

Original Articles

A CLINICAL STUDY OF 89 CASES OF ENCEPHALITIS

By JYOTSNA RANJAN CHATTERJI, M.B.

Medical Registrar

N. GUPTA, M.B., M.R.C.P. (Edin.), D.T.M. & H. (Lond.), D.P.H. (Cantab.)

Professor of Clinical Medicine and

M. N. DE, M.B., M.R.C.P. (Lond.), F.N.I.

Professor of Medicine

(From the Department of Medicine, Medical College, Calcutta)

THE word encephalitis denotes broadly an inflammation of the brain substance characterized clinically by a febrile reaction, an unconscious or semi-conscious state, and various grades of disturbances of the function of the central nervous system. In some cases a complete recovery with restoration of the normal functions of the brain and spinal cord occurs, whilst in others severe degenerative changes take place in the brain leaving the organ permanently damaged. The condition is to be regarded as serious.

The causative factors are many, the chief of which are microbial toxins and viruses. Acute non-suppurative encephalitis of virus aetiology is not uniformly distributed all over the world, neither is its incidence very constant. It usually occurs in epidemic form, but sporadic instances may be found in places where it is least expected. While an epidemic of encephalitis was in progress in middle Europe in 1916-17, hardly any case was reported in India until 1919 when the epidemic spread to this as well as to other far eastern countries such as Japan and Eastern China. Even then, the incidence of the disease never assumed a big proportion as seen in Europe and America. That the epidemic overran our country during its global spread was proved by the presence of a fair number of men and women of our country suffering from the post-encephalitic syndrome.

During the last three years, an epidemic of encephalitis appears to have been prevalent in Calcutta as well as in the south-eastern part of Bengal. During these years, no less than 89 cases were admitted into the Medical College Hospitals under the writers, besides a fair number of cases which came into notice during routine professional work. These latter cases however are not included in the list under review owing to the difficulty of keeping them under continued observation. Out of the 89 cases observed in the hospital, 17 were admitted in 1942, 30 in 1943 and 42 in 1944. It will be seen that the incidence gradually rose and reached the peak in 1944. It is a matter of opinion whether such a steady rise in the incidence is due to the natural spread of the

epidemic amongst the susceptible community or to the unusual social, economic and hygienic conditions consequent on the war situation. It is however certain that the disease is being less frequently noticed during the last three months.

Epidemiology

Seasonal incidence.—Curve 1 (figure 1) shows that the highest incidence of the disease was in the months of September and October and the lowest in March. It was most common in the autumn when there is marked prevalence of all catarrh-producing illnesses, the catarrh of the upper respiratory tract favouring the infection. After October, there was a steady decrease, and in December, the coldest month, the incidence was comparatively low. There was a little rise in the number of admissions in the month of January after which, however, the incidence steadily fell down and reached the lowest limit in March. The summer saw another rise to a maximum in May. The rainy season showed a comparatively low incidence.

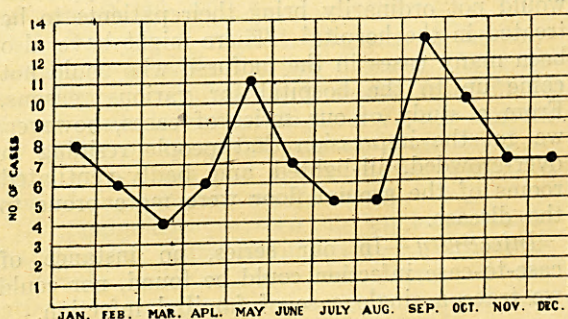


Fig. 1.

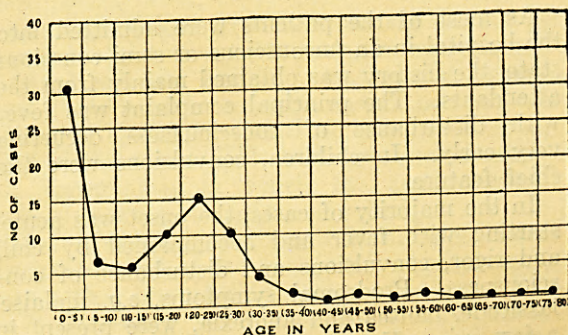


Fig. 2.

Age incidence.—It will be evident from curve 2 (figure 2) that the disease was most common in children under 5 years of age; comparatively rare between the ages of 5 and 15 years, and fairly high between 15 and 30 years. Whereas the maximum number of cases was in children under 5 years of age, the disease was rare after the age of 35 years. This may probably be explained by the lack of immunity in young children.

