pancreas, 1; kidney, 1; costal cartilage, 1; ant. medias-num, 1; skin, 1; palate, 1.

As might have been expected, the primary metastases are most frequent in the lung tissue, and next to the lungs metastatic foci are found most frequently in the bones; having been present in 6 of the 18 cases in which metastases were found. This is equal to 30 per cent. Luke gives the frequency of bone metastases in sarcomata which had produced metastases, as 12.7 per cent., so it appears that bone metastases are $2\frac{1}{2}$ times as frequent in sarcomata of the thyroid as in tumors of this class in general.

Limacher, as stated above, found 44 cases of sarcoma of the thyroid in the post-mortem records of the Berne Path. Institute, and among these 44 cases, 35 showed metastases. The difference between these figures and the figures deduced from the series of cases collected by myself is perhaps explained by the fact that in many cases, a post-mortem examination was not made, or if made, was not reported. So, very probably some metastatic foci have been thus overlooked. Among these 35 cases the distribution is as follows: Lung, 27; liver, 7; bones, 8; spleen, 1; brain, 3; heart, 3.

It will be noticed that in this series also, the metastases are relatively frequent in the lungs and in the bones. As far as my knowledge goes, no adequate explanation has been offered to account for this frequency of osseous metastases.

As the conclusions reached in this paper are based on the study of a comparatively small number of cases, and as it is evidently not possible to enumerate all peculiarities and unusual manifestations of thyroidal sarcomata, it has seemed desirable to arrange in tabular form the chief facts of interest in the pathology of these tumors. Special care has been taken to include in this table several points concerning which there seems to be a difference of opinion among the various writers on the subject. An endeavor has also been made to bring out some of the salient points in the pathology of the disease, in each case, in order that a comprehensive picture of the many and various anatomic features might be presented.

In conclusion, I desire to express my sincere appreciation of the kindly interest and the help rendered by Prof. Ludwig Hektoen, in the preparation of this paper.

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XERODERMA PIGMENTOSUM.*

REPORT UPON THE PRESENT CONDITION OF THE INDIANAPOLIS CASES.

BY ALEMBERT W. BRAYTON, M.Sc., M.D.

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INDIANAPOLIS, IND.

ALSO THE REPORT OF A CASE IN COLUMBUS, OHIO, NOT BEFORE PUBLISHED.

BY ARTHUR H. BOWEN, M.D.

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This "truly wonderful and terrible disease," as Dr. R. W. Taylor designates it, was first described by Hebra and Kaposi in their "Lehrbuch der Hautkrankheiten," in 1870. A disease peculiar to early life, presenting polymorphous symptoms, chronic and unending in its course, indelible in its disfigurements, prone even from its benign lesions to destroy or impair vision, to more or less disfigure and destroy the nose, ears and mouth parts, and by its malignant new growths leading to early death.

Xeroderma pigmentosum is a rare disease; the primary article of Hebra and Kaposi was based on four cases only, out of the multifarious richness of their clinical material. Later, two cases were published by Geber, under the title, "A Rare Form of Nævus." In 1877 Dr. Taylor read, before the American Dermatological Association, a paper giving the history of seven cases of this rare disease; Dr. Heitzmann related a case at the same meeting. In 1878, Dr. Duhring reported a case, under the title, "A Rare Case of So-called Xeroderma of Hebra." In 1882, Kaposi published a paper based on two personal papers, using the name "xeroderma pigmentosum," although Dr. Taylor had applied the provisional but very graphic name of "angioma pigmentosum et atrophicum." In 1883, Vidal, out of enthusiasm for Kaposi, called the disease, "La dermatose de Kaposi," a not uncommon name at the present time. In 1884, Pick wrote a clear account of the disease under the title, "Melanosis Lenticularis Progressiva." In the same year Radcliff Crocker published the histories of three cases, with the title, "Atrophoderma Pigmentosum." These are the only cases reported from England. Dr. White of Boston, in 1884, described two cases from his city; in the same year Dubois Havenith reported a case.

