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REMARKS ON THE HISTOLOGY OF XERODERMA PIGMENTOSUM.

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I HAVE been asked by the Editor of this JOURNAL to supplement Dr. Brayton's description of his two cases of *xeroderma pigmentosum*, with a brief account of the histology of that affection, based on my own observations.

During my residence in London, in 1890, I had an opportunity of seeing one of the three English cases of *xeroderma pigmentosum* through the courtesy of Dr. H. Radcliffe Crocker, and I am indebted to him for some specimens which he removed from one of the tumors in the patient's face and for his kind permission to make use of them in this publication.

Dr. Crocker, it will be remembered, published in 1884 an account of three cases of *xeroderma pigmentosum* (the only examples of this disease observed in England) affecting three members of the same family. In the youngest of these, a boy of nine years, the disease had at that time made not much progress. The face, neck, arms and forearms were deeply pigmented, there was considerable atrophy of the skin of the face, very few telangiectases, some superficial ulceration especially below the eyes, and a few warty growths, which proved to be papillomatous granulomata. When I saw the boy in 1890, he presented the disease in an advanced stage. Fungating and ulcerating tumors had developed in different parts of the face, and the atrophic changes in the skin were very marked. A photograph taken at that time sufficiently illustrates the extent of these changes (See Fig. 1), a description of which need not detain us now. The following extracts from a letter of Dr. Crocker's under date of February 25, 1892, may be of interest: "All three cases are still alive, but I have not seen them since you saw them with me. The boy had made much more progress downwards than either of the other two in whom the disease was



comparatively quiescent. I send you a photograph of him taken on May 1, 1890. . . . Compare it with the portrait of him in the *Med. Chir. Trans.* [1884], and you will see how he has gone to pieces."

A part of the lower tumor on the cheek was excised, and, as it represents a later phase in the development of the disease, the



Fig. 1.

stage of malignant growths, it may be well to precede a description of its histology with an account of the earlier changes in this disease. In presenting this resumé I shall not follow any single author, but shall make use of all previous publications on the subject, especially those of Kaposi, Neisser, Vidal, Crocker, Taylor and Elsenberg. The first change consists, probably, in a hyperæmia. It is true that in many of the re-

corded cases there is no history of erythema ; but in view of the facts that a temporary redness of the face in an infant may so easily be overlooked, and that this symptom is recorded in perhaps the majority of cases, we may assume it to be the rule. Accompanying the vascular dilatation, there will be increased exudation of serum, leucocytic infiltration, and probably more or less red blood-corpuscule diapedesis. We have thus at hand the material for the next marked change, the accumulation of pigment in the skin, located chiefly in the lower layers of the rete. Meanwhile, in consequence of the increased blood supply, there is an increased development of the surrounding connective tissue, which goes on to the production of more or less sclerosis, which in turn compresses the blood vessels in places inhibiting thus the nutrition of other parts. At the same time changes within the vessels are taking place, resulting in endarteritis obliterans. This interference with the circulation explains the occurrence of the next notable clinical changes, the development of atrophic patches, and the telangiectases ; the diminished nutrition explains the first, the occurrence of congestion and of collateral hyperæmiæ the second symptom. The atrophic patches, under the microscope, show nothing characteristic ; the rete is reduced to a few rows of cells ; there is no pigment present ; the papillæ are few and small or entirely wanting, there being a sharp line of demarcation between the epidermis and the cutis. The latter presents a dense connective tissue in which the glandular structures are for the most part reduced in size and evidently in process of atrophy. The blood vessels are sparse in some places, frequently with their lumen diminished through endarteritis, and in others enormously dilated, forming large, irregular vascular channels resembling angioma. Later, patches of connective tissue may undergo myxomatous degeneration. The regions around the vessels are considerably infiltrated with round cells, and we may have at this period—toward the end of the second stage in the progress of the disease—the picture of a granuloma interspersed with patches of angio-myxoma. The warty growths which occur in this period and which form the connecting link between it and the third, the period of malignant growths, are generally granulomata, commonly papillomatous in their structure, and are covered by a thickened epidermis with long rete proliferation into the body of the tumor. The superficial ulcerations like the distortion of the mucodermal orifices, which develop throughout this period, may be regarded as purely secondary lesions. The latter are the effect

of the sclerosis and the atrophy; the ulcerations probably result from the bacterial infection of the cracks and tears—rhagades—which occur naturally in such a skin in so mobile a region as the face.

