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EDITORIAL

Introduction: education teaching article series on hemolytic uremic syndrome

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Introduction

Since its original description by Gasser nearly 50 years ago, hemolytic uremic syndrome (HUS) has been an object of fascination within both the lay and the medical communities. Reports of exotic outbreaks from around the globe and massive numbers of meat recalls have kept "hamburger disease" in the public consciousness, and new insights into the underlying pathophysiology have captured the attention of a broad spectrum of basic scientists and clinicians. In many ways, this situation is unique and difficult to account for. In day-to-day practice, HUS is an easy disease to recognize and diagnose accurately. As a newly identified infectious disease, it has had greater stamina than fellow travelers like Legionnaire's disease or hantavirus infection. The complement cascade is an important part of the innate host defense network, but it is not usually viewed as the vanguard of immunology.

So, what accounts for the continued allure of HUS? I think it is, in part, due to the sudden and overwhelming nature of this rare disease that usually strikes previously healthy children. Second, the multisystem involvement makes HUS that much more dramatic. Third, it fosters interaction between nephrologists and specialists in infectious disease, epidemiology, public heath, intensive care, endothelial function, and complement biology. Finally, despite the extensive knowledge about HUS, it remains a disease searching for a reliable and safe treatment to attenuate disease severity.

Over the past 10 years, it has become increasingly apparent that HUS is one clinical manifestation of a larger entity called thrombotic microangiopathy (TMA). This lesion is a well-defined pathological phenotype that reflects injury to the vascular endothelium and which can be triggered by a number of processes. TMA can result from bacterial toxins, medications, systemic illnesses, abnormalities in the regulation of the alternate complement system, and diminished activity of the von Willebrand factor cleaving protease, ADAMTS13. The understanding of rare and complicated disorders begins with adequate classification. Some have proposed breaking down TMA into diarrhea-related disease, complement-associated disease, ADAMTS13-related disease, and unclassified disease. Because derangements in complement regulatory proteins and ADAMTS13 are generally undefined at the onset of disease, an alternative clinical approach is to break TMA down into four categories: diarrhea-associated HUS, atypical non-familial HUS, atypical familial HUS, and thrombotic thrombocytopenic purpura (TTP). Although these schemes may be useful, they should be considered provisional until a full understanding of the mechanism of disease has been worked out for all forms of TMA.

In recognition of the broad interest in HUS among pediatric nephrologists, a series of educational articles by a range of international experts in this disease has been compiled. Each of the authors has made substantial contributions over long illustrious careers into defining the disease entity, its treatment, and its outcomes. Drs. Copelovitch and Kaplan have written two articles addressing the non-familial causes of atypical HUS [1, 2]. The contribution of pneumococcal-related HUS is especially timely, in view of the recent recognition that the incidence of this entity is increasing [3]. Dr. Taylor, and Drs. Zimmerhackl, Scheiring, and Andreoli, focus on diarrhea-related HUS, the most common form of TMA in children, and provide timely updates on the epidemiology and treatment of this illness [4, 5]. Finally, Dr. Loirat and her coworkers, who, along with their colleagues in France and throughout Europe

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have published numerous articles in this area, summarize what is known about the genetic forms of atypical HUS, focusing on those that have been linked to mutations in complement regulatory proteins [6].

Pediatric nephrologists have been at the forefront of research into HUS, and *Pediatric Nephrology* has provided a forum for the publication of numerous high-quality reports into experimental models of TMA [7], long-term prognosis after diarrhea-related HUS [8, 9], identification of new causes of non-familial atypical HUS [10], and the appropriate treatment of familial atypical HUS [11]. I am confident that this series of Teaching Articles will highlight the key advances made in the past and point the way to research that will lead to better treatments of all forms of TMA and HUS in the future.

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