Pulmonary Edema in Severe Falciparum Malaria

Hemodynamic Study and Clinicophysiologic Correlation

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This study was performed to extend the knowledge of the pathogenesis of PE in severe falciparum malaria. Sequential hemodynamic studies were conducted in 13 patients with severe falciparum malaria. Seven patients developed PE, while the other six patients had NPE. Two patients died, one in each group. Hemodynamic changes were found in both groups, including an initial reduction in SVR and PVR, along with an increased CI and variable values (normal and increased) of PCWP. All abnormalities persisted for at least two days; changes in PVR lasted especially longer (throughout five days). The initial hemodynamic changes cannot predict the development of PE; however, heavy parasitemia of more than 60 percent and severe hypoalbuminemia were found to be more common in PE than NPE. Of three patients with PE who had normal PCWP, one died, with postmortem findings of increased pulmonary capillary permeability. The increased PCWP which was found in the other four cases of PE was proven to be volume overload without evidence of CHF. It was concluded that the pathophysiological changes in severe falciparum malaria were systemic and pulmonary vasodilatation. The abnormal pulmonary vascular change was found to be the cause of PE. Volume overload and hypoaalbuminemia could aggravate further pulmonary capillary leakage in these cases.

Acute PE is a fatal complication and therapeutic problem in severe falciparum malaria in the tropics. Clinical and pathologic aspects have been described. Fluid overload, increased pulmonary capillary permeability from various causes, and decreased colloidal osmotic pressure are believed to be the causes of PE. Despite extensive clinical descriptions, hemodynamic studies are still limited. The clinicophysiological change is still unclear. Since falciparum malaria is a systemic disease, the pathogenesis of PE is probably more complex than previously described. Additional hemodynamic studies with clinical correlations are therefore needed for a better understanding of the pathogenesis. This study is an attempt to explore sequential hemodynamic changes with clinical correlations in severe falciparum malaria.

Materials and Methods

This study was conducted prospectively in the ICU at the Department of Medicine, Ramathibodi Hospital, Bangkok, Thailand. The period of study was from January 1985 to December 1988.

Severe falciparum malaria was diagnosed when one of the following criteria was found in parasitemic patients: (1) more than 10 percent parasitemia; (2) renal failure (BUN level >50 mg/dl or creatinine level >2.0 mg/dl or oliguria; urine from urethral catheterization was less than 100 ml in six hours); (3) respiratory failure (PaO2 while breathing room air was less than 60 mm Hg); or (4) PE. The PE was defined when dyspnea, bilateral rales on chest auscultation, and bilateral alveolar infiltration on chest x-ray films were present. Cerebral malaria, which was difficult to define and was rarely seen without the presence of the previously mentioned conditions, was not cited as a separate criterion for selection.

Thirteen cases of severe falciparum malaria were evaluated on admission to the ICU. Laboratory studies included daily or more frequent hemocrit determinations and a peripheral blood smear for malarial parasite count. Initial complete blood cell and platelet counts were done and repeated as needed. Daily or more frequent blood chemistry measurements included the BUN level and electrolyte levels. Initial blood glucose level was followed more frequently using Hemoglucoest (Boehringer Ingelheim) four to six times per day. The PT, TT, and TT were done (Fibrometer; BBL Co). The FDP was measured initially with the reverse passive hemagglutination method. Daily or frequent arterial blood gas analysis was rapidly accomplished on the freshly drawn sample of arterial blood. The pH, PaCO2, and PaO2 were measured under anaerobic conditions by a blood gas analyzer (Instrumentation Laboratory 1312). A 12-lead ECG and chest x-ray film were done on admission and were repeated as necessary.
Right cardiac catheterization with a balloon-tipped flow-directed thermomodulation catheter (Swan-Ganz catheter; American Edwards Laboratories) was performed through the jugular vein. Zero reference was placed at the midchest level. Hemodynamic measurements were performed daily or more frequently, as necessary. These included a serial record of central venous pressure, pulmonary artery pressure, PCWP, and cardiac output (by thermomodulation technique). The PCWP was obtained at the end of expiration when the catheter tip was in the lower branch of the pulmonary artery, either right or left. When the patient was receiving PEEP, no attempt to wean off the respirator had been made during measurement of PCWP. Systemic blood pressure was obtained from the brachial artery using a sphygmomanometer. Hemodynamic calculations were done (COM-I/Epson HX20; American Edwards Laboratories). Standard formulas were used to calculate CI, SVI, SVR, and PVR.

