Hydrocephalus in Tuberculosis Meningitis in Childern

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Foreword:-

Chairman Mao Said:-

"There are many contradictions in the process of development of a complex thing, and one of them is necessarily the principal contradiction whose existence and development determine or influence the existence and development of the other contradiction."

"..... in studying any complex process in which there are two or more contradictions, we must devote every effort to finding its principal contradiction. Once this principal contradiction is grasped, all problems can be readily solved."

In the process of tuberculosis meningitis the above saying likewise holds true. In the process of tuberculosis meningitis of children the following phenomena are often met with. All late, or even middle stage cases of the disease during antimicrobial treatment may unexpectedly die; in many children under treatment the symptoms due to inflammation markedly improve, the spinal fluid findings normalize, but servere mental disturbances are left behind; in some there is uncontrollable high fever, convulsion or persistent headache and vomiting.....These are undoubtedly the results of hydrocephalus. Although the tubercle bacilli together with the tissue damage on one side and the antimicrobials on the other side are the major contradiction, the use of effective antimicrobials is the determining factor. The specific tratment can determine or influence the coming into being and the development of hydrocephalus; it can control the inflammation of the meninges, hence reduce intracranial pressure as met with in the majority of early and large number of middle stage cases. But in some of the later and many of the late cases, before the

antimicrobials can exert their effect, die of acute hydrocephalus or even when the antimicrobials have brought the inflammation under control, die of chronic hydrocephalus. Thus the coming into being and development of hydrocephalus determine or influence the whole course of event, making its treatment the major and deciding factor, especially in the middle stage and even more in the late stage where it is most often met with as a complication..

Among 614 cases of tuberculosis meningitis children admitted in 1956 to 1966 to the Peking Municipal Children's Hospital and the Children's ward of the Peking Tuberculosis Institute, 365 cases (59.4%) showed definite hydrocephalus. The incidence is even higher in those who died of the disease; 20 out of 22 cases (90.9%) showed this complication that came to autopsy. Of the 365 cases complicated with hydrocephalus 82 (22.5%) died, while among those that were not so complicated there were only two death (0.8%). Therefore in order to reduce the mortality of tuberculosis meningitis hydrocephalus control must be the major concern.

At the beginning we did not fully realize the supreme importance of hyerocephalus in tuberculosis meningitis, with increasing experience, little by little we become convinced of it. Starting with simple antimicrobial treatment we gradually introduced a series of conjugated pressure-reducing procedures and our effort have secured us increasing better curative results from year to year. Thus from 1956 to 1958 we used antimicrobials alone, 1959-63 steroids were added, 1964-66 other intracranial pressure depressants and hydrocephalus-control measures were further introduced. The clinical results of these three periods are shown in table I (see appendix).

DIAGNOSIS OF HYDROCEPHALUS:

The recognizance of the presence of hydrocephalus in the prerequisite of its proper control and treatment. From 1964 to 1966 out of 254 cases of tuberculous meningitis 172 cases were diagnosed of having hydrocephalus, out of which 90 were on grounds of clinical symptoms and findings alone, the rest (82) by puncture of the lateral ventricle.

1, The frequencies of the different symptoms and findings of these cases are shown in Table II (see appendix).

2, Change in the lateral ventricle fluid in hydrocephalus:.

98 punctures of the ventricles were done either on one or both sides, 89.8% of these showed inflammatory changes (table III) (see appendix). These changes induce overproduction of CSF, thus in the acute stage communicative hydrocephalus was often the result. Of the 82 drained cases 71 (86.5%) were of this type, Therefore ependymitis is one of the origins of hydrocephalus.

3, Relationship between incidence of hydrocephalus and age of patient, stage and type of diseases. (table IV, V, VI) (see appendix)

TREATMENT OF HYDROCEPHALUS:

I, Draiage of lateral ventricle:

Significance of ventricular drainage in treatment; with the development of hydrocephalus the increased intracranial pressure of ten endangers the child's life. Therefore hydrocephalus becomes the major contradiction, its control will determine the fate of the the child. In the acute stage of tuberculous meningitis the CSF is over-produced as a result of ependymitis leading to cerebral edema and an intracranial pressure and often cerebral herniation. At this moment a drainage of some ml. of CSF can reduce the pressure to normal value. Besides, the increase of CSF leads to dilatation of the ventricles, pressing on the cerebral tissue, reducing its blood supply, causing in turn cerebral functional disorder, intensifying cerebral edema, forming thus a vicious cycle. If a persistent drainage of CSF is carried out, the normal pressure then can be maintained for a time, giving the antimicrobials time to counteract the inflammation, and the cycle can be disrupted. We started this practice in 1961 with a few late cases and did not maintain it for long (1–3 days). Subsequently it was prolonged to 2–3 weeks and started the treatment earlier than before, yielding gratifying results. Following is an analysis of the 82 cases thus treated.

