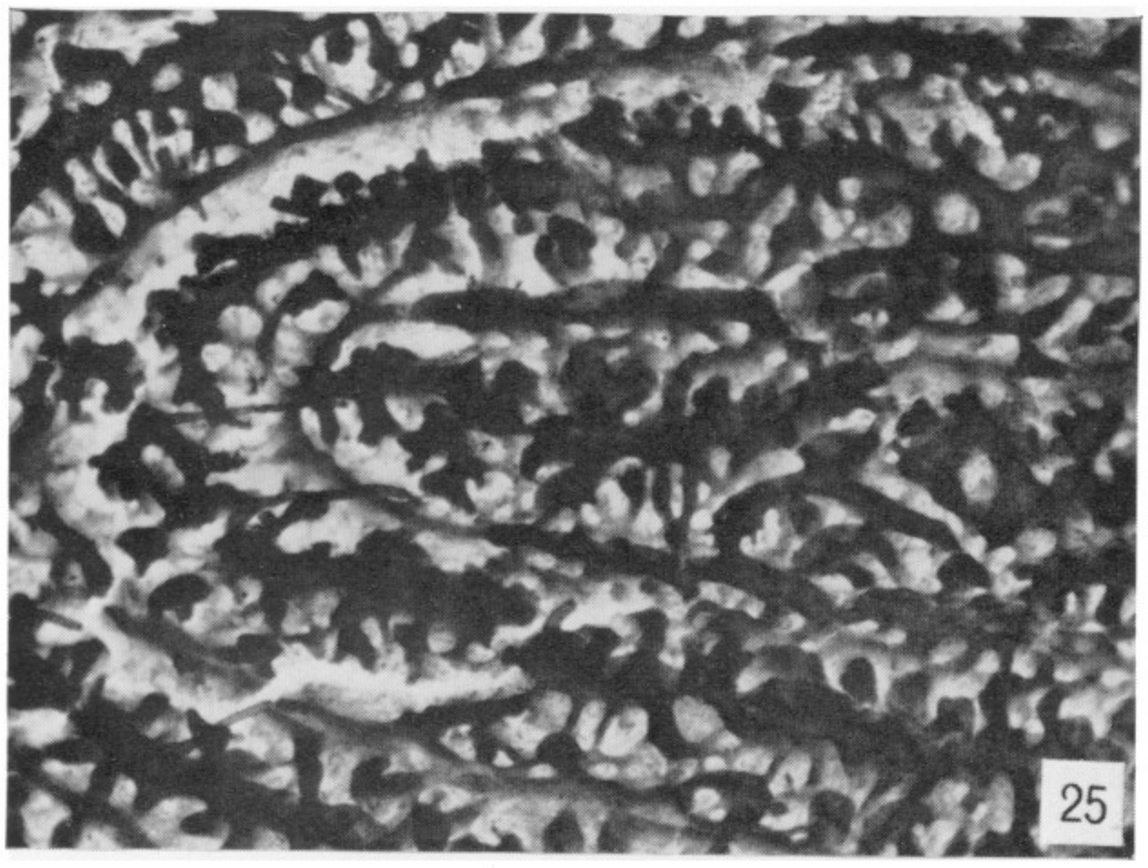
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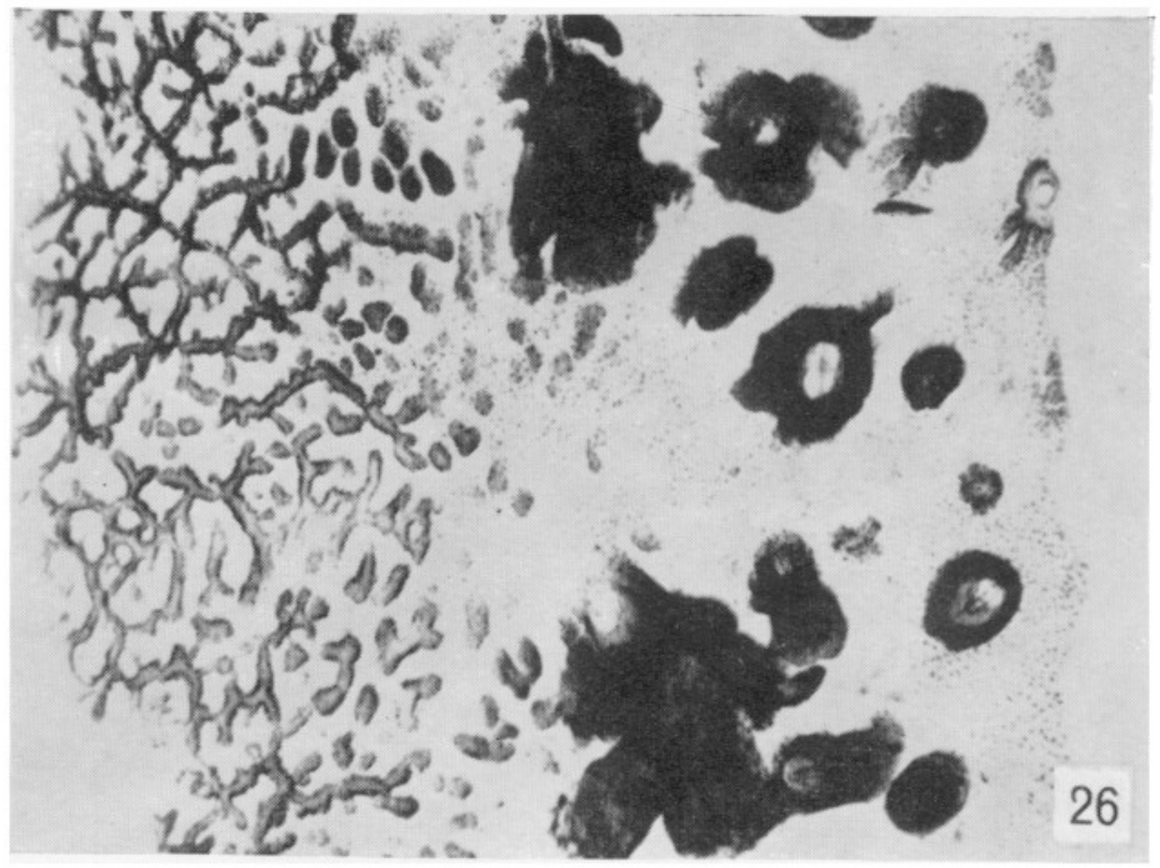
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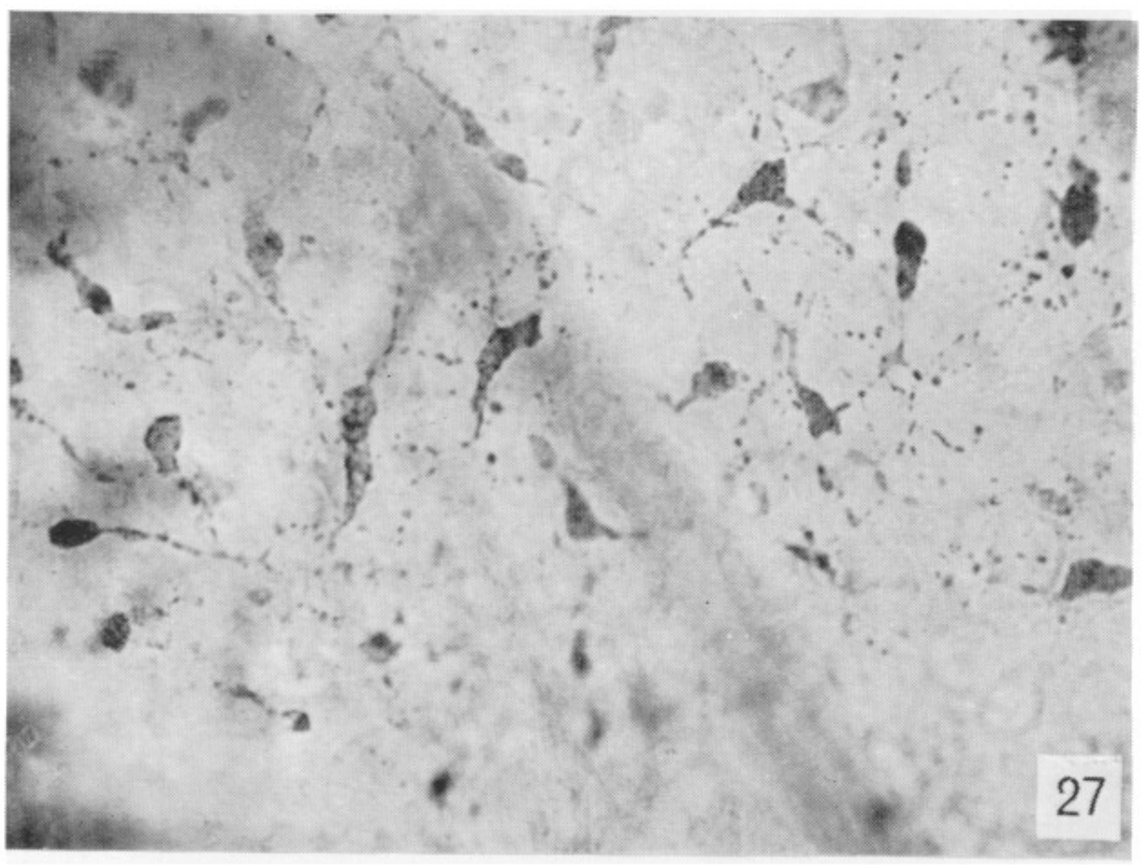
