

### Regarding “Dengue—How Best to Classify It”

TO THE EDITOR—The 2009 World Health Organization (WHO) revised dengue classification has been welcomed by many and questioned by some [1]. Since the 1980s, a broad consensus has developed among the clinical dengue community that the dengue fever (DF)/dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS) classification was both essentially retrospective and overly complex, limiting its usefulness for patient management and global surveillance [2–8]. Following calls for revision of the system, evidence including data from a large prospective study enrolling >2000 patients across 7 endemic countries was reviewed at an expert meeting convened by WHO in 2008, after which the new, simpler classification was adopted. Since then, other studies have looked at the effectiveness of the revised classification in a number of hospitals in different countries [9–11].

A recent Viewpoints article published in this journal outlines the case for retention of the 1997 DF/DHF/DSS classification [12]. We agree with the authors on several points—in particular, that although dengue is a dynamic and multifaceted disease, altered capillary permeability is a critical feature of severe disease and must be identified promptly and managed appropriately—but feel that certain clarifications are warranted.

First, the inclusion of severe organ involvement as the third criterion for severe dengue does not shift attention away from plasma leakage. The term *dengue shock syndrome* is retained and listed first, focusing attention on altered capillary permeability, plasma leakage, and shock as the primary manifestations of severe disease. The inclusion of severe organ involvement gives clinicians the opportunity to report cases that were previously ignored and helps describe the full extent of severe syndromes associated with infection. This is particularly important as dengue spreads to new geographic areas and the clinical picture diversifies.

Second, the authors appear to use the terms *case classification* and *case definition* interchangeably. DHF is clearly a highly specific syndrome and in the past has often been used as a surrogate for dengue diagnosis in the absence of laboratory confirmation. However, it has been repeatedly shown that the DHF/DSS classification misses approximately 20% of confirmed dengue cases with shock [6, 13, 14], and when used as a case definition, the associated sensitivity was only 36% in a recent assessment by the same authors [14]. The authors also express concern that the presence of warning signs might be used alone as diagnostic criteria, thereby overloading local healthcare systems in endemic settings. However, the new system makes clear that when no signs of plasma leakage are present, laboratory confirmation of dengue is important [1]. Improvements in early diagnosis and risk prediction for severe disease are

undoubtedly needed and research efforts in this area are ongoing.

Clinicians have long since wanted a classification that reflects clinical severity in real time. We believe the revised case classification with its simplified structure will facilitate effective triage and patient management and also allow collection of improved comparative surveillance data. Change is often difficult, but with commitment to research focused on improving early diagnosis and risk prediction, it should be possible to harmonize the new scheme globally across all epidemiological settings. The requirements of clinicians and public health officials dealing directly with the global pandemic are clearly paramount, but efforts are also being directed toward development of tighter definitions of severe phenotypes for basic science research.

## Notes

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## References

- World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. New ed. Geneva, Switzerland: WHO, 2009.
- Balmaseda A, Hammond SN, Perez MA, et al. Short report: assessment of the World Health Organization scheme for classification of dengue severity in Nicaragua. *Am J Trop Med Hyg* 2005; 73:1059–62.
- Bandyopadhyay S, Lum LC, Kroeger A. Classifying dengue: a review of the difficulties in using the WHO case classification for dengue haemorrhagic fever. *Trop Med Int Health* 2006; 11:1238–55.
- Deen JL, Harris E, Wills B, et al. The WHO dengue classification and case definitions: time for a reassessment. *Lancet* 2006; 368: 170–3.
- Murgue B, Deparis X, Chungue E, Cassar O, Roche C. Dengue: an evaluation of dengue severity in French Polynesia based on an analysis of 403 laboratory-confirmed cases. *Trop Med Int Health* 1999; 4:765–73.
- Phuong CX, Nhan NT, Kneen R, et al. Clinical diagnosis and assessment of severity of confirmed dengue infections in Vietnamese children: is the World Health Organization classification system helpful? *Am J Trop Med Hyg* 2004; 70:172–9.
- Rigau-Perez JG. Severe dengue: the need for new case definitions. *Lancet Infect Dis* 2006; 6:297–302.

- Sumarmo, Wulur H, Jahja E, Gubler DJ, Suharyono E, Sorensen K. Clinical observations on virologically confirmed fatal dengue infections in Jakarta, Indonesia. *Bull World Health Organ* 1983; 61:693–701.
- Barniol J, Gaczkowski R, Barbatto EV, et al. Usefulness and applicability of the revised dengue case classification by disease: multicentre study in 18 countries. *BMC Infect Dis* 2011; 11:106.
- Basuki PS, Budiyo, Puspitasari D, et al. Application of revised dengue classification criteria as a severity marker of dengue viral infection in Indonesia. *Southeast Asian J Trop Med Public Health* 2010; 41: 1088–94.
- Narvaez F, Gutierrez G, Perez MA, et al. Evaluation of the traditional and revised WHO classifications of dengue disease severity. *PLoS Negl Trop Dis* 2011; 5:e1397.
- Srikiatkachorn A, Rothman AL, Gibbons RV, et al. Dengue—how best to classify it. *Clin Infect Dis* 2011; 53:563–7.
- Alexander N, Balmaseda A, Coelho IC, et al. Multicentre prospective study on dengue classification in four South-East Asian and three Latin American countries. *Trop Med Int Health* 2011; 16:936–48.
- Srikiatkachorn A, Gibbons RV, Green S, et al. Dengue hemorrhagic fever: the sensitivity and specificity of the World Health Organization definition for identification of severe cases of dengue in Thailand, 1994–2005. *Clin Infect Dis* 2010; 50:1135–43.

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