24

Topical dermatological therapy

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Skin diseases are common in small animal practice. Unlike most other organs, skin is readily visible and accessible so topical therapy can be a feasible treatment option for some disorders. This chapter serves as an introduction to topical therapy in small animal practice. After providing details on pathophysiology of the skin, practical tips on topical therapy will be followed by a discussion of the major ingredients in shampoos and conditioners. Relevant examples of creams and ointments and information on topical therapy of otitis externa complete the chapter. It is impossible to list the multitude of products available. Rather than discussing individual products, the focus of the chapter will be on ingredients commonly found in topical medications in most countries. The choice of individual products is up to the veterinarian and will depend on availability and personal experience.

Application of drugs to the skin surface is theoretically easy and limited more by owner and patient constraints than by inherent procedural problems. Owner concern over possible side effects of oral drugs has increased in recent years, resulting in an increased willingness to spend time and money on topical therapy. These products may improve the animal's skin condition, appearance and odor, and relieve pruritus.

However, the hair coat of small animals can limit the use of creams and ointments, especially with skin diseases affecting larger areas of the body. Many pets will try to remove topical agents by licking. This may remove most of the drug before penetration and render it useless. Systemic side effects may also occur due to ingestion of the drug or its vehicle.

Typically, creams or ointments are used in the treatment of otitis externa or localized skin lesions. When applying these agents, it is recommended the patient be distracted by feeding, playing or walking for the first 5–15 min after administration to avoid removal of the active drug prior to penetration into the skin and possible systemic adverse effects.

Relevant pathophysiology

The skin is the largest organ of the body. It is the anatomical and physiological barrier between the animal and the environment and as such has a multitude of functions, summarized in Table 24.1.

The skin consists of epidermis, dermis and subcutis or panniculus. The epidermis is the outermost part of the skin and is formed by several layers of keratinocytes situated on a basal membrane. The basal keratinocytes divide constantly and new keratinocytes gradually move outwards through the stratum spinosum, stratum granulosum and stratum corneum while differentiating into a dead horny cell or corneocyte, which is ultimately shed. Proliferation and differentiation are influenced by a multitude of factors such as hormones, vitamins, cytokines and physical or chemical insults.

The dermis is a part of the body's connective tissue system and provides the tensile strength and elasticity of skin. It contains hair follicles, arrector pili muscles, sebaceous and sweat glands, lymph and blood vessels and nerves.

The subcutis is usually the thickest layer of the skin. It functions as an energy reserve and has a role in thermogenesis, insulation and protective padding.

A disturbance of the cutaneous physiological balance often results in an influx of inflammatory cells and/or release of inflammatory mediators and cytokines in the epidermis and dermis. This leads to increased proliferation of keratinocytes and thus epidermal hyperplasia, which may lead to the clinical feature of scaling. Pathogenic microbial agents may proliferate on the surface of the stratum corneum or in the follicular lumen. They may eventually penetrate the epithelial barrier, causing ulceration or furunculosis. Pruritus, as well as visual changes in the skin and hair coat such as scaling, greasiness and odor, are often associated with chronic inflammation and/or infection and are major concerns for animal owners.

Practical tips for topical dermatological therapy

Shampoos, conditioners and moisturizers are suitable for decreasing or eliminating pruritus and odor temporarily and improving the appearance of skin and coat. If the inflammation and/or infection affects deeper layers of the skin, topicals may also be useful as concurrent therapy. However, they typically cannot penetrate to deeper layers and therefore are not effective as sole therapy in these cases.

Trade names of a selection of shampoos available in the USA, Europe and Australasia are given in Table 24.2

Table 24.1 Functions of the skin	
Sensory perception	Touch Pressure Itch Pain Heat Cold
Protection against	Physical insults Microbes Solar radiation Water loss
Secretion/excretion of	Sweat Sebum
Vitamin D production	
Immune regulation	
Temperature regulation	

and topical ear medications are listed in Table 24.3. Topical insecticides are frequently an essential part of flea or tick control in small animal practice. Repellants, adulticides and combinations of these agents with insect development inhibitors/growth regulators are available and are discussed in Chapter 10.

Topical therapy with shampoos and moisturizers is symptomatic. It is used as sole therapy to resolve clinical signs or as an adjunct to systemic drug therapy. Once clinical signs resolve, shampoos and moisturizers may be used to maintain clinical remission without need for systemic therapy.

The success of topical dermatological therapy will depend on several factors.

- The disease
- The patient

Table 24.2 Selected shampoos and conditioners available in Australia, Europe and the USA

Australia

Shampoos

* Dermocil (Illium; 0.5% hexetidine)
* Malaseb (Dermcare; 2% chlorhexidine, 2% miconazole)
* Pyoben (Virbac; 3% benzoyl peroxide)
* Pyohex (Dermcare; 3% chlorhexidine)
* Sebazole (Virbac; econazole nitrate, sulfur, sodium salicylate)
* Triocil (Parke-Davis; 0.5% hexetidine)
* Allergroom (Virbac; 5% urea, glycerin, lactic acid)
* Aloeveen (Dermcare; 2% colloidal oatmeal, aloe vera)
* Episoothe (Virbac; 2% colloidal oatmeal)

Conditioners

* Aloeveen (Dermcare; 2% colloidal oatmeal, aloe vera)
* Episoothe Conditioner (Virbac; colloidal oatmeal)
* Resisoothe (Virbac; fatty acids, vitamine E, oatmeal)

