INTRODUCTION
Ear problems have been common throughout history and various medications have been administered to the ear for a local effect. Early otic preparations were applied by soaking materials, such as cloth, wood, or plants, in various oils or extracts from plants or animals and placing the soaked materials into the ear. More recently, administration of medications to the ear involve placing a liquid in the ear and inserting a cotton plug to keep the medication from draining out. This method is still used today, along with the use of ear irrigants, which clean debris from the ear. This debris can be the cause of many otic infections.

Otic (aural) preparations may consist of solutions, suspensions, ointments, gels and powders. Liquid ear preparations are usually placed in the ear canal by drops or in small amounts for the removal of excessive cerumen (ear wax) or for the treatment of ear infections, inflammation, or pain. Because the outer ear is a skin-covered structure and susceptible to the same dermatologic conditions as other parts of the body’s surface, skin conditions which arise are treated using a variety of topical dermatological preparations.

ANATOMY AND PHYSIOLOGY
The external ear is made up of the pinna (auricle) and the external auditory canal. Terminating the end of the external auditory canal is the tympanic membrane, which forms the beginning of the middle ear. The auricle consists of a thin layer of highly vascular skin firmly attached to cartilage. There is generally no fatty tissue or subcutaneous tissue in the auricle, except for the ear lobe, which is composed primarily of fatty tissue with fewer blood vessels than the rest of the auricle.

Starting from the exterior and moving along into the external auditory canal, the first one-third to one-half is the outer cartilaginous portion followed by the inner body or osseous portion. The end of the ear canal ends in a cul-de-sac. The external auditory canal of adults tends to be “S” shaped and that of children tends to be shorter and straighter. The auricle is susceptible to bleeding when scratched because it is more rigid and lacks the flexibility normally provided by a subcutaneous layer of fat. The auricle area contains many nerves which can cause enhanced pain sensations when inflamed. Moving further into the external auditory canal, the skin becomes thicker and contains both apocrine and exocrine glands along with hair follicles. The skin lining the external auditory canal is continuous with that forming the tympanic membrane outer layer.

Cerumen is produced as a part of the body’s normal defensive mechanisms. Cerumen is formed when the oily secretions from the exocrine glands mix with the milky, fatty fluid from the apocrine glands. The cerumen serves to lubricate the canal and entrap dust and foreign materials; it also provides a waxy, waterproof barrier to the entry of pathogens. Under normal conditions, bacterial growth is inhibited because the cerumen contains lysozymes and an acidic pH. Normal skin growth results in a continuous shedding of the external layer including the ear canal. The shed skin cells are continually mixed with the cerumen. This mixture normally moves outward to the external opening of the ear when the jaw moves, such as in talking or chewing. The ear canal is usually self-cleaning. The cerumen may progress from an oily and pastelike appearance to that of being dry and flaky. The color ranges from light gray to orange or brown and may darken upon exposure to the air.
COMMON OTIC DISORDERS

Under certain circumstances, the external auditory canal forms an ideal environment for bacterial growth. The canal, if moisture accumulates, will form a dark, warm, moist environment that can support bacterial growth. The protective layer of skin can be challenged and traumatized by fingernails, cotton-tipped swabs, hair pins, or any other object inserted into the ear in attempts at cleaning. Once the integrity of the skin is penetrated, pathogenic organisms can enter and initiate an infection. Other injuries can result from burns, sporting accidents, ear piercing, and improperly fitted ear molds or hearing aids.

Ear complaints affect patients of all ages and range from simple conditions such as excessive ear wax to more complex painful ear infections.

**Impacted Cerumen**

Ear wax impaction may be experienced by up to about 6% of the general population; this is one of the most common ear problems presented to physicians. Some individuals are more prone to impacted cerumen; especially those with narrow or mis-shaped ear canals and those with excessive hair growth in the canal. Others with a greater than average tendency for impacted cerumen are those with overactive glands, those wearing hearing aids as well as those using ear plugs to prevent water from entering the ear and to muffle loud noises. If cerumen is prevented from its natural migration outward to the opening of the ear canal, it may build up and dry out, forming a plug. As cerumen becomes dry, it is more difficult to remove from the ear. Impacted cerumen buildup is experienced by the patient as a sense of fullness or pressure within the ear, some associated with a dull pain.

