

Current Treatments for Scabies and Pediculosis

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ABSTRACT

Scabies and lice have afflicted man since ancient times. Permethrin is generally the treatment of choice for head lice and scabies, because of its residual effect. Toxicity and absorption are minimal. Ivermectin should be reserved for cases where permethrin fails.

KEY WORDS: *scabies, lice, permethrin, ivermectin, malathion, lindane*

How do we get rid of scabies and lice? Treatment options that were formerly available, included sulfur, crotamiton lotion (*Eurax*), and 25% benzyl benzoate¹. Sulfur in 5–10% petrolatum is relatively cheap, but must be applied on three successive nights to be effective. It is considered the safest treatment for pregnant women and very young children, although there are no studies to confirm the lack of toxicity.

For many years lindane was the preferred therapy until concern was voiced about its efficacy and safety. Permethrin, malathion and, most recently, ivermectin have become treatments of choice.

Lindane

For scabies

For the past 50 years, lindane has been the preferred therapy for scabies. This agent needs to be used on successive nights to ensure that the eggs and live mites are adequately exposed to treatment.

For lice

For lice, lindane has a 90% success rate, but there are concerns about side effects involving the central nervous system if improperly used.

Seizures secondary to this medication have been reported, particularly when this medication was applied to wet skin or to skin altered by inflammatory changes that cause easy absorption. The absorption rate may be ≥ 40 times that of permethrin, leading to a significant potential for toxicity². Bathing prior to application should be avoided. Hair should be washed with plain shampoo and dried thoroughly before applying lindane. Children should not apply lindane without adult supervision.

While the topical lotion and shampoo are still available, the topical cream has been withdrawn from the US market. However, it is still available in Canada.

Permethrin

Permethrin is a synthetic compound based on the insecticidal components of naturally occurring permethrins¹². It kills both organisms and eggs, and because of its lack of percutaneous absorption, toxicity is not a consideration. Weekly applications have been very successful in preventing reinfection.

For scabies

The 5% permethrin preparation kills the organisms and eggs, and has an extremely low rate of absorption, making the toxicity potential nonexistent. Weekly applications have been extremely

successful in preventing reinfection. It is probably the most reliable topical scabicide.

For lice

The 1% Permethrin crème rinse is effective, although the 5% lotion may be used if the 1% fails. Washing removes excess medication, but the protective residual remains for about a week, thereby reducing the possibility of reinfestation.

For each of these topical applications, the entire skin, head to toe must be treated, including the fingernails, toenails, soles of the feet, the umbilicus, and the perianal area. When anatomic areas are missed, it is impossible to distinguish reinfection from resistant organisms. All people with whom the patient has come into contact must also be treated to avoid reinfection.

Ivermectin

This drug was released for human use in the US in 1996, for onchocerciasis.

It is taken orally, at a dose of 0.2mg/kg, or two-6mg tablets for a 60kg person. It does not protect against reinfestation, though, so may require a follow-up course of treatment. Merck, who developed ivermectin, has donated over a million doses for the

treatment of onchocerciasis in Africa. This eradication program occurred without significant side effects.

For scabies

A number of clinical studies have shown ivermectin to be an excellent scabicide. A recent study¹⁰ compared the efficacy and safety of ivermectin and lindane when treating human scabies in 53 patients in Buenos Aires, Argentina. Ivermectin was as effective as lindane, and because of its ease of administration, it was felt to be a worthwhile tool for improving compliance and controlling infestations. Several reports^{6-9,17} have stressed the advantage that ivermectin provides in managing the eradication of scabies, including the control of outbreaks of infestation in institutional settings.

For lice

Ivermectin has been reported to be effective in removing head lice. However, a second treatment after 10 days may be needed, because it does not affect the viable eggs on the hair shafts⁵.

The US FDA has not approved Ivermectin for treatment of lice or scabies, and the appropriate doses and dosing schedules for these conditions have not yet been established¹⁶.

