Current Practice

DISEASES OF THE SKIN

Fungal Infections of the Skin

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Candida (Monilia) Infections

Infections of the skin by various species of the yeast *Candida*, commonly *C. albicans*, have become more frequent in recent years, and their recognition and treatment are important. These fungi are frequent commensals in animals and men, and are present in the alimentary tract and mucosa of many people. They may become pathogenic on the skin if local and general conditions become suitable. They prefer moist sites (Fig. 1), scaling cracked skin, and pockets between the nail fold and nail plate; and skin contaminated with sugar from glycosuria or from which bacterial competition has been removed by the use of antibiotics. General conditions favouring growth include debility and serious illness, diabetes, antibiotic and steroid therapy, and rarely hypocalcaemia. *Candida* infection is recognized by the well-defined edge of the inflamed area, which is often undermined, and the adjacent skin may show small superficial pustules, which rupture and leave a tiny circle with a raised edge. Evaluation of mycological reports on scrapings can be difficult, and a positive culture is of little significance unless fungal elements are found on direct microscopy.

FIG. 1.—*Candida* infection in the palm of a patient with rheumatoid arthritis. The thumb and finger deformities caused maceration in the fold of the skin between the thumb and palm.

General Considerations of Treatment

In the management of *candida* infection the various contributory factors must be taken into account, and indeed if the underlying general health and local skin environment can be improved the *candida* may well clear without any specific treatment.

Nystatin, an antifungal antibiotic, is now the most commonly used drug in *candida* infections. It has no effect on

ringworm fungi. When taken by mouth very little is absorbed, and the tablets are of value only in candidiasis of the alimentary tract. Nystatin is not stable in contact with water, and is therefore used on the skin in ointment form. When an underlying eczematous eruption is present nystatin ointment can be used with equal parts of hydrocortisone or one of the more powerful steroid ointments. If the addition of an antibiotic or bactericidal substance is required Triadocortyl (triamcinolone, neomycin, gramicidin, and nystatin), or Nystaform-H.C. (hydrocortisone, clioquinol, and nystatin) may be used.

Amphotericin B is another effective anti-*candida* antibiotic. As a topical preparation it does not seem to have any significant advantage over nystatin. In severe or systemic infections it can be given by daily intravenous injections, but it is highly toxic, and this limits its practical use.

There are a large number of chemical agents effective against *candida*. Gentian violet and the dyes are not now used to any extent because of the staining effect on clothing and skin. Clioquinol (Vioform) and related substances, hydrargaphen (Penotrane), and disulphamethylfuchsonium sulphionate (Pruvagol) are all used, but are less effective than nystatin.

Common Clinical Conditions

INTERTRIGINOUS CANDIDIASIS.—Usually there is an underlying seborrhoeic eczema or occasionally a flexural psoriasis (Fig. 2), and general and local treatment should be directed to this. The most useful application is a steroid combined with nystatin or a quinoline derivative. Patients with candidiasis of the vulval area may have an associated vaginal candidiasis, which will require treatment with nystatin pessaries. Infection round the anus may be secondary to candidiasis of the alimentary tract, and nystatin should be given by mouth. *Candida* grows very readily on a pre-existing rash in the napkin area in infants (Fig. 3). This is usually due to the presence of ammonia derived from the urine urea, but a seborrhoeic eczema or a psoriasis-like eruption may be present, and is often colonized by *candida*. It has become common for these eruptions to be treated with anti-*candida* agents combined with steroids, but it must be realized that steroid absorption will occur, and may be quite marked if the area is large and weeping and if one of the more powerful steroids is used. Babies with obvious "steroid facies" have been seen after such treatment.

CHRONIC PARONYCHIA.—This common condition is due to the skin of the nail fold becoming separated from the nail plate owing to various factors, including maceration from occupations requiring much contact with water and trauma from excessive manicuring and picking habits. The resultant gap is very often infected with *candida*, and the consequent swelling of nail fold may help to keep the gap open. It is seen more commonly in patients with poor peripheral circulation, and with nail-fold skin which is poorly adherent to the nail. The nail plate often

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grows out irregularly owing to the inflammatory changes adjacent to the nail bed, but in some cases the nail itself—particularly at the edges—is invaded by candida. The paronychia gap is usually infected with other organisms, including staphylococci, causing at times acute episodes of inflammation.

Treatment consists in careful explanation and avoiding the maceration and trauma as much as possible. The usual household rubber gloves if worn for long periods probably do more harm than good because of the maceration provoked. More-loose-fitting gloves of the "Glovelies" pattern are better, but should be worn only for periods up to 10 minutes at a time. Nystatin ointment used at least four times a day round the nails will usually clear the candida infection. Hydrargaphen

treatment an anti-candida preparation may help, provided the underlying condition is dealt with.

