OTOGENIC INTRACRANIAL SUPPURATION

By ALAN JEANES (London)*

THE chief danger of otitis media, apart from its possible effect on the hearing mechanism, lies in the tendency for infection to spread inwards to involve intracranial structures. Probably in the majority of cases of pyogenic meningitis and of brain abscess, the source of infection is to be found in the middle ear.

The introduction of sulphonamides and antibiotics has brought about changes in the incidence and mortality rate of these complications, which are now seldom seen in patients with acute otitis media but still occur in occasional cases of chronic otitis media, sometimes with fatal consequences.

In an attempt to examine the current extent of the problem, a survey has been made of a series of cases admitted to two otological hospitals during the past ten years. The results of the survey form the basis of this paper, in which attention is paid to the incidence, ætiology and mortality of these conditions, and particularly to the pathology of the underlying ear disease.

The Series

During the ten-year period 1951-60, thirty-four patients with otogenic brain abscess or leptomeningitis were admitted to the wards of the Royal National Throat, Nose and Ear Hospitals at Gray's Inn Road and Golden Square, London, where there is an annual attendance of 2,000-3,000 cases of acute or chronic suppurative otitis media.

There were fifteen cases with brain abscess and in seven of these the abscess was accompanied by leptomeningitis as indicated by a cerebrospinal fluid cell count of at least several hundred neutrophils per c.mm. Leptomeningitis without brain abscess was present in a further nineteen cases.

Brain abscesses were always single and were situated in the left temporal lobe in seven cases, the right temporal lobe in seven, and in the cerebellum in one case. Cases of extradural abscess are not included in this series unless, as in five cases, this lesion was accompanied either by leptomeningitis or brain abscess.

There were twenty-two male and twelve female patients. Their ages ranged from five to seventy-eight years and the average age was forty-two years. In ten cases there was a relatively short history of aural symptoms,

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i.e. three days to three weeks, but in four of these there was also a history of previous infection. Twenty-three cases presented symptoms of ear infection which had been present for months or years. In eight of these the symptoms and signs of intracranial suppuration developed during the post-operative period following routine surgery for chronic otitis media.

There were eight deaths (23·5 per cent.) among the thirty-four cases, and the average age at death was fifty years.

Bacteriology

The bacteriological findings are shown, together with a summary of general features, in Table I.

The commonest single infecting agent was *Streptococcus pneumoniae*, which was isolated in pure culture from the C.S.F. in five cases of leptomeningitis and in one case of leptomeningitis with brain abscess. Four of the pneumococcal strains belonged to Type III, one to Type I, and one was not typed.

The second commonest organism was Proteus, which was isolated in pure culture from the C.S.F. or brain abscess contents in five cases.

Other organisms encountered included *Streptococcus pyogenes*, *Staphylococcus pyogenes*, *Escherichia coli* and *Pseudomonas pyocyanea*.

The C.S.F. was sterile in twelve cases of leptomeningitis, but organisms were always demonstrated in material aspirated from brain abscesses.

Pathology of Underlying Ear Infection

(a) *Surgical material*

Material from fourteen of twenty-two cases undergoing aural surgery was received for histological examination. The presence of non-specific inflammatory granulation tissue, showing varying degrees of cellularity or fibrosis, was noted in all fourteen cases.

In four cases there was insufficient material to allow a distinction to be made on histological grounds between acute and chronic infection.

In five cases, the features were predominantly those of chronic infection, amongst which were:

(1) Bone reconstruction as shown by prominent lines of apposition and irregular cement lines (Fig. 1).

(2) Conversion of the flattened or cuboidal lining of the tympanic cavity and mastoid air cells into a columnar type of epithelium (Fig. 2) and the formation of gland-like structures (Fig. 3).

(3) The presence of keratinizing squamous epithelium resulting in the formation of epidermoid cholesteatoma (Fig. 4).

(4) Cholesterol granuloma, indicated by collections of cleft-like spaces and foreign body giant cells embedded in fibrous granulation tissue (Fig. 5).