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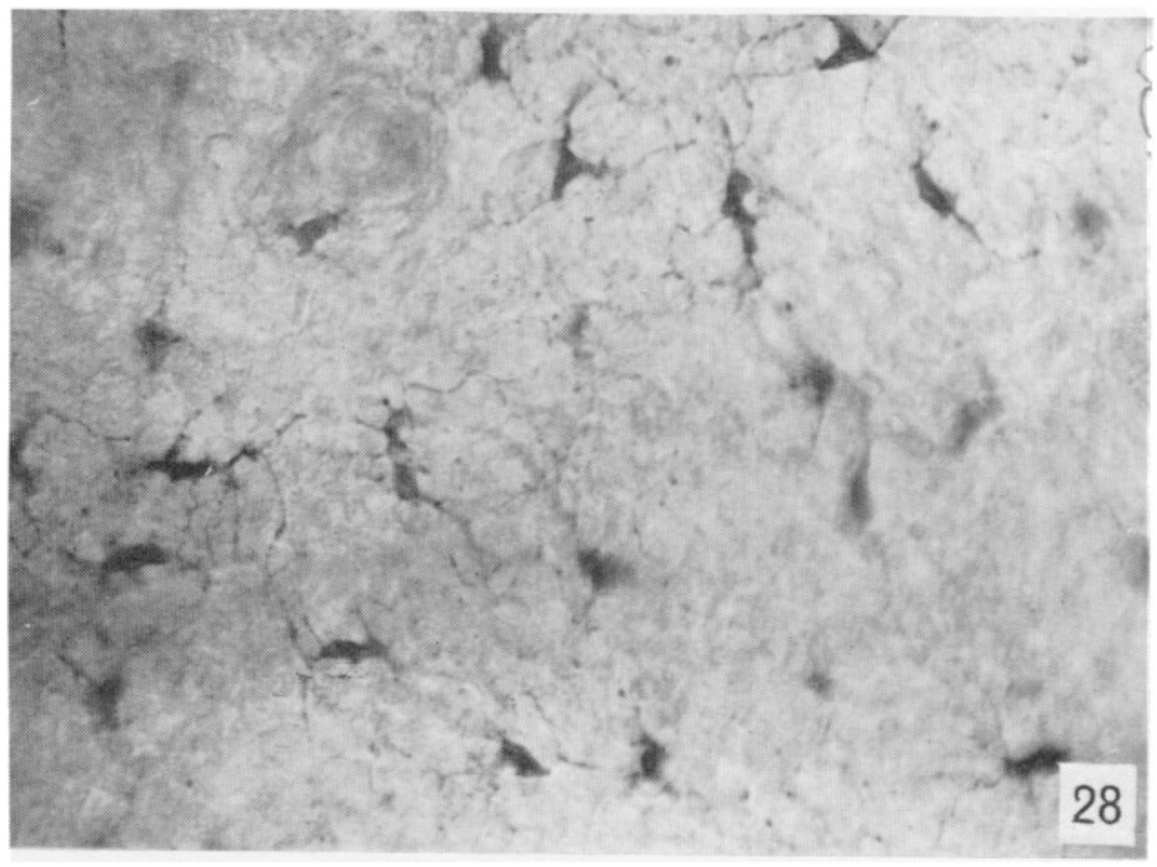
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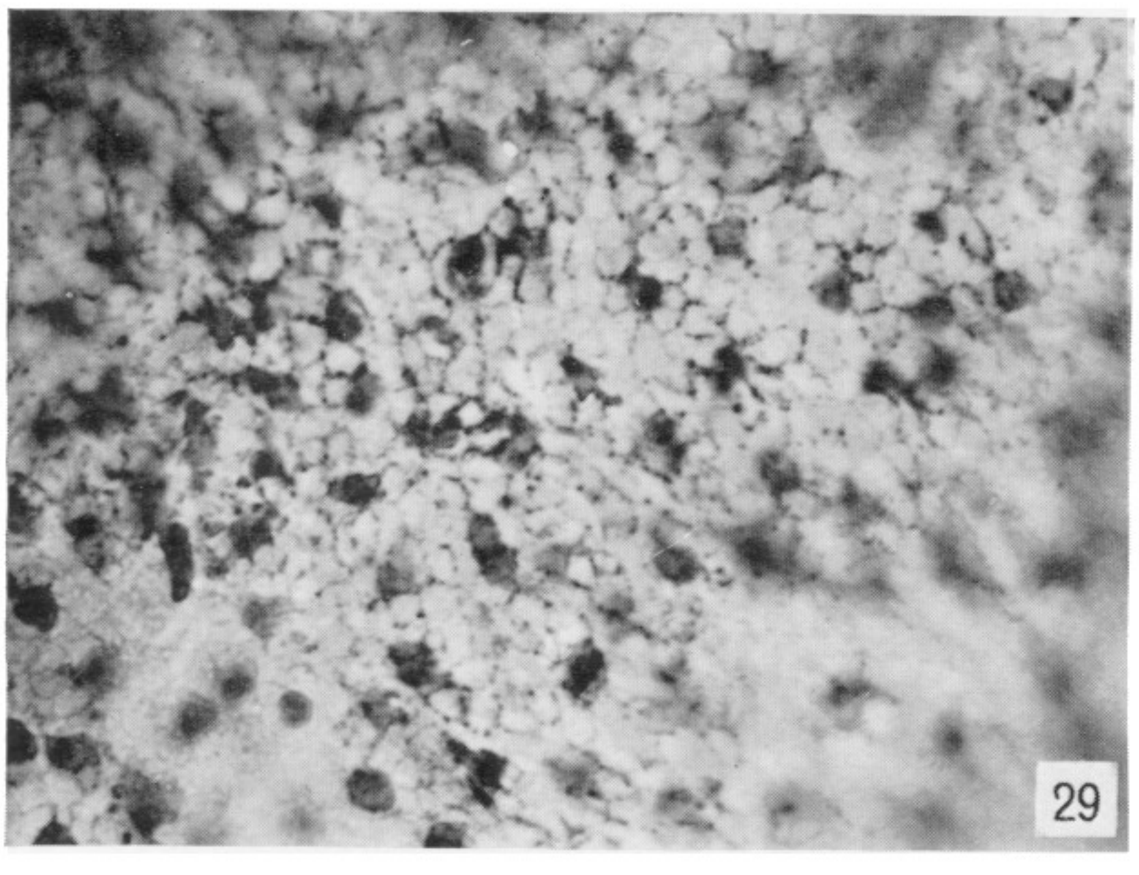
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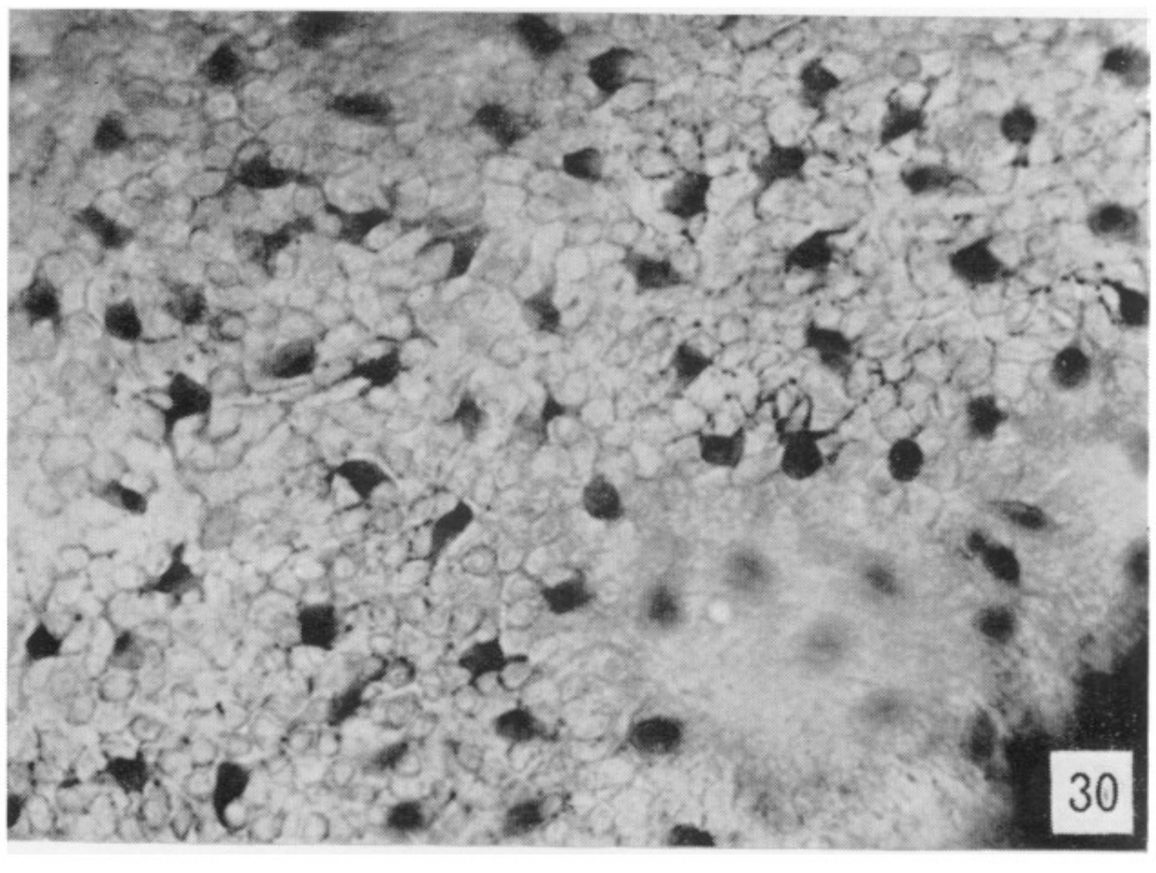
