As a result of their experiments some very definite conclusions and facts can now be said to be in our possession, facts which, even though they were surmised and embodied in hypotheses beforehand, had not been conclusively proved. That the primary hormone of the ovary, oestrin, is responsible for the growth and development of the uterus is now beyond dispute, and by the administration of massive doses of this hormone many a young woman, who ordinarily would have been condemned to a sexually immature, sterile, and probably dysmenorrhoeic life, can now be cured and made normal; just as a potential cretin can be saved by early medication with thyroid extract. The oestrin produced by the ovary is therefore responsible for the growth of the uterus and endometrium, and if this is in excess of the normal, then cystic hyperplasia of the endometrium develops. This is seen in the condition of metropathia haemorrhagica, where one ovary is fibrosed and functionless and the other is cystic and producing oestrin but not forming corpora lutea and hence no progesterin. Progesterin during the last ten to fourteen days of the intermenstrual period is essential for the production of a normal endometrium capable of receiving and embedding a fertilized ovum, and is therefore an integral part of the therapeutic technique.

The balance between oestrin and progesterin is interesting; Kaufmann thought that thirty-five rabbit units of progesterin were necessary, but the English writers state that only five units are needed to produce true menstruation, and the latter appears to be the correct figure. The dosage of oestrin varies with the different workers. Bishop, Cook, and Hampson at Guy's and Kaufmann at Vienna use one and a quarter million international units and the Americans, Werner and Collier, much less. The latter state with certainty that 75,000 international units are the minimum clinical dose of oestrin, but for true menstruation they maintain that nearly a million units are essential. There is almost certain to be a considerable margin of error or discrepancy between the figures of the various workers as each one uses a different preparation, and, even if they are all standardized, it seems doubtful if the products retain their potency with keeping, and the standard itself is open to individual variations of value.

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J. Karaseff (*Journ. de Radiol. et d'Électrol.*, July, 1936, p. 373) found radiographic changes in the bones and joints in 95 per cent. of all cases of leprosy. The changes affect mainly the distal ends of the extremities. They are of a destructive nature. They appear under two different forms: (1) local osteoporosis, seen mainly in persons of the hyposthenic type; (2) osteo-articular destruction, seen only in pronounced cases of leprosy of the nervous system. These changes are met most frequently in the feet. The spine is never affected in leprosy. The bone changes become more pronounced with the general progress of the disease.

L. M. Ruiz (*Arch. Med., Cir. y Esp.*, May 30th, 1936, p. 354), who records an illustrative case, maintains that mononucleosis is of importance in the diagnosis of malaria, and should be studied whenever the presence of the plasmodium cannot be demonstrated. In quotidian fever and atypical forms of malaria a diagnosis must be made from other diseases, especially acute leukaemia and glandular fever or infective mononucleosis. Apart from its diagnostic value a differential leucocyte count is indispensable in the examination of a case of malaria, as the neutrophil picture is a guide to the patient's resistance.

THE PROBLEM OF OTOSCLEROSIS

BY

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The clinical picture of otosclerosis is so indefinite, its symptoms are so often shared by other forms of deafness, and its physical signs are so few and inconstant, that the diagnosis can only be made with varying degrees of probability. When it is added that no treatment is known that has the slightest effect on its course it might well be supposed that the worst had been said. Nevertheless, by constantly diagnosing the disease on insufficient data and by persisting in its treatment otologists have added an aspect to the subject which carries with it something more than the reproach of an unsolved problem.

The outstanding pathological features of otosclerosis are: the bony fixation of the stapes, the occasional involvement of the basal coil of the cochlea, and, though this has not yet been proved, degenerative changes in the auditory nerve. According to the relative time incidence of these factors the clinical picture of otosclerosis may, apparently, vary from that of a middle-ear "obstructive" deafness to that of pure nerve deafness. Moreover, this picture need not possess one symptom that is not constantly present in other and far more common types of deafness. The facile diagnosis of this disease is almost as great a mystery as its aetiology.