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TABLE I

Summary of Cases

Case No. and Year	Age	Sex	Duration of Aural Symptoms	Intracranial Lesion	Bacteriology	Result
1 1951	58	F	> 1 year	Leptomeningitis	C.S.F.—sterile Mastoid cells—sterile	Recovered
2 1951	33	F	18 months	Leptomeningitis	C.S.F.—*Staph. albus.* Mastoid cavity—sterile	Recovered
3 1951	42	M	R. ear—11 weeks L. ear—years	R. temporal lobe abscess	Abscess contents—*Staph. albus.*	Recovered
4 1952	9	M	Not known	L. temporal lobe abscess (recurrent)	Not known	Recovered
5 1952	60	F	2 weeks	Leptomeningitis	C.S.F.— *Strep. pneumoniæ* Aural Swab—*Strep. pneumoniæ*	Died
6 1952	49	M	20 years	Leptomeningitis and R. temporal lobe abscess	C.S.F.—*Strep. pneumoniæ*	Died
7 1953	64	M	10 years	Leptomeningitis and R. temporal lobe abscess	C.S.F.—sterile Mastoid swab—Coliform bacillus	Recovered
8 1953	33	F	6 years	L. temporal lobe abscess	Abscess contents—Paracolon bacillus L. mastoid cavity—*Staph. pyogenes*	Died from recurrence of abscess 18 months later
9 1953	13	M	2 years	Leptomeningitis	C.S.F.—Proteus Mastoid bone chips—Proteus	Recovered
10 1953	78	M	14 months	L. temporal lobe abscess	Abscess contents—*Staph. albus*	Died
11 1954	66	M	27 years	Leptomeningitis	C.S.F.—sterile Aural swab—Proteus	Recovered
12 1954	5	F	8 days	Leptomeningitis	C.S.F.—sterile Aural swab—sterile	Recovered
13 1954	38	F	R. ear—3 weeks L. ear—years	Leptomeningitis and R. extradural abscess	C.S.F.—*Staph. albus* R. aural swab—*Strep. pyogenes* R. mastoid swab and Abscess contents—*Staph. pyogenes*	Recovered
14 1955	42	M	1 year	R. temporal lobe abscess	Abscess contents—*E. coli* R. aural swab—Proteus	Died
15 1955	22	F	Since childhood	R. temporal lobe abscess	Mastoid cavity—*E. coli*	Subsequently admitted to another hospital with severe mental changes
16 1956	20	M	Many years	Leptomeningitis and R. extradural abscess	C.S.F.—sterile Abscess contents—*Strep. pyogenes* and Proteus	Recovered
17 1957	20	M	Since childhood	Leptomeningitis	C.S.F.—sterile Aural swab—Proteus	Recovered
18 1958	53	F	10 days	Leptomeningitis	C.S.F.—*Ps. pyocyanea* Aural swab—*Ps. pyocyanea*	Recovered
19 1958	49	M	3 days	Leptomeningitis and L. extradural abscess	C.S.F.—sterile L. aural swab—*Staph. pyogenes*	Recovered

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TABLE I continued

Case No. and Year	Age	Sex	Duration of Aural Symptoms	Intracranial Lesion	Bacteriology	Result
20 1958	18	M	Not known	Leptomeningitis	Not known	Recovered
21 1959	34	M	Many years	Leptomeningitis	C.S.F.—sterile Aural swab—Proteus	Recovered
22 1959	45	M	3 days	Leptomeningitis	C.S.F.—*Strep. pneumoniæ* Aural swab—*Staph. pyogenes*	Recovered
23 1959	36	F	4 years	Leptomeningitis and L. temporal lobe abscess	C.S.F.—sterile Abscess contents—*Staph. pyogenes* and non-hæmolytic Streptococcus L. aural swab—*Staph. pyogenes*	Recovered
24 1959	31	F	2 weeks (previous mastoidectomy at age of 5)	Leptomeningitis	C.S.F.—*Strep. pneumoniæ* Aural swab—*Strep. pneumoniæ*	Recovered
25 1959	43	M	4 days	Leptomeningitis and extradural abscess	C.S.F.—*Strep. pneumoniæ* R. aural swab Swab from R. mastoid antrum } sterile	Recovered
26 1959	62	M	2 weeks (also 8 years previously)	Leptomeningitis and R. cerebellar abscess	C.S.F.—Proteus Abscess contents—Proteus R. mastoid swab—Proteus	Recovered
27 1959	31	M	8 years	L. temporal lobe abscess	Not known	Died
28 1960	50	M	> 10 months	R. temporal lobe abscess	Abscess contents—Proteus R. aural swab—Proteus	Recovered
29 1960	49	M	20 years	Leptomeningitis	Aural swab—*E. coli* P.M. swab of subarachnoid space—*E. coli*	Died
30 1960	59	M	Many years	Leptomeningitis, R. temporal lobe abscess and extradural abscess	C.S.F.—Proteus Brain abscess contents—Proteus Mastoid bone chips—Proteus	Recovered
31 1960	52	M	5 days (also 2 and 4 years previously)	Leptomeningitis and L. temporal lobe abscess	C.S.F.—sterile Abscess contents—sterile (but Gram positive cocci in direct smear) L. mastoid swab—*Strep. pyogenes*	Recovered
32 1960	57	F	Many years	Leptomeningitis and L. temporal lobe abscess	C.S.F.—sterile Abscess contents—Proteus L. aural swab—Proteus	Died
33 1960	48	M	4 days (also several years previously)	Leptomeningitis	C.S.F.—*Strep. pneumoniæ* Aural swab—*Strep. pneumoniæ* and *Staph. pyogenes*	Recovered
34 1960	42	F	Many years	Leptomeningitis	C.S.F.—sterile Mastoid swab—*Staph. pyogenes* Aural swab—*Staph. pyogenes* and Proteus	Recovered

In the remaining five cases there was evidence of acute infection such as osteoclastic erosion of bone and the formation of trabecular new bone (Figs. 6 and 7), together with additional features indicating the presence of underlying old or chronic infection.

The histopathological findings in these fourteen surgically treated cases are summarized in Table II.