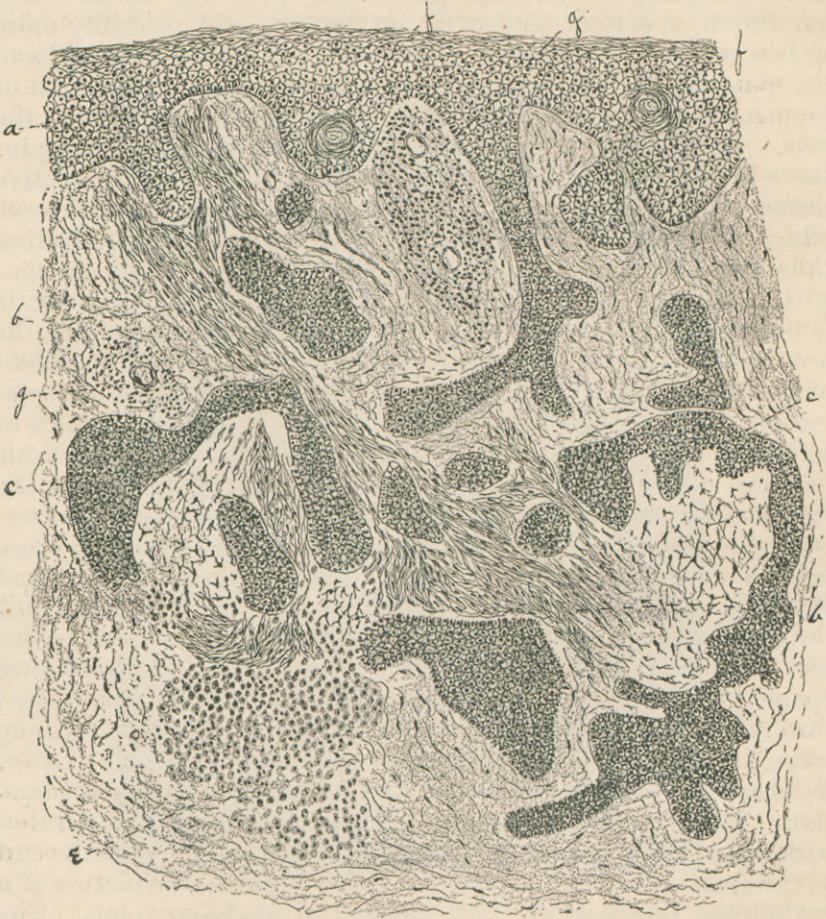


Fig. 2.

a, Epidermis; *b*, Spindle-celled sarcoma; *c*, Epithelioma; *e*, Round-celled sarcoma; *f*, Epithelial "pearls"; *g*, Granulation tissue.

We come now to the third stage, that of malignant growths. Almost every variety of malignant growth has been described by the various authors, and there appears to be considerable differences in different tumors or cases. The specimen from

Dr. Crocker's case shows on examination so many different kinds of neoplastic formation that it may be regarded as a typical case for purposes of histological study. The portions removed included parts which had ulcerated as well as others which were still covered by epidermis. The stratum corneum was in many places very much thickened; the rete malpighii at the seat of the ulcerations thinned or wanting, elsewhere as a rule very much thickened, and its interpapillary processes greatly proliferated, irregular branching processes extending far down into the cutis helping to form there the picture of epithelioma. Below the epidermis there is the greatest conceivable confusion in the arrangement of the new formed tissue; sarcoma, spindle and round-celled, epithelioma, myxoma, with patches of granulation tissue and large vascular channels interspersed. The illustration, Fig. 2, will convey an idea of the variety and arrangement of the elements of this peculiar growth. The sarcoma occurs indifferently in various parts of the tumor. In some sections it appears to form a considerable part of the growth, in others it is entirely wanting; it is commonly of the small spindle-celled variety, but there are patches of round cells which from their size and their dense and uniform aggregation give the impression of being round-celled sarcoma rather than simple granulation tissue. The myxoma occurs in irregular scattered areas of moderate size, and seems to be derived from the connective tissue. The round-cell infiltration is frequently limited to the region around a small blood vessel, but often extends over large areas. The epithelioma forms the one constant feature in all parts of the tumor. It occurs as long bands projecting downward from the rete, and splitting up below into patches, streaks and islands of the most fantastic shapes. At times it lies in the midst of granulation tissue, again the little islands are surrounded by spindle-celled sarcoma, or adjoin myxomatous tissue. In short it occurs throughout the entire extent of every section and forms pre-eminently the important part of the tumor. Epithelial "pearls" occur frequently, and among the cells themselves the most wonderful variety of mitoses normal and pathological, and of nuclear and cellular degeneration may be found. The connective tissue which forms a large part of the tumor appears loose and œdematous in some places, in others contains large and numerous fibroblasts. The blood-vessels are seldom normal, their endothelial lining is often swollen and proliferated. In some places there are broad thin-walled spaces filled with blood. I find no

