The most common fungal infections in infants and children are mucocutaneous candidiasis, pityriasis versicolor, tinea corporis, tinea pedis and tinea capitis. The objective of the present update is to inform clinicians on options for treatment of these symptomatic but non-life threatening fungal infections, given the wide variety of topical, usually over-the-counter (OTC) (Table 1) and oral prescription (Table 2) drugs available. It replaces the previous position statement published in 2007.

### TABLE 1
Selected topical antifungal agents for children

<table>
<thead>
<tr>
<th>Antifungal agents</th>
<th>Dosage</th>
<th>Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clotrimazole: (Canesten, Clotrimaderm)</td>
<td>1% two times daily for 7 days (max 14 days)</td>
<td>$$</td>
</tr>
<tr>
<td>Gentian violet: (1% to 2%)</td>
<td>2 times daily</td>
<td>$</td>
</tr>
<tr>
<td>Ketoconazole shampoo: (Nizoral shampoo)</td>
<td>2% once daily</td>
<td>$</td>
</tr>
<tr>
<td>Miconazole† cream or ointment: (Micatin, Micozole, Monistat)</td>
<td>2% once or twice daily</td>
<td>$$</td>
</tr>
<tr>
<td>Nystatin: Cream or ointment (Candidatin, Mycostatin, Nadostine, Nilstat, Maydern)</td>
<td>Two to three times daily</td>
<td>$</td>
</tr>
<tr>
<td>Nystatin: Oral suspension (100,000 U/ml)</td>
<td>100,000 to 200,000 U three times daily for 7 to 14 days</td>
<td>$$</td>
</tr>
<tr>
<td>Terbinafine: (Lamisil 1%)</td>
<td>1 to 2 times daily</td>
<td>$$$</td>
</tr>
<tr>
<td>Tolinaftute: (Tinactin 1% cream)</td>
<td>1 to 2 times daily</td>
<td>$$</td>
</tr>
<tr>
<td>Selenium sulfide: (Versel lotion 2.5%, Selsun shampoo 1%)</td>
<td>Once daily</td>
<td>$</td>
</tr>
</tbody>
</table>

*The relative cost of 30 g treatment is indicated. Variation in the price of products occur among brands and stores. Relative prices are indicated as follows: $ <$10; $$ from $10 to $25, $$$ from $25 to $50.

† Available by prescription only

### Mucocutaneous candidiasis
*Candida albicans* colonization can occur as early as the first week of life. Symptomatic infections such as thrush and *Candida* diaper dermatitis (CDD) may develop at any age thereafter, particularly following broad-spectrum antibiotic treatment. Systemic candidiasis is rare, but is a particular risk for premature infants.

Although mucocutaneous candidiasis is common, only a few high-quality randomized control studies of drug therapy have been published. In fact, one recent review of oral candidiasis in patients with cancer found only eight studies that met the inclusion criteria. Control trials for diaper dermatitis are also rare, making it difficult to derive recommendations for optimal therapy.
**Oropharyngeal candidiasis (thrust)**

Oropharyngeal candidiasis (thrust) may start as early as seven days after birth, with an incidence in infants of 5% to 10% depending on the population studied [9]. Response to antifungal agents is usually good in neonates with no major underlying condition, but a prolonged course may be required and recurrences are common. Use of an infant soother increases the incidence of thrust and may make treatment less effective, unless the soother is carefully washed after use [10].

Topical gentian violet, the oldest therapeutic agent, is moderately effective against thrust but prolonged use can cause irritation and even ulceration [11]. Gentian violet stains tissue and clothing and, thus, is not well accepted by parents; it also interferes with clinical assessment.

Nystatin suspension has been used since the 1950s [10]. It is well tolerated and remains the most frequently prescribed agent for thrust. The usual dosage of 200,000 units four times daily is highly effective, curing 50% of newborns after one week and 80% of newborns after two weeks of treatment [11]. It should be administered after feeds.

First-generation imidazoles, such as miconazole and clotrimazole, are more effective than nystatin [12]. However, miconazole gel and oral preparation of clotrimazole are not licensed in Canada. Chronic oral candidiasis can respond to clotrimazole troches [13]. There is also anecdotal experience that clotrimazole suppositories in a pacifier or clotrimazole vaginal cream applied to the oral mucosa after feedings are effective against thrust [14,15]. Because these therapeutic approaches have not been evaluated in controlled trials, they are not recommended as first-line therapies.