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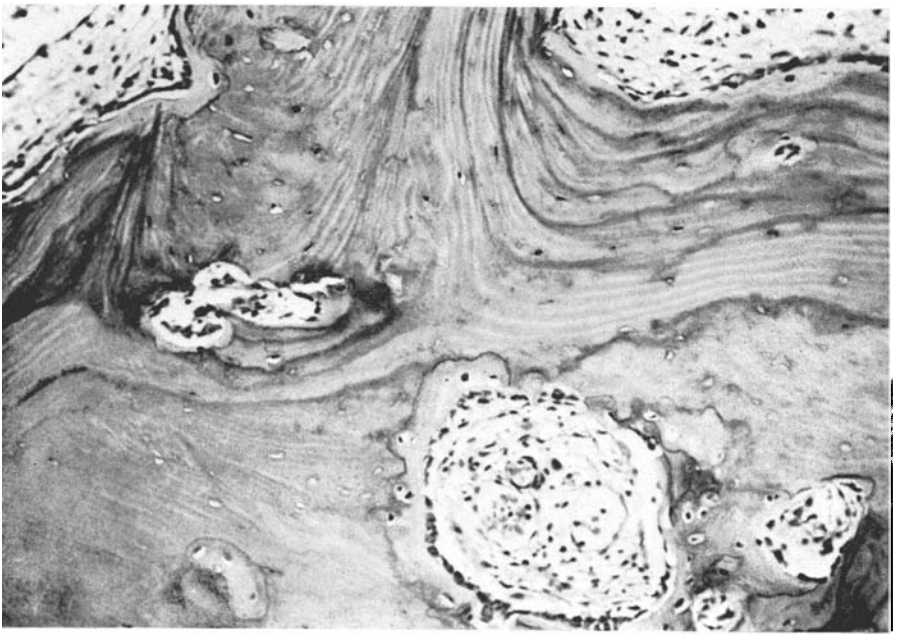


FIG. 1—CASE XXXIV.

Irregular cement lines in mastoid bone indicating bone reconstruction. Note fibrous granulation tissue in perivascular spaces. Hæmatoxylin and eosin ×143.

TABLE II

SUMMARY OF HISTOLOGICAL FINDINGS IN MASTOIDECTOMY SPECIMENS

Case No.	Suppuration	Inflammatory Granulation Tissue	Bone Changes			Epithelial Changes		Glandular Structures	Epidermoid Cholesteatoma	Cholesterol Granuloma
			Erosion	New Bone Formation	Recon-struction	Columnar	Squamous			
7	+	+	+		+					
8		+			+	+		+		
13	+	+	+		+					
15		+								
17		+	+				+	+	+	
18		+								
20		+								
25		+			+	+		+		
26	+	+	+	+	+	+		+		
28		+					+		+	
29		+				+	+	+	+	
30		+			+			+		+
31	+	+								
34	+	+		+	+					

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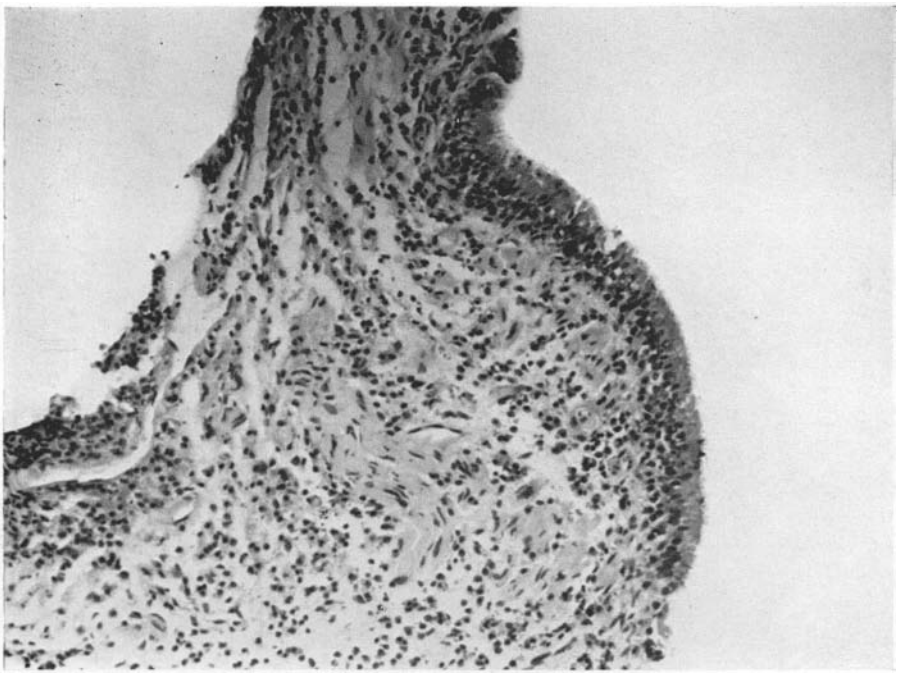


FIG. 2—CASE XXIX.
Columnar epithelium covering chronic inflammatory granulation tissue. Hæmatoxylin and eosin × 165.

