SULPHONAMIDE IN THE TREATMENT OF ACUTE MASTOIDITIS

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We feel diffident in making claims for a preparation which, by reason of its initial success, may have had an inflated popularity, but the results given below seem to be striking enough to warrant publication. The inconclusiveness of first results is well known, and these figures are published in the hope that further investigation and use of the drug by others will lead to its acceptance as a most useful prophylactic during the course of the all-too-common otitis media. The method of administration which has been carried out at the Royal Naval Hospital, Chatham, during the past year has been as follows:

All cases of acute suppurative otitis media (A.S.O.M.) were placed on "colsulanyde" (Crookes's), 1 drachm four-hourly by mouth, *as soon as they were admitted*. In addition they received the treatment of the acute ear which has been accepted practice for generations—namely: myringotomy, if the tympanic membrane was showing evidence of retention of pus, whether perforated or not; syringing of the ear thrice daily with saline or a solution of boric acid, followed by drops, those mostly used being gutt. hydrarg. nit. dil., gutt. acid. boric. in spirit, gutt. glyc. acid. carbol., and where the tympanic membrane was inflamed, intact, but not bulging, "sedonan" or "otalgan"; constant inhalations of tinct. benzoin. co. and menthol, and attention to nasopharyngeal and sinus infection. They also had a smart sulphur-free purge on admission, and a sulphur-free analgesic, such as aspirin.

During the year following the introduction of this routine the ratio of acute mastoiditis to acute otitis media has been greatly reduced, *in this series from 22.7 per cent. to 4.5 per cent.* That the accuracy of these figures is open to question is beyond doubt, for many different factors come into play in assessing results of this kind. The possible causes of error will be discussed later. The figures were obtained from the statistical returns of the hospital, and the average for the years 1934, 1935, 1936, and the early half of 1937, when sulphonamide was not being used, is compared with the year comprising the latter half of 1937 and the early half of 1938, when the above routine was employed. The figures for "acute mastoiditis" are those cases which were actually operated upon, and which were therefore surgically proven.

	A.S.O.M.	Acute Mastoiditis
1934	245	41
1935	177	33
1936	152	58
1937 (first half)	33	6
Total	607	138

Percentage of cases of acute suppurative otitis media to develop acute mastoiditis, 22.7.

	A.S.O.M.	Acute Mastoiditis
1937 (second half)	69	2
1938 (first half)	86	5
Total	155	7

Percentage of cases of acute suppurative otitis media to develop acute mastoiditis (sulphonamide used), 4.5.

Furthermore, during the period January, 1934, to June, 1937, the number of deaths per annum from the complica-

tions of acute suppurative otitis media averaged 2.85, while during the period June, 1937, to June, 1938, there were no deaths from this cause.

No claims are made in regard to the efficacy or otherwise of the drug in the treatment of otitis media *per se* (this side of the question is still under investigation), but the figures are consistent with the view that it is a preventive of the complications of this disease. Secondly, it is not claimed that every case of otitis media was streptococcal in origin, for not all of them were swabbed. All those in which swabs were taken proved to be due to a haemolytic streptococcus, and during the past winter and spring there has been, in the district from which these cases came, almost a streptococcal epidemic, comprising tonsillitis, scarlet fever (which has been very severe), etc.

The incidence during the years 1934 to 1937 (first half) may seem to be unduly high. However, the Royal Naval Hospital at Chatham draws its patients largely from establishments where a great number of individuals are massed together, and especially from those training establishments in which a large number of boys of the ages of 16 and 17 are accommodated. In this environment it is possible that an infecting organism may rapidly reach a high state of virulence, passing as it does through a large number of individuals of the age (at the boys' training establishments) when mastoiditis is most common and, in the case of the newly joined, finding an easy and non-resistant prey, often equipped with predisposing conditions such as massive pads of adenoids. The same treatment was adopted for any case of scarlet fever which developed otitis media, and these have been shown among the "A.S.O.M." section. Only one of these patients developed acute mastoiditis.

From the above it will be seen that the sulphonamide was used in a purely "shotgun" manner, and it is contended that the results justify its use, for, even if the otitis does not respond to the treatment and mastoiditis develops, no harm has been done and the patient's resistance is in no way impaired by the drug. In no case was the administration of sulphonamide prolonged for more than fourteen days, as it was considered that by the end of this time any good which would accrue from this mode of treatment had already been done, and, conversely, if the drug had failed, then no good purpose was being served by its continuance.

Chronic otitis media has not been considered in the above group of patients, the vast majority of whom had no previous record of otitis media.

Points Noted during the Series

In a small minority of cases colsulanyde, 1 drachm four-hourly, caused in the course of a few days a noticeable cyanosis, though no subjective symptoms were complained of by the patients. In these cases the sulphonamide was stopped for a few days and then begun again on a dosage of 1 drachm thrice daily. None of them showed any evidence of a true sulphaemoglobinaemia when tested spectroscopically, and Long and Bliss (1937) mention that they were not convinced of the existence of this condition.

A leucocyte count was performed as a routine on admission, and the tendency appeared to be for this count to drop after a few days' treatment, especially in those cases which already had a raised white count on admission, and a slight relative lymphocytosis appeared to be the rule. There was, however, little change in the blood picture relevant to otitis media, and this subject (the changes in the blood picture during sulphonamide treatment) is under investigation by Surgeon Commander McIntyre, to whom we are indebted for his co-operation.

