Tuberculous Meningitis: A 30-Year Review

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Tuberculous meningitis remains an important illness that can be difficult to diagnose in a timely fashion and carries significant morbidity. We present a retrospective review of the cases of tuberculous meningitis diagnosed and treated at a single institution. Fifty-eight cases were identified and stratified according to stage of disease at presentation. Four patients (7%) died; three (5%) developed severe neurological sequelae. Poor outcomes were largely confined to cases presenting in an advanced stage and at the extremes of age. Corticosteroids were administered to 56 patients and may have contributed to the comparatively good outcome in these cases.

Tuberculous meningitis (TBM) remains a serious health threat in both developed and developing countries [1–7]. Despite the advent of new neuroimaging techniques and antituberculous drugs, the diagnosis of TBM can be difficult and/or delayed because of the relative rarity of the condition, and the associated morbidity and mortality remain high [1]. A growing body of evidence, however, indicates that early treatment can significantly improve the outcome of TBM [1, 8]. Uncertainty remains regarding the role of corticosteroids as adjunctive therapy for TBM [1, 9, 10].

We present a retrospective analysis of 58 patients with TBM who were treated at a single institution over a 30-year period. In addition, we attempt to clarify the elements critical to the diagnosis and successful treatment of this condition.

Methods

The case records of all patients with TBM diagnosed and treated at Fairfield Infectious Diseases Hospital (FIDH) in Melbourne, Australia, between 1960 and 1990 were reviewed. This hospital is the major referral center for infectious diseases in the state of Victoria. Patients either presented initially to FIDH or were transferred from other institutions. The diagnosis of TBM was established on the basis of one of the following criteria (which were evaluated, in the order listed, until one set was fulfilled): (1) culture of *Mycobacterium tuberculosis* from CSF; (2) clinical findings of subacute meningitis (meningeal symptoms lasting for longer than 4 days), with more than 10 cells/mm^3 in CSF and *M. tuberculosis* cultured from another site; or (3) a clinical course of subacute meningitis, with a CSF glucose level of <2.2 mmol/L and a favorable response to specific antituberculous treatment. Diagnosis by the first criterion was considered definite; diagnosis by the second or third criterion was considered presumptive.

No additional cases were identified by cross-referencing of other diagnostic codes or by a review of autopsies performed. The stage of TBM was determined by the method of Gordon and Parsons [7, 8]; in stage 1 the patient was fully conscious; in stage 2 the patient was drowsy or had focal neurological signs, and in stage 3 the patient was comatose or nearly so. In all cases a smear for acid-fast bacilli was prepared with application of a standard Ziehl-Neelsen stain to centrifuged CSF; in addition, the erythrocyte sedimentation rate (ESR) was determined, chest radiography was undertaken, hemoglobin was measured, and white blood cells (WBCs) were counted. Student's *t* test was used for statistical analysis.

Results

Patients

Fifty-eight patients with TBM were identified. A review of the records of the seven other major university teaching hospitals in Victoria revealed another 32 cases. Thus our cases constituted 64% of all cases diagnosed in Victoria over this period. Fifty of our cases were diagnosed by the first criterion, four by the second, and four by the third. In the latter four presumptive cases (in which *M. tuberculosis* was not cultured from any site), the level of glucose in CSF was markedly low at the time of admission (mean, 0.9 mmol/L; range, 0.3–1.6 mmol/L) and remained low for 14–28 days. In addition, the tuberculin skin test with purified protein derivative (PPD) gave a positive result in all four cases (three at 10 U and one at 100 U). The patients were followed for 12 months to 14 years (mean, 3.2 years).

The incidence of TBM treated at FIDH over the 30-year period reviewed is shown in table 1. The number of patients from Asian countries rose during the last 15 years studied (i.e., after 1975). The patients ranged in age from 1 month to 72 years (mean, 31 years); 3 patients were >60 years old, and

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Table 1. Numbers of patients with TBM at FIDH, stratified by year of presentation and country of origin.

Country of origin	No. of patients during indicated period						
	1960–1965	1966–1970	1971–1975	1976–1980	1981–1985	1986–1990	Total
Non-Asian	18	13	12	2	1	3	49
Asian	0	0	0	1	2	6	9
Total	18	13	12	3	3	9	58

11 were <15 years old. There were 32 male patients and 26 female patients. Three patients were pregnant.

