



THE PRESIDENT  
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**Proposals for the revision of the WHO  
essential drugs list  
concerning drugs that are used  
to treat skin diseases**

***International League of Dermatological Societies working group:***

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## **Introduction**

While skin diseases (SD) are a very common reason for visiting a doctor in developed countries, in recent years certain SD have been identified as significant health problems in less developed areas, particularly in children. This is due to their large prevalence and incidence in the general population, as well as to the high level of demand of local populations for treatment of many of these conditions (as shown by the fact that SD are a major reason for visiting a primary health centre in many areas). In addition their management results in disproportionately high costs compounded by ineffective management. With a view to improving the management of the most common SD, the opinion of the ILDS was sought as part of the process of revision of the current WHO list of essential drugs, specifically those used in the management of dermatological conditions in children.

We focused on the 10 diseases that are most prevalent in children and that are the cause of most concern to patients, taking into consideration the disease burden to both individuals and the community. In order to guide our choice, we considered the available epidemiological data (taken, in particular, from a recent exhaustive review on the topic [1]), on SD in the general population as well as in specialized and non-specialized health centres. This work also reflects the opinion of experts on the ILDS advisory group. We have focused on those disorders that are seen in the widest range of countries but we are aware that certain conditions, not on this list, may, in certain areas, deserve to be treated with a similar measure of priority (e.g., albinism, tropical ulcers).

The 10 disorders selected are the following: pyoderma, scabies, lice (head lice and body lice), tinea capitis, other superficial mycosis, herpes (HSV 1 and 2), eczema (dermatitis), prurigo due to insect bites, disorders of keratinisation (psoriasis and ichthyosis), and acne vulgaris.

## **References**

1. Epidemiology and management of common skin diseases in children in developing countries. Discussion papers on child health. WHO/FCH/CAH/05.12.  
[[http://www.who.int/child-adolescenthealth/publications/CHILD\\_HEALTH/DP/Topics\\_5/p](http://www.who.int/child-adolescenthealth/publications/CHILD_HEALTH/DP/Topics_5/p)].

## Methodology

The point of reference was the current WHO essential drugs list (March 2005 revised), focusing on those drugs that are used exclusively for dermatological disorders in children (e.g., topical agents), and drugs that have other indications but that are used in dermatological diseases (e.g., antibiotics). Drugs with a specific dermatological target included in the current WHO list but used for diseases that occur exclusively in adults (fluorouracil ointment, tar) have not been discussed in the following sections. The process of defining essential drugs followed a logical sequence, starting with a detailed consideration of the retention of drugs on the current list. In addition, we have proposed the addition of some drugs in view of their clinical relevance, taking into consideration the level of evidence, their usefulness, worldwide availability cost (where possible we have suggested inexpensive drugs), cost-effectiveness, and the availability of generic versions. Finally, we have suggested removal of a few drugs from the list, either because of their low efficacy, or because of frequent or unacceptable side effects.

The decision to consider drugs for inclusion was taken after an exhaustive review of the literature of the diseases targeted, including recent meta-analyses when available. For disorders where such data were lacking, we relied on experts' opinions or, occasionally, on unpublished data using methods judged to be valid by the group.

## Pyoderma

**Definition** - The term is a synonym for pyogenic infection of the superficial layers of the skin, i.e., infection due to ubiquitous bacteria such as *Streptococcus pyogenes* and *Staphylococcus aureus*. There are different clinical patterns but all have in common bacterial aetiology, prognosis, and management; the most common in children is impetigo, a contagious superficial skin infection characterised by erosions covered by honey-colored crusts, or sometimes by bullae.

Pyoderma is one of the most common skin disease throughout the world, particularly in tropical developing countries where key predisposing factors are hot climate, humidity, poor hygiene, reduced access to water, and overcrowding. Prevalence of pyoderma is very high in children in most tropical developing areas, and it is by far the leading skin disease encountered in primary care health centres in such areas.

