

Remodelling

Estimation of the age of a fracture by this criterion is very difficult because initial deformity, the amount of callus produced, and age of the child are major variables. In the young infant with a stable, undisplaced fracture the remodelling process may be complete at three months while the older child with an angular deformity or a markedly displaced fracture may continue to remodel for two years.

Intracranial haemorrhage

Computed tomography is the primary diagnostic method for the evaluation of head trauma and its value in the management of the abused child is well documented.²⁵⁻²⁹ The appearance of haematoma on computed tomography changes slowly with time and is well understood.³⁰ Freshly clotted blood is of higher attenuation (whiter) than brain, becoming the same density as brain from two to four weeks, and less dense than brain after this time, approaching the density of cerebrospinal fluid by six weeks. Chronic subdural haematomas associated with ventricular dilatation may be difficult to distinguish from cerebral atrophy on computed tomography but magnetic resonance imaging (MRI) easily identifies it as chronic haematoma. MRI has been shown to be superior to computed tomography in the investigation of subacute or chronic head injury³¹ but the MRI appearances during acute haemorrhage are more complex, change rapidly during the first week, and have a wide differential diagnosis.³² Nevertheless, once haemorrhage has been identified on computed tomography, MRI can be used to assess its age more accurately if that is appropriate.

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Fungal skin infections

Fungal skin infections or superficial mycoses are common causes of skin disease in most age groups. They include three main diseases—dermatophyte or ringworm infections, candidosis, and pityriasis versicolor. There are significant differences, though in the epidemiology and clinical behaviour of these infections when they present in childhood. This is in part due to variations in rates of exposure in the case of dermatophytosis but in other examples may reflect real differences in the expression of host resistance.

Resistance to skin infection

The factors that determine the outcome of skin infection are divided into innate mechanisms and those that require the expression of immunological memory.^{1,2} Innate mechanisms include the capacity for epidermal cells to respond to damage to the stratum corneum by increased proliferation. Although scientific proof is lacking there is no reason to suppose that this capacity varies with age, except perhaps in photoaged skin. Likewise fungal inhibition due to reversible binding by unsaturated transferrin,³ present in sweat and serum, is not known to be affected by age. However the

presence of free fatty acids (FFAs) on the skin surface is known to affect fungi as those of medium chain length inhibit the growth of dermatophytes while facilitating the growth of pityrosporum yeasts. The composition of sebum containing these FFAs changes at puberty when the inhibitory moieties of medium chain length come to dominate. This is believed to be the explanation of the comparative rarity of scalp ringworm, tinea capitis, in postpubertal children whereas pityrosporum infections, such as pityriasis versicolor, are seen more frequently. FFAs appear to act by direct inhibition of fungal growth but they may also interfere with adhesion,⁴ the interaction between fungal cell wall receptors with keratinocytes, which is essential for subsequent penetration of the skin.

The other main processes determining the outcome of fungal invasion are antigen reception by Langerhan's cells,⁵ the accumulation of effector cells, principally neutrophils, the site of infection via the production of chemotactic factors by the fungi and the activation of T lymphocytes, predominantly helper cells.^{6,7} The means by which the latter effect fungal clearance is also not understood. Production of cytokines which amplify neutrophil killing or

epidermal growth as well as the activation of keratinocytes themselves to express HLA-DR and elaborate more cytokines such as interleukin-1 are probably equally important. The net effect is that patients with defective T lymphocyte function including AIDS patients are especially susceptible to most superficial mycoses, although unless this is accompanied by appropriate levels of exposure this defect will manifest itself by altered clinical expression of disease rather than by increased incidence. Dermatophytosis in the AIDS patient is an example where bizarre or extensive infections can occur but the diseases are not more common than in the appropriate control groups.⁸

Susceptibility to superficial mycoses may, in some cases, be genetically determined. There is evidence, for instance, for HLA linkage in the candida endocrinopathy syndrome⁹ and for an autosomal recessive mediated trait in the tropical infection, tinea imbricata.¹⁰

Dermatophytosis

The dermatophyte or ringworm fungi are mycelial organisms that produce long chains of cells, hyphae, in order to penetrate the stratum corneum.¹¹ They do this by the production of proteases which can break down keratin. These fungi cause exogenous infections originating either from other humans or animals or, more rarely, soil. They produce a characteristic group of infections known collectively as tineas whose clinical expression is largely determined by the site of infection, the identity of the organism, and the level of host response.

