The Journal of the American Medical Association

Published under the Auspices of the Board of Trustees

VOL. LIV, No. 2

CHICAGO, ILLINOIS

JANUARY 8, 1910

Original Articles

MELANOMAS AND SOME TYPES OF SARCOMA OF THE SKIN*

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The sarcoma group of skin diseases is of exceeding interest to the dermatologist on account of the frequency in which the skin is involved even where the tumors are primary in some other organ, and also from the fact that the type best known to dermatologists, the idiopathic hemorrhagic sarcoma of Kaposi, seems to be independent of any primary growth and apparently originates from the vascular tissue of the extremities. Perhaps the one which carries the greatest interest of all, and certainly the one which has given rise to the most active controversy regarding its nature, is the so-called melanoma—a name which does not commit one to any positive view regarding its genesis. Although it sometimes originates from pigmented moles and even those which are non-pigmented, it also occurs independently of any visible change in the skin, so that perhaps the importance of these pigmented moles as potential melanomas has been somewhat exaggerated. The majority of people possess one or more of these congenital defects, but only few of them become malignant.

Before entering into the discussion of the various views on this fascinating subject I shall cite briefly two melanomas of the foot which have recently come under my observation. In both there was an absence of any history of a mole, the tumor having been preceded by a pigment spot which persisted a variable time before actual growth was noticed.

CASE 1.—A woman aged 54, a native of Germany, stated that for several years she had had a pigment spot on the inner border of her left foot near the heel. It had occasioned her no inconvenience until two years before examination, when she noticed a gradual increase in size and volume. This was slow for about a year and a half, but during the past six months the growth had been augmenting more rapidly.

Macroscopic Examination.—At the time she presented herself the lesion was about 2 inches by 1 in diameter and consisted of an irregular tumor encroaching partly on the sole of the foot. It was unevenly elevated in the center and at the periphery was level with or rose slightly above the surrounding skin. In color it shaded from dark brown to deep black, and it was covered by thick adherent scales except in one area where a dry depression furrowed the surface. This was also the blackest part of the tumor and may have been the starting point. There were no satellite metastases, no lymph node enlargement and no local pain. The patient was well-

nourished and said that her general health had suffered no change.

Microscopic Examination.—The tissue (Fig. 1) presented an enormously hypertrophied horny layer containing lakes of free pigment and chromatophores in groups and isolated. The rete was irregularly thickened and undulating; the basal layer in places was preserved and in others obliterated by the encroachment of the growth. In the interspinous spaces and in lacunae hollowed out by them were to be seen one or more chromatophores. The tumor itself occupied the upper two-thirds of the corium, giving the appearance of a growth of the papillary bodies. The outlines of the latter in some areas were well preserved; they were enlarged and club-shaped and here and there the epidermis was lifted up from them. The growth in these places had a columnar arrangement at right angles to the epidermis. In portions it was so deeply pigmented that neither cells nor intercellular substance could be made out. In areas less dense, the cells had a pale vesicular nucleus, some two, and rather small cell bodies with moderately long processes at either end. Between them was a delicate fibrillary substance. The surrounding connective tissue was markedly sclerosed and divided the growth by band-like partitions. In the tumor area the vascular development was poor, but around it were found a number of dilated vessels with an infiltration of round and pigment cells and free pigment.

CASE 2.—The other case also occurred in a woman, who gave a very indefinite history. She was about 45 years old and when first seen had a large lobulated mass on the inner side of the foot which ulcerated and discharged a bluish-black fluid. Numerous bluish-black metastases were present on the leg and thigh and the inguinal lymph nodes were enlarged. The patient died from cachexia and internal metastases. The initial tumor was from a pigment spot which had appeared several years before. Examination of a very small metastasis from the thigh showed the lesion to be made up of a collection of deeply pigmented branched and round cells. They were filled with coarse granules and clumps of pigment (Fig. 2). The cells were especially numerous about the vessels, the endothelium of which was also pigmented. In a larger secondary growth the pigmented cells formed a network which occupied the middle and lower thirds of the corium. In neither specimen was there any inflammatory reaction.