Clinical Data

The duration of symptoms before presentation ranged from 1 day to 9 months (median, 10 days); it was <2 weeks in 32 cases (55%) and ≤2 days in 3 (5%). In the latter 3 cases, diagnosis and initiation of treatment were delayed by 5–11 days; however, all 3 patients remained in stage 1 and recovered fully after therapy. Patients whose interval from onset to presentation was >4 weeks were more likely to have extrameningeal disease (table 2). Extrameningeal disease was manifested as symptomatic tuberculous chest disease in 22 cases, as urinary tract disease in 3 cases, and as tuberculous arthritis in 1 case.

Twenty-five of the 58 cases were classified as stage 1 at presentation, 25 cases as stage 2, and 8 cases as stage 3 (figure 1). Most cases (44, or 76%) presented as subacute meningitis. Symptoms and signs at presentation are listed in table 3. Fever (>37.5°C) was documented on admission in 32 cases (55%) and within the first 24 hours after admission in 44 cases (76%); it was present on admission as either a symptom (night sweats or rigors) or a sign in 38 cases (66%). Five patients had no fever documented during their hospitalization; all of these patients received antituberculous therapy and glucocorticoids on the day of admission. Fever reached a level of >39.0°C in 10 cases (17%). Six patients reported rigors. Cranial-nerve palsies were noted before therapy in 7 cases and developed 2–13 days (mean, 5 days) after initiation of treatment in another 6 instances.

The provisional diagnoses considered by infectious diseases specialists and fellows on the day of admission were diverse, including TBM in 21 cases, pyogenic meningitis in 9, cerebral abscess in 7, viral meningitis in 6, and encephalitis in 5. Thirty-four of 58 patients were empirically treated on the day of admission with antibiotics active against the bacterial agents of meningitis or cerebral abscess; 10 of these 34 patients were also treated for TBM.

Fourteen patients showed signs of clinical deterioration before treatment was begun. More specifically, 11 patients deteriorated in terms of their level of consciousness (and therefore their stage of TBM), 6 patients developed new cranial-nerve palsies, and 2 patients developed generalized epileptic seizures. Some patients experienced more than one type of deterioration. Treatment was delayed by a mean of 8 days in these 14 cases.

A history of contact with tuberculosis or prior tuberculosis was documented in 16 (28%) of the 58 patients and resulted in the commencement of empirical antituberculous therapy in 7 instances. A history of contact was established for 8 of the 11 patients who were <15 years of age.

Laboratory Data

The level of sodium in serum was <135 mmol/L (range, 108–134 mmol/L) in 29 cases (50%), and the ESR was >20 mm/h in 16 cases (28%). The WBC count was $>11.0 \times 10^9$/L

Table 2. Duration of symptoms of TBM before admission, stratified by stage and presence of extrameningeal disease.

Duration (d)	No. (%) of patients	No. (%) with extrameningeal disease	No. in indicated stage of TBM		
			I	II	III
0–2	3 (5)	0 (. . .)	3	0	0
3–14	19 (33)	3 (16)	8	9	2
15–28	16 (28)	5 (31)	8	5	3
29–270	20 (34)	13 (65)*	6	11	3
Total	58 (100)	21 (36)	25	25	8

* $P = .002$ for a duration of ≥29 days vs. ≤28 days.

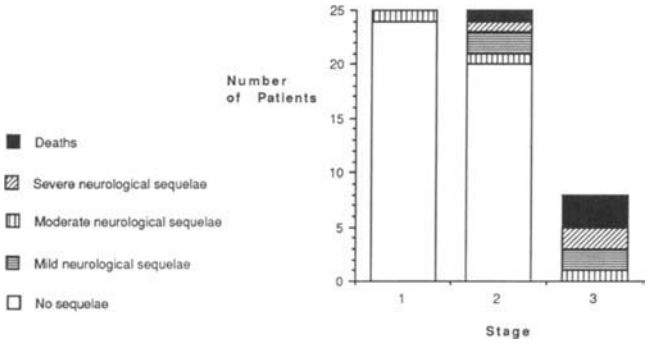

Figure 1. Outcome of 58 cases of TBM, by stage of disease at presentation.

