proach), we have posted a case at NEJM.org. As the series on fluid and electrolyte disorders goes forward, various cases will be posted 2 weeks before publication of an upcoming review article. These cases will be followed by questions about the diagnosis or management of the condition to be considered in the article. We encourage you to read the case and tell us how you would manage the patient's treatment. We will post the results of this online poll to coordinate with publication of the review article.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

1. Berend K, de Vries APJ, Gans ROB. Physiological approach to assessment of acid–base disturbances. N Engl J Med 2014;371: 1434-45.

2. Cirillo M, Capasso G, Di Leo VA, De Santo NG. A history of salt. Am J Nephrol 1994;14:426-31.

3. Manz F. History of nutrition and acid-base physiology. Eur J Nutr 2001;40:189-99.

4. Thomas SJ, Edwards PP, Kuznetsov VL. Sir Humphry Davy: boundless chemist, physicist, poet and man of action. Chemphyschem 2008;9:59-66.

5. O'Shaughnessy WB. Experiments on the blood in cholera. Lancet 1831-32;1:490.

6. Latta T. Relative to the treatment of cholera by the copious injection of aqueous and saline fluids into the veins. Lancet 1832; 2:274-7.

7. Chieffi G. Osmoregulation at the Zoological Station of Naples at the end of the 19th century. Am J Nephrol 1994;14:458-60.

8. Pitts RF, Lotspeich WD. Bicarbonate and the renal regulation of acid base balance. Am J Physiol 1946;147:138-54.

9. Gamble JL. Chemical anatomy, physiology and pathology of extracellular fluid. 5th ed. Cambridge, MA: Harvard University Press, 1949.

10. Darrow DC, Pratt EL, Flett J, Gamble AH, Wiese HF. Disturbances of water and electrolytes in infantile diarrhea. Pediatrics 1949;3:129-56.

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Ebola — An Ongoing Crisis

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In March 2014, an outbreak of a febrile illness associated with a high case fatality rate was identified in the Guéckédou region of Guinea-Conakry, a remote part of West Africa. An international field investigation was initiated. On April 16, the Journal published a preliminary report identifying the outbreak as due to Ebola virus.1 The initial sequence data showed that the outbreak strain was Zaire ebolavirus, but a strain distinct from those identified in prior outbreaks, such as those in the Democratic Republic of Congo (DRC) and Gabon. In Guinea there appeared to be ongoing human-to-human transmission. Over the next 4 to 8 weeks, the outbreak seemed to be resolving, as over 20 previous outbreaks have, with a substantial decline in new cases. We and many others thought it would soon be over.²

We were wrong. Cases started to appear over the summer, and the number increased exponentially as this viral infection spread more widely in Guinea–Conakry and in Liberia and Sierra Leone.³ Cases associated with travel have been identified in Senegal and Nigeria, and there is evidence of ongoing transmission in Nigeria.⁴ Recently, Ebola transmission has been identified in the DRC, although molecular data suggest that this event is unrelated to the ongoing West African outbreak.^{5,6} These molecular data provide the information we need to define important aspects of ongoing transmission dynamics and to guide control strategies. Currently, there is no effective treatment, but human vaccine trials have been initiated.⁷

As of September 18, 2014, there were 5335 identified cases of Ebola virus disease, with more than 2622 associated deaths, which is more than in all previous Ebola outbreaks combined.⁴ These numbers are nonetheless likely to be underestimates, given the limitations of case identification, and the fraction of deaths probably underestimates the case fatality rate, because the interval between case identification and death has been just over 2 weeks. Although clinical data remain sparse, it seems likely that effective basic supportive care may make the difference between life and death for an infected patient. Unfortunately, health care workers have been disproportionately affected owing to the tremendous demands of patient care and the difficulty of implementing the infection-control measures required to prevent transmission.8 The Ebola outbreak is having serious adverse effects on

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travel, commerce, and routine health care, such as care for malaria, which threaten to further disrupt the already precarious conditions in which millions of people in the region live.⁹

The fear associated with a virulent and potentially deadly contagious infectious disease, which respects neither borders nor social status, has captured the attention of the world. The responders, both local and international, have been dedicated and brave. But far more is needed. It is critical that all members of the global health community — health care workers, scientists, regulators, funders, governments, and local communities — collaborate in responding as rapidly as possible if we are to control this enlarging outbreak. For example, the move by regulators to allow vaccine trials to proceed quickly shows flexibility and good judgment.