Sex incidence

	Adult	Child	Total
Male ..	39	17	56
Female ..	12	21	33
	51	38	89

It will be seen from the above that among adults, males were three times more affected than females, while among children the distribution was approximately equal in both sexes.

Racial incidence.—Out of 89 cases, 68 were in Hindus, 17 Muslims, 3 Anglo-Indians and one Buddhist. These figures correspond roughly to the total figures for hospital admissions of the different races, and probably do not indicate any racial variations in susceptibility.

Social status.—Most of the cases came from middle class or poor families. This may not have much significance, as the hospital cases are derived mainly from people coming from such families. The richer section of the population would not ordinarily bring their patients to be treated in the hospital. There might have also been many cases in the mofussil who could not come up to the hospital for various reasons. From a study of our series of cases, however, we got the impression that people residing in over-crowded, ill-lighted and badly-ventilated rooms of the ground floor were more prone to the disease.

Infectivity.—In our series, no instance of case-to-case infection could be found, nor could we trace a single case of familial infection.

Clinical features

As most of the patients were admitted into the hospital in an unconscious or semi-conscious state, the history was obtained mainly from the attendants. The principal complaint was fever with disturbance of consciousness occurring very early. In children, convulsions were the chief feature.

In the majority of cases, the onset was acute, starting with fever and accompanied by chill and rigor, convulsions and disturbance of consciousness. Prodromal symptoms, *e.g.* malaise, lassitude, nausea and anorexia, were present in a few only. Upper respiratory catarrh was not present in the majority of them; at any rate it was not noticed at the time of admission.

Pyrexia.—Except 4 patients who came in a collapsed condition, all had pyrexia. Continuous fever was noticed in 52 cases; in 35 less than one week's duration; and in 8 a month's duration. Intermittent fever was found in 12 cases, and remittent fever in 15. Six had irregular pyrexia of about 2 to 4 weeks' duration, and hyperpyrexia (over 106°F.) was noticed in 7 cases.

Cheyne-Stokes' breathing was noticed in 3 cases and Biot's breathing in one. Slight bronchial catarrh was noticed in a few. Tachycardia in proportion to the rise of temperature was present in the majority of them, none showing any bradycardia. A coated tongue, loss of appetite and constipation were common. Troublesome vomiting was noticed in 4 cases and slight diarrhoea in 6. Except slight albuminuria there was no abnormality in the urine.

Blood.—A moderate leucocytosis was present in 67 patients (75.27 per cent), with relative increase of polymorphonuclear neutrophil cells. Malarial parasites were not found in any one of them. Blood culture was done in 18 cases with negative results except in one which showed *D. pneumoniae*. Widal reaction for enteric group of infections was done in 23 cases, also with negative results. W.R. was negative in the few cases in which it was done.

Psychic and mental symptoms.—Disturbance of consciousness was present in almost every case. Deep unconsciousness was noticed in 57 cases and a semi-conscious state in 17. Sight somnolence or diurnal somnolence with nocturnal wakefulness was not noticed in any of our patients.

Mental symptoms were noticed in 16 patients, the symptoms varying from slight dullness to acute mania. Delirium was present in 6 cases, and was mostly violent; 2 showing delirium as found in the typhoid state. Mental confusion was noticed in 3 cases and emotional disturbances (as laughing or crying without stimulus) were present in 2.

Convulsions.—Convulsions were noticed in 38 patients of whom 27 were children under 10 years. Its incidence was maximal in infants and young children. Generalized convulsions were found in 23 cases (5 adults and 18 children) and localized convulsions in 15 (6 adults and 9 children). A past history of convulsions was given in 5 patients, 4 of whom were children under 10 years.

Meningeal irritation.—The signs of meningeal irritation such as stiffness of the muscles of the neck, a positive Kernig's sign, etc., were present in 42 cases. In some of them the meningeal irritation was so severe that without a lumbar puncture they could have easily been taken for meningitis.

Cranial nerves.—The cranial nerves having their nuclei in the mid-brain were mostly affected. A sluggish reaction to light or accommodation, and dilated, contracted or unequal pupils were noticed in 42 cases; ptosis was present in 4, in one of them it was bilateral, and squint in 3. Facial paralysis was observed in 2 cases.

Motor power.—Two patients showed hemiplegia and one monoplegia of the right lower limb. One developed spastic paraplegia with scissor gait, and a moderate degree of rigidity of the muscles was noticed in 5. One case developed flexibilitas cerea and another Parkinsonism with mask-like face and salivation. Slurring speech with marked intention tremor was seen in one case, and 2 had trismus. Bulbar symptoms, such as difficulty in swallowing, regurgitation of food and nasal voice were seen

in one case only. Torsion spasm producing wry neck was seen temporarily in one. Fine tremors in the tongue, fingers and eye-lids, specially when the latter were closed, could be detected in a few cases and they persisted for a fairly long time but ultimately disappeared completely.

