# Rotavirus infection in adults

Evan J Anderson and Stephen G Weber

Rotavirus has been recognised for 30 years as the most common cause of infectious gastroenteritis in infants and young children. By contrast, the role of rotavirus as a pathogen in adults has long been underappreciated. Spread by faecal-oral transmission, rotavirus infection in adults typically manifests with nausea, malaise, headache, abdominal cramping, diarrhoea, and fever. Infection can also be symptomless. Rotavirus infection in immuno-compromised adults can have a variable course from symptomless to severe and sustained infection. Common epidemiological settings for rotavirus infection among adults include endemic disease, epidemic outbreak, travel-related infection, and disease resulting from child-to-adult transmission. Limited diagnostic and therapeutic alternatives are available for adults with suspected rotavirus infection. Because symptoms are generally self-limiting, supportive care is the rule. Clinicians caring for adults with gastroenteritis should consider rotavirus in the differential diagnosis. In this review we intend to familiarise clinicians who primarily provide care for adult patients with the salient features of rotavirus pathophysiology, clinical presentation, epidemiology, treatment, and prevention.

Infective gastroenteritis causes substantial morbidity and mortality worldwide. Although various bacterial species have long been associated with gastrointestinal disease,[1] specific viral causes of these infections were not delineated until the early 1970s. However, with the discovery of Norwalk virus in 1972[2] and rotavirus in 1973,[3] the causative agents for most non-bacterial gastroenteritis infections were identified. Almost immediately, the spectrum of viruses causing gastrointestinal infection in adults was recognised as differing from that in children. Among children younger than 2 years, nearly half of all cases of diarrhoea requiring admission to hospital can be attributed to rotavirus infection.[4] By contrast, among adults most non-bacterial outbreaks of gastroenteritis can be linked to the Norwalk-like viruses.[5]

The important part played by viral pathogens besides the Norwalk-like viruses in adults with gastroenteritis is not yet fully appreciated. Specifically, the contribution of pathogens that typically affect children is not recognised by most clinicians who take care of adults. Such is the case for adult infections caused by the common paediatric pathogen rotavirus. Here we review important features of rotavirus microbiology and pathophysiology, along with relevant clinical and epidemiological features of rotavirus infection.
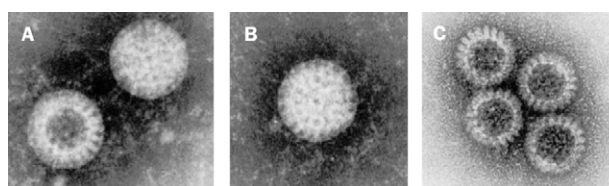
Electron micrographs of a human strain of rotavirus B. (A,B) Complete virus; (A,C) stages in the breakdown of virus particles as seen in preparations of stool samples (courtesy of Cornelia Büchen-Osmond, ICTVdB, the universal virus database of the International Committee on Taxonomy of Viruses).

Structure

In 1973, Bishop and colleagues[3] described unique viral particles obtained from the duodenal mucosa of children with gastroenteritis. Viruses with similar morphological appearance had been seen in 1963 in the intestinal tissue of mice with diarrhoea.[6] Under the electron microscope, the 70 nm diameter viral particles first described in these reports had a wheel-like appearance, prompting the name rotavirus, from the Latin rota (figure).[7]

Rotavirus is a non-enveloped virus now classified within the Reoviridae family. 11 segments of double-stranded RNA reside within the core. The RNA encodes six viral proteins (VP) that make up the viral capsid, and six non-structural proteins (NSP). The core is surrounded by an inner capsid, composed mostly of VP6, the primary group antigen,[1,8] and includes the epitope detected by most common diagnostic assays. Other structural proteins also seem to confer some degree of group specificity.[9] The outer capsid is primarily composed of VP4 and VP7.[10] VP4 contributes the spoke-like projections to the wheel-shaped appearance of rotavirus. This VP is cleaved by trypsin in vitro to yield VP5* and VP8*, which appear to play an important part in cellular attachment.[9] The inner and outer capsids give the viral particle the double-layered icosahedral structure visualised on negative-stain electron microscopy.[10]

EJA is at the Division of Infectious Diseases, Northwestern Memorial Hospital and Children's Memorial Hospital, Chicago, IL; and SGW is at the Department of Medicine, Section of Infectious Diseases, Infection Control Program, University of Chicago Hospitals, Chicago, IL, USA.

