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ON THE PIGMENTATION OF THE CONJUNCTIVA IN NORMAL INDIVIDUALS AND IN CASES OF KERATOMALACIA IN ADULTS

BY

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IN his interesting studies concerning xerophthalmia and keratomalacia in China, A. Pillat^{12, 13} has called attention to a particular conjunctival pigmentation. He finds this to be one of the most striking symptoms of xerosis, being found with a frequency of about 70—80 per cent. of the cases.

In what concerns the origin of that pigmentation, some authors (Kirkpatrick, Wright) think it to be due to a disturbance in the functions of the liver, and see in it a connection with the icteric state of the conjunctiva, signs of cirrhosis, etc., frequently found in such patients.

Opposed to that opinion, Mori and Pillat think that such pigment is melanin accumulated through a mechanism still unknown, as a result of the processes of degeneration going on in a xerophthalmic conjunctiva. In his observations Pillat could not find any notable increase of bilirubinaemia or any liver insufficiency, as verified by the levulose test.

We have been interested in this fact because in our limited observations, which we could follow in the Ophthalmological Clinic of Jassy, we had never noticed such particular pigmentation. Pillat mentions not having found this symptom recorded, excepting in such Oriental races as Indians and Chinese.

From the literature that we have analysed, only the observations made in Poland by Narog¹¹ were found to mention it. In one

case of severe keratomalacia, he describes, in connection with an intense conjunctival pigmentation, the presence of a considerable amount of squamous pigmented detritus, covering the xerotic lesions and the conjunctival sacs.

Quite recently, however, we had the opportunity of finding a case of conjunctival xerosis in which the pigmentation was noticeable. The clinical history is briefly as follows:—

P. V., aged 68 years, a farrier, attended the clinic for a marked diminution of vision and a senile ectropion. Diplobacillary secretion adhered especially to the internal corners of the eyes. The inferior right lid was everted, the left lid showed also some tendency to ectropion. The everted conjunctiva was thickened and had a papillary, vegetant appearance. On the external part near the corneal limbus was found a small xerotic lesion, covered with the characteristic foamy deposit. Very near to it was a larger white dim nodosity. Around both, one saw a very heavy, blackish-brown pigmentation which appeared in marked contrast with the white of the neighbouring lesion. The ocular conjunctiva corresponding to the palpebral aperture, was also yellowish-brown. On slit-lamp examination, the pigment appeared as a diffuse yellowish uniform infiltration, on which were spread irregular darker spots. The inferior part of the globe was also slightly pigmented. The corneal limbus was pigmented especially in the superior and inferior portions, less in the internal and external ones. The pigmentation appeared as a blackish strip composed of little spots like a mosaic-work, separated by lines which were more clear. It had a very clean-cut edge towards the limbus and faded gradually on the external side. The plica semilunaris was intensely pigmented on both sides. The everted tarsal conjunctiva showed a characteristic pigmentation appearing striped like the coat of a zebra. The conjunctival sacs were free from pigment. We did not find the cholesterol crystals described by Narog. Both lenses showed early sclerosis, so we could not examine the fundi. Vision of the right eye was $1/6$, and of the left $1/8$. The patient complained of a still more marked diminution of vision in dim light. Examination with the Birch-Hirschfeld adaptometer revealed a difference of 15 points between the patient and a normal eye. He felt weak, and had indefinite pains in the limbs. There is nothing else to mention except a slight degree of chronic bronchitis. Arterial tension 175-/70. Bordet-Wassermann reaction, negative. Blood Ca. 0.120 mgr. per litre. Cholesterol, 1.66 per litre. Urea, 0.45 per litre. Blood bilirubin (H. v. den Berg) $1/2$ unit. Urine normal. The patient was a gipsy. The whole integument was intensely pigmented. Many white cicatricial spots were distributed irregularly over the whole body, seemingly due to pediculosis. It was very difficult to get

clear information about his diet. He did not have milk as a rule, or eggs and butter. His usual diet consisted of corn, potatoes, soups and less frequently, green vegetables.

The fact which we have found interesting is that our patient belongs to a race which is naturally pigmented, the gipsies. This explains, we think, why his xerosis showed pigmentary changes.

The variations of the physiological normal pigmentation of the conjunctiva among different races is well known. Richly distributed in the negroes (Giacomini), Malay, Javanese (Steiner¹⁵), Algerians (Brauit⁵), Japanese (Kozuo), pigment is seen also in a reduced amount in the white races. Redslob found it in one-third of the examined cases, scantily distributed in the basal layer of the ocular conjunctiva. With the slit-lamp, pigment is found in a greater proportion of cases.