Drug	Products available & cost	Side effects/Risks	Dosage & Frequency	Benefits	Success rate
Permethrin	<i>Elimite</i> \$26 <i>Acticin</i> \$22 <i>Nix</i> 1% \$9.20	Rare contact dermatitis. Missing an area may allow recurrence.	Cover whole area, including fingernails, etc. Apply weekly, if needed.	Minimal absorption. Remains active on skin for 7 days.	90-100% following a single application
Lindane	<i>Kwell Lotion</i> * \$40 <i>Scabene</i> \$18 Generic \$12-15	Exposure to skin with impaired barrier function may lead to nausea, vomiting, and/or neurologic stimulation. Severe toxic effects if ingested.	Cover whole area, including fingernails, etc. Apply over two successive days.		84-91% from single application; 96% when applied for six hours or more.
Malathion	<i>Ovide lotion</i> \$31.25	Significant skin absorption. Can cause respiratory distress, headaches, nausea, diarrhea, sweating.	Must apply all over, including fingernails, etc. Apply a single dose then repeat in 7-9 days as needed.		Rates of ≥ 90% have been reported ³ .
Ivermectin	<i>Stromectol</i> or <i>Mectizan</i> 6mg Tablets @ \$10/tablet	Few known risks. Can still be reinfected from the environment, including untreated contacts.	12mg (2 tabs) in 60 kg adults (0.2 mg/kg)	Total patient treatment	Over 90%; May have to repeat dose in one week.

Table 1: Common treatments for scabies and head lice. Prices are US average wholesale prices. Retail prices are about 40% higher.

*There is some information indicating that the *Kwell* brand has been discontinued in the US by the manufacturer, Reed and Carnick.

Malathion

For lice

Malathion lotion should be applied to dry hair, and then allowed to dry on the scalp. After several hours, the hair can be combed to remove nits and lice. Success rates of $\geq 90\%$ have been reported³.

Ovide Lotion (Medicis), composed of 0.5% malathion in 78% isopropanol, was recently approved by the US FDA for treatment of head lice. The same formulation has been available in the US twice before, as *Prioderm* (Purdue Frederick) and *Ovide* (GenDerm)¹².

Malathion is an irreversible cholinesterase inhibitor that is hydrolyzed by plasma carboxylesterases much faster in mammals than in insects and is considered safe. Resistance to malathion has been reported⁴.

Nit Removal

After using any of the above treatments, the nits may be dead, but will remain on the hair. Most school authorities will not allow students to return unless the nits are gone. The National Pediculosis Association advocates vigilant daily nit removal for at least 7 to 10 days following the initial treatment. Alternatively, malathion lotion loosens the attachment of the nits to the hair.

Reports of Resistance

Resistance to permethrin in developed countries has been reported in 1999^{11,13,18}. In one study, researchers compared the response of head lice to permethrin in US children, where pediculicides are readily available, to children from Borneo, where such products are unknown. They concluded that head lice in the US are less susceptible to permethrin than those found in Borneo¹¹.

A study from England evaluated resistance to permethrin and malathion in lice samples and concluded that head lice are resistant to current over-the-counter treatments in England¹⁸. Treatment failure can be predicted after repeated applications, even with more concentrated formulations¹¹. There have been reports of resistance for lindane¹⁴ and malathion^{4,15}, but not for ivermectin.

Other Treatment Options

Other treatment options that are sometimes used include heavy greases such as petrolatum, which is rubbed into the scalp, and the hair placed under a towel or in a net overnight. The petrolatum probably closes breathing holes and suffocates the lice. Physostigmine ointment, used for eyelash infestation of pubic lice, may have a similar mechanism of action. These therapeutic approaches have not undergone rigorous testing.

Alternative Approaches

Alternative approaches are used and enthusiastically accepted in our present climate. However, there are no well conducted studies that support any alternative medical claims at present.

Conclusion

Permethrin, because it leaves a residual on the skin and hair for several days after use, is the preferred treatment for lice and scabies. Its residual effect on the skin discourages re-infestation and lasts up to a week. The 5% lotion is used for scabies, and the 1% for head lice—although the 5% lotion may be used if the 1% fails. Toxicity and absorption are minimal. Ivermectin should be considered for cases in which there is an increased number of organisms (e.g., “Norwegian” scabies) or a failure following the use of permethrin. Malathion is a third treatment option.

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Update on Topical Acne Treatments

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Abstract

Topical acne treatment can positively benefit patients with acne. This review summarizes clinical and prescribing information on currently available topical agents. The efficacy of the medications included in this report is supported by properly designed randomized clinical trials^{2-8,14}.

KEY WORDS: *acne, tretinoin, adapalene, isotretinoin, tazarotene, clindamycin, erythromycin, azelaic acid, benzoyl peroxide*

Topical acne medications are indicated for treatment of comedonal and mild inflammatory acne, or as adjuncts to

systemic therapy in moderate acne¹. The newer, more frequently prescribed drugs are summarized herein.