Correspondence: Dr Stephen G Weber, Department of Medicine, Section of Infectious Diseases, Infection Control Program, University of Chicago Hospitals, MC 5065, 5841 South Maryland Avenue, Chicago, IL 60637, USA. Tel +1 773 702 6776; fax: +1 773 702 8998; email: sgweber@medicine.bsd.uchicago.edu

Seven distinct groups of rotavirus (named A to G) have been shown to infect various animal species. Of these, only groups A, B, and C have been reported as human pathogens.[9] Group A is the primary pathogen worldwide and is the group detected by commercially available assays. Additional subgroups and serotypes can be identified by further characterisation of VP4, VP6, and VP7 antigens.[10] Group B seems to be limited to causing epidemic infection in Asia and the Indian subcontinent, whereas group C rotavirus causes endemic infections that frequently go unrecognised.

Pathogenesis

Rotavirus spreads from person to person, mainly by faecal-oral transmission. Although rotavirus has been detected in urine and upper-respiratory samples,[11,12] these body fluids are not believed to be commonly associated with transmission. After ingestion, rotavirus particles are carried to the small intestine where they enter mature enterocytes[13] through either direct entry or calcium-dependent endocytosis.[14]

After cytolytic replication in the mature enterocytes of the small intestine, new rotavirus particles can infect distal portions of the small intestine or be excreted in the faeces. More than 10^{10}–10^{11} viral particles per gram of faeces are excreted by children during infection.[8,15] The amount of rotavirus excreted by adults might be more variable. In at least one study shedding was 10–100-fold lower in travellers' diarrhoea.[16] Symptom-free adults can shed rotavirus in quantities so low as to be undetectable by most routine assays.[17]

The mechanism by which rotavirus induces diarrhoea is poorly understood. Few investigations have incorporated the study of human mucosal samples. The reports that are available describe various findings: villous shortening, flattening, and atrophy, denudation of microvilli, mitochondrial swelling, distension of the endoplasmic reticulum, depressed disaccharidase concentrations, and infiltration of mononuclear cells.[14,18,19]

Additional hypotheses about the pathophysiology of rotavirus gastroenteritis have been generated from animal studies. In one review the diminished ability of the intestinal epithelium to absorb fluid and nutrients,[14] stimulation of the enteric nervous system,[20] and local villous ischaemia and shortening resulting in impaired nutrient absorption were noted. A murine model of rotavirus infection suggests that rotavirus NSP4 acts as an enterotoxin, potentially by increasing calcium-dependent signalling of chloride secretion.[21,22] The diarrhoea induced by rotavirus is unlikely to be completely explained by any one process, rather that several mechanisms contribute simultaneously.[14] These mechanisms are summarised in panel 1.[3,13,14,18–28]

Immunity to rotavirus

Resolution of rotavirus gastroenteritis depends greatly on the immunological response of the host. In a normal host, rotaviral antigens are transported to Peyer's patches, undergo processing by B cells, macrophages, or dendritic cells and are presented to helper T cells. This cascade culminates in stimulation of rotavirus-specific B cell and cytotoxic T-lymphocyte-precursor expansion.[29] Bernstein and colleagues[30] noted that stool rotavirus IgA concentrations peaked 14–17 days after infection and persisted for longer than 1 year, but at declining concentrations. The researchers suggested that serum rotavirus IgA is a more consistent marker of rotavirus immunity than other antibody measurements.[30] However, rotavirus-specific IgA is frequently undetectable in duodenal fluid or faeces in the first week of infection, although symptoms might resolve within that time.[29] This pattern suggests a mechanism independent of humoral immunity. Offit[29] notes that infected mature villous epithelial cells are steadily replaced by less-mature enterocytes, which may be less susceptible to rotavirus invasion. Increased peristalsis improves clearance of viral particles and the non-specific activity of interferons can prevent VP translation.[29] De Bouissieu[31] has reported that interferon α concentrations correlate with a trend towards shorter duration of diarrhoea among patients who have rotavirus infection.