Since our attention was called to that fact, we have sought systematically for the existence of conjunctival pigmentation, and have found that gipsies show usually a brown-blackish tinge of the conjunctiva, corresponding to the palpebral aperture. This is the habitual distribution of pigment and corresponds to the part exposed to light. The causal relationship between these two phenomena, is shown also by the fact, that pigment may develop in other parts of the conjunctiva, if they become exposed (ectropion).

But, in richly coloured races, one finds sometimes intensely pigmented irregular spots, on the tarsal conjunctiva and even in the corneal epithelium (van Duyse¹⁵, Asher²). The abnormal distribution of pigment could be observed in diseases other than xerophthalmia. Steiner¹⁵ has recorded it in the trachoma of coloured people: "During the acute stage of the disease, one finds frequently on the superior part of the tarsal conjunctiva, more rarely on the inferior part, some spots, more or less round or of irregular form and size from that of a pin's head to 1 square centimetre or more. Nearly always they are very dark and well delimited, one might say ink spots." "Exceptionally they can be less dense and the mucosa appears powdered with black." During the cicatricial stage, they seem like an agglomeration of points, lines, circles, or a real net, because the pigment, by reason of treatment or otherwise, has been scraped away from the tops of the granulations and left only in the separating sulci.

A pathological pigmentation of the conjunctiva has been observed in the white race in Addison's disease. Apparently in that case too, there is a pathological increase of the same melanotic pigment. (Lubarsch⁹, Alima Chanum¹). Löwenstein⁸ has recently obtained experimentally an abnormal pigmentation of the conjunctiva after subconjunctival injections of adrenalin, and he has observed a patient who has developed such pigmentation, after a long treatment with adrenalin drops. Bittdorf³ believes that

the pigmentation in Addison's disease is due to an increase of oxidation of adrenalin in the skin.

All these facts incline us to accept Pillat's opinion that the xerophthalmic pigmentation is due to melanin. What is the cause of the increase in quantity?

According to Bloch (see Masson¹⁰, Laignel Lavastine⁷) the grains of melanin result from the reaction of an oxidase, produced in special cells, with a particular substance arising from protein, and related to tyrosin, and to adrenalin. Experimentally he can show this oxidase *in situ*, using as chromogenic substance the dioxyphenylamin.

It may be interesting to recall that recently some authors have seen a cutaneous pigmentation appearing after administration of irradiated ergosterol, in children. (Iancu⁶).

In the conjunctiva as in the skin, the production of pigment must be the same. Its presence in increased amount in the coloured races, could be conceived as due to an increased production of ferment, or of the chromogenic substances or of both, resulting from an ancestral adaptation to special conditions of life, of exposure, etc. Similar ideas apply to the pathological conditions (Bittdorf⁴). In what concerns the diseases of the conjunctiva, we should think rather of the excessive production of chromogenic degenerative products due to the local processes. We do not know if the patients of Narog had also a natural tendency to pigmentation (gipsy etc.) or not.

There is no doubt that sometimes a biliary origin may be attributed to the conjunctival coloration, but that could not be made a rule. Hepatic insufficiency was not found in Pillat's cases, and the blood bilirubin in our case was quite low. We could not eliminate, however, an indirect participation of the liver, as a factor in the storing and the utilization of vitamin A, and in the production of xerophthalmia as a whole. Some observations justify such a hypothesis.

In conclusion, we think that the abnormal pigmentation seen in xerophthalmia in the coloured people should be considered as the manifestation of a special reaction, the intensity of which varies according to the particular capacity of the trophopigmentary tissue of different races, being most reduced in the white race.

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A CASE OF MICROPHTHALMOS

BY

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PORT SAID

ON September 28, 1921, an Italian lady brought her daughter, aged 23 days, for my opinion about her eyes. A well-built and developed baby. The eyelids of both eyes presented nothing abnormal. They covered eyeballs of very small size, like large peas, about 9 mm. in diameter. Each eye had a small transparent cornea; they both were of the same size: not more than 4 mm. in the horizontal meridian and 2 mm. in the vertical. Through the cornea some bluish-grey material could be seen, but no anterior chamber, no pupil nor design of iris. The movements of both eyeballs, and the eyelids as well, as their sensibility did not show anything particular. The parents of the baby were young healthy people, without any physical defects. I have observed the child for about nine years. She developed into a pretty looking girl of a gay and lively disposition and not lower in intelligence than the average child of her age. Her eyes did not grow bigger, but the corneae became rather smaller and less transparent than during infancy. The child does not see the brightest light.

A curious family history was told me by the mother of the child. Some 20 months previously to the birth of the child, being in the second month of her first pregnancy, she had occasion to watch the operation on her own mother for acute glaucoma. The operation ended in a catastrophe: copious escape of vitreous and