

EDITORIALS



Intravenous Fluids — Getting the Balance Right

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Acute infections are a major cause of illness and death in children worldwide. In Africa, 50 percent of in-hospital deaths of children occur within 24 hours of admission, and shock complicates many cases.¹ The provision of emergency advanced life support for critically ill children would have an important effect on survival in the developing world, where acute infections are common.^{1,2} Ways must be found of ensuring emergency care in resource-poor settings, where sophisticated point-of-care analyses, intensive monitoring, and specialist care are rarely present; basic laboratory studies cannot be done in a timely fashion; the choice of intravenous fluids is limited; infusion pumps and equipment sized for children are scarce; and often the primary diagnosis is unconfirmed and complicated by delay, poor nutritional status, and possibly HIV infection.

Efforts to lessen childhood mortality have largely ignored triage and emergency care as interventions for child-survival programs, though these interventions are required by millions of children and may be highly cost-effective. It is for people living and working in these resource-poor settings that the study by Wills et al.,³ reported in this issue of the *Journal*, is so important.

Wills et al. investigated fluid treatment for Vietnamese children with dengue shock syndrome. With the use of simple clinical monitoring tools, the authors have shown that the administration of Ringer's lactate leads to the same outcome among children with moderate shock as does the administration of colloids. They confirm reassuringly the World Health Organization (WHO) protocol for patients with dengue and moderate shock. Among children with severe shock, they found that dextran or starch was equally effective but that dextran

caused more hypersensitivity reactions. Whether Ringer's lactate would be as effective remains untested.

The emergency management of dengue shock syndrome is unusual because fluid loss from leaky capillaries into the interstitial space is relatively slow and the development of pulmonary edema and cardiac instability mitigates against rapid fluid replacement. This disease requires a specific protocol, and Wills et al. have provided a safe and available mode of action. But these results cannot be translated to most other cases of shock. It may not be possible to find a single fluid-management protocol that works for all causes of shock — but what can be said to those who face these medical problems with little laboratory and clinical support?

The basic life-support approach to the treatment of a critically ill child is a workable approach. Several studies have shown that frontline staff at district hospitals, taught to use emergency triage, assessment, and treatment (known as ETAT) guidelines, have improved their recognition and treatment of sick children.^{1,2,4} This, rather than a syndrome-based approach, is appropriate at all levels of care. There is considerable overlap in the presentation of severe malaria, septicemia, and gastroenteritis, and often they coexist. The airway must be secured, oxygenation optimized, and vascular access established. Hypoglycemia must be corrected. The type of fluid needed to restore volume and circulatory deficits depends on the cause, the clinical presentation, and coexisting conditions, which are important determinants of potential complications of volume resuscitation.

The choice of resuscitation fluids has been a therapeutic question surrounded by much debate about the optimal fluid. Physiologic crystalloids

such as normal saline (0.9 percent sodium chloride solution) and Ringer's lactate are cheap and widely available. Because they equilibrate freely across the intravascular and extravascular compartments, large volumes may be required to improve perfusion, with the risk of fluid overload.⁵ Many protocols advocate the use in shock of 0.9 percent sodium chloride, which has been shown to be as effective as 4.5 percent human albumin in adults admitted to intensive care units.⁶ However, large volumes of normal saline may cause hyperchloremic acidosis, and with no glucose or potassium, its use in some cases of shock, acidosis, or electrolyte imbalance could make matters worse. Ringer's lactate is a physiologic solution, and large volumes do not cause metabolic acidosis.^{7,8} It has been tried and tested in patients with cholera and other causes of hyponatremic dehydration. Wills et al. have shown its value in dengue shock syndrome, but its place in septic shock is untested.

The use of hypotonic solutions (e.g., half-strength Darrow's solution with 5 percent glucose [sodium, 61 mmol; potassium, 17 mmol; chloride, 52 mmol; lactate, 27 mmol; glucose, 50 g; and calories, 200 per liter]), advocated by the WHO owing to concern about sodium overload in the treatment of shock in patients with severe malnutrition, may be appropriate when the primary problem is depletion of intracellular volume due to dehydration. Hypotonic solutions generally are not advocated for the correction of shock until the circulating volume has been restored with isotonic solutions or colloids. In children with hypernatremic dehydration (clinically identifiable by a doughy feel to the skin and by irritability), the serum sodium concentration may be alarmingly high, and sodium-rich fluids should be avoided. Colloids — human albumin solution and cheaper synthetic colloids — exert plasma oncotic pressure and theoretically offer improved perfusion with less risk of fluid overload. However, they are expensive, are not widely available, and are associated with safety concerns such as coagulation and allergic reactions. Transfused whole blood could act as a physiologic colloid, but it is rarely readily available and carries considerable risk of transfusion-associated HIV transmission in many localities.⁹

