Drug Treatment of Disease

INFECTIONS OF THE EAR

BY

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ACUTE OTITIS MEDIA AND MASTOIDITIS

The introduction of a widening range of antibiotics in the past fifteen years has profoundly altered the treatment of acute otitis media, greatly altered the need for surgery, and diminished the incidence of intracranial spread of infection and permanent deafness. It is also agreed that the virulence of otitic infections has undergone a change, so that to-day we do not see some of the devastating infections prevalent years ago. During this time there has also been a realization of the dangers of antibiotic therapy, and, while the need for early treatment in adequate dosage and the continued necessity for surgical drainage of pus is now widely known, the delayed effects in causing deafness and cholesteatoma are not yet generally realized or accepted. It is easy to place too much reliance on drugs and to delay surgery; this is dangerous, because it ignores basic surgical principles and may lead to catastrophe. The indications for advising surgical intervention may be slight and often require more judgment and experience than was formerly the case.

Acute aural infections may be caused by a variety of organisms whose identity cannot be determined by the clinical features alone. Moreover, the bacteriology may from time to time present considerable variation, not only in the type of infecting organism but in the virulence and drug resistance of a particular organism. Thus Hodgkin (1957) found that more than half (in winter, more than two-thirds) of his cases of acute suppurative otitis media were due to *Streptococcus pyogenes*, but Friedmann (1954) a few years earlier found this organism to be responsible in less than a quarter of his cases. Recently there has been an increase in the proportion of cases infected with *Staphylococcus aureus*, and in many this organism is resistant to some or all of the antibiotics in common use. Because of the variability of the virulence and antibiotic sensitivity of the organism and the natural resistance of the patient—the latter includes the antibody response as well as local factors such as adenoidal hypertrophy, the functioning of the Eustachian tube, and the anatomical configuration and scarring from previous infections in the middle ear and mastoid process—the choice and method of administration of the antibiotic are dictated by the clinical findings and the bacteriological investigation.

Mild Infections

In the case of a mild infection of the middle ear with little systemic reaction seen 12 to 24 hours after the onset of pain and by then showing only slight injection of the drum and minor loss of hearing to the whispered voice, it is possible that resolution will occur promptly with rest in bed, acetylsalicylic acid, and local heat. In the opinion of many, however, it is usually more prudent to treat such a case with sulphonamides or an antibiotic. The choice of sulphonamide drug is wide and open to personal choice, but a good choice is sulphadimidine

3 g. initially, followed by 1 to 1.5 g. subsequently every six hours.

For children the dose should be approximately one-third of the adult dose from 1 to 3 years of age, half the dose from 4 to 10 years of age, and two-thirds of the dose from 11 to 15 years. Unless considerable improvement is obvious after 24 hours this treatment should be discontinued and an antibiotic administered. When the onset of the ear infection is associated with more pronounced general and local manifestations, an antibiotic should be used initially and no reliance placed on a sulphonamide alone.

Penicillins

The object of treatment with an antibiotic is to obtain a rapid concentration in the blood sufficient to exert a bactericidal or bacteriostatic action, depending on the drug used and the antibiotic sensitivity of the invading organism. Penicillin is bactericidal as well as bacteriostatic, and though its spectrum of activity is narrow it is the drug of first choice in middle-ear infections provided the infecting organism is sensitive and the patient has not shown a sensitivity reaction to the drug.

Except in the most severe infections penicillin is usually given by itself but may be combined with a sulphonamide. In pyogenic infections penicillin should be given as soon as possible so as to prevent the formation of pus. Once the middle-ear cleft contains frank pus or even flakes of pus floating in an inflammatory exudate and the drum remains intact, there is a risk that adhesions will form and cause residual deafness. It is probable that this sequela is more likely after infections treated with sulphonamides.

Some otologists advise routine myringotomy to effect drainage in all cases of suppurative otitis, and there is no doubt that this operation should be carried out whenever resolution is delayed.

Penicillin may be given by the intramuscular route as benzylpenicillin (crystalline penicillin G) 500,000 to 1,000,000 units two to four times daily (250,000 to 500,000 units for a child). A long-acting penicillin such as procaine penicillin or benethamine penicillin may be added in doses of 300,000 to 500,000 units but tends to be more potentially allergenic than the crystalline salts. Penicillin can also be given by the oral route either as phenoxymethylpenicillin (penicillin V) in the form of tablets, capsules, or suspension, 250 mg. for adults (125 mg. for children) or benzylpenicillin, 600,000 units for adults, half an hour before a meal at intervals of not more than four hours. A "loading" dose of benzylpenicillin, 1,000,000 units for the adult, should always be given at the outset of a course of oral treatment and preferably once a day afterwards.

The penicillin levels in the blood obtained by oral administration are satisfactory in infants up to the age of 1 year, but with increasing age considerable variation is found, though the levels tend to be more satisfactorily

maintained in children. Many general practitioners find the oral route gives satisfactory results, and it has the advantage of ease of administration. However, some patients will not keep to the prescribed times for taking the drug, and for this and other reasons satisfactory blood levels are not maintained. Delayed resolution resulting in deafness or partial control of the infection, possibly resulting in intracranial spread of the infection, may ensue, and many otologists having to treat such "failures" are strongly of the opinion that oral penicillin therapy should not be used for this disease.