The Bezold Triad

For the past fifty years otologists have reiterated the statement that a case of progressive deafness with the Bezold triad and nothing obvious to account for it is otosclerosis. This "triad" consists of: increased bone conduction, negative Rinne, and loss of low note perception. As the increased bone conduction is caused by the loss of low note perception, and as the "negative Rinne" is merely a quaint way of expressing this ratio, it is not very obvious why there should be this insistence on its being three signs instead of only one. At the best this "syndrome" can only be of diagnostic value in uncomplicated cases in which fixation of the stapes precedes any serious involvement of nerve or cochlea. Yet it is made to apply to cases in which otosclerosis is supposed to coexist, as well it may, with conditions known themselves to produce the Bezold "triad"—that is to say, middle-ear deafness or loss of low note perception.

There are certain other features of otosclerosis the diagnostic value of which I will briefly attempt to assess. It will be noticed that they may all be absent in otosclerosis, while, with very few exceptions, even their presence only becomes significant in the aggregate.

Other Diagnostic Features

The Family History.—At least half the cases are diagnosed in the absence of any family history. Unless it can be investigated, and this is rarely possible, even its presence must often be misleading.

Age of Onset.—Although the disease usually starts round about puberty, it may start at any other period. It has been found, and verified microscopically, in the seven-months foetus, to say nothing of intervening and later stages. Nager cites a case in which recent deafness in a man of 70 was diagnosed as otosclerosis. In the individual case, therefore, the time of onset can scarcely be of more assistance in diagnosis than the greater incidence in the female sex.

Course of the Disease.—Although the deafness in otosclerosis is progressive, it is not uniformly so. There may

be long periods during which it is stationary. There may even be short periods of apparent improvement. There cannot, therefore, be anything pathognomonic about the earlier part of its course.

The Tinnitus.—Typically this is high-pitched, continuous, and precedes the deafness. Often, however, it follows the latter and it may be completely absent. Tinnitus is, moreover, a frequent accompaniment of almost every condition which may affect the ear, from wax in the external meatus to Eustachian catarrh, and from anaemia to blood-pressure changes.

Paracusis Willisii (that is to say, ability to hear better in a noise).—The mechanism of this is not understood. It is certainly not pathognomonic of otosclerosis. It is often absent when this is diagnosed and is often present in other forms of deafness.

Diminished or Absent Secretion of Wax.—Many normal ears have no wax when examined. On the other hand, wax may be present in otosclerosis. Only a prolonged and elaborate investigation could satisfactorily determine that its rate of secretion was below the normal. Yet the reappearance of wax during treatment is frequently taken as an indication of the success of the latter.

Fixation of the Stapes.—It is generally admitted that there is no means of diagnosing this fixation during life, Gellé's test being quite unreliable. Yet Nager states that we can only diagnose otosclerosis in the presence of this fixation.

The Flamingo Flush on the Drum.—This is seen in less than a third of the cases diagnosed as otosclerosis. It is interpreted as the increased vascularity of the new bone in the otic capsule showing through the drum.

The diminished sensitiveness of the meatal skin and the absence of a "vasomotor response" to tactile stimulation of the drum are generally regarded as useless as aids to diagnosis.

There remains the radiological examination of the bony lesion in the otic capsule itself. Although this has been attempted, and plates published purporting to show the osteoporotic area, the general consensus of opinion is that this also gives no help.

Personal Equation of the Observer

After this analysis of the otosclerotic picture it will surprise no one to find that the proportion of deaf patients diagnosed as suffering from this disease differs greatly with different observers. In a series of over one thousand private cases J. A. Wright found only 7 per cent. This was also Bezold's figure. Nager finds 20 per cent. and Shambaugh 30 per cent. Nager suggests that these varying figures may be due to racial differences. This cannot apply to the Edinburgh series, in which Fraser's private ear cases gave 27 per cent. and the out-patient department of the Royal Infirmary just over 6 per cent. Fraser suggests that his private cases are a selected group owing to his well-known interest in this type of deafness. The alternative explanation this survey suggests is that the personal equation of the observer bulks largely in the uncertain diagnosis.