Europe

(Names and availability may differ in various European countries)

Shampoos

* Canoderm (Graeub, 3% benzoyl peroxide)
* Clorexyderm (Jacoby; 2% chlorhexidine)
* Etiderm (Virbac; 10% ethyl lactate, benzalconium chloride)
* Hexocil (Pharmacia & Upjohn; 0.5% hexetidine)
* Lactaderm (Chassot; 10% ethyl lactate)
* Malaseb (Dermcare; 2% chlorhexidine, 2% miconazole)
* Oxydex (3% benzoyl peroxide)
* Peroxyderm (Chassot, 2.5% benzoyl peroxide)
* Sebolytic (Virbac; omega-6 fatty acid, 2% salicylic acid, piroctonolamin, zinc gluconate, 0.25 tea tree oil)
* Sebomild P (Virbac; Piroctonolamin, omega-6 fatty acids, glycerin, lactic acid)
* Polytar (Stiefel, 4.5% tar)
* Allercalm, Episoothe (Virbac; 2% colloidal oatmeal)
* Allermyl (Virbac; omega-6 fatty acids, mono- and oligosaccharides, vitamin E, piroctonolamin)
* Sebocalm (Virbac; 10% sodium oleic sulfonate, 9% lauramide, 1% glycerin)

Conditioners/Sprays

* Allermyl Lotion (Virbac; omega-6 fatty acids, mono- and oligosaccharides, vitamin E)
* Dermacool Spray (Virbac; benzalconium chloride, hamamelis, menthol)
* Sebomild P Lotion (Virbac; vitamin E, piroctonolamin, glycerin, salicylic acid)

USA

Shampoos

* Benzoyl-Plus (EVSCO; 2.5% benzoyl peroxide and encapsulated Novasome moisturizer)
* ChlorhexiDerm (DVM; 2% chlorhexidine)
* Dermazole (Virbac; 2% miconazole)
* Hexadene (Virbac; 3% chlorhexidine, lactic acid, chitosanide)
* Imaverol (Janssen, 10% enilconazole)
* Malaseb (DVM; 2% chlorhexidine, 2% miconazole)
* Mycodex (SmithKline Beecham; 2.5% benzoyl peroxide)
* Miconazole shampoo (EVSCO; 2% miconazole and encapsulated Novasome moisturizer)
* OxyDex (DVM; 2.5% benzoyl peroxide)
* Pyoben (Virbac; 3% benzoyl peroxide)
* Allerseb T (Virbac; 4% coal tar, 2% sulfur, 2% salicylic acid)
* Dermapet (Dermapet; 2% sulfur, 2% salicylic acid)
* LyTar (DVM; 3% coal tar, 2% sulfur, 2% salicylic acid)
* NuSal-T (DVM; 3% salicylic acid, 2% coal tar, 1% menthol)
* Seba-Hex (EVCO; 2% chlorhexidine, sulfur, salicylic acid and encapsulated Novasome moisturizer)
* SebaLyt (DVM; 2% sulfur, 2% salicylic acid, 0.5% triclosan)
* Sebolux (Virbac; 2% sulfur, 2% salicylic acid)
* Seba Moist (EVSCO; 2% sulfur, 2% salicylic acid and encapsulated Novasome moisturizer)
* Sulf/OxyDex (DVM; 2.5% benzoyl peroxide, 2% sulfur)
* SeboRex (DVM; 3% salicylic acid, 2% sulfur, 1% chlorhexidine)
* Relief (DVM; 1% pramoxine, colloidal oatmeal)
* Allergroom (Virbac; 5% urea, glycerin, lactic acid)
* Dermal Soothe Shampoo (EVSCO; pramoxin, novasomes)
* Episoothe (Virbac; 2% colloidal oatmeal)
* Hydra Pearls Rehydrating Shampoo (EVSCO; Novasomes)
* HyLytefa (DVM; humectants, emollients and omega-6 fatty acids)

Conditioners/Sprays

* Dermal Soothe Spray (EVSCO; pramoxin, novasomes)
* Episoothe (Virbac; 2% colloidal oatmeal)
* Hydra Pearls Rehydrating Spray (EVSCO; Novasomes)
* HyLytefa (DVM; humectants, emollients and omega-6 fatty acids)
* Relief (DVM; pramoxine 1%, colloidal oatmeal)

Table 24.3 Selected topical ear medications (names and availability may differ in various countries)

- * Aurimite (Schering Plough; pyrethrins, benzocaine)
- * Aurizon (Bayer; marbofloxacin, clotrimazole, dexamethasone)
- * Baytril Otic (Bayer; enrofloxacine, silver sulfadiazine)
- * Bur-Otic (Virbac; hydrocortisone, Burrow's solution)
- * Cerumite (EVSCO; pyrethrins, squalene)
- * Conofite Lotion (Schering Plough; miconazole)
- * Eradimite (Fort Dodge; pyrethrins)
- * Fucidine (Graeub; fusidic acid, framycetin, nystatin, prednisolone)
- * Gentocin Otic (Schering Plough; gentamicin, betamethasone)
- * Mita-Clear (Pfizer; pyrethrins)
- * Otiprin (Vetoquinol; chloramphenicol, dexamethasone, lidocaine)
- * Otomax (Schering Plough; gentamicin, betamethasone, clotrimazole)
- * Otomite Plus (Virbac; pyrethrins)
- * Panolog (Fort Dodge; nystatin, neomycin, thiostreptone, triamcinolone)
- * Surolan (Jansen; miconazole, polymyxin B, prednisolone)
- * Synotic Otic (Fort Dodge; fluocinolone, dimethyl sulfoxide)
- * Tresaderm (Merial; thiabendazole, neomycin, dexamethasone)
- * Tritop (Pfizer Animal Health; neomycin, isoflupredone)