Streptomycin

Streptomycin has a synergistic activity when given with penicillin. Intramuscular injections of 500 mg. combined with 500,000 units of penicillin will often control an infection when penicillin alone has failed. However, its use in otitis media may not be without danger to the hearing in view of the well-known toxic effect on the auditory nerve.

Ear Drops

Should the ear drum perforate during the course of the infection every effort must be made to prevent secondary bacterial invasion from the external auditory meatus. When rapid resolution is taking place no local medication is required, but, if necessary, ear drops containing a non-irritating, broad-spectrum antibiotic may be instilled. Syringing or dry-mopping of the deeper part of the meatus is not advisable within the first few days of the appearance of the discharge owing to the risk of introducing fresh infection, but thereafter there is no harm in prescribing ear drops containing polymyxin, bacitracin, or neomycin. These antibiotics are not antagonistic to penicillin, as are the tetracyclines (Jawetz *et al.*, 1958). Penicillin drops should never be used owing to the high risk of causing a local skin reaction and suprainfection with resistant organisms.

In most cases, therefore, provided the patient has never previously shown any signs of reaction to the drug, treatment should be started with systemic and possibly oral penicillin. If the ear is already discharging, a swab should be taken for bacteriological examination if laboratory services are available. By the time a report is received the effects of the initial treatment will be apparent and can then be modified if necessary according to the antibiotic sensitivity of the organism found. Here it may be mentioned that intensive treatment with penicillin will sometimes succeed despite a report of a penicillin-resistant organism, and there is no harm in persisting for another 24 hours at least if clinical examination shows an immediate and dramatic response to penicillin therapy.

Tetracyclines

When the use of penicillin therapy is contraindicated, other antibiotics must be used, preferably in the light of the bacteriological findings. The next in order of preference is one of the tetracyclines—chlortetracycline ("aureomycin"), oxytetracycline ("terramycin"), or tetracycline ("achromycin") in doses of 250 to 500 mg. every six hours. For children the usual dose is 2.5 to 7.5 mg. per kg. body weight every six hours.

Vitamins

Vitamins, especially those of the B group and K, may be given concurrently to prevent deficiency arising from

alteration in the bacterial flora of the gut. Suitable preparations are tab. aneurin. co. fort. B.N.F., 2 tablets thrice daily, and tab. acetomenaphthone. B.P. (vitamin K), 5 mg. thrice daily.

Because the virulence of the organism cannot always be judged at the onset, and because early thrombophlebitis may occur in the bone surrounding the middle-ear cleft, those antibiotics which are bacteriostatic only (e.g., the tetracyclines) are slower in their bacteriological effect and are less likely to overwhelm the infection before necrosis of bone has occurred. It is the author's experience that mastoid surgery has to be undertaken more commonly for cases treated initially with the tetracyclines than those treated with penicillin.

Use of other antibiotics, particularly erythromycin, is not recommended in the conditions of general practice, and, if a case is not rapidly responding to treatment as shown by subsidence of pyrexia, toxæmia, pain, and tenderness, diminution of the discharge and the inflammation of the drum, together with some return of hearing, removal to hospital is indicated. It follows that if treatment is started several days after the onset of the disease, particularly if the ear is already discharging, considerable discretion is required in deciding for how long one is justified in continuing antibiotic treatment.

CHRONIC OTITIS MEDIA

Two Varieties

A distinction must be made between the benign and the severe varieties. In the former the condition has been preceded by the manifestations of acute otitis media; an odourless mucoid or mucopurulent discharge flows through a clear-cut central perforation of the membrana tensa, and formation of granulation tissue or polyps is rare. The cause of the chronicity usually lies outside the middle-ear cleft and is due to ascending infection from the nasopharynx or entrance of infection via the meatus through a pre-existing perforation of the drum.

In the severe variety the disease essentially lies in the middle ear or mastoid and often has an insidious onset. A purulent, offensive discharge seeps through a perforation in the edge of the drum or through Shrapnell's membrane. Granulations are common, the incus or body of the malleus is usually necrosed, and the mastoid air cells are absent or partially formed. Cholesteatoma may be present. Resolution can occasionally occur with frequent and scrupulous cleansing, but such a result is generally only temporary, and at best carries a risk of deafness and at worst the possibility of serious or fatal intracranial complications. Thus surgery is advisable in most cases, and drug treatment will not be discussed. However, if there is delay before operation is undertaken, the discharge will be less unpleasant and possibly diminished if aurist. spiritus (50% alcohol in water) is instilled twice daily.

First Essential

For benign chronic otitis media the first essential is treatment of the predisposing causes and removal of decomposing debris from the meatus. Instillation of drops or powder containing an antibiotic will control the entrance of fresh infection, and one having a wide spectrum of activity should be chosen. The meatal skin is often irritated by the middle-ear discharge and is then

more readily sensitized by the preparation used, thus increasing the bacterial swarm.

