BLUE SCLEROTICS AND BRITTLE BONES, WITH MACULAR ATROPHY OF THE SKIN AND ZONULAR CATARACT.

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WHEN the sclerotics are abnormally thin, as in buphthalmus, and even locally after scleritis, the white part of the eye assumes a bluish colour, because the dark uvea shows through. But a bluish colour of the whole sclera may be congenital, and is most often found in connexion with bones so slender and fragile that fractures are occasioned by the slightest cause—as, for example, slight blows or fall from a small height.

The description of the disease "blue sclerae and tendency to fracture" was published for the first time by Eddowes¹ in 1900 in a short report in the *BRITISH MEDICAL JOURNAL*, which, however, gives an almost complete description of the disease. Eddowes saw the disease in a father and his daughter, and he is of the opinion that the blue sclerae, as well as the tendency to fracture, are due to an inherited defective structure of the fibrous tissue of the body. In 1908 Peters² describes a family of four generations, of the 11 members of which 10 had blue sclerae, and he establishes the fact that the disease is congenital and hereditary. In a subsequent report Peters³ mentions that fractures, too, often occurred in this family.

Since then several pedigrees have been published of families in which blue sclerae and the tendency to fracture were found to be inherited. In this way Stephenson⁴ mentions, in 1910, four generations, and Harman⁵ a fifth generation of a family, of the 55 members of which 31 had blue sclerae.

Burrows⁶ found in 1911, in a family of 24, 13 affected with blue sclerae and 9 with the tendency to fracture; Adair Dighton⁷ found among 14 persons 9 with blue sclerae; Cockayne⁸ 6 cases in a family of 17 members. Van der Hoeve and de Kleyn⁹ report two pedigrees in 1918; in one, 10 persons out of the 22 members of the family have blue sclerae, as have, in the other, all the 6 members of the family, while 10 and 5 respectively have the tendency to fracture. Finally, Freytag¹⁰ has recently mentioned a family of 18 members, 11 of which had blue sclerae.

In summing up all these cases it will be seen that among 156 persons, 76—that is, about one-half—had blue sclerae; and among 52 persons, whose bones were examined in addition to the symptoms of the eyes, 24—also about one-half—had the tendency to fracture. If we look at the published pedigrees, for instance, at ours, the conditions of heredity seem to be of such a nature that the whole matter seems to be in accordance with the view adopted by Groenow,¹¹ that the anomaly is inherited as a dominating quality according to Mendel's theory.

Besides blue sclerae and tendency to fracture, other anomalies are described in these patients. One of the most frequent seems to be deafness. Van der Hoeve and de Kleyn,⁹ who were the first to describe this symptom in connexion with the blue sclerae, found hardness of hearing or deafness in all the members of the two families in question who suffered from blue sclerae and tendency to fracture. Bronson¹² found deafness in 7 cases, Voorhoeve¹³ the same in 4 cases. Late development of the teeth is further mentioned by Crocco,¹⁴ syndactyly and astigmatismus by Van der Hoeve and de Kleyn,⁹ embryotoxon by Peters,² haemophilia, congenital vitium cordis, palatum fissum and rachischisis by Voorhoeve,¹³ projecting frontal and occipital bones by Bronson,¹² and a tendency to luxations and subluxations by Freytag¹⁰ and Behr.¹⁵

As regards the cause of the disease, a great deal seems to indicate that this is due to an inherited anomaly of the mesoderm. The blue colour of the sclerae is, as mentioned above, due to the sclerotic being so transparent that the uvea shows through more than normally; the transparency, in its turn, is due to the sclerae being thinner than usual, as Buchanan²⁰ proved by measuring an enucleated eye, the sclera of which was only one-third of the ordinary thickness.

The tendency to fracture is due—as is proved by several

examinations by *x* rays (Stenvers in Van der Hoeve and de Kleyn's report,⁹ Freytag,¹⁰ Crocco,¹⁴ Reye²¹)—to thinness of the bones and defective calcareous development. Further, a relative thickening of the compacta at the expense of the spongiosa is found—probably a result of former fractures—in addition to older and newer fracture lines as well as flexures of separate bones and of the whole bony system.