It is obvious from this discussion that any object placed in the ear may tend to compress the cerumen and alter the normal flow of the cerumen from the ear. In fact, cotton-tipped swabs can result in pushing the cerumen back deeper into the ear.

**Water-Clogged Ears**

If cerumen builds up in an ear and the ear is exposed to water, as in taking a shower or going swimming, water may get in behind the cerumen in contact with the tympanic membrane. The presence of this moisture may result in maceration of the skin lining the ear and the tympanic membrane contributing to inflammation and infection of the external auditory canal; a condition known as swimmer’s ear. This situation can also result from excessive sweating in humid environments as well as from the improper use of aqueous products to clean the ear.

Symptoms of water-clogged ears include a feeling of fullness and wetness of the ear; this may be accompanied by some gradual loss of hearing. As the condition progresses, it can result in tissue maceration leading to itching, pain, inflammation and/or infection.

**Disorders of the Skin of the Ear**

Disorders of the skin of the ear can include contact dermatitis, seborrhea, psoriasis and boils.

**Contact dermatitis** may result from either an allergy or an irritant. It may present as maculopapular rash and vesicles. The rash may be associated with pruritus, erythema and/or edema. Mild irritants include soaps and detergents and can cause an inflammatory response similar to allergic contact dermatitis.

**Seborrhea** affecting the ear is presented with visible drying and flaking of the skin, with or without fissuring of the skin.

**Psoriatic lesions** present as thickened, erythematous, silvery scales that occur most frequently on the knees, elbows, torso and scalp, including the ear.

**Boils**

Localized infections of hair follicles can result in boils, or furuncles. The causative organism often is a Staphylococcus species. The boil generally begins as a red papule and develops into a superficial pustule with a core of pus and a reddened area around the base. The lesion slowly enlarges and becomes firm prior to softening and opening in a couple of weeks discharging its contents. Pain can be caused by the swelling and tight skin.

**TREATMENT OF OTIC DISORDERS**

**Cerumen**

There are a number of methods of breaking up the cerumen and aiding its removal from the ear, including preparations containing carbamide peroxide, glycerin, hydrogen peroxide and olive oil. The carbamide peroxide and hydrogen peroxide contribute a mechanical “bubbling” action that can serve to soften and break up dried cerumen and move the pieces of ear wax towards the outer portion of the ear canal; they also have anti- infective properties. Glycerin is hygroscopic and can absorb some moisture from the environment and serve to soften the cerumen. The olive oil can also serve as a softening agent for the cerumen so it can be easily removed. These liquids are viscous and will tend to stay in the ear canal if a small piece of cotton is placed at the entrance to the ear.

Recently, solutions of synthetic surfactants have been developed for their cerumenolytic activity in the removal of ear wax. One of these agents, triethanolamine polypeptide oleate-condensate, commercially formulated in propylene glycol, is used to emulsify the cerumen thereby facilitating its removal.

The procedure for removing cerumen usually involves placing the otic solution in the ear canal with the patient’s head tilted at a 45º angle, inserting a cotton plug to retain the medication in the ear for 15 to 30 minutes. This is followed by gentle flushing of the ear canal with lukewarm water using a soft rubber ear syringe.

**Water Clogged Ears**

Preparations used to treat water-clogged ears (otitis externa, swimmer’s ear) include isopropyl alcohol, glycerin, boric acid, hydrocortisone, ethyl alcohol and acetic acid. Also effective, when infection occurs, are otic drops containing a mixture of aminoglycoside antibiotics and anti-inflammatory corticosteroids in an acidic vehicle. The alcohol aids in reducing surface tension mixing with the water to aid in its removal through the ear canal. Glycerin also will aid in absorbing the water. Acetic acid will reduce the pH in the ear canal minimizing bacterial growth. Hydrocortisone will assist in reducing inflammation and the antibiotics will help reduce infection.

