In several patients with congestive heart failure the symptoms were slight and the presence of pulmonary infarction was overlooked. In post-operative and puerperal patients the condition was often misdiagnosed as pleurisy, pulmonary collapse, or pneumonia.

The importance of paying serious attention to every case of femoral thrombosis and pulmonary embolism is reiterated, and measures of prophylaxis and therapy are briefly discussed.

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DEAFNESS WITH USE OF DIHYDROSTREPTOMYCIN IN TUBERCULOUS MENINGITIS

BY

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Attention has recently been drawn to the reduced success and increased deafness resulting from the use of dihydrostreptomycin instead of other forms of streptomycin in the treatment of tuberculous meningitis (Minkenhof, 1950; Biagi, 1951; Cathie and Garrow, 1951; Somner, 1951). My experience in Ayrshire Central Hospital, Irvine, and Belvidere Hospital, Glasgow, seems to confirm the latter finding, although the results, in terms of percentage recovery, have not been adversely affected. Deafness itself, however, is a most perplexing problem, especially since, in my experience, hearing-aids have been of no value to the patients developing it. Lip-reading tuition has been given during their stay in hospital and after dismissal, but this, of course, is a very poor substitute for normal hearing, although it does help them to enter into conversation.

For several months dihydrostreptomycin was suspected as being the cause of increased deafness complicating recovery from tuberculous meningitis—and indeed this was mentioned to representatives of Glaxo Laboratories, who have recently provided supplies of the calcium chloride complex to conduct a controlled

investigation on a series of new cases. Unfortunately the introduction of dihydrostreptomycin coincided with an intensification of intrathecal (but not intramuscular) streptomycin therapy, and the possibility that this may have been responsible for the increased incidence of deafness required to be first excluded. Accordingly, when this discovery of increased deafness was made in April of last year, the course of intrathecal streptomycin was reduced to one more closely resembling that previously used, the intramuscular regime being unaltered. It is too early to assess the ultimate results with this course. So far, it does not appear to have affected the recovery rate; but cases of deafness have already occurred. For comparison, this latter course is now being used, the calcium chloride complex being substituted for dihydrostreptomycin. It is hoped to publish later a report on the results.

The courses given and the results obtained are outlined below:

1. Results Prior to Use of Dihydrostreptomycin

The adult course in average cases extended over a period of six months, as follows:

Intramuscular Streptomycin	Intrathecal Streptomycin
2 g. daily in 2 doses for 3 months 1 g. daily for 1 month 1 g. on alternate days for 1 month 1 g. twice weekly for 2 weeks 1 g. weekly for 2 weeks	100 mg. daily for 2 weeks Rest for 1 week 100 mg. daily for 1 week 100 mg. on alternate days for 2 weeks 100 mg. weekly until end of 6 months

Of 26 patients treated, 13 died and 13 survived for periods varying from two to three and a half years. Only one of these became slightly deaf during treatment of a relapse. The deafness has not progressed.

2. Results Using Dihydrostreptomycin

A. *Intense Intrathecal Course.*—The adult course in average cases extended over a period of six months, as follows:

Intramuscular Dihydrostreptomycin	Intrathecal Dihydrostreptomycin
Exactly as above	100 mg. daily for 2 weeks 100 mg. on alternate days for 8 weeks 100 mg. weekly till end of 6 months
Para-aminosalicylic acid was given concurrently and for a further six months	

Of 51 patients treated 17 died and 34 survived for periods ranging from eight months to two years: 20 cases became deaf.

B. *Less Intense Intrathecal Course.*—The adult course in average cases extended over a period of six months as follows:

Intramuscular Dihydrostreptomycin	Intrathecal Dihydrostreptomycin
Exactly as above	100 mg. daily for 2 weeks 100 mg. on alternate days for 4 weeks 100 mg. weekly till end of 6 months
Para-aminosalicylic acid was given concurrently and for a further six months	

Fourteen patients received this course and were observed over a period varying from three and a half to seven months. So far, four have died. Of the survivors two are already becoming deaf.

Modification of Dosage for Children

Intrathecal.—In all series the intrathecal dosage was the same as for adults except in patients under 5 years of age, in whom the maximum intrathecal dose was 50 mg.

Intramuscular.—On the basis that 1 g. was given at each injection to adults, the quantity for children was reckoned as follows:

Aged 15 and over ..	1 g.
„ 10 to 14 ..	0.75 g.
„ 5 to 9 ..	0.5 g.
„ 0 to 4 ..	10 mg. per lb. (450 g.) body weight

Results

An analysis of the results obtained with these three courses is given in Table I.

