

EPITHELIAL CHANGES IN ANAEMIC EAST AFRICANS

BY

ALLAN JACOBS, M.D.

*Institute of Pathology, Welsh National School of Medicine, Cardiff*

Many patients suffering from severe iron-deficiency anaemia have symptoms and clinical signs related to the mouth, the pharynx, and the finger-nails. Soreness of the tongue with signs of atrophy are commonly found, and difficulty in swallowing localized to the post-cricoid region is felt by 10–20% of patients with iron deficiency. Koilonychia, when it occurs, appears to be associated with atrophy of the buccal mucosa (Jacobs, 1961). It is often assumed that the changes giving rise to these symptoms are due to the effect of iron deficiency on the squamous epithelium, though similar changes may be caused by other deficiencies.

These stigmata of chronic iron deficiency, although common in Great Britain (Witts, 1956) and Scandinavia (Lundholm, 1939), are said to be rare in East Africa despite a high incidence of severe chronic iron-deficiency anaemia (Foy and Kondi, 1958; Trowell, 1960). The present inquiry was undertaken to investigate this difference in symptomatology and to attempt a correlation with the histology of the buccal epithelium.

Symptomatology

The case records of all patients admitted to the King George VI Hospital, Nairobi, and the Coast Province General Hospital, Mombasa, during 1959 and 1960 with iron-deficiency anaemia, uncomplicated by any other haematological disorder or major disease, were examined. There were 114 such cases. In 57 of these cases there was evidence of hookworm infestation. Thirty-eight additional cases were personally examined clinically and haematologically. The degree of anaemia in all these patients is shown in Table I. There was no difference between the two groups in this respect. A quarter of the patients had a haemoglobin concentration of 3 g./100 ml. or less, a level which is not commonly found in Britain. The frequency of the major symptoms related to iron deficiency are shown in Table II. Conversations with the doctors who had cared for these patients and with others confirmed the impression that buccopharyngeal symptoms and koilonychia are uncommon in Kenya Africans and that the Paterson-Kelly syndrome is a rarity.

TABLE I.—Degree of Anaemia in 152 African Patients

Hb (g./100 ml.)	0–3	3.1–6	6.1–8.9
No. of cases	39	75	38

TABLE II.—Frequency of Symptoms in 152 African Patients with Iron-deficiency Anaemia

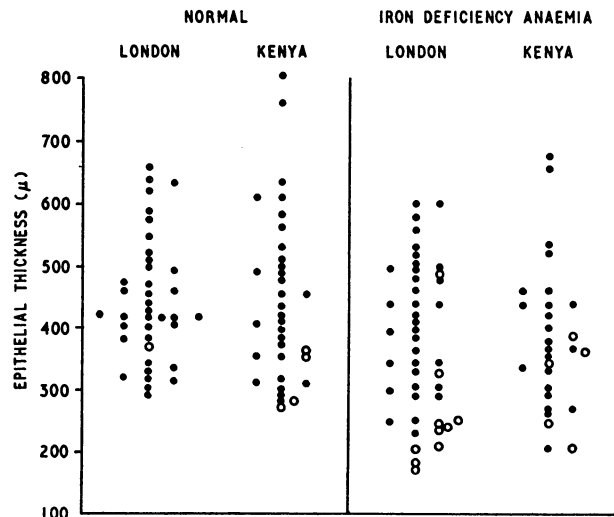
	No. of Cases
Weakness and tiredness	43
Dizziness and fainting	45
Breathlessness	61
Headache	31
Diarrhoea	8
Glossitis and/or stomatitis	1
Koilonychia	0
Dysphagia	1

Epithelial Histology

*Materials and Methods.*—Biopsy specimens of the buccal mucosa were taken from the 38 cases of iron-deficiency anaemia mentioned above by the method

previously described (Jacobs, 1960). The haematological diagnosis was confirmed by estimation of haemoglobin concentration, packed cell volume, and examination of a blood film in each case. Specimens were also taken from 56 healthy Africans with a haemoglobin concentration of 12 g./100 ml. or more. The biopsy fragments were fixed in acetic-acid-alcohol-formalin and, after processing, sections were stained in the standard manner with haematoxylin and eosin, periodic acid-Schiff, and periodic acid-Schiff after treatment with diastase. Maximum epithelial thickness was measured in those specimens where adequate vertical sections were obtained.

*Normal Subjects.*—There is little essential difference between the mucosal histology in normal Africans and the English subjects studied previously (Jacobs, 1961). A comparison of epithelial thickness and glycogen content in these groups is shown in the Chart. Four specimens from the African group showed glycogen depletion and may have come from cases of latent iron or other deficiency. Two of these were the thinnest



Maximum epithelial thickness in Africans compared with the measurements from London subjects (Jacobs, 1961). ● Normal glycogen content. ○ Glycogen depleted or absent.

epithelia seen in normal subjects. One other specimen showed the presence of an abnormal amount of diastase-resistant polysaccharide, previously seen only in anaemic epithelia (Jacobs, 1961). The African mucosae contain more melanin, both in the epithelium and beneath it, than the English, but this is not as striking as might be expected, and there is considerable variation from subject to subject and also between areas in the same biopsy.