The deafness is, in some cases, due to oto-sclerosis (Bronson,¹² Crocco,¹⁴) and in other cases to labyrinthic disease (Voorhoeve¹³). Stenvers (loc. cit.) found on examination by *x* rays that the labyrinthic parts were covered by a thick calcareous substance, so that the deafness in this case was due probably to a secondary disease of the labyrinth as a consequence of disturbances of nutrition caused by the osseous affection in this region.

The real cause of all the symptoms is quite unknown as yet. Some authors think that it is due to disturbances of the internal secretion (Bolten,¹⁵ Behr,¹⁶ Hoffmann¹⁷), while others connect the disease with inherited syphilis; but none of these theories has, however, yet been proved.

We shall now bring forward a case of this rare disease which has not, to our knowledge, yet been described in this country.* The case is more interesting because the patient suffers from a cutaneous disease, which perhaps is connected with the other symptoms, and which has not before been described as part of this disease.

DESCRIPTION OF DISEASE.

Condition of Heredity.—The existence of blue sclerae and the tendency to fracture in all the other members of the family is illustrated by the accompanying pedigree, composed according to information given by the patient. It has only been possible to examine one member, a maternal aunt; she had typical blue sclerae, was dull of hearing, and had formerly had several fractures, but presented no changes in the skin.

Pedigree.

Anamnesis.—The blue colour of the sclerae has existed as long as the patient remembers, and does not seem to have changed in the course of the years. She has not noticed any subjective symptoms of her eyes, and has not complained of an impaired eyesight.

The patient states that she had broken her right upper arm twice, her left forearm once, both her legs once, her right collar-bone once, and one of her ribs once. Each fracture had occurred after a very slight trauma. The patient is not able to give any more detailed information about these repeated fractures, the last having occurred at the age of 13. Subjective ear symptoms have not been observed.

Three years ago—in summer time—brownish spots as big as a pea began to appear on the neck. They grew in the course of the winter, and other spots of the same nature as the first ones continued to appear. From that time cutaneous affection has spread slowly, developing especially in winter, while the disease has in summer been rather stationary. There has been no itching, pains, or paraesthesias. The state of the general health has been good. There have been no symptoms from the lungs or heart and no febrilia.

OBJECTIVE INVESTIGATION.

The patient is 23 years old, unmarried, the daughter of a cottager. Weight 35 kg., height 142 cm., the distance between the finger-tips at outstretched arms 152 cm.

Eyes.—The eyelids are natural, the conjunctivae free from injection. The corneae have distinct arcus juvenilis above and below, otherwise normal. Javal: 3.00 (0°) above, on the left; 3.00 (170°) above, on the right.

* A case of osteogenesis imperfecta congenita with blue sclerae, described by Johannesen and Eiken in *Hospitalstidende*, 1919, No. 7, should, however, perhaps be referred to here.

Corneal radius horizontally is 7.7 mm., vertically 7.3 mm. Visual acuity, on right, 6/9 Am. 200 (15°); visual acuity, on left, 6/9 Am. 200 (165°). She reads with correcting glasses the finest writing (Jaeger N.1) at a distance of 10 cm.

Both sclerae are of a rather deep grey-blue colour, especially in the foremost part corresponding to the ciliary body, which is sharply outlined through the sclerotics. By transillumination by means of Sach's lamp a deep reddish light is seen peripherally everywhere, while a distinct radially striped shadow of the ciliary body is seen in front. The irises are grey-blue, the pupils normal. By maximum dilatation of the pupils a *cataracta zonularis* is seen on both eyes. Otherwise the refractive media are clear; the fundus of both eyes is normal. The tension is between 10 and 7.5 (Schiotz).