- The owner
- The environment

The disease

The pathomechanism of the skin disorder will determine whether an agent may be useful and if so, which one. **Seborrheic disorders** cause epidermal hyperplasia and hyperkeratosis, clinically evident as scaling. This may be primary or (much more commonly) secondary to a variety of underlying diseases such as infection, allergy, hormonal disorders and others. Secondary seborrhea will resolve after the underlying cause is appropriately treated. Seborrhea may benefit from keratoplastic and keratolytic agents such as sulfur, salicylic acid and tar.

Treating **bacterial infections** with appropriate antimicrobial agents will eliminate the organism and resolve secondary signs such as scaling or odor. Antibacterial agents such as ethyl lactate or benzoyl peroxide, and antifungal agents such as ketoconazole are available in shampoo formulations. Shampoos may also contain chlorhexidine, iodine and miconazole, which are antibacterial as well as antifungal. Additional antimicrobial agents in some topical products are benzalconium chloride, PCMX (para-chloro-meta-xylenol) and piroctonolamin.

Pruritic skin diseases such as hypersensitivity may be treated with nonspecific antipruritic agents such as oatmeal or emollient shampoos or conditioners in conjunction with regular moisturizing rinses or sprays. Fatty acids, vitamins, urea, lactic acid, glycerine and mono- and oligosaccharides may also be included in antipruritic shampoos and lotions.

Topical ear medications are indicated in almost every patient with otitis externa. If the ear canal is dry and scaly, ointments are more suitable than solutions or lotions. Otitis externa purulenta should be treated with solutions or lotions rather than ointments where possible. Almost all ear medications contain a glucocorticoid to suppress inflammation in addition to antimicrobial or antiparasitic drugs. Which particular product is most effective will depend on the underlying cause of the otitis as suggested by history, otoscopic examination, ear cytology, microbial culture and sensitivity and microscopic examination of debris for parasites.

The patient

Species, size, hair coat and temperament will determine the suitability of the patient for topical therapy. Cats tend to dislike immersion in water (with or without shampoo) or spraying and often express their displeasure aggressively. Dogs are more readily convinced to accept shampoos, sprays or moisturizers. In general, it is more difficult (and more expensive and time-consuming) to bath larger breeds than small or toy breeds. Long-haired and plush-coated breeds are more difficult to shampoo than short-coated breeds. Last but not least, some dogs enjoy their bath, others tolerate it and a small percentage dislike it enough to make the bath an unpleasant experience for all involved. It is essential to identify dogs in the last group early on as long-term shampoo therapy is an unrealistic goal for them and their owners.

The owner

Regular and long-term topical therapy requires time, dedication and money. Clear, simple, written instructions will avoid misunderstandings and good communication will ensure that owners unable to comply are identified early. Owners with a busy lifestyle may have more difficulty coping with long-term topical therapy than those with a more relaxed lifestyle. If the pet is considered a family member, the motivation to undertake treatment regimens will be higher. If, however, the patient has a low priority within the family, compliance may be problematical. If financial constraints are present, the author recommends using an inexpensive nonmedicated cleansing shampoo prior to the typically more expensive medicated product. This is more time-consuming but decreases the amount of medicated shampoo needed per bath and thus the long-term cost to the owner.

The environment

Climate and seasonal temperature will be relevant. Shampoo therapy for a Jack Russell terrier can be accomplished easily indoors but bathing a St Bernard

regularly may be unrealistic during the cold seasons in temperate or colder climates, as most clients will shampoo big dogs outdoors.

Long-term maintenance

The author initially recommends shampooing once to twice weekly. Whether therapy will be continued beyond the first few weeks depends, of course, to a large degree on the efficacy of the treatment. Once the condition has responded to topical agents, it may be possible to taper therapy to weekly or fortnightly baths to maintain remission. Important to achieving long-term compliance is the ability to communicate well with the client and reassure them that they are contributing significantly to their pet's wellbeing.

Technical tips

It is important at the start of therapy that clients are shown in the clinic how to apply topical products. This applies particularly to creams, ear medication, sprays and spot-ons. If the owner does not feel comfortable spraying the animal, it may be more effective to schedule appointments for this to be done by a veterinarian or veterinary technician/nurse at regular intervals.

The method of administration of ear medications should be explained carefully and then demonstrated to the owner using one of the patient's ears. After the demonstration, the owner should treat the other ear under supervision of the veterinarian or veterinary nurse/technician to maximize compliance and minimize chances of procedural problems.

Specific tips for shampoo therapy

It is often not possible to demonstrate shampoo therapy in a clinical setting, so thorough oral and written instructions are crucial.