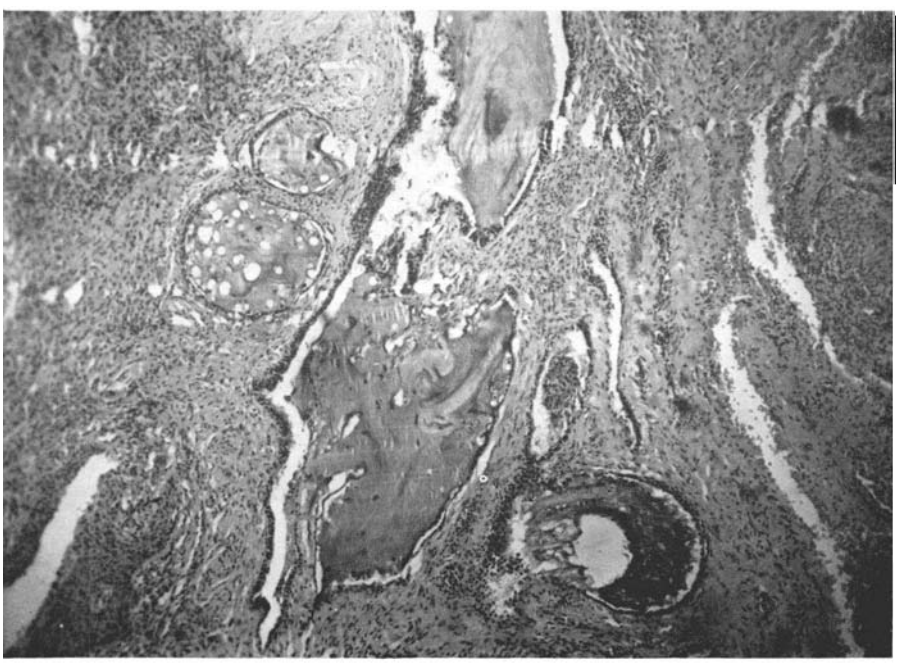


FIG. 3—CASE XVII.
Gland-like structures surrounded by chronic inflammatory granulation tissue. Hæmatoxylin and eosin × 45.

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FIG. 4—CASE XXIX.
Keratinizing squamous epithelium forming part of the wall and contents of epidermoid cholesteatoma. Hæmatoxylin and eosin × 165.

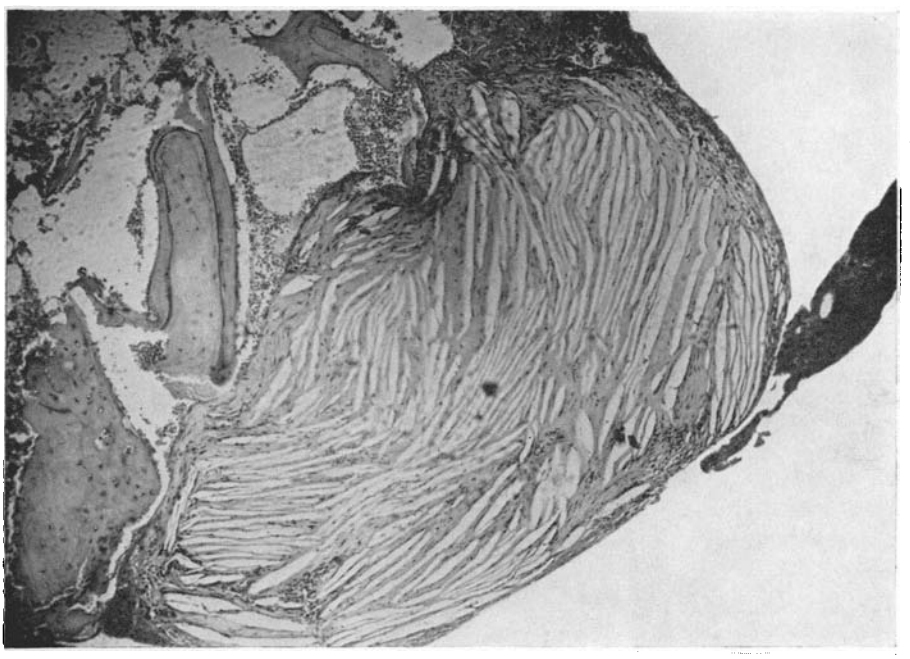


FIG. 5—CASE XXX.
Cholesterol granuloma. Hæmatoxylin and eosin × 41.

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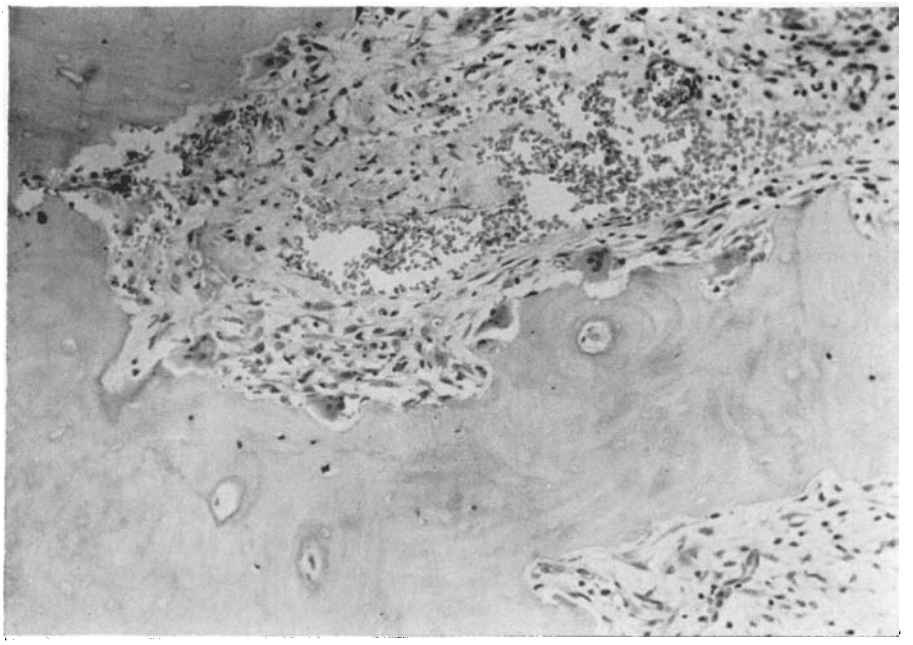