This brought our knowledge of the subject to 1888, under ten observers of forty-one cases. Dr. Taylor's cases were the second, sixth and seventh daughters of a family of ten children. The sister of the mother of these children married a maternal second cousin; of their five children, the second and fourth were victims of this dread disease. Dr. Taylor observed two other cases in different families. This distinguished and fortunate observer contributed a paper to the New York Medical Record, March 10, 1888, under title of "Xeroderma Pigmentosum and its Relation to Malignant New Growths of the Skin," in which may be found a résumé of the forty cases known at that time. Accompanying this paper is an extended table of two pages, giving the essential facts of all the then recorded cases; the age, sex, age at onset, age when tumors appeared, nature of the tumors, name of the

* Presented to the Section on Cutaneous Medicine and Surgery, at the Forty-ninth Annual Meeting of the American Medical Association, held at Denver, Colo., June 7-10, 1898.

observer, and extended remarks, critic, historic and suggestive, on the individual cases. There was also a series of six half-tones of five of Dr. Taylor's personal cases—one showing the progress from the eighth to the thirteenth year, with the development at the latter age of well-marked malignant tumors of the eyelid and cheek.

It would seem that the wide dissemination of the knowledge of this disease through Dr. Taylor's paper, in the *Record*, should have brought the disease into such prominence that all the cases scattered through our country would at once have been recognized. But such was not the case. A family of Low German descent, which had lived for two generations within a half-hour's ride of Indianapolis, presented three cases covering a period of twenty-six years, without recognition of the true nature of the disease. Dr. Taylor's paper was the source of my knowledge of the disease, and enabled me, with the help of the articles in the atlases of Taylor and Morrow, and the brief notes in the various works on dermatology, to identify two cases in the family cited. I wrote a description of the cases for Dr. Taylor, and also sent to him a life-size water-color drawing, made by Mr. Richard Gruelle of Indianapolis, of one of the cases—a girl of 16 years. Dr. Taylor was kind enough to present the case to the Section on Cutaneous Medicine and Surgery at the Washington meeting in 1891. This was published with an excellent chromo-lithograph in the *Journal of Cutaneous and Genito-Urinary Diseases* for April, 1892, and also, with the same plate, in the *Indiana Medical Journal*, September, 1892. In the meantime a third case of the disease developed in an infant daughter of the family, and the two cases, with the plate, were published in the "Transactions of the Indiana State Medical Society" for 1892, so that, altogether, some six thousand copies of this excellent colored plate—the best graphic representation of the disease extant, according to Dr. Taylor's view—were widely distributed throughout the country.

The most extended histologic studies of the tumors of xeroderma pigmentosum known to me are those made by Dr. S. Pollitzer of New York City. They were published with sections in the same issue of the *Journal of Cutaneous and Genito-Urinary Diseases*, in which occurred the plate and description of my own case. Dr. Pollitzer's material was from one of Dr. Crocker's three London cases; the material was taken in 1890. In 1892, Dr. Crocker's three cases were still alive, but two of them were progressing to a rapidly fatal termination, and in one the disease was quiescent. They comprised two brothers and a sister of the same family; in each case the disease was discovered soon after the first year of infancy. They were respectively 12, 10 and 9 years of age at the time they were reported.

The sections presented by Dr. Pollitzer exhibit a wildness of growth equivalent to pathologic riot. In a pin's head area are seen epithelial ramifications as the prevailing type. Intermingled with these are islands of spindle-celled sarcoma and round-celled sarcoma; also epithelial pearls and granulation tissue. Illustrative of the variety of structure in these tumors is a remark of Dr. Ludwig Hektoen, professor of pathology in Rush Medical College, Chicago, who wrote me that he made careful sections and studies of some of the material sent him from my cases, and "knew less of the pathology of the disease than ever before."