The patients were not placed on a sulphur-free diet, as has been recommended by some, though sulphur-containing drugs were avoided in the concomitant treatment.

Discussion of the Results

It will be at once apparent that the percentages given above for the fall in mastoid incidence are open to question as regards their absolute accuracy. The seasonal and yearly incidence of mastoiditis varies widely and is naturally worse in an epidemic year, but it is claimed that, so far as Chatham is concerned, the last twelve months have included an epidemic. This, then, may be taken, if not as an error on the right side, at least to cancel out, more especially as the streptococcus had been active in many parts of the country during the early spring of this year.

Another cause of error which weights the scales in favour of the drug is the tendency of the surgeon, striving to show results such as these, to adopt a more expectant line of treatment of mastoiditis than he has formerly been accustomed to carry out. While the existence of the "doubtful" mastoid is undeniably common, there are a large number of cases which anyone would be forced to diagnose as acute mastoiditis, and even the most expectant treatment would not be able to reduce the mastoid ratio to the extent given above without an increase in the fatalities. Nor was the drug found to produce a "false cure," as Anwyl-Davies (1937) alleges it to do in gonorrhoea, though this side of the question is still under investigation and to be proved conclusively will need figures taken over more than one year.

It is reasonable, too, to assume that sulphonamide would have a beneficial effect on the course of acute streptococcal mastoiditis, because this drug is known now to be specific for the organism. The figures already published, from the original ones of Colebrook and Kenny to the most recent, all show that the virulence of the organism to the human body is reduced; and since in the type of mastoiditis under review the virulence seems to be a big determining factor in the infection or escape of the mastoid process, the results might almost have been forecast, though it is gratifying to see them work out in practice.

What, in our opinion, is of the utmost importance is the early administration of the drug at a time when there is no question of mastoid infection. Probably pus is present in the mastoid antrum in many cases of otitis media, but this is still confined within a layer of mucous membrane. It is asking too much of any non-surgical measure to effect a cure after this membrane has broken down and there is already osteitis of the mastoid process, though Montandon (1937) reports two cases in which sulphonamide was given as a premedication before mastoidectomy and the condition settled without the need for operation.

It seems plausible to imagine that the sulphonamide reduces the streptococcus in the middle ear to a virulence low enough to enable the antrum to shut itself off by granulations (which it undoubtedly does in middle-ear infections of a low virulence), and thus guards against the all-too-common type of case where very acute mastoiditis develops within a few days of the onset of the otitis media. None of the seven cases operated upon during the second half of 1937 and the first half of 1938 were of this type; they were all operated upon because of a persistence of the discharge, coupled with a low pyrexia, slight mastoid tenderness, and a high leucocyte count. Sulphonamide in these cases appeared to have failed; this is a well-known phenomenon, and one for which no explanation is offered.

In all cases the mastoid cells were found to be hopelessly involved.

In fact, since the adoption of this line of treatment the classical "acute mastoid" has become a rarity in the hospital.

Conclusions

In spite of the possible sources of error in the figures published above, the incidence of acute mastoiditis in the Royal Naval Hospital, Chatham, has been notably reduced. Since the only difference in the accepted treatment of the acute ear has been the introduction of routine administration of sulphonamide *on admission*, it is reasonable to suppose that the aforementioned drop in mastoiditis is due to the drug. Therefore the sulphonamide group of drugs have a very real place in the treatment of acute suppurative otitis media.

We would like to express our indebtedness to Surgeon Rear-Admiral Dudley for his invaluable assistance in compiling these results.

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Clinical Memoranda

The Use of Prontosil in Sprue

As early as 1914 I recorded two cases of sprue, with prominent soreness of the mouth, in which lasting benefit followed the use of autogenous streptococcal vaccines prepared from cultures from the sore tongue. In 1918 I published seventeen further cases, and suggested that oral streptococcal infection might play a part in the aetiology of sprue, even if it is only a secondary infection. Later in that year Dr. Lucius Nicholls confirmed my observations regarding the beneficial effects of autogenous oral streptococcal vaccines in sprue, and pointed out that his cultures belonged to the non-haemolytic *Streptococcus viridans* type. In 1920 I reported on forty-four cases of sprue treated in Calcutta by the vaccines, in addition to milk diet and drugs for controlling the looseness of the bowels, and compared the results with those in forty-five cases that I had analysed from the earlier Calcutta European Hospital records (Rogers, 1921). In the old series, which were probably more severe on the whole than the vaccine series, there were no recoveries while in hospital, and only five cases had greatly improved. In the vaccine series twenty-one had recovered, eighteen of them remaining well for upwards of one year, and thirteen, mostly more recent cases, had greatly improved. In six other cases relapses occurred. Later I obtained good results with the vaccines in clearing up the symptoms of sore mouth, followed by much gain in weight with cessation of the diarrhoea, in patients treated at the Hospital for Tropical Diseases, London; but it is difficult to assess the relative influence of diet and vaccines respectively.

A recent experience leads me to return to the subject. During the last five years I have from time to time attended for sprue a retired Indian tea-planter living in the country and now over 80 years of age. Since he moved to Southwold I had not seen him, until recently Dr. E. C. Cordeaux reported to me that his condition had become serious, being complicated by a fall of haemoglobin to 48 per cent., and by febrile bronchitis. On August 2, 1938, I saw the