

Oral medicine for the general practitioner: red, white and coloured lesions

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This series of five papers summarises some of the most important oral medicine problems likely to be encountered by practitioners.

Some are common, others rare. The practitioner cannot be expected to diagnose all, but has been trained to recognise oral health and disease, and should be competent to recognise normal variants, and common orofacial disorders. In any case of doubt, the practitioner is advised to seek a second opinion from a colleague. The series is not intended to be comprehensive in coverage either of the conditions encountered, or all aspects of diagnosis or treatment: further details are available in standard texts, in the further reading section, or from the internet. The present article discusses aspects of red, white and coloured lesions.

Red lesions

Red oral lesions are commonplace and usually associated with inflammation in, for example, mucosal infections. However, red lesions can also be sinister by signifying severe dysplasia in erythroplasia, or malignant neoplasms (Table 1).

Inflammatory lesions

Most red lesions are inflammatory, usually

- Viral infections; (e.g. herpes simplex stomatitis)
- Fungal infections

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Table 1: Causes of red lesions

Localised
Inflammatory
Candidosis
Other mycoses
Lichen planus
Reiter's disease
Graft versus host disease
Drugs
Epithelioid angiomatosis (Bartonella infection)
Reactive lesions
Pyogenic granulomas
Peripheral giant cell granulomas
Atrophic
Geographic tongue
Lichen planus
Lupus erythematosus
Erythroplasia
Burns
Avitaminosis B12
Purpura
Vascular
Telangiectases (Hereditary haemorrhagic telangiectasia or scleroderma)
Angiokeratomas (Fabry's disease)
Angiomas
Neoplasms
Giant cell tumour
Squamous carcinoma
Kaposi's sarcoma
Wegener's granulomatosis
Generalised
Candidosis
Avitaminosis B complex (rarely)
Irradiation or chemotherapy-induced mucositis
Polycythaemia



Figure 1: Median rhomboid glossitis.



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Figure 2: Pemphigus.

Figure 3: Desquamative gingivitis.

Candidosis

- Denture-related stomatitis; usually a form of mild chronic atrophic candidosis consisting of inflammation beneath a denture or other appliance
- Median rhomboid glossitis; a persistent red, rhomboidal depapillated area in the midline dorsum of tongue (Figure 1)
- Acute oral candidosis; may cause widespread erythema and soreness sometimes with thrush, often a complication of corticosteroid or antibiotic therapy. Red lesions of candidosis may also be seen in HIV disease, typically in the palate

Deep mycoses - rare in the developed world, except in HIV disease and other immunocompromised persons

- Histoplasmosis
- Cryptococcosis
- Blastomycosis
- Paracoccidioidomycosis
- Bacterial infections: these are rare causes of red lesions but Bartonella infection may cause epithelioid

angiomatosis, mimicking Kaposi's sarcoma

- Cancer treatment-related mucositis; common after irradiation of tumours of the head and neck, or chemotherapy e.g. for leukaemia
- Immunological reactions; such as lichen planus, plasma cell gingivostomatitis, granulomatous disorders (sarcoidosis, Crohn's disease, orofacial granulomatosis), amyloidosis, and graft versus host disease.

Neoplastic lesions

Red neoplasms include:

- Peripheral giant cell tumours
- Angiosarcomas such as Kaposi's sarcoma - a common neoplasm in HIV/AIDS, appears in the mouth as red or purplish areas or nodules especially seen in the palate
- Squamous cell carcinomas
- Wegener's granulomatosis
- Midline granulomas.

Vesiculobullous disorders

These include erythema multiforme, pemphigoid and pemphigus (Figure 2).