Impetigo may be primary or secondary, reflecting superinfection of other skin disorders, e.g., scabies, atopic dermatitis, prurigo, or head lice. In some cases, varying from less than 1% to 10%, glomerulonephritis may occur; but very rarely this complication may be epidemic in communities. Pyoderma may also occasionally cause bacteremia, particularly in young infants [1].

**Aims of treatment** - To accelerate cure, and to prevent spread of infection and (although rare) systemic complications (glomerulonephritis, bacteremia).

**Evidence** - Two systematic reviews about treatment of individual cases are available [2,3]. There is no good evidence to support the use of disinfectants alone, although they are widely used and their efficacy in milder cases probable. For cases with

limited involvement, the topical antibiotics mupirocin and fusidic acid have similar efficacy. Topical mupirocin was found to be significantly better than oral erythromycin in pooled analysis. However, topical antibiotics are expensive and not available in many areas over the world. For extensive lesions, systemic antibiotics appear to be the only reasonable treatment option. Many RCTs of systemic antibiotics deal with a range of infections including impetigo, but only a few report separate results for pyoderma. Two RCTs compared penicillin and erythromycin, both concluding that erythromycin was more effective. Moreover, cloxacillin was significantly superior to penicillin in two studies. It should be noted that the bacteriological profile of pyoderma in tropical developing countries may noticeably differ from that encountered in developed countries, with *Staphylococcus aureus* predominating in the latter while *Streptococcus pyogenes* is still very prevalent in the former. Amoxicillin has been shown in a recent RCT to be as efficacious as erythromycin in the treatment of pyoderma in Mali [4]. Erythromycin may rarely cause adverse cardiological events.

No evidence is available about therapeutic strategies to limit dissemination of the disease in the community. Soap, associated with hand washing, has been shown to have a preventive effect, but only if used in combination with intensive educational programmes (5).

### References

1. Mulholland EK., Ogunlesi OO., Adegbola RA., Weber M., Sam BE., Palmer A., Manary MJ., Secka O., Aidoo M., Hazlett D., Whittle H., Greenwood BM. Etiology of serious infections in young Gambian infants. *Pediatr. Infect. Dis. J.* **18**, S35-41 (1999).
2. George A. *et al.* A systematic review and meta-analysis of treatments of impetigo. *Br. J. Gen. Pract.* **43**, 247-52 (2003).
3. Koning S. *et al.* Interventions for impetigo. *Cochrane Database Syst. Rev.* **4**, CD003261 (2004).
4. Faye O., Hay RJ., Diawara I., Mahé A. Oral amoxicillin versus oral erythromycin in the treatment of pyoderma in Bamako, Mali: an open randomized trial. *Int. J. Dermatol.* **46**, S19-22 (2007).
5. Luby SP., Agboatwalla M., Feikin DR., Painter J., Billhimer W., Altaf A., Hoekstra RM. Effect of handwashing on child health: a randomised controlled trial. *Lancet* **366**, 185-7 (2005).

### Scabies

**Definition** - Scabies is an itchy condition associated with skin infestation by the mite, *Sarcoptes scabiei* [1]. Transmission of mites occurs during relatively prolonged skin to skin contact. The spread of the disease increases with overcrowding. It is very common in tropical developing countries, with a total annual number of cases in the world that has been grossly estimated as 50 to 300 millions. It is a very common reason for presentation at a health centre in many tropical developing areas. Superinfection (secondary pyoderma) is common when hygiene is poor and where there is little access to water; this may lead to the same complications as primary



pyoderma (e.g. glomerulonephritis). Epidemics in small communities, such as jails, refugee camps, or villages, can severely impair normal social relations within these communities.

**Aims of treatment** - To alleviate itching and to eliminate infestation in individuals affected, and to prevent superinfection, as well as spread within the community.