It is not always possible after growth has taken place to determine whether the melanoma originated from a congenital malformation or not. In the above cases no connection with a nevus could be established, and with the history of a pigment spot developing in middle age the antecedent condition was probably the malignant lentigo of Hutchinson. This begins as a pigment spot late in life on the face, more frequently the eyelid, and the extremities, and after some years takes on growth.

Owing to the assumption of an etiologic connection between pigmented growths and nevi the nature of melanomas is still one of the disputed questions in tumor pathology, and until the histogenesis of nevi is settled the controversy will probably be left open. Following the work of von Demiéville¹ in 1880 and von

* Read in the Section on Dermatology of the American Medical Association, at the Sixtieth Annual Session, held at Atlantic City, June, 1909.

1. Von Demiéville: Virchow's Arch. f. path. Anat., 1880, lxxxi, 333.

Fig. 1.—Melanoma of the foot. Zeiss Planar 20 mm. Showing extensive pigmentation of the tumor and epidermis. The growth is situated in the upper two-thirds of the corium and is made up of spindle cells, the majority of which are densely pigmented, and a fibrous stroma.

Fig. 3.—Melanotic whitlow. Zeiss 8 mm., C. O. 4. Showing bundles of spindle cells cut in various planes, large chromatophores and a central focus of lymphocytes. Pigment is present in the large cells and in variable amount in the smaller ones.

Fig. 2.—Melanoma metastasis. Zeiss 8 mm., C. O. 4. Showing chromatophores in a secondary nodule of the thigh; large irregular, round and spindle cells with fine and coarse granules of melanin.

Fig. 4.—Papillary nevus. Zeiss 3 mm., N.A. 1.40, C. O. 4. Showing the "nevus cells" with vesicular nucleus, some having two. The cell bodies are clear, more or less rounded and have a sharp outline. In places they are closely apposed and form a mosaic; in others they are separated by fibers from the connective tissue stroma.

Fig. 5.—Idiopathic multiple hemorrhagic sarcoma. Zeiss Planar 20 mm. Showing the growth in the corium made up of spindle cells and numerous capillaries and spaces filled with blood.

Fig. 7.—Angiosarcoma. Zeiss 8 mm., C. O. 4. Showing large cavernous blood channels lined by endothelium or sarcoma cells and the intervening tumor tissue of round and polygonal cells, and a supporting reticulum.

Fig. 6.—Idiopathic multiple hemorrhagic sarcoma. Zeiss 8 mm. C. O. 4. Showing the bundles of spindle cells cut in various planes and an intercellular substance.

Fig. 8.—Myeloma of the finger. Zeiss 8 mm., C. O. 4. Showing the giant cells, surrounding round and small spindle cells and the delicate reticulum.

Recklinghausen² in 1882 these malformations were regarded as endothelial in origin; and to harmonize, all melanomas were placed in the sarcoma group. In 1893, however, Unna³ promulgated his views on the epithelial nature of moles, and for the sake of consistency melanomas were then placed in the carcinoma group by the adherents of Unna's school. He maintained that nevus cells were true epithelial cells which had been snared off and had undergone a metaplasia from prickle cells to "soft plastic ameba-like clumps without prickles or fibrillation." Hodara⁴ claimed to have demonstrated in snared-off cells the degeneration which led to the disappearance of the epithelial prickles, and, more recently, Zieler, in his experimental work at the Breslau Clinic, produced changes in the skin which he considered as further proof of the epithelial origin of nevi. He treated a healthy portion of skin in a patient with xeroderma pigmentosum for twenty minutes with Kromayer's quartz lamp and produced a marked reaction with necrosis of the papillary bodies. After several weeks a pigmented scar ensued, on examination of which he found pigment in the cutis and epidermis and in the basal layer pale cells of epithelial character and groups of the same at the periphery of and in the scar tissue.

