MODERN TOPICS IN

PAEDIATRIC DERMATOLOGY

MTP 5

Edited by
JULIAN VERBOV
MD FRCP

MODERN TOPICS IN PAEDIATRIC DERMATOLOGY

Edited by
JULIAN VERBOV MD FRCP

MTP 5

WILLIAM HEINEMANN MEDICAL BOOKS LIMITED
London

Contributors

D. J. ATHERTON, M.A., M.B., M.R.C.P., Senior Registrar, Dermatology, Guy's Hospital, St. Thomas Street, London.

J. MARTIN BEARE, M.D., F.R.C.P., Consultant Dermatologist, The Royal Belfast Hospital for Sick Children, N. Ireland.

G. W. BEVERIDGE, M.B., Ch.B., F.R.C.P.(Ed.), Consultant Dermatologist and Senior Lecturer, Department of Dermatology, The Royal Infirmary, Edinburgh.

E. ANN BINGHAM, M.B., M.R.C.P., Senior Registrar in Dermatology, The Royal Belfast Hospital for Sick Children, N. Ireland.

S. S. BLEEHEN, M.B., F.R.C.P., Consultant Dermatologist, Hallamshire Hospital, Sheffield.

J. J. CREAM, B.Sc., M.D., F.R.C.P., Consultant Dermatologist, Charing Cross Hospital, London.

R. P. R. DAWBER, M.A., M.B., F.R.C.P., Consultant Dermatologist, The Radcliffe Infirmary, Oxford.

R. W. EMMERSON, M.B., F.R.C.P., Consultant Dermatologist to the Reading group of Hospitals.

W. FRAIN-BELL, M.D., F.R.C.P., Consultant Dermatologist, University of Dundee.

W. A. D. GRIFFITHS, M.A., M.D., M.R.C.P., Consultant Dermatologist, Liverpool Area Health Authority (Teaching).

M. ANN HALL, M.B., M.R.C.P., Medical Assistant, Rheumatology Unit, Canadian Red Cross Memorial Hospital, Taplow, Berks.

CHRISTINE I. HARRINGTON, M.B., M.R.C.P., Senior Registrar in Dermatology, Hallamshire Hospital, Sheffield.

F. HARRIS, M.D., M.Med.(Paed.)., F.R.C.P.(Ed.)., Professor of Child Health, University of Liverpool.

E. J. MOYNAHAN, F.R.C.P., Consultant Dermatologist, Guy's Hospital, St. Thomas Street, London.

P. PINKERTON, M.D., F.R.C.Psych., D.P.M., Consultant Physician-in-Charge, Dept. of Psychological Medicine, Royal Liverpool Children's Hospital, Myrtle Street, Liverpool.

J. SAVIN, M.A., M.D., F.R.C.P., D.I.H., Consultant Dermatologist, The Royal Infirmary, Edinburgh.

JULIAN VERBOV, M.D., F.R.C.P., Consultant Dermatologist, Liverpool Area Health Authority, and Isle of Man Health Services Board. Clinical Lecturer in Dermatology, University of Liverpool.

A. D. B. WEBSTER, M.R.C.P., Consultant Physician, Division of Immunological Medicine, Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex.

R. S. WELLS, M.D., F.R.C.P. (Ed. and Lond.), D.C.H., Consultant Dermatologist, The Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London.

C. B. S. WOOD, F.R.C.P., D.C.H., Professor of Child Health, St. Bartholomew's Hospital, London and The London Hospital.

Acknowledgements

I should like to thank the Editor of the *British Journal of Dermatology* for permission to reproduce Fig. 5.4 and the Editor of *The Practitioner* for permission to reproduce Fig. 10.10. I am indebted to Mrs A. F. Pearcey of the Royal Liverpool Hospital Department of Medical Illustration for providing and allowing reproduction of some of the photographs in Chapters 2 and 5, copyright of which remains with the aforementioned institution.

J. V.

Preface

This book considers skin problems in children. The basic aim in editing such a book has been to provide an easily readable text on numerous topics, both common and not so common. It is not intended to be a formal textbook of paediatric dermatology.

It is my experience that, in general, doctors other than those with a special interest in dermatology, have difficulty in recognizing, diagnosing and correctly treating skin conditions occurring in children, and many practitioners have told me just this.

All the contributors were asked to write their chapters with emphasis on producing a book of practical use with wide appeal containing something of interest to paediatricians, family practitioners, school medical officers, as well as dermatologists. In addition to chapters on the all-important common conditions such as atopic eczema and infections I felt that other topics less commonly discussed should be included in a modern work. Thus, steroids and growth, the child and light, rheumatic diseases, immunodeficiency and the skin, and psychosomatic aspects of skin disease are considered in separate chapters. The chapter on tropical dermatology should be of special interest to doctors both at home and abroad.