Age:	0– 1 yrs.	35 cases
	1– 3 yrs.	37 cases
	3– 7 yrs.	9 cases
	7–14 yrs.	1 case

Type and Stage of disease:

Basal	7 cases
Meningo-encephalitic	70 cases
Spinal	5 cases
Middle stage	6 cases
Late	73 cases
Chronic	3 cases

Character of Hydrocephalus:

Communicative	71 cases
Obstructive	11 cases

2, Clinical effect of lateral ventricle drainage:

In the 82 cases where triple antimicrobials (a few also with 1314Th added) together with corticosteroids were used plus drainage, the effect on reducing the intracranial pressure and the prevention of further development of hydrocephalus was satisfactory. In 41 cases drainage alone was used together with pre-while-or post-drainage use of hypertonic solution of urea, mannitol or sorbitol.

In 44 cases the hydrocephalus was completely brought under control; in 22 cases of the 38 that were have hailed, showed transient favorable effect, such as disappearance of head ache, vomiting and convulsion, respiration regularized and the immediate return of normal mental state deprived of by the increase of intracranial pressure. Life endangered by cerebral herniation can be saved by ventricle drainage. In 16 cases the result was poor, probable due to severe and long-sustained hydrocephalus having had already caused irreducible damage to the brain tissue. It is evident that early recognition and prompt treatment is of great importance.

The frequency of puncture in the 41 favorable cases was various; in 28 cases. once; 8 cases, twice; 4 cases, three times; 3 cases, 4 times; 1 case, 7 times; each time in general lasting 7-10 days, the longest being 25 days. There was no incidence of secondary infection or unfavorable reaction.

The amount of CSF drained also varied; the least was 15 ml/day, up to 300-400 ml/ day. In most children the amount drained increased as

the days increased, in general in 7–10 days the total amount drained is 1,000–1500 ml. Time needed to control the hydrocephalus: 15 cases (30%) in a week, a further 11 cases in the second week, making a total of more than 50% in two weeks. The longest took 4 months, drained 7 times; 3 days after the last drainage symptoms improved and gradually brought under control.

This case has been followed up for 19 months; except for slight squinting of the left eye, impairment of movement of the left hand, the mental development was taken as satisfactory although somewhat inferior to other children of the same age

(1) Relationship between age of patient and effect of drainage:

0–1 yr of age
18 cases under control
17 not under control

1–3 yrs. of age
20 cases under control?
17 not under control

3–7 yrs. of age
5 cases under control
4 not under control

7–14 yrs. of age
1 case under control

There seems to be no direct relationship between the age of the child and the effect of drainage.

(3) Relationship between the type and stage of disease and effect of drainage:
(see table VII)

(3) There is no direct relationship between the character of hydrocephalus and effect of drainage:

Communicative hydrocephalus 71 cases:
39 were brought under control
32 not

Obstructive hydrocephalus 11 cases:
5 were brought under control
6 not

(4) Intraventicular injection of drugs:

It was found that with hydrocephalus by CSF examination, 89.8% showed ventricular inflammatory changes; increased of protein in 55.8%. With a view of controlling this condition (reducing exudation and adhesion) intraventricular injection of drugs was carried out in 27 children, once a day for 7–10 days. The effect of this measure is shown in Table VIII (see appendix).

In these 27 cases after injection of drugs cell count reduced in 17 cases (62.9%), increased in 6 cases (22.2%), protein reduced in 8 cases (29.6%), increased in 4 (14.8%); those unchanged were in the majority in the normal range, while in those without medication reduction of cell count and protein, each in 2 cases only. The effect of this measure appears to be good. In injection drugs strict aseptic technic should be followed to prevent secondary infection, and slowly administered; dilution of the drug should preferrable be with CSF.

(5) Analysis of 38 cases where hydrocephalus was not brought under control: (Table IX) (see appendix)

Although ventricle drainage reduces intracranial pressure effectively but in very late stage of the disease where cerebral damage had gone too far, where there is obstruction or when the drainage was applied too late the effect is not evident. In case of drug resistance or in retreatment cases special caution must be taken to achieve the desired aim.

(6) Case history:

Shui, H.H, 704373 female, age 1 yr. 4 months. Admitted on Jan. 16, 1966, as emrgency case. Slight cough for 1 mos. vomiting 1–2/ days for 1/2 month, projectile; come for 1 day, comatose, ashy, shallow and weak breathing, crack-pot sign pefinite, fontanelle full definite pathologic reflexes; lungs showed acute miliary tuberculosis and primary complex. Six hours after admission Cheyne-Stokes respiration, opisthotonus, rigidity of the extremities and clinic convulsion of the arms set in. 10% chloral hydrate was given, when ventricle puncture was done, the pressure was found to be very high; after 20 min. of drainage breathing became stalized, convulsion stopped. On the 3 day of drainage the child opened its eyes

and began to react to the surroundings; on the 5th day the kneejerk came back, 6th day, eyes began to move, light reflex recoved. On the 10th day the swallowing reflex came back, eyes appeared to perceive objects, feeding well, Discharged on the 65 th day, well. Followed up for 8 months, condition good, mental development normal, no sequalae.