**Evidence** - Two systematic reviews are available, mainly focusing on treatment strategies to control disease in individual patients and looking at short term results [2,3]. The evidence indicates that permethrin is more effective than crotamiton, lindane and malathion, and that it is associated with fewer side effects than lindane. Lindane has been withdrawn from some markets as it has the potential to cause neurotoxicity where it has been used incorrectly. 12-25% benzyl benzoate is also widely used, but there is a lack of data on its efficacy compared with other scabicides, although there is global agreement that it is equivalent to, or slightly less efficacious than, permethrin. Systematic treatment of close or family contacts is an essential complementary procedure that is necessary in order to avoid reinfestation. Limited data are available concerning the use of oral ivermectin, especially in children; it is contra-indicated during pregnancy. Oral ivermectin has not yet been widely licensed for use against scabies, except in France. In a RCT (85 people), topical permethrin was more effective than oral ivermectin at 14 days, but a second dosage at day 14 showed a 95% efficacy at day 28 [4]; in another RCT (181 people), ivermectin was less effective than 12.5% benzyl benzoate at 14 and 28 days [5]. While the level of efficacy of oral ivermectin compared to topical scabicides in individual cases is insufficiently documented, nor has the optimal dose regimen been established (1 or 2), it has been shown to be very useful in the control of epidemics in small closed communities. There is also evidence that oral ivermectin given to treat scabies in an epidemic context may reduce the occurrence of glomerulonephritis [6]. There are limited data concerning strategies to control dissemination in the community. A programme to control scabies among the whole Kuna Indian population in the small San Blas islands of the Republic of Panama documented that simultaneous treatment of the whole population with permethrin 5% cream caused the prevalence to fall from 33% to less than 1%; as long as continued surveillance and treatment of newly introduced cases was maintained, prevalence of scabies remained below 1.5% for over 3 years [2].

### **References**

1. Chosidow O. Scabies. *N. Engl. J. Med.* **354**, 1718-27 (2006).
2. Walker GJA., Johnstone PW. Interventions for treating scabies. In: *The Cochrane Library*, Issue 3, 2005. Chichester, UK: John Wiley & Sons, Ltd. Search date 1999; primary sources Medline; Embase; records of military trials from UK, USA, and Russia; and specialist register of the Cochrane Diseases Group.
3. Strong M., Johnstone PW. Interventions for treating scabies. *Cochrane Database Syst Rev.* **3**, CD000320 (2007).
4. Usha V., Gopalakrishnan Nair TV. A comparative study of oral ivermectin and topical permethrin cream in the treatment of scabies. *J. Am. Acad. Dermatol.* **42**, 236-40 (2000).



5. Ly F., Caumes E., Ndaw C., Ndiaye B., Mahé A. A randomised controlled, open trial comparing oral ivermectin and two modalities of applications of 12.5% benzyl benzoate for the treatment of human scabies in Dakar, Senegal. *Bull. World Health Organ.* (submitted).
6. Lawrence G., Leafasia J., Sheridan J., Hills S., Wate J., Wate C., Montgomery J., Pandeya N., Purdie D. Control of scabies, skin sores and haematuria in children in the Solomon islands: another role for ivermectin. *Bull. World Health Organ.* **83**, 34-42 (2005).
7. Taplin D., *et al.* Community control of scabies: a model based on use of permethrin cream. *Lancet* **337**, 1016-8 (1991).

## Head and body Lice

**Definition** - Head lice is an infestation caused by the blood-feeding insect, *Pediculus humanus var capitis*. In some communities low socioeconomic status is a risk for this infestation, possibly due to inability to treat it effectively. It has worldwide prevalence, sometimes resulting in high rates of infection, although there is much more public concern in Northern developed countries than in the South. Bacterial superinfection may occur, although not commonly. Body lice potentially transmit serious bacterial infections such as endemic typhus, particularly if there is gross overcrowding such as in refugee camps.