Second-generation imidazoles, such as fluconazole and itraconazole or other new oral antifungals, may be considered if conventional topical treatments fail, particularly among immunocompromised patients. Although these drugs are effective, they are not recommended as first-line management of thrust in normal children because of limited paediatric data, potentially significant adverse effects and high costs.

**Candida diaper dermatitis (CDD)**

CDD is common during the second to fourth months of life in healthy infants [16]. *Candida albicans* is present in the feces of 90% of such infants [17,18]. Treatment should include decreasing maceration of the skin by eliminating impervious diaper covers, changing diapers frequently and leaving diapers off for long periods of time. Topical antifungal therapy is also necessary. In one randomized, double-blind, controlled trial comparing miconazole ointment with zinc oxide petroleum base, miconazole was safe and more effective, particularly in moderate to severe cases. Ointments, creams and powders of nystatin, miconazole and clotrimazole are available (Table 1). It is still not clear whether concomitant oral and topical antifungals should be recommended. In two studies [18,19], relapses were decreased (although not significantly) when an oral supplement of nonabsorbable nystatin was added to the topical ointment of nystatin (16% versus 33%).

There are no well-designed trials to assess the efficacy of adding a topical anti-inflammatory agent in treatment of CDD. Potent anti-inflammatory preparations, such as those with high concentrations of steroids, may impair the response to antifungal agents and should be avoided. The place for low concentrations of steroids (eg, 1% hydrocortisone) is unclear. Although some experts never use steroids with antifungal agents, others advocate them in CDD.

**Pityriasis versicolor (Tinea versicolor)**

Pityriasis versicolor is a mild or chronic condition characterized by scaly hypo- or hyperpigmented lesions on the trunk. Infection often occurs in adolescents when the sebaceous glands are active. *Malassezia*, an organism restricted to invading the stratum corneum [20], causes the infection [21]. Antifungal preparations can be effective, but recurrences are common [22].

Topical ketoconazole, selenium sulfide and clotrimazole are the most common treatments [23]. Treatment usually consists of applying shampoo preparations, such as ketoconazole 2% or selenium sulfide as a 2.5% lotion or 1% shampoo, to the affected area for 15 min to 30 min nightly for one to two weeks, and then once a month for three months to avoid recurrences [24]. In one randomized trial using ketoconazole shampoo for three days or one day compared with placebo, the response was 73%, 69% and 5%, respectively.

**Tinea corporis**

Tinea corporis (ringworm) is a superficial infection of the skin that is not covered by hair. It can occur at any age. Lesions are circular (thus the name ringworm). Common causes in Canada include *Trichophyton*...
rubrum, Trichophyton mentagrophytes and Microsporum species (especially Microsporum canis and Epidermophyton floccosum). These are transmitted by direct contact with infected humans, animals (usually dogs and cats) or (rarely) by fomites [28]. There is little difference in efficacy among clotrimazole, ketoconazole, miconazole or terbinafine. A good response usually occurs when any of these agents are applied once or twice daily for 14 to 21 days. Topical agents mixed with corticosteroids should be avoided [24].

Tinea pedis

Tinea pedis (athlete’s foot) is a common superficial fungal infection of the foot. Causes include T rubrum, T mentagrophytes and E floccosum. Although tinea pedis often spreads among household members, it is uncommon in young children [26][27].

Many topical antifungals are effective against tinea pedis. Drying agents, such as Burrow’s solution, may be a useful adjunct for macerated or vesicular lesions. Recurrence of the infection can be prevented with good foot hygiene. Oral antifungals are indicated for infections involving the toenails. Clinical studies in children are limited, but suggest that fluconazole, itraconazole and terbinafine are effective [28][29].

Tinea capitis and seborrhoeic dermatitis

Tinea capitis (fungal infection of the scalp) is the most common paediatric superficial dermatophyte infection. The causative species vary geographically; M canis predominates in Europe, whereas Trichophyton tonsurans predominates in North America. Because tinea capitis does not respond well to topical therapy alone, oral therapy is required (Table 2) [28].

Seborrhoeic dermatitis and pityriasis capitis (cradle cap) are common, but usually mild, scalp infections caused by Malassezia species (eg, Malassezia furfur). The condition often resolves with mild soap application. Shampoos containing selenium sulfide or an azole are useful in severe forms.