Although many physicians presume that rotavirus infection will confer lifelong immunity, multiple investigations show that re-infection can occur. Bishop and colleagues[32] noted that infection with rotavirus during the neonatal period did not protect against developing rotavirus infection during the first 3 years of life but did lessen the severity of such infections. In a prospective study of 200 Mexican infants followed up from birth, Valazquez and colleagues[33] noted that by age 2 years 96% of infants had experienced a primary rotavirus infection. During the same period, nearly 70% of the infants experienced a second infection. More than 10% of the children studied had five or more rotavirus infections during the first 2 years of life. Yolken and colleagues[34] had previously noted that by age

2 years, more than 85% of children had antibodies to two different rotavirus serotypes. Therefore, although nearly all adults have antibodies to rotavirus,[35] they might still be susceptible to infection.

Rotavirus can elude host defences and induce repeat infection through several mechanisms. There are multiple groups, subgroups, and serotypes of rotavirus. Initial antibody response to infection is serotype specific, with limited production of cross-reactive antibodies.[36] Subsequent rotavirus infections increase antibodies that cross-react with multiple serotypes.[36]

Additionally, certain elements of the rotavirus-specific immune response are short-lived. Rotavirus-specific secretory IgA is sometimes not detectable in faeces as early as 1 year after infection.[37] Elias[38] reported that rotavirus fluorescent antibody titres peaked in children at age 1–3 years but subsequently fell to almost undetectable concentrations in individuals older than 70 years.[38] In a review of multiple studies, Jiang and colleagues[36] noted that serum concentrations of rotavirus-specific antibodies were a marker for protection against future infection. Correlates of protection from studies of natural infection, challenge studies, and vaccine studies are detailed in panel 2.[29,35–37,39–50]

Clinical presentation

An appreciation of the typical presentation of rotavirus infection in children is critical to understanding the spectrum of disease among adults. Primary infection with rotavirus typically occurs in infants between ages 6 months and 2 years, although infection in neonatal intensive-care units and severe infection in infants younger than 6 months are well documented.[51,52] In all age-groups, the classic presentation of rotaviral infection is fever and vomiting for 2–3 days, followed by non-bloody diarrhoea.[53] The diarrhoea may be profuse, and 10–20 bowel movements per day are common. When examined, the stool from affected patients is generally devoid of faecal leucocytes. Especially when associated with vomiting, the diarrhoea of rotavirus infection can precipitate severe and even life-threatening dehydration. Infants with repeat rotavirus infections are generally less-severely affected than those with primary disease.[33]

Among adults, rotavirus infection has been associated with a wide spectrum of disease severity and manifestations. As such, it is difficult to provide a concise description of a typical clinical presentation. Nevertheless, prospective studies of voluntary rotavirus ingestion have provided some insight, although the participants in these studies were primarily young healthy adults. Data from several such trials are summarised in the table.[35,46–48,54] For these volunteers, illness most frequently began 2–6 days after ingestion and continued for 1–4 days. About two-thirds of study participants had an antibody response, with more than half of all participants eventually shedding rotavirus. Symptoms were less common than evidence of infection, but most frequently included diarrhoea, fever, headache, malaise, nausea, or cramping. One participant passed 11 stools in 1 day.[35] Among the volunteers, rotavirus particles were detectable in the stool

Panel 2. Correlates of protection against rotavirus[29,36,39]

Natural infection
Quantity of cross-reactive neutralising antibody responses against multiple serotypes,[40–42] of virus-specific secretory IgA at intestinal mucosa surface,[37,43] and of virus-specific IgA and IgG in serum[41,44]