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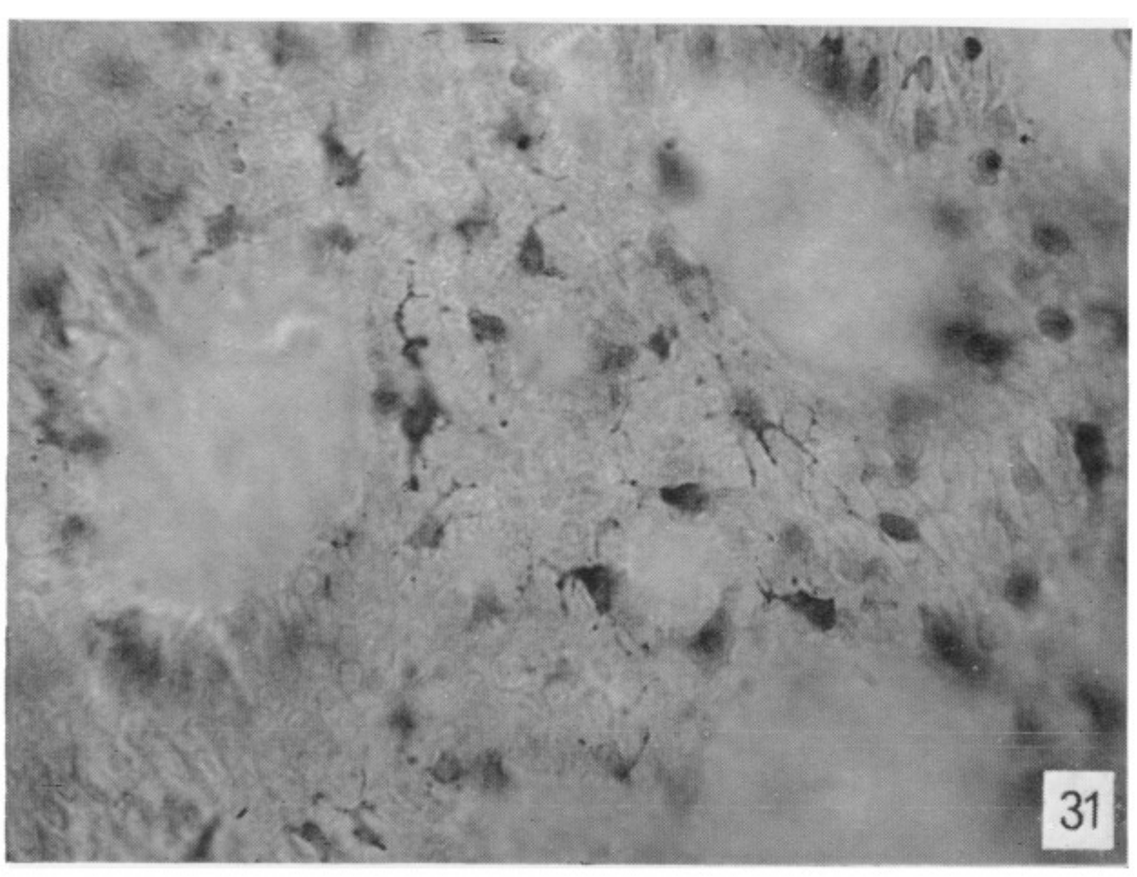
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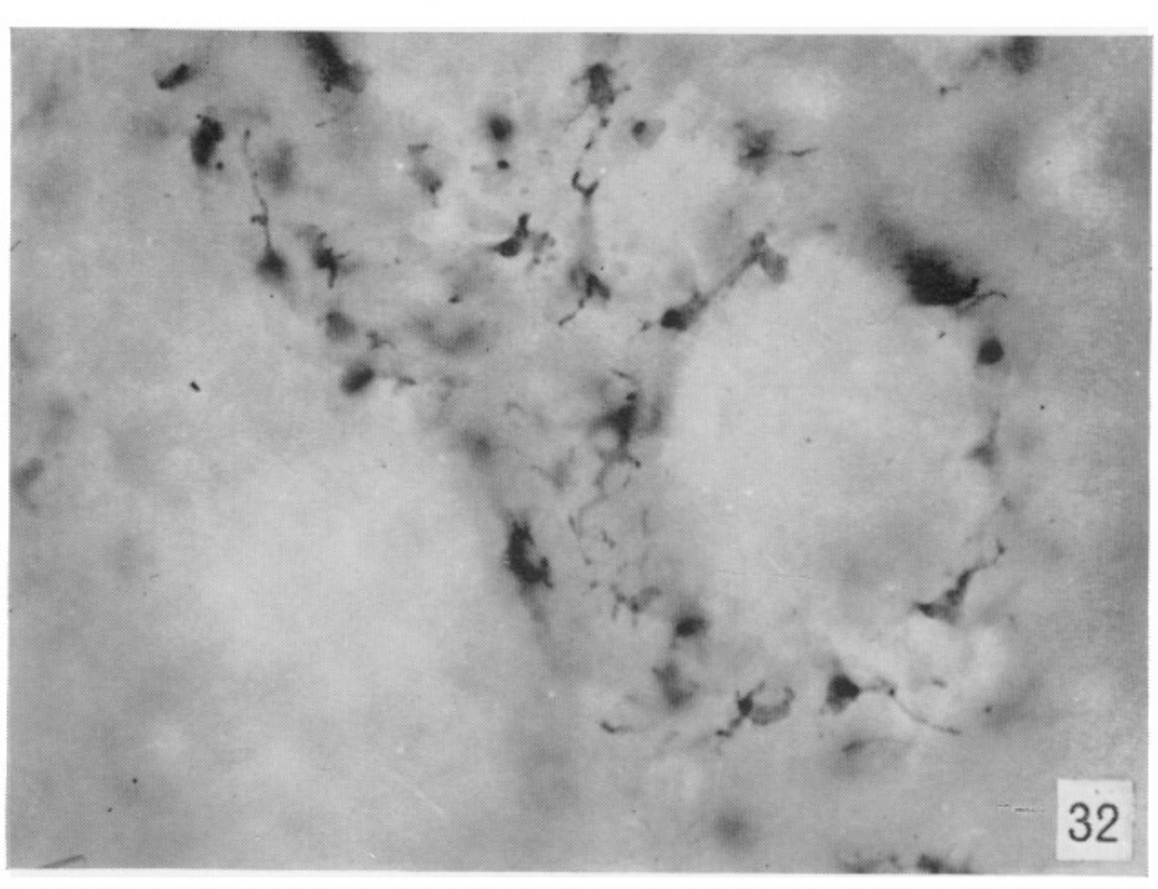
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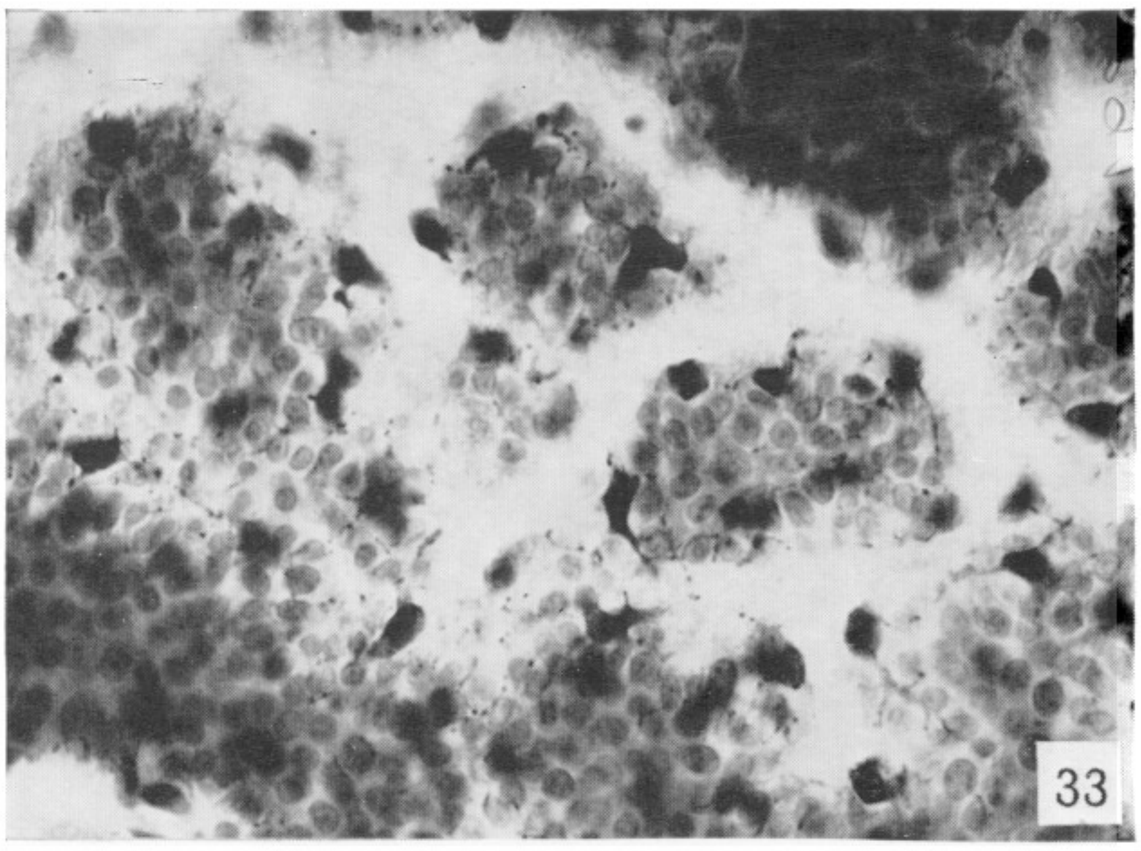