Fig. 9.—Myeloma of the finger. Showing tumefaction of the terminal phalanx, discoloration of the nail and fungating growth beneath.

These had the arrangement and form of typical nevus cells. The question which arises is if this was not in reality an experimental epithelioma. This would not be an unnatural supposition with a predisposed skin like that in xeroderma pigmentosum.

On the side of the mesodermal origin of moles are ranged the investigators who favor the proliferation of lymphatic endothelium or vascular endothelium and perithelium or both. Virchow and others believed them to be derived from young connective-tissue cells; and, according to Soldan,⁶ they had their origin in the vessels following the sheaths of nerve fibers. Borst⁷ and Kreibich regard nevi as melanofibromata and Ribbert⁸ invokes a distinct cell type of connective tissue origin, the chromatophore. He holds that nevi consist of two

kinds of cells—alveoli of polymorphous cells and fully developed chromatophores—both genetically identical, the round ones being sharply less differentiated. Others incline toward a dual genesis. Thus Wilfred Fox⁹ believes that the majority of nevi with regular columns of cells are derived from the epidermis, while a rare variety with a less uniform distribution arises from the mesoderm. Adami,¹⁰ while favoring the connective-tissue origin of chromatophores, admits that they may also be derived from the epidermis, but argues against a purely epithelial genesis that "pigmented tumors of pure epitheliomatous type are unknown." While I agree in the main with Adami, it must not be overlooked that pigmented rodent ulcers described by Johnston¹¹ and the pigmented carcinoma reported by Gilchrist¹² were epithelial.

From my own studies of this perplexing subject I am in accord with the view that attributes a twofold origin to nevi. In some, the characters of the cells conform more closely with those of the epidermis and can hardly be distinguished from prolongations of the latter which enter the mole. In others, there appears to be another variety, consisting of cells with vesicular nuclei, with faint or no tinctorial properties and a well-defined border (Fig. 3). Their shape in general is round, but this may be modified by mutual pressure. Fibers from the connective tissue may be seen between individual cells and groups of them.

The sites of predilection for melanomas are the eye and the skin of the face and extremities, especially the foot. While nevi and pigment spots form a predisposing base for the development of melanomas, the latter also occur independently of them in the normal skin or other organs. Regions normally rich in chromatophores show a certain proneness, as the anus and genitalia.

Ribbert and Borst look on the primary occurrence of melanomas elsewhere than in the skin, mucous membranes or choroid with skepticism. This seems hardly justifiable in view of the number of authentic reports. Duval¹³ reported a melanoma of the gall bladder, Rössle of the ovary and Frankel of the thyroid. Orth¹⁴ published a report of a primary melanosarcoma of the adrenal and Martini¹⁵ three cases from the axillary and cervical lymph nodes. In his report he incorporates accounts of similar primary lymph node tumors recorded by Cena, Birch-Hirschfeld, Putiate, Berger and Marchand, and seeks the explanation for this location in the common mesodermal origin of the lymph ganglia and corium and the aberration of chromatophores during fetal life into the stroma of certain nodes, which cells after a time give rise to tumor formation. In connection with the central nervous system there are also a number of instances. Virchow,¹⁶ in 1859, reported a case of the arachnoid, all the other organs being free. Stoerck's case showed involvement of the pia and spinal cord, without other findings. Sternberg's case was a primary growth of the brain, as was also Minelli's. Hirschberg¹⁷ reported one of the lower dorsal and upper lumbar segments of the spinal cord with metastases into the neighboring soft tissues; nowhere else was

