at Lennox Castle Maternity Hospital, and Dr. R. A. Tennent at Bellshill Maternity Hospital (Table IV). These men,

TABLE IV.—“Trial Induction” (Premature Surgical Induction followed by Trial of Vaginal Delivery)

	No. of Cases Induced	Maternal Mortality	Foetal Mortality	Caesarean Section Rate
R. A. Tennent, Bellshill Maternity Hospital	121	Nil	1.7%	9.9%
R. J. Wotherspoon, Lennox Castle Maternity Hospital	43	„	Nil	21.0%

working quite independently, have, I think you will agree, produced results which compare favourably with any other method of delivery, and in so doing have avoided many caesarean section operations.

Conclusion

Caesarean section has, in the last 15 years, become a boon. Let us avoid the pitfalls of the past and let us prevent this operation from falling into disrepute and becoming the first resort of the lazy obstetrician, the escape of the timid obstetrician, and the cloak of the incompetent. Let us use it wisely without holding it like the sword of Damocles over the head or body of the mother, whose only fault is that her pelvis lacks by a centimetre or so the proportions which would normally ensure natural childbirth.

Summary

Changes which have occurred during the last fifty years in the methods of managing labour in patients with contracted pelvis are outlined. It is shown that the destructive operation has now almost disappeared and that classical caesarean section has been largely superseded by the lower segment operation.

Reference is made to the alteration in the severity of contracted pelvis during the last fifty years, and the importance of the rachitic factor in the production of present-day pelvic contraction is mentioned. The role of the minor degrees of pelvic contraction as a cause of dystocia in labour is emphasized.

The tendency towards an ever-increasing elective caesarean section rate is fully discussed and criticized, and an attempt has been made to justify the use of trial of induction of premature labour in specially selected cases.

Where there is a minor degree of pelvic contraction premature surgical induction may initiate labour at a point where disproportion is minimal or non-existent.

REFERENCES

- Caldwell, W. E., and Moloy, H. C. (1933). *Amer. J. Obstet. Gynec.* 26, 479.
 D'Esopo, D. A. (1949). *Ibid.*, 58, 1120.
 — (1950). *Ibid.*, 59, 77.
 Hewitt, J. (1950). Presidential Address to Glasgow Obstetrical Society.
 Ince, J. G. H. (1939). *J. Obstet. Gynaec. Brit. Emp.*, 46, 1003.
 Johnstone, R. W. (1952). *William Smellie*, 1st ed., p. 106. Livingstone, Edinburgh.
 MacLennan, H. R. (1944). *J. Obstet. Gynaec. Brit. Emp.*, 51, 293.
 — Hay, A. B., and Paterson, M. L. (1953). *Lancet*, 2, 19.
 Marshall, C. M. (1949). In *Trans. 12th Brit. Congr. Obstet. Gynaec.*, p. 19. London.
 Thoms, H. (1935). *The Obstetric Pelvis*. Williams and Wilkins, Baltimore.

An annotated bibliography on *Pulmonary Fibrosis in Soft Coal Miners* has been published by the U.S. Public Health Service. The annotations, 83 in number, cover papers published from 1834 to 1953, and reveal the comprehensive studies which have been made of this condition in Britain and the U.S.A. The bibliography (Public Health Bibliography Series No. 11) is obtainable from the Superintendent of Documents, Government Printing Office, Washington, price 25 cents.

STREPTOMYCIN AND ISONIAZID IN ACUTE MILIARY TUBERCULOSIS

BY

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The present investigation consists of two series of patients suffering from acute miliary tuberculosis uncomplicated by meningitis at the beginning of treatment. The first group (series A) comprises 24 patients admitted to hospital during the period August, 1948, to June, 1951, and treated with streptomycin. All have been followed up for a period of two or more years. The second group (series B) comprises 12 cases treated with isoniazid, or isoniazid in combination with streptomycin or with streptomycin and P.A.S. These patients were admitted to hospital during the period April, 1952, to February, 1953.

The diagnosis of miliary tuberculosis was made primarily on radiological grounds; in 20 cases in series A, and in all cases in series B, additional confirmation was obtained from sputum examination and gastric lavage and by the presence of choroidal tubercles. Radiographs of the chest were taken at monthly intervals during the patient's stay in hospital, and at three- to six-monthly periods following dismissal.

The purpose of the investigation is to relate our experience of acute miliary tuberculosis treated with streptomycin and with isoniazid and to consider whether the use of isoniazid holds promise of advantage. It is realized that the investigation has the disadvantage that the patients in the two studies were not treated contemporaneously, and, further, that the smaller number of cases, plus the shorter follow-up period, in series B does not permit comparable therapeutic inferences. Nevertheless the difference between the two series in respect of the incidence of meningitis, despite the small number of cases involved, prompts us to publish our results.