Table 2: Causes of oral white lesions

<p>Local causes</p> <ul style="list-style-type: none"> • Materia alba (debris from poor oral hygiene) • Keratoses <ul style="list-style-type: none"> • Frictional keratosis (and cheek/lip biting) • Smoker's keratosis • Snuff-dipper's keratosis • Burns • Grafts • Scars • Furred or hairy tongue <p>Neoplastic and possibly pre-neoplastic</p> <ul style="list-style-type: none"> • Leukoplakia • Keratoses • Carcinoma <p>Inflammatory</p> <p>Infective</p> <ul style="list-style-type: none"> • Candidosis • Hairy leukoplakia • Syphilitic mucous patches and keratosis • Koplik's spots (measles) • Some papillomas • Reiter's disease • Koilocytic dysplasia (papillomavirus) <p>Non-infective</p> <ul style="list-style-type: none"> • Lichen planus • Lupus erythematosus <p>Congenital</p> <ul style="list-style-type: none"> • Leukoedema • Fordyce spots • Inherited dyskeratoses <ul style="list-style-type: none"> • White sponge naevus • Focal palmoplantar and oral mucosa hyperkeratosis syndrome • Darier's disease • Pachyonychia congenita • Dyskeratosis congenita

Reactive lesions

These include:

- Pyogenic granulomas
- Peripheral giant cell granulomas

Burns

Atrophic lesions:

Table 3: Types of leukoplakia with high malignant potential

<ul style="list-style-type: none"> • In certain at-risk sites (floor of mouth/ventrum of tongue: lower lip; commissures) • Associated with Candida species • Verrucous or nodular lesions • Lesions mixed with red lesions (speckled, or erythroleukoplakia)
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- Erythroplasia is one of the more important causes of a localised red lesion, since it is often dysplastic (see below).
- Erythema migrans (geographic tongue) manifests with irregular depapillated red areas, which change in size and shape, usually on the dorsum of the tongue
- Desquamative gingivitis is a frequent cause of red gingivae, almost invariably caused by lichen planus or pemphigoid (Figure 3).
- Iron or vitamin deficiency states may cause glossitis or other red lesions.

Purpura

Bleeding into the skin and mucosa is usually caused by:

- Trauma, occasional small petechiae are seen at the occlusal line in perfectly healthy people
- Suction (e.g. fellatio may produce bruising in the soft palate)
- Platelet disorders such as thrombocytopenia can result in red or brown pinpoint lesions (petechiae) or diffuse bruising (ecchymoses) at sites of trauma, such as the palate.
- Localised oral purpura or angina bullosa haemorrhagica is an idiopathic, fairly common cause of blood blisters, often in the soft palate, in older persons.

Vascular anomalies

Also known as angiomas and telangiectasia, these include:

- Dilated lingual veins (varices) may be conspicuous in normal elderly persons
- Haemangiomas are usually small isolated developmental anomalies, or hamartomas. Rarely, they may be part of the Sturge-Weber syndrome (haemangioma with epilepsy and hemiplegia) or other rare conditions
- Telangiectasias - dilated capillaries - may be seen after irradiation and in disorders such as hereditary haemorrhagic telangiectasia and systemic sclerosis.



Figure 4: Keratosis.

Diagnosis

Diagnosis of red lesions is mainly clinical but lesions should also be sought elsewhere, especially on the skin or other mucosae. It may be necessary to take a blood picture (including blood and platelet count), and assess haemostatic function or exclude vitamin deficiencies. Investigations needed may include other haematological tests and/or biopsy or imaging.

Management

Treatment is usually of the underlying cause, or excision.

White lesions

Some common whitish conditions, notably Fordyce granules are really yellowish, but may cause diagnostic confusion.

Truly white oral lesions appear white usually because they are keratotic (composed of thickened keratin, which looks white when wet) or may consist of collections of debris (necrotic epithelium or materia alba), or fungi - such as candidosis.

White lesions have a range of causes (Table 2) but are usually painless. The morphological features may give a guide to the diagnosis. For example, focal lesions; are often caused by keratoses; multifocal lesions; are common in thrush (pseudomembranous candidosis) and lichen planus; striated lesions; are typical of lichen planus; and diffuse white areas are seen in the buccal mucosa in leukoedema, and in the palate in stomatitis nicotina.

Leukoedema

Leukoedema is a common benign congenital whitish-grey filmy appearance of the mucosa, seen especially in the buccal mucosae bilaterally in persons of African or Asian descent. Diagnosis is clinical - the white appearance disappears if the mucosa is stretched. No treatment is available or required.

Inherited disorders of keratin

Inherited dyskeratoses are rare but include:

- White sponge naevus
- Focal palmoplantar and oral mucosa hyperkeratosis syndrome
- Darier's disease
- Pachyonychia congenita
- Dyskeratosis congenita.

