Some Experiences on the Treatment of Japanese Encephalitis

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It is widely accepted that there is no known specific chemotherapeutic agent against arbovirus-encephalitis. One who is interested in Japanese encephalitis will easily appreciate the fact that, as there are great variations in its pathological changes as to its location, extent of invasion, and accordingly in its pathophysiological aspects, real pathogenesis of encephalitis cannot easily be grasped.

We must confess that there has been no systematic research into the biochemical explanation on the pathogenesis of encephalitis to the present day, though it is a very difficult task.

At present we cannot but treat the encephalitis cases symptomatically, but the importance of basic knowledge which will be used as a therapeutic guide can not be denied. Our concept and basic knowledge of this disease, however, was lacking in objectivity and was at most conventional up to this day.

As the authors try to establish a therapeutic principle, though a symptomatic one, we first put an emphasis on the “objective” evaluation of its symptoms and causes of death, and we are eager to get the methods which will enable us to get rid the patient of the causes of death and lower the fatality rates. So we made a comprehensive filing of the result of observations for these three years (1958, 59, 62) that our data might serve as a guide in our future treatment. We dare to publish some of our practical experiences (furthermore definite results of them are lacking at this stage) in the hope that better therapeutic methods will come up through the criticisms and instructions of other coresearchers. (Table I).

The factors which are concerned with the causation and mechanism of fatal outcome in encephalitis can be mentioned circulatory failure, complications, respiratory disturbances and prostration as shown in the Table I.

The circulatory failure, one of the causes of death in encephalitis, is primarily a peripheral vascular failure with minimal or no change in the heart, resulting in rapid feeble pulse, cold extremities and cyanosis (so-called “shock”).

These cases present vague but invariably toxic pictures from the initial stage of the disease and respond to adequate anti-shock therapy and vasotonics with rather prompt relief from their signs.

It is also probable that a more frequent cause of peripheral circulatory failure in encephalitis is dehydration which results in secondary shock (peripheral vasomotor collapse). This occurs because of the lack of desire to drink water and inability to swallow food, increased perspiration, increased secretion in the upper airway, hyperventilation and vomiting with resultant hemococoncentration.

According to a study done in the epidemic of 1949, the amount of blood-volume in encephalitis patients is diminished to such a marked degree that its decrease is directly related to final prognosis and it increases gradually to normal level with the recovery of the patient. (A phenomenon seen also in cholera patient) So the replacement of lost fluid and electrolytes is essential and mandatory in the treatment of encephalitis. But to what degree the replacement should be done is not so simple a problem. In autopsies of encephalitis cases the most prominent pictures of the gross pathology are brain edema and congestion of cerebral vessels. In connection with this finding it is thought that the excessive administration of fluid will most probably be harmful and that a method which enables us to relieve this congestion and edema will be highly effective. in
Table 1. Causes of death in Encephalitis Cases (acute stage)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Mechanisms</th>
<th>Signs and Symptoms</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Circulatory failure</td>
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<tr>
<td>a) Peripheral c.f.</td>
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<tr>
<td>1) Essential→</td>
<td>(toxic)</td>
<td>Weak pulse, Cyanosis, shock</td>
<td>Antishock therapy, Vasculotonica</td>
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<td>b) Cardiac insufficiency</td>
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<tr>
<td>←</td>
<td>damage on circulatory-center in medulla oblongata, Vago-Vagal reflex, Vago-Sympathetic reflex</td>
<td>Cardiac arrest (no changes or occ. Hyperpotassemic changes on ECG.)</td>
<td>Fatal †</td>
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<tr>
<td>Complication</td>
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<td>2)</td>
<td>atelectasis due to bronchial secretion ↓ (Bacterial infection) pneumonia</td>
<td>Dysspnoea, Rales on Chest Dulness, occ. dense shadow on chest X-ray. (Atelectasis, Pneumonia)</td>
<td>Suction, Antibiotics.</td>
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<td>Respiratory failure</td>
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<tr>
<td>a) Damage of resp. center</td>
<td>No regulation of resp.</td>
<td>Irregular breathing (Cheyne-stokes, Biot type)</td>
<td>Fatal †</td>
</tr>
<tr>
<td>3) Resp. M. paralysis</td>
<td>Can not breathe</td>
<td>Usually complicated with 3a)</td>
<td>Iron-lung. Respirator (almost fatal †)</td>
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<tr>
<td>c) Mechanical resp. failure</td>
<td>Air way disturbance, Hypoxia(Cranial N. paralysis in bulbar type)</td>
<td>Cyanosis, Dysspnoea, Rales, Stridor, Dulness</td>
<td>Suction, postural drainage (Trendelenburg position) Tracheotomy, O₂ supply)</td>
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<tr>
<td>4) Exhaustion</td>
<td>prostration</td>
<td></td>
<td>Nasal feeding, plasma and blood transfusion.</td>
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</table>