**Aims of treatment** - Clearance of the insect from individual patients, and disease control in the community.

**Evidence** - There are two systematic reviews [1,2]. Permethrin and malathion are effective against head lice when resistance is not present. There is limited evidence for the efficacy of other insecticides such as d-phenotrin. Resistance to pyrethroids may occur [3]. In a RCT (253 people), dimeticone lotion was compared with d-phenotrin; no significant difference was found in the number of individuals free of lice at 14 days. Dimeticone may represent a treatment option when other modalities have failed. Oral cotrimoxazole should not be used because there is both little evidence of efficacy and a risk of severe cutaneous drug reaction. There is insufficient evidence for combing and wet combing with conditioner (i.e., bug-busting). Analysis of a trial using oral ivermectin is in process.

In the case of body lice, apart from treatment with oral antibiotics indicated because of associated bacterial infection, washing clothes may be sufficient. Permethrin and gamma benzene hexachloride are also efficacious.

## References

1. Dodd CS. Interventions for treating head lice. In: *Cochrane Database Syst. Rev.* **2**, CD001165 (2001).
2. Vander Stichele RH. *et al.* Systematic review of clinical efficacy of topical treatments for head lice. *BMJ.* **311**, 604-8 (1995).



3. Chosidow O. *et al.* Controlled study of malathion and *d*-phenothrin lotions for *Pediculus humanus var capitis*-infested schoolchildren. *Lancet* **344**, 1724-7 (1994).

## **Tinea capitis**

**Definition** - Tinea capitis (scalp ringworm) is a fungal infection of the scalp skin and hair caused by *Dermatophytes* (mainly the genera *Trichophyton* and *Microsporum*). The clinical hallmark is the presence of single or multiple patches of hair loss, which may be accompanied by signs of inflammation. It is seen predominantly in pre-pubertal children in disadvantaged communities. It is contagious amongst children, in whom it is highly prevalent in many tropical developing countries, particularly sub-Saharan Africa. Bacterial superinfection and other significant sequelae (such as kerion) are uncommon. Spontaneous remission most commonly occurs around puberty, and represents the most common outcome in developing countries, although scarring and permanent hair loss can result from this infection.

**Aims of treatment** - To achieve complete clearance with minimal sequelae in individual patients, and to prevent spread to other children as well as re-infection.

**Evidence** - A Cochrane systematic review is in press and data have been summarised in a book chapter [1]. The evidence indicates that griseofulvin for 6-8 weeks is effective and safe for tinea capitis. Compared to griseofulvin, oral terbinafine appears more, or as, efficacious, over short periods of treatment (1 month or less). It is now licenced for use in children in some countries. It is also now available in generic forms. The evidence also indicates that terbinafine, itraconazole and fluconazole can cure most patients with tinea capitis with a shorter course of treatment and a good safety profile. There are no RCT's that focus on strategies to reduce spread and reinfection. Topical treatment (e.g., imidazole creams, lotions or shampoos) is ineffective as a means of curing this infection, but its use may reduce transmission. Accompanying procedures include screening and treatment of contacts.

## **References**

1. Gonzalez U. Tinea capitis. In: Evidence-Based Dermatology 2<sup>nd</sup> Ed. Williams HC, Bigby M, Diepgen D, Herxheimer A, Naldi L, Rzany B, eds. BMJ Books 2008.

## **Other fungal infections**

**Definition** – Apart from scalp involvement (tinea capitis), fungal infections may involve other locations: body folds (including interdigital spaces of feet, so-called "athlete's foot"), and groins. Athlete's foot or tinea pedis is the most common variety of infection, and is most frequently caused by dermatophytes. It usually presents in one of three ways: macerated soggy interdigital skin, recurrent vesicular eruption, or



dry scaly skin of the soles. Ideally, cases should be confirmed by the laboratory tests, microscopy and culture, where these facilities are available, since in many tropical areas an identical picture may be caused by mould fungi other than dermatophytes (*Scytalidium*).

**Aims of treatment** - To suppress symptoms and to cure the infection. Also to control a major risk factor for cellulitis of the leg (tinea pedis was a main risk factor in 3 case control studies).