(range, 11.2–27.0 × 10^9/L) in 18 cases (31%) and was <4.0 × 10^9/L (range, 2.9–3.9 × 10^9/L) in 4 (7%). When 10 U of PPD was used, the tuberculin skin test elicited a reaction of >10 mm in 18 of 40 patients; when 100 U was administered to those who initially had a negative result, another 12 patients reacted. Thus the cumulative rate of reactivity was 75%. Of the 10 patients with negative results at both 10 U and 100 U, 5 were clinically ill (2 in stage 3 and 3 in stage 2) and—in light of possible anergy—were given antituberculous therapy before a CSF smear revealed *M. tuberculosis.*

Table 3. Clinical findings at presentation in 58 cases of TBM.

Finding	No. (%) of patients
Symptoms	
Headache	50 (86)
Fever*	30 (52)
Vomiting	24 (41)
Confusion	20 (34)
Lethargy	14 (24)
Neck stiffness	14 (24)
Cough	8 (14)
Back pain	5 (9)
Hemiparesis	4 (7)
Epilepsy	4 (7)
Poor eating	2 (3)
Weight loss	2 (3)
Limb pain	2 (3)
Signs	
Fever	32 (55)
Meningism	21 (36)
Abnormal mental state	33 (57)
Drowsy	27
Semiconscious	4
Comatose	2
Abnormal respiratory examination	16 (28)
Localizing neurological signs	9 (16)
Hemiparesis	3
Sixth-nerve palsy	5
Seventh-nerve palsy	4
Choroidal tubercles	4 (7)
Epididymo-orchitis	1 (2)
Chronic septic arthritis	1 (2)

* Night sweats or rigors.

Table 4. CSF findings on admission in 58 cases of TBM.

Finding, range	No. of patients (%)
WBC count (no./μL)	
0–50	8 (14)
51–100	10 (17)
101–200	14 (24)
201–400	15 (26)
401–800	11 (19)
801–4,000	1 (2)
Polymorphonuclear cell count (% of total WBC count)	
0–10	17 (29)
11–20	14 (24)
21–30	8 (14)
31–40	2 (3)
41–50	7 (12)
51–100	10 (17)
Glucose level (mmol/L)	
0–0.5	9 (16)
0.6–1.0	7 (12)
1.1–1.6	10 (17)
1.7–2.2	9 (16)
2.3–2.6	15 (26)
2.7–4.3	8 (14)
Protein level (mg/L)	
450–1,000	14 (24)
1,001–1,500	21 (36)
1,501–2,000	12 (21)
2,001–2,500	5 (9)
2,501–3,000	4 (7)
3,001–4,800	2 (3)

Findings on chest radiography were abnormal in 24 cases (41%). A miliary pattern was evident in 9 patients, upper-lobe infiltration in 12, and lobar consolidation in 3. *M. tuberculosis* was recovered from the sputum of 17 of the 24 patients. (None of the sputum samples was obtained by bronchoscopy.) All 8 patients whose TBM was diagnosed after 1986 were tested for antibodies to human immunodeficiency virus (HIV); none was positive by ELISA (Abbott Laboratories, Abbott Park, IL).

Most patients had predominantly lymphocytic meningitis, with a total WBC count in CSF of 50–800/μL (table 4). The total WBC count ranged from 7 to 4,000/μL. One patient had predominantly polymorphic meningitis, with a WBC count of 4,000/μL; this person had recently had a cerebral infarction. The CSF glucose level was normal in 23 cases (40%), although it subsequently fell below the normal range in 17 (74%) of these cases; in 12 cases this fall preceded therapy. Depression of the CSF glucose level at presentation was not related to prognosis. The CSF protein level was elevated in all cases, with a range of 478–4,800 mg/L (normal

range, 100–400 mg/L). The CSF smear for acid-fast organisms was positive in 26 cases (45%); in 20 cases this result was positive before treatment, while in 6 the positive result followed the initiation of therapy by a mean of 2 days (range, 1–6 days). The smear was positive when prepared with CSF from the initial lumbar puncture in 13 cases (all before the start of therapy), with CSF from the second lumbar puncture in 8 cases (2 after the start of therapy), with CSF from the third lumbar puncture in 3 cases (2 after the start of therapy), and with CSF from the fourth lumbar puncture in 2 cases (both after the start of therapy).