Challenge studies
Serum serotype specific neutralising antibody;[35,45] intestinal neutralising antibody;[46,47] serum rotavirus IgG, but not necessarily with large doses;[46–48] and raised prechallenge titres of antibody to specific epitope of rotavirus VP7[49]

Vaccine studies
Vaccine-induced serum antibodies might be important in protection from natural infection, but interpretation is complicated because of differences in methods of existing studies;[36] and heterotypic antibody response to rotavirus vaccination might be protective against usual infecting serotypes[36,50]

from the start of symptom onset and persisted for more than 10 days in some. Three studies document rotavirus readministration to volunteers, noting that symptoms and antibody response were much less common.[35,47,54]

In several reports of rotavirus outbreaks among adults similar symptoms have been described. In a prospective study of 98 families with neonates followed up from shortly after birth, only 17 of 43 adults who had serological evidence of rotavirus infection were symptomless.[55] 14 had diarrhoea and 11 had abdominal cramping. None had symptoms that necessitated medical care or absence from work. In a separate study, 14 parents of children with rotavirus gastroenteritis developed serological evidence of infection, but only three had diarrhoea.[56] Grimwood and colleagues[57] found, in a study of children with rotavirus in 28 families, that 18 of 54 adult family members exposed to rotavirus developed evidence of infection, and all but four were symptomatic. In a study of college students during a rotavirus outbreak, of the 83 individuals who met the criteria for rotavirus infection, 93% had diarrhoea, 90% abdominal pain or discomfort, 83% loss of appetite, 81% nausea, and more than 50% had fatigue, vomiting, headache, chills, subjective or low-grade fever, or myalgia.[58]

Patients with underlying immunodeficiency are at risk of sustained symptoms and rotavirus dissemination, a phenomenon already recognised among children. This pattern was first described in 1980 when two of four children with underlying primary immunodeficiency who had rotavirus infection developed chronic diarrhoea that at least temporarily responded to administration of human milk containing a high titre of rotavirus antibodies.[59] A geriatric patient with impaired natural-killer-cell activity and impaired cellular and humoral immunity had rotavirus shedding for at least 35 days.[60] Gilger and colleagues[61] noted that in four children who had various immune deficits and chronic diarrhoea from rotavirus, rotavirus was identified in the liver and kidney. Whether the involvement of liver or kidney was important is unclear.

Symptoms of adult volunteers after rotavirus ingestion

Study	Dose administered	Evidence of infection			Proportion of patients with specific rotavirus-related symptoms								
		Symptoms	Antibody response	Shed rotavirus	Diarrhoea	Vomiting	Headache	Anorexia	Malaise	Cramping or gas	Temperature >37·2°C	Chills	Nausea
Middleton et al, 1974 (n=1)[54]	1×10⁸ viral particles	0	0	0	0	0	0	0	0	0	0	0	0
Kapikian et al, 1983 (n=18)[35]	1 mL 0·2% stool filtrate	22%	67%	28%	22%	11%	22%	22%	17%	11%	17%	NR	NR
Ward et al, 1986 (n=36)[48]*	>9 ffu	50%	64%	58%	36%	8%	14%	NR	17%	17%	19%	11%	22%
Ward et al, 1989 (n=38)[46]†	9×10¹ to 9×10³ ffu	39%	66%	58%	NR	NR	NR	NR	NR	NR	NR	NR	NR
Ward et al 1990 (n=4)[47]‡	9×10³ ffu	25%	75%	50%	NR	NR	NR	NR	NR	NR	NR	NR	NR
Summary percentages§	··	39%	65%	52%	31%	9%	16%	21%	16%	15%	18%	11%	22%

ffu=focus forming unit. NR=data not recorded in original paper and taken as not having occurred in calculation of summary percentages. *Data included when >50% infectious dose ingested (>9 ffu). †15 of 38 patients had mild illness (including one patient with no antibody response or shedding). ‡One of four volunteers experienced illness but no specific symptoms were recorded. §Summary percentages after rotavirus ingestion calculated only from data from studies in which full clinical syndrome of illness described. All percentages have been rounded to the nearest whole percentage point.