M-mode and two-dimensional echocardiograms (aTL model 851B) were done within 24 hours of admission. The ejection fraction was calculated from the difference between the end-diastolic and end-systolic dimensions divided by the end-diastolic dimension.

**Treatment**

Treatment included intravenous administration of quinine sulfate (1,200 mg as a loading dose, followed by 600 mg every 8 to 12 hours for maintenance, depending on the degree of renal impairment). An exchange blood transfusion was done in cases with very heavy parasitemia (>60 percent), and blood transfusion was given to keep the hematocrit reading at 30 to 35 percent. Continuous peritoneal dialysis was performed through a Tenckhoff Silastic peritoneal catheter using 1 to 1.5 L of dialysate in patients with acute renal failure who either had oliguria or rising BUN level (more than 50 mg/dl). The dwell time was adjusted for adequate removal of waste products, fluid, and electrolytes. When negative fluid balance was required, ultrafiltration through the peritoneum with 4 percent glucose dialysate was instituted. Hemodialysis was substituted when complications of peritoneal dialysis developed.

Oxygen inhalation was given when clinical hypoxia developed or the PaO₂ was below 60 mm Hg. Endotracheal intubation and assisted ventilation with a volume respirator were initiated when a desirable quantity of oxygen could not be met with inhalation of high-flow oxygen connected to a reservoir bag or when clinical exhaustion developed. Inspired oxygen concentration was adjusted and PEEP was initiated if inhalation of 60 percent or more oxygen could not raise the PaO₂ to 60 mm Hg in patients who had diffuse bilateral alveolar infiltration.

Strict fluid balance was carefully monitored by recording daily fluid intake (oral and parenteral) and output (urine; vomitus; diarrhea; dialysate). Fluid was given in an amount equal to or a little less than output in those with no pulmonary congestion. If that pulmonary complication developed, increased urinary output was forced by giving intravenous furosemide in nonoliguric renal failure or mild renal impairment. The volume of fluid removed by peritoneal dialysis or hemodialysis was adjusted in oliguric renal failure. In case of hypotension, fluid replaced to raise the PCWP to 10 cm H₂O was tried. If there was no response, an additional vasopressor, such as dopamine, was given to keep systolic pressure at 90 to 100 mm Hg. Nutritional support was started via the oral or parenteral route as soon as possible, in order to prevent hypoglycemia and to maintain adequate caloric intake.

**Statistical Analysis**

Hemodynamic data were compared between the PE and NPE groups. The data were expressed as individual data and the mean ± SEM, and statistical comparisons were made with Student's unpaired t-test.

**RESULTS**

Patients were divided into two groups; one was the PE group, and the other was the NPE group. A summary of clinical data is shown in Table 1. Pulmonary edema developed in seven patients (cases 1 to 7); four cases developed on admission, and the other three patients developed PE in the ICU, one on the second and two on the third day after admission. Six patients (cases 8 to 13) had NPE. Both groups had male predominance. The age range, except for case 10 (80 years of age), was similar in both groups, ranging from 18 to 58 years in PE and from 21 to 51 years in NPE. Involvement of more than one organ was found

<table>
<thead>
<tr>
<th>Group and Case, Sex, Age (yr)</th>
<th>PE†</th>
<th>Renal Failure</th>
<th>Hepatic Impairment</th>
<th>Bleeding</th>
<th>CNS</th>
<th>CVS</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1, M, 21</td>
<td>+ +</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>2, M, 20</td>
<td>+ +</td>
<td></td>
<td>(- +)‡</td>
<td>+</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>3, M, 58</td>
<td>+ †</td>
<td></td>
<td>(- +)‡</td>
<td>(+ +)§</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>4, F, 47</td>
<td>+ +</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Died</td>
</tr>
<tr>
<td>5, M, 34</td>
<td>+ +</td>
<td></td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>6, M, 18</td>
<td>+ +</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
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</tr>
<tr>
<td>7, M, 25</td>
<td>+</td>
<td></td>
<td>-</td>
<td>+</td>
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<td></td>
<td>Survived</td>
</tr>
<tr>
<td>NPE</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8, F, 21</td>
<td>-</td>
<td>(+ +)‡</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>9, M, 23</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>10, M, 80</td>
<td>-</td>
<td>(+ +)‡</td>
<td>+</td>
<td>-</td>
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<td>Died</td>
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<td>11, M, 25</td>
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</tr>
<tr>
<td>12, F, 51</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
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<td>+</td>
<td>-</td>
<td></td>
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<td>Survived</td>
</tr>
</tbody>
</table>