Series A—Streptomycin

Adult patients admitted during the period 1948–50 were given 2 g. of streptomycin daily; for subsequent admissions this dosage was reduced by half. Patients under 15 years were given a dose of 20 mg. of streptomycin per lb. (44 mg. per kg.) body weight daily. Treatment was continued for four months or more.

With the exception of three patients admitted during 1948–9, all received sodium P.A.S. in addition to streptomycin. Adult patients were given 15 g. of sodium P.A.S. daily; the dose for patients under the age of 15 years was 0.25 g. per kg. body weight daily.

The figures in Table I show the fatality in age groups and illustrate the poor prognosis in children compared with a more favourable outcome in older patients. The death rate in the age group 0–3 years is 45.4% (5 out of 11), in contrast to 7.7% (1 out of 13) over the age of 3 years.

Table II shows the incidence of a complicating tuberculous meningitis in the 24 treated patients. Eight patients (33.3%) developed tuberculous meningitis, and of these 3 died, 2 of them being in the age group 0–3 years. In all cases the complication supervened during the course of

TABLE I.—*Age and Fatality*

Age Group (Years)	Alive	Dead	Total
0-3	6	5	11
4-15	7	1	8
16-25	4	—	4
26+	1	—	1
Total	18	6	24

TABLE II.—*Incidence of Tuberculous Meningitis: Series A*

Age Group (Years)	Alive	Dead	Total	Total Cases
0-3	2	2	4	11
4-15	1	—	1	7
16-25	2	1	3	5
26+	—	—	—	1
Total	5	3	8	24

streptomycin therapy. It will be seen that meningeal involvement occurred in one-third of the 24 patients and was responsible for 50% of the total deaths (see Table I).

The figures in Table III indicate that the time taken for the lungs to show complete clearance of miliary opacities is somewhat similar for all age groups in the 13 patients who recovered and who did not develop meningitis. The term

TABLE III.—*Radiological Progress in Uncomplicated Recoveries*

Age Group (Years)	Interval from Diagnosis to Clearing (Weeks)	Total
0-3	26 (12-36)	4
4-15	18.5 (8-28)	6
16-25	18 (12-24)	2
26+	16	1
	Mean 20.5	13

Figures in parentheses denote minimum and maximum values.

"uncomplicated" used in the title of this Table refers to meningitis and does not take account of other complications of miliary tuberculosis (see Table V). For the purposes of comparison the value 20.5 is regarded as the average time in weeks necessary for complete radiological clearing in uncomplicated recoveries.

In Table IV are analysed the eight cases complicated by meningitis. The shortest period of time for meningitis to develop from the diagnosis of miliary tuberculosis was four weeks (Cases 5 and 7); the longest period was six months (Cases 6 and 8). All cases occurred during the course of streptomycin therapy and within a period of six months of its inception. The average time of onset of meningitis was 14.8 weeks.

Table IV also shows the interval of time between diagnosis of miliary tuberculosis and complete radiological clearing of the lung lesions in those cases complicated by meningitis. In Case 3 calcified foci were seen after a follow-up

TABLE IV.—*Analysis of Cases Complicated by Meningitis*

Case No.	Age (Years)	Onset T. B. M. (Weeks)	Period of Observation (Years)	Interval from Diagnosis to Clearing (Weeks)	
				Recovery	Death
1	8; 12	12	2	10	Lungs I.S.Q.
2	11; 12	12	3 1/2	Calcified lesions in lungs	
3	2	20	2		
4	3	19	9 1/2	16	27
5	9	4	2		
6	17	24	2		
7	22	4	6 1/2	20	16
8	25	24	2		
				32	
	Mean 14.8			Mean 20.16	

period of two years. Analysis of the remaining seven patients reveals that in all cases of meningitis which survived more than six months radiological clearing took place in a minimum period of 10 weeks (Case 1) to a maximum period of 32 weeks (Case 8). The average time of clearing was 20.16 weeks, which is similar to the value of 20.5 weeks in the uncomplicated recoveries (Table III). (The figures are

in agreement with those in the report of the Medical Research Council (1950) and support the view expressed in that report that clearing of miliary opacities in the lungs is no guide to prognosis.)

In Table V are enumerated complications occurring in patients in whom meningitis did not develop. Of the three fatal cases, all were under the age of 3 years. All died

TABLE V.—*Complications in Non-meningitis Cases*

Age (Years)	Complication	Result
1	Tuberculous abscess of chest wall	Recovered
1	Fulminating infection	Died
1	Tuberculous bronchial pneumonia	"
2	Tuberculous peritonitis	"
10	Renal tuberculosis	Recovered

within three months of the beginning of treatment; one, a baby of 1 year with a fulminating infection, died 48 hours after admission to hospital.