In addition to the antibiotic-steroid combinations that are often used to treat otitis externa, a combination of acetic acid (2%) in aluminum acetate solution and boric acid (2.75%) in isopropyl alcohol is used. These drugs help to re-acidify the ear canal and the vehicles serve to dry the ear canal. By drying the ear canal, the growth medium for the offending microorganisms, usually *Pseudomonas aeruginosa*, is kept in check. Pharmacists may also be called on to extemporaneously prepare a solution of acetic acid, 2 to 2.5% in rubbing alcohol (70% isopropyl alcohol or ethanol), propylene glycol or anhydrous glycerin. The source of the acetic acid can be glacial acetic acid USP or acetic acid NF. Boric acid, 2 to 5%, dissolved in either ethanol or propylene glycol has also been recommended for use in the ear. This substance, however, may be absorbed from broken skin and be toxic. Thus, its use is usually limited and should be avoided in treating children with burst ear drums.

**Skin Disorders of the Ear**

Topical treatment of ear infections is frequently considered adjunctive, with concomitant systemic treatment of orally administered antibiotics also undertaken.

Liquid ear preparations of the anti-inflammatory agents hydrocortisone, triamcinolone and dexamethasone sodium phosphate are prescribed for their effects against the swelling and inflammation which frequently accompany allergic and irritative manifestations of the ear, as well as for the inflammation and pruritus which sometimes follow treatment of ear infections. In the latter instance, some physicians prefer the use of corticosteroids in ointment form packaged in ophthalmic tubes. This packaging allows the placement of small amounts of ointment in the ear canal with a minimum of waste. Some of the commercially available products used in this manner are labeled “eye-ear” to indicate their dual use.
Contact dermatitis can be treated with a 2.5% aluminum acetate solution which has antipruritic, anti-inflammatory and some antibacterial properties. This astringent precipitates proteins and dries the affected area. It can also reduce the pH of the area inhibiting bacterial and fungal growth.

The associated itching of seborrhea can be treated with topical hydrocortisone-containing preparations.

Psoriatic lesions can be treated with routine medications used to treat psoriasis as well as hydrocortisone-containing preparations for the discomfort.

Boils are generally self-limiting. Treatment can include warm compresses and topical antibiotics, as previously listed.

In the event of an excessively dry ear canal skin, the application of mineral oil or olive oil (sweet oil) may help to counteract dryness and repel moisture.

**Ear Pain**

Pain in the ear frequently accompanies ear infection or inflamed or swollen ear tissue. Frequently, the pain is far out of proportion to the actual condition. Because the ear canal is so narrow, even a slight inflammation can cause intense pain and discomfort for the patient. Topical analgesic agents generally are employed together with internally administered analgesics, as aspirin, and other agents, such as anti-infectives, to combat the cause of the problem.

Topical analgesics for the ear are usually solutions and frequently contain the analgesic antipyrine and the local anesthetic benzocaine in a vehicle of propylene glycol or anhydrous glycerin. The hygroscopic vehicles reduce the swelling of tissues (and thus some pain) and the growth of microorganisms by drawing moisture from the swollen tissues into the vehicle. These preparations are commonly employed to relieve the symptoms of acute otitis media.

**Physicochemical Considerations**

Physicochemical considerations in developing otic preparations include solubility, viscosity, tonicity, surfactant properties, and preservatives. Although sterility is not generally a consideration, the products need to be "clean."75

Many drugs are soluble in the vehicles commonly used in these preparations. If a drug is insoluble in these vehicles, the preparation can be prepared as a suspension. Because most of these vehicles are relatively viscous agents, the addition of suspending agents may not be necessary. The viscosity of the preparation is important in keeping the medication in the ear canal. If the preparation is too thin, the medication will drain out of the ear. On the other hand, if the medication is too thick, it may not reach the inner recesses of the ear.

Tonicity and hygroscopicity are important in the product’s ability to aid in withdrawing fluids from the immediate area of the ear. If the product is hypertonic, some fluid may be withdrawn from the ear, thereby releasing some of the pressure. If the product is hypotonic, however, some fluid may flow into the area.

Because many ear conditions are related to the difficulty in cleaning the ear, the presence of a surfactant in the preparation helps the medication spread out and aids in breaking up ear wax. This action makes it easier to remove any foreign material.

Many otic preparations are self-preserving because of the high concentration of glycerin, propylene glycol, and the like. If these agents are not present, it may be wise to add a preservative to minimize the chance of introducing bacteria that might grow in an unpreserved product. As determined on an individual product basis, some liquid otic preparations require preservation against microbial growth. When preservation is required, such agents as chlorobutanol (0.5%), thimerosal (0.01%), and combinations of the parabens are commonly used. Antioxidants, as sodium bisulfite, and other stabilizers are also included in otic formulations, as required. Ear preparations are usually packaged in small (5 to 15 mL) glass or plastic containers with a dropper.