TABLE I

Course Used	Total Cases	Alive	Dead	Deafness
1. Streptomycin ..	26	13 (50%)	13	1
2A. Dihydrostreptomycin ..	51	34 (67%)	17	20
2B. Dihydrostreptomycin	14	10	4	2

Incidence of Deafness

As the cases in group 2B have been under observation for only three and a half to seven months, it is not yet possible to discuss the incidence of deafness in this series. The following discussion therefore relates only to the 51 patients in the second series, of whom 20 (39.2%) became deaf. Three of these have subsequently died, so that 17 (50%) out of the 34 cases surviving are deaf. Of the 17 patients who died, 5 survived more than three months; thus 39 out of the 51 cases lived more than three months. The incidence of deafness in these 39 cases is 20 (51.3%). This figure is given, since the earliest time at which deafness has been noted is two to three months; 51.3% of patients surviving for this period became deaf.

Of the 20 cases of deafness, 12 were totally deaf, 6 were moderately deaf, and 2 had only slight impairment of hearing. No relationship could be found to the stage of disease and degree of illness when treatment was begun. The usual classification was adopted, and the cases were divided into three categories:—(1) Early: conscious, with only slight meningeal signs and no focal signs, but positive C.S.F. findings. (2) Intermediate: drowsy, with more marked meningeal signs and symptoms, and, possibly, focal signs. (3) Advanced: comatose or semi-comatose, with marked meningeal signs, and focal signs. Table II gives the incidence of deafness in these three groups

TABLE II

Stage of Disease	Total Cases	Dead	Alive	Surviving More Than 3 Months	
				No.	No. Deaf
Early ..	2	0	2	2	1 (50%)
Intermediate ..	33	7	26	28	14 (50%)
Advanced ..	16	10	6	9	5 (55.6%)

In all groups the proportion of deaf cases among those who survived long enough for deafness to occur is the same. Likewise, the incidence of deafness could not be correlated with the presence of miliary tubercles in the lungs, or of adult pulmonary tuberculosis, or with other known factors.

The earliest date of onset of deafness was three months from the beginning of treatment, the average time being five months. In a few cases deafness occurred after completion of treatment or during a second course. Although a small proportion of cases developed deafness when their condition was not progressing favourably, most patients appeared either to have fully recovered or to be steadily improving when their hearing began to be impaired. The following brief descriptions of cases treated in Belvidere Hospital, Glasgow, illustrate these findings.

Case Reports

Case 1.—A boy aged 15 was admitted on March 25, 1950, in a comatose state, on the ninth day of illness, with marked meningeal signs. During the first six weeks of treatment progress was slow, but thereafter he improved steadily and by the sixth month was very well, with no meningeal signs, a normal temperature, and C.S.F. returning to normal. During the sixth month he was noticed to be slightly deaf, and in the course of a few weeks the deafness became total. Otherwise he is perfectly well.

Case 2.—A boy aged 9 was admitted on April 17, 1950, with a history of headache and sickness for four days. He was drowsy and listless and had definite meningeal signs. He made a steady uninterrupted recovery, but, though clinically well at the end of six months, the C.S.F. still contained 61 lymphocytes per c.mm. and 100 mg. of protein per 100 ml. After a fortnight without treatment these findings increased and, despite nothing abnormal being found clinically, he was given a further course of treatment. In the fourth month of this course slight deafness developed. In a few weeks this became complete and has remained so. Otherwise he was well, the C.S.F. findings subsequently returning to normal. Deafness is still the only abnormality.

Case 3.—A girl aged 16 was admitted on April 22, 1950, the seventh day of illness, moderately ill with definite meningeal signs, miliary tubercles in the lungs, and choroidal tubercles, but quite bright mentally. She responded to treatment during the first 10 weeks, then her condition remained stationary. In the 14th week of treatment she had a convulsion and went into coma. Retention of urine developed, followed by incontinence and a spastic paresis of her legs, which later became flaccid. The course of dihydrostreptomycin was begun over again and she improved steadily, regaining control of her bladder and power of her legs. After a further 12 weeks, when she was progressing well, she complained of buzzing in her ears and was slightly deaf in the right ear. In six to eight weeks she was totally deaf in both ears but was very well, apart from stiffness of her knees, which required orthopaedic treatment. She is still well but remains totally deaf, although very proficient in lip-reading.

Case 4.—A boy aged 7 was admitted on May 21, 1950, the seventh day of illness. He was only mildly ill, a bit listless, and had slight neck stiffness and very slight left facial palsy. He made an excellent recovery with dihydrostreptomycin and at the end of six months appeared completely well, was up and about, and had no signs of disease and a normal C.S.F. Then he was noticed to be slightly deaf. In a few weeks' time he became totally deaf and has remained so, although perfectly fit otherwise.

Case 5.—A man aged 26 was admitted on October 21, 1950, after three weeks' illness. He was quite bright mentally but had marked meningeal signs. Tuberculin (P.P.D.) was given intrathecally during the first three months of treatment. C.S.F. protein was 460 mg. per 100 ml. on admission. Within a fortnight he had a fully developed spinal block, and intrathecal dihydrostreptomycin was then given by both lumbar and cisternal routes. While tuberculin was being given his condition appeared to be deteriorating and he had many reactions. By the end of the third month deafness was noticed, and in a few weeks was complete. After cessation of tuberculin his condition steadily improved and, apart from his deafness, he made an uninterrupted recovery.