Treatment

Antituberculous treatment was started within a week of presentation in 46 cases; in fact, it was begun on the day of admission in 24 of these cases. In the remaining 12 cases, such treatment was delayed for up to 3 weeks. The decision to initiate treatment was based on the patient's history and on results of the initial CSF examination and chest radiography in 20 cases. In 11 cases, this decision was based on the finding of acid-fast bacilli in a second or subsequent CSF smear; in 13 cases, on a decline in the CSF glucose level; and in 14 cases, on a deterioration in clinical state. A history of contact with tuberculosis was elicited more frequently, the duration of symptoms was longer, the percentage of smear-positive cases at the time of the first lumbar puncture was higher, and the mean glucose level in CSF was lower among the 24 patients whose antituberculous treatment was started on the day of admission than among the 34 patients whose treatment was initiated later (table 5).

Fifty-six of the 58 patients received prednisolone orally for 4–9 weeks (mean, 6 weeks); the initial dose of 0.5–1 mg/(kg·d) was reduced after the first 2 weeks. The 2 patients who did not receive glucocorticoids were classified as having stage 1 TBM at presentation and recovered with no sequelae. No severe adverse effects resulted from steroid therapy. A minor relapse of either headache or fever after the initial reduction in the steroid dose was noted in 11 (20%) of 56 cases. Repeated lumbar puncture in these 11 cases only confirmed a steady improvement in the CSF profile. Antibiotic therapy consisted of isoniazid and streptomycin in 41 cases (all occurring before 1975); isoniazid, streptomycin, and rifampin in 6 cases; isoniazid, rifampin, and pyrazinamide in 6 cases; and isoniazid, rifampin, pyrazinamide, and ethambutol in 5 cases. No significant differences among the responses to the various regimens were detected. Two patients died and two developed severe sequelae with isoniazid-streptomycin treatment; two patients died and one developed severe sequelae with the other three regimens together ($P = .4$). Three of the 54 isolates of *M. tuberculosis* tested exhibited antibiotic resistance (to streptomycin in all instances). All patients with resistant isolates were receiving streptomycin and isoniazid alone; their uneventful recovery emphasizes the usefulness of isoniazid.

Neurosurgical intervention was required in four cases for the treatment of hydrocephalus. Two of the patients died, one suffered severe neurological sequelae, and one was left with minor sequelae. Three of the four patients presented in stage 3 and one in stage 2. Computed tomography was performed in 13 cases and showed at least one abnormality in eight. Six patients had evidence of basilar meningeal enhancement, three patients had some degree of hydrocephalus, and one patient had evidence of parietal infarction.

Clinical Outcome

Fifty-four of 58 patients survived; 44 of the surviving patients had no neurological sequelae (table 6). Four patients developed minor neurological sequelae: incomplete deafness (two patients, both given streptomycin), vertigo (one patient given streptomycin), and mild short-term memory loss (one patient). Patients whose TBM was classified as stage 3 at presentation had a poor prognosis, even when treatment was begun on the day of admission. All eight such patients died or developed a neurological deficit (figure 1).

Most patients with poor outcomes were at one of the extremes of age. Only 1 of the 44 patients between 11 and 59 years of age either developed severe neurological sequelae or died, whereas 6 of the 14 patients who were either ≤ 10 or ≥ 60 years of age had these outcomes ($P < .001$). A poor prognosis was clearly related to an advanced stage of disease at presentation (figure 1). All 3 pregnant patients (2 in stage 1 and 1 in stage 2 at presentation) recovered uneventfully. None of their children developed congenital tuberculosis.

The prognosis for patients with radiographic evidence of miliary tuberculosis did not differ from that for patients with either radiographic findings of localized disease or normal radiographic results. Death or a severe neurological deficit was the outcome for one of nine patients with a miliary pattern on chest radiography and for six of 49 patients with localized changes or normal findings ($P = .9$).