FIG. 6—CASE VII.
Erosion of bone by inflammatory granulation tissue. Note the presence of osteoclasts. Hæmatoxylin and eosin × 158.

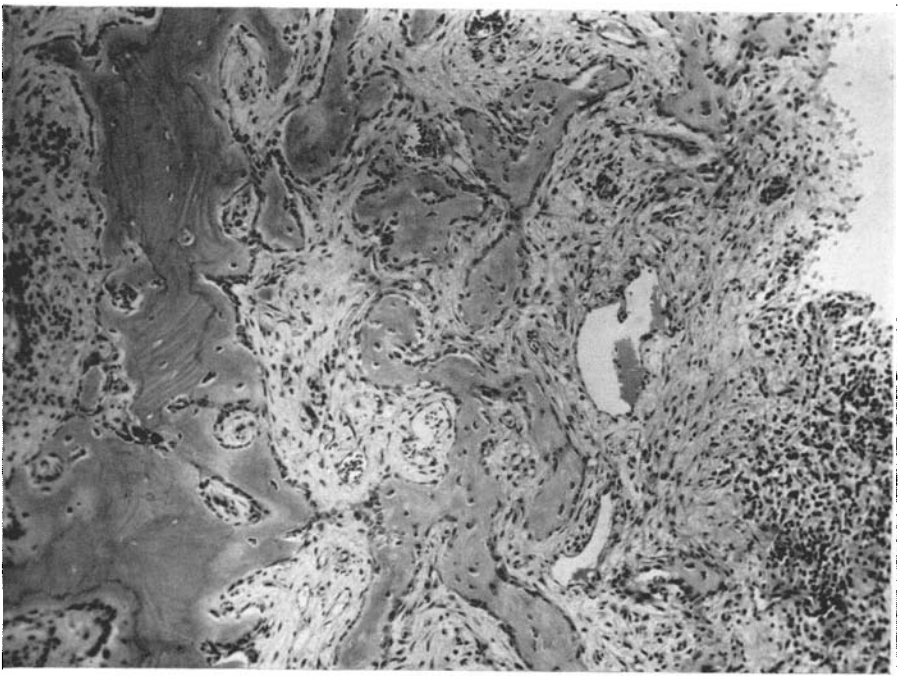


FIG. 7—CASE XXVI.
Trabeculae of new bone forming in granulation tissue. Note proliferation of osteoblasts. Hæmatoxylin and eosin × 90.

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(b) *Autopsy material*

Histopathological studies were made of the temporal bones obtained at autopsy from five of the eight fatal cases. The findings are summarized as follows:

CASE V

Mastoid is mainly diploetic, but there is evidence of bone reconstruction in vicinity of tympanic cavity, with inflammatory granulation tissue in air cells. Tympanic cavity is filled with purulent exudate, and lined by polypoid columnar ciliated mucosa. There is extensive submucosal inflammatory granulation tissue enclosing numerous gland-like structures.

CASE VI

Mastoid bone shows evidence of reconstruction, and air cells are filled with inflammatory granulation tissue. Tympanic cavity contains purulent exudate and is lined by columnar ciliated epithelium thrown into polypoid folds. There is extensive submucosal inflammatory granulation tissue enclosing numerous gland-like structures. There is total bony obliteration of the cochlea. An aural polyp projects into the external auditory meatus (Figs. 8 and 9).