There may be a family history or other features associated, such as lesions on other mucosae, or skin appendages such as the nails. Specialist care is indicated.

Local causes of white lesions

Debris, burns (from heat, chemicals such as mouthwashes), grafts and scars may appear pale or white. Materia alba can usually easily be wiped off with a gauze.

Keratoses and leukoplakias

Leukoplakia is nowadays defined as 'a whitish patch or plaque that cannot be characterised clinically or pathologically as any other disease and which is not associated with any physical or chemical causative agent except the use of tobacco'.

Thus frictional keratosis and specific tobacco-induced lesions such as smoker's keratosis are now termed keratoses (not leukoplakias). Keratotic lesions, being inherent in the mucosa, will not wipe away with a gauze swab (Figure 4).

Leukoplakia is in fact not a single entity, rather it is a heterogeneous group of lesions of different aetiologies and of different potential for malignant change. Most leukoplakias - up to 70% in large series - are benign without evidence of dysplasia, but clearly biopsy is indicated to define the remaining 10 to 30% that are either dysplastic or already invasive carcinomas. Overall the rate of malignant transformation is of some 3 to 6% over 10 years but rates up to 30% have been reported, especially in leukoplakias in at risk sites, those associated with Candida, or in speckled or verrucous lesions (Table 3).

Frictional keratosis

Frictional keratosis is caused particularly by friction from the teeth and seen mainly at the occlusal line, particularly in adult females and especially in those with temporomandibular pain-dysfunction syndrome. Patients with missing teeth may develop keratosis on the alveolar ridge. Any sharp edges of teeth or appliances should be removed and the patient counselled about the habits. Malignant change is rare.

Table 4: Causes of oral brown or black hyperpigmentation

LOCALISED
Amalgam, graphite, carbon, dyes, inks or other tattoos
Ephelis (freckle)
Epithelioid angiomas
Kaposi's sarcoma
Malignant melanoma
Melanoacanthoma
Melanotic macules
Naevus
Pigmented neuroectodermal tumor
Verruciform xanthoma
MULTIPLE OR GENERALISED
Genetic
Racial
Carney syndrome
Complex of myxomas, spotty pigmentation and endocrine overactivity
Laugier-Hunziker syndrome
Lentiginosis profusa
Leopard syndrome
Peutz-Jegher's syndrome
Drugs
ACTH
Amiodarone
Antimalarials
Betel
Busulphan
Chlorpromazine
Clofazamine
Contraceptive pill
Ketoconazole
Menthol
Metals (bismuth, mercury, silver, gold, arsenic, copper, chromium, cobalt, manganese)
Methyldopa
Minocycline
Phenothiazines
Smoking
Zidovudine
Endocrine
Addison's disease
Albright's syndrome
Nelson's syndrome
Pregnancy
Post-inflammatory
Others
Gaucher's disease
Generalised neurofibromatosis
Haemochromatosis
HIV disease
Incontinentia pigmenti
Thalassaemia
Whipple's disease
Wilson's disease

Tobacco-induced keratoses

Tobacco is a common cause of keratosis, seen especially in males.

- **Cigarette-induced keratosis**

Mild keratosis may be seen especially on the lip (occasionally nicotine-stained) and at the commissures, occasionally in the palate, and the teeth are usually nicotine-stained. Malignant change is rare.

- **Pipe smoking**

Diffuse whiteness over the palate is termed smoker's keratosis or stomatitis nicotina. The palatal minor salivary gland orifices appear red against this white background. Malignant change is uncommon

- **Cigar smoking**

Cigar smokers may develop stomatitis nicotina and nicotine-stained teeth. Malignant change is uncommon.

- **Snuff use**

Snuff may produce keratosis, together with gingival recession. Malignant change is rare.

In contrast, two habits are especially dangerous:

- **Reverse smoking (Bidi)**

In some communities, especially Asians, cigarettes are smoked with the lit end within the mouth. Palatal or other oral carcinoma can result.

- **Tobacco chewing**

Chewed tobacco may induce keratosis. In many communities, tobacco is a component of the betel quid (Scully, 2002). Buccal carcinomas can result.

