Dr. W. J. Newlands presented a case of Essential Hypercholesterolæmiac Xanthomatosis with involvement of the pharynx. The patient was a 73-year-old female who had presented 15 months previously with nasal obstruction. This was found to be due to Xanthomatosis involvement of the retropharyngeal tissues in relation to both naso- and oro-pharynx. The soft palate was pushed forward—the larynx was normal. Removal of nasopharyngeal tissue relieved the nasal obstruction while Atromid successfully lowered the blood cholesterol. The patient remained improved; "details of blood chemistry and microscope slides of the Xanthoma were shown". Dr. Newlands commented that the condition was believed to be the result of increased cholesterol metabolism, the site of this being the liver. Laryngeal involvement, frequently necessitating a tracheotomy, is common in such cases; the present case was particular in that the larynx was entirely normal.

The President then declared the meeting closed.

ROYAL SOCIETY OF MEDICINE—SECTION OF OTOLOGY

March 5th, 1965

PROFESSOR D. F. N. HARRISON: We have listened today to two erudite and informative papers. There are, however, several aspects of this interesting condition which I feel might be considered in further detail.

It was Dr. Haddow of Entebbe who first commented that this condition appeared to be limited to certain areas in Africa where the altitude was less than 5,000 feet, a yearly rainfall of more than 20 inches and where the temperature did not fall below 60°F during the coldest season of the year. This geographical distribution also corresponds with that of some mosquito-borne diseases, and this has led to the suggestion that the tumour might be of virus origin, perhaps carried by an arthropod vector. A virus, antigenically related to reovirus 3, has in fact been isolated from a case of Burkitt's lymphoma!

If these "geographical postulates" are really important, then it might be of value to consider whether there are other regions in the world where similar climatic conditions exist. Map B showing mean temperatures and rainfall throughout the world, demonstrates that in both the northern part of South America and in Indonesia there are regions which match the conditions found in Central Africa. Maps showing annual rainfall and the presence of mosquitoes also confirm these features and thus one should consider those regions as potential habitats for Burkitt's lymphoma. ten Seldam has found some cases in New Guinea (1960) and as this country is explored further, more patients may materialize. However, an American expedition into the Panama Canal zone

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found no evidence of lymphoma, although the technical difficulties of exploring the dense jungle of this region must make any definite pronouncement of incidence somewhat unreliable. No doubt further surveys will be carried out in those regions in the near future.

The dramatic response of this tumour to Cyclophosphamide (Endoxana, Cytoxan) is not surprising for we have seen that the tumour contains a high quantity of phosphatase. This particular drug is only activated in the human when the warhead: di-2-Chloroethylamine (nor-HN2) is released by enzymic action. This occurs primarily in the liver from the action of the phosphatase and phosphamidases but also occurs in tumour tissue where the concentration of these enzymes is high. It is interesting to note that Dr. Burkitt uses a high dose therapy of 30-40 mg. per kg. given as a single intravenous injection for this is the régime followed at the Royal National Throat, Nose and Ear Hospital in the treatment of adult squamous carcinoma affecting the head and neck, with unfortunately less success.

In those cases where massive tumour destruction occurs within several days, it is somewhat surprising that there has been no mention of secondary hæmorrhage or systemic toxicity from absorption of the breakdown products of the tumour. This might well be expected in those cases with large abdominal tumours.

There is obviously much work yet to be carried out but Dr. Burkitt is to be admired not only for his pertinacity and enthusiasm in elucidating the clinical features of this interesting condition but also for his wisdom in applying modern chemotherapeutic techniques to its control.

MR. MCKENZIE discussed the treatment of cholesteatoma and agreed with Mr. McGuckin that a patient with a cholesteatoma had the disease for life, and any treatment had to take account of that fact. Cholesteatoma was no longer an urgent indication for surgery, and the behaviour of the condition could be studied for weeks or months before surgery. Most otologists were now accustomed to the use of the Zeiss microscope in Out-patients, and the rate of growth of the cholesteatoma could sometimes be measured by regular observation, and so could the natural resistance of the patient. Treatment after operation must never cease and emphasis must be laid on regular visits to hospital, because a cholesteatoma might recur in the mastoid cavity at any time, even if the ear had been dry for twelve months or longer.

MR. W. STIRK ADAMS (Birmingham) said he would like to discuss the role of the stroma of the petromastoid in the pathology and treatment of cholesteatoma, as he thought the epithelial breakdown which produced the clinical cholesteatoma was due to a preceding keratogenic dysfunction of the soft tissue stroma of the middle ear and mastoid.

