atrium. A convenient external reference point for this in a supine patient is the mid axillary point. This level was presumably used by A. E. Baue, whose review we quoted. Some prefer to use the sternal angle as a reference level, in which case the recorded pressures will, of course, be lower. Since the usefulness of C.V.P. measurements is not in their absolute values but in changes of C.V.P. that take place it is of little importance which reference point is chosen, provided the same point is used consistently.—Ed., *B.M.J.*

Mild Ulcerative Colitis

SIR,—Some aspects of the management of the ulcerative colitis (or procto-colitis, as Avery Jones *et al.*¹ would prefer to describe the condition, so as to include the milder forms without mucosal ulceration, or those proved only by microscopical features) seem conflicting to me and need clarification.

Firstly, it has been claimed that the success rate of medical treatment in mild ulcerative colitis is about 90%.² The "success" is defined as control of acute attacks and keeping the disease in prolonged remission and/or aborting further exacerbation as quickly as possible. Although the value of steroids (systemically and/or as retention enemas) is undoubted in the treatment of acute attacks, their long-term use to prevent relapses has been disappointing. Salazopyrine, on the other hand, has been proved to be the only drug which can prolong remission³ and, therefore, is the mainstay of medical treatment. However, it is known that a substantial number of patients cannot tolerate this drug because of reactions, the most important of which is hypersensitiveness to sulpha or aspirin or to both components.

Here comes the important question. Are we to accept the exclusion of this group of salazopyrine-hypersensitive patients from the medically treated ones, although they belong to the "mild" group, and hence should escape radical surgical treatment? Or could it be possible to desensitize these patients and continue medical treatment effectively? This led me to find out that N. Svartz⁴ made limited trials of desensitization. Her method was to start with quarter of a 0.5 g. tablet two or three times daily for a period of 8-10 days and then gradually build up the dosage. However, it succeeded only in a comparatively few cases. J. Arnold Bagen⁵ is said to have come across no individual who could not tolerate the drug if given in a suitable dosage.

Secondly, if we do find that the mild colitic group of patients can be reasonably treated medically (perhaps with long remissions and fewer subacute exacerbations), are we justified in following such a course of management? What are the dangers of colitic cancers in this group? Brooke⁶ recently emphasized that this group is more at risk because radiological diagnosis of early lesions may not be made in a large number of cases, and surgical treatment will not be advised because of absence of severe complications or serious debility. He, therefore, advised total excision of the large bowel if total history of disease is 10 years and more, though in the future there may be a kind of

selection of patients for this radical procedure, dependent on finding precancerous changes in rectal biopsy specimens as claimed by Morson and Pang.⁷ His argument in favour of this line of treatment is an improved 5-year survival rate of 32% compared to 18.6%,⁸ presumably owing to early detection and improved management.

Thus, it seems to me there exists a fundamental difference of opinion and experience as to the management of the mild colitis group of patients. On the one hand we are led to believe that this group of patients has the best prognosis with a medical regimen and presumably the best chance of escaping surgery. On the other hand, in the event of precancerous changes in rectal biopsy not being universally present, this is the very group which is most at risk and better dealt with by surgery as early as possible.—I am, etc.,

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Thalassaemia Genes

SIR,—I have read with much interest the attractive hypothesis of two α -polypeptide chain loci for human haemoglobin posed for debate by Professor H. Lehmann and Dr. R. W. Carrell (21 December, 1968, p. 748). This would explain the variability of α thalassaemia syndromes, since they may result from one to four α thalassaemia genes. It is also suggested that haemoglobin H disease, at least in a proportion of the patients, arises from three α thalassaemia genes, and hydrops foetalis from four such genes.

We have proposed that there are at least two α thalassaemia alleles;¹⁻³ the classical one is α thalassaemia₁ and the milder form is α thalassaemia₂. The former leads to complete and the latter to partial inhibition of α chain synthesis. Haemoglobin H disease results from double heterozygosity between the two types of α thalassaemia. Homozygosity for α thalassaemia₁ leads to lethal hydrops foetalis with haemoglobin Barts. According to the hypothesis of Professor Lehmann and Dr. Carrell, it may well be argued that what is apparent as α thalassaemia₁ is really a result of two α thalassaemia genes, and α thalassaemia₂ represents one α thalassaemia gene. The finding¹ that the ratio of persons with haemoglobin H disease among sibs is $\frac{1}{4}$ and not $\frac{1}{2}$ indicates that the hypothetical two α thal-

assaemia loci are not independent. If the two α chain loci are closely linked and their products are identical, they would behave and be known as one gene. We are then left in an ugly position, not able to prove or disprove the hypothesis.