The three patients who did not receive P.A.S. were under the age of 2 years. One made an uneventful recovery, one died of tuberculous meningitis (Case 2, Table IV), and one died from a fulminating tuberculous infection 48 hours after the starting of treatment (Table V).

Series B

The 12 patients in this series were treated with isoniazid, or with isoniazid, streptomycin, and P.A.S., or with isoniazid and streptomycin. Patients who received P.A.S. were all over the age of 10 years and were given 15 g. of the sodium salt daily.

Six of the patients were given isoniazid alone in a daily dosage of 8 mg. per kg. in four cases, and 6 mg. per kg. in two cases. The duration of treatment was 18 weeks in four cases, 14 weeks in one case, and 24 weeks in one case. The chest x-ray films of one of these patients showed a focus of tuberculosis in addition to the miliary lesions; consequently, two months after the initial isoniazid therapy was completed, a further course of treatment—isoniazid, 8 mg. per kg. twice a week, and streptomycin, 1 g. twice a week on the same days as isoniazid, plus P.A.S. 15 g. daily—was instituted and continued for 18 weeks.

Two cases were treated with isoniazid 8 mg. per kg. daily, streptomycin 1 g. daily, and P.A.S. 15 g. daily. One of these received this treatment for 10 weeks, this being repeated for a further 12 weeks except that 1 g. of streptomycin was given twice a week instead of daily. The other was under the regime for 12 weeks, and then, owing to the development of sensitivity to streptomycin and P.A.S., isoniazid, 8 mg. per kg. daily, was given alone for a further 16 weeks. Two cases were treated with isoniazid 8 mg. per kg. daily, streptomycin 1 g. twice a week, and P.A.S. 15 g. daily; the duration of treatment was 28 weeks in each case. One case was treated with isoniazid 8 mg. per kg. three times a week, and streptomycin 1 g. three times a week, on the same days, plus P.A.S. 15 g. daily; the duration of therapy was 17 weeks. One case was treated with isoniazid, 8 mg. per kg. twice a week, and streptomycin twice a week on the same days; the duration of therapy was 28 weeks.

Age.—Seven patients were aged 4 to 15 years, three were 16 to 25, and two were 26 or more.

Length of Observation.—All patients were observed for over one year. There were no fatalities.

Clearing of X-ray Films.—The average time taken for the chest x-ray films to clear in series B was 19 weeks, and the average time taken in the six cases treated with isoniazid alone was 18 weeks. The longest time taken was 32 weeks and the shortest 11 weeks; in both these cases the treatment was isoniazid alone.

Complications.—No complications occurred.

Discussion

The results in series A, in which 24 patients were treated with streptomycin or streptomycin and P.A.S. daily are in accordance with those in similar series. The aspect with

which we are particularly concerned is the development of tuberculous meningitis during or after treatment, and it is seen that this complication occurred in one-third (33%) of the patients under this therapeutic regime. The Medical Research Council (1950) reported an incidence of 32% in 25 similarly treated patients, and the Ministry of Health Report (1950) stated that one-third of all cases of miliary tuberculosis will develop tuberculous meningitis despite streptomycin therapy.

The average time from the start of treatment to the development of tuberculous meningitis in series A was 14.8 weeks, and the longest time was 24 weeks.

In series B 12 patients were treated with isoniazid, alone or in combination with streptomycin or streptomycin and P.A.S., and tuberculous meningitis did not develop in any of them during a period of over one year.

Great stress cannot be placed on the results of series B, because the numbers involved were small and do not happen to include patients aged 3 years or less, in whom, judging from the experience of series A, tuberculous meningitis is most likely to develop. Nevertheless, the findings encourage hopes, based on the work of Elmendorf *et al.* (1952), Mackaness (1952), Mackaness and Smith (1952), and Suter (1952), that isoniazid therapy may reduce the incidence of tuberculous meningitis in cases of miliary tuberculosis under treatment. Elmendorf *et al.* found that isoniazid, unlike streptomycin, passes in practically full concentration from the blood to the C.S.F., and the other workers reported that isoniazid readily penetrates the cell membrane of histiocytes, so that it can attack any contained tubercle bacilli, whereas streptomycin does not. Further, Ritchie *et al.* (1953), on the basis of pathological studies of miliary tuberculosis and tuberculous meningitis, have reported that in both these conditions isoniazid causes a resolution of the lesions not seen with streptomycin.