Reflexes.—The tendon jerks were exaggerated in 10 patients, and in 3 of them the exaggeration was unilateral. A positive Babinski was seen in 12 cases, it being unilateral in 3. Well-developed ankle clonus was seen in 2 cases.

Sphincters.—Retention of urine was present in 8 patients. The majority of patients were constipated.

Sensory disturbance.—Sensory disturbances of the nature of hyperæsthesia, hyperalgesia and increased tenderness to pressure on the muscles were present in a few of them. Most of the patients being unconscious or semi-conscious did not respond to the sensory tests.

Cerebro-spinal fluid.—Lumbar puncture was done in 63 patients, the pressure being high in 52 and normal in 11. It was not done in the remaining cases owing to their low condition or for some other reason. The fluid in every instance was clear, and its culture yielded uniformly negative results. The proteins were increased, the sugar and chloride content remaining normal. Colloidal gold reaction was done in 4, the results being as follows—(1) 4444322000, (2) 0043222300, (3) 2111000000 and (4) 2234442000.

Prognosis

Out of the 89 patients, 64 died (71.9 per cent), the disease being more fatal in children under 5 years of age (86.8 per cent) than in adults (60.7 per cent). Those that came in deeply unconscious or with severe convulsions had invariably a bad prognosis. Hyperpyrexia was always serious and not a single patient with it survived.

Sequela.—Out of 25 recoveries, only 3 showed some residual signs at the time of discharge. One of them had mental symptoms, the second had ataxia, intention tremor and slight paresis of the lower limbs, and the third had facial palsy. These patients were progressing favourably but were discharged on request.

Discussion

At the beginning of the epidemic, the disease in some of the cases was mistaken for other maladies, such as acute cerebro-spinal meningitis, typhoid fever and cerebral malaria. As more and more patients came to the hospital, the clinical features became more pathognomonic and diagnosis clear. Those admitted with localized neurological findings were at once suspected to be cases of encephalitis, but quite a large proportion of them came in with pyrexia and disturbances of consciousness, the two symptoms which could be met with in a

large number of other conditions as well, especially in Calcutta. While routine clinical and laboratory investigations suggested encephalitis, the subsequent development of definite neurological signs ultimately clinched the diagnosis. The important points on which stress was laid for suspecting encephalitis were fever, disturbances of consciousness, meningeal irritation and convulsions, but with clear cerebro-spinal fluid and a moderate leucocytosis. Cerebral malaria, acute cerebro-spinal meningitis, eruptive fevers, septicæmic conditions, the enteric group of fevers and typhus fever were all considered in the differential diagnosis. The two conditions which caused the worst confusion clinically were cerebral malaria and cerebro-spinal meningitis; this was removed by a blood examination and lumbar puncture. On clinical grounds alone, this appears to be an epidemic form of encephalitis. In our series, however, we observed the following features which were different from the clinical picture of classical epidemic encephalitis.

(1) The incidence was highest in infants and young children who are least affected in epidemic encephalitis.

(2) There is a marked difference in the mortality rate between the two diseases. Whereas in epidemic encephalitis, it varies from 27 to 50 per cent, it was as high as 72 per cent in our series of cases. Moreover, most of these ran a very acute and severe course which is unusual in epidemic encephalitis.

(3) Somnolence as seen in epidemic encephalitis, *viz.* light somnolence by day with nocturnal delirium, was not found in our patients. Unconsciousness was, in the majority of them, very deep and early. Early interrupted lethargy and inversion of sleep rhythm were not detected.

(4) Convulsions were a prominent feature as opposed to its rarity in epidemic encephalitis.

(5) Meningeal irritation was also a prominent feature and the intracranial pressure as estimated by lumbar puncture was increased in most of the cases. This is different from epidemic encephalitis in which the cerebro-spinal fluid pressure is usually not raised.

(6) Localizing neurological findings were absent in many of the cases, and, when present, were rather prominent.

(7) Mortality was highest in the first week, and recovery after that period was more hopeful.

(8) Residual signs after recovery from the acute stage were infrequent.

Summary

(1) Clinical features of 89 cases of encephalitis admitted into the Medical College Hospitals under the writers during the years 1942, 1943 and 1944 are given.

(2) The differences in the clinical features observed in the present series from those of epidemic encephalitis are discussed.