In the extended paper of Kaposi, pp. 728 to 742, in

the volume on "Diseases of the Skin" (Twentieth Century Practice, 1896), the author gives nine sections illustrating the pathologic anatomy. The sections and discussion of them show that the development of carcinoma and sarcoma in xeroderma pigmentosum is due to the disproportionate growth of the epithelioid structures, as distinguished from the connective-tissue stroma. The author further states, that essentially the same condition is met with in the senile skin in those cases where sarcoma or carcinoma arises from preexisting papillary warts, or pigment naevi. In the old people, we attribute the cancer growth to the senile changes in the vessels and the senile degeneration of the connective tissue of the cutis. These multiple epithelioid growths in old people, while akin histologically to those of xeroderma, do not warrant us in calling such cases Kaposi's disease—a disease which always begins in the first year of life. Indeed, its congenital tendency is its most marked etiologic characteristic, and is further emphasized by the occurrence of the disease in several children of the same family. Among the forty-three cases first presented by Kaposi in tabular form, two brothers and sisters were affected in six families, three children in each of four families, and in one family seven children. Kaposi gives the total number of cases published up to 1895, as 76, reported by thirty different authors. The American reporters are: Drs. Taylor of New York, 7 cases; J. C. White of Boston, 2 cases; Duhring of Philadelphia, 1 case; M. B. Hutchins of Atlanta, Ga. (not Hutchinson, as in Kaposi's paper), 1 case; C. Heitzmann of New York, 1 case; Arthur H. Bowen of Columbus, Ohio, 1 case, and the three Indianapolis cases which are the subject of this note—a total of sixteen American cases, as far as the present writer can determine. I have not calculated from the literature the number of families in which the seventy-six cases occurred—probably less than thirty families have furnished all the cases. The Portugal cases, occurring in late life—40 to 80 years of age—it seems to me ought not to be recorded as xeroderma pigmentosum.

But it is not necessary to pursue further the histopathology of a disease of which perhaps not more than threescore cases are authentically known. Dr. Taylor has summed up the microscopic findings of Kaposi, Geber, Neisser and Pick (*American Text-Book of Genito-Urinary, Venereal and Skin Diseases*), and he refers the reader to the elaborate exposition of the histology of the morbid growths given by Dr. Pollitzer and already referred to in this article.

I quite agree with Dr. Taylor in his insistence that xeroderma pigmentosum is a disease of infancy, and is rarely, if ever, developed in childhood and adolescence, and probably never in adult life. The undoubted cases occurred in the first and second years of life, and probably every true case began before the sixth month. In the early stages, the brown spots are easily mistaken for ordinary freckles; the red flush is not uncommon in infancy; unobserving parents would not take alarm, generally speaking, until extreme bronzing, contractions or tumors appeared.

Certainly, the three cases under my observation developed an aberrancy of redness and freckling noticed by the parents by the sixth month of life. In the case of the little girl, now 6 years old, whom I have frequently seen since her third month of life, atrophic macules not larger than an eighth of an inch in diameter, were the first symptoms observed. These atrophic spots were not preceded, as far as I could learn from

the parents or observe for myself, by any preliminary rash, pigmentation or telangiectatic areas. Dr. Hardaway has quoted this order of development observed by me in his description of xeroderma pigmentosum ("Morrow's System," vol. iii, p. 405, foot-note).

Dr. Taylor has had his series of cases under observation for twenty years; I do not know that any one of them has survived for twenty years, but various members of the two families have, some one or other, been suffering from this disease through that time. He is very emphatic as to the disease commencing in very early life. Of the cases reported by Kaposi, Vidal, Heitzmann, and others, as beginning as late as 9, 16, 72, and even 88 years of age, he is skeptic, as any one would be who is practically conversant with genuine cases of xeroderma pigmentosum. "It should be distinctly borne in mind," he says, "that the coincidence of the various pigmentations of the skin, with attendant epitheliomatous and other malignant growths does not of necessity constitute xeroderma pigmentosum." A child may have freckles in early life and malignant tumors in later life, and yet not suffer from true xeroderma. The weight of all testimony goes to show that the disease is one of early childhood, up to 5 or 10 years of age, frequently limiting itself to the skin alone—showing only redness, white atrophy, intense freckles, or even glossy black patches of pigment, contraction and ectropion of the lower lids. The tumors may come by the fifth year; they may be longer delayed, but their appearance marks the stage of the disease dangerous to life, unless they are promptly and thoroughly eradicated.