As an adjunct to the above mentioned measures polyvinylpyrrolidone derivative was used to relieve cerebral edema, to accelerate detoxifying mechanism and to replace lost fluid. But the results were not so good as reported by other authors.

We experienced four cases of sudden death due to cardiac arrest. The diagnosis of acute cardiac insufficiency was made as those cases presented little evidence of cardiac disturbance on ward round several hours before death. Those sudden cardiac arrests came probably as a result of so-called vagovagal, vagosympathetic reflex or the invasion of the medullary cardiovascular center. It is generally claimed that marked change in myocardium was an infrequent finding in encephalitis autopsies. We also found no significant change in ECG in 20 odd cases of encephalitis in 1958.
As the next cause of death should be considered complications, especially complicating pneumonias. Some clinicians laid stress on bacterial complications especially pneumonias leading to death. But according to our observations the chance of primary pneumonias was almost nil and most of the so-called primary pneumonia cases were misdiagnoses of infected atelectasis from obstructions of bronchi or bronchioles due to accumulations of secretion.

In the bulbar type of this disease the increase in amount and change in character of oral and upper-respiratory tract secretions, narrowed bronchial lumina and ineffective coughing mechanism due to vagus and allied cranial nerve disturbances are frequently found and easily lead to obstructive atelectases. Surely superimposed bacterial infections may lead to pneumonias, but this occurrence isn't so frequent as reported previously. Rather mechanical respiratory failure (q.v. (c) of (3) in the table) was found to be the principal factor.

By adequate suctioning of the upper airway, we could promptly relieve the patient of the obstructing tracheal and bronchial secretions which caused dyspnea and various physical signs of the chest, such as rales, dullness, and weak breathing sounds.

The importance of antibiotic administration (penicillin and streptomycin) together with suctioning of the airway cannot be overemphasized in an unconscious patient with disturbances in swallowing or coughing mechanism.

In the author's experience the greatest number of deaths were due to the respiratory failures. So-called bulbar and pons type which is the gravest of all types of encephalitis causes death mainly by respiratory disturbance.

As shown in the table (8 of 3) cranial nerves (especially 7th, 9th, 10th, 11th) which pass through the pons and medulla (cranial nerves 6th, 7th, 9th, 10, 12th) lead to the accumulation of secretions, airway obstruction, atelectasis, dyspnea and cyanosis, and may result in fatal end. In those cases, tracheotomy, tracheal intubation, endotracheal suctioning, postural drainage with Trendelenburg position and oxygen inhalation should be done to keep airway free and clear as the patency of the airway determines the final outcome in them.

The above mentioned emergency measures are nothing but the clinical applications of recent advances in respiratory physiology and anesthesiology.

In practice the cooling of body surfaces in hyperpyretic patients (surely most cases of encephalitis are hyperpyretic) influences the clinical course in a good way by relieving dyspnea and reducing unnecessary, harmful energy expenditure. This is especially true in the case of infant and small children where the surface area is proportionately larger, pulmonary ventilatory capacity smaller and basal metabolic rate higher than adult. These physiological handicaps of the infant and small children predispose to hypoxia, asphyxia and the excessive accumulation of CO₂ in the body when the patient is hyperpyretic and unconscious as in the case with encephalitis. Moreover hypothermia decreases cerebral edema, intracranial pressure and, above all, the oxygen demand of the central nervous
These considerations led us to lay heavy weight on body surface cooling in encephalitis patient.

