Chapter 9
Immunology of Norovirus Infection

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Abstract Noroviruses are the leading cause of epidemic non-bacterial gastroenteritis worldwide. Despite their discovery over three decades ago, little is known about the host immune response to norovirus infection. The purpose of this chapter is to review the field of norovirus immunology and discuss the contributions of outbreak investigations, human and animal challenge studies and population-based studies. This chapter will survey both humoral and cellular immunity as well as recent advances in norovirus vaccine development.

9.1 Introduction

9.1.1 Norovirus Disease Etiology

Noroviruses (NoV) are the major cause of epidemic gastroenteritis in the United States and a significant cause of severe diarrhea in young children in developing countries [1, 2]. NoV is also the most frequent cause of acute gastroenteritis after ingestion of raw shellfish [3, 4, 5]. NoV symptomatic infection causes vomiting, watery diarrhea, nausea, abdominal cramps, fever and general malaise. Gastroenteritis induced by NoV is self-limiting and rarely fatal. Fatality in children and the elderly is usually caused by severe dehydration after NoV infection [2, 6, 7].

9.1.2 Classification

NoV belong to the family Caliciviridae, genus norovirus, and are currently divided into five distinct genetic classifications called genogroups (GI-V). Genogroups are
further subdivided into clusters, each categorized with a number and the name of the prototype strain. Each cluster is comprised of individual strains identified from various outbreaks and human and animal infections. GI, GII, and GIV affect humans, and currently there are 8 clusters for GI, and 17 clusters for GII [8]. It is not possible to determine the exact number of strains for each cluster and genogroup because new strains continue to be added.

9.1.3 Transmission

Transmission of NoV may occur via ingestion of fecal-contaminated food or water, exposure to contaminated fomites or aerosolized vomitus, and direct person-to-person contact [9, 10, 11, 12, 13, 14, 15, 16, 17]. In rare cases, transmission can occur through organ transplantation [16, 17]. A low infectious dose of less than 5 genomic copies (viral particles) could be enough to infect a healthy adult (Moe, C.L. et al., unpublished data). In certain symptomatic and asymptomatic individuals, virus can be shed for more than 3 weeks post-challenge or exposure [18, 19, 20]. In immunocompromised individuals, such as transplant recipients, NoV has been detected in stool specimens for up to two years after initial infection [16, 17, 21, 22, 23]. These individuals may be asymptomatic carriers of NoV and a possible reservoir for human NoV in a population.

9.1.4 Epidemiology

NoVs are the second most important cause of severe gastroenteritis in young children [24, 25], and may cause about 20% of endemic gastroenteritis in families [26]. Each year in the U.S., the public health impact of NoV is evidenced by the estimated 23 million infections that result in an estimated 50,000 hospitalizations and 310 fatal cases [27]. This number is probably a severe underestimate of the true burden of disease. In 2004, in the U.S., NoV was responsible for 48% of outbreaks among all reported gastroenteritis outbreaks and 79% of outbreaks among reported non-bacterial gastroenteritis outbreaks [28]. GI and GII strains cause the majority of human outbreaks. Analyses, based on published outbreak reports and national surveillance systems, suggest that most outbreaks are associated with GII strains [29]. Within GII, cluster 4 (GII.4), “Bristol”, has been currently associated with most of the published outbreak reports among all the GI and GII clusters.

NoV are classified by the Centers for Disease Control and Prevention (CDC) and the National Institute of Allergy and Infectious Diseases (NIAID) as a Bioterrorism Category B Priority Pathogen based on their high transmissibility, low infectious dose, and serious public health and economic impact. No vaccine is currently available.