- Product warnings should be discussed prior to therapy.
- Grooming prior to shampooing reduces coat matting.
- Ocular ointments to protect the eyes are not only ineffective but may enhance the irritant potential of shampoo, perhaps by trapping irritant solution in the eye.
- It may be useful to remove debris and dirt with a nonmedicated shampoo before using a medicated shampoo. This decreases the amount of medicated shampoo required and thus treatment cost.
- Shampoo therapy is effective only if the right shampoo is used at the right frequency and for the right time. Most shampoos require a contact time of 10–15 min, a long time when trying to restrain a wriggly or bouncy animal. Contact times should be accurately timed using a watch or stopwatch.
- To facilitate patient compliance, the patient may be petted or massaged in the bath. In warmer climates it may be possible to play with the animal outside for 5–10 min once the shampoo has been applied and then return to the tub for the recommended 10 min of rinsing.
- Adverse reactions after shampoo use are rare. If there is concern that a patient may be at risk, shampoo reactions can be identified by 'patch testing'. The shampoo is applied to a small area of nonhaired skin on the ventrum, left on for 10 min and then rinsed off. The area is inspected regularly during the following 24 h for signs of inflammation. If inflammation is observed this indicates that this particular shampoo is not suitable for this patient. During shampoo therapy patients must be monitored as adverse effects may occur at any time. If the skin appears inflamed and/or the patient is irritated beyond the normal rubbing and shaking that occurs to assist drying in the first 5–20 min after a bath, topical therapy should be discontinued or different products used.
- The use of a whirlpool has been advocated for treatment of skin disease in dogs. In a double-blinded, randomized and placebo-controlled study, shampooing pruritic dogs in a whirlpool achieved better results than conventional shampoo therapy or water treatment alone. This effect was particularly pronounced in long-haired dogs.

Specific tips for application of topical preparations to the external ear canal

- Ear medications should be warmed to 'skin temperature' by placing them in a pocket for 5–10 min prior to administration.
- All attempts should be made to make the experience enjoyable. Patting, giving a treat or playing a game after every treatment may all be helpful.
- In pets with recurrent ear disease, it can be beneficial to handle the ears regularly twice weekly, even when the ears are healthy. Pretending to apply ear drops then rewarding with a game or treat can reduce the anxiety the pet associates with administration of ear drops.
- Animals should not be restrained by pulling or holding the affected and painful ear. If the pet struggles, altering the restraint method or seeking assistance may be necessary.
- Once the pet is appropriately restrained on the floor, table, chair or lap, the tip of the ear should be lifted to visualize the opening of the ear canal. Once the opening has been clearly identified, the top should be taken off the tube or bottle and the prescribed amount squeezed into the opening. Alternatively a syringe can be used to draw up the correct amount and then squirt the contents into the ear canal. Gently moving the ear will straighten the angle of the ear canal and assist the medication to reach the deeper

areas. If the pet shakes the head immediately when the drops are applied, swabs should be held over the opening to stop the drops being flicked out again.
- If the inner part of the pinna is affected, a very thin layer of medication should be applied to cover the affected area.
- After the drops are administered, the ear should be gently massaged for 1–2 min. The animal will then shake the solution from the ear. Excess medication may be removed with a tissue but only from the outside of the ear. Cotton swabs should never be pushed down into the ear canal as this will only force debris down further.

Special tips for application of topical drugs to smaller skin lesions

- Application of a thin layer of the cream or ointment to cover the affected area is sufficient; application of large amounts of the topical does not increase efficacy.
- Prevention of licking or rubbing is most important in the first 5–10 min after application and is best achieved by either feeding, walking or playing with the pet for the first 10 min after treatment.
- The frequency and duration of drug administration must be communicated clearly to the owner and should be adhered to. It is necessary to treat until clinical and microscopic remission (determined by impression smears or tape preparations) is achieved.

SHAMPOOS, MOISTURIZERS AND CONDITIONERS

Shampoos typically are soap or detergent based. Soaps are composed of sodium or potassium salts of high-molecular-weight aliphatic acids and emulsify skin oils and sebum with water to remove dirt. The associated alkaline reaction can be irritant. Thus, soaps are not commonly used in veterinary shampoo formulations.

Detergents are mild cleansing soap substitutes consisting of emollient oils, emulsifiers, surfactants and stabilizers and typically are tolerated well by sensitive or inflamed skin. Other added ingredients include antioxidants, conditioners, pH adjusters, preservatives, coloring agents and fragrances. Some shampoos also contain moisturizing agents such as glycerin, lactic acid, urea and essential fatty acids. 'Hypoallergenic' shampoos contain a smaller number of ingredients, presumably with a lower chance of an irritant or allergic reaction.

The pH of canine skin is less acidic than that of human skin and some companies attempt to formulate veterinary shampoos with a pH close to that of normal canine skin. However, in general the most important factor for pH determination is not the patient's skin pH but the qualities of the active ingredients and their solubility at various pH levels. Thus, the difference between human and veterinary shampoos with similar ingredients may not be sufficient to avoid use of human formulations in small animal patients.

Many ingredients, particularly tar, benzoyl peroxide and chlorhexidine, are difficult to formulate, package and keep in solution and therefore should be bought from reputable companies.

New technologies have led to formulation of shampoos where the active ingredients are trapped in microvesicles. Once the shampoo is applied to the skin, the lipid membrane of the microvesicles attaches to the skin and hair. A positive exterior charge contributes to binding to the negatively charged skin and hair. In the dry environment, the active ingredient is gradually released, leading to sustained activity. Microvesicles may contain water (e.g. Novasomes®, EVSCO) or active ingredients (e.g. Spherulites®, Virbac). The benefit of sustained action may be less pronounced with antibacterial shampoos, as one of the proposed mechanisms for antibacterial action is the pH change on the skin surface associated with shampooing. This pH change leads to a decrease in bacterial adherence and bacteria are easily removed from the skin surface.

Shampoos contain a variety of active ingredients singly or in combination.