There was a correlation between a marked elevation of the CSF protein level at admission (>2.0 g/L) and an advanced stage of disease at presentation. One of 25 patients in stage 1, 5 of 25 patients in stage 2, and 5 of 8 patients in stage 3 had such an elevation on admission ($P < .05$ for stage 1 vs. stage 3 and for stage 2 vs. stage 3; $P = .08$ for stage 1 vs. stage 2).

Sequential CSF Changes with Treatment

Before 1980 it was routine at FIDH to repeat lumbar punctures at monthly intervals in all cases of TBM until the CSF profile returned to normal—a change that sometimes took 24 months or longer. Hence a large amount of information is available on CSF parameters after the initiation of therapy and their relation to stage of disease and prognosis. Data obtained by reexamination of CSF from a varying number of patients up to 12 months after the start of treatment are shown in table 7.

Table 5. Features of patients with TBM, by time of initiation of antituberculous therapy.

Group (*n*)	No. (%) with history of contact with *M. tuberculosis*	Mean duration (d) of symptoms before admission ± SD (range)	No. (%) with stage 2 or 3 on admission	No. (%) with initial CSF smear positive for AFB	No. (%) with CXR changes typical for *M. tuberculosis*	Mean CSF glucose level on admission (mmol/L) ± SD (range)	Mean total WBC count/μL of CSF on admission ± SD (range)	Mean % of PMNs in CSF ± SD (range)
All patients (58)	16 (28)	29 ± 46 (1–270)	33 (57)	13 (22)	24 (41)	1.75 ± 0.98 (0.1–4.3)	326 ± 555 (7–4,000)	30 ± 26 (0–100)
Treatment within 24 h of admission								
Yes (24)	12 (50)	47 ± 62 (3–270)	17 (71)	13 (54)	16 (67)	1.31 ± 0.92 (0.1–3.1)	268 ± 230 (17–790)	36 ± 27 (0–90)
No (34)	4 (12)*	16 ± 16 (1–60)†	16 (47)‡	0 (. . .)§	8 (24)*	2.07 ± 0.90 (0.3–4.3)‖	372 ± 719 (7–4,000)#	24 ± 23 (0–100)**

NOTE. Abbreviations: AFB = acid-fast bacilli; CXR = chest radiography; and PMNs = polymorphonuclear cells. All *P* values given below are for treated vs. untreated patients within 24 hours of admission and were obtained with use of Student's *t* test.

* $P = .001$.
† $P = .01$.
‡ $P = .07$.
§ $P < .001$.
‖ $P = .004$.
$P = .50$.
** $P = .06$.

For all of 45 patients tested, the CSF culture was negative for *M. tuberculosis* at 1 month. The smear for acid-fast bacilli was negative at 1 month of treatment for 24 of 25 patients tested; for the remaining patient (who had stage 2 disease at presentation and recovered uneventfully), it was negative by 2 months.

The CSF glucose level returned to the normal range in 23 of 40 cases after 1 month of treatment; in 12 cases this restoration took 2 months, and in 1 patient it took almost 4 months. The rate of rise of the glucose level was not related to stage of disease or prognosis. The patient whose glucose level took 4 months to return to normal had an uneventful clinical recovery within the first 2 weeks of treatment.

The CSF protein level fell to the normal range within 6 months of treatment in only 2 of 45 cases. In 6 instances this return to normal took longer than 12 months. The range for all 45 patients was 4–26 months, with a median of 8 months. A prolonged elevation of the CSF protein level was more common among patients who had advanced disease at presentation and developed neurological sequelae; specifically,

Table 6. Clinical features of cases of TBM ending in death or in moderate or severe neurological sequelae.

Outcome, patient's age (y)	Time from onset to presentation (d)	Stage of disease at presentation	Day of treatment commencement	Nature of sequelae	Time from start of treatment to death (d)
Death					
40	49	2	6	. . .	7
4	10	3	. . .*	. . .	2
63	10	3	4	. . .	22
75	300	3	1	. . .	6
Survival					
Severe sequelae					
69	60	3	1	Vegetative	. . .
4	42	2	2	Vegetative	. . .
4	9	3	2	Vegetative	. . .
Moderate sequelae					
34	60	3	1	Hemiparesis	. . .
46	10	1	1	Late spinal syrinx	. . .
41	10	2	8	Cerebellar dysfunction	. . .