If this uncertainty exists in the uncomplicated case, what of those cases in which the disease is diagnosed in the presence of middle-ear changes known to produce the same functional disturbance? Gray in his monograph diagnoses even early otosclerosis in the presence of aural sepsis. Fraser admits the difficulty, but nevertheless regards aural sepsis as a predisposing factor. Lowndes Yates describes cases of subacute and recurring otitis media in which the graph of the deafness was identical with that usually postulated for otosclerosis. These cases were apparently treated by the intermittent suction of

pus from the Eustachian tube. It is not surprising to find that in at least one case the associated deafness increased with each recurring exacerbation of the sepsis. Yet Yates suggests that otosclerosis may be the terminal stage "of subacute otitis media in which the products of the inflammation are conveyed away by the Eustachian tube." It might well be suggested that any complications arising from this condition would be due to the Eustachian tube not "conveying away" in anything like an adequate manner. He adds that if the condition is more acute, and a perforation forms, the case is not regarded as otosclerosis, "though the impairment in hearing may be similar."

Diagnosis on Inadequate Data

This brings us to the consideration of the cases in which the deafness is accompanied by little in the way of objective signs of infection other than the retraction and fixation of the drum. The latter is, of course, the expression of the gradual scar fixation of the ossicles, including the stapes. The causal condition may be catarrhal involvement of the middle ear, or it may be a "latent" epitympanic or mastoid suppuration "drained by the Eustachian tube." Yet from the literature one would gather the impression that this progressive atrophy and scar contraction of the middle-ear contents—"if such a condition has any real pathological existence," to quote Dr. Gray—was itself regarded as otosclerosis. The frequent good hearing of the patient with a discharging ear and with drum and malleus destroyed is a commonplace. So also is the rapid onset of deafness after the radical mastoid operation. Apparently only the fact that it takes place in weeks instead of years prevents this also being diagnosed as otosclerosis. Of what use is it to maintain that the diagnosis is made on the Bezold syndrome when it is made in the presence of conditions which can themselves amply account for this "pathognomonic" syndrome?; when, moreover, it is assumed that the pathology permits the disease to appear as a pure nerve deafness? Nager, after emphasizing the Bezold syndrome—"Above all the tuning-fork tests"—says that he does not hesitate to diagnose otosclerosis in cases of progressive deafness in spite of pathological "residues" in the drum. He regards progressive deafness in such cases, without otosclerosis, as extremely rare. It would at least be more logical to admit that the only constant feature on which the diagnosis of otosclerosis is made is the existence of progressive deafness.

Treatments, New and Old

Were there a specific treatment for otosclerosis this desire to diagnose it on inadequate data would be explicable. It would not only be giving the patient the benefit of the doubt, but there would be the possibility of a therapeutic confirmation of the diagnosis. There is, however, no treatment known to affect the course of the disease. What, then, are we to say of the various forms of treatment so assiduously practised? Fraser gives a dismal list and asks why, when the general surgeon has given up trephining microcephalic skulls, we should not follow his lead and abandon methods of treatment that have proved useless? Others, including the unfortunate patients, may well ask the same question.

A treatment that has had its day rested on the wholly unwarrantable assumption that paracusis Willisii was pathognomonic of otosclerosis and that an atrophic drum was its cause. The patient started the treatment with the deafness of an acute myringitis and ended, if she was fortunate, with her original hearing. Throughout the treatment, however, she remembered only the steady improvement. The electrophonoide treatment of Zund-

Burguet is of more recent origin. It is said to work by "re-educating" the ear by minimal auditory stimuli. As one exponent of the method claims that it acts by producing a local hyperaemia, and another places the lesion in the cerebral cortex and regards it as due to intestinal toxæmia, the rationale of the method is a little difficult to grasp. It is, however, significant that the patient is warned that one or two years' treatment may be needed.

