

Preface

Respiratory syncytial virus (RSV) was first isolated from chimpanzees in 1955, and shortly thereafter from young children, and recognized as an important cause of serious lower respiratory tract disease in infants and young children, i.e., pneumonia and bronchiolitis. Shortly after its discovery efforts to develop a vaccine began. It is now over 50 years since its discovery and no safe and effective vaccine is yet available. The fact that the peak of disease occurs in young infants despite the presence of maternally acquired antibody and that humans have multiple disease-associated infections throughout life, foretell the challenge in inducing protective immunity with a vaccine. The first RSV vaccine, formalin-inactivated tissue culture grown virus (FI-RSV) formulated with alum, was ineffective, associated with enhanced respiratory disease, and raised concerns that other vaccines might also predispose to FI-RSV vaccine enhanced respiratory disease. Older children did not experience FI-RSV vaccine enhanced respiratory disease suggesting that prior infection establishes a safe immune response pattern. Therefore, development of RSV vaccines for the RSV naïve infant has focused on live-attenuated RSV or other live viruses expressing RSV genes, while other types of vaccines are being developed for older children and adults. Subsequent to the FI-RSV vaccine trial, a number of live-attenuated RSV strains, live virus and other gene expression systems, and protein subunit vaccines in different platforms have been developed and tested in animals and a few have also been studied in humans. No vaccine has yet shown sufficient promise to move toward licensure. However, the prospects for many candidate vaccines, as well as different vaccine platforms, will remain unknown until clinical trials in the selected target population for the vaccine are performed. Though the lack of success to date highlights the biological difficulties in developing an RSV vaccine, the efficacy of immune prophylaxis suggests a safe and effective vaccine is achievable. The availability of ever more powerful tools to study the immune response and pathogenesis of disease and ability to construct a wide variety of vaccines using different vaccine platforms suggest that an RSV vaccine should be within reach. Caren Hall who made so many contributions to our understanding of RSV wisely noted in a poem one of the ongoing challenges to achieving an RSV vaccine (Anderson and Heilman 1995).

*Immunity and RSV**What is this thing we call immunity?**Does it exist for ills from RSV?**Perhaps for mice within their splenic soul,**But in the babe, the old, what is its role?**Is there a pattern of response we can discern?**Or is it like night skies that change with each earth's turn,**With season, angle viewed, and light years passed?**Has each from different, fluid molds been cast?**Thus, is it only solitary stars we see.**And not a constellation called immunity?*

Caroline Breese Hall

We feel this book brings together in one place what we know about RSV and helps to organize the constellation of facts about the virus and host factors that can guide successful development of an RSV vaccine. We feel that a better understanding of the of clinical and epidemiologic features of infection, functional and structural features of the virus, pathogenesis of the associated disease, and the immune response it induces provide the underpinnings for success.

Finally, we mourn the passing of Caren Hall. She has been the queen of RSV and authored most of the seminal studies on the clinical and epidemiologic features of infection and transmission of the virus. Equally important, she has been



Caroline Breese Hall (center) teaching and mentoring

a wonderful friend to so many in the field and an example to all of an outstanding scientist with a kind and nurturing spirit. In recognition of what she accomplished and the person she was, we dedicate this book to her. We refer the reader to the obituaries published in the Journal of Pediatric Infectious Disease Society in May 2013 Plotkin et al. (2013); Caserta and Long (2013); Englund et al. (2013). These three tributes provide a glimpse into why we felt so honored to have known and worked with her.

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