Other investigators have assessed the course of rotavirus infection in patients with malignant disease. A wide spectrum of clinical manifestations and severity of illness have been reported. Bolivar[62] screened 90 adults who had various solid tumours and leukaemia, with and without diarrhoea. He noted that two patients had rotavirus infection, both of whom had undergone bone-marrow transplantation and had developed graft-versus-host disease. Diarrhoea lasted for 10 days before resolution.

In three subsequent studies in bone-marrow-transplant patients results varied. Yolken and colleagues[63] prospectively assessed patients undergoing bone-marrow transplantation for infectious gastroenteritis and found that rotavirus occurred less frequently than *Clostridium difficile* or adenovirus, but still occurred in nine of 78 patients. In one patient, adenovirus occurred concomitantly with rotavirus infection. Of the eight remaining patients, all developed vomiting, seven had abdominal cramps, six had respiratory illness (infiltrates on chest radiography with appropriate clinical signs and symptoms) and four had diarrhoea. Five of the eight rotavirus-infected patients eventually died. Troussard and colleagues[64] also prospectively assessed patients undergoing bone-marrow transplantation and noted rotavirus infection in eight of 94 patients. Adenovirus occurred concomitantly in two patients. Seven of the patients had isolates positive for rotavirus in the winter months, with acute onset, vomiting, and diarrhoea. In a later study of the same topic, rotavirus was noted in four of 60 adult asymptomatic stem-cell-transplant patients followed up prospectively.[65] No patient with gastroenteritis had rotavirus isolated.

Rotavirus infections in adult patients infected with HIV-1 frequently present as a chronic diarrhoea with sustained viral shedding in stools. Albrecht and colleagues,[66] between 1987 and 1991, detailed a retrospective assessment of 106 samples from 66 patients infected with HIV-1 who had otherwise unexplained diarrhoea. 35 samples from patients without diarrhoea served as controls. 13 samples from nine case patients were positive for rotavirus; two of these samples were rotavirus recurrences 6 months after the initial episode. No symptom-free patients had rotavirus infection. Rotavirus was associated with diarrhoea of 2–8 weeks' duration in all patients and with abdominal cramping in eight patients. Thomas and colleagues[67] looked prospectively at 862 samples from 377 UK HIV-1-positive patients with diarrhoea. Rotavirus was third in frequency to adenovirus and coronavirus, occurring in 11 (2·4%) samples. The median CD4 count of patients with rotavirus infection was nine.

Epidemiology

Hrdy[68] described five typical settings for rotavirus infections in adults. We propose modification of these classifications to the following: endemic disease, epidemic outbreaks, travel-related gastroenteritis, and infections transmitted from children to adults. Although substantial overlap exists between the groups, our classifications clarify separate risk factors and clinical features.

Endemic disease

Rotavirus infection in children is seasonal, with peak incidence in winter months in temperate climates. Iturriza-Gomara and colleagues[69] noted that, in the UK between 1995 and 1998, notable numbers of infections began in December or January, peaking in March or April and falling to almost zero by July. In the USA, Kapikian and colleagues[56] found that rotavirus cause 59% of diarrhoea cases necessitating admission to hospital in children between November and April, but could not be linked to cases from May to October.

In several studies findings suggest that adult disease is not as season-specific as childhood disease. Cox and Medley[70] noted that IgM antibodies to group A rotavirus in

adult serum in routine hospital samples are present throughout the year. IgM concentrations increased with older age, and antibodies reached 20% in March and fell to 10–11% during the summer months. Cox and Medley attributed the high rates to IgM persistence, IgM cross-reactivity, or possibly to non-seasonal high infection rates in adults. Other researchers have also found that rates of adult disease do not mirror the winter seasonality of infection in paediatric patients.[71] These studies suggest that endemic disease in adults may not arise solely from unrecognised transmission of rotavirus from children to adults.