As a general rule I have tried to avoid repetition. However, on occasions I have allowed some repetition of a topic, if this proved necessary to the continuity of a particular chapter. Sometimes different views on the same subject have been deliberately allowed to remain.

Julian Verbov

Royal Liverpool Children's Hospital
Myrtle Street
Liverpool

Contents

Chapter 1

Inherited Disorders

D. J. Atherton and R. S. Wells

CHROMOSOMAL ABNORMALITIES

SINGLE GENE DISORDERS
The ichthyoses
Epidermolysis bullosa
Ectodermal dysplasia
Palmoplantar keratoderma
Familial multiple tumour syndromes
Inherited disturbances of pigmentation
Disorders of collagen and elastin
Deposition diseases
Miscellaneous conditions

Genetic factors play a role in the aetiology of diseases by operating in one of three ways. In many common conditions such as atopic eczema and psoriasis, genetic factors are known to be important, though the pattern of inheritance is complex, and is generally considered to involve a number of different genes. This is known as multifactorial inheritance. A large number of comparatively rare conditions result from abnormalities of single genes. Probably the most common in this country is autosomal dominant ichthyosis vulgaris, which affects about 1 in 1000 of the population. A small number of disorders have been found to result from chromosomal abnormalities, either numerical or structural. These conditions are not inherited in the normal sense, but since they have their origin in the genetic material, they are usually classified as genetic. This chapter will be concerned with diseases of the skin in which the genetic influence is of the last two types. We will not describe all known skin diseases in these categories, but will limit ourselves to those most commonly seen in ordinary dermatological and paediatric practice with the exception of a few rarer conditions which are of especial interest or importance.

There still seems to persist in a great part of the medical world a saddeningly fatalistic attitude towards hereditary diseases. These diseases can often be avoided altogether by genetic counselling, and the technique of amniocentesis is being increasingly employed for the prenatal diagnosis of both single gene disorders and chromosomal anomalies. Many inherited diseases which formerly were invariably fatal, such as acrodermatitis enteropathica, can now be treated successfully, and the future possibility of 'gene therapy' seems increasingly feasible.

For an account of basic genetic principles the reader is referred to the excellent textbook by Fraser Roberts (1972). However, because of frequent misuse, we are keen to define certain terms used in this chapter. *Expressivity* describes the degree of manifestation of a gene in an individual in whom its presence is detectable. This may refer to the variety of abnormal features present as well as to their severity. The term '*forme fruste*' is sometimes used to denote extremely mild expression of a gene. The *penetrance* of a gene is said to be reduced when it is not always expressed in individuals in whom its expression would be expected.

CHROMOSOMAL ABNORMALITIES

Dermatological manifestations occur in some of the major chromosomal anomalies, though they rarely constitute the presenting clinical features. In *Down's syndrome*, cutaneous livedo is often a feature in the neonatal period. Thereafter, the skin becomes increasingly dry, and often develops a prematurely aged appearance. The hair is fine and sparse. Syringomata (eccrine sweat duct adenomata) occur quite commonly, and elastosis perforans serpiginosa appears in a few of these patients. The latter comprises annular or arcuate groups of horny papules most commonly occurrring on the back of the neck, and is frequently associated with other genetically determined disorders, particularly those of collagen and elastin. Also of dermatological interest are the consistent and characteristic dermatoglyphic abnormalities, and the pale areas often seen in the outer part of the iris, known as Brushfield's spots.

Dermatoglyphic abnormalities also occur in *Patau's syndrome* in which the most common cutaneous feature is the high incidence of capillary haemangiomata, often arising on the forehead. Excessive hyperconvexity of the nails and scalp defects also frequently occur. Cutaneous livedo is also often noted in *Edward's syndrome*, in which other common cutaneous manifestations include downy hypertrichosis of the back and forehead, laxity of the skin of the neck, dermatoglyphic abnormalities, and hypoplasia of the nails.

Dermatological abnormalities may be a major feature of *Turner's syndrome*, and the most characteristic of these is the frequent occurrence of multiple melanocytic naevi.

Chromosomal breaks are a characteristic finding in several rare inherited conditions. In *Bloom's syndrome*, dwarfism, facial telangiectasia and erythema, with photo-sensitivity are associated with a marked predisposition to neoplastic disease, and acute leukaemia in particular. Chromosomal breaks and a greatly increased susceptibility to malignant disease also occur in *Fanconi's familial panmyelopathy syndrome*. Many patients with this condition show mottled cutaneous hyper- and hypopigmentation in addition to bone marrow failure, skeletal and other abnormalities. The condition is transmitted by an autosomal recessive gene and is almost certainly not related to dyskeratosis congenita as has been widely suggested.