**Evidence** - Two systematic reviews are available. One systematic review [1] documents that many topical products are effective in treating tinea pedis, with allylamines most effective and azoles, undecenoic acid and tolnaftate in decreased order of effectiveness. In a French recommendation (2007 and book chapter in 2008), it was stated that topical terbinafine and azoles are the first line options; topical terbinafine is effective after a shorter course of treatment than the imidazole alternatives (1 week vs 4 weeks) but is much more expensive (Scrivener Y, personal communication 2008). The last two agents are the cheapest, while terbinafine is the most expensive. The evidence provided by another systematic review suggests that systemic agents are no more effective than topical drugs in producing cures for the average patient with athlete's foot [2].

### **References**

1. Crawford F. *et al.* Topical treatments for fungal infections of the skin and nails of the foot. *Cochrane Database Syst. Rev.* **2**, CD001434 (2000).
2. Bell-Syer SEM. *et al.* A systematic review of oral treatments for fungal infections of the skin of the feet. *J. Dermatol.* **12**, 69-74 (2001).

## **Herpes simplex**

**Definition** - *Herpes simplex virus* (HSV) is a human DNA virus with two species, HSV-1 and HSV-2, that causes a variety of disease manifestations, the most common being localised recurrent skin and mucous vesicular lesions, occurring after primary infection (e.g., acute herpetic gingivostomatitis). Genital HSV is a sexually transmitted disease and there is strong evidence that it increases the risk of other infections through genital contact, in particular HIV infection.

**Aims of treatment** - To suppress symptoms and reactivation, and to reduce transmission.

**Evidence** - No systematic reviews are available for cutaneous manifestations while a protocol for a systematic review on suppressive therapy for recurrent genital herpes in immunocompetent individuals is available [1]. For primary infection in children, i.e., herpetic gingivostomatitis, small RCTs [2,3] suggest that oral aciclovir reduces the mean duration of pain and other symptoms. A few RCTs document that the frequency of recurrent herpes labialis can be reduced by antiviral therapy [4]. Similarly, daily treatment with an oral antiviral therapy reduces the frequency of



recurrence of herpes genitalis as shown in a recent meta-analysis [4, 5]. Valaciclovir appears to be as effective as oral aciclovir and somewhat better than famciclovir. Aciclovir is available in generic forms, contrarily to other more recent antiherpetic drugs. For recurrences, aciclovir 400 mg x 3 for 5 days should be used as it is the most effective (cheapest, more convenient than ACV 200 x 5, and as efficacious as VACV) [6].

### **References**

1. Evans AL. *et al.* Suppressive antiviral therapy for recurrent genital herpes in immunocompetent individuals (protocol). *Cochrane Database Syst. Rev.* **1**, CD004091 (2003).
2. Ducoulombier H. *et al.* Herpetic stomatitis-gingivitis in children: controlled trial of acyclovir vs placebo. *Ann. Pediatr.* **35** 212-6 (1988).
3. Amir J. *et al.* Treatment of herpes simplex gingivostomatitis with aciclovir in children: a randomised double-blind placebo controlled trial. *Br. Med. J.* **314**, 1800-3. (1997).
4. Mahler V. Herpes simplex. In: Evidence-Based Dermatology 2<sup>nd</sup> Ed. Williams HC, Bigby M, Diepgen D, Herxheimer A, Naldi L, Rzany B, eds. BMJ Books (2008).
5. Lebrun-Vignes B *et al.* A meta-analysis to assess the efficacy of oral antiviral treatment to prevent genital herpes outbreaks. *J. Am. Acad. Dermatol.* **57** 238-46 (2007).
6. Cernik C., Gallina K., Brodell RT. The treatment of herpes simplex infection: an evidence-based review. *Arch. Intern. Med.* **168**, 1137-44 (2008).

### **Eczema (atopic dermatitis)**

**Definition** - Atopic eczema (also known as atopic dermatitis) is a chronic, relapsing, and itchy inflammatory skin condition commonly observed in children, characterised mainly by flexural involvement. The condition which is genetically determined (the "atopic" background) is influenced by several environmental factors.