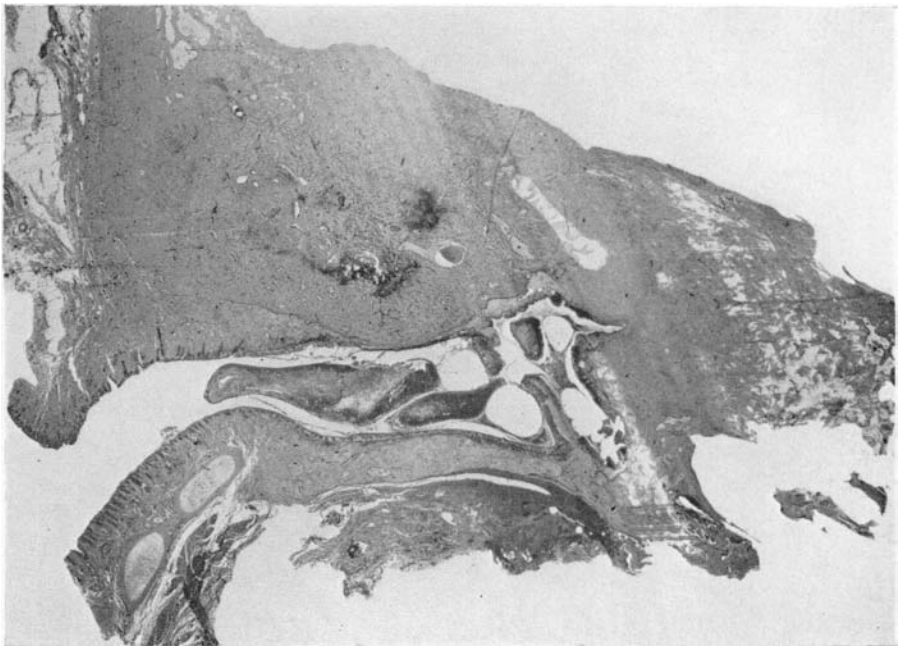


FIG. 8—CASE VI.

Section of temporal bone showing polyp in external auditory meatus. There is total bony obliteration of the cochlea. Hæmatoxylin and eosin × 2·7.

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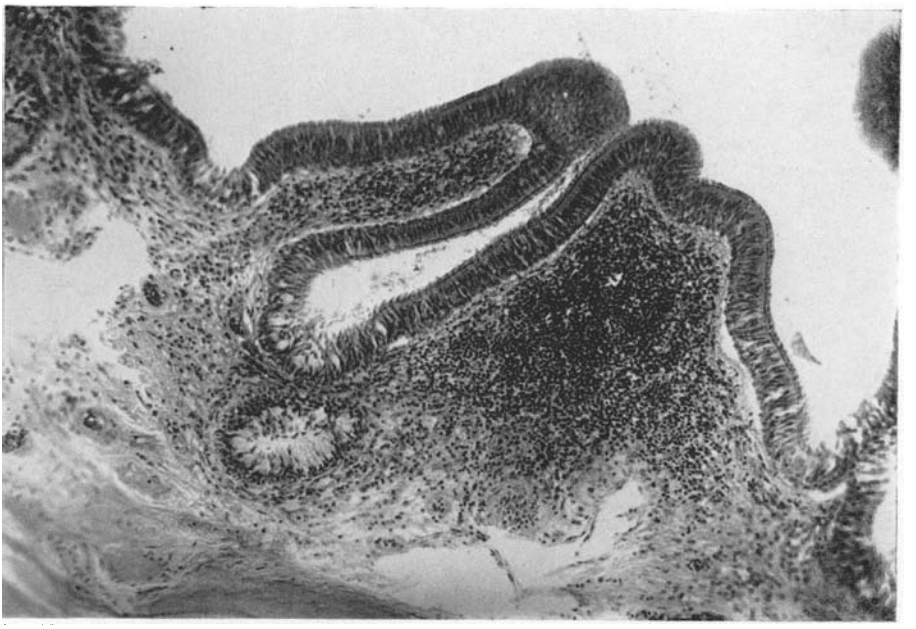


FIG. 9—CASE VI.
Polypoid columnar ciliated epithelium lining tympanic cavity. Hæmatoxylin and eosin × 75.

CASE X

Mastoid is mainly pneumatized or diploetic, but there is evidence of bone reconstruction in vicinity of tympanic cavity, with fibrous granulation tissue in air cells. Tympanic cavity contains small amount of pus and is lined by columnar epithelium. Fibrous granulation tissue, enclosing numerous glandular structures, lies deep to the mucosa.

CASE XXVII

Mastoid is mainly pneumatized but there is evidence of bone reconstruction in vicinity of tympanic cavity, and some of the air cells contain fibrous granulation tissue. The tympanic cavity contains purulent exudate and is lined by columnar epithelium with much submucosal granulation tissue enclosing gland-like structures.

CASE XXIX

Mastoid bone shows evidence of reconstruction, and inflammatory granulation tissue is present in air cells. Tympanic cavity contains much granulation tissue covered by keratinizing squamous epithelium forming the wall and contents of an epidermoid cholesteatoma. Some trabeculae of new bone have formed in the granulation tissue. Numerous gland-like structures are also present. The cochlea contains pus and there is infiltration of the auditory nerve by mixed inflammatory cells (Figs. 10, 11 and 12).

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FIG. 10—CASE XXIX.
Section of temporal bone showing epidermoid cholesteatoma in tympanic cavity and pus in cochlea. Hæmatoxylin and eosin × 5·3.