Case 6.—A boy aged 13 was admitted on December 9, 1950, moderately ill, listless, and drowsy, with slight but definite meningeal signs. Tuberculin was given intrathecally for a month, during which his condition remained poor. After discontinuing tuberculin he made steady progress. At the end of the fourth month, when symptoms and signs had abated and his temperature had settled, he was noticed to be slightly deaf. Further recovery was uninterrupted, but deafness has become total.

Case 7.—A girl aged 11 was admitted on December 18, 1950, with a history of a week's illness. On admission she

was semi-comatose and delirious and had fairly marked meningeal signs. In two days she became completely comatose and did not recover full consciousness till after a month, by which time she had a right hemiparesis. Her progress thereafter was slow but steady. During the fourth month of treatment she became deaf: her deafness was moderate and never became complete. A month later her condition deteriorated, spinal block developed, and she died on May 2, 1951.

Case 8.—A man aged 24 was admitted on January 19, 1951, with bilateral pulmonary tuberculosis complicated by tuberculous meningitis. He was irrational and resentful and had marked meningeal signs. Pneumoperitoneum was induced to control the pulmonary tuberculosis, which appears to have healed. His progress was slow, but by the end of the fifth month signs and symptoms had subsided and his temperature had settled. Then he developed slight impairment of hearing, which has now become moderate. Otherwise he is fit, the chest having cleared and the C.S.F. returned to normal.

Conclusions

The results in this series contrast with those outlined by Cathie and Garrow (1951). Their results with dihydrostreptomycin were poorer than those obtained earlier. In the present series the recovery rate with dihydrostreptomycin was 67%, as compared with 50% prior to its use. Other factors, however, have probably contributed to the improvement in results—increasing knowledge and experience of streptomycin, concomitant administration of P.A.S., etc.—and it is doubtful whether any significance can be attached to it. It seems reasonable to deduce, however, that dihydrostreptomycin is at least as effective as other forms of streptomycin in the treatment of tuberculous meningitis.

The series confirms the findings of Cathie and Garrow and other workers in relation to deafness. In contrast with 1 case of deafness out of 13 survivors before the use of dihydrostreptomycin, 50% of survivors became deaf after using this drug. The occurrence of nerve deafness late in the course of treatment in most cases, when the patients appeared to have recovered from the disease and were normal in other respects, suggests that the deafness is unlikely to be caused by the meningitis, but that it is a toxic manifestation—apparently irreversible—of the drug used. It is true that in this series other factors may have contributed to the increased incidence of deafness with dihydrostreptomycin, especially the increased intrathecal dosage of the drug in the second group of cases, but there is enough evidence to warrant caution in using dihydrostreptomycin, and to indicate a controlled investigation of its advantages and disadvantages compared with other forms of streptomycin.

Summary

The results obtained in a series of 26 cases treated with streptomycin are compared with those in a series of 51 cases treated with dihydrostreptomycin. While the latter showed a 67% recovery rate as compared with 50% in the former, 50% of the survivors in the second series were deaf, whereas only 1 out of 13 survivors in the first series had impairment of hearing.

Some of the features of the deafness are stated, and brief descriptions are given of some illustrative cases.

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ADDENDUM.—Since this paper was submitted for publication one further case in Group 2A has developed slight deafness, and four more cases in Group 2B—making a total of six cases in this group—have become deaf. These facts confirm the conclusions already reached and stated above, and are in keeping with papers which have appeared more recently. It is hoped to incorporate these further results in a later publication.

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GROWTH OF BIPARIETAL DIAMETER OF FOETAL HEAD IN THE LAST WEEKS OF PREGNANCY

BY

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Those who favour the early induction of labour for the prevention of cephalo-pelvic disproportion base their practice on the beliefs that during the last weeks of pregnancy the foetal head becomes harder and larger. The second of these two beliefs has been questioned by Josephs (1949), who could not detect radiologically any increase in the biparietal diameter during the last four weeks of pregnancy. This paper is concerned with examining this rather surprising finding.

Methods.—Steel callipers (Fig. 1) fitted with a sprung platform so that measurements could be made under standard conditions of pressure were used to measure the biparietal diameter of infants' heads 48–96 hours after birth.

Results

The individual biparietal diameters of 1,059 infants were plotted against the respective durations of pregnancy as estimated from the first day of the last menstrual period of the mother. A statistical calculation was then made to delimit the area within which two-thirds of all these points fell. This area is represented by the shaded portion of Fig. 2, from which it can be seen that in general the greater the duration of pregnancy the greater the biparietal diameter of the head. In addi-

FIG. 1.—Sketch of callipers used in measuring the biparietal diameter of the head, showing the sprung platform.