This view originated with Politzer's observation in the Fourth Edition of his textbook "Diseases of the Ear", Ballin and Heller translation 1902, where he wrote: "The epidermic blind pouches first described by Schwartze and observed by the author in a vast number of specimens, extend from the external meatus into the cavum tympani and mastoid antrum, and may persist as such during the entire life of the patient", and it may be deduced that if clinical cholesteatoma only occurs in a small proportion of these penetrations a local

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factor must be responsible, and this probably lies in a preceding stroma damage.

In discussing treatment he thought the local excision of the cholesteatoma insufficient, as in a consecutive series of 31 cases in which mastoid bone and stroma were examined histologically it had been shown that both keratinizing and non-keratinizing multilayered squamous epithelium were frequently associated with other infective mastoid pathologies.

In his view the objective should be to prevent recurrences of cholesteatoma by achieving the recovery of normal stroma function in the walls of the operative cavity after a full excision of the superficial cementation in the mastoid.

The basis of stroma recovery with the resulting long-term security of the post-operative radical cavity had been regarded by his senior colleague, B. Seymour Jones, in Birmingham (1945) as determined by the biological development of the post-operative twelve day collagen response from the fibroblasts in the walls of the cavity (then described as granulation tissue), and it had been the speaker's aim, in facilitating its development, to ascertain the biological factors responsible.

Recently these have been recorded in experimental physiology (Mills Moyer, 1962) where the collagen response has been widely studied in closed wound repair by the Carrageenin granuloma, the Ivalon Sponge and the tissue scaffolding techniques, and many studies of open wound repair have followed Metchnikof's original observations and the recent experiments of Parker in the R.C.S. laboratories have again confirmed the response of the mobile cells to injury (R.C.S. Annual Reports 1963/64).

Over the same period the pH changes during the repair of the experimental wound from the initial alkaline swing, back through neutral to an acid pH level of 5·5 in four days, have been accepted as the normal, and such a swing can be regarded as a normal biological occurrence immediately after the radical mastoid operation.

Hitherto there does not appear to have been any work in experimental physiology on the effect of artificially accelerating this swing during repair to the acid side, but recently an investigation has been carried out in the Biochemical Department of the Queen Elizabeth Hospital, Birmingham, to discover whether movement of pH changes in the post-operative tissues are likely to have been affected by the pH of the topical applications used post operatively.

The Table indicates that with B.I.P.P.—originated by Rutherford Morrison in Newcastle on Tyne in 1916, and reported by his otological colleague, Sam Whyllis, as having revolutionized mastoid surgery, the tissues are flooded with an acid medium of 3·5, and the effect would seem to be a biological shock to intensify and accelerate the response of the tissue to injury.

The Bismuth and Glycerin preparation aa with a more acid pH of 3·1 was developed 30 years ago in the department of clinical otolaryngology of the University of Birmingham for the stimulation of fibroblast activity in the post-operative cavity after excision of the upper jaw. It has retained its position as a post-operative cavity dressing ever since and has proved even more effective than B.I.P.P. in promoting rapid tissue collagenosis with a resulting high level of post-operative security in the mastoid cavity.

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pH TABLE OF TOPICAL AURAL APPLICATIONS

MR. J. H. JOHNSTONE, B.Sc., DEPUTY HEAD OF THE DEPARTMENT OF BIOCHEMISTRY, QUEEN ELIZABETH HOSPITAL, BIRMINGHAM.

No.	pH	Application	Prescription
A. External Auditory Canal			
1	3·0	Methylene Blue	1% Aq. Soln.
2	3·3	Salicylic Acid	Unguentum
3	3·6	Boric and Iodine	Pulv (I_2 0·75 gr. to oz. P.A.B. 10% suspension)
4	3·8	Hydrocortisone	1% ung.
5	4·5	Gentian Violet	1% Aq.
6	4·5	Aluminium Acetate	8% (Aq. sat. sol.)
7	5·0	Cu Zn SO_4 Sol.	Cu SO_4 3 gr. Zn SO_4 10 gr. Aq. ad. oz. 4
8	5·9	Ichthyol 20% in Glycerin	
9	6·4	Neocortef aural drops	Upjohn 1·5%
10	6·8	Xeroform	Dimol
11	9·0	Argyrol	5%
12	6·45	Spirit	70%
13	6·45	Spirit	30%
14	4·5	5 vol. Hydrogen Peroxide	
B. The Mastoid Cavity			
1	3·1	Bismuth Subnitrate in Glycerin	Cream
2	3·5	B.I.P.P.	Bismuth subnitrate 1 part, Iodoform 2 parts and Paraffin Q.S. (1 gm. cream mixed with 5 ml. aq.) pH of Aq. 3·5
3	4·35	Arsenicus Trioxide	1/5000 in Boric Acid pulv. (Ref: Alfred Lowy, *Jl. Arch.* O.R.L., Vol. 22, 1935, p. 636)
4	6·5	Amino Acridine	1/1000
5	6·5	Glycerin	50% sol. in H_2O
6	7·2	Eusol	0·27% Hypochlorous Acid

Discussion on Cholesteatoma Auris

MR. FRANCIS MCGUCKIN (Newcastle) said: Sir Terence Cawthorne has been generous enough to send me an advance abstract of his paper and Mr. Brian Pickard has been kind enough to invite me as a guest in his home so that there can be nothing malicious or vicious about my intervention. Nevertheless, my opinions are not quite in accord with theirs and such differences as there are will presently become apparent.