SINGLE GENE DISORDERS

The ichthyoses

The term ichthyosis implies a disorder of keratinization of the skin which results in obvious scaliness. There are a number of disorders in which ichthyosis is the principal abnormality, and it is only fairly recently that a satisfactory classification of these disorders has emerged, based to a great extent on genetic studies. Considerable variability of phenotypic expression appears to be responsible for the vast number of apparently different clinical varieties of ichthyosis which have been described in an extensive literature, and the situation is not yet entirely clear. There are four common conditions, and a number of less common ones which will be described briefly because of important associated features.

Ichthyosis vulgaris is an autosomal dominant condition. It is the commonest of the ichthyoses and the mildest; indeed, many patients do not consider their skin abnormal. The skin is normal at birth and scaling usually appears during early childhood, tending to become more prominent over a period of years, though spontaneous improvement is common after puberty. The scales are usually small, fine, and translucent and are most apparent on the extensor aspects of the arms and legs, and also on the cheeks in younger children. Follicular hyperkeratosis (keratosis pilaris) is often present, giving a roughened feel to the extensor aspects of the upper arms and thighs. Another characteristic feature is an increase in the markings of the palms and soles. There is a well established association of this type of ichthyosis with atopy, and particularly with atopic eczema. It is possible that dryness of the skin actually provokes the development of eczema in the predisposed child.

X-linked ichthyosis (Fig. 1.1) is less common but more severe. The scales are much larger, polygonal, and have a dirty-brown colour, giving the skin a rather reptilian appearance. The scaliness is frequently obvious at birth and usually starts during the first year of life. Virtually the entire skin surface may be involved including the flexures, though these are usually only relatively mildly affected. The face is largely spared and increased palmar and plantar markings are not a feature, nor is follicular hyperkeratosis. Improvement during the summer is characteristic. The condition is persistent and spontaneous resolution cannot be expected. In both affected males and carrier females, slit-lamp examination of the cornea reveals small opacities in the posterior capsule or on Descemet's membrane, although vision is usually normal.

Mental retardation and hypogonadism appear in association with X-linked ichthyosis in some patients; this may represent a separate disorder inherited by a different gene.

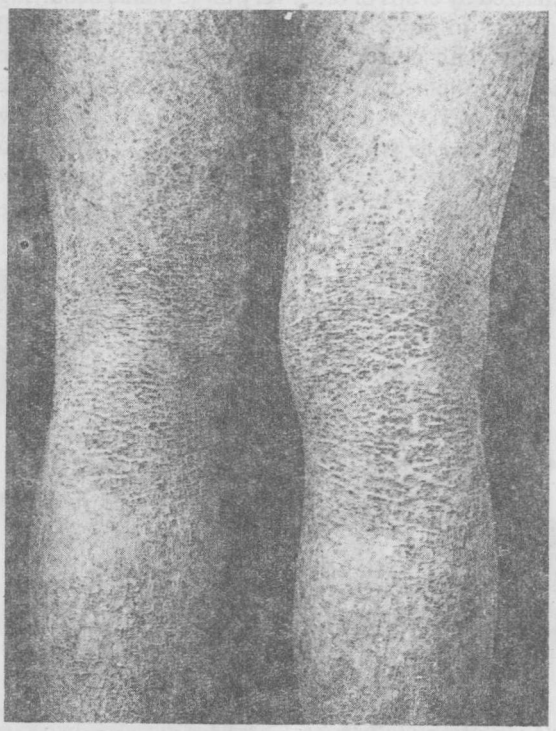


Fig. 1.1 X-linked ichthyosis, showing the typical large, dark scales. Note the involvement of the popliteal fossae

Non-bullous ichthyosiform erythroderma is a condition transmitted by an autosomal recessive gene of variable expressivity. It is a more severe form of ichthyosis than those already considered and is the underlying disorder in most babies born with the appearance described as 'collodion baby' (see later). In a typical case, a brightly erythematous child is encased in a shiny, transparent, but rather rigid membrane, which cracks and peels off after a few days, when the more typical clinical features of the disorder become apparent. In the few babies who seem normal at birth the condition will also usually manifest itself at this stage. There is a generalized dull erythema which tends to be most conspicuous in the flexures. Superimposed on the erythema is hyperkeratosis, so that the skin feels generally thicker and more rigid than normal. In many cases there is also a tendency for large scales with raised edges to form; this condition is known in some countries as 'lamellar' ichthyosis. Hair and nail growth may be abnormal, and rigidity of the skin may result in ectropion. The severity of the condition is very variable, and the course reflects this variability. Some patients die in early infancy but most patients survive and will be affected throughout life, although there is a gradual tendency for the erythema to fade leaving only generalised hyperkeratosis.

A probably different autosomal recessive gene transmits the *Sjögren-Larsson syndrome*, in which the cutaneous features of non-bullous ichthyosiform erythroderma are associated with mental retardation, and spasticity which is not usually present at birth, but becomes manifest during infancy. Macular degeneration will occur later in a few children.