Infections

White lesions which can result from infections include candidosis, hairy leukoplakia (caused by Epstein-Barr virus), and the mucous patches and leukoplakia of syphilis. Specialist care is indicated.

Mucocutaneous disease

Lichen planus is the main skin disease that can present with oral white lesions but lupus erythematosus can present similarly. Darier's disease (keratosis follicularis) is a rare cause. Specialist care is indicated.

Diagnosis

The nature of white lesions can sometimes only be established after further investigation. Biopsy is usually indicated, particularly where there is:

- A need to exclude malignancy
- Admixture with red lesions (erythroleukoplakia or speckled leukoplakia)
- A raised lesion (nodular or verrucous leukoplakia)
- Candidal leukoplakia

- Floor of mouth leukoplakia (sublingual keratosis)
- A rapid increase in size
- Change in colour
- Ulceration
- Pain
- Regional lymph node enlargement.

The finding by the pathologist of epithelial dysplasia may be predictive of malignant potential but this is not invariable, and there can be considerable inter- and intra-examiner variation in the diagnosis of dysplasia. Thus there has been a search for molecular markers to predict exactly which lesions are truly of malignant potential and may develop into oral squamous cell carcinoma (OSCC).

The most predictive of the molecular or cellular markers thus far assessed for OSCC development apart from dysplasia, include chromosomal polysomy, the tumour suppressor p53 protein expression, and loss of heterozygosity (LOH) at chromosome 3p or 9p. Routine use of these is, however, hampered by their complexity and lack of facilities in many routine laboratories.

As a surrogate for individual molecular markers, measurement of gross genomic damage (DNA ploidy) may be a realistic option, uses automated image cytometry of nuclei obtained from routinely processed tissue samples and is now available in some histopathology laboratories.

Management

Perhaps surprisingly, management is very controversial since there are no studies that prove the best course of treatment (Figure 5). The dilemma in managing patients with potentially malignant oral lesions and field change has been of deciding which mucosal lesions or areas will progress to carcinoma. Cessation of dangerous habits and the removal of the high-risk lesions is probably the best course of action.

Hyperpigmentation

Most oral discolouration ranges from brown to black. Oral mucosal discolouration may be superficial (extrinsic) or due to deep (intrinsic - in or beneath mucosa) causes. Extrinsic discolouration is rarely of consequence and is usually caused by:

- Coloured foods or drinks, (such as liquorice, beetroot, red wine, coffee, tea)
- Drugs (such as chlorhexidine, iron salts, griseofulvin, crack cocaine, minocycline, bismuth subsalicylate, lansoprazole, and HRT)
- Habits such as tobacco or betel use.

Black hairy tongue is one extrinsic type of discolouration seen especially in patients on a soft diet, smokers, and