2. Von Recklinghausen: Ueber die multiplen Fibrome der Haut, Berlin, 1882.

3. Unna: Berl. klin. Wehnschr., 1893, xxx, 13.

4. Hodara: Monatsh. f. prakt. Dermat., 1897, xxv, 205.

6. Soldan: Arch. f. klin. Chir., 1899, lix, 261.

7. Borst: Die Lehre von den Geschwülsten, 1902, p. 117.

8. Ribbert: Beitr. z. path. Anat. u. z. allg. Path. (Ziegler's), 1897, xxi, 471; Geschwulstlehre, 1904, p. 277.

9. Fox: Brit. Jour. Dermat., 1906, xviii, 15.

10. Adami: Principles of Pathology, 1, 764.

11. Johnston: Jour. Cutan. Dis., 1905, xxiii, 1.

12. Gilchrist: Jour. Cutan. Dis., 1899, xvii, 117.

13. Duval: Montreal Med. Jour., 1908, xxxvii, 270.

14. Orth: Berl. klin. Wehnschr., 1906, xxvi.

15. Martini: Ztschr. f. Krebsforsch., 1907-8, vi, 200.

16. Virchow: Virchow's Arch. f. path. Anat., xvi, 180.

17. Hirschberg: Virchow's Arch. f. path. Anat., clxxvi, 229.

there a trace of melanotic pigmentation. As Hirschberg points out, physiologic chromatophores with iron-free pigment are present in the central nervous system, and there is also an embryologic relationship between those of the skin, choroid and leptomeninges in that they have a common matrix in their development. Furthermore, from the observations of Ribbert,¹⁸ Kölliker, and others, chromatophores are present in the adventitia, especially of the pial arteries which pass into the central nervous system, and these may undergo primary proliferation.

Melanomas developing on moles may give rise to marked local changes, or, more rarely, to none at all, the first indication of malignancy being metastasis. Or, the mole may ulcerate and partially heal or take on slow growth; meanwhile, the neighboring lymph nodes enlarge and, if ulceration over them takes place, discharge an inky black fluid, the patient dying from recurrent hemorrhages or from ulceration of some large vessel in the neighborhood. Again, the mole may increase in size and color and produce lymph node and visceral metastases, death ensuing from cachexia or interference with some vital organ. In the benign type, the so-called melanotic "rodent ulcer," the node becomes locally malignant, but no metastasis takes place. In Galloway's¹⁹ and Crocker's²⁰ cases of melanoma of the foot the tumor began as a "blister" which ruptured and healed several times and then developed into a growth.

Melanotic whitlow, which, according to Hutchinson, is due to injury, is seen at the base of one of the finger- or toe-nails, has the features of an onychia with pigmentation, and soon develops into a fungating tumor which is as malignant as the other forms. Figure 4 shows a section of such a growth, in which the sarcoma element was very evident. It was made up of fasciculi of connective-tissue cells with intercellular fibrillae. The cells varied in size, were spindle or oval in shape and had pale-staining nuclei. Some were pigmented, others not. In outlying areas there was also an alveolar arrangement of round and polymorphous cells of large size with a sparing amount of intercellular substance. Pigment in this portion was lacking. The tumor was very vascular and in the lumina of a number of vessels a growth was noted. A number of multinucleated cells were also seen. A round-celled infiltration was quite marked, a focus being present in the center of the illustration.

The rule is for melanomas to form more metastases than do any other tumors, dissemination taking place both by the lymph and the blood stream, so that the regional lymphatics and all the viscera, intestines and serous membranes may show secondary involvement. This tendency to metastasize is due to growth near the vessels and into them, so that the cells are carried through the entire vascular system. In advanced cases the leucocytes and the endothelial cells lining the vessels take up pigment so that the tissues in general may be tinged and there may be in addition melanemia and melanuria. Not all tumors are equally malignant and dissemination may be delayed for a long period. Just gives the average duration as three years, but death within a year has followed, and as an outside limit may be mentioned Dobbertin's case of brain tumor which appeared ten years after a primary tumor of the eye. Whitfield²¹ divides melanomas into two classes, the com-

mon highly malignant type with early and general dissemination and the slow-growing variety with little tendency to metastasis. Rarely the regional lymph nodes escape even in the malignant type, as in Gilchrist's²² case in which dissemination took place by the blood stream only, and hundreds of metastases were present without involvement of the lymphatics.