Bullous ichthyosiform erythroderma is determined by an autosomal dominant gene, again of markedly variable expressivity. Large sheets of epidermis peel off shortly after birth leaving raw areas, and the condition may be mistaken at this stage for epidermolysis bullosa. The next phase of the disease is characterized by crops of often very large bullae occurring at virtually any site, rapidly becoming 'de-roofed' to leave further raw areas which heal swiftly without scarring. Gradually the bullae occur with decreasing frequency and warty hyperkeratosis develops, becoming characteristically prominent and linear in the flexures (Fig. 1.2).

Patches of similar warty hyperkeratosis can occur in isolation in otherwise normal children, and in some at least this seems to represent a phenotypic 'forme fruste' of the same gene, because other members of the family have the typical generalized form of the disorder. Oral retinoic acid is often helpful in both varieties of ichthyosiform erythroderma, and deserves a therapeutic trial in more severely affected cases.

Fig. 1.2 Bullous ichthyosiform erythroderma. Characteristic linear hyperkeratosis of the neck

There are a number of other rarer ichthyotic conditions, and, of these, ***Refsum's syndrome*** is of particular interest since it is the only ichthyosis in which the essential biochemical lesion has been identified. Phytanic acid accumulates in the tissues as a result of deficiency of a single enzyme, determined by an autosomal recessive gene. Ichthyosis occurs in many patients, though it may be confined to a minor degree of palmar and plantar hyperkeratosis. The major clinical abnormalities are retinitis pigmentosa, peripheral neuropathy, and ataxia, all of which usually appear in childhood. The diagnosis is confirmed by plasma lipid analysis which reveals an excess of phytanic acid. Diets low in phytol may result in clinical improvement, though this is not entirely established.

Considerable confusion surrounds the term '*collodion baby*' (Fig. 1.3). This term describes a clinical appearance, which can be the phenotypic expression of a number of different genes. Although the most striking examples are seen in babies with non-bullous ichthyosiform erythroderma, there is no clinical distinction between these and others who will turn out to be cases of X-linked ichthyosis, or the Sjögren-Larsson syndrome. Furthermore, this condition may occur in a mild form as a non-genetically determined phenomenon in both post-mature and dysmature neonates, in whom it is believed to result from a failure to shed the embryonic epitrichium.

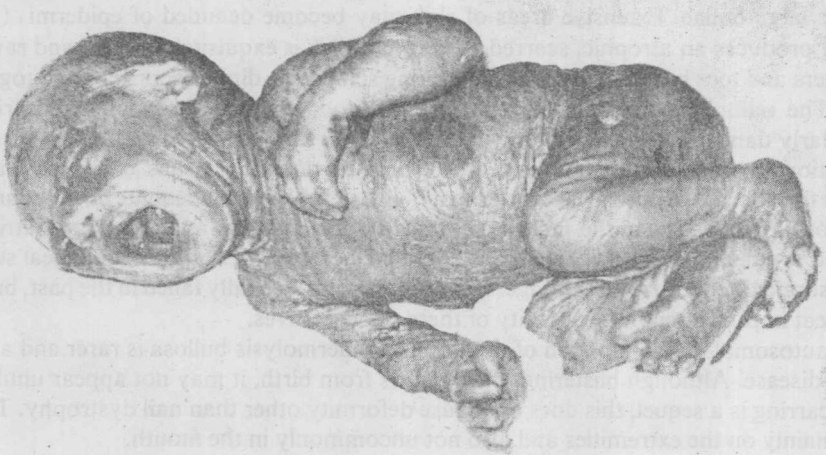


Fig. 1.3 'Collodion' baby

'Harlequin fetus' is a clinical description of babies born with the very rare and rapidly fatal autosomal recessive trait, *ichthyosis fetalis*. The baby is often born prematurely, encased in skin so rigid that it splits along lines of cleavage into huge armour-like plates. Although genetically distinct, the phenotype resembles a very severe example of the 'collodion baby' situation. Every medical museum has one.

Epidermolysis bullosa (see Chapter 9 also)

Epidermolysis bullosa comprises a number of genetically quite distinct disorders whose common effect is undue susceptibility to blister formation.