INDICATIONS OF VENTRICULAR DRAINAGE:

(1) acute hydrocephalus producing high fever, irregular breathing, convulsion, repeated vomiting, stupor (or mentally clear) where other measures failed to reduce the intracranial pressure, especially in young infants,

(2) sudden slowing or stopping,of breathing, shallow and rapid and irregular pulsementally cloudiness or coma, ashy grey appearance, cold seeat, cyanosis of tups of extremities, lips and nose or convulsion of extremities, suspecting cerebral herniation,

(3) acute exacerbation of chronic hydrocephalus,

(4) progressive hydrocephalus where other measures to reduce the intracranial pressure failed,

SIDE REACTIONS:

Too rapid withdrawl of CSF may lead to rupture of intracranial veins.; too rapid and too much withdrawl may cause back-herniation of the cerebellus and the brain stem thru the incisura tantorii/cerebelli and the herniation of the gyrus cinguli. Having these possibilities in mind we have not encountered any of these mishaps.

SUMMARY:

44/82 cases of hydrocephalus treated with ventricular drainage resulted favorable; 22 showed temporary relief, 16 failed. This treatment can effectively reduce intracranial pressure, break up the vicious cycle of hydrocephalus, gaining time for the antimicrobials to on the inflammatory process in the meninges, thus solving the problem at its root. This

method of treatment is specially indicated in case of cerebral herniation. It is a relatively safe procedure.

II. Use of hypertion solution in the management of hydrocephalus:

In recent years there has been a good deal of investigation on the use of hypertonic solution to reduce intracranial pressure. Of the substances used urea, mannitol showed the best results. In China there have been many reports on their use in neuro-surgery. The mode of action of their use with rapid intravenous drip is mainly due to the creation of osmotic pressure difference between the blood and CSF.

Increased intracranial pressure is a common finding in tuberculous meningitis and progressive hydrocephalus is often the cause of death in children suffering from tuberculous meningities. From Feb. 1963 we have used this way of treatment in 74 such patients and obtained encouraging results. The clinical analysis of the 30 cases where hypertonic solution was used as the principal measure follows:

(1) age:

0–1	yr.	3 cases
1–3	yrs.	9 cases
0–7	yrs.	6 cases
7–12	yrs.	12 cases

(2) Stage and type of disease
middle and late each 15 cases,
type II and III each 15 cases.

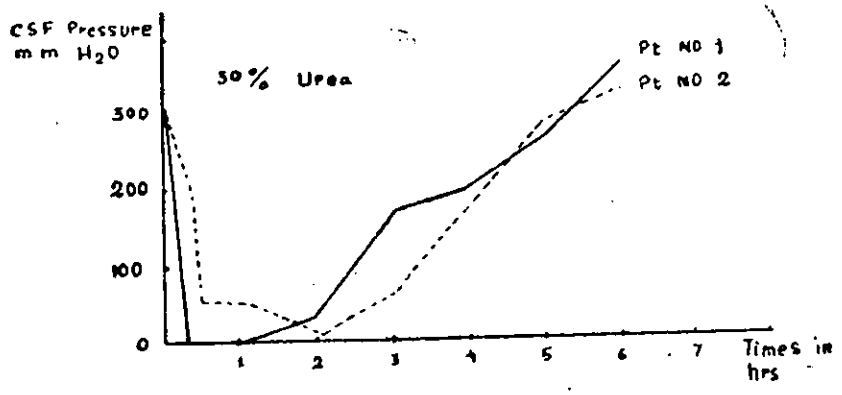
(3) Character of hydrocephalus:
Communicative 29 cases
Obstructive 1 case