Sir Terence's judgment has been influenced by an almost unique experience of congenital petrous epidermoids. There are reasons why he sees a number of these somewhat exotic canaries, but there are also reasons why I see a vast collection of very ordinary sparrows. We should, I think, dismiss the uncommon congenital entity altogether from today's argument. It is something special, though I would say that even here the use of the word cholesteatoma is faintly silly and nostalgic. Our time may be more fruitfully spent on everyday affairs.

Now an appeal to Harvey Cushing in 1922 is not impressive. With all respect, I suggest that Cushing's otological experience was such as to justify no

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more than wild speculation. Dan McKenzie's 1931 paper was a fine essay in philosophy and it dazzled me for a few years, but not longer, because it became clear that though the deductions were logical enough, the premisses were faulty; the whole magnificent edifice could not stand the test of observation—and this condemnation goes also for those cases in which keratin (or cholesteatoma) is or seems to be enclosed, cases which are seldom too difficult to interpret. Again, I imply no disrespect to a distinguished man.

It is unlikely that the opinions of Virchow, announced in 1863, are any more germane to this morning's discussion than would be his 1863 views about the reticulo-endothelial system. The otological observations of clinicians like Toynbee and Von Troltsch about that time, of Albert Gray before 1910, and of Arthur Juers today may command more respect. In any event Virchow saddled us with the term cholesteatoma, a word which is worse than faintly silly—it has proved disastrous.

In short I reject the neoplastic theory of cholesteatoma. I also reject the word itself and all concepts based on it. The so-called cholesteatoma consists almost wholly of dead epidermis. (It is true there is a germinal layer.) Why not call it a mass of keratin or, as Mr. John Gray says, skin in the wrong place? After all it is epidermis.

Non-malignant destructive ear disease is initially silent and the damage is done by keratin derived from the external auditory canal. We may not understand the precise mechanism, but it is virtually certain that basically it is not one of pressure or infection or suppuration, though these things may be added. Keratotic erosion may destroy canal bone in any direction; it may erode not only into the attic but also into any part—*any part* of the mesotympanum; it may even bore through from the canal into the mastoid to produce a meato-mastoid fistula, in that sequence, meatus first and mastoid second. When infection or suppuration occurs it is secondary. When the patient first has a symptom it is because a silent pathology has been complicated by some process which produces an overt symptom, such as discharge, bleeding, deafness and so on. The aberration of canal skin is always there long before the symptom.

I plead that you do not accept the plausible theory put forward this morning if only because it demands the further exhumation of a corpse already interred half a dozen times. Why not let the poor soul rest in peace? There is nothing of prophylactic hope about the neoplastic idea. It is something which is demonstrably wrong, at least to those who spend many hours each week with the microscope in the out-patient clinic.

I believe that the old concept of chronic suppurative otitis media, with or without what is called cholesteatoma, is almost untenable. It matters little whether my present interpretations are right or wrong—and there is no time now to argue the problem in detail—but my views are at least based on massive factual observation of enormous numbers of cases. Keratin inside the middle-ear cleft has arrived there from the outside. Keratin may make a hole, or it may enter through a hole already present, or it may occasionally make a hole which closes behind it because it is sterile and because of regeneration of mucosa. Clearly, Sir Terence and I are not wholly in accord.

Before offering a few colour-transparencies as a mere fraction of my evidence, I should mention some small disagreement between Mr. Pickard and myself.

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Skilled surgical techniques have their place and one has or has not the talent to acquire them. Secretly I think some of his techniques savour of the mediæval. In non-malignant destructive ear disease, it is important not to be carried away by technical splendour, perhaps even more important to know when not to do a thing than how to do it. In this sphere, it is certain that definitive operations do not necessarily produce definitive results, that exact diagnosis of type and extent of disease is paramount, that *ad hoc* surgery or no surgery at all should displace set operations, that the idea of absolute cure is not to be countenanced though control may be a legitimate ambition. We cannot afford preconceived surgical notions about a disease that is never the same twice.

(Eleven colour-transparencies of six cases were quickly described but it was stressed that these represented no more than a tiny fraction of the evidence.)