Epidermolysis bullosa simplex is inherited as an autosomal dominant trait. Bullae usually first appear during infancy but rarely are apparent during the first few days of life. The patient's only

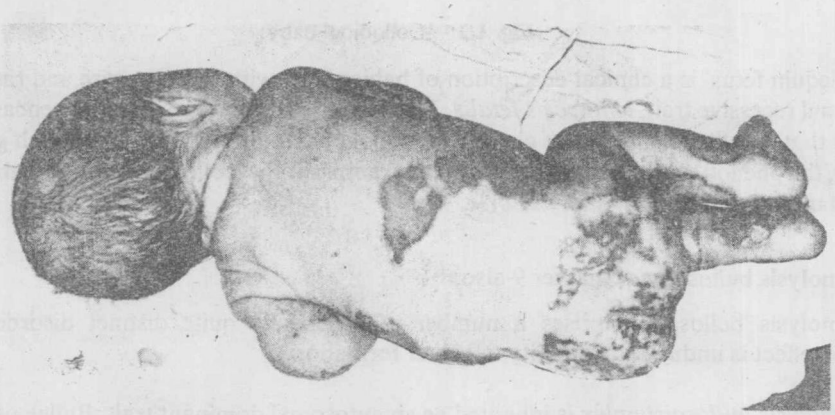
disability is a tendency for blisters to follow relatively minor trauma. Crawling, and later, walking result in the formation of clear tense blisters, particularly on the hands and feet, and especially in hot weather. Blisters heal without scarring, and occasionally occur on the oral mucous membrane. The condition improves with increasing age and rarely causes significant disability.

Epidermolysis bullosa of the hands and feet. This condition is also inherited as an autosomal dominant trait. It is even milder than epidermolysis bullosa simplex, blistering not usually appearing until late childhood, and almost always restricted to the feet, following heavy exertion. As with epidermolysis bullosa simplex, blistering is usually only troublesome during hot weather, and tends to improve with increasing age.

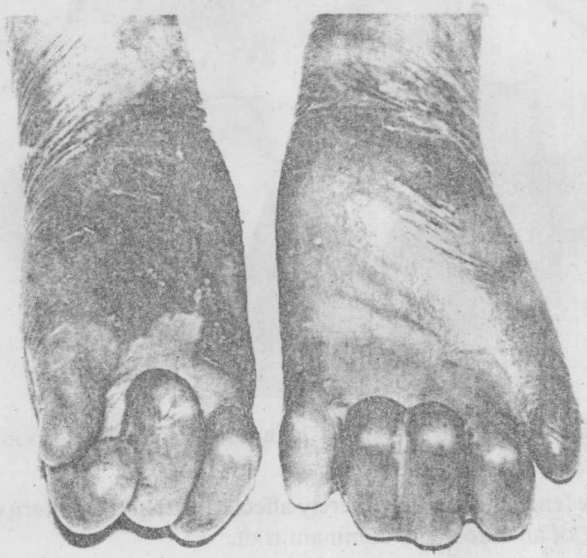
Dystrophic epidermolysis bullosa (dermolytic bullous dermatosis). There are two varieties of epidermolysis bullosa in which scarring follows the blistering: these are known as the 'dystrophic' forms. They are transmitted by distinct genes, one autosomal dominant and relatively mild, one autosomal recessive and serious.

In the autosomal recessive form, blistering is present at birth. The conjunctiva and mucous membrane of the mouth, pharynx, and oesophagus are also affected, and the scarring that follows the blisters is the major cause of disability, which can be dreadful. The very mildest trauma will cause blistering: merely lifting the newborn baby is likely to result in the appearance of tense large bullae. Extensive areas of skin may become denuded of epidermis (Fig. 1.4a). Healing produces an atrophic, scarred epidermis which is exquisitely fragile, and raw areas on the fingers and toes become fused during healing so that the digits become bound together (Fig. 1.4b). The nails and teeth tend to be lost. The occurrence of oesophageal stricture is a particularly dangerous complication which is likely to be aggravated with lethal consequences by dilation by bouginage. Judicious use of oral corticosteroids has completely altered the outlook for affected children. This treatment if given early and in adequate dosage can minimize the deformity and reduce the incidence of such complications as oesophageal stricture, and acquired syndactyly. Later on, steroids should be used to cover both oesophageal surgery and plastic surgical separation of the fingers, operations which usually failed in the past, but can now offer great improvement in the quality of these patients' lives.

The autosomal dominant form of dystrophic epidermolysis bullosa is rarer and a much less serious disease. Although blistering often occurs from birth, it may not appear until later, and while scarring is a sequel, this does not cause deformity other than nail dystrophy. The blisters occur mainly on the extremities and also not uncommonly in the mouth.



(a)



(b)

Fig. 1.4 Autosomal recessive dystrophic epidermolysis bullosa. (a) Widespread areas of denuded epidermis in a neonate; (b) Acquired syndactyly.

Epidermolysis bullosa letalis. In this very rare variant, blistering of skin and mucous membrane is severe from birth, and the blisters are usually haemorrhagic. Healing is poor, and extensive raw areas tend to persist. In spite of corticosteroids, the condition is usually fatal within the first 3 months of life.

We have not considered the pathological distinctions between the genetically and clinically distinct disorders, though electron microscopy is yielding fascinating clues into the fundamental abnormalities responsible for blistering in these conditions.