Ringworm Infections

With the development of mycology it is now difficult to discuss ringworm infections of the skin without brief consideration of some of the different species of ringworm fungi common in this country and their epidemiology. The common ringworm fungi can be divided into two groups according to their natural habitat: those which are exclusively human parasites (the anthropophilic species) and those which are primarily parasites of animals (zoophilic) but can be contracted by man from their natural host.

In ringworm of human origin undefined factors in the receptivity of the skin are very important; there are many instances of a husband or wife in whom the fungus has been present for many years without the partner's becoming infected, though the children of such a couple often contract the disease. Also one hand or foot may be involved for many years without the condition developing on the other limbs. The constant presence of inoculum in a family or group where one or more persons are infected must obviously increase the likelihood of cross-infection.

Ringworm of animal origin is usually contracted only by direct or indirect contact with the animal, and seldom from another human case. Most zoophilic ringworm fungi are confined to one animal host, so that the source of a human infection can be traced once the identity of the causal fungus is known.

An accurate mycological diagnosis is important in determining the source of infection, treatment, general management, and prognosis. Scrapings can be taken easily and sent to a mycologist or to the local laboratory, where, if mycological facilities do not exist, they can be sent on for microscopy and culture. The scales are scraped off with a scalpel blade on to a piece of paper, preferably black, to show up the tiny pieces of skin.

Anthropophilic Species

TRICHOPHYTON INTERDIGITALE.—This is the most common cause of foot and nail ringworm in this country, though because the symptoms it produces are usually mild and limited

FIG. 2.—Candida infection secondary to a flexural psoriasis. Satellite lesions are seen below the patient's right hand.

tincture (Penotrane) by day and chlorquinaldol (Steroxin) at night is a useful combination, and will be more likely to control any secondary bacterial infection. In an occasional case eczematization round the nail fold may play a part, and in these a steroid in combination with an anti-candida preparation may help.

ANGULAR STOMATITIS.—This common condition is usually due to an overlap of the mouth angle skin secondary to an edentulous state in old age, sagging of the cheeks, or an exces-

FIG. 3.—Candida infection secondary to an ammonia napkin irritation. A group of typical satellite lesions are seen particularly on the left side of the abdomen, just above the edge of the main eruption.

sive closing of the bite from faulty dentures. It may be due to an iron-deficiency anaemia or sometimes to a general eczematous tendency; but in Great Britain almost never a vitamin-B deficiency. Whatever the cause, candida are common secondary invaders, and may play a part in preventing healing. In the

FIG. 4.—*Epidermophyton floccosum* infection in a 1½-year-old girl who had previously had a long-standing ammonia napkin irritation. The father had this fungus involving his toe-webs.

in extent it is seen less often than *T. rubrum* in dermatological clinics. It is usually confined to the toe-webs and feet, rarely spreading to the legs, groins, or hands.

TRICHOPHYTON RUBRUM.—The incidence of infection with this fungus is increasing rapidly. Infection usually starts in the toe-webs, and from there spreads to the toe-nails and other parts of the body. It may involve the groins and anogenital areas, and an important property is its ability to spread over the general skin surface, particularly over the hands and feet, where it occurs as a scaling eruption with often only slight erythema. It can thus be difficult to distinguish from eczema, though the history of gradual spread, a well-defined edge, localized distribution, and association with nail ringworm would help. In some cases the fungus may be infecting pre-existing eczematous areas. The final diagnosis may well have to await the mycological examination of scrapings.

EPIDERMOPHYTON FLOCCOSUM.—This fungus is the least common of the human ringworm fungi, and usually affects only the toe clefts and groins. It rarely involves nails, and may appear in such unexpected sites as, for example, the hands, beneath the breasts, in the axillae and anogenital region, sometimes secondary to a pre-existing eruption involving these areas (Fig. 4).

Zoophilic Species

MICROSPORUM CANIS.—Scalp ringworm in children, which up to 15 years ago was of much importance, is now uncommon, and the human type (*M. audouini*) is a rarity in this country. *M. canis* is acquired from cats and dogs, commonly a kitten, and leads to patches of redness and scaling with partial hair loss and broken hairs, sometimes with a pustular reaction. Exposed sites other than the scalp may be involved. Hairs infected by the fungus fluoresce under Wood's light.