Penicillin should never be used. Chloramphenicol rapidly sterilizes the area but will almost certainly be followed by a skin reaction if used for more than two to three weeks. There are, however, numerous proprietary preparations containing the tetracyclines, neomycin, bacitracin, or polymyxin in varying proportions which have a broad spectrum and only rarely cause sensitivity even after prolonged use. Some also include a hydrocortisone derivative and can be employed with advantage if there is an obvious otitis externa.

These preparations are at present expensive, but their use is justified in the speed with which infection is brought under control. It is probably true that treatment can now be completed in days compared with weeks taken in the pre-antibiotic era.

OTITIS EXTERNA

The acute diffuse form is less common in Great Britain than in warmer climates, and tends to occur in summer and after bathing. Because of the extreme tenderness and swelling of the meatal skin, pus and debris have to be removed gently; this care will avoid abrading the surface and exacerbating the infection. A wick of "selvedge" gauze, $\frac{1}{2}$ in. (1.3 cm.) wide, soaked in 10% glycerin and ichthammol inserted deeply into the meatus and changed daily, will relieve the pain and remove pus and debris.

When the swelling subsides the meatal walls can be painted with 1 or 2% crystal (gentian) violet in alcohol/water solution. Alternatively an ointment in a water-miscible basis containing hydrocortisone and a wide-spectrum non-sensitizing antibiotic can be inserted with a fine wool-tipped probe twice a day.

It should seldom, if ever, be necessary to incise a furuncle of the external meatus, and the treatment described above is usually sufficient. Systemic antibiotics may be given, but many consider that their use predisposes to a second attack a few weeks later and should therefore be reserved for the relapsing case.

Scratching

Chronic otitis externa is associated in at least a third of the cases with seborrhoea of the scalp, and, while energetic treatment to the ear will temporarily clear the condition, relapse is likely unless the scalp is treated at the same time. Subsequent neglect of the scalp will predispose to relapse of the otitis. In a few individuals emotional strain will precipitate an attack, and complete resolution of the otitis will not occur until the anxiety has been overcome.

As local irritation is usually the first symptom to appear and the last to disappear with treatment, exacerbation of the lesion from scratching is commonly found unless the patient is warned. If the finger-nail is used, excoriation and weeping will be confined to the concha and may spread to the surrounding skin. Occasionally a hair clip or the side-piece of a spectacle frame may be used in the meatus.

Removal of Debris

Removal of epithelial debris is an essential part of the treatment. In some cases there is a pronounced hump on the bony meatal floor forming a "gutter" against

the lower margin of the tympanic membrane. Daggett (1942) stressed that until epithelial debris, which may not be visible because of the hump, is removed and the gutter subsequently kept clean, the otitis will not resolve.

Removal of debris is best carried out by dry mopping under direct vision with fine straight and bent wool-tipped probes. Gentleness is essential to avoid pain and additional trauma. Alternatively, syringing may be carried out provided the meatus is carefully dried afterwards. The inflammation and infection can then usually be controlled by application of 1% hydrocortisone and a broad-spectrum antibiotic and is the treatment of first choice. Initially, an ointment with a water-miscible base is preferable, because aural drops tend to keep the surface layers of epithelium sodden. Later a change may be made to a greasy base, though this is often not required. Most patients may be taught to use a probe tipped with the minimum of cotton-wool, first to remove debris and then to apply a thin smear of the ointment. A suitable probe can be made from a wire paper clip which has been straightened and a series of nicks to grip the wool tip made near one end with a fine file or wire cutters.

Treatment should be carried out at least twice a day. Alternative preparations are too numerous to mention here, but 2% crystal violet in 50% alcohol/water solution, 0.1% thiomersal ("merthiolate") in water or as the tincture in alcohol, acetone, and water, or aurist. alumin. acetat. B.N.F. are useful.

Sensitization

The meatal skin is probably more readily sensitized to drugs than other parts of the body. Most drugs can cause trouble, but some, such as neomycin and the tetracyclines, rarely do so and usually only after continuous application for several weeks. Particularly with neomycin the reaction may be so mild, and in addition be modified by hydrocortisone applied at the same time, that it passes unrecognized. Unsatisfactory progress after two to three weeks' treatment should therefore be an indication to change the therapy, either to another antibiotic or to another substance. Dermatologists have for long held that penicillin should never be applied in an ointment or lotion to the skin, and the author wishes to support this view most strongly in relation to otology.

Experience with chloramphenicol has shown that, while it is efficient at controlling a wide range of bacterial infections, continued use in the ear for more than two to three weeks will result in an acute skin reaction in almost all cases. Furthermore, such sensitivity will persist for several months. There are also considerable advantages in using antibiotics which are not given systemically, such as neomycin, polymyxin, and bacitracin, to avoid the development of drug-resistance to bacteria that may cause a more serious infection. Some patients may become sensitized to propylene glycol, which is used as the vehicle for most antibiotic ear drops.

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