the epidermis returns to normal if and when the affection resolves. Rüedi (1963) states that the epidermis of the external auditory meatus, adjoining the tympanic membrane superiorly in healthy infants, shows an increased growth in the sense of hyperkeratosis: this may be more marked when activated by the irritation of acute or chronic inflammations of the middle ear.

What is the possible significance of these findings? Is there any relationship between exudative otitis media and chronic suppurative otitis media? I believe there is. A marginal perforation may occur, which has been noted on several occasions. A further question also arises: Is it possible for cholesteatoma to form in these cases? I think so. It has been observed that keratinous debris forms in the meatus and that the squamous epithelium of the deep posterior meatal wall shows both hyperplasia and hyperkeratinization; this structural change is identical to cholesteatoma. It is quite possible for this proliferating epithelium of the deep meatal skin to invade the middle ear through a marginal perforation.

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The Ætiology and Treatment of Cholesterol Granuloma in the Middle Ear

Cholesterol granuloma is found in any part of the body where crystals of cholesterol may be deposited; that occurring in the middle ear is not markedly different from one in an accessory nasal sinus or even in an atheromatous patch in an artery.

The condition is becoming more frequently recognized, which does not necessarily mean that it is becoming more common, as the symptoms and signs can be overlooked. It is possible that many cases of adhesive otitis media represent the end-result of untreated cholesterol granuloma of the middle ear.

Ætiology

There is as yet no agreement on the ætiology of cholesterol granuloma in the middle ear. Ranger (1949) considered the possible sources of the cholesterol crystals to be (1) a deposit from the blood stream, (2) from degeneration of epithelium or (3) from degenerated cell elements of the blood deposited by repeated hæmorrhages; he felt that the first two were unlikely as there was no raised serum cholesterol or degenerated epithelium found in his cases. Shambaugh (1929) cultured the fluid obtained by paracentesis in his two cases and found no specific organisms; this finding of a sterile middle ear has been confirmed by subsequent workers. Simpson (1954) suggested that deposits of cholesterin crystals might occur when a high serum cholesterol coincided with a serous middle ear exudate and that such crystals caused a tissue reaction with small and recurring mucosal hæmorrhages and even resorption of bone. Birrell (1958) found that many of his patients had received insufficient treatment by oral antibiotics previously, and on several occasions he noted the presence of true cholesteatoma accompanying cholesterol granuloma; he differentiates chronic nonspecific inflammation, where there is mucosal hypertrophy and mucoid middle ear discharge without cholesterol deposition, from cholesterol granuloma of the middle ear. Friedmann (1959) injected a sterile suspension of cholesterol into the middle ear of the guinea-pig. He found that cholesterol granulomata formed in two to three weeks but cleared completely after a month. Dota and his co-workers (1963) injected a 1% solution of oxalic acid through the tympanic membrane of the rabbit at weekly intervals to a total of 5, 10 or 20 injections. They produced typical cholesterol granulomata and also invasion of the middle ear by true cholesteatoma. Experimentally it is therefore possible to produce cholesteatoma and cholesterol granuloma with the same stimulus.

A reasonable hypothesis to explain the ætiology of this condition may be found by a careful study of cases seen in the acute phase; I will mention only two.

Case 1 presented with a three weeks' history of bleeding from the left ear and no other history. The appearances were of a ruptured bulla of the drum head. Cholesterol granulomata were found in both ears, with extensive middle ear fibrosis. The blood cholesterol was within normal limits. No growth was obtained from the contents of the middle ear. Cortical mastoidectomy was unsuccessful in clearing the condition and later cholesteatoma was found in each attic region, so radical mastoidectomy was required; this also failed and, at musculoplasty, small nests of cholesteatoma were found under the skin lining.

Case 2 had a history of repeated earache and deafness in both ears. Both drum heads and hearing were found to be normal but infected tonsils and adenoids were removed. Three months later he returned with a keratosis obturans in his left auditory meatus; when this was cleared there were seen marginal posterior granulations (Fig 1) on the drum head, which was intact. Hearing was poor and investigation showed a

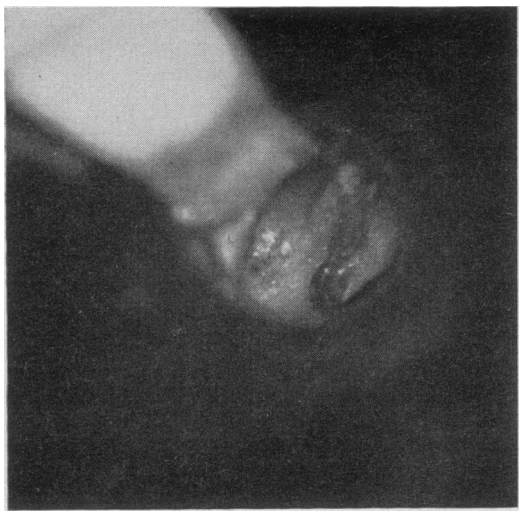

Fig 1 **Case 2** *Drum head seen immediately after removal of keratosis obturans, showing sessile posterior granulations*

fully developed cholesterol granuloma of the middle ear and mastoid, with soft granulations in Prussak's space arising from the drum head (Fig 2). Thus in only three months a double condition developed affecting the epithelium of the middle ear and the external auditory meatus.