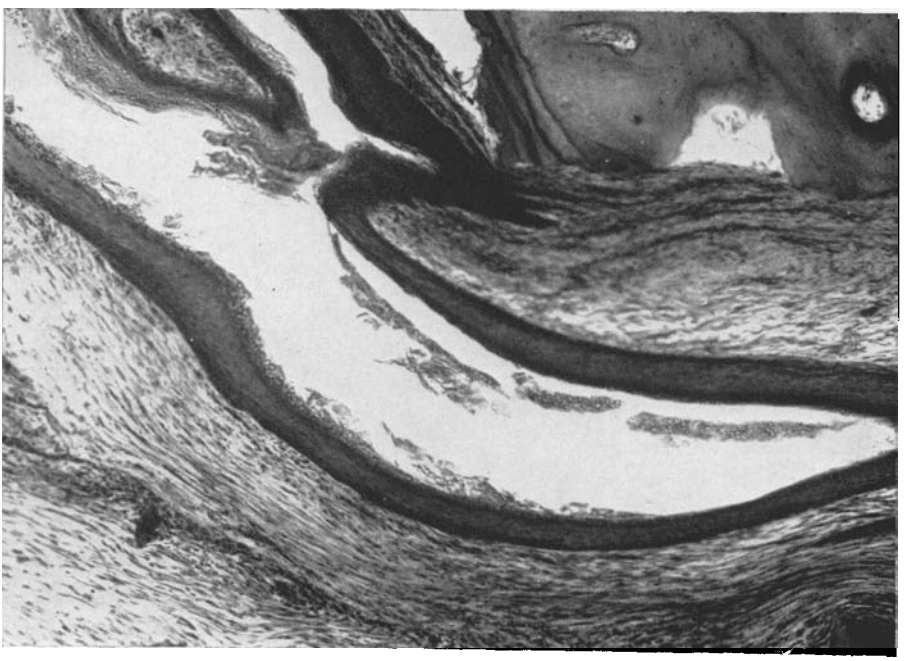


FIG. 11—CASE XXIX.
Part of epidermoid cholesteatoma shown in Fig. 10. Hæmatoxylin and eosin × 96.

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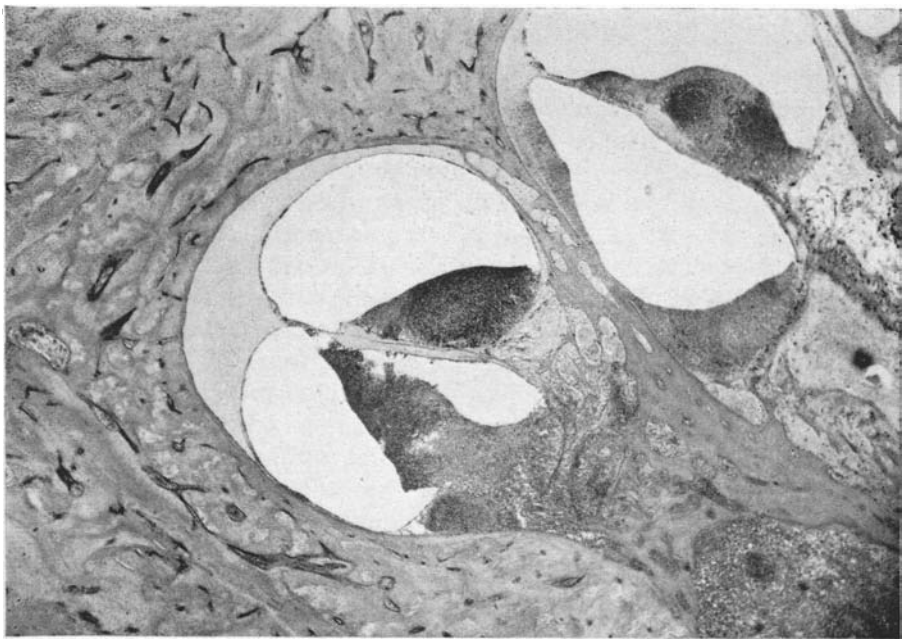


FIG. 12—CASE XXIX.
Part of cochlea shown in Fig. 10 showing the presence of pus. Hæmatoxylin and eosin × 30.

Discussion

The thirty-four cases described here presented at two hospitals during a ten-year period in which 2,000-3,000 cases of acute and chronic suppurative otitis media were seen annually. Viewed in this context, the incidence of intracranial suppuration as a complication of otitis media is seen to be small (less than 0·15 per cent.) at the present time, contrasting with the figures given by authors writing in the pre-antibiotic era. Fraser and Halliday (1936), for instance, found fifty-one cases of meningitis or brain abscess amongst 2,731 cases of acute otitis media attending the Edinburgh Royal Infirmary between 1920 and 1934, an incidence of 1·9 per cent. Cawthorne (1955) quotes Hegener (1908) who found 223 cases with intracranial complications, excluding extradural abscess, among 10,187 cases of otitis media, a proportion of 2·2 per cent. Although these sets of figures are not strictly comparable one with another, they provide sufficient evidence to show that the incidence of intracranial suppuration as a complication of otitis media has undergone a very considerable reduction since the introduction of sulphonamides and antibiotics.

Otogenic intracranial suppuration as a cause of death has fallen from a major position amongst ear, nose and throat conditions to one of comparative rarity as shown by the occurrence of thirteen deaths from this

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cause at one of these two hospitals in 1936 (unpublished data) compared with only eight deaths in the present series during the whole of the past ten years. This observation is in agreement with the findings of Courville (1955) who reported a reduction of 90 per cent. in the number of deaths from these conditions since 1934. It seems, however, that this dramatic improvement is due more to the reduction in the incidence of these complications than to a reduction in case mortality. While the eight fatal cases in this series form a very small proportion of the total number of cases of otitis media seen during the period, they are of greater importance when considered in relation to the total number of cases of intracranial suppuration, of which they form the not inconsiderable proportion of 23·5 per cent. In another recent series reported from the Royal Victoria Infirmary, Newcastle-upon-Tyne by Dawes (1961) there were thirty-five deaths amongst ninety-eight cases of otogenic meningitis admitted during the years 1944-60, and fifteen deaths amongst thirty cases of otogenic temporal lobe abscess, though most of the deaths occurred during the earlier years of this period. It is clear that these conditions are still dangerous to life and that since even survivors are liable to suffer from permanent mental changes or other defects, early diagnosis is essential if patients are to be given the full benefits of modern therapy.