* = Not present; +, present; and + +, present and severe.
†D, Day PE developed; and A, PE on admission.
‡Oliguric renal failure.
§Hepatic encephalopathy.

**Table 1—Clinical Data**
Table 2—Laboratory Data*

<table>
<thead>
<tr>
<th>Group and Case</th>
<th>Infected RBCs, percent†</th>
<th>Hematocrit, percent</th>
<th>Total Bilirubin, mg/dl</th>
<th>Albumin, g/L</th>
<th>BUN/Creatinine, mg/dl</th>
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<td>A</td>
<td>PE</td>
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<td>Normal value</td>
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<td>...</td>
<td>0.2-1.2</td>
<td>42-52</td>
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</tr>
<tr>
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<td>5.9</td>
<td>25.5</td>
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<td>1</td>
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<td>6</td>
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<td>7</td>
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<td>11</td>
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<td>36</td>
<td>2.6</td>
<td>33.6</td>
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*A, Admission.
†Parentheses indicate infected red blood cells before admission.
‡Exchange transfusion.
§Negative.
(U) = Unquantified.

in all except case 13. Varying degrees of renal impairment were found in five of the seven cases with PE and four of the six cases with NPE. Four patients from both groups (cases 2, 3, 8, and 10) had oliguria. All patients in both groups had hepatic impairment; one patient with PE developed hepatic encephalopathy (case 3). One patient (case 1) had a convulsion after one day of treatment. Sensory changes occurred in four patients, two from each group. Circulatory disturbances occurred in five patients, three with PE and two with NPE. One had transient hypotension (case 1), while the other four (cases 4, 6, 10, and 12), two from each group, had persistent hypotension (more than 24 hours) and needed vasopressor therapy to maintain systolic blood pressure between 90 and 100 mm Hg. The lowest systolic blood pressure of 70 mm Hg was found in two patients (cases 10 and 12); one (case 10) of these two had clinical shock and later died.

Table 3—Initial Arterial Blood Gas Levels, Chest x-Ray Films and Echocardiogram

<table>
<thead>
<tr>
<th>Group and Case</th>
<th>pH</th>
<th>PaO₂, mm Hg</th>
<th>PaCO₂, mm Hg</th>
<th>Saturation, percent</th>
<th>Oxygen Therapy</th>
<th>Chest X-Ray Film*</th>
<th>EF, percent</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Early</td>
<td>Late</td>
</tr>
<tr>
<td>PE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7.394</td>
<td>269.5</td>
<td>37.8</td>
<td>99.6</td>
<td>Mask; 10 L/min</td>
<td>Normal; P1</td>
<td>52.07</td>
</tr>
<tr>
<td>2</td>
<td>7.329</td>
<td>76</td>
<td>31</td>
<td>92.8</td>
<td>Mask; 7 L/min</td>
<td>↑ Marking; P2</td>
<td>86.69</td>
</tr>
<tr>
<td>3</td>
<td>7.35</td>
<td>70</td>
<td>33</td>
<td>92.3</td>
<td>Mask; 6 L/min</td>
<td>PE</td>
<td>...</td>
</tr>
<tr>
<td>4</td>
<td>7.372</td>
<td>80</td>
<td>30</td>
<td>94.3</td>
<td>Room air</td>
<td>Normal; P1</td>
<td>89.20</td>
</tr>
<tr>
<td>5</td>
<td>7.363</td>
<td>34</td>
<td>45</td>
<td>56</td>
<td>Room air</td>
<td>PE</td>
<td>76.17</td>
</tr>
<tr>
<td>6</td>
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<td>125.5</td>
<td>33.8</td>
<td>98.7</td>
<td>FIO₂, 0.7</td>
<td>PE</td>
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</tr>
<tr>
<td>7</td>
<td>7.502</td>
<td>67</td>
<td>34</td>
<td>94</td>
<td>Cannula; 3 L/min</td>
<td>PE</td>
<td>62.53</td>
</tr>
<tr>
<td>NPE</td>
<td></td>
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<tr>
<td>8</td>
<td>7.412</td>
<td>59.3</td>
<td>31</td>
<td>89.2</td>
<td>Room air</td>
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<td>75</td>
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<tr>
<td>9</td>
<td>7.463</td>
<td>64</td>
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<tr>
<td>10</td>
<td>7.240</td>
<td>108</td>
<td>51</td>
<td>97</td>
<td>Cannula; 5 L/min</td>
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<tr>
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<td>95.3</td>
<td>Room air</td>
<td>↑ Marking</td>
<td>...</td>
</tr>
<tr>
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<td>82</td>
<td>35.5</td>
<td>96.3</td>
<td>Room air</td>
<td>Normal</td>
<td>89.20</td>
</tr>
<tr>
<td>13</td>
<td>7.369</td>
<td>107</td>
<td>34.2</td>
<td>97.9</td>
<td>Room air</td>
<td>Normal</td>
<td>53</td>
</tr>
</tbody>
</table>

