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,