EDITORIALS

From Alchemy to Fluid, Electrolyte, and Acid–Base Disorders

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The article by Berend et al.[1] in this issue of the *Journal* is the first in a series of review articles that consider approaches to the understanding and management of fluid, electrolyte, and acid–base disorders. These disorders are among the most common conditions that we encounter as clinicians.

The topics discussed are long-standing concerns. The history of salt and its medicinal uses goes back for millennia,[2] and compounds that we currently call acids and bases[3] were identified in ancient times. During the Middle Ages, acids were known by alchemists, who were seeking to change base metals into gold. However, current knowledge about fluid compartments and the handling of electrolytes is based on work that began about 400 years ago with Santorio Sanctorius, who may be considered to be among the first investigators in quantitative experimental medicine.[3] Yet, although the foundations that permitted progress occurred earlier, little was known about the actual management of disorders of water and electrolyte balance until the 19th century. For example, Joseph Black recognized carbon dioxide and Antoine Lavoisier, oxygen, in the 18th century.[3] Sodium as an element was discovered by Sir Humphrey Davy only in the first decade of the 19th century.[4] Davy also isolated potassium, calcium, and chloride, but his research was not clinical.[4]

The modern understanding of the role of fluids and electrolytes in physiological homeostasis was triggered by the cholera pandemic that began in 1829.[5,6] The needs of people with that disease soon led to the earliest attempts at using intravenous electrolyte-replacement fluids, some of which were successful. The experience with cholera, as well as a growing body of knowledge about chemistry and body composition, led to more studies.

In the ensuing two centuries, much has been learned. Once the chemistry was known, efforts to understand the physiology thrived. Early experiments with osmoregulation were performed at the Zoological Station of Naples and elsewhere.[7] These investigators learned more about how the kidney and the lungs participated in maintaining homeostasis. In the mid-20th century, Pitts[8] and others discovered many of the basic principles of acid–base metabolism, and the studies by Gamble,[9] Darrow et al.,[10] and others led to an understanding of the role of individual anions and cations in maintaining electrolyte balance, as well as the need to correct abnormalities in fluids and electrolytes. Advances continue in many centers worldwide.

Today, we routinely expect to obtain measurements to determine acid–base and electrolyte status, and these measurements can be performed in minutes in regions of the world where advanced technology is available. And yet, in much of the world, far less information is available. Indeed, death due to fluid and electrolyte imbalance — as occurs in patients with cholera and probably Ebola virus infection — is still all too common in many areas.

This series in the *Journal* cannot, by the nature of the subject, be even close to complete. But we hope that the topics covered will provide a useful compendium of approaches to the questions that arise when fluid, electrolyte, and acid–base disturbances occur.

In preparation for the first two articles in the series, both of which focus on acid–base disorders (the first on the physiological approach and the second on the strong ion, or Stewart, ap-

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.

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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