The color of the metastases bears no relation to that of the original tumor, as the latter may be deeply pigmented and the daughter cells colorless, and conversely, with a slightly pigmented growth the metastases may show all the shades from a light brown to an intense blue-black.

Microscopically, melanomas show a varying picture, not only in different growths but in different portions of the same tumor. There may be an alveolar arrangement of large or small cells in one part and bundles of spindle or branched and stellate cells in another. The amount of pigment is also a varying factor; in some areas it may be so dense as to obscure the nucleus and cell body and in others it may be entirely lacking. In spite of this polymorphism, Ribbert²³ believes that all of the cells originate from one and the same type—namely, the chromatophore—by reason of which he designated these tumors "chromatophoromata." The round unpigmented, indifferent elements represent an embryonal stage of the chromatophore and are found in the most active infiltrating parts of the tumor, while the fully developed chromatophores represent the adult and less active stage. The large, round, densely pigmented cells he regards as degenerated forms, which, like dead amebas, have become rounded, the diffuse pigmentation being the final stage in the life history of the cell. The small, round polymorphous cells are collected into alveoli, many of which have arisen by the growth of the cells into the lymph and blood vessels and filling and distending them. The spindle cells are collected into bundles, which in the main run parallel to the blood vessels. Ribbert found that in nevi the pigmented cells were usually of spindle shape and had a tendency to arrange themselves about the vessels. They may, however, also be pigment-free, although the pigmented ones are the characteristic element, and it is most likely that melanomas arising from nevi do so from the fully developed chromatophore rather than from the cell clusters, though these can not be ruled out. When they do arise from pre-existing developmental anomalies, he adds, it is probable that in them the chromatophores were more numerous from the beginning and were undergoing a slow but continuous increase.

Borst and others also pointed out that the most pigmented portions of melanosarcomas were those closely related to the vessels. Lubarsch and Rössle explain this by the fact that the cells lying nearest the vessels receive more nourishment; hence develop and pass through their evolution more rapidly. The intensity of pigmentation then does not point to its hematogenous origin, but to more favorable conditions for development.

Melanin consists of fine amorphous granules varying from golden brown to inky black. It is soluble in ether, alkalies and strong acids and is bleached by chlorin, peroxid of hydrogen and potassium permanganate. Being the final stage of the cell, its increased production leads to death of the cell, and nucleus and protoplasm may disappear, leaving only heaps of pigment. Von Rindfleisch is of the opinion that pigment

18. Ribbert: Cited by Hirschberg, Virchow's Arch. f. path. Anat., 1906, clxxxvi, 229.

19. Galloway: Brit. Med. Jour., 1897, p. 873.

20. Crocker: Diseases of the Skin, Edition 3, p. 1020.

21. Whitfield: Brit. Jour. Dermat., 1900, xii, 274.

22. Gilchrist: Jour. Cutan. Dis., 1899, xvii, 122.

23. Ribbert: Geschwulstlehre, p. 255.

accumulation leads to an irritative condition of the cell and proliferation, resulting in daughter cells with the inherent property in a certain stage of development to form pigment again.

In the discussion of the origin of melanin the points at issue are whether it originates in the cutis or epidermis or in both, and whether or not it is derived from the blood. Kölliker²⁴ believed that it was formed in the cutis and through the leucocytes or connective tissue cells was transported to the epidermis; Jarisch and Post,²⁵ that it was of epidermic origin and streamed into the cutis direct or was carried there by wandering cells. Ehrmann,²⁶ Borst, and Neumann were of the opinion that it was derived from the hemoglobin of the blood. Ehrmann²⁶ attributed to a specific cell in the cutis, the melanoblast, the function of pigment formation, and believed that this cell extended into the epidermis and deposited pigment there. This cell is identical with the chromatophore of Ribbert. The hematogenous origin of melanin, however, is not supported by chemical examination, as it contains sulphur and not iron. Various investigators, among them Martini, found iron only in those portions where hemorrhage had taken place, so that the presence of iron in melanotic areas is generally looked on as a contamination with blood.