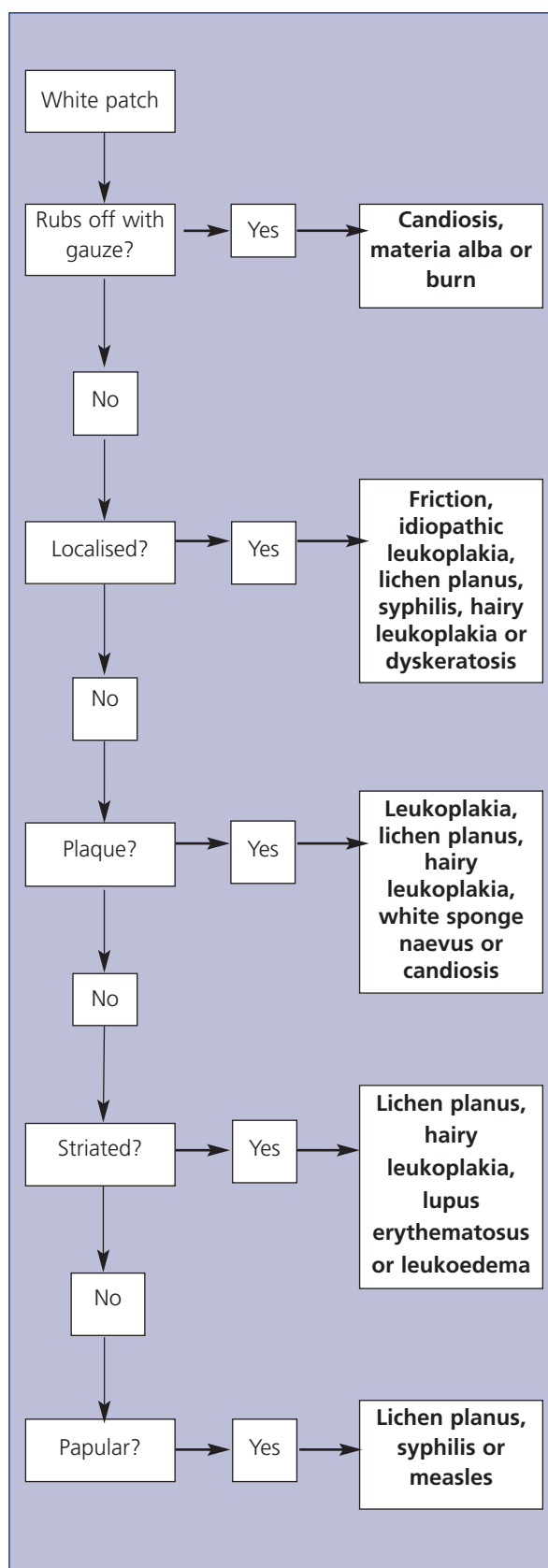


Figure 5: Management of white lesions



Figure 6: Racial pigmentation



Figure 7: Amalgam tattoo.



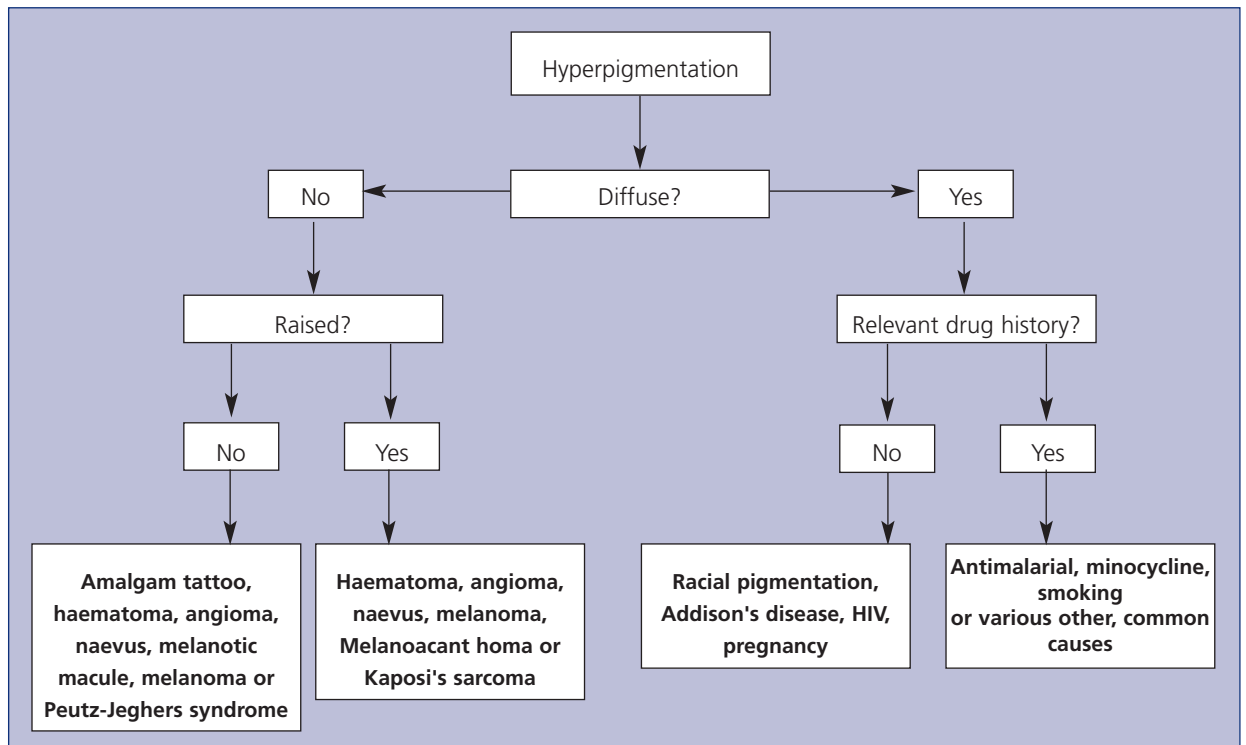
Figure 8: Naevus.