**Vehicles**

Vehicles used most often in otic preparations are glycerin, propylene glycol, and the lower molecular weight polyethylene glycols (PEGs), especially PEG 300. These vehicles are viscous and will adhere to the ear canal. Water and alcohol (ethanol and isopropyl) can be used as vehicles and solvents for some medications; however, they are used primarily for irrigation, since one of the therapeutic aims of these preparations is to keep the ear canal dry to minimize bacterial/fungal growth. Alcohol can be used full strength. Vegetable oils, especially olive oil, are also good vehicles. Mineral oil has been used as a vehicle for some antibiotics and anti-inflammatory medications. Otic ointments primarily contain petrolatum as a vehicle, whereas otic powders may contain talc or lactose as a vehicle.
QUALITY CONTROL
The compounding pharmacist should follow standard quality control procedures. These include checking the volume/weight, pH, viscosity, appearance, and odor of these products.

PACKAGING, STORAGE AND LABELING
Otic preparations should be packaged in dropper containers, puffers, syringes (without needles) or tubes as appropriate for the product and method of administration. Generally, otic preparations should be stored at either room or refrigerated temperatures. They should not be frozen. These preparations should be labeled “For the Ear,” “Discard after [appropriate date],” and “Use Only as Directed” and “Keep Out of Reach of Children”.

STABILITY AND BEYOND-USE DATES FOR OTIC PREPARATIONS
The following beyond-use recommendations can be exceeded if there is valid scientific information to support the stability of the product.

Beyond-use dates for water-containing formulations are no later than 14 days, when stored at cold temperatures, for products prepared from ingredients in solid form. If nonaqueous liquids are prepared using a manufactured product, the beyond-use recommendation is no later than 25% of the time remaining on the product’s expiration date or 6 months, whichever is earlier and six months if prepared from ingredients with a USP-NF monograph. For all other products, the beyond-use recommendation is the intended duration of therapy or 30 days, whichever is earlier.

PROPER ADMINISTRATION AND USE OF OTIC DROPS
Patients should be instructed on how to apply drops to the ear from dropper bottles. They should also be told to place a cotton or gauze pad in the ear to keep the liquid from escaping.

When ear drops are prescribed, it is important for the pharmacist to first determine how the drops are to be used. For example, ear wax removal drops should be instilled and then removed by the patient with an ear syringe. Alternatively, drops intended to treat external otitis infection are intended to be instilled and left in the ear.

The pharmacist should make sure the patient or parent understands that administration is intended for the ear and the frequency of application. To facilitate patient acceptance, the pharmacist should point out that the bottle or container of medication should first be warmed in the hands, and if the product is a suspension, shaken well prior to withdrawal into the dropper. The pharmacist should also explain the need to store the medication in a safe place out of the reach of children and away from extremes of temperature.

When instilled into the ear, to allow the drops to run in deeper, the earlobe should be held up and back. For a child, the earlobe should be held down and back. For convenience it is probably easier to have someone other than the patient to administer the drops.

Some ear drops by virtue of their formulation, i.e., low pH, may cause stinging upon administration. Thus, parents and children should be forewarned especially if a child, for example, has tympanostomy tubes in the ear. The patient should also understand the length, in days, to use the product. For antibiotic ear drops, it is not necessary to finish the entire bottle because therapy could last 20 to 30 days depending upon the dosage regimen. Therefore, patients should be instructed to continue using the drops for 3 days beyond the time ear symptoms disappear. Products for swimmer’s ear or otitis externa may take up to 7 to 10 days to demonstrate efficacy.

If a child is prone to develop ear infections as a result of swimming or showering, it might be advisable to recommend the parents to consult a physician for prophylactic medication to use during swimming season, and consider using form-fitting ear plugs that fit snugly in the ear when swimming or showering. Further, after the child emerges from the water or shower, the parents can be advised to use a home hair blow dryer on a low setting to dry out the ear. It will dry out the ear quickly without trauma. The dryer should not be placed too close to the child’s ear.