Rössle,²⁷ in studying protozoa under pathologic conditions, found that certain nuclear changes took place—namely, hypertrophy and hyperchromatosis—with discharge of a portion of the nuclear substance into the plasma and its conversion into brown or black pigment. Turning his attention to melanomas, he came to the conclusion that similar changes took place in young cells—namely, an overproduction of nuclear substance with passage into the protoplasm and metamorphosis into pigment. He demonstrated that the chemical reaction in both was the same—namely, iron-free.

Staffel²⁸ confirmed the studies of Rössle and applied them to various pigmented conditions in the skin. He concludes that in human skin pigmentation is the result of cellular activity, is formed by the epidermic as well as plasma and mast cells, and that the mode of formation is the same in all—i. e., an accumulation of nuclear substance and its conversion into pigment.

In further support of the nucleolar theory are the experiments of Meirowsky.²⁹ He produced pigmentation with the Finsen light and found that pigment was produced only in the epidermis and not in the cutis. He was able here to follow the same cycle of development as his predecessors had reported—viz., accumulation, discharge and metamorphosis of nucleolar matter. Pigment being a portion of the nucleus, he suggests that this point may help to clear up the question of the inheritance of pigmentation, the nuclei transmitting inherent properties and tendencies to the offspring.

Adami³⁰ argues that identical nuclear changes having been described in connection with so many cell deposits, each individual cell deposit instead of being a direct development from the plasmasomes or chromidia is due to the interaction between the discharged nuclear matter and certain cytoplasmic substances. He also suggests that instead of being a progressive acquire-

ment, marked pigmentation indicates a deficiency in the disintegrative mechanism of the cell, the normal final stage of colorless chromogen formation not being reached. From the investigations of von Fürth³¹ it seems that melanin is developed by the action of intracellular oxidases or enzymes on the aromatic or chromogen group of the protein molecule.

The true factor in the causation of melanomas, as in all tumors, is still unknown, and the extent to which increased vascularity due to irritation or inflammatory changes plays a rôle still undecided. The majority of cases begin after the third decade, chiefly in the fourth and fifth. Bland-Sutton mentions one in a girl of 13. It would seem that melanomas of the foot occur more frequently in women than in men. These tumors appear to have a wider distribution in the lower animal kingdom, where they are not so malignant as in man. They are frequent in horses, and also occur in cows, having the same tendency to metastasis, but with a more benign course.

Among the other pigmented growths of the skin is Kaposi's idiopathic multiple hemorrhagic sarcoma, differing from the melanoma in having a multiple and usually symmetrical origin, a slower course and little tendency to metastasize. Its color is due to blood pigment and not to melanin. As shown in Figure 5, the tumors are situated in the corium, are very vascular, and consist of capillaries and blood spaces lined by endothelium or tumor cells and a connective tissue growth. The blood spaces are very delicate and rupture easily, the hemorrhagic extravasation giving rise to the pigment present in these tumors. Under higher magnification (Fig. 6) the growth is seen to be made up of spindle cells and an intercellular stroma collected into bundles which on section appear in various planes and give rise to an appearance of streaming or radiation from different centers.

I have previously called attention to the fact that single brownish-red tumors are met which present all the histologic features of Kaposi's angiosarcoma, remain localized and show no recurrence after removal. On the other hand, we find tumors originating from the endothelium or perithelium of blood vessels in which the cells are not spindle-shaped as in the Kaposi type, but round or polygonal (Fig. 7), with deep-staining nuclei and a slight intercellular substance between. The large cavernous blood channels are lined by endothelium or tumor cells and, owing to the delicacy of the walls, hemorrhage readily occurs into the tissue.