*P1, PE developed on day 2 in ICU; and P2, PE developed on day 3 in ICU; ... not done.
from septic shock. The cause of death in the other patient (case 4) was PE, with postmortem findings of fibrosis, edema, hemorrhage, and hyaline membrane formation in both lungs.

Initial laboratory data are shown in Table 2. Six patients, three from each group, were initially treated at another hospital. Heavy parasitemia of 60 percent or more was found in three of seven patients with PE, while only one patient with NPE had 55 percent parasitemia or less. Exchange transfusion using 4,400 ml of blood in two cases (cases 1 and 2) resulted in a marked reduction in the rate of parasitemia to 3 to 4 percent at the end of the blood exchange. Jaundice, with the total bilirubin level ranging from 2.3 to 30.6 mg/dl and from 1.4 to 24.6 mg/dl, was noted in the PE and NPE groups, respectively. In PE, the BUN level ranged from 10 to 80 mg/dl, while the creatinine level was 1.4 to 5.6 mg/dl on admission. The respective values were 10 to 85 mg/dl and 1.4 to 8.0 mg/dl during PE. Hypoalbuminemia (35 g/L or less) was found in all patients in both groups (except case 7) on admission. Six of the seven patients with PE had persistent hypoalbuminemia on the day that PE developed. Thrombocytopenia of less than 100,000/cu mm was found in all cases except case 13. Increased FDP was found in three cases (cases 1, 3, and 9); however, the PT, PTT, and fibrinogen level were found to be normal in these three cases. Therefore, there was no case fulfilling the criteria of DIC in this study.

Table 3 shows initial arterial blood gas levels, chest x-ray films, and echocardiographic results. Varying degrees of alveolar-arterial oxygen gradient were found in all cases in both groups, except case 13. All cases were corrected with oxygen therapy. Four cases (cases 3, 5, 6, and 7) had initial PE characterized by a bilateral alveolar infiltrate which equally distributed throughout both lungs, except case 3, who had central predominance on the left side. All patients had a normal cardiac shadow. Three patients (cases 1, 2, and 4) who initially had NPE, developed a bilateral alveolar infiltrate similar to that previously mentioned on days 2 and 3. A reduction in the ejection fraction with cardiac dilatation was observed in two cases (cases 1 and 13); the abnormality reverted to normal in both cases within seven days.

**Hemodynamic Data**

Five cases had initial hemodynamic measurements when PE had already developed. The other eight patients had NPE at the beginning of the study, but two of these patients (cases 2 and 4) later developed PE on the second and third day of hemodynamic study. Therefore, the PE group consisted of seven cases, while the NPE group consisted of six cases. Five of the seven patients with PE and all patients with NPE had serial hemodynamic studies for at least four days.