TRICHOPHYTON VERRUCOSUM.—This is the cattle ringworm fungus, and though there is commonly a history of direct or indirect contact with cows or calves it may turn up under unusual circumstances and in sites other than the usual exposed areas. A patient recently seen had not been out of the city, but had ridden for a short time in a cattle lorry, and in another the infection involved the vulval area (Fig. 5). Particularly on the scalp and beard, a severe pustular eruption occurs (kerion), and is often misdiagnosed as a primary staphylococcal infection,

FIG. 5.—*Trichophyton verrucosum* (cattle ringworm) involving the vulva.

causing impetigo or boils. The hairs readily fall out over the area involved (Fig. 6). The uncommon "toxic" eruption, consisting of widespread follicular papules, which can occur with other fungi, is more often seen in association with severe cattle ringworm.

TRICHOPHYTON MENTAGROPHYTES.—Members of this group occur naturally on small mammals, both domesticated and wild, and animals carrying them may have no apparent lesions. Small laboratory animals, pet mice, wild rodents, and hedgehogs are all potential hosts, and human infection can often be traced to direct or indirect contact with these. Lesions usually occur on exposed parts of the body, and may be vesicular or pustular (Fig. 7).

FIG. 6.—*Trichophyton verrucosum* (cattle ringworm) involving the scalp.

FIG. 7.—*Trichophyton mentagrophytes* var. *erinacei* acquired from handling baby hedgehogs. Note pustules and similarity to a secondary infected pompholyx.

General Considerations of Treatment

The most important drug is griseofulvin, which acts on all ringworm fungi mentioned, but has no effect on *Malassezia furfur* (pityriasis versicolor), *aspergillus*, or *candida*. This latter fact needs the greatest publicity, as the majority of cases of chronic paronychia referred to dermatologists have been given completely useless prolonged courses of griseofulvin. It is given by mouth, is absorbed well, and appears to act by modifying keratin, so that the fungus will not invade the keratin laid down after the commencement of treatment. With ringworm of non-hairy skin, some three to four weeks' treatment is therefore sufficient. When hair is involved the infected part can be removed when the newly grown non-infected hair is long

enough, and in scalp ringworm treatment is often continued for two to three months. Nails obviously take longer to grow non-infected keratin, and a period of treatment of eight to twelve months is often necessary for finger-nails and one to two years for toe-nails. Toe-web ringworm may improve, but very rarely is infection cleared from this site by griseofulvin.

The dose of griseofulvin is important. In an average case the fine particle preparation Grisovin-F.P. is given in a dose of 250 mg. twice daily, preferably after meals. Some cases do not respond unless this dose is doubled, and smaller doses are often ineffective. The older preparation of griseofulvin is still available in tablets of 250 mg., and this can lead to confusion over the dose given.

Apart from the rare effect of altering porphyrin metabolism serious side-effects are very unlikely. Headaches, a curious distended feeling of the face, epigastric discomfort, and skin eruptions, including actinic sensitivity, may make it necessary to stop treatment.

The position with regard to topical fungicides is unsatisfactory. The very fact that there are so many different preparations available suggests that none is really effective. Ung. acid. benz. co. *B.N.F.* (modified Whitfield's ointment), is still one of the most useful. New preparations are continually being marketed, and two of the latest are Variotin and Tolnaftate. In common with many older preparations they appear to have excellent in-vitro effects on fungi, but there will have to be considerably more clinical evidence than is yet available before it is known whether they have a really worth-while clinical effect.

The persistence and tendency to recurrence vary from fungus to fungus, and may be linked to the presence of some focus which is impossible to eradicate, such as infection of the nails and toe-webs. *T. rubrum* and at times *Epidermophyton floccosum* can be extremely difficult to clear up completely. On the other hand, the ringworm infections acquired from animals usually clear completely, and further attacks are uncommon.

There is considerable debate about the practice and value of isolation of patients and treatment of fomites. The infectivity of the present common ringworm fungi is low, and elaborate precautions are unpractical. The regular use of an ointment will reduce the dissemination of infected scale, and the use of personal towels for drying and standing on in the bathroom is advisable. Obvious cases should not use the public swimming bath until treated, but a much more important consideration in this connexion is the facilities to wash down the sides of the bath and changing-room regularly. Paddling in a foot bath with added fungicidal chemical, prior to using the swimming bath, is of no value. Children with scalp ringworm are usually kept away from school until clear, but at the present time the human type is uncommon, and that acquired from cats is much more likely to be spread in a community by the cat than from patient to patient. Diagnosis of suspected cases in children and animals is helped to a great extent by looking for fluorescence under Wood's light.