**Aims of treatment** – To control flares, to minimise the impact of established atopic eczema on the wellbeing of children and their family, and eventually to prevent occurrence in predisposed infants and children.

**Evidence** - Around 400 RCTs have been published on the subject of atopic eczema, but only one systematic review [1]. No clear indications are available about prevention. Short term treatment with topical steroids is the mainstay of treatment of flares. Calcineurin inhibitors are also effective in reducing symptoms; however, they are expensive and there is insufficient information on their long term use. As for control of established manifestations, there is evidence that emollients and specific patient education are useful. The value of long term therapeutic strategies to control symptoms (e.g., intermittent topical steroid treatment) has not been established by RCT but is widely practiced as a means of achieving optimal risk benefit. There is one RCT published in the BMJ showing that intermittent topical steroid (fluticasone) may



prevent relapse vs placebo [2]. Oral antihistamines are of limited benefit for control of itching.

### **References**

1. Hoare C., Li Wan Po A., Williams H. Systematic review of treatments for atopic eczema. *Health Technol. Assess* **4**:1–191 (2000).
2. Berth-Jones J., Damstra RJ., Golsch S., Livden JK., Van Hooteghem O., Allegra F., Parker CA. Twice weekly fluticasone propionate added to emollient maintenance treatment to reduce risk of relapse in atopic dermatitis: randomised, double blind, parallel group study. *Br. Med. J.* **326**, 1367 (2003).

## **Acne**

**Definition** - Acne is a disease of the pilosebaceous duct with a range of clinical manifestations frequently occurring simultaneously, including comedones, papules, pustules, and nodules. It usually involves the face and/or upper back. Its first appearance is most common during adolescence. It is extremely common in all populations, and may have a major impact on the quality of life of patients because of its tendency to cause scarring and post inflammatory hyperpigmentation.

**Aims of treatment** - To alleviate symptoms short term, and to limit disease activity and sequelae long term.

**Evidence** - There is at least one systematic review [1]. Topical retinoids and benzoyl peroxide are effective in mild to moderate acne alone or in combination. Benzoyl peroxide appears to have similar activity to topical antibiotics including tetracyclines, erythromycin, or clindamycin, against inflamed lesions and greater activity against noninflamed lesions, but may cause local irritation. Oral antibiotics including erythromycin and tetracyclines are effective in inflamed lesions but there is no good evidence about their optimal dose or duration. One cycline, minocycline, does not have a good benefit risk ratio. Oral 13-cis retinoic acid is highly effective in severe acne or in cases of "difficult-to-treat" moderate acne, but is highly teratogenous and its use in child-bearing age women is possible only if there is strict supervision and if adequate contraceptive measures are taken. Topical retinoids should not be used during pregnancy. Salicylic acid preparations and 5% sulphur lotions are cheap and well tolerated, but only moderately active.

### **References**

1. Lehmann HP. *et al.* Management of acne. Rockville, MD: Agency for Healthcare Research and Quality, 2001 (Evidence Report/Technology Assessment, 17; AHRQ publication no. 01-E019).



## **Prurigo due to insect bites**

**Definition** - Prurigo is an exaggerated skin reaction to insect bites that very commonly affects children in tropical areas. It is a frequent source of pyoderma (secondary pyoderma). The tendency to react to insects decreases with age and usually disappears after several years of evolution when children are older. It is important to distinguish between the prurigo due to insect bites and the early manifestations of onchodermatitis in endemic areas. An itching condition very similar to insect prurigo is commonly observed in HIV-infected adults.

**Aims of treatment** – To alleviate symptoms, and to prevent superinfection.

**Evidence** - No systematic reviews or RCTs are available to inform treatment. Topical anti-itching compounds (calamine, crotamiton), including topical steroids, may be helpful. Antiseptics are important in order to prevent superinfection and to alleviate milder cases of superinfection. Oral anti-histamines may be helpful.

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