Bony System.—The patient is little and slender, the face flat, the chin small, the shape of the head brachycephalic, the prothesis full. The palpable long bones show no changes except that they are slender, while a considerable kypho-scoliosis, together with a pronounced curvature to the right, is noticed in the dorsal part, with a curvature to the left in the lumbar part and a corresponding deformity of the thorax. Photographs by x rays of all the bones, except the skull, did not show any trace of previous fractures. On the other hand, they proved to be but slightly calcareous and on the whole defectively developed.

The Ears.—Both tympanic membranes are red and retracted. The hearing is slightly reduced on both sides, probably on account of a double-sided chronic catarrh of the middle ear. There is no trace of disease of the inner ear, the vestibular function being normal.

The Skin.—The lower part of the neck and the upper part of the chest are affected with a strange cutaneous disease which appears zonularly. In front there are definite spots varying in size from a millet seed to a farthing, of a greyish purple colour, and of a somewhat irregular or oblong form. The surface is below the level of the surrounding skin, and the veins show through distinctly. At the edge of these parts, which at some places join into great patches, a narrow hyperaemic border is seen. The surface of the skin in the affected parts is atrophic, smooth, without scales or crusts, and the hair follicles seem to be natural. The sebaceous glands come out strongly as small white points. On the back of the neck, where the spots are smaller but of the same form, they have a somewhat different appearance. The colour is more red-purple and the atrophy less pronounced, and in some of them there seems even to exist a slight infiltration. The healthy skin is richly covered with hair and has no anomalies of pigmentation. The colour of the hair is dark blonde.

Microscopy of the affected skin did not show any changes in the epidermis, but an atrophy of the corium was present, accompanied by a slight cell infiltration along the vessels. By elastin colouring it was proved that the atrophy especially attacked the elastic tissues, whereas the connective tissue was only slightly altered.

Other Organs.—The examination of the lungs and heart showed a normal condition, except a displacement caused by the kypho-scoliosis. The abdomen was normal, without any soreness or perceptible growths. The examination of the sensibility of the affected parts of the skin did not show any difference, as regards the senses of touch, pain, and temperature, from the surrounding normal skin. There was no swelling of the thyroid gland. The pulse averaged a rate of about 80, and was regular and strong.

Special Investigations.—Haemoglobin 85 (Sahli); red corpuscles 4.1 million; white corpuscles 6,300, of which 75 per cent. were eosinophiles and 1 per cent. large mononuclears; number of blood plates 398,000 per c.mm.; coagulation time six minutes; volume of cells 39 per cent.; quantity of febrin in plasma 0.30 per cent. The Wassermann reaction was negative. Mantoux's, von Pirquet's, and Moro's tuberculin reactions were strongly positive. There was no focal reaction on the affected parts of the skin. Ewald's test meal showed normal figures of acid. The urine did not contain albumin or sugar.

According to the pedigree, the anamnesis, and the objective findings, there can scarcely be any doubt that the disease of the patient must be referred to the syndrome described by Eddowes. The examination by x rays has

not corroborated the statement of the patient about previous fractures, but it is possible that the ten years have effaced the traces, and the fact of the bones being tiny and slightly calcareous is, from a diagnostic point of view, just as valuable as existing fractures. The hardness of hearing, which, as has been said above, is very slight, seems in our case to have another etiology than in the cases previously described.

The most interesting feature of the present case is the zonular cataract, which, as is generally recognized, is a hereditary affection, and which, as far as one knows, has not been described before in connexion with Eddowes's complex of symptoms. Further, there is the particular change in the skin which, in its development and appearance, corresponds to a description given for the first time by Thibierge,²² who called it *athrophodermie érythémateuse en plaques à progression exentrique*. A similar case, differing, however, in some points, was reported later by Yadassohn,²³ who proposed the name *anetodermia erythematodes*. The name that has been used in most of the recent publications is, however, *atrofia maculosa cutis*.

In addition to the rather considerable foreign literature of this disease there exists a report by L. Nielsen²⁴ in the proceedings of the Danish Dermatological Society (March, 1899). It appears from the descriptions that the disease generally begins with round, slightly elevated, bluish-red spots, varying in size from a lentil to a shilling; these spots are, subsequently, slowly changed into atrophic areas; the beginning stage of infiltration has, however, in many cases not been seen. The histological investigations correspond entirely with the description given above.