Antiseborrheic agents

Sulfur

Clinical applications

Sulfur shampoos are indicated for the treatment of seborrheic dermatitis and primary seborrhea sicca and oleosa. If the seborrhea is secondary to another skin disease, treatment of the primary disorder will resolve the seborrhea. In pets with dry skin, the use of a moisturizer after the shampoo is recommended.

Mechanism of action

Sulfur is keratoplastic; it slows down the epidermal cell proliferation by a cytostatic effect on the basal cell layer. It is also keratolytic. Hydrogen sulfide and pentathionic acid are formed and cause damage to corneocytes and subsequent softening of the stratum corneum and shedding of cells. They are also responsible for the antibacterial and possible antifungal action of sulfur. Sulfur is not a good degreasing agent and is therefore not as drying as other antiseborrheic agents.

Adverse effects

- Occasionally, irritant reactions can occur. Dogs and cats may show pruritus and/or inflamed skin after shampooing.
- Sulfur can stain jewelry!

Known drug interactions
Sulfur has synergistic keratolytic activity with salicylic acid. Thus the two agents are frequently combined. The synergy is most pronounced when the concentrations are similar. Typically, shampoos contain 2% sulfur and 2% salicylic acid.

Salicylic acid
Clinical applications
Salicylic acid is usually combined with sulfur and is recommended for the treatment of seborrheic dermatitis and primary seborrhea sicca and oleosa. If the seborrhea is secondary to another skin disease, therapy of the primary disorder will resolve the seborrhea. In pets with dry skin, the use of a moisturizer after the shampoo is recommended.

Mechanism of action
Salicylic acid is keratolytic by lowering the pH of the skin, resulting in increased hydration of the keratin and swelling of the corneocytes. It also solubilizes the intercellular cement substance in the stratum corneum, facilitating desquamation. Salicylic acid does not change the mitotic rate of the basal keratinocytes. It is mildly antipruritic and anti-inflammatory.

Adverse effects
Occasionally, irritant reactions can occur. Dogs and cats may show pruritus and/or inflamed skin after shampooing.

Known drug interactions
Salicylic acid has synergistic activity with sulfur.

Tar
Tar shampoos are prepared typically from coal tar but may occasionally be derived from wood or bituminous tars (prepared from shale deposits). Distillates of coal contain some 10,000 different constituents and it is not clear which of these components are responsible for the clinical efficacy. It is possible that very potent and clinically efficacious components are not responsible for the smell of crude tar. The smell may influence owner compliance. Coal tar solution may be found in shampoo formulations and contains only 20% coal tar. Some products combine tar with sulfur and salicylic acid. Tar shampoos are now used less commonly than in the past as other effective products have been developed.

Clinical applications
A tar shampoo is recommended for the treatment of primary seborrhea oleosa. It is probably the most effective antiseborrheic shampoo available. Tar is not only keratoplastic and keratolytic but also degreasing. Dogs with normal or dry skin will often deteriorate without the concurrent use of a moisturizer to prevent excessive dryness. Greasy seborrhea, however, will respond better to tar shampoos than to sulfur or salicylic acid as the degreasing action removes the grease and debris caused by the disease.

Mechanism of action
Tar is keratolytic and keratoplastic, antipruritic, degreasing and vasoconstrictive. The exact mechanism of the keratolytic and antipruritic action is unknown. Tar suppresses epidermal growth and DNA synthesis. Crude coal tar and some of its photoreactive ingredients produce oxygen and superoxygen radicals and interstrand cross-links in DNA, causing the keratoplastic effect. In the human literature, the role of concurrent ultraviolet (UV) B radiation in enhancing this effect is controversial.

Adverse effects
- Irritant or allergic reactions are more common in shampoos with higher concentrations of tar (>2%) and 'patch testing' is recommended prior to the use of products containing tar.
- Folliculitis can be observed in some patients and should be considered if the patient seems to develop 'hive-like' reactions.
- Sun sensitivity may occur. Sparsely-haired dogs should not be allowed outside on the day of the bath.
- Tar products should not be used in patients with dry skin.
- Tar shampoos must not be used in cats.

Known drug interactions
- Tar induces microsomal drug-metabolizing enzymes. It has been suggested that even topically applied tar could influence the rate of biotransformation of concomitantly administered oral drugs in some patients.
- Coadministration of photosensitizing drugs such as sulfonamides and phenothiazines may aggravate the tendency of sun sensitivity in sunbathing, sparsely-haired dogs.

Selenium sulfide
Clinical applications
Selenium sulfide is an older antiseborrheic agent and is considered for severe cases of oily seborrhea nonresponsive to tar and/or sulfur/salicylic acid. It also has been used to treat cutaneous yeast infections.

Mechanism of action
Selenium sulfide interferes with hydrogen bond formation in the keratin and thus is keratolytic. It is kerato-

plastic by depressing epidermal cell turnover rate. Selenium sulfide is fungicidal at higher concentrations.

Adverse effects

Selenium sulfide is drying and may be irritant. It will also stain the coat and is thus not recommended as a first-line shampoo.

Antimicrobial agents

Benzoyl peroxide

Clinical applications

Benzoyl peroxide is indicated for superficial and deep pyodermas. Because of its presumed follicular flushing activity, it also is recommended in patients with demodicosis, acne, comedone syndromes and sebaceous adenitis. Benzoyl peroxide has prominent degreasing activity so it is the agent of choice for patients with greasy or oily skin. However, its use must be followed by a moisturizing rinse in any dog with normal or dry skin. It is generally used at concentrations of 2–3%.