The average age of the cases reported here was forty-two years, and there were only two children under the age of twelve years although approximately 25 per cent. of the patients attending with otitis media are in this age group. There were no children among the eight fatal cases, whose average age was fifty years. By contrast, the thirteen patients who died in 1936 at an average age of eighteen included no less than six children under the age of twelve years. These figures indicate that the greatest improvement in the rate of incidence and hence of mortality has occurred amongst the younger age groups. This is of course to be expected since it is in the more acute forms of acute otitis media, which commonly occur in children, that antibiotics are most likely to be effective.

The sex incidence shows a male to female ratio of 11 : 6. This male preponderance, which is in agreement with the observations of most other authors, might be explained by the greater incidence of otitis media amongst males. In a recent series of 1,000 consecutive cases of otitis media attending these hospitals, there were 565 males and 435 females. Even if these figures are significant, however, they still require explanation; it is probable that the sex incidence both of otitis media and of its complications is determined by a greater susceptibility amongst males to infection in general.

The bacteriology of the intracranial lesions, as might be expected, follows that of otitis media. Neumann (1925) found that among 101 cases of otogenic meningitis forty-five were due to infection with *Streptococcus pyogenes* and thirty-eight to infection with *Streptococcus pneumoniae*.

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These were also the commonest organisms found in eighteen cases of otogenic meningitis reported by Cawthorne (1939), and in twenty-two cases of otogenic brain abscess reported by Atkinson (1934). Since fewer cases result from acute otitis media than formerly, it follows that infection due to these pyogenic cocci is becoming relatively less common while those organisms which are commonly found in chronic otitis media, such as Proteus, are being found more often. It is of interest to note, however, that *Streptococcus pneumoniae* was still the commonest organism to be isolated in the present series, and that in four out of six pneumococcal cases the strain was found to belong to Type III, which has earned a special reputation in the past as a cause of otogenic intracranial suppuration.

The widespread use of antibiotics in otitis media has resulted in a greater proportion of cases of leptomeningitis in which the C.S.F. is found to be sterile, or in which an organism of only doubtful significance is isolated. It is often found that the C.S.F. becomes sterile within twenty-four hours of commencing antibiotic therapy. It is evident, therefore, that lumbar puncture should be performed before the commencement of therapy if a full bacteriological diagnosis is to be made. The choice of antibiotics will depend on the identity of the organisms isolated, but once the specimen of C.S.F. has been obtained the patient can be treated empirically while the bacteriology report is awaited.

As far as possible from the surgical material available, histopathological studies confirmed the clinical impression that the majority of cases occurred amongst patients whose ear infection was chronic rather than acute. Evidence of chronic infection was provided by such features as reconstruction of bone, reversion to a columnar ciliated type of mucosa lining the tympanic cavity or mastoid air cells, formation of glandular structures, the presence of keratinizing squamous epithelium forming the wall and contents of epidermoid cholesteatoma, and cholesterol granuloma, all of which are typical of chronic otitis media (Friedmann, 1956).

The features of acute or sub-acute infection such as osteoclastic erosion of bone and the formation of trabeculae of new bone were seen in five cases but in all of these there was evidence of chronic infection also, the histological picture being that of acute on chronic otitis.

Similar evidence of chronic infection was observed in the five temporal bone specimens obtained at autopsy. All five specimens showed a greater or lesser degree of bone reconstruction, together with extensive granulations enclosing glandular structures. The tympanic cavity was lined by columnar epithelium in four cases; in the fifth the presence of keratinizing squamous epithelium had resulted in the formation of an epidermoid cholesteatoma. This last case was also notable for the presence of pus in the cochlea and inflammatory infiltration of the auditory nerve, illustrating one of the pathways by which infection may spread to the meninges.

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It is not intended in this paper to discuss the clinical aspects or treatment of these conditions. It is suggested, however, that the development of headache, mental changes or other untoward symptoms occurring in the course of otitis media should always arouse the suspicion of intracranial complications, so that patients suffering from these conditions may benefit from the early application of modern diagnostic techniques and when necessary of the timely surgical intervention and adequate antibiotic therapy upon which survival depends.

Summary and Conclusions

An analysis is made of thirty-four cases of otogenic meningitis or brain abscess admitted to the Royal National Throat, Nose and Ear Hospitals during the past ten years, with special reference to the pathology of the underlying ear disease.

The incidence of these complications of otitis media underwent a considerable reduction after the introduction of sulphonamides and antibiotics, but has not continued to fall during the past ten years.

The greatly diminished death rate from these conditions appears to be due more to a reduction in incidence than to a reduction in case mortality, which has remained relatively high.

The greatest reduction in incidence has occurred amongst children with acute otitis media; the majority of cases in this series were adults with chronic ear infection.

Since these conditions must still be regarded as dangerous to life, the need for early diagnosis is stressed.

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