The contribution of rotavirus as a cause of endemic gastrointestinal disease varies according to geographic distribution and characteristics of patients. In a small prospective study in the UK, rotavirus caused 4·1% of acute diarrhoea in adults admitted to hospital.[72] Similarly, 3% of acute diarrhoea in Switzerland,[73] 3% of infectious diarrhoea pathogens in a Swedish clinic for infectious diseases,[74] 5% of adults with gastroenteritis requiring admission in Thailand,[75] 2–4% of adults older than 15 years with gastroenteritis presenting to their family physician in the Netherlands,[76] and nearly 4% of individuals older than 45 years in Michigan[77] were due to rotavirus.

In studies in other geographic areas even higher rates of infection have been seen. In Japan, Nakajima and colleagues[71] reported that group A rotavirus had a role in 14% of patients with diarrhoea. Pryor and colleagues[78] noted that rotavirus was second only to *Campylobacter* spp as a cause of diarrhoea among Australian adults, accounting for 17% of all cases. In Indonesia, 42% of patients presenting with diarrhoea had rotavirus-positive stools compared with 11% of control samples.[79] In a study of Mexican adults, 63% of patients presenting with acute gastroenteritis during winter months were positive for rotavirus.[80]

Even these results might underestimate the true prevalence of endemic rotavirus infection. Group C rotavirus is not routinely detected by commercial assays but it does contribute to endemic rotavirus infection worldwide. In a study in the UK, 43% of patients were seropositive for group C rotavirus.[81]

Epidemic outbreaks

Among adults, clusters of rotavirus infections most frequently occur in communities that are otherwise sheltered from more routine exposure to rotavirus-infected children.[82] One of the largest outbreaks involved nearly 3500 people in 1964, in an isolated area of Micronesia.[83] Since then, other outbreaks have occurred among closed communities, including a Finnish military base,[84] an Israeli kibbutz,[85] and an isolated South American Indian community.[86]

Outbreaks of rotavirus infection have also occurred in long-term health-care facilities, particularly those with close living quarters; compromised host immunity and multiple comorbid disorders might help facilitate the spread of infection.[87–91] Cubitt and colleagues[88] described an epidemic of rotavirus among staff and patients in an extended-stay geriatric hospital, in which 15 of 39 residents developed symptoms and seven had confirmed rotavirus infection. Halvorsrud and Orstavik[92] described an outbreak of 92 cases

of acute gastroenteritis among nursing-home patients with identification of rotavirus by comparing acute and convalescent antibody titres. Rotavirus has been suggested as the causal pathogen in 5% of diarrhoea outbreaks in a study of institutions caring for elderly residents.[93]

Among adults, rotavirus outbreaks are not confined to geriatric populations. Group A rotavirus was associated with an outbreak of gastroenteritis among college students in the District of Colombia.[58] Rotavirus also caused a waterborne outbreak of gastroenteritis in 1981 in Eagle-Vail and Avon, CO, USA in which severity of symptoms correlated with the amount of tap water consumed.[94] Finally, Griffin and colleagues[95] screened 263 outbreaks of gastroenteritis in the USA between 1998 and 2000 and found that rotavirus was implicated in three outbreaks. Uniquely affecting Asia, group B rotavirus has been associated with outbreaks affecting large numbers of adults in broad geographic distributions of China and India.[96,97]

Travel-related gastroenteritis

Rotavirus has been implicated as an important contributor to travellers' diarrhoea among adults, especially among those visiting Central America and the Caribbean. In a study of travellers returning from Jamaica, rotavirus was identified in 9% of individuals with diarrhoea, making the virus second only to enterotoxigenic *Escherichia coli* as a cause.[98] In two studies of US students travelling in Mexico, electron microscopy identified rotavirus in about 25% of patients who had diarrhoea, compared with 3% and 15%, respectively, of symptom-free patients.[99,100] In a third study, a substantial rise of antibodies to rotavirus was seen in 17% of two student groups travelling to Mexico.[101] By contrast, only 5–6% seroconverted to Norwalk virus.[101] Ryder and colleagues[102] found rotavirus in 26% of Panamanian travellers to Mexico who had diarrhoea. Sheridan and colleagues[103] similarly found that 36% of US Peace Corps volunteers and 30% of Panamanian travellers visiting Mexico had at least a four-fold increase in rotavirus antibody titres. Adult travellers with rotavirus shed 10–100 times less rotavirus than do paediatric patients.[99,100]