Life-support courses^{10,11} and now Wills et al. have all shown that shock can be assessed and monitored effectively without high-tech facilities. Pulse rate, pulse pressure, blood pressure, capillary refill,

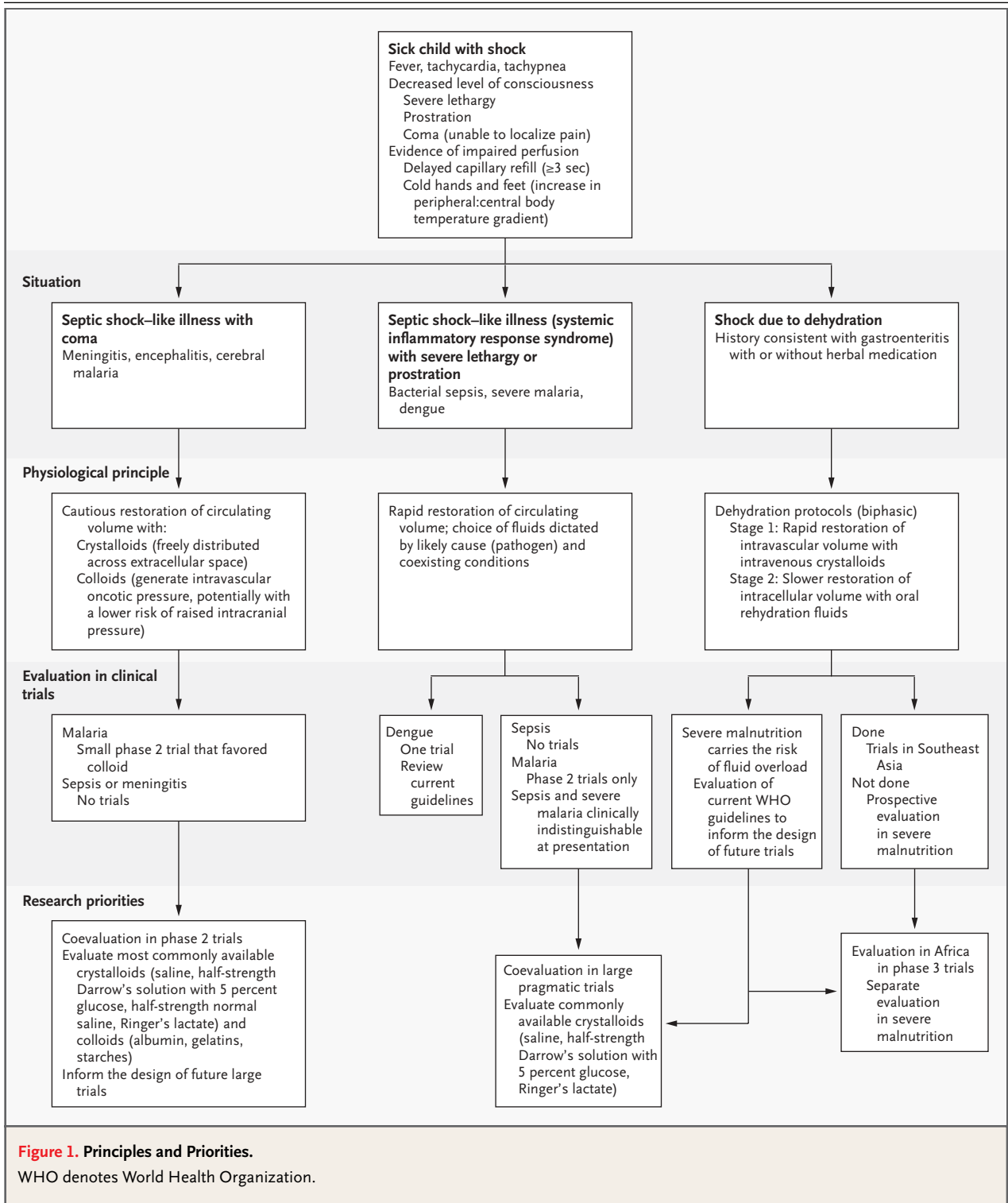
peripheral temperature, coma score, urine output, and oxygen saturation are simple and effective both in diagnosis and as serial measurements to monitor treatment response.