We, as a global health care community, must move decisively to bring this dangerous epidemic under control and then to improve the health care systems in the affected region.¹⁰ This will require more resources and more health care workers on the front lines (see the Ebola Outbreak page at NEJM.org for volunteer opportunities). It will also require communication and teamwork to win the trust of those in the affected communities. The *Journal* will continue to report on this unprecedented outbreak with updates on the efforts to control it, the biomedical findings emerging from it, and the difficult stories of those who are suffering through it. Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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1. Baize S, Pannetier D, Oestereich L, et al. Emergence of Zaire ebola virus disease in Guinea — preliminary report. N Engl J Med 2014. DOI: 10.1056/NEJMoa1404505.

2. Center for Disease Control and Prevention. Outbreaks chronology: ebola hemorrhagic fever (http://www.cdc.gov/vhf/ebola/ resources/outbreak-table.html).

3. World Health Organization. Ebola Response Roadmap situation report 1: 29 August 2014 (http://apps.who.int/iris/bitstream/10665/131974/1/roadmapsitrep1_eng.pdf?ua=1).

4. World Health Organization. Ebola Response Roadmap update: 18 September 2014 (http://apps.who.int/iris/bitstream/ 10665/133833/1/roadmapsitrep4_eng.pdf?ua=1).

5. Gire SK, Goba A, Anderson KG, et al. Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. Science 2014;345:1369-72.

6. Virological analysis: no link between Ebola outbreaks in West Africa and Democratic Republic of Congo. Geneva: World Health Organization, September 2, 2014 (http://www.who.int/mediacentre/news/ebola/2-september-2014/en).

7. Cohen J. Ebola vaccines racing forward at record pace. Science 2014;345:1228-9.

8. Unprecedented number of medical staff infected with Ebola. Geneva: World Health Organization, August 25, 2014 (http://www.who.int/mediacentre/news/ebola/25-august-2014/en).

9. Ebola: economic impact already serious: could be "catastrophic" without swift response. Washington, DC: World Bank Group, September 17, 2014 (http://www.worldbank.org/en/news/ press-release/2014/09/17/ebola-economic-impact-serious -catastrophic-swift-response-countries-international -community-world-bank).

10. Investing in global health systems: sustaining gains, transforming lives. Washington, DC: Institute of Medicine, September 16, 2014 (http://www.iom.edu/Reports/2014/Investing-in-Global -Health-Systems-Sustaining-Gains-Transforming-Lives.aspx).

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Transfusion Threshold of 7 g per Deciliter — The New Normal

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Holst and colleagues¹ now provide definitive evidence in the *Journal* that a restrictive approach to blood transfusion not only reduced blood use by half but also did not cause harm to 998 critically ill patients with septic shock. It has been 15 years since the publication of the results of the Transfusion Requirements in Critical Care (TRICC) trial in the *Journal*.² In that Canadian Critical Care Trial Group study, 838 critically ill patients were randomly assigned to receive blood transfusions on the basis of a threshold of 7 g per deciliter or 10 g

per deciliter while also agreeing to undergo transfusion 1 unit at a time. Much like the results of the Transfusion Requirements in Septic Shock (TRISS) trial by Holst et al., approximately 50% less blood was administered in the restrictivestrategy group than in the liberal-strategy group. In contrast to this latest trial, overall trends and all the secondary analyses suggested that a liberal transfusion strategy may have resulted in increased mortality, increased rates of pulmonary edema, and increased rates of organ failure.

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