Patients with α thalassaemia/haemoglobin Q disease have the major haemoglobin types of Q and H without haemoglobin A.⁴⁻⁷ Haemoglobin Q is an α chain variant. If there is only one α chain locus the α thalassaemia gene—presumably α thalassaemia₁—completely suppresses the α -gene on one chromosome and the α^Q gene occupies the allelic position on the other chromosome. There is no room for α^A synthesis and haemoglobin A is thus absent in α thalassaemia/haemoglobin Q disease. On the other hand, if there are two α chain loci two positions are supposedly occupied by α thalassaemia genes, one by haemoglobin Q gene and the other by a normal gene. In this circumstance haemoglobin A should be synthesized in about a quarter of the normal value. The absence of haemoglobin A in this condition is not in favour of the concept of two α chain loci. However, the lack of haemoglobin A should be further substantiated; also it must be ruled out that there is no α thalassaemia gene adjacent to that of haemoglobin Q.—I am, etc.,

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Glue Ear

SIR,—Your leading article on glue ear (6 December, p. 578) was timely and highlighted one of the major difficulties encountered in this disease, that of accurate diagnosis. The relationship between hearing loss and the presence of fluid behind the tympanic membrane is not always great, and repeated studies¹ have shown that children with glue ear may pass school screening tests for hearing loss. As your leading article states, "at an early stage the membrane may have an almost normal appearance," and to the untrained eye the membrane may seem entirely normal. I was therefore surprised you did not mention impedance audiometry as a rapid and accurate method of establishing the diagnosis. By use of the electro-acoustic impedance bridge it is possible to measure accurately and simply both the state of the middle-ear conducting mechanism and the middle-ear pressure. The bridge very reliably differentiates between an ear with fluid in it and a normal ear in the presence of an intact tympanic membrane. Children tolerate the instrument well,

and the responses are objective. It has been used in school screening programmes in the United Kingdom and the results reported by Brooks.² Extensive use in Scandinavia, and my own experience, confirms the value of the instrument, the use of which obviates the need for a diagnostic, as opposed to a therapeutic, myringotomy.

The advice to prescribe a hearing-aid in cases where repeated myringotomy is required is good only as long as the patient is carefully followed. In the presence of chronic glue ear permanent damage may occur to the tympanic membrane, particularly in its posterior segment, which becomes thin, loses its middle layer, and becomes flabby. This may eventually be indriven into the sinus tympani and to the mastoid air cells, forming a cholesteatoma. Indeed, this is one of the commoner pathogenetic mechanisms of a cholesteatoma at present. Only a small proportion of children are so involved, but any child with an abnormally thin tympanic membrane should be vigorously treated and observed until complete resolution occurs. Even though this may take several years, it is not safe to discharge these children with a hearing-aid.—I am, etc.,

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SIR,—Having read your leading article on "Glue Ear" (6 December, p. 578), I am frankly amazed at the last paragraph, which must be absolute medical heresy. I am quite sure that every otolaryngologist would continue to insert Teflon tubes as long as they are required. If this is not done, a grave risk of chronic adhesive otitis is incurred, with possible or probable permanent deafness. To even suggest a hearing-aid for a form of deafness that is remediable by a simple surgical procedure is absolutely absurd, apart from the just-mentioned possible sequelae.

The exact cause of chronic seromucinous otitis is certainly not known, but many of these cases are certainly cured by an adequate adenoidectomy. I would certainly question your statement "nor has the removal of the adenoids been shown to prevent or mitigate glue ear." I think the possible allergic aetiology of this condition has been somewhat overemphasized, but a possible focus of infection in the paranasal sinuses should always be sought. I agree with your statement that the tendency to this type of otitis seems to decrease as these children grow older, and the long-term outlook for their hearing, in my experience, is very good as long as the middle ears are kept normal by artificially aerating them with some form of Teflon tube. It is in the adult patient that permanent malfunction of the Eustachian tube can be a problem, and in these cases I have no hesitation in keeping

these Teflon tubes in place permanently. This is a small price to pay for normal hearing, and the patient can lead a perfectly normal life apart from his inability to swim. It has to be admitted, however, that these Teflon tubes are not curing the basic malfunction of the Eustachian tube, but neither does an artificial stapes have any effect on the underlying pathology of otosclerosis. I really feel that the final paragraph of your leading article is appalling, and I am very worried that some general practitioners and paediatricians might accept your advice and fail to refer these patients to an otolaryngologist for the appropriate therapy.

