that its "true effectiveness as a preventive and therapeutic agent remains unknown because of the strict secrecy surrounding its operations."

Thus although this service is to be valued, it will probably not be sufficient. Other measures, including real career reforms, will be necessary.

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Hairy leucoplakia

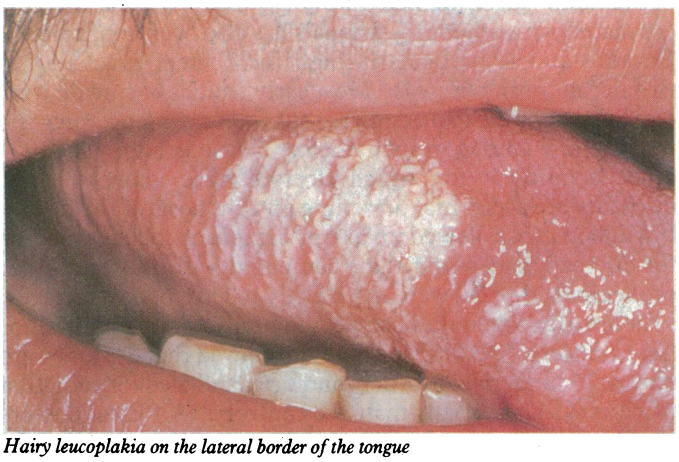
Three quarters of patients develop AIDS in two to three years

Hairy leucoplakia is a clinical entity that is particularly seen on the lateral border of the tongue in those who are at risk of developing AIDS.[1] Prompt recognition of the condition is important as it is one of the early signs of infection with HIV and some three quarters of those affected develop AIDS within two to three years. Hairy leucoplakia was first observed among male homosexuals in the United States,[1] but it also affects patients belonging to other risk groups, including intravenous drug abusers,[2,3] recipients of blood or blood products,[4] patients with haemophilia, and female partners of men infected with HIV.[4,5]

Clinically hairy leucoplakia appears as an asymptomatic, greyish white to white, most often corrugated, or, rarely, hairy, lesion on the tongue either unilaterally or in most instances bilaterally (figure).[6] Although this is the classic presentation, minor degrees of hairy leucoplakia may be present as barely discernible white areas on the posterolateral lingual border; these areas may escape attention without a thorough clinical examination. In contrast, hairy leucoplakia may present as large, atypical plaque like lesions or spread downwards on to the ventral surface of the tongue, where it usually has a flat appearance. It has also been described on the floor of the mouth, the buccal mucosa, and the palate,[6,7] although it has not been shown in either vaginal or anal mucosa.[8]

Several intraoral lesions clinically resemble hairy leucoplakia. The differential diagnosis includes chronic hyperplastic candidosis, pseudomembranous candidosis (which is common among those at risk of AIDS), lichen planus, idiopathic leucoplakia, tobacco associated leucoplakia, geographic tongue, "galvanic" lesions, and occlusal trauma. Histological examination of hairy leucoplakia shows a thick epithelium with hyperparakeratosis, hair-like projections of keratin, areas of koilocytes (ballooned cells with clear cytoplasm), and pycnotic nuclei surrounded by an empty halo. Abundant hyphal elements of yeasts may be seen in the superficial epithelium.[3,6] The subepithelial connective tissue is free of or contains a few inflammatory cells.[3,9]

A viral aetiology has been proposed for hairy leucoplakia,[1,10,11] and some researchers have shown both Epstein-Barr virus and human papillomavirus in the lesions,[1,12] whereas others have found only Epstein-Barr virus.[10,13] HIV has not been recovered from tissues taken from hairy leucoplakia. The candidal hyphae within the epithelium and the isolation of candida from the surface may imply that yeasts are important in the pathogenesis of hairy leucoplakia, but antifungal treatment eradicates the fungal elements without causing the lesion to regress.[6,9]



Hairy leucoplakia on the lateral border of the tongue

Antiviral agents have been used successfully in treating hairy leucoplakia. Oral[14] or topical[3] acyclovir and trisodium phosphonoformate (Foscarnet)[15] have caused the lesions to regress in many patients, lending further credence to the viral aetiology of hairy leucoplakia. Topical tretinoin has led to resolution of the lesions in one case,[16] and ganciclovir in another.[17] None the less, the best treatment for hairy leucoplakia remains unknown as there are no controlled trials of any antiviral agent and relapses and remissions occur spontaneously in many patients who apparently recover.