What about vulnerable groups? For children with hypovolemic shock, it is often impossible to distinguish between severe invasive bacterial disease and malaria. Severe dehydration may be differentiated by history and clinical signs. An additional problem is that often an herbal medication is given by parents to children with gastroenteritis, causing a profound hypernatremic metabolic acidosis. Whereas severe hypernatremia (serum sodium concentration, >150 mmol per liter) and hyponatremia (serum sodium concentration, <130 mmol per liter) can often be diagnosed correctly from clinical signs, the concentrations in between are far less clinically predictable.

Both sepsis and severe malaria are complicated by central nervous system involvement, with the risk of raised intracranial pressure. In pediatric critical care units with ample resources, the coexistence of hypovolemic shock and impairment of consciousness in suspected sepsis has led to the development of protocols that include the administration of colloids. A small phase 2 trial involving patients with cerebral malaria complicated by shock has provided some support for the use of colloids but needs confirmation in larger trials.¹² However, the adoption of these protocols is difficult in Africa owing to the prohibitive costs. Furthermore, many children in Africa have coexisting conditions — namely, anemia and malnutrition — that are seen as relative contraindications to fluid resuscitation, and hypovolemia is often left uncorrected, resulting in cardiovascular collapse and death.

Cerebral edema will develop in some children who have infections of the central nervous system or severe systemic disease. Approximately one third of children with bacterial meningitis will have hyponatremia (serum sodium concentration, <130 mmol per liter). Maintenance fluids may be given in the form of half-strength Darrow's solution with 5 percent glucose or as 0.45 percent sodium chloride solution with 5 percent glucose. Shock requires rapid delivery of fluid; maintenance should be at normal requirements.¹³

More research is required, especially among children with severe malnutrition who are in shock (with or without severe dehydration), to improve the evidence base of current guidelines. Large, prag-



matic trials are needed in which the treatment assignment takes into account the major syndromes associated with shock (Fig. 1).

High-quality trials are essential to inform patient management and guide policy. Improving child survival with the development of a simple management protocol will have benefits beyond the boundaries of any one illness. But to achieve large-scale success with a simple protocol, it will be vital to increase human resources and train and support the staff in small hospitals in developing countries.

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Hepatitis A — The Price of Progress

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Hepatitis A tends to be a self-limited disease without serious sequelae and with a low case fatality rate¹; unlike hepatitis B and hepatitis C, hepatitis A is not a cause of chronic liver disease. On the other hand, approximately 1.4 million clinical cases of hepatitis A occur each year worldwide, and in the United States, hepatitis A is a common cause of acute hepatitis and one of the most frequently reported vaccine-preventable diseases,¹ responsible for a substantial economic burden on society.²

A seemingly welcome observation has been the recent decline in the incidence of new cases reported yearly in the United States. From an average annual incidence of 28,000 cases (9 to 14 cases per 100,000 population) reported to the Centers for Disease Control and Prevention during the 1980s and 1990s, the incidence of reported cases has been declining during the past 10 years toward the lowest ever recorded — 7600 cases annually (2.7 cases per 100,000 population) in 2003.³

The downside of the reduction in new infections with hepatitis A virus has been a declining prevalence of antibody to hepatitis A in the population and the emergence of an adult population with limited immunity to infection. This temporal trend

parallels an important dichotomy in the clinical expression of hepatitis A infection that relates to geographic differences in the endemicity of infection. In communities with a high prevalence of hepatitis A, infections with this enteric agent are most likely to occur in children, in whom the disease tends to be asymptomatic or mildly symptomatic.¹ With advances in environmental hygiene that are typical of developed countries, the frequency of enteric infections, such as that with hepatitis A, declines, and children are spared, but the level of natural immunity in the population declines, and adults remain susceptible.¹ When adults are infected, however, the resulting illness tends to be more severe.⁴ Paradoxically, then, as hepatitis A becomes less common, the burden of new infections shifts from children to adults, and the frequency of clinically severe acute hepatitis A increases — an unintended consequence of progress.

In the United States, despite declining rates of infection, sporadic outbreaks of foodborne hepatitis A continue to occur, and with increasing regularity, foodborne outbreaks unrelated to an index food handler have attracted attention. In this issue of the *Journal*, Wheeler and colleagues⁵ describe an