FORMULATIONS FOR TREATING OTIC DISORDERS
Formulations for Removing Cerumen

<table>
<thead>
<tr>
<th>Rx</th>
<th>Urea and Hydrogen Peroxide Otic Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>10 g</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
<td>3 %</td>
</tr>
</tbody>
</table>

Dissolve the carbamide peroxide in sufficient glycerin to volume, package and label. A beyond-use date of up to six months can be used for this preparation.

Formulations for Treating Water-Clogged Ears

<table>
<thead>
<tr>
<th>Rx</th>
<th>Boric acid 2% in Isopropyl Alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boric acid</td>
<td>2 g</td>
</tr>
<tr>
<td>Isopropyl alcohol 70%</td>
<td>qs</td>
</tr>
</tbody>
</table>

Dissolve the boric acid in sufficient isopropyl alcohol 70% to volume, package and label. A beyond use date of up to six months can be used for this preparation.

Formulations for Treating Disorders of the Skin of the Ear

<table>
<thead>
<tr>
<th>Rx</th>
<th>Aluminum Acetate Otic Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum subacetate topical solution</td>
<td>54.4 mL</td>
</tr>
<tr>
<td>Glacial acetic acid</td>
<td>1.5 mL</td>
</tr>
<tr>
<td>Purified water</td>
<td>qs</td>
</tr>
</tbody>
</table>

Slowly and with stirring add the glacial acetic acid to the aluminum subacetate topical solution. Add sufficient purified water to volume and mix well. Package and label. A beyond use date of up to six months can be used for this preparation.

<table>
<thead>
<tr>
<th>Rx</th>
<th>Hydrocortisone and Acetic Acid Otic Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>1 g</td>
</tr>
<tr>
<td>Glacial acetic acid</td>
<td>2 mL</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>qs</td>
</tr>
</tbody>
</table>

Add the hydrocortisone and glacial acetic acid to sufficient propylene glycol to volume and mix well. It will slowly dissolve. Gentle heat can be used if required. Package and label. A beyond use date of up to six months can be used for this preparation.

<table>
<thead>
<tr>
<th>Rx</th>
<th>Acetic Acid and Glycerin Otic Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glacial acetic acid</td>
<td>0.5 mL</td>
</tr>
<tr>
<td>Glycerin</td>
<td>20 mL</td>
</tr>
<tr>
<td>Purified water</td>
<td>qs</td>
</tr>
</tbody>
</table>

Mix the glacial acetic acid and glycerin. Add sufficient purified water to volume and mix well. Package and label. A beyond use date of up to six months can be used for this preparation.
Pulverize sufficient ciprofloxacin tablets to a very fine powder. Add the propylene glycol slowly and mix well. Add sufficient glycerin to volume and mix well. Package and label. A beyond use date of 14 days can be used for this preparation.

Add the triamcinolone to the propylene glycol. Add sufficient glycerin to volume and mix well. Package and label. A beyond use date of up to six months can be used for this preparation.

Add the gentamicin sulfate to sufficient glycerin to volume and mix well. Package and label. A beyond use date of up to six months can be used for this preparation.

Add the lidocaine hydrochloride to the glycerin and sufficient propylene glycol to volume and mix well. Package and label. A beyond use date of up to six months can be used for this preparation.

Add the nystatin to the propylene glycol and mix well. Add sufficient glycerin to volume and mix well. Package and label. A beyond use date of up to six months can be used for this preparation.

Add the gentamicin sulfate to sufficient glycerin to volume and mix well. Low heat can be used if needed to effect solution. Package and label. A beyond use date of up to 6 months can be used for this preparation.

Add the tetracaine to sufficient propylene glycol to volume and mix well. Package and label. A beyond use date of 30 days can be used for this preparation.

Add the antipyrine and benzocaine to sufficient glycerin to volume, mix well and allow to set until all dissolved. Package and label. A beyond-use date of up to six months can be used for this preparation. Note: As an option, 0.25% phenylephrine hydrochloride can be added to this preparation. A beyond-use date of only 14 days could be used for this modified formulation, when stored in a refrigerator.

Add the tetracaine to sufficient propylene glycol to volume and mix well. Package and label. A beyond use date of 30 days can be used for this preparation.

Add the ciprofloxacin to sufficient propylene glycol 300 to volume and mix well. Low heat can be used if needed to effect solution. Package and label. A beyond use date of up to 6 months can be used for this preparation.

REFERENCES