*Iron-deficient Subjects.*—Some English patients with iron-deficiency anaemia have an abnormally thin epithelium, and this is usually associated with glycogen depletion (see Chart). It is also associated with the presence of koilonychia, which was found in five of the English patients, all of whom had an epithelial thickness of 250  $\mu$  or less (Jacobs, 1961). Although some of

the African group showed mucosal atrophy it was not so strikingly attended by glycogen depletion as in the English patients, and in no case was it associated with koilonychia. In neither group was it related to the degree of anaemia. Two of the African cases showed the abnormal polysaccharide previously described in the English group, where six samples were found. No evidence of mucosal depigmentation was found. A few examples of infiltration by inflammatory mononuclear cells were found in anaemic and non-anaemic subjects of both racial groups.

### Discussion

The syndrome of anaemia, glossitis, and dysphagia, often in association with koilonychia, was first described by Paterson (1919) and Kelly (1919). Later authors have commented on the frequency of these symptoms in chronic iron-deficiency anaemia. Wintrobe (1961) states that a sore tongue or sore mouth is found in about 28% of cases and nail changes in one-third. Lundholm (1939) found glossitis in 44% of his patients with hypochromic anaemia and koilonychia in 41%. Dysphagia probably occurs in 15–20% of patients with chronic iron-deficiency anaemia (Lundholm, 1939; Whitby and Britton, 1957); though not all of these have demonstrable lesions in the pharynx or oesophagus. It is often assumed that these symptoms are due to the effect of iron deficiency on the epithelium, but, with the exception of koilonychia, the symptoms are common to a number of conditions, including the megaloblastic anaemias (Brown, 1946; Whitby and Britton, 1957). An examination of the histology of the buccal epithelium in iron-deficiency anaemia shows a combination of atrophy and glycogen depletion in some cases, but the appearance is in no way different from that found in cases of vitamin-B<sub>12</sub> deficiency, where the changes are more common (Jacobs, 1961). The histological lesions do not appear to be related to the presence of symptoms (Jacobs, 1960).

The present findings regarding the symptoms of iron deficiency in East Africans are in agreement with the views of Foy and Kondi (1958) and Trowell (1960). The rarity of glossitis, dysphagia, and koilonychia is a striking contrast to their frequency in Great Britain, particularly in view of the high incidence and greater severity of iron deficiency. It seems unlikely that these symptoms, when they occur in Europeans, can be the direct result of iron deficiency alone. They may result from an associated factor, either constitutional or environmental, or from iron deficiency acting together with such a factor.

Although six epithelial specimens taken from anaemic African patients were thinner than normal, only two were characterized by the glycogen depletion usually found in the atrophic European epithelia, and in none of these cases was koilonychia found. Atrophic changes were not related to the degree of anaemia and did not give rise to symptoms. They may have been related to other deficiencies than iron.

It has been suggested that the Paterson-Kelly syndrome is not solely a result of iron deficiency (Jacobs, 1962), and its rarity in iron-deficient Africans lends support to this. In addition to the uneven geographical distribution of this syndrome the finding, in some cases, of other affected members of the family

(Simpson, 1939; Kruisinga and Huizinga, 1959; Jacobs and Kilpatrick, unpublished observations) suggests a constitutional factor in its aetiology. Wynder and Fryer (1958) found normal serum iron levels in 68% of cases of Paterson-Kelly syndrome in women. The recurrence of dysphagia in such cases does not appear to be related to the discontinuance of iron therapy (Kirchenberger and Flett, 1946; Jones, 1961), and indeed the syndrome can occur in pernicious anaemia with no iron deficiency (Jacobs, 1962).

Valberg *et al.* (1961) have shown that rats rendered anaemic by dietary restriction of iron do not develop any macroscopic or microscopical changes in the nails, mouth, tongue, or oesophagus.

The role of iron deficiency in determining the symptoms and lesions of the mouth, throat, and nails is uncertain. The findings in Kenya Africans indicate that they do not always result even from severe iron deficiency and that other factors must be involved.

### Summary

Glossitis, stomatitis, dysphagia, and koilonychia are common stigmata of iron deficiency in patients of North European origin. A review of a series of 152 Kenya Africans with iron deficiency shows that they rarely have these symptoms and signs. A comparison of oral epithelial histology in 39 normal Londoners and 34 normal East Africans shows no essential difference between the two groups, but whereas epithelial atrophy and glycogen depletions were found in 11 out of 44 anaemic Londoners these signs were not so striking in a group of 28 anaemic East Africans.

The relative scarcity of buccopharyngeal symptoms and the lesser extent of epithelial atrophy in a population where chronic iron deficiency is common indicate that they are not an inevitable consequence of it and that lack of iron by itself does not cause these lesions.

It is suggested that iron deficiency plays a secondary or even an incidental part in the aetiology of the Paterson-Kelly syndrome and that a constitutional factor relatively common in this country may be important.

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