Drug	Mechanism of Action
Tretinoin <i>Retin-A</i> (Janssen-Ortho) <i>Stieva-A Retisol-A</i> (Stiefel) <i>Vitamin A Acid</i> (Dermik) <i>Vitinoin</i> (Penederm)	<ul style="list-style-type: none"> • Facilitates removal of existing comedones and inhibits formation of new ones • Believed to suppress keratin synthesis • (Inhibition of <i>P. acnes</i>)
Adapalene <i>Differin</i> (Galderma)	<ul style="list-style-type: none"> • Prevents microcomedone formation • Enhances keratinocyte differentiation • (Inhibition of <i>P. acnes</i>) • (Anti-inflammatory)
Isotretinoin <i>Isotrex</i> (Stiefel)	<ul style="list-style-type: none"> • Comedolytic and anti-inflammatory • (Inhibition of <i>P. acnes</i>)
Tazarotene <i>Tazorac</i> (Allergan)	<ul style="list-style-type: none"> • Comedolytic and believed to inhibit cross-linked envelope formation in human keratocyte cultures
Clindamycin <i>Dalacin T</i> (Upjohn Pharmacia)	<ul style="list-style-type: none"> • Inhibition of <i>P. acnes</i> • Anti-inflammatory
Erythromycin <i>Staticin, T-stat</i> (Westwood-Squibb) <i>Sans-Acne</i> (Galderma) <i>Erysol</i> (Stiefel)	<ul style="list-style-type: none"> • Inhibition of <i>P. acnes</i>
Azelaic Acid <i>Azelex</i> (Allergan)	<ul style="list-style-type: none"> • Inhibition of <i>P. acnes</i> • Slowly releases active oxygen • Some keratolytic effect
Benzoyl Peroxide <i>Benzac, Benzac AC</i> (Galderma) <i>Solugel, Panoxyl, Acetoxyl</i> (Stiefel) <i>Desquam-X</i> (Westwood-Squibb) <i>Benzagel</i> (Dermik)	<ul style="list-style-type: none"> • Inhibition of <i>P. acnes</i> • Anti-inflammatory • (Comedolytic)
Benzoyl Peroxide and Erythromycin <i>Benzamycin</i> (Dermik)	<ul style="list-style-type: none"> • Inhibition of <i>P. acnes</i> • (Comedolytic) • Anti-inflammatory
Tretinoin and Erythromycin <i>Stievamycin, Stievamycin mild, Stievamycin Forte</i> (Stiefel)	<ul style="list-style-type: none"> • Comedolytic • Inhibition of <i>P. acnes</i>

Table 1: Mechanism of action for topical acne medications⁹

Any mechanism that is enclosed in parentheses denotes a minimal effect.

Pathogenesis

Some of the factors responsible for acne include heredity and the role of hormones. Exposure to ultraviolet light and the use of certain drugs can also affect acne¹³. Acne is multifactorial, involving (1) sebaceous hypersecretion due to increased levels of circulating androgens and/or sebaceous gland hypersensitivity, and (2) follicular hyperkeratinization leading to pore occlusion. Inflammatory acne includes (3) the proliferation of *Propionibacterium acnes* (*P. acnes*) within the comedone and (4) the generation of chemotactic and proinflammatory factors¹.

Treatment Options

The presence of multiple comedones suggests the use of agents directed at follicular hyperkeratinization. Inflammatory lesions may warrant the use of agents with antimicrobial and/or anti-inflammatory effects. Other factors that should be considered in therapeutic selection are *side effect profile, cost, and individual patient preference*.

In a recent survey, acne patients who were referred to a dermatologist's office were asked, "Which form of treatment would you prefer: topical or systemic?" Female patients were five times more likely than males to prefer topical treatments, as were those with lesser grades of acne severity (see Table 2).