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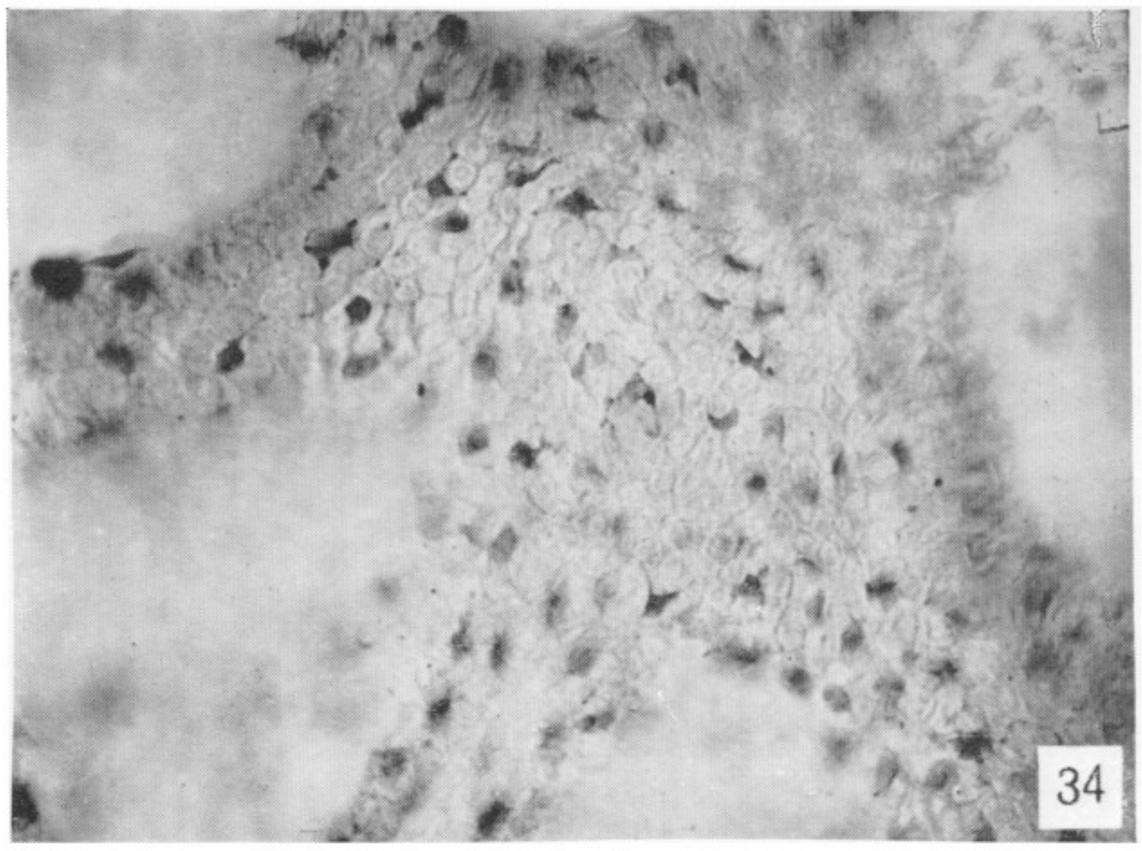
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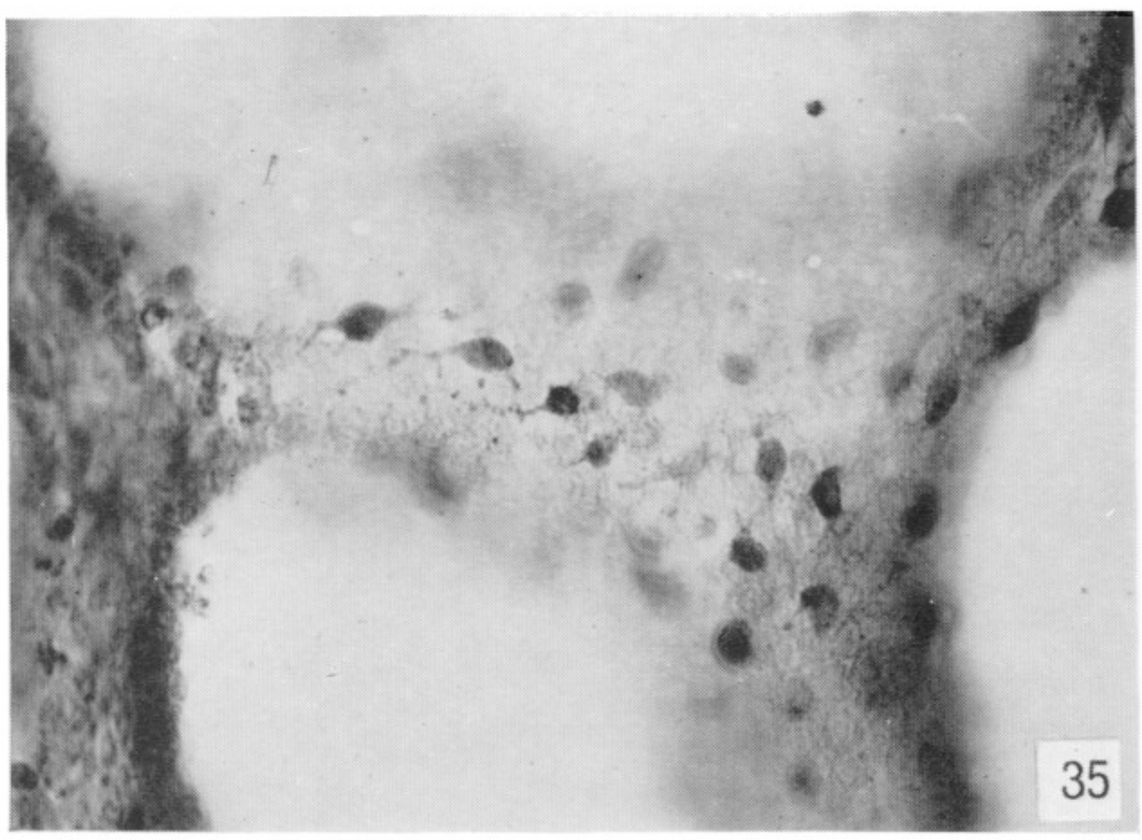
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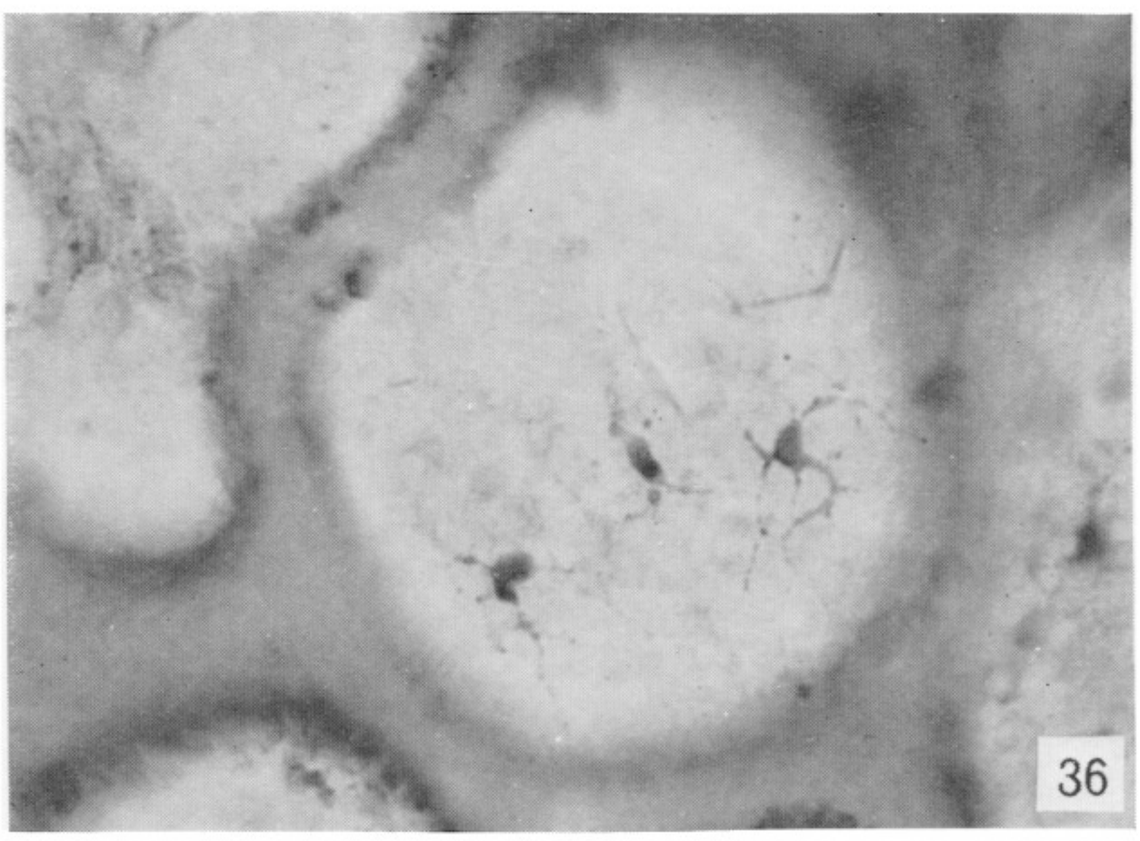