evidence of proliferating blood-vessels. Of glandular structures and hairs there was for the most part nothing to be seen. In only one section was there a thinned degenerated hair follicle and the remains of a sebaceous gland.

All these various changes have been described in different cases by previous writers on the anatomy of xeroderma pigmentosum. The tumor which I have briefly described has, however, the peculiarity of presenting at once, frequently in a single section, all these varieties of new growth and degeneration.

I have observed, however, two kinds of degeneration which I

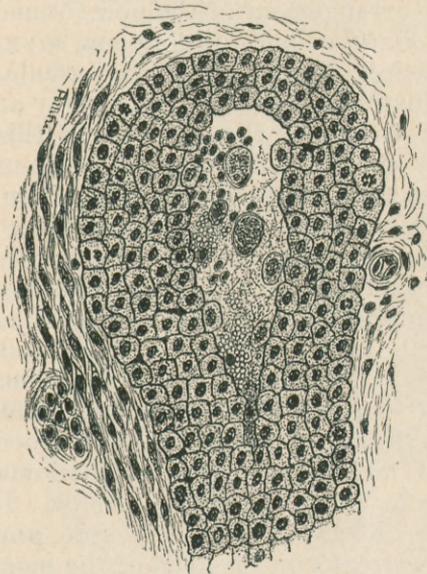


Fig. 4.

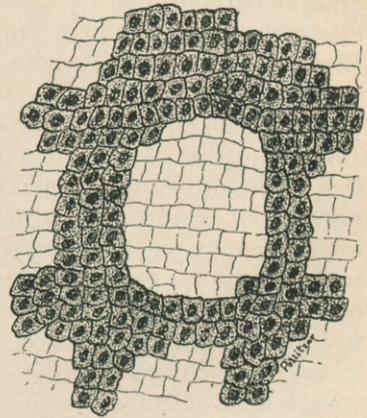


Fig. 3.

believe have not before been described in these tumors. First, in some places in the deeper part of the tumor the epithelial new growth appeared to form a network inclosing quite regular clear spaces, suggesting the rare form of neoplasm known as *cylindroma carcinomatodes*. With a higher power, however, these clear spaces were found to contain a delicate reticulum looking like skeletons of cornified cells containing no trace of a nucleus or protoplasm (see Fig. 3). In the *cylindroma carcinomatodes* the clear spaces are filled with a perfectly homogeneous colloidal matter, and the peculiar degeneration referred to here cannot therefore be classed with that variety of cancer.

The cells of the epithelial reticulum show no signs of growth, no mitoses, but on the contrary many of them are undergoing degeneration. I have never seen anything like it. Is it possibly an early stage in the formation of cylindroma?

Second, in some parts of the tumor, in the upper regions as well as in the deeper, there were exudations of serum, generally into a mass of epithelial tissue, constituting parenchymatous vesicles, of various sizes, sometimes microscopic, at others large enough to be visible in the section to the unaided eye. The borders of these vesicles were generally the epitheliomatous cells into which the exudation had taken place; often, however, only one side of the vesicle was lined with epithelium, the other sides being less sharply defined granulation tissue. The vesicle itself was filled with granular matter, fibrin, red-blood corpuscles, a coarsely granular amorphous matter probably disintegrated red-blood corpuscles, leucocytes, and epithelial cells. The latter showed the forms of degeneration which we commonly see in vesicles formed in the rete, as in Herpes zoster for instance. The peculiar large dropsical cells, with compressed crescentic nuclei and body filled with leucocytes, which Pfeiffer has described in zona as forms of protozoan parasites, occurred commonly.

These forms of degeneration must play an important role in the breaking down of the tumors which marks the last stage of xeroderma pigmentosum.

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