Mechanism of action

Benzoyl peroxide is metabolized in the skin (predominantly in the upper layers of the epidermis) to benzoic acid and free oxygen radicals. The former lowers skin pH, the latter disrupts microbial cell membranes. Benzoyl peroxide has broad-spectrum antimicrobial activity that persists for 48 h even when conditions for bacterial growth are optimal. It has also been shown to be keratoplastic by inhibiting the epidermal metabolism and DNA synthesis.

Benzoyl peroxide has been shown to decrease metabolism of sebaceous gland cells in humans but whether sebum production is actually decreased is controversial. Free fatty acids decrease in sebum of human patients treated with benzoyl peroxide, presumably because of its antibacterial effect, as bacterial lipases are responsible for production of free fatty acids. Benzoyl peroxide is also believed to have a follicular flushing action.

Adverse effects

- Erythema, pain and pruritus can occur, especially in cats. This occurs more commonly when concentrations over 3% are used. Thus, most veterinary products have a benzoyl peroxide concentration of 2–3%.
- Ocular irritations have also been reported.
- Alone, benzoyl peroxide has no known carcinogenic effect. It is, however, a tumor promoter by enhancing chemical carcinogenesis with 7,12-dimethylbenzanthracene in hairless mice. Conversely, it appears to protect against ultraviolet carcinogenesis.
- Owners must be informed that benzoyl peroxide may bleach fabrics.

Chlorhexidine

Clinical applications

Chlorhexidine is indicated for dogs and cats with skin infections and dry to normal skin. It appears to have greater efficacy for bacterial infections, particularly *Staphylococcus* spp, than for yeast or dermatophyte infections. It is usually added in concentrations between 0.5% and 3%. Shampoos containing combinations of chlorhexidine and miconazole are available and have superior action against yeast and fungal infections compared to shampoos containing chlorhexidine only.

Mechanism of action

Chlorhexidine is a cationic surfactant synthetic biguanide with broad-spectrum antibacterial and less pronounced antifungal activity. It disrupts microbial cell membranes and coagulates cytoplasmic proteins. Chlorhexidine has a residual activity of several hours. It is nonirritant, nontoxic and works in organic debris.

Adverse effects

Irritant reactions may rarely be seen.

Ethyl lactate

Clinical applications

Ethyl lactate is used for mild superficial bacterial infections in normal to dry skin. Conflicting results are reported from various studies: some show it to be as effective as benzoyl peroxide, others that it is no more effective than water.

Mechanism of action

Ethyl lactate is metabolized to ethanol and lactic acid by bacterial lipases in hair follicles and sebaceous glands. Ethanol solubilizes lipids and lactic acid and lowers the skin pH, resulting in a bactericidal effect. Both agents are short-lived in vivo.

Adverse effects

Occasionally, patients show irritant reactions following treatment.

Iodine

Clinical applications

Iodine products are indicated for bacterial or fungal infections of the skin. However, they are considered to be cosmetically inferior to other equally effective products and thus are less commonly used.

Mechanism of action

Iodine is an excellent bactericidal, fungicidal, virucidal and sporicidal agent. Povidone-iodine is elemental iodine complexed with the carrier molecule pyrrolidone nitrogen, which augments sustained release, dispersibil-

ity and penetration. It must be diluted for proper dissociation of the complex. It has a mild degreasing activity.

Adverse effects
Iodine usage may cause irritations and cutaneous hypersensitivities, and stains light hair coats.

Triclosan
Clinical applications
Triclosan is an antibacterial ingredient in some shampoos used for seborrheic disorders and may be helpful in preventing infections of seborrheic skin.

Mechanism of action
Triclosan is a bisphenol disinfectant. It is bacteriostatic against predominantly Gram-positive bacteria and has been reported to be effective in treating meticillin-resistant staphylococcal infections at a concentration of 2%. At a concentration of 0.5% it was less effective than benzoyl peroxide or chlorhexidine in inhibiting the growth of *Staphylococcus intermedius*.

Miconazole
Mechanism of action
Miconazole inhibits the synthesis of ergosterol, a major component of fungal cell membranes. This interferes with the barrier function of the membrane and with membrane-bound enzymes.

Clinical applications
Miconazole is an azole derivative that, because of its poor oral absorption and rapid clearance, is used predominantly for topical treatment of localized superficial infections. A formulation containing chlorhexidine and miconazole has been shown in double-blinded studies to be effective in the treatment of canine *Malassezia* dermatitis. Miconazole in various ear medications is effective against yeasts complicating canine otitis externa. Miconazole also has activity against Gram-positive bacteria such as *Staphylococcus intermedius*, the predominant organism involved in bacterial skin infections in small animals.

Adverse effects
Irritation characterized by erythema, pruritus and occasionally exudation may rarely be seen.

Antipruritic and moisturizing agents

Emollients
Clinical applications
Emollients include fats such as lanolin, hydrocarbons such as paraffin, petrolatum and mineral oil, humectants such as carboxylic acid and lactic acid and oils such as olive, cottonseed, corn, almond, peanut and coconut oil. These agents are added to shampoos as vehicles and for their local effects in softening and protecting the skin.

Mechanism of action
Emollients soften the skin by forming an occlusive oil film on the stratum corneum, thus decreasing the transepidermal water loss.

Moisturizing agents
Clinical applications
Urea, glycerin and propylene glycol are classified as demulcent polyhydroxy compounds. They are added to many shampoos for protection and moisturizing of the skin. Essential fatty acids and colloidal oatmeal are also added to some products.