Ectodermal dysplasia

This term is used to describe a number of inherited conditions in which there are concurrent abnormalities of a variety of ectodermal structures, in particular hair, skin, nails, and teeth.

Anhidrotic ectodermal dysplasia is the most important of these conditions. It is inherited as an X-linked trait and its most serious component is the virtually total absence of eccrine sweat glands. The facies is characteristic, the skin is dry, thin and shiny, the hair is sparse and the eyebrows and eyelashes are absent. The teeth are few in number and conical in shape (Fig. 1.5), and the nails are often thin and ridged. The lacrimal and salivary glands may be hypoplastic, as may be the mucous glands of the respiratory and gastro-intestinal tracts. Taste and smell are often defective. Limited expression of the gene is common. Affected boys are intolerant of heat and may present with recurrent and unexplained hyperpyrexia in early childhood. They have often been exhaustively investigated for an infective cause for pyrexia before the abnormality of temperature regulation is appreciated. A hot environment, hot food, or exertion can cause great discomfort, and affected children learn to avoid these stimuli from an early age. Carrier females often show minor abnormalities, such as a degree of diffuse alopecia or minor dental defects.

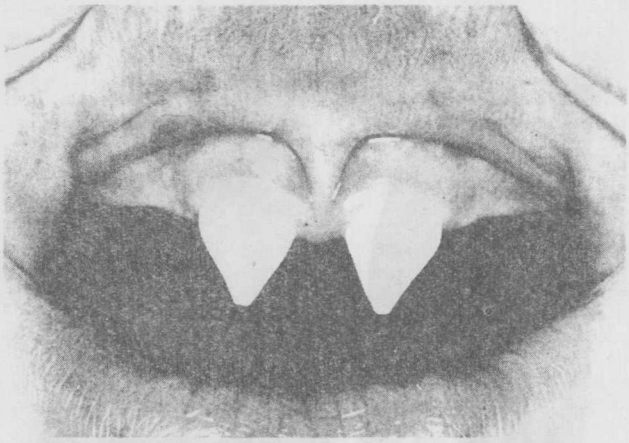


Fig. 1.5 Anhidrotic ectodermal dysplasia. Characteristic conical incisors in a 2-year-old boy

In some families the females are more severely affected so that the pattern of inheritance more closely resembles that of an autosomal dominant trait.

Hidrotic ectodermal dysplasia is a commoner and less disabling condition. Inheritance is determined by an autosomal dominant gene of widely variable expressivity, and nail dystrophy is the most consistent abnormality. The nails are usually short, thickened, discoloured and longitudinally striated, and may be missing. The hair is sparse, fine and fragile, or completely missing. Typically there is diffuse palmar and plantar hyperkeratosis, with coarse ridges and furrows and often painful fissures. Pebbly hyperkeratosis of the skin around the distal margin of the nails is characteristic. The teeth appear normal but tend to be prone to early caries. The facial appearance is normal, and sweating is not impaired.

Palmoplantar keratoderma

There are a number of inherited disorders of keratinization whose principal manifestation is localized thickening of the skin of the palms and soles. Different varieties are distinctive both clinically and genetically. Palmo-plantar keratoderma also occurs as a manifestation in several other cutaneous syndromes including both types of ichthyosiform erythroderma, hidrotic ectodermal dysplasia, and pachyonychia congenita.

Diffuse palmoplantar keratoderma, or tylosis, is the commonest form and is transmitted by an autosomal dominant gene of variable expressivity. The condition is apparent soon after birth, and comprises diffuse but well demarcated hyperkeratosis of the palms and soles. Erythema of the affected skin soon fades and the thickened skin develops a yellow colour. Fissuring is often a problem in severely affected cases.

Rarer varieties of palmoplantar keratoderma have been described in which the hyperkeratosis takes on a punctate or a linear pattern; most varieties are autosomal dominant traits. A strong association between palmoplantar keratoderma and later development of oesophageal carcinoma has been described in a number of familes of Irish extraction. In these families the hyperkeratosis is of a diffuse pattern but appears after the age of 5 years, and almost all cases subsequently develop oesophageal malignancy unless prophylactic oesophagectomy is undertaken.

Familial multiple tumour syndromes

Neurofibromatosis is an uncommon autosomal dominant disorder characterized by the occurrence of widespread over-growth of various cell types, all sharing a common neural crest origin. Cases occurring as a result of fresh mutations are relatively common. It is rare for any abnormality to be apparent at birth, and the disease usually manifests itself during childhood or in early adolescence. The earliest feature to appear are cutaneous 'café au lait' macules. These are well defined areas of light brown hyperpigmentation, usually oval in shape and more or less any size. They may occur at any site and their number gradually multiplies with increasing age. In about one third of patients, small freckle-like lesions of this type are found in the axillae; this important finding is virtually pathognomonic. Similar café au lait spots occur in *Albright's fibrous dysplasia*, though in this condition:

(1) they tend to be relatively few in number (usually less than 6);
(2) the edge of the lesion is often irregular;
(3) axillary lesions do not occur; and
(4) the giant melanosomes characteristic of neurofibromatosis are absent.