Common Clinical Conditions

TOE-WEB RINGWORM.—In various surveys some 30% to 90% of normal people have been found to have some abnormality of the skin between the toes. Of these, from 75% to 95% have no ringworm fungus present on repeated examination. Therefore most cases of what is loosely called athlete's foot are not basically a ringworm infection, though in the more severely affected cases the incidence of fungus infection will be higher.

The cause of non-ringworm athlete's foot is debated, but many cases may be due to simple maceration between the toes, and some may be an intertriginous eczema. Other organisms,

including staphylococci and candida, have been isolated, but could often be secondary invaders, although the *Corynebacterium minutissimum*, which is the cause of erythrasma, may well have a primary infective role. Apart from the possibility of an intertriginous eczema simulating a fungus infection toe ringworm can be associated with a local eczematous change. There is debate whether this represents a true allergic response to the fungus or not. There is also disagreement about the nature of the association of an eczematous pompholyx eruption on the hands with ringworm of the toes, and in recent years such an eruption on the hands is less frequently considered to be due to a toxic allergic response to the toe ringworm.

These considerations have considerable practical importance on the management of athlete's foot. Scrapings will usually indicate whether or not ringworm fungus is present. Mild cases of toe-web ringworm will do very well on a simple dusting powder, and one containing undecylenic acid is often used. Ung. acid. benz. co. *B.N.F.* has also a place in treatment. More severe cases, particularly if associated with itching and weeping, often do well on a combined steroid and quinoline derivative, such as clioquinol hydrocortisone ointment (Vioform—hydrocortisone). Few dermatologists recommend disinfection of footwear and socks, but in some cases of *T. rubrum* infection of toes and nails, if an all-out attack is undertaken, including removal of nails, it would be logical to disinfect or discard footwear.

GROINS AND ANOGENITAL AREA.—The first problem in this area is one of diagnosis. Seborrhoeic eczema and flexural psoriasis involve the crevices of the folds. The latter condition will have a well-defined edge, and both may be secondarily infected with candida. Erythrasma has a superficial scale and slight redness, with a well-defined edge, and commonly involves the groins and adjacent thigh; examination under Wood's light reveals a salmon-coloured fluorescence. Ringworm usually affects the area of thigh just distal to the fold, and has a well-defined scaling edge. However, in some cases an accurate clinical diagnosis is impossible, and may rest on mycological findings. To make matters more difficult in some cases of ringworm infection there has been a pre-existing eruption, usually of the seborrhoeic eczema type. Many local fungicides are therefore not tolerated and may give rise to an eczematous response. If the condition appears to be uncomplicated ringworm infection, apart from griseofulvin by mouth, local treatment with half-strength ung. acid. benz. co. *B.N.F.* applied gently may help. If there is an eczematous element a combined steroid quinoline derivative cream might be a more effective local application. There is likely to be an associated ringworm of the toes, which will require local treatment to try to prevent relapses.

CATTLE RINGWORM.—The reaction and pustulation seen with cattle ringworm are largely due to fungus, but there is sometimes a secondary staphylococcal infection, and treatment with an antibiotic for a few days, in addition to griseofulvin, will occasionally be indicated. Locally, compresses of normal saline applied every few hours may help, and later ung. acid. benz. co. *B.N.F.* can be used.

TRICHOPHYTON RUBRUM INFECTIONS.—Patches on skin often respond well to griseofulvin, together with ung. acid. benz. co. *B.N.F.* locally. The difficulty is, however, that the eruption is likely to relapse, as the infection may remain in the toe clefts and in nails. Toe-web infection is not usually cleared by griseofulvin, and nail infection may well take up to eight to twelve months of continued griseofulvin for finger-nails and one to two years for toe-nails before clearing. Indeed, after all this time the fungus can still often be isolated, and many dermatologists doubt the wisdom of these prolonged treatments of griseofulvin for such infection in toe-nails and toe-webs. Short courses of six to eight weeks, repeated when necessary, will usually keep eruptions under control. Persistently infected nails may be removed during the course of griseofulvin, and some dermatologists claim success with these measures.

Tinea versicolor (*Malassezia furfur*)

The eruption from this fungus usually involves the upper trunk, and consists of numerous patches of a light red-brown colour with superficial scaling and well-defined edges. The patches are more clearly demonstrated by examination under Wood's light. After a period of exposure in sunny weather the surrounding skin becomes brown, but the patches infected with the fungus do not pigment so readily and are much lighter in colour. The fungus can easily be demonstrated by examination of scrapings. It does not respond to griseofulvin, but clears quickly with the use of local fungicides, including ung. acid. benz. co. *B.N.F.*, applied in a thin smear twice per day. The infection will readily relapse, and the use of the ointment just at night for a prolonged period after apparent clearing is advisable.