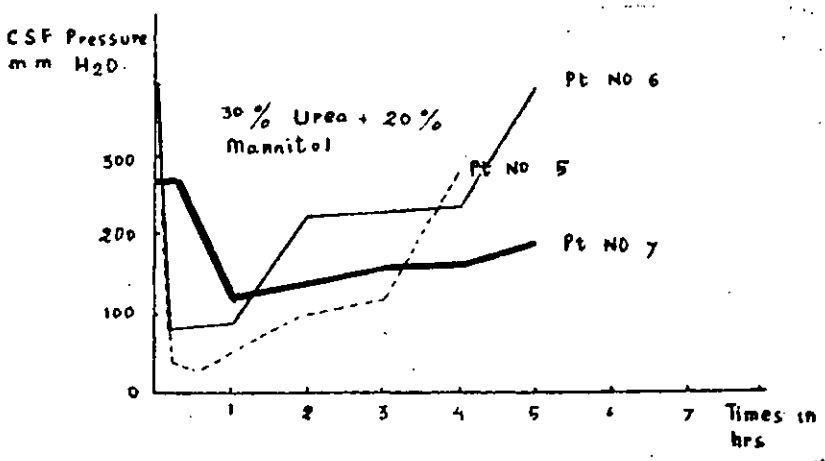
(4) Treatment, dosage and course: In the literature mannitol dosage is 1–4.25 g / kg / injection, urea 1 g / kg / injection, administered by venous drip in $\frac{1}{2}$– 1 hour. Our dase with mannitol or urea H.S. g/kg injection sorbitol 2 g / kg / injection administered by venous drip in 1/2–1 hour. Our dose with mannitol or urea was 1–1.5 g / kg/ injection, sorbitol 2 g / kg / injection by benous drip in 1/2 hour, rarely all three drugs in combination or singly injected with syringe

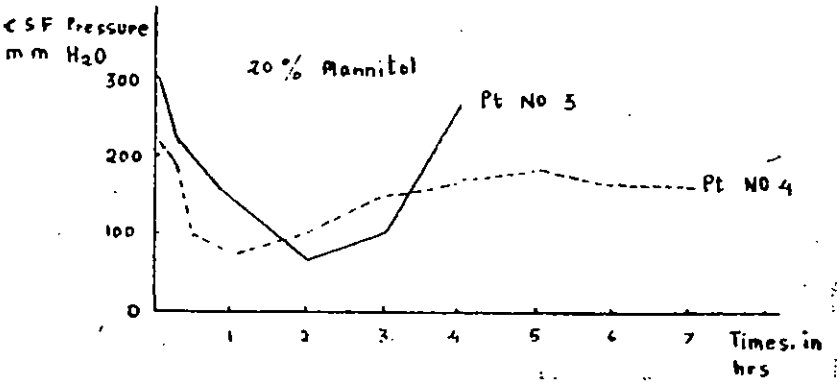
or urea plus 20% mannitol, 30% urea plus 25% rbitol. When used in combination, each 0. 5–1 g / kg / injection: 4–6 hours after using urea singly by drip a shot of 40 ml 25–50% glucose was given to prevent rebound. Treatment was given 1–2 times a day. In some cases one injection is enough, the most 15 times.

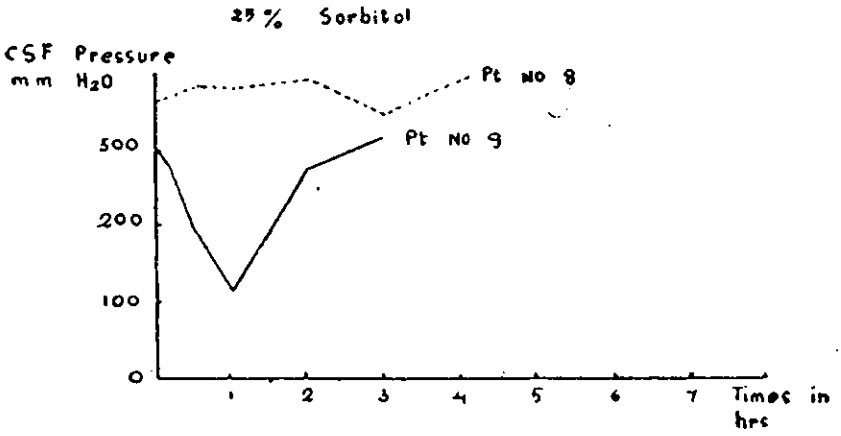
(5) Curative effect: In all 30 cases where hypertonic solution was given by intravenous drip there was immediate relief of symptoms (headache, vomiting and convulsion ceased, irregular breathing normalized and recovery from coma). Together with the use of anti microbials in 28 cases the hydrocephalus was brought under control; in the other two, although the immediate result was euident, but the cerebral damage was too far gone to relief the hydrocephalic symptoms, ended fatally.

In a few patents whose celebral lateral ventricle was drained the ffect on intracranial pressure of these drugs was recorded.




