virus-specific IgA production at the intestinal surface is short lived, complete protection against disease is only temporary. However, each infection and subsequent reinfection confers progressively greater immunity; thus severe disease is most common among young children with first or second infections. Immunologic memory is believed to be important in the attenuation of disease severity upon reinfection.

Diagnosis Illness caused by rotavirus is difficult to distinguish clinically from that caused by other enteric viruses. Because large quantities of virus are shed in feces, the diagnosis can usually be confirmed by a wide variety of commercially available EIAs or by techniques for detecting viral RNA, such as gel electrophoresis, probe hybridization, or PCR.

TREATMENT ROTAVIRUS INFECTIONS

Rotavirus gastroenteritis can lead to severe dehydration. Thus appropriate treatment should be instituted early. Standard oral rehydration therapy is successful for most children who can take fluids by mouth, but IV fluid replacement may be required for patients who are severely dehydrated or are unable to tolerate oral therapy because of frequent vomiting. The therapeutic roles of probiotics, bismuth subsalicylate, enkephalinase inhibitors, and nitazoxanide have been evaluated in clinical studies but are not clearly defined. Antibiotics and antimotility agents should be avoided. In immunocompromised children with chronic symptomatic rotavirus disease, orally administered immunoglobulins or colostrum may result in the resolution of symptoms, but the best choices regarding agents and their doses have not been well studied, and treatment decisions are often empirical.

Prevention Efforts to develop rotavirus vaccines were pursued because it was apparent—given the similar rates in less developed and industrialized nations—that improvements in hygiene and sanitation were unlikely to reduce disease incidence. The first rotavirus vaccine licensed in the United States in 1998 was withdrawn from the market within 1 year because it was linked with a low incidence of intussusception, a severe bowel obstruction.

In 2006, promising safety and efficacy results for two new rotavirus vaccines were reported from large clinical trials conducted in North America, Europe, and Latin America. Both vaccines are now recommended for routine immunization of all U.S. infants, and their use has rapidly led to a >70–80% decline in rotavirus hospitalizations and emergency department visits at hospitals across the United States. Indirect benefits from vaccination (i.e., herd immunity) have also been documented in many settings. In April 2009, the World Health Organization recommended the use of rotavirus vaccines in all countries worldwide. As of May 2013, a total of 42 countries, including 5 low-income countries in Africa and Asia, have incorporated rotavirus vaccine into their national childhood immunization programs. In Mexico and in Brazil, a decline in deaths from childhood diarrhea following introduction of rotavirus vaccines has been documented. Postmarketing surveillance has identified a low risk of intussusception in some countries; however, the benefits of vaccination exceed the risks, and no changes in vaccine administration policy have been implemented.

The different epidemiology of rotavirus disease and the greater prevalence of co-infection with other enteric pathogens, of comorbidities, and of malnutrition in developing countries may adversely affect the performance of oral rotavirus vaccines, as is the case with oral vaccines against poliomyelitis, cholera, and typhoid in these regions. Therefore, evaluation of the efficacy of rotavirus vaccines in resource-poor settings of Africa and Asia was specifically recommended, and these trials have now been completed. As anticipated, the efficacy of rotavirus vaccines was moderate (50–65%) in these settings when compared with that in industrialized countries. Nevertheless, even a moderately efficacious rotavirus vaccine would be likely to have substantial public health benefits in these areas with a high disease burden.

OTHER VIRAL AGENTS OF GASTROENTERITIS

Enteric *adenoviruses* of serotypes 40 and 41 belonging to subgroup F are 70- to 80-nm viruses with double-strand DNA that cause ~2–12% of all diarrhea episodes in young children. Unlike adenoviruses that cause respiratory illness, enteric adenoviruses are difficult to cultivate in cell lines, but they can be detected with commercially available EIAs. Adenovirus types 31 and 42–49 have been linked to diarrhea in HIV-infected and other immunocompromised persons.

Astroviruses are 28- to 30-nm viruses with a characteristic icosahedral structure and a positive-sense, single-strand RNA. At least seven serotypes have been identified, of which serotype 1 is most common. Astroviruses are primarily pediatric pathogens, causing ~2–10% of cases of mild to moderate gastroenteritis in children. The availability of simple immunoassays to detect virus in fecal specimens and of molecular methods to confirm and characterize strains will permit more comprehensive assessment of the etiologic role of these agents.

Toroviruses are 100- to 140-nm, enveloped, positive-strand RNA viruses that are recognized as causes of gastroenteritis in horses (Berne virus) and cattle (Breda virus). Their role as a cause of diarrhea in humans is still unclear, but studies from Canada have demonstrated associations between torovirus excretion and both nosocomial gastroenteritis and necrotizing enterocolitis in neonates. These associations require further evaluation.

Picobirnaviruses are small, bisegmented, double-strand RNA viruses that cause gastroenteritis in a variety of animals. Their role as primary causes of gastroenteritis in humans remains unclear, but several studies have found an association between picobirnaviruses and gastroenteritis in HIV-infected adults.

Several other viruses (e.g., enteroviruses, reoviruses, pestiviruses, and parvovirus B) have been identified in the feces of patients with diarrhea, but their etiologic role in gastroenteritis has not been proven. Diarrhea has also been noted as a manifestation of infection with recently recognized viruses that primarily cause severe respiratory illness: the severe acute respiratory syndrome–associated coronavirus (SARS-CoV), influenza A/H5N1 virus, and the current pandemic strain of influenza A/H1N1 virus.

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Jeffrey I. Cohen

ENTEROVIRUSES

CLASSIFICATION AND CHARACTERIZATION

Enteroviruses, members of the family Picornaviridae, are so designated because of their ability to multiply in the gastrointestinal tract. Despite their name, these viruses are not a prominent cause of gastroenteritis. Enteroviruses encompass more than 100 human serotypes: 3 serotypes of poliovirus, 21 serotypes of coxsackievirus A, 6 serotypes of coxsackievirus B, 28 serotypes of echovirus, enteroviruses 68–71, and multiple new enteroviruses (beginning with enterovirus 73) that have been identified by molecular techniques. Human enteroviruses have been reclassified into four species designated A–D. Echoviruses 22 and 23 have been reclassified as parechoviruses 1 and 2 on the basis of low nucleotide homology and differences in viral proteins. Enterovirus surveillance conducted in the United States by the Centers for Disease Control and Prevention (CDC) in 2007–2008 showed that the most common enterovirus serotype, coxsackievirus B1, was followed in frequency by echoviruses 18, 9, and 6; together, these four viruses accounted for 52% of all isolates.

Human enteroviruses contain a single-stranded RNA genome surrounded by an icosahedral capsid comprising four viral proteins. These viruses have no lipid envelope and are stable in acidic environments,