PATCHES OF DEEP PIGMENTATION OF THE ORAL MUCOUS MEMBRANE NOT CONNECTED WITH ADDISON'S DISEASE

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PATCHES of blackish pigmentation in the mucous membrane of the cheeks, lips, and mouth proper, are occasionally met with which cannot be attributed to disease of the suprarenal capsules. They are, it has been supposed, sometimes analogous to simple pigment-naevi of the skin. Some of them may be, as Dr. G. Pernet suggests, allied to the black patches which are not uncommon on various parts of the mucous membrane of the mouth in dogs and other animals. In some cases it has been suggested that they are of racial (ethnic) or atavistic origin. In other cases they have been considered to represent a disturbance in the distribution of pigment in the mucous membrane analogous to that which occurs in the skin in freckling (ephelides, lentigines), and they are occasionally associated with circum-oral freckle-like spots on the face. In a few cases it has been claimed that they were causally connected with pernicious anaemia. In some cases they may have been set up by local haemorrhages and inflammatory complications connected with foul teeth and pyorrhoea alveolaris.

A man (M. G.) aged 57 years, a Hungarian Hebrew tailor, was admitted to hospital on March 11, 1916, under my care, suffering from advanced and acute pulmonary tuberculosis and tuberculous spinal caries. He had remarkable, deep (blackish) pigmentation of the buccal mucous membrane and pigmentation, to a less extent, of the mucous membrane of the palate and lips. There was likewise considerable pigmentation of the skin of the face and he was of dark complexion. He did not show the pigmentation typical of Addison's disease elsewhere on his body. He did not know when the pigmentation in his mouth and buccal mucous membrane first appeared—in fact, he seemed to be unaware of its existence until we asked him about it. In the hospital there was considerable pyrexia and progressive loss of weight. The brachial systolic blood-pressure was low, varying from 95 to 105 mm. Hg. A blood-count (March 11, 1916) gave 6,800,000 red cells and 8,125 white cells to the cubic millimetre of blood. The Wassermann reaction was negative. The urine contained a trace of albumin. Examination of the gastric contents after a test breakfast proved the presence of a normal amount of free hydrochloric acid.

The patient died on March 29, 1916, and the *necropsy* showed extensive miliary tuberculosis of both lungs with breaking-down at the apices, tuberculous caries (with abscess-formation) of the mid-dorsal vertebral column. Miliary tubercles were in the liver and spleen. There was likewise a small tuberculous focus in one kidney. No evidence of disease was detected by macroscopic or microscopic examination in the pancreas, pituitary gland, pineal body, or either

suprarenal gland. The solar plexus was not specially examined. In regard to the pathological examination of this case I am much indebted to Dr. H. Schmit.

What the cause was of the pigmentation in the mouth in this case I am at a loss to know. The case was not one of Addison's disease, nor was it one of haemochromatosis. There may perhaps have been a racial or atavistic element in it (see farther on); the patient came from Hungary, and was of Hebrew family. On the whole, I am inclined to regard the pigmentation as analogous to that discussed by Sir Jonathan Hutchinson and Radcliffe Crocker, to which I shall allude farther on.

Certain French observers maintain that there may be a 'physiological' pigmentation of the mucous membranes, occasionally (in Lascars and some Roumanian Jews, for instance) of racial (ethnic) origin (1). Cases of pigmentation of the buccal or oral or both buccal and oral mucous membrane of unknown causation have been demonstrated by H. Dufour and Alardo (2), and by O. Crouzon (3) and others. Milian (4), in Paris, attributed to syphilis the pigmentation of the buccal mucous membrane and lips which he had observed and demonstrated in a syphilitic Roumanian woman, but I am inclined to question whether the pigmentation was really due to the syphilis (see remarks farther on, at the end of this paper).