* No treatment was given.

Table 7. CSF parameters before and after therapy for TBM.

Time relative to initiation of treatment	No. of patients with indicated finding/total no. (% with finding)				
	CSF culture positive for *M. tuberculosis*	CSF smear positive for acid-fast bacilli	CSF glucose level of <2.2 mmol/L	CSF protein level of >450 mg/L	CSF WBC count of >5/μL
Before	50/58 (86)	20/58 (34)	35/58 (60)	58/58 (100)	58/58 (100)
After					
1 w	7/58 (12)	9/40 (23)	32/58 (55)	45/45 (100)	45/45 (100)
1 mo	0/45 (. . .)	1/25 (4)	17/40 (43)	45/45 (100)	45/45 (100)
2 mo	. . .	0/25 (. . .)	5/40 (13)	44/45 (98)	44/45 (98)
4 mo	. . .	. . .	0/40 (. . .)	44/45 (98)	32/45 (71)
6 mo	. . .	. . .	. . .	43/45 (96)	16/45 (36)
12 mo	. . .	. . .	. . .	6/45 (13)	9/45 (20)

4 of the 6 patients whose CSF protein level took longer than 12 months to normalize developed neurological sequelae.

The CSF cell count fell by at least 50% from the initial value within the first month of therapy in 43 of 45 cases but still had not returned to the normal range by 6 months in 16 instances. In 7 cases the cell count was still abnormal after 24 months of therapy (6–23/μL), although it was within the normal range in all cases by 34 months. One of the 7 patients whose cell count was slow to return to normal had minor neurological sequelae; the other 6 patients recovered fully.

Discussion

We review a series of 58 patients with TBM presenting to an Australian infectious diseases hospital. The diagnosis of TBM was established by CSF culture in 86% of cases. The smear for acid-fast bacilli was ultimately positive in 45% of cases, although half of the CSF smears from the first lumbar puncture were negative. Seventy-six percent of patients survived without sequelae, 7% died, and 5% developed severe neurological sequelae. Glucocorticoid therapy was given to 97% of patients. A poor clinical outcome was related to an advanced stage of disease at presentation and to the occurrence of TBM at the extremes of age.

The diagnosis of TBM can be difficult unless a high degree of suspicion is maintained [1, 11]. Unfortunately, in 14 of the 58 cases in this series, treatment was delayed until after clinical deterioration had commenced. In this review no contribution of a delay in diagnosis to a poor prognosis was documented. Specifically, 1 of 14 patients with a delayed diagnosis and 3 of 44 patients without such a delay died; moreover, the remaining 13 patients with a delayed diagnosis survived without sequelae. An association between a delay in treatment and a poorer prognosis has been documented previously [1, 8, 12]; in light of the correlation between stage and prognosis that we did document (as have other investigators [7]), our study might have confirmed the former association had the number of patients been larger.

A typical presentation of TBM includes subacute lymphocytic meningitis with a depressed level of glucose in CSF; however, this combination of findings was noted at presentation in only 10 patients (17%). The cases of TBM that were treated appropriately on the day of admission had a presentation and CSF profile more typical of TBM than did those in which treatment was delayed (table 5). Laboratory investigations other than CSF examination and chest radiography were of little diagnostic help; this point emphasizes the need for vigilance with regard to the possibility of TBM.

Since currently used antituberculous drugs are not particularly toxic in the short term, empirical treatment should be initiated as early as possible (given a reasonable suspicion of TBM) to reduce morbidity and mortality [8, 11]. In the first week after the start of treatment, the diagnosis can be made without excess difficulty by smear and subsequent culture. In this series a positive smear was demonstrated for 16 of 25 patients who were tested 1–6 days following commencement of treatment.

Efforts to diagnose TBM have a higher positive yield if repeated large volumes of CSF (10–20 mL) are examined [1, 8]. Although lumbar puncture was repeated routinely in this series when the diagnosis was suspected but not confirmed by smear, the volume of CSF examined was generally <10 mL. Forty-five percent of the cases reported here were positive for acid-fast bacilli on CSF smear. In some series up to 90% of cases of TBM have been smear-positive, although in general the figure is lower [1, 8].