With the melanoma at one pole of the sarcoma group representing the highest type of malignancy, we have the giant-celled sarcoma or myeloma at the opposite end as the least malignant. It is still a question whether it properly belongs to this group, many pathologists being inclined to place it in a class by itself, for this reason denominating it "giant-celled myeloma" instead of a giant-celled sarcoma. It is made up of tissue similar to the red marrow of young bones and occurs in the medulla and in the periosteum, as in the lower jaw, where it is known as epulis. In the long bones the site of predilection is near the epiphyses, almost always beginning in the medulla and growing out to the periosteum. These tumors may attain the size of a head and undergo cystic softening. The vascular development is very marked, and the hemorrhage may be so great that the tumor regresses and is no longer thought a growth. Such cases have been called "bone aneurisms." These

24. Kölliker: *Ztschr. f. wissensch. Zoöl.*, 1887, xlv.

25. Post: *Virchow's Arch. f. path. Anat.*, 1894, cxxxv, 479.

26. Ehrmann: *Monatsh. f. prakt. Dermat.*, 1907, xlv, 166.

27. Rössle: *Ztschr. f. Krebsforsch.*, 1904, ii, 291.

28. Staffel: *Verhandl. d. deutsch. path. Gesellsch.*, 1908, xi, 136.

29. Meirowsky: *Monatsh. f. prakt. Dermat.*, 1906, xlii, 541; xliii, 155; 1907, xlv, 166.

30. Adami: *Principles of Pathology*, i, 765.

31. Von Fürth: *Centralbl. f. Path.*, 1904, xv, 617.

tumors are not very malignant; they grow slowly, recur sometimes, but do not as a rule metastasize.

CASE 3.—The case under consideration, kindly referred to me by Dr. Dougal Bissell of this city, had a more unusual location, viz., in the terminal phalanx of the left middle finger. The patient was a woman of 33.

History.—Ten years before examination, the patient had had a chancre of the lip for which she was treated over a period of two and a half years. She was married the first time at twenty, and the second time six years before she came under observation. She had never been pregnant. Eight years before examination she was operated on for tubal disease, a portion of one ovary being left. She had menstruated normally since. Three years before she came under observation she had a "sore" on her elbow. Eight months before she presented herself to me she noticed a swelling of the terminal phalanx of the left middle finger. Later the nail became discolored and tender on pressure. After this a dark red infiltration appeared beneath the nail and projected some distance beyond the tip of the finger. It subsequently ulcerated and was followed by a fungating condition (Fig. 9). On palpation of the terminal phalanx, marked crepitation was evident, probably due to the disintegration of the bone.

On account of the history of syphilis, the patient was treated energetically with antisyphilitic remedies without avail. A biopsy was then made to confirm the clinical diagnosis of myeloma. She was given numerous x-ray exposures, but as they were unproductive of result, she finally yielded to operation. Amputation of the terminal phalanx was made by Dr. Bissell and the tissue sent to me for further examination.

Examination of Specimen.—On section, the entire phalanx showed soft cancellous tissue with a few spicules of bone and a central cavity. Microscopically, (Fig. 8), the typical feature was the giant cell, which has the characteristic structure of myeloplasm. The rest of the tumor was made up of spindle and round cells arranged about the giant cells or blood vessels, which were very numerous in some areas. They varied from small capillaries to large blood spaces and hemorrhage was marked in places. The supporting stroma consisted of an intercellular reticulum of variable amount. The giant cells were more or less grouped, had a finely granular protoplasm and many nuclei, oval or round, situated throughout the cell body. Their number was so great sometimes that they filled the entire cell. Occasionally tumors were found in which the nuclei had a peripheral arrangement as in the Langhans cell.