<table>
<thead>
<tr>
<th>Antifungal agent</th>
<th>Availability</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketoconazole†</td>
<td>200 mg tablet</td>
<td>$$$</td>
</tr>
<tr>
<td>Fluconazole†</td>
<td>100 mg tablet</td>
<td>$$$$</td>
</tr>
<tr>
<td>Itraconazole†</td>
<td>100 mg capsule</td>
<td>$$$$</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>250 mg tablet</td>
<td>$$$</td>
</tr>
<tr>
<td></td>
<td>250 mg capsule</td>
<td>$$$</td>
</tr>
<tr>
<td></td>
<td>250 mg tablet</td>
<td>$$$</td>
</tr>
</tbody>
</table>

†Azoles (Ketoconazole, Fluconazole and Itraconazole) may interfere with metabolism of other drugs (see drug interaction). Prescription is required for all mentioned agents. *Except for Terbinafine, the approximate relative cost is based on treatment for two weeks for a 20 kg child, including the prescription fee (data from 2012). Major variation in the price of products and prescription fees occur among provinces and stores. Relative price has been indicated as follows: $$$ from $25 to $50, $$$$$ from $50 to $100, and $$$$$$ over $100.

Oral antifungal agents absorbed systemically

Fluconazole

Fluconazole is a triazole with activity against Candida species, some dermatophytes and many systemic mycoses. The drug is hydrophilic and, thus, present mainly in bodily fluids rather than in keratin or lipids [30]. It is, therefore, not useful for routine treatment of most superficial fungal infections [31][32].

Griseofulvin

Griseofulvin is no longer available in Canada.

Itraconazole

Itraconazole is an azole with activity against many dermatophytes, Candida species, M furfur and some moulds. It has a long half-life in the skin and nails, an affinity for both lipids and keratin, and reaches the skin
primarily through sebum. The drug may be excreted in sebum for one month after therapy has been discontinued. Itraconazole is available in tablet and liquid formats. Clinical trials and case series using itraconazole to treat tinea capitis have shown it to be effective (approximately 90% of the time) for infections caused by either *Trichophyton* and *Microsporum* species \[33\]-\[37\]. Few side effects were seen in most studies using 3 mg/kg/day to 5 mg/kg/day for four to six weeks. Although more studies on safety are needed, itraconazole may become a good first-line agent for tinea capitis.

**Ketoconazole**

Ketoconazole was the first azole evaluated for efficacy in the treatment of resistant superficial fungal infections such as tinea capitis. Ketoconazole was found to be equivalent to griseofulvin for such cases in these clinical trials \[38\]-\[41\].

**Terbinafine**

Terbinafine is a lipophilic and keratinophilic fungicidal agent, active in vitro against dermatophytes and some moulds. It diffuses to keratinocytes from the bloodstream to reach the stratum corneum and hair follicles \[42\]. Because it is not metabolized through cytochrome P-450, many of the drug interactions seen with the azoles do not occur. Terbinafine is well tolerated, with gastrointestinal and skin reactions in only 2% to 7% of patients. Loss of the sense of taste has been reported, but resolves after therapy has ended.

Oral terbinafine is effective in the treatment of relatively resistant superficial dermatophyte infections including tinea unguium (onychomycosis), tinea pedis and tinea corporis or tinea cruris, achieving mycological cure in over 80% of adult patients \[43\]. It is effective for children with tinea capitis at a dose of 62.5 mg/day to 250 mg/day for four weeks \[44\]-\[48\]. Topical terbinafine 1% formulations have been effective when applied once or twice daily for two weeks. Gupta et al \[49\] concluded that terbinafine may be the drug of choice for superficial fungal infections in children. Terbinafine is available in Canada as a topical 1% cream and orally as a 250 mg tablet. No liquid formulation is available.

**Drug interactions**

The extent to which an antifungal agent interacts with the hepatic P-450 enzyme system has implications on its potential to cause significant drug interactions \[50\]. Azoles are metabolized by cytochrome P-450 3A (CYP 3A) and may inhibit the elimination of other drugs metabolized by this enzyme, such as antiarrhythmics, cortisol, cyclosporin, estradiol and tacrolimus. Terbinafine is not an azole; it does not affect CYP 3A and it has few drug interactions.

For further details on the use of antifungal agents for common paediatric infections, the reader is referred to recent review articles \[1\]-\[4\].

**References**

42. Faergemann J, Zehender H, Denouël J, Mille-rioux L. Levels of terbinafine in plasma, stratum corneum, dermis-epidermis (without stratum corneum), sebum, hair and nails during
and after 250 mg terbinafine orally once per day for four weeks. Acta Derm Venereol 1993;73:305-9.


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