CSF Pressure
mm H2O
30 % Urea + 20 %
Mannitol
Pt NO 6
Pt NO 5
Pt NO 7
500
200
100
0
1
2
3
4
5
6
7
Times in
hrs


CSF Pressure
mm H2O
20 % Mannitol
Pt NO 5
Pt NO 4
300
200
100
0
1
2
3
4
5
6
7
Times. in
hrs


25 % Sorbitol
CSF Pressure
mm H2O
Pt NO 8
Pt NO 9
500
200
100
0
1
2
3
4
5
6
7
Times in
hrs

From the above graphs it can be seen:

i, Urea: The action of 30% urea is sure and rapid; 10 min. after injection the fall in intracranial pressure is evident; it may fall to 0. The highest effect is reached in 15 min. to 2 hrs. after completing injection; the effect lasts for about 5 hrs. then there appeared a rebound.

ii, Mannitol: 20% solution 15–30 min. after completing injection it begins to act, highest at 15 min. to 2 hrs. There is no rebound. Effect lasts 4–5 hrs. 64% reduction of pressure.

iii, 30% plus 20% Mannitol: Act also rather promptly, becoming evident in 15 min. highest in 15 min. to 2 hrs. no rebound. Effect lasts 4–5 hrs. 75% reduction of pressure.

iv, 25% sorbitol: action slow, duration of action, 2 hrs; no rebound. In one case pressure was reduced by 67%, in another no effect. Table X (see appendix)

Illustrative case report:

Chao, F. H. 704123, male 5 yrs. of age admitted Jan. 1966.

Vomiting for 20 odd days, severe in last week. Barium meal showed narrowing of ileocaecal region, admitted for surgery. General condition fair; given penicillin and SM; nothing by mouth, intravenous fluid 2,400 ml. in 24 hrs. Next day became stuporous with convulsion of lower extremities. Lumber tap produced typical tuberculous meningitis findings. 3rd day, comatous, loss of swallowing reflex. With large infusion, hydrocephalus intensified. Beside 3 antimicrobials and steroid, 20% mannitol (1 g/kg/injection) by drip insituted; one hour afterwards swallowing reflex returned; 3 hrs afterwards eye movements became active and became reactive to external stimuli. Next day mentally clear, can answer questions. Hypertonic solution used for 4 consecutive days, ventricle drained for 7 days: combined treatment for 4 months; hydrocephalus brought under control. On discharge CSF essentially normal.

Indication for use:

1. In acute increase of intracranial pressure leading to convulsion,

temporary stopping of breathing and mental disturbance–symptoms of cerebral herniation; quick administration with syringe is indicated, followed by ventricle drainage to prolong the effect of this treatment.

2. In cases of increased intracranial pressure producing headache, nausea and vomiting.

3. Where ventricle draining failed to relief symptoms when cerebral edema is suspected.

4. In children above 4 yrs. of age, where it is difficult to drain the ventricles.

5. Where ventricle draining failed to relief hydrocephalus it can be alternately used.

Side Effects:

It is reported in the literature that 30% urea can lead to anorexia, diarrhea, nausea, vomiting, local irritation, hemoglobulinuria and prolonged prothrombin time and abnormalities in EKG; and EGG 20% mannitol and 25% sorbitol show no side effects. In our series we have not encountered any of these side effects.

SUMMARY:

Observation of 30 cases of tuberculos meningitis complicated with hydrocepholus using hypertonic solution infusion as the major treatment measure showed good immediate results and in 28 of these the hydrocephalus came under control. Of the three drugs urea acted most quickly but there was a rebound after 5 hrs.; 20% mannitol acted rather slowly but no redound; 25% sorbital was slow and least easting in effect, 30% urea plus 20% mannitol combined seem to be better than either singly. Hypertonic solution infusion is best suited for emergency use in cerebral herniation cases and in children above 4 years of age where ventricle draining is difficult to perform.

III, ACETAZOLAMIDE:

Although ventricle drainage and hypertonic solution infusion are definitedly effective in treating hydrocephalus in general but in chronic

progressive hydrocephalus they are not entirely satisfactory. Further it is difficult to use these two measures for long period of time. Therefore an orally admitted drug-acetazolamide was tried out.

The mode of action of acetazolamide is as yet poorly understood. It is a potent inhibitor of the enzyme carbonic anhydrase which catelyzes the reaction $Co_2 + H_2{}^0 = H_2Co_3$' and is present in high concentration in the choroid plexus. It has been suggested that carbonic anhydrase activity in the choroid plexus yields an excess of H+ and $HCo_3^=$ ions in the CSF. These ions are rapidly exchanged for Na + and C 1- ions from the plasma. Water, which moves freely from the plasma into CSF, follows passively to reestablish osmotic equilibrium. The net result, therefore, is an almost complete inhibition of brain carbonic anhydrase activity and would, therefore, be expected to interfere considerably with CSF production. In 1963 Pollay and Davson found, following the intravenous administration of acetazolamide in the rabbits, that the rate of ventricular fluid production was reduced to about 50% of normal. In 1965, Huttenlocher reported that acetaxolamide was effective in 10 of 15 children with congenital hydrocephalus and thought that it may be superior to the presenty available shunting procedures for the chronic, slowly progressive hydrocephalus patients. We have not been able to find any report on its use in hydrocephalus in tuberculous meningitis.