Owing to the history of lues which this patient gave, it is interesting in this connection to cite the case of syphilitic dactylitis with recurrence after operation reported by Nicolas, Durand and Moutot.³² The patient was a man with a fusiform tumefaction of the left index finger, which was diagnosed on clinical and histologic examination as a myeloma of the synovial sheath. An operation was performed, but a month afterward the patient returned with a tumor the size of a pigeon's egg, which was then diagnosed as a rapidly infiltrating sarcomatous recurrence. An antecedent history of syphilis, however, and a closer study of the microscopic features of the case, suggested to one of the authors its possible luetic nature. The patient was accordingly most energetically treated on this supposition with injections and iodids and in four weeks was well.

Tertiary lesions of syphilis present under the microscope such a variety of phases that they may simulate a vast number of pathologic conditions. Giant cells conforming more or less to the myeloid type are often present in great numbers, but they do not possess so many nuclei, and on closer examination their vascular relationship can usually be established. I believe that the majority, if not all, giant cells in syphilis are the

result of endothelial proliferation and vascular occlusion. As other differential points may be mentioned the endarteritis and periarteritis of the vessels in lues, and also that the spindle cells with the reticulum met with in myeloma are not a feature of syphilis.

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ABSTRACT OF DISCUSSION

DR. D. W. MONTGOMERY, San Francisco: In my opinion Dr. Fordyce has acted wisely in speaking of the melanomas as sarcomas, without further comment; for although some of the melanomata look like epitheliomata because of their highly developed alveolar structure, yet they are, almost without exception, sarcomas. A pigmented epithelioma is a very rare form of tumor.

DR. JAY F. SCHAMBERG, Philadelphia: One of the photomicrographs shown by Dr. Fordyce recalls to me a picture in my possession which appeared some time ago in the *Journal of Cutaneous Diseases*, and which represented an epithelioma developing on a papillary nevus on the forehead of a young man which had been injured by an umbrella ferule. The nevus had been present since birth and only underwent malignant change subsequent to the injury. The growth appeared to have its origin from an off-shoot of the hair follicle so that it probably belongs to the type of epithelioma designated trichoeplithelioma. Large masses of epithelial cells were seen proliferating in the lymph spaces.

DR. M. B. HARTZELL, Philadelphia: We have learned in recent years that many of the cases of malignant neoplasms formerly called alveolar pigmented sarcoma are not sarcomata at all, but pigmented epitheliomata; and it seems to me that we ought to be somewhat cautious about accepting as sarcoma some of these lesions of the skin showing a pigmented alveolar structure. Most of these are epitheliomata.

DR. WILLIAM S. GOTTHEIL, New York City: I have had two of these cases of pigmented sarcoma and in both of them, in spite of early and repeated operations, general sarcomatosis of the skin and internal organs led to a fatal issue, in one case within six months; in the other within nine months.

DR. J. A. FORDYCE, New York: I intended to use the term melanoma as a non-committal one, including melanosarcoma and melanoepithelioma. I think it is yet undecided where these tumors originate. I do not believe that the view expressed by Dr. Hartzell that many of them are melanoepitheliomata is accepted by leading pathologists. The view is commonly held that these growths originate from the chromatophores, presumably connective tissue cells, and not from the epithelial cells. Unna's contention that they are melanoepitheliomata is now losing ground, and the view is being held that they originate in this special tissue. In one case, a tumor of this kind existed on the foot for a number of years without giving rise to metastases, although as a rule these growths metastasize early and are rapidly fatal.

THE ROLE OF ANIMAL EXPERIMENTATION IN THE DIAGNOSIS OF DISEASE *

"The humanity which would prevent human suffering is a deeper and truer humanity than the humanity which would save pain or death to animals."—Charles W. Elliot.

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We must recognize a disease before we can hope to prevent or cure it. The diagnosis is, therefore, of fundamental importance; indeed, on correct diagnosis rests the entire structure of preventive and curative medicine. The power of recognizing a large number of diseases with unerring certainty has raised medicine from a de-

32. Nicolas, Durand and Moutot: *Ann. de dermat. et de syph.*, 1908, Series 4, ix, 208.

* This is Pamphlet III in a series issued for public information by the Council on Defense of Medical Research, referred to editorially last week. See advertisement in this issue.