There are major differences in the epidemiology of infection caused by dermatophytes in children and adults. Foot infection including nail disease (onychomycosis) is rare in childhood¹² whereas it is the commonest pattern in adults. The reasons for this are not clear. Childhood nail infections, for instance, are seen occasionally, indicating that the nail is susceptible to attack. One possible reason is the lowered opportunity for exposure to a suitable environment for transmission of infection which is provided ideally by communal changing rooms. Tinea pedis begins to peak in incidence in the teens and early adult life.

The converse is true of tinea capitis, scalp ringworm, which with few exceptions, is a disease of childhood.¹³ There are two main sources of infection, animals (zoophilic infections) and other children (anthropophilic infections).¹⁴ With the former the main cause in most countries is the cat or dog ringworm, *Microsporium canis*, although cattle ringworm, *Trichophyton verrucosum* may also occur. Here exposure is sporadic depending on contact with an infected animal. Increased susceptibility in children, as mentioned previously, is the main reason for the development of the infection in childhood compared to adult life. In Europe, the Middle East and some US and Latin American cities *M canis* is now the dominant organism. By contrast ringworm infections caused by anthropophilic fungi are more common in Africa, India, and the USA.^{15 16} While host susceptibility may explain the prevalence of childhood infections to some extent exposure to an infected population is important. Carriage rates of organisms in clinically normal scalps in endemic areas may be as high as 4%.¹⁷ Some of these children may subsequently develop ringworm or the carrier status may be reversed. The combination of high rates of endemicity, mild clinical signs of infection, and inability to mount effective control measures has led to the perpetuation of hyperendemic foci for scalp ringworm. Typical causative organisms are *Trichophyton tonsurans* (USA), *Trichophyton soudanense* and *Microsporium audouini* (Africa), and *Trichophyton violaceum* (North Africa, Middle East, and the Indian subcontinent).

Scalp ringworm is easily treated with griseofulvin; most

topical antifungal treatments are ineffective on their own.¹⁸ Newer antifungal drugs such as itraconazole or terbinafine are effective, although their limitations are still not clear. Treatment of *M canis* infections with ketoconazole, however, is often unsuccessful.¹⁹ Griseofulvin is normally given in doses of 10 mg/kg daily for six to eight weeks. Though with zoophilic infections it is not necessary to keep children off school, some measure of caution is advisable with the anthropophilic fungi. Here the traditional method of control is griseofulvin combined with exclusion of infected children from school. There is no study that has examined the combined use of oral antifungals and topical applications such as ketoconazole shampoo as methods of limiting spread. With anthropophilic infections it is comparatively easy to screen for spread within classrooms as even though the organisms of the trichophyton unlike microsporium species do not usually fluoresce under ultraviolet (Wood's) light they can be grown from screening scalp samples. One method is the isolation of fungi from scalp massage brushes passed through children's hair.²⁰ Our practice is to treat infected individuals with griseofulvin and carriers, that is those with positive culture but no clinical or microscopic evidence of hair shaft invasion, with ketoconazole shampoo.

Cost in developing countries is often a contraindication to effective control. While the cost of griseofulvin is low compared with newer alternatives the price of a six week course for large numbers of children is high where resources are limited. However there is evidence that the use of single doses of up to 1 g of griseofulvin may be effective methods of eradicating infection in the majority of infected children.¹³ This method is also highly appropriate as the drug can be administered under supervision by a medical assistant or nurse.

Candidosis

Superficial infections affecting the skin and mucous membranes caused by species of the genus candida are very common in clinical practice. These fungi are normal commensals in healthy hosts, although disease is more likely where there is a defect in individual susceptibility. The carriage rates of candida in normal hosts range from 18% (range 4–66) in the mouth to 12% (range 0–33) in the gastrointestinal tract.² In children carriage rates vary considerably. For instance in newborn infants they may reach over 70% in those in neonatal intensive care units.