Drs. Wm. G. Corlett of Cleveland, Guido Bell and Louis Burckhardt of Indianapolis, were good enough to visit my cases with me in March, 1888. Dr. Corlett had seen the oldest case, now 22 years of age, five years before at the meeting of the Mississippi Valley Medical Association, in Indianapolis, where they were also seen by Dr. Ravogli of Cincinnati, Dr. W. T. Belfield of Chicago, and others interested in dermatology. The young woman is physically well preserved; she has been usually strong and robust, fond of work, from which she is only deterred by her photophobia and the gradual encroachment of the disease upon the lower conjunctival surfaces. The lower lids are destroyed; the cornea is clouded; the pupils are sadly malformed by the contracting iris; the tears flow on the face; vision now only amounts to the perception of light and the appreciation of large objects. The nose is eaten away to the bridge; the rims of the ears are eroded; the hands are warty and rough. The largest single tumor was on the right hand at the base of the little and ring finger. This I removed several times with the curette, going to the periosteum, but never entirely prevented its return at the margin in ever-widening circles until, at the suggestion of Dr. Burckhardt, I applied Fowler's solution several times a day to the scraped out areas. I have removed numerous warty tubercles from the fingers, ears, cheeks, lips and lower eyelids. Sometimes the electric needles were applied, under chloroform, to the tumors on the lids, with the happiest results; again the curette was used. Bleeding is profuse, but easily checked by pressure; sometimes the tumors drop off and disappear, as in the case of ordinary warts. Arsenic internally has no effect. At one time I removed a fibrosarcoma from the inner surface of the arm, just above the joint. It was the size of a large egg; the skin over it was normal. The general skin

of the body is always dry; the legs and arms are branny, the trunk and scalp not affected, nor the hair or nails. The mucous membranes are normal; menstruation was regular from the sixteenth year; the weight is about 150 pounds. Within the year just closed (1898) she has developed some cachexia, palpitation, rapid breathing and insomnia; these symptoms are in abeyance this spring (1899).

The little sister, six years old, is in the freckled stage, with white areas and beginning contraction of the lower lids, and ectropion. The few epitheliomatous nodules which have appeared upon her lips and chin have been removed sometimes by the fingernail, again by the spoon, and afterward treated with Fowler's solution, with good results. By proper care I think such a case may go on to womanhood without noticeable mutilation of the ears, fingers, nose, lips or cheeks. But the ectropion and the involvement of the conjunctiva is the most difficult symptom to control. In no case should the nodules be allowed to grow to the size they are shown in the graphic representations of the disease, as for example in the case figured by Dr. Taylor in plate xix of the "American Text-book," already mentioned. The danger of the disease is in the warty tumors. These were allowed to grow in the case of the brother, two years older than the patient above, who died of the disease in his ninth year. The nose and lips were destroyed; the child died of exhaustion subsequent to inanition and possible sepsis.

There are no metastatic growths in xeroderma; the glands and lymphatics are free. It is a disease of the skin primarily and especially of those parts exposed to the light, although it has developed upon the feet and ankles of children who have worn shoes and stockings from infancy. Left alone, any of the nodules may become deep ulcers; the ears are cropped, the nose destroyed, the capsule of the eyeball eroded, the teeth exposed, and the patient passes swiftly on to death, as was the case with the boy above described. In the absence of the knowledge of the disease the cases were regarded as an aberrant form of lupus; indeed, that was the name given by Jonathan Hutchinson—"multiple pigmented lupus."

Xeroderma pigmentosum is a family disease; it is not hereditary; not all in the family are affected. In the present family were seven children; the first-born, a male, is 29 years and healthy; the second, a boy, died of the disease; the third is Mary, above described, and probably the best preserved and most typical of all the cases tabulated in the literature of this disease; the fifth and sixth are healthy boys with fair skins and no trace of disease; the seventh is the child of 6 years, whose case I have watched from infancy. When I first saw Mary in the City Hospital of Indianapolis, she was brought to the clinic to be treated with Koch's tuberculin. Three bottles had been sent to President Harrison, by the German government. A bottle was sent to me for experiment in the Hospital of President Harrison's adopted city, and she was the second case treated in the United States, as far as I can determine, with Koch's tuberculin. It was given under the direction of Dr. Theodore Potter, at my request, but produced no reaction. I had been negligent of the literature of xeroderma pigmentosum, and it was through Hutchinson's picture of his "multiple pigmented lupus," in "Sajous' Annual" that I correctly diagnosed the disease and was led to the study of Dr. Taylor's paper of 1888.