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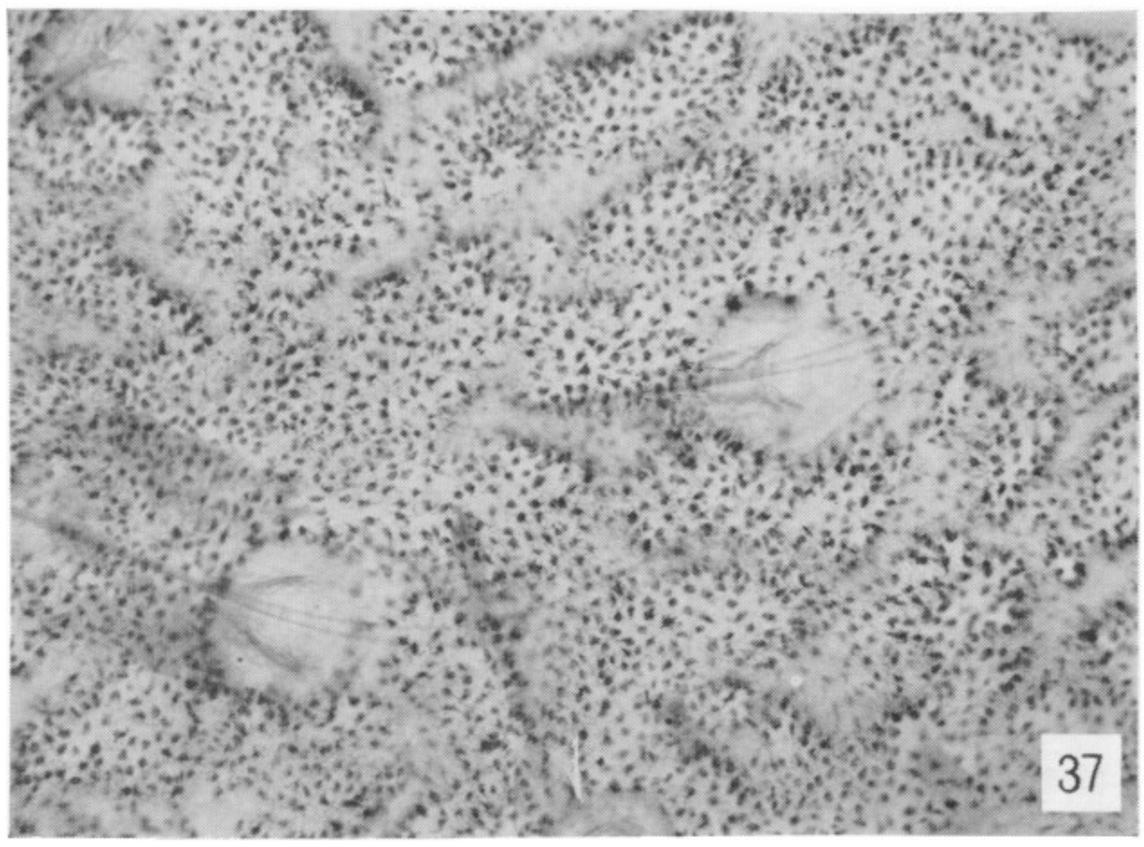
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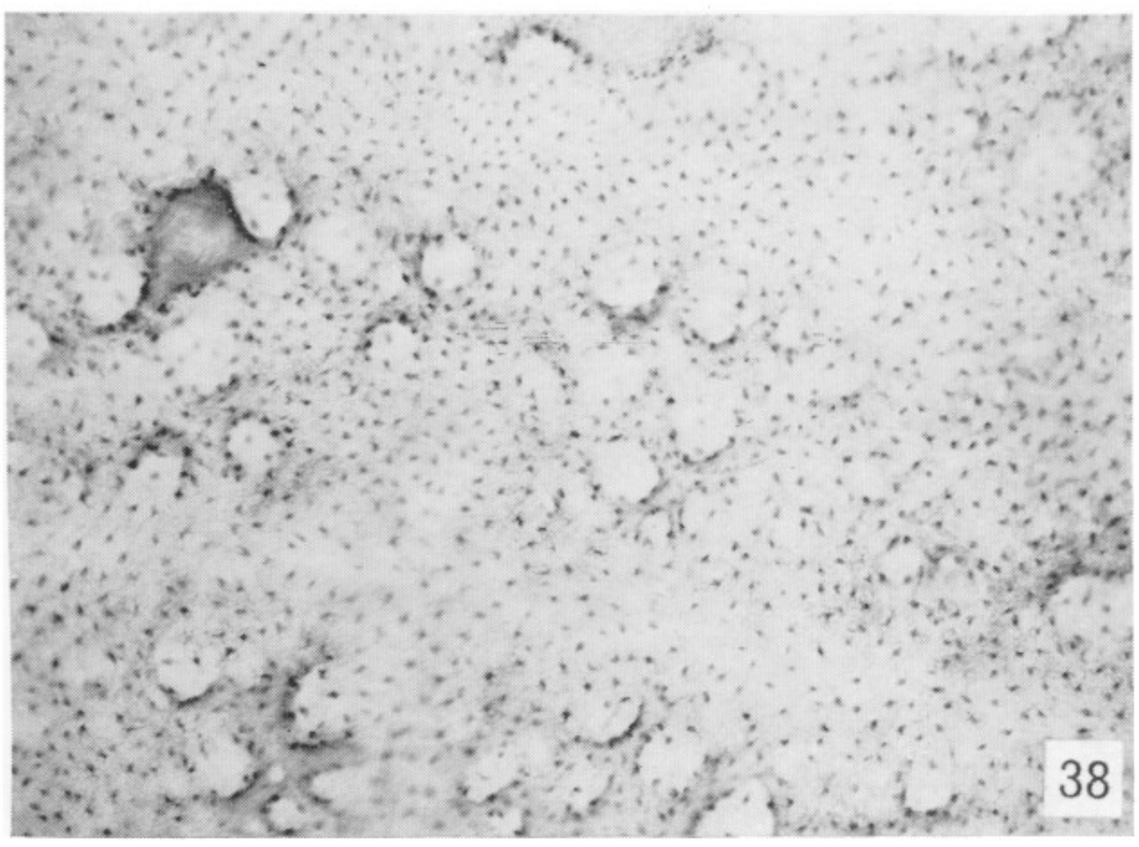