Multiple cutaneous tumours are the second principal feature of the disease. These usually occur when café au lait hyperpigmentation has been present for some years. When they first appear these tumours are soft and may have a violet hue. It feels possible to push the swelling through a button-hole like defect in the skin; this is a very characteristic clinical sign. Later on, the typical assortment of cutaneous and sub-cutaneous neurofibromata become evident.

Apart from the often devastating cosmetic disability caused by this disorder, its main importance lies in its internal effects. In childhood, neurological sequelae are of particular importance. A variety of tumours of the brain, spinal cord and peripheral nerves occur, and the most critical of these are acoustic neurofibromata which are often bilateral, optic and pontine gliomata which are usually malignant, and various tumour types causing spinal cord compression. Mental retardation, when present, tends to be mild. Another common effect in childhood is scoliosis, which may be of severe degree; the cause is not known. A number of endocrine disturbances occur, mostly in adulthood, though in children hypothyroidism and precocious or delayed puberty are the most common. Renal tubular rickets has been reported.

Tuberous sclerosis. This is another complex dysplasia transmitted by an autosomal dominant gene. Approximately half of all cases arise as a result of new mutations, and within affected families variability of expression may be marked. Tumour-like lesions occur in almost any organ, and these include cells of both mesodermal and ectodermal origin.

The disease can usually be diagnosed at birth by the presence of 'ash leaf' macules (Fig. 1.6a) which should be sought with the aid of a Wood's lamp. These are present in almost all affected infants at birth, and comprise oval hypopigmented macules varying considerably in size and number, and occurring at virtually any site on the trunk and limbs.

The typical facial lesions, which are in fact angiofibromata rather than sebaceous adenomata, are usually apparent by the age of 10 years, and often by the age of 4 years. They take the form of glistening, telangiectatic, yellow papules clustering around the nasolabial folds, the cheeks and the chin (Fig. 1.6b).

More unusual but also characteristic is the so called 'shagreen' patch, a soft irregularly lobulated plaque resulting from a naevoid dysplasia of dermal connective tissue (Fig. 1.6c). This lesion tends to appear during childhood on the lumbosacral area, though it may be found elsewhere and may occur in otherwise normal patients.

