

## Correspondence

## Volume Status in Severe Malaria: No Evidence Provided for the Degree of Filling of the Intravascular Compartment

Kathryn Maitland, Charles Newton, Kevin Marsh, Mike Levin

The study by Planche et al. [1] provides important new information addressing intracellular volume depletion in children with severe childhood malaria, but does not address the question of whether intravascular volume depletion (hypovolemic shock) is present. Using sophisticated methodology to determine total body water and extracellular water, they demonstrate a 6.7% deficit in total body water and an 11.7% deficit of intracellular water, providing an important indication of the volumes of fluid that may be required to optimize hydration. The data, however, do not address the degree of filling of the intravascular compartment, nor should they be used to answer the question about the state of tissue and organ perfusion. Indeed, we believe that these new data present no conflict with our previously reported findings. Using methods to study critical illness physiology that are widely employed within pediatric intensive care units for interpretation of circulatory status, we have demonstrated evidence for hypovolemia in 53 Kenyan children with severe malaria complicated by metabolic acidosis [2]. Our children were younger, had longer capillary refilling times (>3 s), lower central venous pressures (mean 2.9 cm H<sub>2</sub>O) and higher creatinines (>80 μmol/l): all features of compensated hypovolemic shock. Furthermore, hypotension (systolic BP < 80 mm Hg) was present in 44% of children with severe acidosis (base deficit >15). These findings also indicate important baseline differences in two cohorts of children studied. We agree that reconsideration of guidelines for acute fluid management is warranted, particularly when current recommendations await an adequate evidence base. Nevertheless, conflicting opinions on the question of volume status in children with severe malaria can be satisfactorily resolved only through prospective randomized trials that include both fluid resuscitation and control groups. While the design and conduct of such trials will involve considerable challenges, optimal fluid management will never be resolved on the basis of theoretical consideration alone. ■

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### Authors' Reply

We are pleased that Dr. Maitland and colleagues consider our data on volume status (intra- and extracellular) of Gabonese children to be important. We did not consider our children with severe malaria to have intravascular volume depletion for the following reasons. When we measured central venous pressures in a proportion of children on admission, there was no evidence of intravascular volume depletion (median [interquartile range] = 6.5 [3–7.5] cm water), and these values did not change significantly over 24 h, suggesting that our severely ill children had adequate filling pressures. Consistent with this observation, our severely ill children improved rapidly when markers of tissue hypoxia (blood lactate concentrations, tachycardia, and tachypnoea) were serially monitored and children were managed with a relatively conservative fluid replacement regimen. Interestingly, extracellular volume was not increased at admission or afterwards either. Capillary leakage, which commonly accompanies hypovolaemia associated with septic shock, was therefore unlikely to be a significant pathophysiological process in these children with malaria. There may be differences in the severe syndromes of malaria seen in different geographical locations, perhaps accounting for the clinical features attributable to compensated hypovolemic shock reported by Maitland and colleagues. Such differences can be assessed using simple and recently calibrated bioelectrical impedance analysis methodology as well as other techniques that monitor intravascular volumes. The design of optimal fluid management regimens for children with severe malaria can thus be informed not only by theoretical considerations, but also by appropriate physiological assessments. ■

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## Completing the Public Health HIV/AIDS Alphabet

**Arthur Ammann**

Dr. Gerberding outlines critical steps for arresting the HIV/AIDS epidemic [1]. She suggests moving ahead with “ABCs” and with “D” for diagnosis and “R” for responsibility. These are good suggestions—with increased HIV testing and individuals taking responsibility for their role in HIV spread, the epidemic might be slowed. We could continue to add incrementally to the alphabet soup of public health. But instead, we could choose to immediately implement the mainstays of public health—universal testing and contact tracing [2,3,4]. Every sexually active individual and every individual at risk for HIV deserves to know their HIV status. Thus, every HIV-infected individual must be called upon to be accountable for preventing HIV transmission. Contact tracing should be instituted for HIV just as it is for other infectious diseases. Those who have been exposed to HIV have a right to know how to protect themselves and if they too are infected, to be offered treatment [5]. HIV testing has too often focused on testing of women in a perinatal setting rather than universal testing in routine clinical care. Without universal voluntary HIV testing and contact tracing, we will see the continued tilt of the epidemic toward women, now at 55% of all HIV infections and in all likelihood at 75%–80% in another 8 to 10 years [6,7]. For too long the debate has been that contact tracing will result in physical abuse of women. Confining our definition of abuse of women to physical abuse alone is to have too narrow an ethical focus—HIV infection itself is an abuse of women or of anyone else. Universal HIV testing and contact tracing adds an essential comprehensive public health approach to the epidemic that will be successful in reducing the ever-escalating numbers of new infections. ■

