ABC of Dermatology

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THE SKIN AND SYSTEMIC DISEASE I

When a man has on the skin of his body a swelling or an eruption or a spot . . . and the disease appears to be deeper than the skin it is a leprous disease.

Leviticus xiii,

Although arguments continue about what the Old Testament writers understood by "leprous," there was clearly an appreciation of the connection between the skin and systemic illness. As in ancient times, clinical signs in the skin may give valuable diagnostic clues to underlying disease. Sometimes the same condition affects both the skin and other organs, or severe skin disease itself may be the cause of generalised illness.

The skin is also a common target organ for allergic reactions to drugs, with a rash being the first clinical sign. The florid skin lesions of the acquired immune deficiency syndrome (AIDS) illustrate the results of infections when the immune response is impaired.

The cutaneous signs of systemic disease is a very large subject, on which much has been written, so a skin eruption that might indicate systemic disease is good reason to consult the large textbooks. Nevertheless, it is possible to give an outline of the more common skin changes that may be associated with systemic illness.

Erythematous rashes

Rash from penicillin.

Erythema multiforme.

Allergic reactions to drugs, commonly the penicillins. There may be a widespread rash developing from a few days to two weeks after treatment with moderate illness (type III) or an acute life threatening anaphylactic reaction (types I and III) with acute angio-oedema and renal failure.

Infection—The characteristic rash of the various viral infections is, in a broad sense, also an allergic response. Less specific reactions such as erythema multiforme are commonly associated with infection—for example, herpes and other viral infections and streptococcal infection—but also with connective tissue disease and drugs such as sulphonamides.

In *carcinoid* and *phaeochromocytoma* vasoactive substances cause episodes of flushing and telangiectasia.

Figurate erythema.

Erythema of nailbeds.

Dermatomyositis.

Neoplasia—Numerous patterns of widespread erythema have been described—the "figurate erythemas"—which may be associated with underlying carcinoma. Dermatomyositis, also a rare condition, has very high association in adults with underlying carcinoma commonly of the breasts, lung, ovary, or gastrointestinal tract. It is characterised by localised erythema with a purple hue, predominantly on the eyelids, cheeks and forehead. There may be similar changes on the dorsal surface of the fingers often with dilated nail fold capillaries. These changes may precede the discovery of an underlying tumour and may also fade away once it is removed. There is variable association with muscle aching and weakness.

Erythema of the nailbeds may be associated with connective tissue disease—such as lupus erythematosus, scleroderma, and dermatomyositis. "Clubbing" of the fingers may be associated.

CRST syndrome.

Telangiectasia—Clubbing may be a feature of scleroderma in the CRST (Calcinosis, Raynaud's phenomenon, Scleroderma, and Telangiectasia) syndrome.

Vasculitis.

Spider naevi, which show a central blood vessel with radiating branches, are frequently seen in women (especially during pregnancy) and children. If they occur in large numbers, particularly in men, they may indicate liver failure. Palmar erythema and yellow nails may also be present.

Vasculitis and purpura of the skin may be associated with disease of the kidneys and other organs, as has already been discussed. "Splinter haemorrhages" under the nails are usually the result of minor trauma but may be associated with a wide range of conditions, including subacute bacterial endocarditis and rheumatoid arthritis.

Changes in pigmentation

Vitiligo.

Hypopigmentation

A widespread partial loss of melanocyte functions with loss of skin colour is seen in hypopituitarism and is caused by an absence of melanocyte stimulating hormone. In the various types of autosomal recessive albinism there is a very considerable loss of pigment from the skin, hair, and eyes.

Localised depigmentation is most commonly seen in vitiligo, in which a family history of the condition is found in one third of the patients. In the sharply demarcated, symmetrical macular lesions there is loss of melanocytes and melanin. There is an increased incidence of organ specific antibodies and their associated diseases (table).

Other causes of hypopigmented macules include: postinflammatory conditions, such as psoriasis, eczema, lichen planus, and lupus erythematosus; infections, such as tinea versicolor, and leprosy; chemicals, such as hydroquinones, hydroxychloroquine, and arsenicals; reactions to pigmental naevi, such as halo naevus; and genetic diseases, such as tuberous sclerosis ("ash leaf" macules).