But why, it may be asked, is so much attention given to a disease which has no practical interest because of its extreme rarity? No case has been observed in Chicago, with her cosmopolitan population of over one and one-half millions—more than all the people of California. Only three cases are reported from the British Islands. The publication of the Indianapolis cases led to the diagnosis of one case in Ohio. Save these four cases I know of no other childhood cases in the United States, except those of Dr. Taylor and those of Dr. White of Boston. One case from Michigan was described to me in such clinical detail that I am reasonably certain it was xeroderma pigmentosum, but I can not make it matter of record, as the child is dead and the relator is now insane. The cases are valuable, as all knowledge is valuable. A

Dr. Arthur H. Bowen's case of xeroderma pigmentosum.

species is none the less a species in botany or zoölogy because it is restricted to a small area or is represented by but a few individuals.

I will close this paper by the addition of the Ohio case which was recognized upon the publication of the Indianapolis cases in the *Journal of Cutaneous and Genito-Urinary Diseases*. The case fell under the observation of Dr. Arthur H. Bowen, lecturer on dermatology, in Starling Medical College, Columbus, Ohio. This case has never been published. I submit also the photograph of Dr. Bowen's case. Dr. Bowen's report was received June 1, 1898.

I also include the report upon the histopathology of the tumors, which was made in the fall of 1892, by Dr. J. C. Graham, then lecturer on bacteriology and pathology in Starling Medical College, but now resident in Denver, Colo.

REPORT BY DR. BOWEN, COLUMBUS, OHIO, OF HIS CASE OF XERODEMA PIGMENTOSUM.

The patient, T. J., aged 9 years, was admitted into St. Francis Hospital in August, 1892. His parents are both living; are healthy, and give no history showing any hereditary disease of any kind. The father is Welsh, the mother American; at time of marriage the mother was 17 years of age. The patient is one of five children, all living except one, who died of "inflammatory croup." The patient is the only one affected; the others show no symptoms of this or any other skin disease. He weighed 14 pounds at birth, and was perfectly healthy up to the age of 8 months, when the present trouble made its first appearance.

The patient was of light complexion, with brown hair and blue eyes, and was three feet eight inches in height. At time of admission into the hospital he was spare and slightly emaciated, but quite strong; digestion fairly good; bowels slightly constipated; skin dry, rough and slightly scaly; sebaceous and coil glands inactive. The affected skin was more thickened and inelastic than the normal skin, and more sensitive.

The history corresponds with that of other cases reported. The mother says the disease first appeared upon the cheek below the eye, as bright red spots, which she called "sunburn." The spots increased and spread rapidly, the skin in places broke, discharging a light-colored pus. After the red spots disappeared the freckles and white, glazed, pearly condition of the skin appeared. The affected surface was not completely covered with the pigmented spots, until about the age of 7 years. The drawn or contracted appearance of the mouth and nose followed the subsidence of the erythematous lesions.

The patient complains of his eyes being weak, and the mother says he has had conjunctivitis.

The ulceration in the ear, for which the boy was brought to the hospital for treatment, began as a wart about six months before. It had been cauterized by the family physician every second day, but continued to grow worse.

The eruption involves entire face and neck, extending from the edge of the hair to the border of the third rib; the hands, fingers, wrists and forearm to the elbow; the feet and legs to the knees.

The eruption began upon the face, spread slowly, involving in the order named the neck, hands, arms, feet and legs, becoming general over affected surface in about six years. The lesion consisted of erythematous spots, pigmented spots, telangiectases, atrophic spots, warts, tumors and ulceration. The erythematous patches began at about the eighth month of age, irregular in outline and of a pinkish red color. Pigmented spots or freckles followed the erythema, appearing about the second year, becoming general over the affected surface at about the sixth year.

The freckles over forehead vary in size, brown or blackish in color, irregular in outline, and in distribution most marked upon face, neck and hands, most numerous upon neck and hands.

The atrophic spots appeared first during the second year, and are most marked about the mouth and upon the back of the hands. These spots varied in size, were irregular in shape, and of a white, glistening or pearly appearance.

These caused a partial stenosis of the mouth and nose, giving them the drawn or contracted appearance seen in the photograph.