The mean CI (±SEM) of both the PE and NPE groups was shown in Figure 1. The initial values for CI were elevated in both groups and remained so for two days. The PE group tended to have a higher initial CI (4.89 ± 0.3 L/m²/sq m) than did the NPE group (4.43 ± 0.6 L/m²/sq m), but the difference was not statistically significant (p > 0.05). The initial and subsequent values for SVI were found to be normal or high normal in both the PE and NPE groups. There were no statistically significant differences between the initial SVI of the two groups (50.6 ± 2.6 ml/beat/sq m in PE vs 47.3 ± 6.9 ml/beat/sq m in the NPE group; p > 0.05).

The mean SVR (±SEM) is shown in Figure 2. The mean SVR was initially low in both groups and remained so for two days. There was no statistically significant difference in the initial mean SVR between the PE group (849 ± 55 dynes-s-cm⁻²) and the NPE group (815 ± 136 dynes-s-cm⁻²) (p > 0.05).

Because of marked variations in the PVR, individual PVR was shown instead of mean PVR in Figure 3. Initially, a low PVR was found in all cases in both groups except one in the NPE group (case 12). The values remained low throughout five days in all except two cases in the NPE group (cases 10 and 12).

Individual values for PCWP are shown in Figure 4. In the PE group (Fig 4A), the initial PCWP measurement was done during the PE period in five of the seven cases. Three of the cases had elevated PCWP.
The other two patients, who had no initial PE, had normal PCWP. One patient later developed PE with a concomitant rise in PCWP on the second day of hemodynamic measurement. The other patient developed PE on the third day, with a normal PCWP. Initial PCWP was elevated in three of the six cases with NPE (Fig 4B). Two remained high for one more day, and all except one had normal or low normal values from day 3 to 5. When initial mean values for PCWP were compared between the two groups, there was no statistically significant difference between the PE group (12±2.5 mm Hg) and the NPE group (13±3.2 mm Hg) (p>0.05).

DISCUSSION

Hemodynamic changes observed in most cases of falciparum malaria included a reduction in the SVR and PVR, along with an increased CI and a variable value for PCWP (both normal and increased PCWP were found). There was no difference in these parameters when comparison was made between the PE and NPE groups. Reduction in the SVR and PVR were found early in the course, with the latter being persistent throughout the study. This indicates that the initial pathophysiologic change in severe falciparum malaria was due to vascular dysfunction. We found in both groups an early abnormal alveolar-arterial oxygen tension gradient and hypoalbuminemia, which might imply the existence of pulmonary vasodilatation and increased pulmonary vascular permeability. Further support for pulmonary vascular changes were the postmortem findings of fibrosis, edema, hemorrhage, and hyaline membrane formation in both lungs of one patient with PE in the present

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21612/)

**Figure 2.** Mean SVR (± SEM) plotted against time for both PE and NPE. Hatched area represents normal minimum to mean resting SVR.

![Figure 3](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21612/)

**Figure 3.** Individual values for PVR of both PE and NPE plotted against time. Closed circles represent PE; open circles represent NPE; each circle represents one case in each day. Hatched area represents normal minimum to mean resting PVR.
study. Our findings are in agreement with previously
described reports regarding the role of pulmon-
ary vascular dysfunction as the cause of PE in severe
malaria; however, not all severely ill patients who had
pulmonary vascular dysfunction developed PE. The
fact that severe hypoalbuminemia of 25 g/L or less
was found more commonly in PE (five of seven cases)
than NPE (one of six cases) indicates that pulmonary
vascular dysfunction with protein leakage might be
more severe in PE than NPE initially. The severity of
pulmonary vascular dysfunction might determine the
development of PE.

The causes of pulmonary vascular dysfunction are
unknown. The hemodynamic changes in the present
study seem to be related to the presence of parasite-
ia. Heavy parasitemia (more than 60 percent infected
red blood cells) was found more commonly in PE than
NPE. Pulmonary vascular dysfunction might be
related to parasitemia and its severity, or to the follow-

ing possibilities which are known to be associated with
malaria: In experimental malaria, catecholamine-in-
duced PE was more in favor of the role of mediator-
induced increased pulmonary permeability than va-
soconstricting effect. Among the mediators which
had been found in experimental animal and human
malaria were kinins, histamine, complement, and TNF.
The role of a histamine-induced increase in pulmonary
vascular permeability was debatable and unlikely. Endotoxin, which had been
found in human and animal malaria, might activate