The treatment of TBM should generally commence with at least three drugs known to be active against *M. tuberculosis* [13]. At FIDH the combination of isoniazid, rifampin, and pyrazinamide is currently used, with ethambutol added if resistance is suspected.

The use of corticosteroids has been controversial, with some investigators advocating their routine use, some suggesting their use only in patients with an advanced stage of disease at presentation, and some recommending only rare use [1, 5, 8, 9, 13]. This review and other reports have noted that the prognosis of TBM is generally good for patients presenting with stage 1 disease, poor for those with stage 3 dis-

Table 8. Outcome of TBM for patients with stage 2 disease at admission.

Years of review, country [reference]	No. (%) of patients dying	No. (%) of patients dying or left with sequelae*	Percentage of patients treated with corticosteroids
1960–1990, Australia [PR†]	1/25 (4)	3/25 (12)	100
1982–1987, Egypt [9]	4/27 (15)	NA	100
1966–1967, India [14]	3/6 (50)	NA	100
1952–1958, United States [15]	1/11 (9)	NA	100
1979–1985, Thailand [16]‡	0/23 (. . .)	5/23 (22)	100
1952–1971, Lebanon [17]‡	5/33 (15)	26/33 (79)	84§
1976–1989, United States [18]‡	0/10 (. . .)	5/9 (55)	83§
1960–1976, Scotland [8]	5/30‖ (17)	9/30‖ (30)	83§
1961–1984, Hong Kong [19]‡	1/78 (1)	10/78 (13)	73§
1968–1983, United States [11]	6/25 (24)	NA	56§
1982–1987, Egypt [9]	14/35 (40)	NA	0
1966–1967, India [14]	3/8 (38)	NA	0
1952–1958, United States [15]	4/11 (36)	NA	0

* Moderate or severe sequelae are included; NA = data not available.
† PR = present report.
‡ These studies reviewed childhood TBM only.
§ Data are percentages of all patients (stages 1–3) receiving steroids; figures on steroid therapy for stage 2 only are not given.
‖ Total number of patients represents those with stage 2 disease at initiation of therapy, not at admission.

ease, and intermediate for those with stage 2 disease (a subgroup that may be particularly amenable to intervention). We compared our data on outcome for patients in stage 2 with the corresponding data from other published series [9, 11, 14–19] (table 8). Few definitive conclusions can be drawn because in many studies the exact number of patients with stage 2 disease who received corticosteroids was unknown and the time of initiation of corticosteroid therapy (at the start of or during antibiotic treatment) was unclear; however, there was a trend towards a more favorable outcome when corticosteroids were used in the treatment of TBM. The rationale for the recent use of corticosteroids in the treatment of bacterial (pyogenic) meningitis in children [20] may also be applicable to TBM, but direct and conclusive evidence is still lacking.

Two criticisms of corticosteroid treatment for TBM are that they may interfere with interpretations of CSF studies and with the penetration of antituberculous drugs into the CSF [13]. Through extensive follow-up of sequential CSF samples, our review showed low CSF glucose levels and positive smears despite the use of corticosteroids (table 7). In addition, a recent study of the penetration of current antituberculous drugs into CSF found no difference between antibiotic levels in corticosteroid-treated patients and those in patients not given corticosteroids [21].

The role of neurosurgery in the management of TBM requires emphasis [1]. If long-term sequelae due to raised intracranial pressure are to be minimized, patients must be monitored for hydrocephalus [2, 22]. The introduction of new neuroradiological techniques has played an important role in this regard: the combination of basilar meningeal enhancement and hydrocephalus is strongly suggestive of TBM [23].

Pregnancy and HIV infection may be important risk factors for the development of TBM [24–26]. However, no patients with TBM have yet been diagnosed as concurrently infected with HIV, and the three pregnant patients in this series have fared well, as have their children.

In summary, this series represents the experience with TBM at FIDH in the last 30 years. This relatively large series from a Western country illustrates that the prognosis of TBM can be good provided that the disease is diagnosed early. The use of corticosteroids may have contributed to the good outcome in our patients.

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