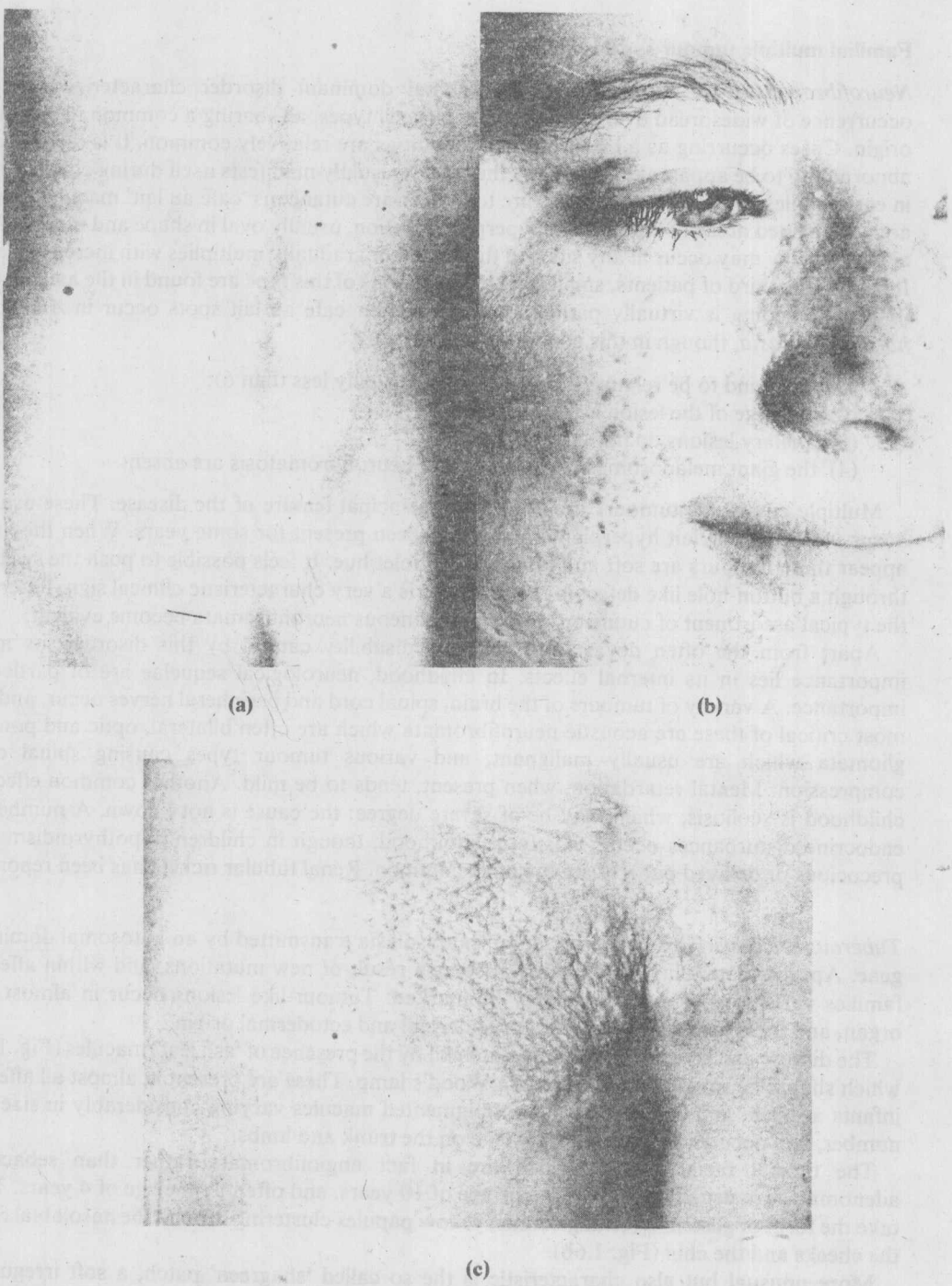


Fig. 1.6 Tuberous sclerosis. (a) 'Ash-leaf' macules on the back; (b) Facial angiofibromata; (c) 'Shagreen' patch over sacrum

The fourth typical cutaneous lesion, the periungual fibroma, does not usually appear until after puberty and is therefore less helpful in early diagnosis. Other naevoid lesions are commonly found on the skin, including café au lait macules, also in the mouth, particularly on the gums and palate.

Multiple gliomata occur in the brain, and mental retardation is present in about 70% of cases. Epilepsy almost invariably occurs at some time in mentally retarded patients, and in up to 70% of those of normal intelligence. Electroencephalogram abnormalities are common but the pattern of findings is very variable and non-specific. Intracerebral calcification, particularly in the region of the basal ganglia, occurs with increasing frequency throughout life, but is rarely evident in early childhood. There is little relationship between the severity of the cutaneous and cerebral lesions. Retinal gliomata are rarely symptomatic, but can be seen ophthalmoscopically in about 20% of patients. Cardiac rhabdomyomata are a significant cause of death in children in whom the classical triad of facial angiofibromata, mental retardation and epilepsy is fully manifest in infancy. Renal angiomyolipomata have also been described.

The basal cell naevus syndrome, also known as Gorlin's syndrome, is transmitted by an autosomal dominant gene of variable expressivity. It is a rare condition whose importance lies in the development by affected patients of multiple basal cell carcinomata. These tumours usually first appear around the time of puberty, on the trunk, neck and in the axillae, as well as in the more typical site for this tumour on the face. Other skin lesions such as epidermoid cysts are common. A characteristic finding are circular pit-like defects of the palmar and plantar keratin.

However, the most constant feature of the syndrome are odontogenic keratinizing cysts of the jaw, which often become symptomatic before the appearance of any skin lesions. Skeletal abnormalities are common and particularly characteristic are bifid ribs, and short metacarpals. Developmental abnormalities of the central nervous system, and defective renal tubular phosphate re-absorption also occur.

Gardner's syndrome. The most important feature of this well known though rare autosomal dominant condition is large intestinal polyposis. The polyps are pre-malignant and differ in no way from those found in familial adenomatous polyposis coli. In half the patients, no polyps are present before the age of 20 years. Since these polyps are rarely symptomatic before malignant change occurs, recognition of other features of the syndrome is crucial. The two important types of skin lesions are cysts and fibrous tumours. The cysts are epidermoid cysts and probably occur eventually in every case, though they may not do so in childhood. They occur principally on the scalp, face, and limbs, and may be numerous. Fibrous tumours of many histological varieties have been reported in the skin and the so-called desmoid tumour is particularly characteristic, typically appearing in the abdominal scar following colectomy.

Skeletal abnormalities are very common and take various forms, though osteomata are the most typical, affecting the facial bones and mandible in particular, but rarely present before puberty.

Inherited disturbances of pigmentation

Hypopigmentation

Oculocutaneous albinism is not uncommon in man and results from a failure of the melanocytes in skin, hair and eye to synthesize normal amounts of melanin; the condition is inherited as an autosomal recessive trait. The skin colour is very light and the hair whitish-yellow. The skin is unusually sensitive to solar radiation. In the short term, even minor exposure to sunlight results