The commonest superficial infection is oral candidosis, which is seen in infants. Chronic oropharyngeal infection is much less common. Where it occurs it is important to consider the possibility of inherited or acquired immunodeficiency including AIDS and the rare infection chronic mucocutaneous candidosis (see below).

Chronic mucocutaneous candidosis (CMC) is a persistent superficial infection with candida species affecting principally the mouth, the skin, and nails.²¹ While originally it was hoped that a deeper understanding of the immunological basis of this syndrome would provide a potential answer to our knowledge of the nature of resistance to infection, the true nature of the immunological defect(s) in this condition is still elusive. It has become apparent though that some of the supposed defects such as reduced delayed type hypersensitivity and neutrophil killing of candida are reversible with successful antifungal treatment. This suggests that some form of immunomodulation by the organism itself may be involved and, for instance, an immunosuppressive effect of circulating cell wall mannan has been proposed as one possible mechanism.²² The expression of a human iC3b receptor-like epitope by *Candida albicans* is of interest in this context as the presence of antibodies to this substance in the serum of CMC patients has been shown to block iC3b

rosetting.²³ It has also been found that patients with CMC are susceptible to other cutaneous infections notably dermatophytosis and human papilloma virus infections and so the defect is not specific to candida.

The classification of CMC has also changed with time. The best known variant is one associated with the polyendocrinopathy syndrome, usually hypoparathyroidism and hypoadrenalism. This is inherited as an autosomal recessive trait.²⁴ Patients with this form generally have evidence of autoantibodies to other organs and some have involvement of other systems, for example pernicious anaemia or primary ovarian failure. In addition to this type some patients may have underlying hypothyroidism, inherited as an autosomal recessive trait. Other patients have no clear predisposition and are said to have sporadic type CMC. In addition in some families without endocrinopathy there is evidence of either autosomal recessive or autosomal dominant susceptibility.²⁵ All forms are usually clinically indistinguishable and range from mild to severe, although those with the sporadic form appear more likely to have extensive disease. Rare adult forms of the disease may also occur. It is important to screen children periodically for endocrinopathy because they may develop endocrine disease years after their first presentation with CMC. One further risk factor is the appearance of leukoplakia on the tongue that may progress to squamous carcinoma. However progression appears to be a particular problem in smokers. Other complications include bronchiectasis and potentially fatal bacterial septicaemia.²¹

Treatment of CMC is now easier, although relapse of infection is common. The drug ketoconazole¹⁹ is very effective and itraconazole²⁶ or fluconazole²⁷ are alternatives. In each case relapse of oral infection is common and it is important to stop treatment once the mouth is clear, instituting further treatment should this be necessary. The reason for this cautious approach is the risk of drug resistance developing where an azole is used continuously. It is not clear whether this will occur with all azoles but resistant candidosis has been described with both ketoconazole and fluconazole. In future studies it will be important to combine monitoring of changes in the patterns of drug sensitivity with genetic typing (karyotyping, restriction fragment length polymorphisms) to check that resistance has truly evolved in the original strains.²⁸ For severe infections other drugs such as intravenous amphotericin B can be used instead.

Pityrosporum infections

The pityrosporum yeasts are common skin commensals, although their emergence is usually delayed until after puberty.²⁹ They may cause disease in childhood in two ways. Firstly they have been isolated in large numbers from cradle cap eczema giving rise to the suggestion that they may be responsible for this condition.³⁰ The situation is analogous to that seen with adult seborrhoeic dermatitis. In addition these fungi have also been found to be a cause of septicaemia in premature neonates; intravenous feeding with intralipid appears to be a risk factor for infection.³¹ The route of infection is not clear but is thought to be via an intravenous line. The commonest disease caused by the pityrosporum yeasts, pityriasis versicolor, is rare in childhood.

Conclusions

While superficial mycoses are common in adults, infections in children present specific challenges. In the healthy child scalp ringworm remains a problem although in industrialised countries, with the exception of the USA, it tends to be a

sporadically occurring disease. In the developing world, however, the prevalence of infection is likely to persist in the face of other more pressing financial priorities. In the immunocompromised patient, including those with HIV infection and CMC, there are still a number of challenges, not only in treatment but also in our knowledge of basic immunopathological mechanisms. The new understanding of the function of epidermis as an immunologically active organ may provide some of the answers that have been so elusive.

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