The last factor to be considered in the fatal outcome of encephalitis is exhaustion. In serious cases as oral food intake is practically impossible, nasal feeding is required.

As a mean of supplying nutrient, fluid and antibodies, plasma (rather than whole blood because of preexisting hemococoncentration) in small children and whole blood in adult were given. This therapy impressed us as a good one.

As the urinary excretion of vitamin B₁ is increased in the acute stage of this disease, vitamin B and C were given in sufficient amount to our patients.

Though the evaluation of the effects of other drug therapy in the treatment of encephalitis is very difficult and confusing, we will briefly review the experiences of drug therapy in our cases and results obtained therefrom.

As a standard in evaluating the severity of individual case author calculated the fatality rate of patients with any one clinical sign or symptom. (Table 2)

**Table 2. Clinical Manifestations and Prognosis**

<table>
<thead>
<tr>
<th>Fever</th>
<th>Vomiting</th>
<th>Consciousness</th>
<th>Dyspnea</th>
<th>Swallowing Disturbance</th>
<th>Tendon reflex</th>
<th>Abs Wall reflex</th>
<th>Trismus</th>
<th>Pupil Edema</th>
<th>Stiffness</th>
<th>Arterial Sign</th>
<th>Babinski Sign</th>
<th>Convulsion</th>
<th>Light reflex</th>
<th>Convulsion</th>
<th>M. Rigidity</th>
<th>Strial Syndrome</th>
<th>Clinical apnoea</th>
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For example the number of patient with palpebral edema was 34 of which 24 ended fatally, so the case mortality with palpebral edema is 71%. In this wise it was found that 7 symptoms and signs, namely, coma, dyspnea, excessive orotracheal secretions, trismus, palpebral edema with slight exophthalmos, positive Babinski sign and absent light reflex have fatality rates over 40%.

We arbitrarily defined as severest those cases with any 5 out of the above mentioned 7 symptoms and signs.

We administered some drugs to these severest cases and assessed the effectiveness of drugs by comparing their prognosis with those of the cases to whom drugs were not given.

**Cortisone and other Steroids**

Opinions differ greatly as to whether cortisone is effective in viral encephalitis. We used cortisone in 6 cases in which 4 ended fatally and one recovered with severe neurological sequelae. After all our impressions are against cortisone therapy in encephalitis. Another steroid prednisolone was used in 12 cases but the results were little better than those cases not given. The claim that it ameliorates sequelae is not very acceptable yet.

**Polyvinylpyrrolidone derivatives**

The effect of these preparations (periston, polybon etc.) was noted in some reports but in our experience with 6 cases 4 died and no direct improvement in clinical picture was seen. Although these preparations are not very hopeful theoretically they can be effectively used as sources of electrolytes and anti-shock agent. But its relatively high cost greatly restricts its general use.

**Tranquilizers**

No appreciable difference in case mortality was noted between cases given and those not given. Of the preparations chlorpromazine was used intramuscularly in the years 1958, 59, and librium (Roche) and librax (in cases with increased orotracheal secretions in doses of 5-10 mg in children and 10-20 mg in adult). in 1962. The case mortality of chlorpromazine-administered patients was 39.1% (6 deaths out of 23 cases) and that of non-users was 34.2% (13 out of 38).

The case mortality with librium and librax (administered for a period of over 3 days) was 20% (6 out of 30) whereas those of non-users was 22%. These drugs cannot be said to be an effective agent.
in encephalitis but in our experience they're somewhat effective in suppressing those symptoms such as anxiety, insomnia, irritability, convulsion, and involuntary movement.

At least we haven't received any unfavorable impression on their use in encephalitis. Rather we were impressed that these drugs (especially librax) were effective in reducing salivation and airway secretion.