	Overall group (n=78)	Males (n=29)	Females (n=49)	Acne Grade I and II(n= 39)	Acne Grade III and IV(n=39)
Topical	26%	7%	37%	38%	13%
Systemic	21%	32%	14%	10%	32%
No Preference	53%	61%	49%	51%	55%

Table 2: Acne survey results (in percent of responses) when patients were asked, "Which form of treatment would you prefer: topical or systemic?"¹⁵

Generic Name	Dosage Forms	Frequency	FDA Pregnancy Category*
Tretinoin	Cream: 0.01%, 0.025%, 0.05%, 0.1%, 0.4% ¹⁷ Gel: 0.01%, 0.025%, 0.05% Microsponge: 0.1% Solution: 0.025%, 0.05%, 0.1% ¹⁷ , 0.2% ¹⁷	Before retiring	C
Adapalene	Cream: 0.1% Gel: 0.1%	Before retiring	C
Isotretinoin	Gel: 0.05%	Two times per day	C
Tazarotene	Gel: 0.05%, 0.1%	Once per day	X
Clindamycin	Solution: 1%	Two times per day	B
Erythromycin	Solution: 1.5% Erythromycin, 2% Erythromycin	Two times per day	B
Azelaic Acid	Cream: 20.0%	Two times per day	B
Benzoyl Peroxide	Cleansing Lotion: 2.5%, 4%, 5%, 8%, 10% Cream: 5%, 10% Gel: 2.5%, 4%, 5%, 6%, 8%, 10%, 15%, 20% Lotion: 2.5%, 5%, 5.5%, 10%, 20%	One or two times per day	C
Benzoyl Peroxide and Erythromycin	Benzoyl Peroxide 5%, Erythromycin 3%	Two times per day	C
Tretinoin and Erythromycin	Tretinoin: Regular – 0.025% Mild – 0.01% Forte – 0.05% All contain Erythromycin 4%	Before retiring	C

Table 3: Topical acne preparations.

*FDA Pregnancy categories are A: Controlled studies show no risk, B: No evidence of risk in humans, C: Risk cannot be ruled out, D: Positive evidence of risk, X: Contraindicated in pregnancy^{11,12}.

Generally, topical acne agents require a trial period of at least 8–12 weeks to determine therapeutic benefit. During this time, the patient should be given appropriate advice to minimize the potential for adverse effects. Maintenance of improvement thereafter requires ongoing treatment with periodic tapering to establish ongoing need.

When prescribing for female patients the clinician should be aware of possible teratogenicity. For example, the potential link between topical tretinoin and the fetal malformation is not clear. *The USP Drug Information for the Health Care Professional* (1999) carries the Pregnancy category C for tretinoin. To be safe, topical tretinoin should not be used during pregnancy.

A multicenter, single-blind, randomized 12 week study in Europe compared clindamycin with a clindamycin phosphate/tretinoin gel formulation (*Velac*) which is approved for use in France. *Velac* was found to reduce overall acne scores and was faster acting¹⁴.

A new drug application for this drug for acne treatment is currently awaiting approval by the US FDA.

Adverse Effects

The most common adverse effect of topical acne therapy is mild irritation. Aqueous-based gels may be less irritating than their alcohol-based counterparts, and creams tend to be less irritating and drying than gels. Irritation can be minimized by advising shorter initial application times. These can then be progressively titrated upwards, with less frequent application, and the use of appropriate nonacneogenic moisturizers.

Summary

Mild acne can be effectively managed by topical medications based on lesional morphology. Appropriate counselling on the use of these medications can minimize adverse effects and enhance compliance.

Generic Name	Erythema	Scaling	Burning	Initial Flare	Photo-Sensitivity	Other
Tretinoin	3+	3+	2+	2+	2+	Photodegraded, apply only at night.
Adapalene	1+	1+	1+	1+	0	Photostable.
Isotretinoin	2+	2+	1+	1+	0	Photoisomerizes with light exposure. Plasma levels not detectable with topical application.
Tazarotene	3+	3+	3+	1+	0	Photostable.
Clindamycin	1+	1+	1+	1+	0	Allergic contact dermatitis (rare). May lead to <i>P. acnes</i> resistance with prolonged use.
Erythromycin	1+	1+	1+	1+	0	Irritation somewhat more frequent than for clindamycin. Allergic contact dermatitis (rare). May lead to <i>P. acnes</i> resistance with prolonged use.
Azelaic Acid	1+	1+	1+	1+	0	Less irritating than tretinoin cream and 5% benzoyl peroxide gel.
Benzoyl Peroxide	2+	2+	1+	1+	1+	May bleach clothing. Allergic contact dermatitis (rare).
Benzoyl Peroxide and Erythromycin	2+	2+	2+	2+	2+	Less irritating than benzoyl peroxide alone.
Tretinoin and Erythromycin	3+	3+	3+	2+	2+	Photodegraded, apply only at night.

Table 4: Adverse effects of topical acne medications⁹.