Since May 1965 we have used acetazolamide in 34 cases of tuberculous meningitis with hydrocephalus.

(1) Age:

0—3	yrs.	18 cases
3—7	yrs.	8 cases
7–14	yrs.	8 cases

(2) Type and stage of disease:

type	II	13
type	III	18 and
type	IV	3 cases

(3) Method, dosage and course: All cases where given SM, INH and steroids, a few with PAS or 1314Th in addition. In 8 cases, before

giving acetazolamide ventricle drainage or hypertonic solution failed to manage the hydrocephalus and have become chronic, progresive; in 22 cases the ventricle was drained for a shart period or having aeen given hypertonic solution 3-13 times. Acetazolamide was given in general 20–40 mg/kg/ day, a few up to 80 mg/kg/day, in 3-4 divided doses, some consecutively, other for 4 days then stop for three days; 27 cases (80%) for less than 2 mos., (mostly 1/2/to 2 mos.), a few for 3+mos., one case for 6 mos.

(4) Therapeutic offect: 18/34 showed favovable results–disappearance of headache, vomiting, convulsion and irregular breathing and irritability improved. In 16 cases there was no improvement.

Illustrative case report:

Liu, K.L. female 10 yrs. of age. Chronic basal meningitic type; headache vomiting, shrieking, excitable, convulsion, semi-comatous. On the 5th day of administration of acetazolamide, mentally imdroved, convulsion headache, vomiting and excitability disappeared; by the 14th day mentally clear. After stopping the drug for 5 days, headache and aching of the eyes returned, intracranial pressure rose to 280 mm water. 4 days later the drug was reinstituted, symptoms disappeared the next day. Further medication for 2 weeks, symptoms did not return, 2 weeks after ceasation of medication headache and mental dulness came back, but on giving the drugs for 3 day, these symptoms again disappeared. Further course uneventful. The time of appearance of the drug effect is various, in general rather slow; in 9 cases (50%) it appeared in 1–3 days; in 7 cases in the 2–3rd week, another 2 in 4th and llth week respectively. So if by the 4 the week on effect is forthcoming further administration is of doubtful value.

Effect of acetazolamide and type and stage of disease:

9/13 of basal meningeal type responded well with the drug, while only 9/21 (43%) of meningo–encephalitic and spinal types did so. 8/12 of the middie stage responded well, 9/19 of the late stage. So it seems that even in the meingo–encephlitic type and late stage of the diseasd the drug is worth trying. Of the 16 failures there mere 5 retreatment and

protracted chronic cases; obstructive type or with separation of the cranial sutures, resulted from severe hydrocephalus, 5 cases; severe cerebral tissue damage, 2 cases; resistant to the major anticrobials, 1 case and in the other 3 cases the reason of failure unexplained.

(5) Indication: Summarizing the above findings it seems that acetazoliamide is indicated in the following conditions:

(i) children over 4 years of age, where ventricle drainage is difficult to perform.

(ii) supplementing with or after ventricle drainage or hypertonic infusion solution, aiming to prevent the hydrocephalus becoming chronic.

(iii) when encountering difficulties in prolonged ventricle drainage or hypertonic infusion.

(6) **Side effect:** Except in one case that developed metabolic acidosis there appeared no other side effects.

(7) **Summary:** An analysis of the 34 cases of tuberculous meningitis complicated with acute or chronic hydrocephalus shows that acetazolamide is effective in reducing intracranial pressure and bringing the hydrocephalus under control. But its action is rather slow and in severe cases it should be supplemented with ventricle drainage and/or hypertonic infusion. It is specially indicated in tuberculous meningitis complicated with chronic progressive hydrocephalus because it can be given for long period of time.

(IV) THE USE OF ETHIONAMIDE (1314Th)

Ventricular drainage, hypertonic infusion and acetazolamide have proved to be of definite curative value. But in case of drug-resistant or retreatment patients such measures were often unable to bring the disease process under control. Therefore the use of an effective second line anti-

microbial is raised to be the major contradiction. Ethionamide has been reported to be useful in cases resistant to the three major antimicrobials. From Jan. 1965 this drug was used in 42 cases, 38 of which were cases of tuberculous meningtis.

(1) Age:

0—1	yrs.	8 cases
1—3	yrs.	17 cases
3—7	yrs.	9 cases
7–14	yrs.	4 cases

(the youngest 6 mos., oldest 12 yrs.)

(2) Stage and type of disease:

Basal	8 cases
meningo-encephalitic	27 cases
spino-lepto-meningitic	3 cases;
early	1 cases,
late	22 cases,
middle	11 cases,
chronic	4 cases.

(3) **Mode of administration, dosage and course:**

All 38 cases were treated per oral route, in doses of 10-20 mg/kg/day, never more than 0.3 g/day: in course of 1–4 mos. (30 cases–1–3 kos., 8 cases over 3 mos.). The best course should be 3-4 mos, if too short there would be relapse of smptoms.