In the first six cases of series B isoniazid alone was employed. As with a similar series of cases reported by Clark *et al.* (1952), the results were satisfactory, but as reports of various studies (Medical Research Council, 1953; and others) indicated that isoniazid combined with streptomycin was more effective against *M. tuberculosis* than either drug alone, various forms of combined therapy were used in the later cases.

Intermittent therapy was effective in the cases in which it was tried. Indeed, in one case in which streptomycin, 1 g., and isoniazid, 8 mg. per kg., were given on the same days twice a week, the x-ray films cleared in the short period of 12 weeks. Recent work by Hobby and Lenert (1953), however, does not suggest that intermittent therapy will prove superior to continuous therapy in acute cases of tuberculosis, for when mice which had been injected intravenously with tubercle bacilli were treated with isoniazid alone, streptomycin alone, and a combination of streptomycin and isoniazid (streptomycylidene isonicotinyl hydrazine), the treatment being given on two days a week, it was found that before comparable results were achieved the dosage given on these days had to be three to six times as great as the daily dosage required when treatment was given on five days a week.

Whatever may prove to be the most effective therapeutic regime in miliary tuberculosis, the results of the present investigation suggest that the use of isoniazid tends to prevent the development of tuberculous meningitis.

Summary

Twenty-four patients were treated with streptomycin or streptomycin and P.A.S. daily, and 33% developed tuberculous meningitis.

A later and not strictly comparable series of 12 patients was treated with isoniazid alone or with isoniazid in combination with streptomycin or with streptomycin and P.A.S., and none of them developed tuberculous meningitis over an observation period of at least one year.

Our thanks are due to Dr. A. L. K. Rankin, physician-superintendent, Belvidere Hospital, who kindly made available to us the case records of six patients included in series A; also to Dr. J. McIntosh, physician, Western District Hospital, who allowed one of us to treat two of his patients with isoniazid.

ADDENDUM.—Since this paper was written two further cases of miliary tuberculosis for inclusion in series B have been under observation for one year, making 14 cases in all in that series. In addition, 10 further cases of miliary tuberculosis have been observed for more than 24 weeks (which was the longest period of time taken for meningitis to develop in series A). In these further 12 cases there have been no fatalities and no complications. However, of four recent cases observed for less than 24 weeks, one patient, aged 9 months, developed tuberculous meningitis six weeks after the commencement of treatment.

REFERENCES

- Clark, C. M., Elmendorf, D. F., jun., Cawthon, W. U., Muschenheim, C., and McDermott, W. (1952). *Amer. Rev. Tuberc.*, **66**, 391.
 Elmendorf, D. F., jun., Cawthon, W. U., Muschenheim, C., and McDermott, W. (1952). *Ibid.*, **65**, 429.
 Hobby, G. L., and Lenert, T. F. (1953). *Ibid.*, **68**, 292.
 Mackaness, G. B. (1952). *J. Path. Bact.*, **64**, 429.
 — and Smith, N. (1952). *Amer. Rev. Tuberc.*, **66**, 125.
 Medical Research Council (1950). *Lancet*, **1**, 841.
 — (1953). *British Medical Journal*, **1**, 521.
 Ministry of Health Report (1950). *Lancet*, **2**, 230.
 Ritchie, G. M., Taylor, R. M., and Dick, J. C. (1953). *Ibid.*, **2**, 419.
 Suter, E. (1952). *Amer. Rev. Tuberc.*, **65**, 775.

MILIARY TUBERCULOSIS OF THE BONE MARROW

WITH PARTICULAR REFERENCE TO THE POSSIBILITY OF DIAGNOSTIC ASPIRATION BIOPSY

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Miliary tuberculosis may be diagnosed by the radiological appearance of the lungs in less than half of the cases in which the disease is found at necropsy. Steiner (1937) found the characteristic x-ray picture in 48% of 46 cases, and Chapman and Whorton (1946) in only 25% of 63 cases. The systematic search for choroidal tubercles provides an additional means of diagnosis, and Emery and Lorber (1950) showed that, in a series of 52 histologically proved cases of miliary tuberculosis, 18 were diagnosed by x-ray examination, 25 by retinoscopy, and 28 by a combination of the two methods. Thus the present methods of diagnosis are insensitive, and other methods warrant investigation.

Stahel (1939) described finding a miliary tubercle in an aspiration biopsy of sternal marrow. Schleicher (1946) published a series of eight cases in which he found miliary tubercles in the aspirated bone marrow of adults during clinical investigation. The investigation reported here is an attempt to assess the incidence of miliary tubercles in the bone marrow in cases of generalized miliary tuberculosis and to determine the potential value of bone-marrow aspiration in the clinical diagnosis of the condition.