The Need for a Scientific Approach

At a discussion on this subject at the B.M.A. Meeting in Edinburgh in 1927, Dan McKenzie deplored the attitude of regarding all forms of treatment for otosclerosis as useless, and maintained that we should pass all therapeutic measures under strict scientific examination. Some hints of what members regarded as scientific methods emerged during the discussion. Guthrie, who had seen no conclusive results from the Zund-Burguet method, thought that the mental attitude of both doctor and patient entered very largely into the treatment. Another member of the Section, who said that he would rather lie under the false stigma of quack and charlatan than break his Hippocratic oath to do the best he could for his patients, admitted that in a considerable proportion of his cases treated by this method there was a functional element. Yet another member, after objecting to Jenkins' method of using the term "otosclerosis" so as to include, as he considered, other middle-ear conditions in addition to true otosclerosis, quoted the case of an "otosclerotic" lady who after a course of the Zund-Burguet treatment, had her hearing increased from five to forty-eight feet. "In view of such a case, and it was not unique," the member said he did not consider himself justified in abstaining from giving this treatment in otosclerosis. He then added that he believed the improvement in the case quoted to have been entirely functional! It is true that "you can perform any miracle if you only make a wrong diagnosis," but the miracle fails to impress when the absurdity of the diagnosis is thus flaunted in our faces. Are we out to compete with the faith cures of the revivalist meeting? Professor Nager, who, like Fraser and many others, had never seen any result from the Zund-Burguet method, touched upon another aspect of the question when he said that he had seen patients coming from the celebrated Coué who were convinced of very marked improvement, though the tuning-fork tests remained unchanged. There is probably no class of patient so ready to believe himself better when he is not than the deaf—perhaps a not unnatural result of the urgent wish. These cases and the hysterical *malade imaginaire* are the backbone and mainstay of such forms of treatment, each exponent presumably remaining "true to his oath" but not, apparently, obliged to pass his methods under "strict scientific examination."

Gray's treatment by the intratympanic injection of thyroxine was based on the assumption, as yet unproved, that this would produce a local increase in the circulation similar to the general increase seen after its internal administration. This improved local circulation was expected to produce an improvement in the hearing analogous to that seen in his "paradoxa" cases. Only fourteen cases were published, and of these seven were unaffected. In the remaining seven the improvement, though claimed by Gray as great, was well within the limits of variation seen in so many cases of deafness. Apparently no controls were used, and when in one case this was inadvertently present in that the untreated ear showed greater improvement than the one treated, Gray attributed this to a "crossed reflex." Although the treatment was claimed to be the rational outcome of the author's theory of the pathogenesis of otosclerosis, it was

described as a treatment for "allied types of deafness" also. These "allied types" appear to be "so-called chronic dry middle-ear catarrh—if such a condition has any real pathological existence." Indeed, a warning was uttered against attempting to differentiate between the two conditions, since it is apparently in the latter type that the greatest improvement was expected. Subsequent investigation has entirely failed to justify Gray's expectations.

Admittedly the problem of otosclerosis is a difficult one. It is not likely to be solved by doubtful diagnosis and still more doubtful observations on the results of treatment.

ESTIMATION OF THE COAGULATION TIME OF THE BLOOD: A SIMPLIFIED METHOD

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Numerous techniques for estimating the coagulation time of the blood have been devised during recent years, varying from elaborate procedures involving lengthy times of observation and the use of expensive apparatus to the simpler methods employed in the ordinary clinical laboratory. Since the estimation of the coagulation time of the blood is of great importance in the differential diagnosis of various haemorrhagic conditions there is no apology needed, it seems, for the introduction of yet another technique, the ease and simplicity of which serve as its own recommendation.

Apparatus Required

One glass tube drawn out into a capillary open at both ends is the only essential piece of apparatus. Gross variations in the size of the capillary bore are to be avoided, but the minor variations of capillary tubing drawn out in the ordinary laboratory do not influence the experiments significantly. A filter paper divided by pencil into segments from the centre is required for receiving the drops of blood expelled from the tube. An ordinary watch with a second hand attached can be used for marking the time intervals, but a stop-watch, if available, is more accurate and convenient.

Method

Blood is drawn up into the capillary tube by surface tension, and at minute intervals the end is placed in a slanting direction on to the segments of the filter paper. Before coagulation the drop of blood is absorbed into the filter paper. After an interval varying from five to nine minutes for normal bloods a tiny thread of fibrin stretches out from the filter paper to the end of the capillary tube. The appearance of this thread of fibrin is taken as the coagulation time of the blood in question, and there is no possibility of mistaking the appearance of the fibrin thread in practice, so that uniform results can easily be obtained on repetition.

Experimental Work

The modified method was tried out in comparison with the well-known standard Wright's capillary tube technique in twenty normal cases and in ten pathological ones. The advantage of the newer method is obvious here in that only one capillary tube is needed instead of the ten or twelve tubes used for Wright's technique.

In the first six of the normal cases variations at three temperatures were observed, and comparison of venous