We have, consequently, a condition of the middle ear that is known to occur in association with lesions of the meatal aspect of the drum head. It is characterized by a history of recurrent attacks of otitis media, in which no organisms can be found and in which eustachian obstruction is not necessarily a feature. There is no convincing evidence of a high serum cholesterol nor is eosinophilia common. It would seem reasonable, then, to suggest a viral condition. There is a very common virus which is found with a predilection for mucocutaneous junctions. The lesions produced by it may be symmetrical and tend to recur in the same location over a long period, gradually diminishing in frequency and intensity. The virus is that of herpes simplex and it is easily possible to determine whether it is present in any individual.

We have tested serologically a tiny series of 5 cases of cholesterol granuloma which have been proved histologically and were all the undoubted cases we could muster. We sent as controls blood from one child with proved secretory otitis media and from another who had had suppurative otitis media; we sent blood from house surgeons and nurses to make up 12. The 5 cases of cholesterol granuloma gave serological antibodies to herpes simplex. The 7 controls were negative. This preliminary investigation will require to be confirmed.

Fig 2 **Case 2** *The same anteverted after mastoidectomy, showing cholesterol granuloma arising from medial surface of tympanic membrane and filling Prussak's space*

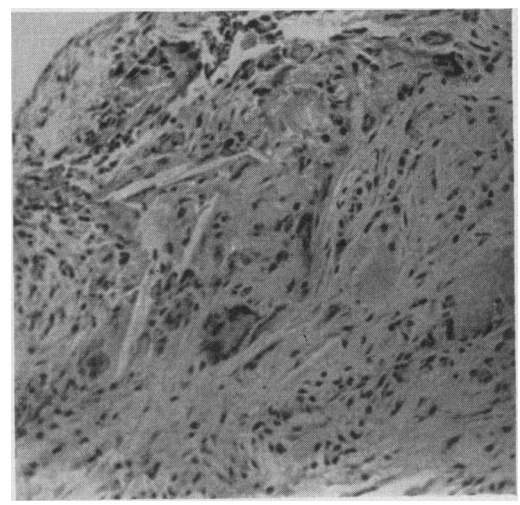

Fig 3 **Case 2** *Low-power photograph of a section showing cholesterol clefts and giant cells*

Pathology

For an account of the characteristics of herpes simplex I am indebted to 'Virus and Rickettsial Diseases of Man' (Bedson *et al.* 1961). This virus is probably more widely distributed and more

constantly present in man than any other virus. It produces lesions most often in mucocutaneous regions and in many cases these are bilateral; in persons liable to repeated attacks the eruption tends to appear in the same area of skin or mucous membrane. The lesions are superficial and usually heal without scarring in a week or ten days. Sixty per cent of the population are infected with the virus and remain carriers through life, while primary infection usually occurs in early childhood. Histologically a vesicle in the skin shows great thickening in the epidermal layer; the affected cells show ballooning and reticular degeneration; multinucleated cells arise from the amitotic nuclear division in epithelial cells. A serous exudate separates the damaged cells, forming the vesicle beneath the stratum corneum which contains fibrin and leucocytes. The dermis shows vascular engorgement and leucocyte infiltration. In a mucosal lesion the mucous membrane over a vesicle tends to be shed and fine granulomatous tissue is formed, the structure of which is a delicate fibrous stroma with collections of polymorphs and lymphocytes in varying proportions. When recovery occurs, the mucosa reforms, cutting off the granuloma and releasing debris consisting of fibrin and white and red blood corpuscles. In the middle ear it is the hæmosiderin so released that gives the clinical picture of the 'blue' drum, described by so many authors. The nuclei of the white cells degenerate with the release of cholesterol, which crystallizes out and behaves as a foreign body, initiating the giant cell response which gives rise to the formation of cholesterol granulomata.

If the condition is mild and resolution is early, the cholesterol crystals are walled off by fibrocellular scar tissue and little harm is done; on the other hand, repeated deposits of cholesterol will lead to massive adhesions forming and the development of adhesive otitis media (MacNaughtan 1956).

Clinical Features

The patient usually presents with deafness and a history of recurring, mild attacks of otitis media, with or without discharge, often associated with upper respiratory infections. The condition may be bilateral or unilateral; usually the deafness is progressive. The drum membrane is typically intact but may be a little dull or may show any gradation of blue up to an inky black. In the acute phase there may be a serosanguineous discharge, with a plum-coloured tympanic membrane showing superficial desquamation or, earlier still, a bullous myringitis. The eustachian tube may or may not be patent but inflation of an obstructed tube rarely brings improvement. In some cases there is evidence of instability of the squamous epithelium of the drum head, with keratosis obturans or actual invasive cholesteatoma. X-ray of the mastoids is helpful, as there will be clouding of the air cells. Culture of the middle ear exudate will be sterile and the fluid cannot be dispersed by suction and inflation. In the final event the diagnosis will be made by exploration of the mastoid.

Treatment

The purpose of treatment is first to remove any invasive cholesteatoma, if this is encountered, then to clear all cells that are involved in the granulomatous process. The middle ear also has to be inspected, using the microscope after reflection forward of the drum head; we find that an endaural approach is convenient and normally dissect out the cells using the dental drill and binocular microscope. Any gross sepsis in the nose and nasopharynx is dealt with at another time. It may be impossible to prevent further attacks of myringitis or otitis media but at least the drainage of the middle ear may be improved by this method and fewer adhesions formed.

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The Treatment of Cholesteatoma in Children

In this paper I shall discuss only intratympanic cholesteatomata in the child whose meatal skin is not constitutionally abnormal.

The term cholesteatoma is traditional and sonorous but I prefer the term intratympanic epidermoid because I believe the condition is essentially a skin-lined cyst within the tympanum.