MR. I. B. THORBURN showed colour photographs of the ears of a 17-year-old youth. In both ears a thin posterior segment of the membrana tensa was adherent to the medial tympanic wall and recessed into the sinus tympani. There was also marked retraction of Shrapnell's membrane.

In the left ear active cholesteatoma was shown to have developed by migration of a keratinizing epithelium from the upper part of the sinus tympani, underneath the body and short process of the incus, in the line of the isthmus tympani posticus described by Bruce Proctor. The long process of the incus had been destroyed and the stapes, together with the antero-inferior part of tympanic cavity, were shut off from the disease by the original retraction of the posterior segment.

It was interesting that in the right ear the anterior part of the mesotympanum contained fluid and air bubbles but as yet no active keratinizing disease had developed in the sinus tympani.

This illustrated what Mr. Thorburn believed was the common ætiology of cholesteatoma auris. There was immigration of a keratinizing epithelium from a recessed segment of the tympanic membrane. This was a late sequel of Eustachian tubal dysfunction, which in its active phase was not infrequently associated with a secretory otitis media. The congenital theory advocated by Sir Terence did not seem to explain the common types of cholesteatoma which most of us encounter. Neither did the standard atticotomy operation advocated by Sir Terence and Mr. Pickard appeal to Mr. Thorburn as appropriate in the management of a condition of such varied and unpredictable extent as cholesteatoma of the middle-ear cleft.

REFERENCE

PROCTOR, B. (1964) *J. Laryng.*, **78**, 631.

Experimental Observations on Vein Graft Myringoplasty

WING-COMMANDER P. F. KING congratulated Mr. Richards on his excellent paper, and said it was interesting to see such accurate confirmation in experimental animals of what happens in clinical practice. While he agreed that there was little to choose between the behaviour of vein auto- and homografts, and the end results, he had found homografts much more satisfactory when under-

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taking a major repair of the middle ear. In this connection, he noted that no technique and no particular grafting material could hope to be successful unless the focus of disease was removed, and all cholesteatoma—whatever its origin—removed. To this end, extensive excisive procedures were often called for when cholesteatosis was present. With these cases one could not obtain sufficient vein autograft properly to cover and heal the middle ear and mastoid.

He had used vein homografts in some 150 cases and was pleased with the high proportion of healed ears obtained.

MR. S. H. RICHARDS thanked Wing-Commander King for his remarks and said that the results of the author's experiments for the most part corroborated Wing-Commander King's work on the use of vein homografts for myringoplasty in humans. He wished to re-emphasize, however, that the authors had never found it necessary to use homografts to repair perforations in humans' ears because they had found that an adequate length of vein from the antecubital fossa would, when stretched, cover even the largest perforation. He agreed that it was of the utmost importance to ensure that grafting is not undertaken when there is active disease in the middle ear or mastoid and the authors adhered to the strictest criteria in their selection of cases for operation. He was aware that Wing-Commander King used vein grafts not only to repair tympanic membrane defect but also to line the mastoid segment, and he appreciated the difficulty in getting a vein autograft large enough to cover both the tympanum and the mastoid cavity. The authors, however, believed that the correct method of dealing with the mastoid cavity was to obliterate it with muscle flaps and this rendered it unnecessary to use a vein to line the mastoid segment.

MR. PHILIP H. BEALES said: I would like to congratulate Mr. Alberti on his interesting paper and to say a few words about the blood supply of the incudo-stapedial region from the point of view of the practising otologist.

It is clear from Mr. Alberti's study and from the work of Nager and Nager that if the whole stapes is removed the blood supply of the long process of the incus is impaired and necrosis will occur in a proportion of those subjected to the various techniques of stapedectomy. I believe that time will show that this incidence is higher than we now think. Because of the risks of failure in the long term, I practise platinectomy in many cases and use the Teflon piston prosthesis for those patients who show an obliterative footplate at operation. In a recent paper McGee has shown that this is only about 5 per cent. of cases in a long series. Revision operations show that the stapes crura survive well after platinectomy and if the stapedius tendon is cut close to the pyramid it becomes reattached to the surrounding mucosa or even to the pyramid itself, and its function can remain. I believe this is the nearest approach to the normal mechanism that can be obtained, and that techniques similar to this should be practised more frequently. It is not widely appreciated that operations of this type can be very straightforward and simple to perform.

DR. A. BROWNLIE SMITH said he would like to congratulate Dr. Alberti on a very excellent piece of work. He appreciated the difficulties involved in such delicate anatomical investigations. He thought there were two methods of

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approaching the problem of the blood supply to the long process of the incus: one was the anatomical approach which Dr. Alberti had carried out; the other was the pathological one. This consisted in a careful examination of what remained after parts of the ossicles had been destroyed by disease.

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