Whether this rather rare cutaneous disease, in its nature quite unknown, is found accidentally in our patient together with Eddowes's complex of symptoms, or whether there really exists a connexion between them, will, of course, be impossible to state from this single case. If we consider that changes in the sclerotics and bones are due to a defective development of the mesodermal tissue, we are, however, apt to conclude that the cutaneous atrophies form a part of the entire disease. By going over the available literature regarding Eddowes's complex of symptoms, it has not been possible, however, to find any case in which cutaneous atrophies are mentioned; the only cutaneous affection which is mentioned is an eczema in Eddowes's¹ own patient. On the other hand, the attempt to find information about blue sclerotics and fractures in the literature of *atrophia maculosa cutis* has also been unsuccessful, only one author, Gottheil,²⁵ mentioning a patient with defectively developed bones and infantilism, but he says nothing about blue sclerae or fractures.

It will consequently require to be proved by future investigations whether a connexion exists between the cutaneous symptoms and the other symptoms of the disease. In addition to the possibility that the cutaneous atrophy may be a symptom parallel with the blue sclerotics, the brittle bones and the hard hearing, it is probable that the debility of the mesodermal tissue may predispose to the development of the cutaneous atrophy, although the latter may be produced by other causes.

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LITERATURE.

- (Those marked with * are not referred to from the original.)
¹ Eddowes: BRITISH MEDICAL JOURNAL, 1900, ii, p. 222. ² Peters: Klin. Monatsbl. f. Augenheilk., 1908, p. 130. ³ Peters: Ibid., 1911, i, p. 594. ⁴ Stephenson: Ophthalmoscope, 1915, p. 278. ⁵ Harman: Ibid., 1910, p. 559. ⁶ Burrows: BRITISH MEDICAL JOURNAL, 1911, ii, p. 16. ⁷ Dighton: Ophthalmoscope, 1912, p. 188. ⁸ Cockayne: Ibid., 1914, p. 271. ⁹ Van der Hoeve and de Kleyn: Arch. f. Ophth., 1918, 95, p. 81. ¹⁰ Freytag: Klin. Monatsbl. f. Augenheilk., 1921, p. 507. ¹¹ Groenow: Graefe-Saemisch Handbuch, 1920. ¹² Bronson: Edin. Med. Journ., 1917-18, p. 240. ¹³ Voorhoeve: Lancet, 1918, ii, p. 740. ¹⁴ Crocco: Comm. d. Hosp. oph. Buenos Aires, 1920, ii, p. 38. ¹⁵ Holtzen: Nederl. T. dschr. v. Geneesk., 1918, i, p. 560. ¹⁶ Behr: Klin. Monatsbl. f. Augenheilk., 1913, ii, p. 281. ¹⁷ Hoffmann: Arch. f. Klin. Chirurgie, 1915, 107, p. 279. ¹⁸ Rolleston: Proc. Roy. Soc. of Med., April, 1911, p. 96. ¹⁹ Antonelli: Arch. d'Ophthalmologie, 1913, 33, p. 91. ²⁰ Buchanan: Trans. of the Ophthalm. Soc., 1903, 23, p. 267. ²¹ Reye: Deut. med. Woch., 1917, p. 125. ²² Thibierge: Ann. de Dermat. et Syph., 1891, p. 1001. ²³ Yadassohn: Verh. d. deutsche dermat. Ges., 1892, p. 347. ²⁴ Nielsen: Dansk dermat. Selskabs Forh., 1-3, 1899. ²⁵ Gottheil: Journ. of Cutaneous Diseases, 1916, p. 133.

THE nineteenth Dutch Congress of Natural Science and Medicine will meet at Maastricht in Easter, 1923, under the presidency of Professor Spronck of Utrecht.

THE great parade ground at Berlin has been transformed into a field for light and sun baths for children with surgical tuberculosis.