

2. Title: Malaria and the Nervous System. Clinical
Experience with a Hospital Population in
an Endemic Area in Thailand

Principal Investigators: Martin Chipman, Major, MC.
Francis C. Cadigan, Jr., Major, MC.
Wisit Benjapong, MD. 1

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Objective: This study attempts to outline and describe the course of the cerebral symptoms which occur with malaria.

Description: During a thirteen-week period from August through November, 1965, all patients with malaria confirmed by examination of blood smears who were admitted to the 180-bed Prabuddhabat Hospital, Saraburi Province, Thailand, were examined for the presence of neurological abnormalities. Those patients who had abnormal findings were placed into one of the following five groups depending upon the predominant symptom.

- I Seizures, focal or generalized.
- II Disturbances of consciousness (coma, semi-coma, stupor, somnolence).
- III Acute behavioral changes and organic psychosis.
- IV Confusion, disorientation, and memory deficits.
- V Focal Signs (e.g., hemiplegia, aphasia).

A clinical study was done on each patient. This included a detailed history and mental status evaluation and a complete physical examination with particular emphasis on neurologic evaluation. Laboratory studies included blood smears for determination of parasite densities, complete blood counts, blood chemistries (glucose, blood urea nitrogen, sodium, potassium, chloride, and CO₂) blood cultures, lumbar puncture, and examination of cerebrospinal fluid and serological tests for spirochills. Viral studies were not done and serological tests for leptospira were incomplete. An attempt was made to exclude neurological diseases which might be responsible for the abnormalities.

Progress: This study uncovered twenty-two cases with neurological deficits. Table 1 shows the distribution of our cases both by age groups and by sex. All twenty-two patients had P. falciparum infection; one of these, case 101, had both P. falciparum and P. malariae. Table 2 lists the cases and shows the distribution of symptoms.

Seizures occurred in ten patients, and were the most common clinical manifestation of central nervous system involvement in malaria. Disturbances of consciousness were present in seven cases. Three patients developed acute behavior disturbances. A single case had disorientation, confusion, and memory deficit. Hemiplegia and aphasia occurred in an elderly patient shortly after he became ill with malaria. Seventeen out of the twenty-two patients had severe occipital and bitemporal throbbing headaches which subsided at about the same time that the major neurological deficits disappeared. There were four patients who had evidence of acute liver disease which cleared as the patients returned neurologically to normal.

Seizures: The histories in all ten patients with seizures are similar. No patient had a previous history of convulsions. The patient usually had the onset of chills, fever, myalgia, and headache eight to ten days before hospitalization. The day before admission, the patient had a generalized seizure during which he was incontinent, bit his tongue, and had tonic-clonic movements. On admission, the patient was

Notes

1. Physician, Prabuddhabat Hospital, Saraburi Province, Thailand.

usually postictal. Seven of the ten cases were treated with oral or intravenous quinine and three received chloroquine. All cases were placed on Dilantin during hospitalization. Case 115 was admitted in status epilepticus. After the first day of treatment, seizures did not recur during the hospital stay except in case 113 in whom generalized seizures continued for three days. No deaths occurred in this group.

Disturbance of Consciousness: Of the seven cases in this group, four died. Those who did not survive were either admitted in coma or like case 111 progressed from somnolence to coma within a few hours. All Cases were treated with intravenous quinine. In four of the seven cases we noted initial parasite counts which were higher than in other groups. Rapid, sudden alterations in levels of consciousness characterized those cases which survived. Case 5 is an example of this type of course.

Acute Behavior Disturbances and Organic Psychosis: The three cases in this group are characterized by sudden changes in personality and by thought disorders.

Case 103 had a two-day history of chills and fever. His parents noted that he subsequently began acting peculiarly. On admission his oral temperature was 100°F. When he arrived on the ward he was giggling and mumbling. He suddenly fell on his knees and began kissing and licking the examiner's shoes. During his two-day hospitalization, he was entirely out of contact with the environment, spoke of being watched and pursued and kept repeating "I'm not to blame."

Case 118 was admitted five days after the onset of chills and fever. She had no prior history of abnormal behavior. The day before admission she began to sing nonsense songs, repeated meaningless proverb-like statements, and complained of ghosts rising out of the ground and annoying her. During the first four hospital days, she appeared to be detached from her surroundings.

Case 120 was a Chinese-Thai adolescent who had always been a model of good behavior. The day before hospital admission, he began spitting at his parents. The content of his speech became disorganized and socially inappropriate. His oral temperature did not rise above 102°F. One day after the start of treatment with intravenous quinine, his behavior reverted to the premorbid pattern.