(4) **Effect:** 31–38 improved: 2 cases showed improvement in the CSF findings only, 29 cases showed that of clinical picture as well: 7 showed no improvement. In the 38 cases 9 cases showed positive culture of the CSF; 5 of these were highly resistant to the major antimicrobials.

The improvement manifested in the normalized temperature disappearance of cranial symptoms, amelioration of meningeal irritation symptoms both CSF cell count and protein content came down and hydrocephalus brought under control.

Illustrative case report: Wang, C.Y. female, age 10 mos. middle stage basal meningitic type and acutemiliary tuberculosis, admitted on Feb. 11, 1966, CSF cell count 242/mm ^{3}, protein 100 mg%; given SM, INH and steroids, symptoms improved for a period then the cranial circumstance gradually increased; sudden high temperature on the 32nd day, convulsion set in, breathing became irregular, the child became comatose. It was thought that the infective organism to be drug resistant, ethionamide was added. Ventricle was drained twice. After 15 day's administration of this drug the clinical improvement was evident, the child became mentally clear; CSF cell count has come down to 16/mm ^{3}, protein to 40 mg%.

(5) **Indication:**

(i) the source of infection had been irregularly treated or treated without effect,

(ii) the patient had been treated for a long time before admission without effect or even became worse.

(iii) after a period of treatment with the major antimicrobials with unsatisfactory result. These three condtions are most prone to show drug resistant organisms, either primary or secondary.

(6) **Side-effect:**

The side effects of ethionamide are mostly in the digestive system, liver damage; some are neuropsychial, dermal or mucosal. Used in the adults its side effects are rather common appearing in general early in the course. Digestive disturbance according to Japanese workers come to 20-45%. In the present series side effects and infrequent, only 3 out of 38 cases. In 2 there was slight liver damage (SGOT raised), in 2 nausea and vomiting (including one with liver damage) and after stopping the medication liver function normalized.

SUMMARY:

(1) Ethionamiade was used in 38 cases, 31 of these showed favorable response. The dose used was 10-20 mg/kg/day, course 3-4 months.

(2) Side effects were infrequent, probably due to the better tolerance of the drug in children and also of the relatively small dose used.

(3) The drug is produce in the country, it is cheap and effective.

SUMMARY AND CONCLUSIONS

(1) Tuberculous meningitis is often complicated with hydrocephalus. In this series of 614 cases the incidence is 59.4%. Among those that came to necropsy it was 90.9%. Further the mortality of the combined condition was 22.5%, against that of those without hydrocephalus, 0.8%. Therefore to bring up the therapeutic effect and bring down the mortality, the early diagnosis and prompt control of hydrocephalus is the crucial point.

(2) The following clincial findings are of great significance in the diagnosis of hydrocephalus: crack-pot sign, irregular breathing, remittent high fever, seperation of sutures, engorgement of scalp veins, edema of the scalp and eyelids, increase of cranial circumference or parietal prominence, excitability, largygeal spasm, glindness, "setting sun" sign of the eyes, exophthalmos and papillary edema.

(3) Hydrocephalus occurs most frequently in infants under 3 years of age, suffering from tuberculous meningitis 81% in the present series. It is mostly associated with the meningo encephalitic type of the disease, 91.3%; next the basal type, 42.4%. 92.3% of late stage cases. 89.8% of the CSF drawn from the ventricle showed abnormal findings, proving that the incidence of ependymitis is high, and this may be one of the factors of the coming into being of hydrocephalus.

(4) Treatment of hydrocephalus: In addition to the use of SM, INH and steroids we used ventricular drainage, hypertonic infusion, oral acetazolamide and ethionamide:

(1) In the acute stage of hycrocephalus, when the condition is serious or when it is rapidly progressing, especially when there is the possibility of herniation or when herniation is beginning, ventricle drainage and rapid hypertonic infusion should be immediately instituted.

(2) If the hydrocephalus is slight or the child is higher in age, hypertonic infusion can be first used; acetazolamide can be added at the same time. If these measures failed then ventricle drainage must be attempted.

(3) After ventricle drainage if the hydrocephalic symptoms are only somewhat relieved but not brought under control, or when the hydrocephalus is passing into the chronic stage then acetazolamide can be used with intermittent hypertonic infusion.

(4) Should drug-resistance is suspected or if after a period of treatment meningitic symptoms do not improve, hydrocephalus is not being brought under control, ethionamide can be added to combat the inflammatory process. At this juncture if the treatment is supplemented with anticranial pressure measures then the possibility of the complete control of hydrocephalus his ensured.

Table I.