those with dry mouth or poor oral hygiene. Intrinsic discolouration may have more significance (Table 4) but generalised pigmentation, often mainly affecting the gingivae, is common in persons of colour, and is racial and due to melanin. Seen mainly in blacks and Asians it can also be noted in patients of Mediterranean descent, sometimes even in some fairly light-skinned people. It is most obvious in the anterior labial gingivae and palatal mucosa (Figure 6) and pigmentation is usually symmetrically distributed. Patches may be seen elsewhere. Pigmentation may be first noted by the patient in adult life and then incorrectly assumed to be acquired rather than congenital in origin.

In all other patients with widespread intrinsic pigmentation, systemic causes should be excluded. These may include:

- Drugs
- Tobacco
- Antimalarials
- Adrenocorticotrophic (ACTH) therapy
- Busulphan, oral contraceptives, phenothiazines, anticonvulsants, minocycline, gold and other drugs

- Many heavy metals (such as mercury, lead and bismuth) not used therapeutically now, rarely cause industrial exposure.
- Pregnancy
- Hypoadrenalism (Addison's disease). Hyperpigmentation in this is generalised but most obvious in normally pigmented areas (e.g. the nipples, genitalia), skin flexures, and sites of trauma. The mouth may show patchy hyperpigmentation. Patients also typically have weakness, weight loss, and hypotension
- Rare causes; HIV infection, internal malignancy, Von Reckinghausen's disease, Albright's syndrome or Peutz-Jegher's syndrome - a rare autosomal dominant condition, of oral and circumoral patchy brown pigmentation with small-intestinal polyps. Localised areas of pigmentation may be caused by intrinsic causes, mainly:
 - Amalgam tattoo (embedded amalgam). Typically this is a single blue-black macule in the mandibular gingiva or at least close to the scar of an apicectomy (Figure 7), is painless, and does not change significantly in size or colour. Amalgam tattoo is best excised to exclude naevi



or melanoma. Similar lesions are caused by other foreign bodies (e.g. graphite tattoo), local irritation or inflammation

- Melanotic macules are usually flat single brown, collections of melanin-containing cells, seen particularly on the vermilion border of the lip and on the palate. They are best removed to exclude melanoma
- Naevi are blue-black often papular lesions formed from increased melanin-containing cells (naevus cells) seen particularly on the palate (Figure 8). They are best removed to exclude melanoma
- Melanoacanthomas are from 5mm to 2cm diameter, seen mainly in the buccal mucosa or palate in African females, and may appear rapidly. These are probably reactive lesions, best removed
- Malignant melanoma is rare, seen usually in the palate or maxillary gingivae. Features suggestive of malignancy include a rapid increase in size, change in colour, ulceration, pain, the occurrence of satellite pigmented spots or regional lymph node enlargement. Radical excision is indicated
- Kaposi's sarcoma is usually a purple lesion seen mainly in the palate or gingival of HIV-infected and other immunocompromised persons.

Diagnosis

The nature of oral hyperpigmentation can sometimes only be established after further investigation. If early detection of oral melanomas is to be achieved, all pigmented oral cavity lesions should be viewed with suspicion. The consensus of opinion is that a lesion with clinical features as above seriously suggestive of being malignant melanoma, are best biopsied at the time of definitive operation.

In patients with localised hyperpigmentation, in order to exclude melanoma, radiographs may be helpful (they can sometimes show a foreign body) and biopsy may be indicated, particularly where there is a solitary raised lesion, a rapid increase in size, change in colour, ulceration, pain, evidence of satellite pigmented spots or regional lymph node enlargement.

In patients with generalised or multiple hyperpigmentation, in order to exclude Addison's disease, blood pressure should be taken (hypotension is a characteristic), plasma cortisol levels may be indicated (low levels found) and a Synacthen (adrenocorticotrophic hormone stimulation) test may be indicated (impaired response found).

Management

Management is of the underlying condition.

Further Reading

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