Adult Blood Products

Adult blood products seemed to be more effective than any above mentioned drug in our encephalitis cases as means of supplying nutrients, fluid and electrolytes, immune bodies, and reducing cerebral edema. Whole blood was given to adult and plasma to children.

Whole blood 500 cc daily or blood plasma 200-250 cc daily were used to 32 patients of which 6 died (case mortality 18.7%). This rate is far lower than that of 45 nonusers in serious state of which 16 died with a case mortality of 35.5%. We think these product should better be recommended to those patients who can afford economically.

國家抄錄

日本腦炎治療에 대한 몇 가지 경험이

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Virus 빈혈인 일본뇌염에 있어 아직特殊化学療法이 없다는 것은周知의 사실이다. 本病에 대한病理學的變化가 복잡하여 그 侵犯部位、程度、範圍가 다르며따라서 그 나타나는病理生理이一向的이 아니고複雑多段하므로病理의本態을把握하기 힘든 상태에 있는것도本病에 대하여関心을 가지는人々이 누구나 쉽게理解할 수 있는 것이다.

이제 症状의이나或治療方針을 親立하여有하여筆者들은 먼저 그 나타나는 症状과 腦炎死의 原因을 客觀의로서 検討分析함에 努力하였고 그 死因을 究明하여 除去할 수 있는 것은 그를 改善함으로써 死死를 低減시킬 수 있으리라는考慮于下数年間 얻은 바 觀察結果는 綜合整理想第1表을 作成하였으며 이에 依하여 患者의 治療에 臨하여였던 것이라.

第1表에서 또는 따라서 脳炎死因으로서 循環障害(末梢血管循環障害 및 急性心機能不全)、合併症、呼吸障害 및 脳症狀等を 視するのに 이 중에서 呼吸障害에 起因한 것이 제일 重要なる意義을 가진다고 믿어왔다. 筆者들은 腦炎死의 大多数는 이 呼吸로서 気道障害 및 이에 따 르는合併症에 該當するもの들 일임을 경험이었다.

腦炎治療에 있어서는 아직까지特殊療法은 없으므로 一 般療法으로는 合併症의 痛苦을的 方向으로 治療할 것 이에 急性期에는 隔離 安静 臥床 등 其他 熱練된 護理處置를 必要로 하며 특이 分泌物에 의한 氣道閉塞等의 障碍에 대하여는 他覚的な 注意が必要하다. 腦瘻型에 있어서는 氣道내에 附着 없이 滲漏하는 分泌物을 除去를 위하여 또는 聲音障害로 機能障害等에 대한 注意が必要하여 氣道、喉頭炎等에 있어서는 氣道内에 附着 없이 滲漏하는 分泌物の 除去を 要請される。脱水状態에 야기 하므로등으로 或者 各種葡萄糖溶液 pydyingl pyrroldione 剤剂 세로는 血漿의 静脈内注入에 의한 血分 및 規律供給、其他 異常狀態에 들어 自覚的に 知なし 못할 때에는 規律注入에 의한 規律供給도 必要하다.

臨床症例의 出現彼方하 그 致命率로서(第2表) 標準重症症例를 設定하여 보았는데、応急、呼吸困難、口腔及び 氣道内分泌過多、牙周緊急 眼浮腫omaly 眼球突出、陽性 Babinski症候及び光反応(瞳孔)消失等の7個徵候群은 腦瘻가 有する症例에 많이 경험하였다。 따라서今後는 治療法의 適宜良否를 決定할 때에는、上記の7項目에 ならざる 5項目を 極端な症例を 重症と 設定하고 それ 被例に 対象으로 하여 試験하여 그 成績으로서 判定지은 것을 提案하였다。

이와같이 설정된 重症患者에各種 特殊療料들이 試用 되었으나 部分の結果によれば有効だと思われているのが 아직 없고 오로지 水分、栄養、血圧 및 抗菌の供給と 脲末梢循環を 視対策할 수 없으나 あらゆる 他症にとって 血漿、全血 또는 高血圧 Albumin 등의 投与は 若干 有効하였으나 有意義하다고 생각하였다。

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