Non-dermatophytes

Various species of *Aspergillus*, *Scopulariopsis brevicaulis*, and other non-ringworm fungi may affect nails already badly damaged by trauma, disease, or old age, but they never attack the adjacent skin. They are insensitive to griseofulvin, and in the nails are rarely cleared by local fungicides. The *aspergillus* fungi may also play a part in otitis externa and infection of postoperative aural cavities. In these sites the fungi will usually clear with frequent aural toilet and application of local fungicides.

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TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Propranolol

This drug is marketed under the name of Inderal by Imperial Chemical Industries Ltd.

Chemistry and Pharmacology

Propranolol is 1-isopropylamino-3-(naphthyl-2-yl)propan-2-ol hydrochloride. It is a specific adrenergic beta-receptor blocking drug. Pronethalol (Alderlin) was the first drug introduced for this purpose, but it was found to be carcinogenic to mice. It has been replaced by propranolol, which is not only free from this hazard but is also more potent. Although propranolol is primarily an adrenergic antagonist it does have other, though less important, pharmacological properties, including a quinidine-like action on the heart.

Sympathetic innervation in man and the effects of circulating catecholamines are mediated by two types of receptor. Alpha-receptors are concerned with smooth-muscle excitation. It is predominantly alpha-receptors that are stimulated by nor-adrenaline and antagonized by phenoxybenzamine (Dibenyline). Beta-receptors are concerned with the excitatory effects on cardiac muscle, and are stimulated by isoprenaline and blocked by propranolol. Adrenaline stimulates both alpha- and beta-receptors. Thus the increase in heart rate and power of myocardial contraction produced by sympathetic stimulation can be prevented by blockade of the beta-receptors. The sympathetic nervous system was so called because it co-ordinated bodily functions and teleologically it was concerned with the response to emergency situations in the external environment—the preparation for fight or flight. The mobilization of carbohydrate reserves and the increase in blood-pressure and heart rate were preparatory measures. However, this response results in excessive and wasteful oxygen consumption by the heart. Opposing this haemodynamic response to stress and exercise may thus be of benefit to patients whose coronary circulation is restricted, for it will have an "oxygen-sparing" effect.

Nevertheless, in patients with severe impairment of myocardial function the drive of the sympathetic nervous system is necessary to maintain cardiac function. If in such patients adrenergic blockade removes this stimulus, cardiac failure will be provoked or aggravated. Severe impairment of myocardial function thus provides the main contraindication to treatment with propranolol.

Indications

Because propranolol modifies the haemodynamic response to stress and exercise, it may help patients with angina of effort. Indeed, it is in the treatment of angina that propranolol has its greatest therapeutic application. Numerous trials have confirmed its effect, and it is the drug of choice for patients who do not respond to conventional methods of treatment.

The response of patients with angina is, however, variable, and the effect on any individual patient is unpredictable. Nervous patients in whom angina is readily provoked by anxiety are most likely to benefit.

As the sympathetic beta-receptors are concerned with excitatory effects in cardiac muscle, it might be expected that their inhibition would be of advantage in cardiac arrhythmias. The therapeutic application of this action is limited, but propranolol does appear to be of undoubted value in the management of arrhythmias due to digitalis intoxication and in certain patients with auricular fibrillation where adequate control of the ventricular rate cannot be obtained by digitalis alone. Theoretically, adrenergic inhibition might be expected to reduce the incidence of the fatal arrhythmias which complicate myocardial infarction, but unfortunately there is no evidence that propranolol influences the mortality of cardiac infarction, and there is a risk that heart failure may be produced.

Emotions are expressed through the autonomic nervous system, and anxiety states are associated with increased secretion of catecholamines. Propranolol may therefore have a place in the treatment of anxiety, especially when the symptoms are related to the cardiovascular system. Improvement in the effort syndrome following propranolol has been reported, but the place of propranolol in the management of anxiety states has not yet been adequately assessed.

Adrenergic inhibition is of obvious importance in the management of patients with phaeochromocytoma. Propranolol should be used in combination with an alpha-receptor antagonist, such as phenoxybenzamine. These drugs are indicated in the preparation of patients with phaeochromocytoma for surgical operations and for maintenance therapy in inoperable cases.

Toxic Effects

Nausea, vomiting, tiredness, dizziness, and diarrhoea are occasional side-effects, but the overall incidence is less than 2%, and it is rarely necessary to stop treatment. Visual hallucinations, paraesthesiae, and purpura have been recorded occasionally. Increases in blood urea and serum transaminase