H. Radcliffe Crocker (5) refers in his text-book to the association of pigmentation of the oral mucous membrane with freckle-like spots on the skin of the lips. In a woman, aged 43 years, under the care of W. Knowsley Sibley (6) for tachycardia, there were spots of deep pigmentation on the skin about the mouth, which had first commenced to appear four years previously. There were similar spots on the mucous membrane of the cheeks and hard palate, but not on the gums. The patient was of dark complexion, much freckled about the face, and in early life she was very liable to bronze on exposure to the sun. Sir Jonathan Hutchinson, when he demonstrated this case (Sibley's patient), said that the pigmentation was of a rare kind, liable to affect persons of dark complexion. He had seen a clergyman, aged 62 years, with a similar pigmentation. Sibley's patient, 22 years later, when she was aged 65, was shown by H. C. Samuel at the Dermatological Section of the Royal Society of Medicine (meeting of January 16, 1919). The pigmentation of the oral mucous membrane was still present, and so was the chronic tachycardia. The heart was slightly enlarged and there was a mitral systolic murmur to be heard.

Sir Jonathan Hutchinson (7) also recorded the case of two girls, who were patients of Dr. J. R. T. Conner. They were twins, brunettes, and quite healthy, and in both of them at the age of 9 years there developed freckling or freckle-like pigment-spots about the mouth—on the lower lip, including the red part (mucous membrane), and (slight pigmentation) on the upper lip. The distribution of the pigmentation in both girls was exactly the same, and it remained unaltered. Dr. Conner has kindly (1919) given me further information regarding these twins. He himself demonstrated them on August 8, 1896, at the Third International Congress of Dermatology, London, 1896 (8). They were first brought to him in

that year, at the age of 12 years, and according to the mother the pigmentation had appeared only three years previously (there seems in this respect to have been an error in Hutchinson's account). From the time when it was first noticed the pigmentation did not vary, excepting that the spots were darker in summer. One of the twins died at the age of 20 years, from intussusception, at the Metropolitan Hospital (London), but the other (B. H.) is still living and is in good health, now (1919) aged 35 years. By the kindness of Dr. Conner I have just seen her. She appears in good health, and the pigmentation is at present not very striking, but perhaps that may be owing to the time of year (commencement of February 1919). The mother is still living. The father, now dead, was a professional rat-catcher. They had nine children, six girls and three boys. None of the other children showed the pigmentation, and there was no history in the family of pigmentation, nor of any admixture of foreign blood.

In this connexion Crocker also refers to a case described by Balzer, Gaucher, and Milian (9), of a woman aged 29 years, in whom pigmentation was present not only round the mouth, but on the eyelids, back of the hands, and forearms; it was first noticed during convalescence from an attack of typhoid fever.

Sir H. D. Rolleston, at the Clinical Section of the Royal Society of Medicine (10), showed a man, aged 25 years, with marked freckle-like pigmentation of the lower half of the face, especially round the mouth. The lower lip presented 'inky' pigmentation towards the angles of the mouth. There were similar patches of pigmentation on the buccal mucous membrane. The patient had not been taking arsenic, but he was thought to be suffering from pernicious anaemia. A subsequent post-mortem examination confirmed the diagnosis of pernicious anaemia and showed that the suprarenal glands were not diseased (11).

At the Dermatological Section of the Royal Society of Medicine, in 1910, Willmott Evans (12) showed a little girl, aged 11 years, with freckle-like spots all round her mouth, and black spots of pigmentation on the buccal mucous membrane, very similar to what was seen in Rolleston's above-mentioned case. The pigmentation, according to the mother, began to appear soon after birth and gradually increased. Evans suggested that the case was an early or mild form of xeroderma pigmentosa, but that diagnosis was not accepted by those who took part in the discussion.