Mechanism of action
A demulcent is a high molecular weight compound in aqueous solution that coats the skin surface, thus protecting the underlying cells and alleviating irritation. Urea promotes hydration and is antibacterial. It accelerates the digestion of fibrin and is proteolytic; thus it helps in removal of excess keratin and crusting.

Glycerin is a popular vehicle as this trihydric alcohol is miscible with water and alcohol. It is a hygroscopic agent that is absorbed into the skin. Similarly, propylene glycol is a good vehicle, miscible with water and dissolving many essential oils. Linoleic acid is important for the barrier function of the stratum corneum, particularly in relation to transepidermal water loss.

Topical application of fatty acids has been shown to affect epidermal fatty acid concentrations and may hydrate the stratum corneum by reducing transepidermal water loss. Colloidal oatmeal hydrates the stratum corneum hygroscopically by attracting and binding water passing through the epidermis.

Adverse effects
Irritant and more commonly, allergic reactions are possible with oatmeal preparations.

Antipruritic agents
Hydrocortisone, antihistamines and aloe vera extracts have been incorporated in shampoos.

Clinical applications
Shampoos containing antipruritic agents are recommended for pruritic patients without secondary infection or seborrhea and dry to normal skin. Their long-term use depends on their efficacy in each patient; relief of pruritus may be negligible or the shampoo may be effective in controlling pruritus for up to 3 d.

Mechanism of action

Antihistamines and hydrocortisone presumably penetrate the epidermis and exert antihistaminic and anti-inflammatory effects in the upper dermis. Their mechanism of action is discussed in Chapter 11.

Systemic absorption of hydrocortisone from shampoo formulations used twice-weekly for 6 weeks has been shown to be clinically insignificant.

Aloe vera has been reported to have anti-inflammatory activity in rats as a result of inhibition of cyclo-oxygenase activity and neutrophil migration. Further studies are needed to evaluate the efficacy and side effects of these shampoos in small animal dermatology.

CREAMS, EMULSIONS AND OINTMENTS

Many creams and ointments are available and it is beyond the scope of this review to discuss them in detail. Most of these products are a combination of anti-inflammatory and antimicrobial agents, commonly glucocorticoids with antibacterials and/or antifungals in a base of solvents, emollients and moisturizing agents discussed above. They form a protective cover and, if occlusive, may prevent transepidermal water loss.

Because of the typically dense hair coat of small animals and their tendency to remove administered topicals by licking or rubbing, creams and ointments are useful for small, local lesions only. Pyotraumatic dermatitis or 'hot spots', skinfold pyoderma, otitis externa and feline acne are common examples of localized problems that may be successfully treated with creams, emulsions or ointments.

Numerous topical anti-inflammatory and antibacterial agents are available. The mechanism of action of most of these drugs is covered elsewhere in this textbook. However, some common ingredients of topical products are discussed below.

Mupirocin

Clinical applications

Mupirocin is an antibacterial agent recommended for localized bacterial infections in dogs and cats. It has been reported to be efficacious in the treatment of feline acne, even when *Malassezia* spp rather than bacteria were documented to be the etiological organism.

Mechanism of action

Mupirocin inhibits bacterial protein synthesis by binding to bacterial isoleucyl transfer RNA synthetase. It is mainly efficacious against Gram-positive aerobes such as staphylococci.

Adverse effects

Mupirocin is supplied as a 2% solution in a water-soluble ointment base of polyethylene glycol. The base can be toxic, especially in cats with impaired renal function, if large amounts are applied for extended treatment periods and the cat licks off some of the ointment.

Tacrolimus

Clinical applications

Tacrolimus is a macrolide immunomodulator synthesized by the fungus *Streptomyces tsukubaensis*. Tacrolimus is reported as an effective treatment for canine atopic dermatitis, perianal fistula and discoid lupus erythematosus. It is also used for other immune-mediated skin diseases such as pemphigus foliaceus in the dog. In veterinary medicine, tacrolimus is applied as a 0.1% ointment initially twice daily topically and then may be tapered down after disease remission to daily or once every alternate day.

Mechanism of action

Tacrolimus is a calcineurin inhibitor similar to ciclosporin and has numerous inhibitory effects on a number of immune cells such as lymphocytes, dendritic cells, mast cells and eosinophils. Its mechanism of action is discussed in more detail in Chapter 12.

Adverse effects

- Tacrolimus may cause a transient burning sensation in dogs and humans.
- When blood concentrations were measured in dogs, they were shown to remain below toxic levels and no hematological or biochemical abnormalities were reported.

TOPICAL THERAPY OF OTITIS EXTERNA

Ear preparations usually consist of a vehicle (such as oil, solution or ointment) and a variety of active ingredients, including anti-inflammatory, antimicrobial and/or antiparasitic agents. The detailed mechanism of action of the active ingredients is discussed in other relevant chapters. Owner education is crucial prior to topical therapy of otitis externa. Patients with otitis frequently resent administration of medication because of associated discomfort and pain. It may be necessary in severe cases to begin therapy with an ear flush under anesthesia to remove debris.