One final point—a pneumatic otoscope is essential for the diagnosis of these cases, and any general practitioner can be taught to use it in a matter of minutes.—I am, etc.,

JOHN KEOHANE.

Edmonton,

SIR,—I read Mr. F. Bauer's letter on this subject (10 January, p. 111) with great interest, and I agree with him that there is some value in using mucolytics and considerable value in attempting to inflate the middle ear by Valsalva's procedure or by others methods. There is indeed uncertainty about all forms of non-inflammatory otitis media because they are often difficult conditions to treat, but, having investigated Eustachian tubal function in a large number of children and adults during the past five years, I have found that one of the most constant factors is that they all show some degree of tubal malfunction.

The Eustachian tube is not a simple pipe; the membranous tube is a physiological mechanism with muscular control which must open actively to allow air to pass up to the middle ear. Its anatomy changes throughout childhood, becoming more efficient with age. The cartilage changes in shape and position, the two important muscles alter in their relationship to the tube, and the mucous glands diminish in number and size during childhood. These anatomical facts account in part for the age incidence of glue ear and serous otitis, conditions which I have found not to be so distinct as has been implied. I am sure that tubal malfunction is only one factor in their development, but in my opinion your leading article (6 December, p. 578) understated the importance of the tube rather than the reverse.

In many cases the adenoids are only of moderate size. I do not think that size is very significant; small infected adenoids may cause lymphatic obstruction leading to swelling in the peritubal tissues, thus making it more difficult for the relatively inefficient childhood tube to open. I have found that adenoidectomy in these cases is of real value. If we look on the Eustachian tube as a passive pipe in good order, provided that air can be forced through and provided that adenoids are not actually blocking the nasopharyngeal opening like a cork in a bottle, then treatment with grommets may seem unreasonable. If, however, we accept that tubal malfunction is an important cause of these conditions, then grommets are a logical and relatively harmless method of allowing

the equalization of middle-ear air pressure acting as temporary artificial Eustachian tubes and allowing time for the real tube to resume its normal activity.

Like Mr. Bauer, I hope that very few of these children would have to be considered for hearing-aids.—I am, etc.,

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Treating Preinfected Wounds

SIR,—With reference to the letter of Mr. J. W. S. Rickett and Mr. B. T. Jackson, (3 January, p. 48) we would like to ensure that no misunderstanding arises from the quotation of our paper on the same subject.

We agree completely with the criticism in your correspondence (15 November, p. 428, 22 November, p. 493) of their double blind trial using lactose as a placebo which was associated with an infection rate of 26% (5 cases from 19) where the appendix removed was normal. In our trial in the cases where the appendix removed was normal there was no wound infection (judged on the same criteria for sepsis), whether ampicillin was instilled into the wound or not. Because the presence of lactose in a pre-infected wound may cause an increase in the incidence of infection, we decided at the outset against a double blind procedure, and these results appear to justify our decision.

Although our results were analyzed in rather more detail than the above mentioned paper, our conclusions were broadly similar if a little more specific. Our paper is to be published in the *British Journal of Clinical Practice* in the near future.—We are, etc.,

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Vagotomy for Peptic Ulcer

SIR,—Vagotomy for peptic ulcer is becoming increasingly popular but there is an appallingly high incidence of incomplete vagotomy,^{1,2} which means failure to cure the ulcer diathesis. In his contribution to this problem, Lee³ has developed a stain (leuco-methylene blue) which is claimed to aid identification of smaller vagal fibres by staining them selectively at operation. We have been using this stain recently and shall publish full details later. Meanwhile, our findings are disappointing. We feel it is important to report the main results because the stain is conceptually attractive but it does not seem to work.

After dividing the obvious nerve trunks at operation, we applied the stain and removed stained structures for histological examination. In a consecutive series of 30 structures from 10 patients, 21 contained no nerve tissue at all, one contained an appreciable amount of nerve tissue, and the remainder contained connective tissue with an occasional isolated nerve fibre so minute as to be invisible to the naked eye.

We therefore found that the stain did not pick out nerve fibres selectively. In these