kinin and the complement system, causing hemody-
namic changes similar to those found in uncomplicated
bacteremia. Tumor necrosis factor, which has a wide
variety of biologic actions, might cause pulmonary
vascular injury and unexplained pathologic findings in
malaria; however, clinical shock is not a common
complication of severe malaria, except in terminal
cases. Mediators of pulmonary vascular dysfunction
might be different from those implicated in other
infections where pulmonary insufficiency is often
accompanied by systemic circulatory failure. We could
not find any evidence implicating DIC as a cause of
pulmonary vascular injury in one postmortem case.
Fulfilled criteria of DIC (thrombocytopenia less than
100,000/cu mm; prolonged PT and PTT; decreased
fibrinogen; and increased FDP) were not found in
both groups; only a raised level of FDP was found in
cases. As a matter of fact, renal failure in these
cases may be responsible for these findings. It is thus
unlikely that DIC is the cause of pulmonary vascular
injury.

Increased PCWP was found in both PE and NPE
cases. The finding either indicates the presence of
CHF or fluid overload. High CI, which was found in
almost all cases in both PE and NPE groups, might
indicate normal cardiac function; however, in the
presence of severe infection, CI was not a good
indicator of cardiac function. Further confirmation
showing normal ejection fraction and cardiac con-
traction in most of our cases provided good evidence that

*Figure 4. Individual values for PCWP plotted against
time in PE (A, top) and NPE (B, bottom). Each circle
represents one case in each day. In A (top), asterisks
represent patients who had PCWP measured during
PE. Closed circles represent PCWP measured without
PEEP. Open circles with central dot represent PCWP
during PEEP. Dashed line represents normal resting
PCWP.
high PCWP was not due to CHF but should be due to fluid overload. Although there was no evidence of positive fluid intake in these cases, endogenous fluid accumulation, which has been demonstrated in human malaria, 9,36,37 might be responsible for high PCWP.

During PE, both normal and increased PCWP, along with increased CI, were found; and increased PCWP, which favored volume overload, was found in both PE and NPE groups. Lowering PCWP to a normal value did not clear PE on chest x-ray films. Volume overload should not be the contributor but only an aggravating factor for the genesis of PE. The fact that PE commonly occurred on the second and third day of hospitalization (patients with PE on admission were known to be treated for a few days prior to admission at another hospital) indicates that poor intake and excessive perspiration might prevent fluid overload, while poorly monitored fluid therapy might aggravate PE. Hypoalbuminemia, the cause of reduced colloidal osmotic pressure, was found initially and persistently during PE. Hypoalbuminemia, when added to volume overload, can aggravate PE in the presence of increased pulmonary vascular permeability.11 This complex mechanism might be needed for the genesis of PE in some patients who had less severe pulmonary vascular dysfunction.

Our findings might offer a better understanding of clinicophsyologic change and its therapeutic implications. Early diagnosis and treatment with a specific antimalarial drug is undoubtedly the best way to prevent systemic complications. Only good supportive care was needed when systemic complications did occur. Heparin and the corticosteroids previously used to treat DIC (an uncommon finding) and permeability change might result in severe complications and a high mortality. These agents have not been given in this study. Avoidance of aggravating factors, close monitoring of fluid therapy, good nutrition, and correction of hypoalbuminemia are mandatory. Early dialysis and respiratory support should be instituted when needed. The use of PEEP instead of IPPB in patients who had intractable hypoxia might prevent hypoxic death, which has been found in other series. All supportive measures used in the present series could result in a low mortality.

In summary, hemodynamic changes in severe falciparum malaria were found to be compatible with systemic and pulmonary vasodilatation. Although early hypotension was quite common, clinical shock was an uncommon finding and may serve to distinguish severe malaria from other infections. The hemodynamic changes could not predict the outcome and the subsequent development of PE; however, severe pulmonary vascular changes seemed to be more common in PE than in NPE, and increased pulmonary vascular permeability was found to be the cause of PE. Fluid overload and hypoalbuminemia in severe malaria were found to be the aggravating factors for the development of PE. There was no evidence that CHF was a contributor to the development of PE.

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