Confusion and decreased awareness are among the earliest signs of developing sepsis and yet very little is understood about brain dysfunction in systemic sepsis. A number of authors have tried to define septic encephalopathy but as the quoted incidence of between 9 and 71% of all patients with sepsis illustrates [1-4], the exact definition remains vague.

It was Hippocrates (460-370 B.C.), over 2000 years ago, who first described the relationship between systemic illnesses and brain dysfunction. He wrote of liver dysfunction and personality changes, “those who are mad on account of phlegm are quiet, but those on account of bile are vociferous, viscous and do not keep quiet” [5]. For septic encephalopathy he described “phrenitis” as a complication of fever, abscesses or spreading redness and swelling of the limbs [6]. Galen (131-200 A.D.) too, observed these relationships [7,8], stating that inflammation affected the mind “sympathetically” causing delirium. Yellow bile was thought to induce acute diseases running a rapid course and accompanied by a high temperature and black bile was believed to cause disease such as mental derangement, apoplexy and convulsions [5].

Sepsis and its sequelae is the leading cause of death in intensive care units (ICUs), accounting for 10 -50% of all deaths [1]. Mortality increases as the number of organs failing increases, reaching almost 100% with six organ failure [9]. Brain failure or septic encephalopathy is included in this analysis and its individual effect on mortality verified by the Veterans Administration systemic sepsis study [2] which found that hypothermia, hypotension, thrombocytopenia and the absence of shaking chills plus an altered mental status were predictive of mortality.
CLINICAL FEATURES

The exact definition of septic encephalopathy remains elusive, primarily because it is usually considered after the patient has been sedated for treatments such as mechanical ventilation. In a prospective study, prior to such interventions, of 69 patients with fever and a positive blood culture, Young and colleagues [3] found 49 (71 %) had evidence of brain dysfunction on detailed clinical testing. Seventeen had a mild encephalopathy and 32 had severe brain dysfunction and it is this study that provides us with one of the better clinical descriptions of septic encephalopathy.

The diagnosis requires evidence of extra-cranial infection and an impaired mental state. Patients behave inappropriately becoming, agitated, disorientated and confused and as severity worsens they become increasingly less responsive. Paratonic rigidity (a velocity dependent resistance to passive movement of the limbs) is said to be typical but focal signs, seizures and cranial nerve palsies are rare and warrant careful search for an alternative explanation. Asterixis, tremor and multifocal myoclonus, found in hepatic and uraemic encephalopathies are not typical of septic encephalopathy. Table 1 lists some of the alternative diagnoses that might be considered in a patient with fever and an altered mental state. Most will be obvious from the presenting history or associated signs and symptoms.

Other clinical indices of sepsis or septic shock have been suggested to correlate with the severity of the septic encephalopathy. Eidelman and colleagues [4] in a prospective study of 50 patients with altered mental status found that a deteriorating Glasgow Coma Score was the best measure of encephalopathy and predictive of mortality. They also found a correlation with blood urea concentrations and bilirubin but not with other metabolic or physiological indices. In contrast, Young and colleagues [3] found a variety of abnormalities correlated with the severity of brain dysfunction, including, axonal neuropathies, increased white cell count, increased blood concentrations of alkaline phosphatase, bilirubin, creatinine, urea, phosphate and potassium and decreased blood pressure and serum albumin levels. However, none of the markers of other organ damage were severely enough deranged to account for the encephalopathy independently.

INVESTIGATIONS

In septic encephalopathy, lumbar puncture may reveal a mild elevation in protein content in the cerebrospinal fluid (CSF), but cell counts and glucose concentrations are unaffected. The value of performing lumbar punctures in all patients with fever and an altered mental state is disputed but they may be