Legend: 3+ very strong, 2+ strong, 1+ moderate

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News about Photodynamic Therapy

On November 5 1999, the US FDA's Dermatologic and Ophthalmic Drugs Advisory Committee considered certain issues related to Dusa Pharmaceuticals' New Drug Application (NDA) for *Levulan Photodynamic Therapy* (5-aminolevulinic acid). Following presentations by Dusa and the FDA, the agency asked the panel for feedback with respect to proposed product labelling and postmarketing studies.

Earlier this year the US FDA issued an approvable letter for this device for the treatment of actinic keratoses of the face and scalp. The letter said that certain items had to be completed before final FDA marketing approval would be granted. These included:

- Compliance with the FDA's Good Manufacturing Practices (GMPs) by all Dusa's manufacturers
- Agreement on revised labelling for the product.

Dusa recently submitted revised labelling to the FDA, and reported that re-inspection of its drug manufacturer had taken place.

Because the FDA had already designated Dusa's NDA as approvable, the agency did not ask for a panel vote on approvability. The FDA is now expected to take these suggestions into consideration when developing final labelling and postmarketing study recommendations. Though nothing is cast in stone, it is possible that this device and associated technologies might be given approval sometime during December 1999.

The US FDA has just granted Dusa Pharmaceuticals a labelled indication for the use of their photodynamic process to treat actinic keratoses of the face and scalp.

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Update on Drugs

Class	Name/Company	Approval Dates and Comments
Pediculocides	Pyrethrins/Piperonyl butoxide <i>Rid</i> aerosol foam mousse Pfizer	The US FDA approved this mousse formulation in July 1999 for the treatment of head lice.
Atopic Dermatitis Agent	Fluocinolone acetonide 0.01% <i>Derma-Smoother/FS</i> Hill Dermaceuticals	The US FDA approved this topical oil in October 1999 for the additional indication of treating moderate to severe stable atopic dermatitis in patients ≥ 6 years of age.
Antibiotic Agents	Quinupristin/Dalfopristin <i>Synercid IV</i> Rhône-Poulenc Rorer	The US FDA granted accelerated approval in September 1999 for this antibacterial drug for the treatment of infections associated with vancomycin-resistant <i>Enterococcus faecium</i> bacteremia (VREF) and skin-structure infections (SSSI) caused by methicillin-susceptible <i>Staphylococcus aureus</i> or <i>Streptococcus pyogenes</i> . <i>Synercid</i> is the first drug in the streptogramin class approved for human use in the US.
Drug News		
Wound Care	In September 1999 <i>Regranex Gel</i> (becaplermin 0.01% gel) (Ortho-McNeil) was launched in the UK for the treatment of diabetic ulcers. It is the first product to have a marketing authorization in Europe for this indication. It is available in the US and Canada.	
Antipruritic Agents	The <i>British Journal of Dermatology</i> (140(5):979-980,1999) reported that cetirizine, used in the treatment of allergic disorders such as allergic rhinitis and chronic urticaria, can itself cause maculopapular eruptions and generalized chronic urticaria in rare cases.	
Leprosy	The World Health Organization (WHO) states that leprosy is nearing elimination worldwide as a public health problem. The use of multidrug therapy (MDT) since 1985 has already reduced the global prevalence of the disease by 85%. The number of countries above the target level has dropped from 122 to 28. However, by the end of 2000, there may still be about 10 countries whose leprosy burden is greater than WHO's target level of less than one case per 10,000.	
Antihistamine Agents	Janssen announced its decision to voluntarily discontinue manufacturing, distributing and marketing <i>Hismanal</i> (astemizole) tablets. <i>Hismanal</i> is an antihistamine indicated for relief of symptoms associated with seasonal allergic rhinitis and chronic idiopathic urticaria. It has been available since 1988.	
Pediculocides	<i>Rid Lice Egg Loosener Gel</i> Pfizer	In June 1999 Pfizer introduced a new approach to loosen nits from the hair shaft. It is to be used after the shampoo to dissolve the substance that glues the nit to the hair shaft.
Immuno-suppressant	Tacrolimus <i>Protopic Ointment</i> Fujisawa Healthcare	A US NDA was filed in September 1999 for this ointment for the treatment of atopic dermatitis. This drug has been approved for marketing in Japan, but has not yet been launched.
Antiviral Agents	Docosanol Avanir Pharmaceuticals	In July 1999 the US FDA asked for more data before it would approve the NDA for this topical cream for oral-facial herpes.

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