Confusion, Disorientation and Memory Deficits: These symptoms of generalized brain dysfunction may occur post-ictally or may especially be found in cases of somnolence. In the one case in this group, case 2, there were no findings indicating either seizures or a disturbance of consciousness. After a three-day history of fever, headaches, and nausea, the patient was admitted to the hospital with an oral temperature of 100°F. She was confused about whether it was day or night, she was unable to count, could not judge simple distances, and could not remember how many children she had or their names. The day after receiving antimalarial treatment, her neurological deficits disappeared. The patient left the hospital before she recovered completely.

Focal Signs: Case 53 was the only one in the series who developed focal neurological findings during the course of malaria. Two days after the onset of fever, he gradually became unable to walk and talk. Examination on admission revealed a thin, elderly Thai male with an oral temperature of 100.6°F, a blood pressure of 130/90 mm Hg., and a blood smear with malaria parasites too numerous to count (over 500,000 parasites per mm³). The patient had a spastic right hemiplegia, more severe in the upper extremity, decreased appreciation of pain over the entire right side, conjugate deviation of the eyes towards the left, a right supranuclear facialy, paralysis and a global aphasia. No peripheral field defects found. On the tenth hospital day the patient could move his eyes past the mid-line. The other neurological abnormalities did not improve. The question of whether this patient's left hemisphere infarction was directly attributable to malaria or was completely untreated, is unanswerable.

Liver: Four patients, Cases, 15, 28, 101, and 112 had enlarged, tender livers. Complete liver function tests were done only on cases 101 and 112 and were abnormal. With the exception of Case 15, patients with hepatic involvement had disturbance of consciousness. Case 15 had asterixis during his first four days of hospitalization. In all cases neurological improvement closely paralleled decrease in liver size and the disappearance of liver tenderness.

Cerebrospinal Fluid: Spinal fluid examinations and measurements were normal in most of our cases. Table 3 lists the three cases which had increased spinal fluid pressure; of these, case 123 died after five days of coma.

Summary: During a thirteen-week period August to November, 1965 all patients with a blood smear positive for malaria who were admitted to the Prabuddhabat Hospital, Saraburi Province were examined for acute neurological abnormalities. Twenty-two patients had involvement of the central nervous system. Seizures were present in ten cases, disturbances of consciousness in seven; acute behavior disturbances and organic psychosis in three; disorientation, confusion, and memory deficits in one; and focal signs in one.

Four deaths occurred in patients whose principal neurologic abnormality was disturbance of consciousness. One of these had an elevated spinal fluid pressure and another had malaria with hepatic involvement.

Further work will be designed to explore the pathogenesis of the nervous system abnormalities in malaria patients.

Table 1

The Distribution of 22 Cases of Nervous System
Malaria
By Sex and Age Groups

Age Group	Male	Female
0-10	1	0
11-20	4	1
21-30	3	2
31-40	3	2
41-50	0	1
51-60	2	1
61-70	1	1
70+	0	0
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Total	14	8
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Table 2

Distribution of Neurological Abnormalities in 22 Cases of Nervous System Malaria

Case	Age	Sex	Seizures	Disturbance of Consciousness	Acute Behavior Disturbances & Organic Psychosis	Confusion, Disorientation & Memory Deficits	Focal Signs	Liver Involvement*	Headaches	Additional Clinical Data
2	58	F				X			X	
5	33	M		X					X	Incontinent of urine
13	30	M	X						X	
*15	52	M	X					X	X	Asterixis
16	36	F	X						X	
25	23	M	X						X	
*28	42	F		X				X	X	
37	40	M	X							
53	61	M					X		X	Incontinent of urine
54**	65	F		X						
*101	39	M		X				X	X	Incontinent of urine
102	22	M	X						X	
104	18	M	X						X	
106	16	M	X						X	
108	19	M			X					
111**	19	F		X						
*112**	59	M		X				X	X	
113	24	F	X							
115	9	M	X						X	Status epilepticus
118	33	F			X				X	
120	13	M			X				X	
123**	21	F		X					X	

Total number of cases 10
with neurological
abnormalities

7

3

1

1

4

17

* Acutely enlarged tender liver with increase in indirect bilirubin.

** Died.

Table 3

Cases of Nervous System Malaria with Elevated Spinal
Fluid Pressures

Cases	Opening Pressur (in mm. of CSF)
113	260
120	240
123	230