Clinical applications

Topical treatment of otitis externa is indicated when the external ear canal is inflamed and/or infected. However,

otitis externa may be caused by a variety of conditions from allergies, hormonal disease and ectoparasites to foreign bodies and neoplasia. Symptomatic treatment may be successful in achieving temporary remission but without diagnosis and therapy of the primary disease, long-term success is highly unlikely. In addition, a careful assessment of potential middle ear involvement is indicated. Otitis externa without otitis media may usually be treated successfully with topical medications. If otitis media is present, long-term systemic therapy is often needed. Otoscopic examination may reveal a ruptured tympanum, indicating middle ear disease. However, otitis media has been reported in patients with intact ear drums. In these patients, the tympanum most likely has healed after initial trauma and infection of the middle ear. If clinical signs of otitis media such as Horner's syndrome or head tilt are not present, imaging methods such as radiography, computed tomography or magnetic resonance imaging may be needed to exclude otitis media in patients with recurrent otitis externa or ear disease unresponsive to appropriate topical therapy.

Glucocorticoids

Glucocorticoids are included in most products. Because of the anatomical structure of the external ear and the cartilaginous structures, inflammation and associated swelling of the aural epithelium lead to a smaller canal lumen, which decreases ventilation and contributes to the development and persistence of infection. The anti-inflammatory effects of glucocorticoids decrease exudation, swelling, scar tissue and proliferative changes, all of which help to promote drainage and ventilation.

Betamethasone valerate and fluocinolone acetonide are some of the more potent glucocorticoids found in ear medications. Moderately potent glucocorticoids include triamcinolone acetonide and dexamethasone. All of these are systemically absorbed and influence the pituitary-adrenal axis, thus long-term treatment with these drugs should be carefully considered. Once active inflammation is controlled, long-term and prophylactic therapy should utilize glucocorticoids of lower potency such as hydrocortisone.

Antibacterial agents

Antibacterial agents frequently included in topical ear medications include aminoglycosides such as neomycin or gentamicin, polymyxin, chloramphenicol, bacitracin, framycetin, enrofloxacin, marbofloxacin, miconazole, silver sulfadiazine, povidone-iodine, chlorhexidine and acetic acid. Before choosing an appropriate formulation, cytological evaluation of an ear swab is recommended and will identify inflammatory cells, cocci, rods and/or yeast organisms.

Cocci are typically *Staphylococcus* spp or *Streptococcus* spp. The former respond to most antibacterial agents. Miconazole and bacitracin are used most commonly in the author's practice for otitis externa complicated by coccal infection, as determined by cytology. When appropriate therapy based on cytology is not effective, bacterial culture and sensitivity are recommended to assist in the choice of antibacterial agents.

Rods are typically *Pseudomonas aeruginosa, Pasteurella multocida, Escherichia coli* or *Proteus* spp. Their response to antibacterial therapy is much more unpredictable and culture and sensitivity tests are recommended as a base for the selection of therapy even in patients not previously treated. If culture is not possible because of financial constraints, the most effective commercial ear preparations for rod infections in the author's practice contain gentamicin in combination with a potent glucocorticoid. *Pseudomonas* isolates are often susceptible to polymyxin B, but this antibiotic is inactivated by purulent discharge and thus should only be applied after thorough ear cleaning. Commercial products containing fluoroquinolones may also be effective.

However, if the tympanum is ruptured, most commercial preparations have ototoxic potential and alternatives need to be considered. Acetic acid at a concentration of 2% appears to be effective against *Pseudomonas aeruginosa*, but administration into ulcerated ear canals is not tolerated well. A solution of silver sulfadiazine at 1% (1 g of silver sulfadiazine in 100 mL of sterile water) administered twice daily has also been reported to be effective. In a more recent study, a solution containing 0.1% silver sulfadiazine also was effective but more liquid and thus easier to apply and disperse in the external canal.

Injectable ticarcillin or fluoroquinolones may be diluted with physiological saline solution and applied to the external ear canal. Ticarcillin is reconstituted to a concentration of 100 mg/mL. This solution is not stable at room temperature and should be frozen in aliquots (stable for 1 month) and thawed on the day of use. Enrofloxacin may be diluted to a 0.3–0.5% solution.

Antifungal agents

Yeast organisms, particularly *Malassezia pachydermatis*, are commonly involved in otitis externa. Dermatophytes and *Candida* spp are less frequently present. Clotrimazole and miconazole are most useful in the treatment of *Malassezia* otitis. Thiabendazole and nystatin have also been effective in some cases. Povidone-iodine or chlorhexidine may also be useful. In patients with chronic otitis externa and media due to yeast organisms, systemic antifungal medication with azoles may be used in combination with acetic acid flushes.

Antiparasitic agents

Antiparasitic agents such as pyrethrins, fipronil, selamectin, moxidectin, ivermectin or amitraz are indicated for mite infestations such as *Otodectes cynotis*. Recurrent clinical signs may be due to resistance of the mites. However, asymptomatic carrier animals are a potential source of reinfestation and all in-contact animals should be treated. *Otodectes cynotis* can be found on other body parts and whole-body treatments with effective miticidals may be needed to eliminate infection. Systemic therapy for ectoparasites is covered in Chapter 10.

Adverse effects

Ototoxicity is of concern with most commercial otic preparations if the tympanum is ruptured and penetration into the middle ear is possible. In patients with chronic otitis externa it may be difficult to evaluate the tympanum even under general anesthesia. However, as antimicrobial topical treatment is the most effective medical therapy for an infected otitis externa (oral antimicrobials do not achieve the same concentrations in the ear canal), the risk of ototoxicity has to be balanced against the benefit of eliminating the infection. Fortunately, ototoxicity does not occur frequently in small animal practice.

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