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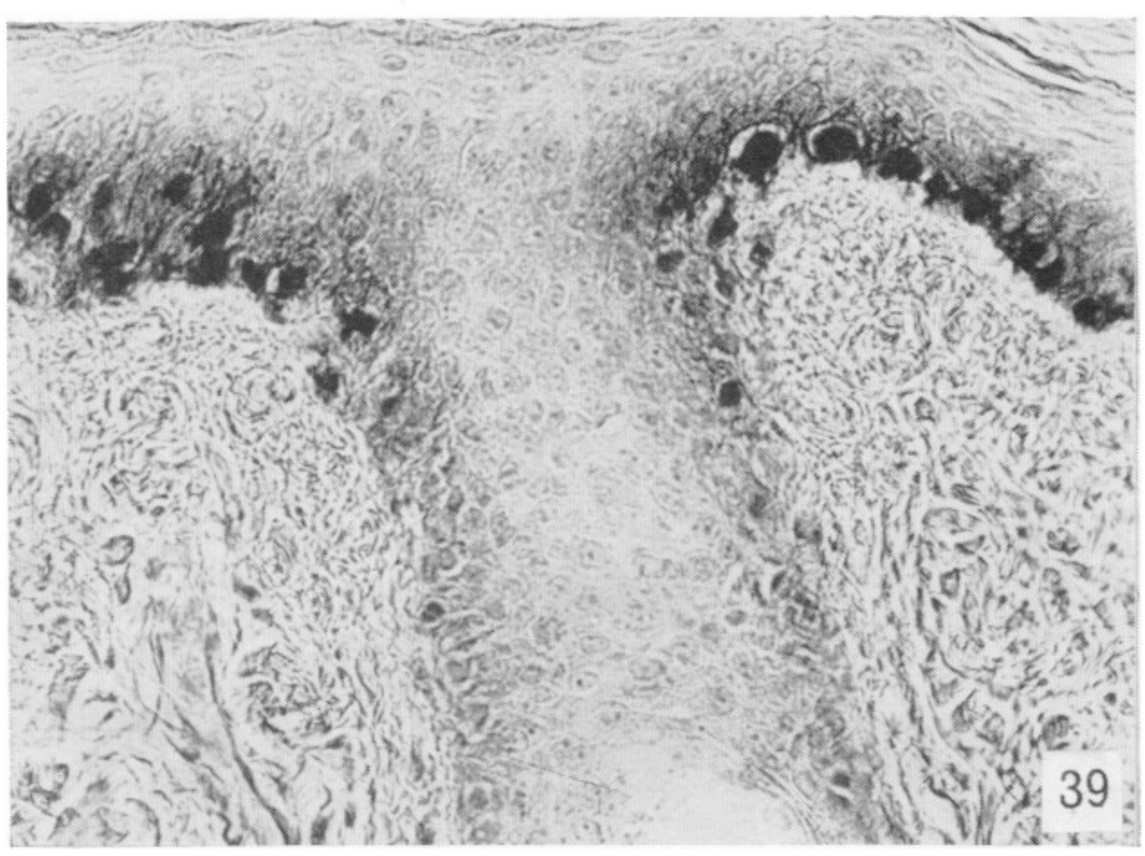
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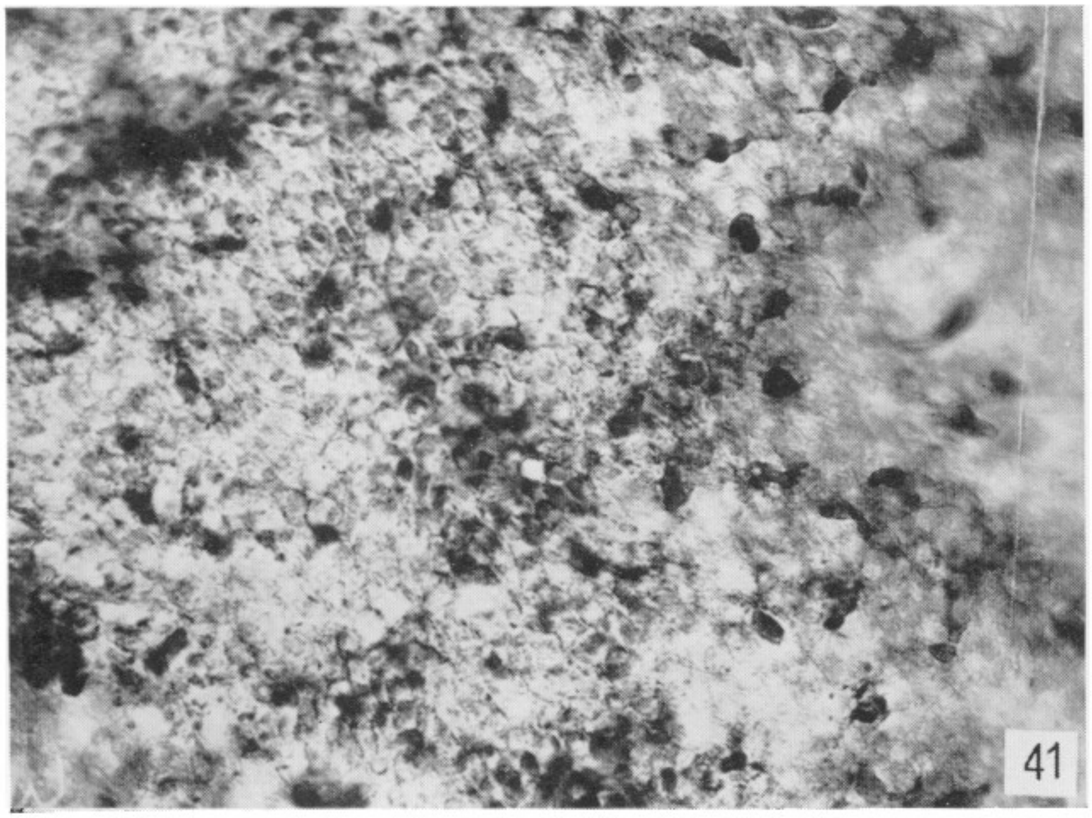

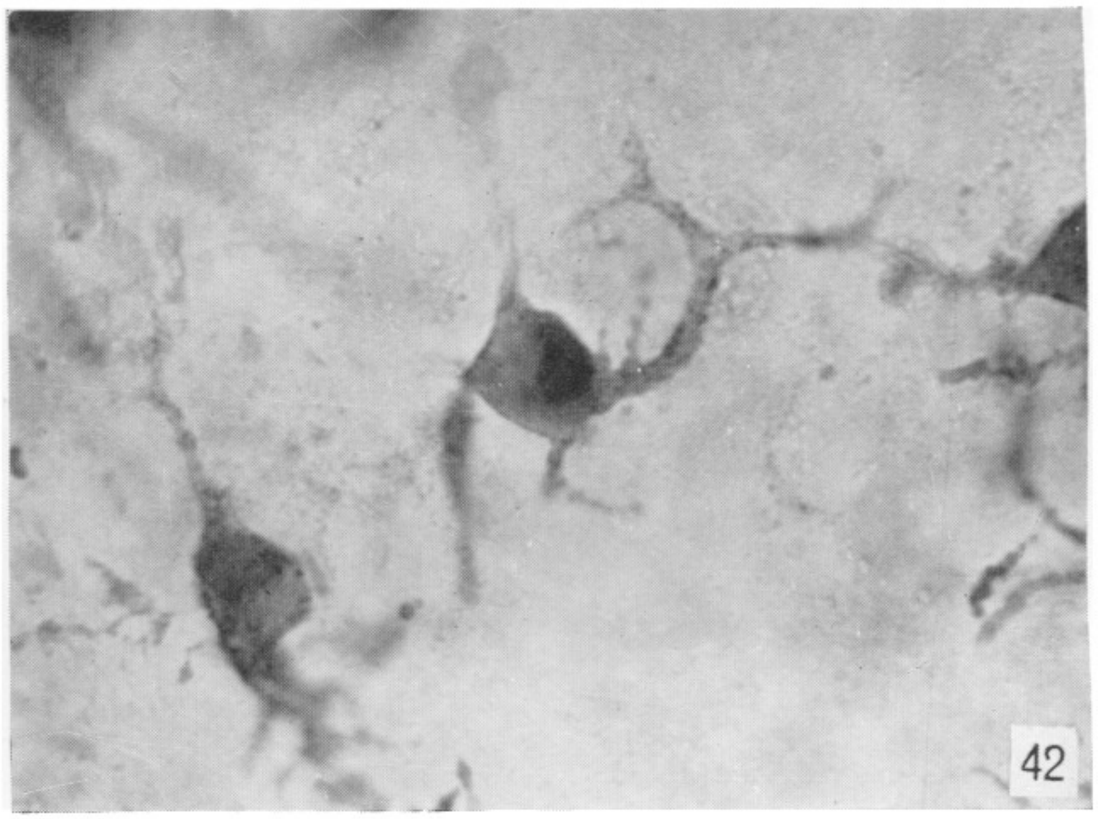

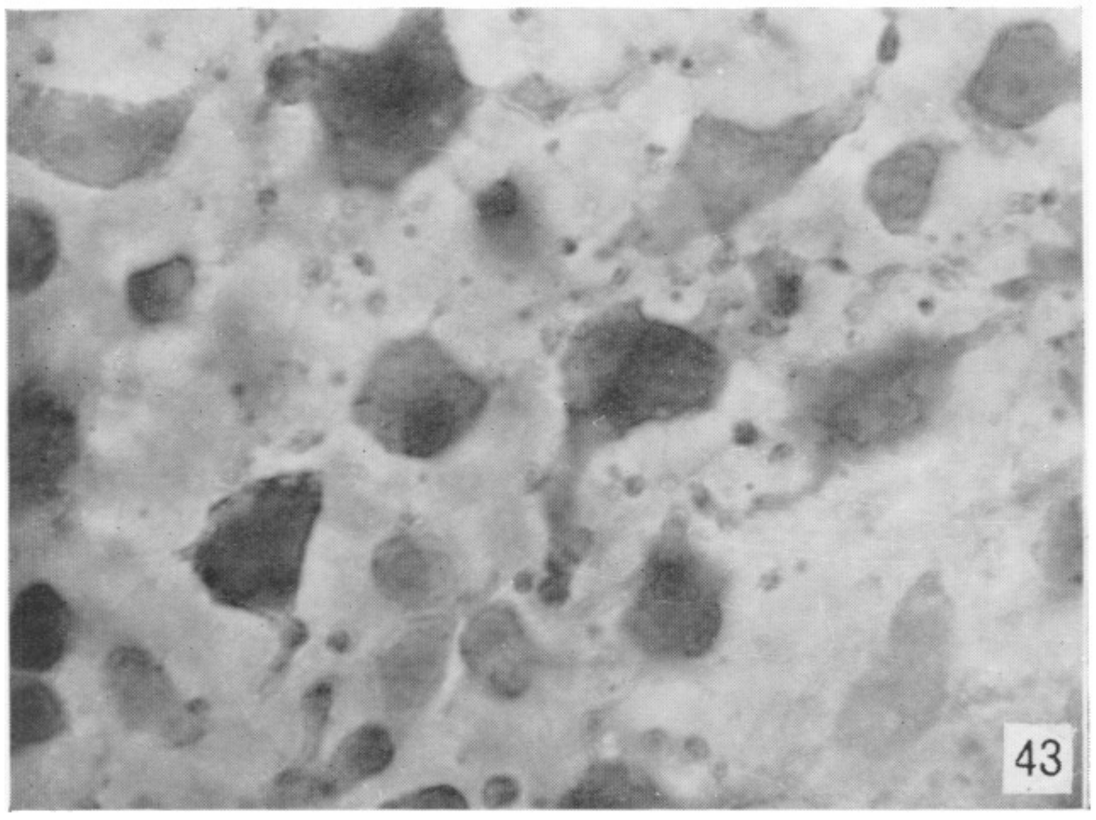