Hyperpigmentation

There is wide variation in the pattern of normal pigmentation as a result of heredity and exposure to the sun. Darkening of the skin may be due to an increase in the normal pigment melanin or to the deposition of bile salts in liver disease, iron salts (haemochromatosis), drugs, or metallic salts from ingestion.

Causes of hyperpigmentation include the following.

Hormonal—An increase in circulating hormones that have a melanocyte stimulating activity occurs in hyperthyroidism, Addison's disease, and acromegaly. In women who are pregnant or taking oral contraceptives there may be an increase in melanocytic pigmentation of the face. This is known as melasma (or chloasma) and occurs mainly on the forehead and cheeks. It may fade slowly. Sometimes there is a premenstrual darkening of the face.

Autoimmune associations with vitiligo

Thyroid disease	Myasthenia gravis
Pernicious anaemia	Alopecia areata
Hypoparathyroidism	Halo naevus
Addison's disease	Morphoea and
Diabetes	lichen sclerosus

Argyria (silver salts in skin).

Melasma.

Increased deposition of haemosiderin is generalised in haemochromatosis. Localised red-brown discoloration of the legs is seen with longstanding varicose veins. It also occurs in a specific localised pattern in Schamberg's disease, when there is a "cayenne pepper" appearance of the legs and thighs.

Acanthosis nigricans.

Pseudoacanthosis nigricans.

Neurofibromatosis.

Neoplasia—Lymphomas may be associated with increased pigmentation. *Acanthosis nigricans*, characterised by darkening and thickening of the skin of the axillae, neck, nipples, and umbilicus, occurs with internal cancers, usually adenocarcinoma of the stomach. *Pseudo acanthosis nigricans* is much more common, consisting of simple darkening of the skin in the flexures of obese individuals. There is also a benign juvenile type.

Drugs—Chlorpromazine and other phenothiazines may cause an increased pigmentation in areas exposed to the sun. Phenytoin can cause local hyperpigmentation of the face and neck.

Inflammatory reactions—Post inflammatory pigmentation is common, often following acute eczema, fixed drug eruptions, or lichen planus. Areas of lichenification from rubbing the skin are commonly darkened.

Malabsorption and deficiency states—In malabsorption syndromes, pellagra, and scurvy there is often frequently increased skin pigmentation.

Congenital conditions—There is clearly a marked variation in pigmentation and in the number of freckles in normal individuals. There may be localised well defined pigmented areas in neurofibromatosis with "café au lait" patches. Increased pigmentation with a blue tinge occurs over the lumbosacral region in the condition known as Mongolian blue spot.

Peutz-Jeghers syndrome.

Peutz-Jeghers syndrome is inherited as an autosomal dominant characterised by pigmented macules of the oral mucosal membranes, lips, and face that appear in infancy. Benign intestinal polyps, mainly in the ileum and jejunum, which very rarely become malignant, are invariably associated with the condition.

Malignant lesions

Lymphoma.

B cell lymphoma.

Mycosis fungoides.

Poikiloderma.

Malignant lesions may cause skin changes such as acanthosis nigricans and dermatomyositis or produce secondary lesions. Lymphomas can arise in or invade the skin and pruritus may be associated with Hodgkin's disease.

Mycosis fungoides is a T cell lymphoma of cutaneous origin. Initially well demarcated erythematous plaques develop on covered areas with intense itching. In many cases there is a gradual progression to infiltrated lesions, nodules, and ulceration. In others the tumour may occur de novo or be preceded by generalised erythema.

Poikiloderma, in which there is telangiectasia, reticulate pigmentation, atrophy, and loss of pigment, may precede mycosis fungoides, but it is also seen after radiotherapy and in connective tissue diseases.

Parapsoriasis is a term used to cover maculopapular erythematous lesions that occur in middle and old age. Some cases undoubtedly develop into mycosis fungoides and a biopsy specimen should be taken of any such fixed plaques that do not clear with topical steroids.

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