The sinister importance of hairy leucoplakia was shown in a cohort of 123 patients with the disease: half developed AIDS within 16 months after diagnosis and four fifths within 30 months.[18] Thus the appearance of hairy leucoplakia has been

described as "a constant reminder of the sword of Damocles that is suspended above the unfortunate victim's head."[19]

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Diagnosis of adrenal insufficiency

The short tetracosactrin test can almost always replace the insulin stress test

The clinical diagnosis of adrenal failure is not difficult in patients presenting acutely with features of both glucocorticoid and mineralocorticoid deficiency, such as nausea, vomiting, diarrhoea, prostration, hypotension, and pigmentation. Such patients are usually young, and treatment with saline, hydrocortisone, and fludrocortisone is urgent and lifesaving. The results of emergency laboratory tests showing typical hyponatraemia, hyperkalaemia, moderate uraemia, and often hypoglycaemia strongly support the diagnosis, which is subsequently confirmed by hypocortisolaemia and the short tetracosactrin (Synacthen) test.[1]

The short tetracosactrin test is performed once the patient has been stabilised; treatment with hydrocortisone should be stopped for 24 hours, though not that with fludrocortisone. Typically the basal cortisol values are <100 nmol/l, do not rise after giving tetracosactrin, and, together with a plasma concentration of adrenocorticotrophic hormone of >200 ng/l (which should always be measured on the basal sample), this pattern establishes the diagnosis.[2,3] Most cases of acute adrenal crisis are due to autoimmune or tuberculous adrenalitis, but too rapid withdrawal of glucocorticoids or overtreatment with adrenal blocking drugs are other causes. Rifampicin and other drugs that induce cytochrome *P*-450 enzymes accelerate the metabolism of cortisol[4] and can precipitate an adrenal crisis early in the course of antituberculous chemotherapy.[5,6]

Glucocorticoid insufficiency with normal production of aldosterone is associated with a more insidious clinical onset. The symptoms are fluctuating and non-specific, such as lassitude, weakness, anorexia, abdominal pain, and weight loss. These are common in outpatient practice and often raise the question of adrenal insufficiency, especially in patients coming from communities with a high prevalence of tuberculosis. In most cases, however, adrenal insufficiency is excluded by finding a basal plasma cortisol concentration of >200 nmol/l, rising to >500 nmol/l after giving tetracosactrin. These values are based on cortisol measurement by the old fluorimetric method, but most laboratories now measure cortisol by direct radioimmunoassay, which gives values 20-30% lower.[7] Consequently, a peak cortisol value of >400 nmol/l is probably acceptable as normal if found with radioimmunoassay, although there is no published formal evaluation of this.

An absent cortisol response to tetracosactrin with a low basal concentration of adrenocorticotrophic hormone (<10 ng/l) points to secondary adrenal failure, which may be confirmed by giving 1 mg tetracosactrin acetate (Synacthen Depot) every day for five days. Because adrenocorticotrophic hormone induces cortisol synthesising enzymes the plasma cortisol concentration rises progressively to normal by the end of the test. Nevertheless, difficulty arises when the cortisol response to tetracosactrin is equivocal. Should the clinician invariably proceed to further investigations of hypothalamic-pituitary function? Much will depend on the clinical context, and here additional clinical clues such as signs of other pituitary hormone deficiency or of a pituitary tumour may help. If the clinical index of suspicion is low it is reasonable to wait and repeat the test six to eight weeks later. If the result is then normal the doctor may reassure the patient with confidence; if it is still abnormal an insulin stress test should be considered.

Patients in whom it is essential to assess hypothalamic-pituitary function fall into three broad groups: firstly, those with pituitary tumours and other hypothalamic-pituitary diseases in whom acute adrenal failure may result from severe stress; secondly, those who have had a hypophysectomy or pituitary irradiation, when the test will indicate the continuing need for glucocorticoid replacement treatment; and thirdly, those who are being weaned off long term glucocorticoid treatment for chronic systemic diseases.

The traditional assessment with the insulin hypoglycaemia stress test has the advantage of assessing the integrity of the hypothalamus and the pituitary simultaneously.[8] Unfortunately, it is unpleasant, expensive, and not without risk. The test is contraindicated in those aged 70 and over and at any age in patients with angina, heart failure, cerebrovascular disease,