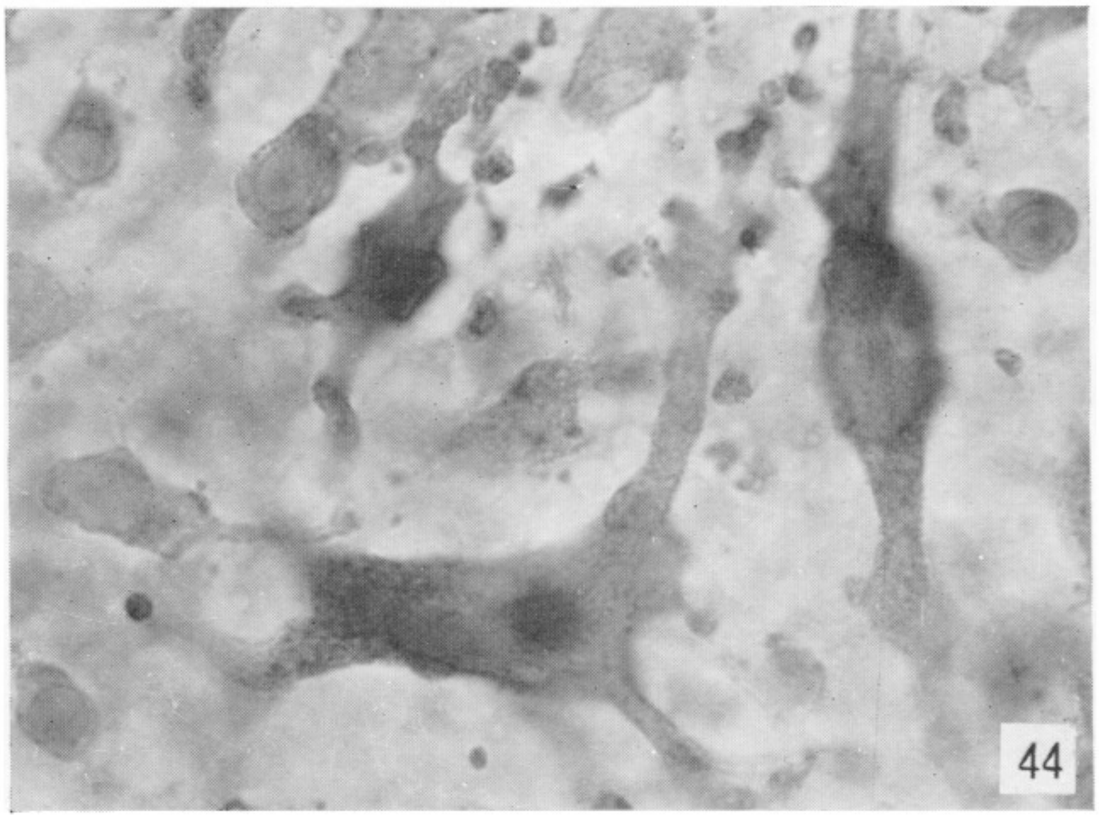

MELANOCYTE CYTOLOGY

FIGURE 41. Lower leg, adult, Negro. Malpighian cells deeply pigmented. Melanocytes dopa-positive. Dopa, × 330.

FIGURE 42. Thigh, adult. Angular melanocyte characteristically present in regions of low melanocyte density. Long dichotomizing processes. Dopa, × 950.

FIGURE 43. Behind ear, 9-year-old child. Round melanocyte from region of high melanocyte density. Short processes with terminal end-buttons. Dopa, × 950.

FIGURE 44. Cheek, adult. Giant melanocytes. Dopa, × 950.