The telangiectases, were innumerable, small, stellate, pin-head sized, most distinct upon the neck.

The affected surface became a bright pinkish red color when the circulation was slightly excited.

The warts were more numerous on hands and neck. They were pea-sized and smaller, roundish, elevated and rough.

The tumors appeared at the fifth year. They were few in number and of slow growth, round and oval, pea-sized, smaller and longer, freely movable, firm and slightly elevated, with a covering of normal skin. They were better felt than seen. They were situated on the temples at outer angle of either eye, on nose between eyes, and on the neck.

The ulceration upon the right ear involved the entire thickness at one place and extended into the external meatus. It developed from a wart of six months' duration. The ulcer is irregular in shape with rough edges. The discharge was pustulous, abundant and offensive, forming yellow crusts. The ulcer was painful at times.

As the prognosis was unfavorable the patient remained in the hospital but a short time.

I learned recently, indirectly, that the patient was dead. I wrote to a physician where the patient lived asking for some information regarding the boy, but have had no reply to my letter. I enclose the report made by Dr. J. C. Graham of Columbus.

DR. GRAHAM'S REPORT.

"The growths given me for examination were three in number, two the size of a white bean, one of which was removed from the forehead, the other from the back of the neck, the third, about as large as a split pea, came from the forehead. I was not present when the growths were cut out and did not have an opportunity to examine them fresh; they were placed in alcohol and subsequently imbedded in celloidin for cutting. In attempting to cut them I found the two larger growths were calcified, necessitating their removal from the celloidin and decalcification before sections could be made.

"There was very little of interest in the smallest growth. The epidermal layer was thin, having only a few strata of cells, the rete was much atrophied, papillæ were almost entirely wanting, and glands were altogether absent. The cutis consisted of firm connective tissue whose nuclei stained fully. The hair follicles were much atrophied, the lymph spaces were filled with small round cells, and the blood-vessels were few in number.

"Sections of the large tumors made subsequent to decalcification showed the following: Epidermis thin, no papillæ, glandular structures and hair follicles wanting, and the greater part of the mass made up of epithelial cells supported by a scanty reticulum of connective tissue; the cells were greatly degenerated and took the stain very slightly. Calcification began in the centers of the nests of epithelial cells, and was present in nearly every one. The degenerated condition of the structures made an exact histologic analysis difficult.

"I regret very much not having secured a specimen from the ulcerated mass on the ear, since it might perhaps have shown a malignant character, such as growths described by a number of writers on the histology of xeroderma pigmentosum.

"So far as I have been able to review the literature of this disease, no former case has presented calcification of the nodules."

A RARE AFFECTION OF THE EYE: CONGENITAL IRIDEREMIA.*

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L. M. W., a girl of 12 years, was brought to my office by Dr. T. S. Greer of Edgerton, Kan., Feb. 15, 1899. As the Doctor presented the child with her father, he said that he thought he had a very singular case. Looking at the child's eyes, I remarked to him: "You have succeeded, Doctor, in dilating the pupil *ad maximum*," to which he replied, "No, I have never used any mydriatic in this case, nor has the girl taken any medicine that would induce mydriasis." Upon a closer examination I discovered that instead of the pupils being dilated, there was an absence of all the

Figure 1.

iris excepting a narrow rim at the ciliary border, about 1.5 mm. wide (Figs. 1 and 2), and this was ragged or serrated, having no circular fibers. There was a slight scallop at the zenith of both irides. (Fig. 2). By either the direct or indirect method there could be seen a black zone encircling the entire periphery—the ciliary body—with a transparent space all around, through which the bright reflex of the choroid and retina could be seen. Encircling the lens at its ciliary margin was a narrow crown of centripetal striæ resembling arcus senilis lentis; this I named *arcus juvenilis lentis*, the first I had ever seen; probably this was the suspensory ligament where it joined the lens capsule.

The little patient was suffering from photophobia, always closing the palpebral aperture as in albinism, thus regulating the amount of light to the fundus of the eye. Her vision was but 20/100 of either eye, and a convex spheric glass of 2.50 D. only improved

*Read before the Midland Ophthalmological Society, March, 1899.