The writers express their sincere gratitude to Lieut.-Colonel H. E. Murray, Superintendent, Medical College Hospitals, for his permission to carry out the work and utilize the records of the hospital.

SULPHANILYLGUANIDINE IN CHOLERA

By S. K. GUPTA, M.B., D.T.M.,
B. C. CHATTERJEE, M.B., D.T.M., D.P.H.,
B. M. PAUL, L.M.P., L.T.M.

and

R. N. GHOSE, L.M.F.

(Bowel Diseases Research Department, School of Tropical Medicine, Calcutta)

By reason of its solubility in water (200 mg. per cent according to Marshall *et al.*, 1940), and low absorbability from the gastro-intestinal tract [Marshall *et al.* (1941), Crossley *et al.* (1938)] sulphanilylguanidine remains in the intestine for a long time to act on bacteria. With this idea in view, sulphanilylguanidine was used (Chopra *et al.*, 1941) in the cholera epidemic of 1941 with good results. The mortality among the sulphanilylguanidine treated cases was 3.84 per cent whereas the death rate among the control cases treated with saline transfusions only was 8.97 per cent. The preliminary work revealed the harmless nature of the drug in cholera and we decided to administer the large doses which had lately been recommended.

While the efficacy of sulphanilylguanidine was being tried in cholera patients in the Campbell Hospital, studies were also made of its action on *V. cholerae in vitro*.

Vibrio cholerae and sulphanilylguanidine

Three tubes were taken as noted below :—

- (1) 1 gm. of sulphanilylguanidine added to 4 c.cm. of nutrient broth.
- (2) 1 gm. of sulphanilylguanidine added to 4 c.cm. of nutrient broth and autoclaved.
- (3) Sterile nutrient broth 4 c.cm.

Equal amounts of *Vibrio cholerae* were inoculated into each of the above three tubes. Thereafter cultures in bile salt agar plates were made from each of these test tubes at various intervals and the results recorded next day as stated below :—

Six tubes containing 9.9 c.cm. of nutrient broth with 0.5 per cent sulphanilylguanidine were prepared. By serial inoculation of a 20 hours' culture of cholera vibrio (Ogawa) (0.1 c.cm. of culture into tube 1, 0.1 c.cm. from tube 1 to tube 2, etc.) dilutions from $1/10^2$ to $1/10^{12}$ were prepared. Similar tubes of the same broth without sulphanilylguanidine were prepared and inoculated with cholera vibrio in the same way and in the same dilutions. The tubes were incubated for 28 hours and at the end of that time were sub-cultured on the half per cent bile salt agar plates. The results were as follows :—

Dilution of inoculum	Tubes seen after 24 hours	0.1 c.c. plated after 28 hours' action
<i>With sulphanilylguanidine (0.5 per cent)</i>		
$1/10^2$	Good growth	Heavy growth
$1/10^4$	No growth	210 colonies
$1/10^6$	"	No growth
$1/10^8$	"	"
$1/10^{10}$	"	"
$1/10^{12}$	"	"
<i>Without sulphanilylguanidine</i>		
$1/10^2$	Good growth	Many colonies
$1/10^4$	"	"
$1/10^6$	"	"
$1/10^8$	"	"
$1/10^{10}$	"	"
$1/10^{12}$	"	"

Five c.cm. were taken from each of the sulphanilylguanidine culture tubes (except the first tube) into 100 c.cm. of nutrient broth and incubated, the idea being to dilute the sulphanilylguanidine. In 24 hours there was no growth but in two of the flasks there was growth in 48 hours. The original dilution in these two cases had been 10^4 and 10^8 .

These experiments indicate the bacteriostatic and bactericidal properties of sulphanilylguanidine on the cholera vibrio.

Sulphanilylguanidine in cholera cases

The average weight of an Indian adult admitted to the cholera ward of the Campbell Hospital was roughly 50 kilograms and 5

Time of plating after addition of young culture of <i>V. cholerae</i>	Presence of <i>V. cholerae</i> or other colonies in		
	Tube 1	Tube 2	Tube 3
Immediately	Large numbers of <i>V. cholerae</i>	Large numbers of <i>V. cholerae</i> .	Large numbers of <i>V. cholerae</i> .
4 hours after	Do.	Do.	Do.
24 " "	Fair number of <i>V. cholerae</i>	Do.	Do.
48 " "	Few of <i>V. cholerae</i> and of other bacteria.	Do.	Do.
72 " "	None of <i>V. cholerae</i> but large numbers of other bacteria.	Do.	Do.
96 " "	Do.	Do.	Do.