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## Nepal's War and Conflict-Sensitive Development

**Sonal Singh**

I would like to share my experience from nearly a decade of civil war between the Maoist rebels and the Royal Nepalese Army in Nepal in reference to the article by Zwi [1] on the expanding role of health communities in times of conflict. The current war in Nepal has led to widespread destruction of limited infrastructure and has adversely impacted access to health-care services and personnel, affecting family planning, maternal and child health programs, and immunization services throughout the country. While Nepal is flooded with non-governmental organizations, paradoxically, humanitarian assistance may have unknowingly exacerbated the conflict by perpetuating the same inequalities that led to the conflict in the first place. This has brought to the fore the need for “conflict-sensitive development” [2]—development sensitive to the (conflict) environments in which they operate, in order to reduce the negative impacts of their activities—and to increase their positive impacts—on the situation and its dynamics. Development projects can continue in less affected areas with a need for transitional programs in conflict areas that can adapt to the rapidly changing environment. If agencies are unable to function, they have required the help of humanitarian agencies such as Médecins Sans Frontières with experience in conflict settings. Some agencies have adopted a participatory role in development and have involved neutral local agencies, increasing community participation in their projects with good success. But there is a need for increasing coordination between organizations working in various health-related projects. Health-care workers across the world in different conflicts are in a unique position to leverage something of universal importance—the promise of good health [3]. Raising awareness of the issues surrounding conflicts will act as a catalyst for change. ■

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## Three More Learning Points

### Ignacio Garcia-Doval

After reading the Learning Forum by Fleming and Lynn [1], I would like to suggest three learning points that, in my opinion, should receive more attention.

(1) Morphology: the essential point of dermatological diagnosis is morphology, a low tech, but hard to master, skill. Dermatological diagnosis, as any other medical diagnosis, starts by collecting adequate information from the patient, and follows by its elaboration. Many doctors consider that dermatological diagnosis can be made on a quick recognition basis, but an ordered and syndromic approach is essential to get to an adequate diagnosis. I think that most dermatologists would agree that a good description of a patient by an experienced colleague is a better starting point for diagnosis than many pictures. I would describe the lesions seen in Figure 1 of [1] not simply as shallow ulcers, but as clearly polycyclic erosions (a finding highly suggestive of herpetic infection).

(2) Indicated investigations: Tzanck test is the microscopic evaluation of cell morphology on a cutaneous smear. It can be done in about 15 minutes, requiring a microscope and a trained doctor. Access to this test is probably much easier than to viral cultures or polymerase chain reaction tests. In this setting, a positive Tzanck test would be enough to confirm the clinical diagnosis at a minimum cost. Considering the widespread audience of *PLoS Medicine*, with many readers in less developed countries, this test should not be forgotten.

(3) This case, and the suspicion about systemic manifestations of skin disease, is a wonderful opportunity to disseminate an old concept, very frequently forgotten in medical literature: the skin is an organ, in fact, the biggest

one in the body. Its main functions are to act as a barrier, to control temperature, to serve immunological and hormonal roles, and, physiologically less important but very important for patient well-being, to participate in personal relationships. When these functions are not adequately performed, skin failure appears, exactly as is the case with heart or renal failure. Skin failure can have many manifestations, including noninfectious fever, bacteremia, or sepsis. As is the case with renal or cardiac failure, it is easier and more practical to learn about this syndrome than to discuss the systemic manifestations of the many diseases that can cause it. I would highly recommend the following references for doctors interested in the subject: [2,3]. ■

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