Comparison Of Tuberculous Meningitis Of Three Different Periods

Case Number		Those With Hyorocephalus		Death In Those Without Hydrocephalus			
		No	%	Death No.	%	Number	%
1956–58	113	68	60.1	26	38.2	0	
1959–63	247	127	51.4	28	22.0	0	
1964–66	254	170	66.9	28	16.4	2	2.3
Total	614	365	59.4	82	22.5	2	0.8

Table II.

Frequencies Of Symptoms And Findings In 82 Confirmed Cases	Number	%
Crack-pot sign	75	95
Vomiting	74	90
Headache	9/10	90
Fulnes or bulging of fontanelle	43/49	88
Convulsion	69	84
Coma	61	74
Opisthotonus	48	59
Irrgular breathing	38	46
Remittent fever	36	44
Separation of cranial sutures	33	40
Engorgement of cephalic veins	32	39
Decerebrate rigidity	28	34
Increase of cephalic circumstance	26	32
Papillary edema	21	25
Irregular pulse	19	23
Unilateral sweating	14	17
Excitabality	13	16
Laryngeal spasm	13	16
Blindness	13	16
"Setting sun" sign of the eyes	13	16
Head shaking	12	15
Unequal pupils	7	9
Drowsiness	6	7
Striking patient's own head	5	6
Exophthalmia	4	5
Eyelid edema	3	4
Shrieking	3	4

Table III.

Findings In The Ventricular Fluid													
Cells/Mm^3				Sugar (Mg%)			Protein (Mg%)			Chloride (Mg%)			
0-4	5-10	11-50	51-462	15-20	21-45	45-90	10-20	21-40	41-240	500-600	601-650	651-725	
Number	10	16	47	25	2	28	63	43	26	28	44	35	22
%	10.2	16.3	48	25,6	2.1	29.9	68	44.2	26.8	29	43.6	34.7	21.7

Table IV.

Relationship Between Incidence Of Hydrocephalus And Age Of Patient, Stage And Type Of Disease

Age	No. Of Cases	With Hydrocephalus		With Hydrocephalus	
		No.	%	No.	%
0-3 yrs.	158	128	81	30	19
3-7 yrs.	62	35	56.4	27	43.6
7-14 yrs.	34	9	26.5	25	73.5

Note: The incidence of hydrocephalus falls with increasing age.

Table V

Type	No. Of Cases	With Hydrocephalus		Without Hydrocephalus	
		No.	%	No.	%
1) Serous	7	0		7	100
2) Basal	106	45	42.4	61	57.6
3) Meningo-encepha-litic	138	12.6	91.3	12	8.7
4) Spino-lepto-encepha-litic	3	1	33·3	2	66.7

Note: Type 3 showed the highest incidence, 91.3%, Type 2 next 42.4%.

Table VI

Stage	No. Of Cases	With Hydrocephalus		Without Hydrocephalus	
		No.	%	No	%
Early	18	0		18	100
Middle	84	38	45.2	46	54.8
Late	130	120	92.3	10	7.7
Chronic	22	14	63.6	8	36.4

Note: The later the stage of the disease the higher the incidence: late 92.3%, middle 45.%2% and early none.

Table VII

Relationship Between The Type And Stage Of Disease And Effect Drainage

	Hydrocephalus Type II		III		IV	
	Middle	Late	Middle	Late	Middle	Late
Under control	5	1	—	33	—	2
Not under control	1	—	—	34	—	3

including 22 cases with temporary improvement

Note: It appears that with type II and middle stage disease the effect of drainage is good.

Table VIII

Drug Injected	Cell Cout			Protein		Total	
	Reduced	Increased	No Change	Reduced	Increased	No Change	
Cortisone acetate 10 mg or Hydrocortiode 5mg	7	3	2	6	1	5	12
INH 50mg alternating with steroid	9	3	2	2	3	6	14
Streptomycin	1	–	–	–	–	1	1
No medication	2	7	–	2	2	4	9

Table IX.

Analysis Of 38 Cases Where Hydrocephalus Was Not Burought Under Control

	Very Late Stage, Severe Convulsion, Deep Coma, Acephalic Spasticity, Separation Of Cranial Sutures	Drugre Re-treatment	Sistant Case	Too Late	Protracted Drainge Course Of Disease, Obstructive Type	Total
Temporary amelioration	9	3	4	4	2	22
No effect at all	9	2	2	2	1	16
%	47.7	13.1	15.7	15.7	7.8	

Table X

	Action	Duration	Strength	Rebound	Side Effect	Not
30% ureatol	rapid	5 hrs.	strong	present	local irritation	good for cerebral herniation
20% mannitol	rather slow	4–5 hrs.	ratherweak	none	none	safe
25% sorbitol	slow	1–2 hrs.	weak	none	none	economical
urea plus mannitol	rathe ra pid	4–5 hrs.	rather strong	practically none	practically none	better than either singly