Whether there is any real causal connexion between pernicious anaemia and pigmentation of the buccal and oral mucous membrane is still, I think, unsettled, in spite of T. G. Moorhead's writing on the subject (13). Moorhead's own case was that of a man, aged 28 years, with typical pernicious anaemia. In addition to the uniform lemon-yellow colour of the body there were present a few scattered freckle-like patches of deep brown pigmentation on the face below the eyes and around the angles of the mouth. 'The most striking feature, however, was the pigmentation of the lips and mucous membrane of the inner aspects of the cheeks.' The lower lip on its inner surface was of a bluish, 'inky' colour, and this discoloration was prolonged over the buccal mucous membrane on both

sides, in the form of scattered 'inky' patches, principally on a level with the line of junction of the teeth. The teeth were in an exceedingly foul condition.

Moorhead refers to four other cases of pernicious anaemia showing pigmentation of the buccal mucosa, including Rolleston's above-mentioned case. The earliest one was that described by Hale-White in 1907 (14). His patient was a man aged 22 years, and the diagnosis of pernicious anaemia was confirmed by a subsequent post-mortem examination. Besides the pigmentation of the buccal mucosa there was abnormal pigmentation of the face, trunk, and limbs, partly in the form of small, dark-brown, freckle-like spots, partly in more diffuse brown areas. Another case was recorded by Herbert French in the *Guy's Hospital Reports* for 1909 (15). His patient was a woman aged 33 years, who, in addition to the typical symptoms of pernicious anaemia, showed widespread pigmentation of the skin in patches and specks, pigmentation of the mucous membrane on the inside of the cheeks, and purulent tooth sockets. The diagnosis of pernicious anaemia was also in that case confirmed by a subsequent post-mortem examination. Another case is mentioned by A. Lazarus in Nothnagel's *Encyclopaedia of Practical Medicine* (16). The patient, when seen by him, was suffering from pernicious anaemia, and the tip and back of the tongue and the buccal mucous membrane were the sites of small spots and patches of circumscribed reddish-brown mahogany-like discoloration, which were hyperaesthetic; and Lazarus thought they were probably the result of haemorrhages.

It seems that in some such cases the relation of the pernicious anaemia to the intra-oral pigmentation may have been an *indirectly* causal one, and that the pigmentation may have been set up by local haemorrhages and local inflammatory conditions associated with foul teeth and pyorrhoea alveolaris. In this connexion a case shown by Sir H. D. Rolleston at the Medical Society of London in 1902 (17) may be referred to. The patient was a man aged 40 years, who complained of abdominal pain and constipation. There was a peculiar black pigmentation of the mucous membrane of the lower lip. When the lower lip was turned down, vertical lines of black pigment were seen arranged in the same direction as, but superficial to, the blood-vessels. The pigmentation was strictly limited to that portion of the lower lip opposed to the lower incisor teeth, which were loose, very foul, and coated with much tartar. The patient was a French-polisher by trade, but there was no definite evidence of saturnism, though there was a doubtful 'blue line' (lead line) on the gums. There was no satisfactory evidence in favour of Addison's disease or haemochromatosis.

In conclusion, I venture to make the following suggestions: (1) There is a certain group of cases in which pigmentation, not connected with Addison's disease, occurs in the mucous membrane of the mouth. The pigmentation is in the form of blackish spots and patches in the mucous membrane of the lips or cheeks and sometimes of other parts of the mouth. It is associated with pigmentation of the skin of the face, especially about the mouth, and possibly (in one or two cases) of other parts of the body. (2) It occurs in persons of dark complexion, perhaps especially in Roumanian Jews and in certain races such as Lascars. (3) It is of

unknown causation, and seems in some cases to be of a 'physiological' or perhaps of atavistic origin. It may be analogous to the black patches often present in the oral mucous membrane of dogs and other animals. It appears to be allied to simple pigment-naevi of the skin on the one hand and to freckles (ephelides, lentigines) on the other. (4) Jonathan Hutchinson was probably the first to call attention to this class of pigmentation, which perhaps should include various cases published by French authors under the headings, 'physiological pigmentation' and 'racial (ethnic) pigmentation'. (5) It is possible that Milian's case (see p. 405) really belonged to this group, though the patient undoubtedly had syphilis. (6) It is possible that a similar kind of pigmentation may be in some indirect way causally connected with pernicious anaemia.

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