Infection transmitted from children to adults

Although rotavirus can be linked to adult gastroenteritis in each of the other settings, adults who are in contact with children are at particularly high risk of infection. Transmission of rotavirus within families from children to parents seems to be a common event. Wenman and colleagues[55] showed prospectively that rotavirus infection occurred in 36 of 102 adults caring for children with rotavirus infection. By contrast, only four of 86 adults whose children had no documented rotavirus infection became infected.[55] Grimwood and colleagues[57] confirmed this finding in a report that a third of adult family members in New Zealand developed evidence of rotavirus infection. The same phenomenon has been seen among parents of more severely ill children. Kim and colleagues[104] found evidence of rotavirus infection in 55% of adult contacts of children who were admitted to hospital with rotavirus, compared with 17% of adult contacts whose children were

not infected. More casual contact might also be sufficient to facilitate rotavirus transmission from children to adults. Rodriguez and colleagues[105] reported that nine of 12 adults experienced illness after exposure to children infected with rotavirus in a playgroup. Although substantial evidence is lacking, child-to-adult transmission of rotavirus is accepted to occur with some frequency on paediatric wards. Many paediatric nurses, medical students, and house officers experience symptoms of gastroenteritis during the winter months when most paediatric rotavirus infections are encountered. Von Bonsdorff and colleagues[106] described paediatric nurses at several different locations with acute gastroenteritis caused by rotavirus. Among seven hospital staff that developed diarrhoea after direct contact with children with diarrhoea staying in hospital, a rise in antibody titres was detected in three.[104] Interestingly, in the same study, six of 45 medical students reported gastroenteritis. Three of the students had rotavirus particles present on electron microscopy and were noted to be more ill than the parents of the children who were infected. All had diarrhoea for 3–6 days and two of the three had low-grade fever and vomiting. Another case report supports transmission of rotavirus from children to hospital caretakers.[107]

Diagnosis

Electron microscopy, which permits visualisation of the pathognomonic wheel-like appearance, was initially used for diagnostic purposes, but ELISA or EIA have become more commonly used. Commercial assays are reliable, convenient, and inexpensive, but require at least 10^4–10^7 virions to generate a positive result.[108,109] The false-positive rate of commercial assays is 3–5%.[69] One of the biggest limitations of most commercial assays is that they do not detect non-group-A rotavirus.[68,110] Other more sensitive and newer methods are being used in research. One such method is PCR, which is up to 1000 times more sensitive than immunoassays.[109] In one study using PCR, 30% of otherwise healthy children shed virus for 25–57 days after symptoms developed.[111]

Although stool cultures are routinely tested for bacterial pathogens, the low frequency of detecting a positive result calls the usefulness of this practice into question. Rotavirus infection can occur in a similar number of patients to some bacterial pathogens. Sending a sample of rotavirus antigen for testing by ELISA or EIA could potentially cut costs if by doing so either hospital stay or procedures could be avoided. Such a cost-benefit analysis in adult patients has not been published. One limitation is that adults might shed less rotavirus in faeces than do children, further hampering diagnosis.[100] We suggest that obtaining rotavirus antigen testing for patients admitted to hospital with risk factors for rotavirus infection will be cost effective if additional inpatient studies can be avoided. Determination of rotavirus infection may also be beneficial if infectious patients can be isolated to prevent nosocomial spread. A positive rotavirus antigen test might also allow physicians to avoid prescribing antibiotics for travel-related rotavirus infections.

Treatment

Treatment of rotavirus infections is primarily directed at symptom relief and restoration of normal physiological function. Oral rehydration should be attempted initially. In most developing countries, oral rehydration salt solutions are used extensively in children. Most adults can be managed by encouraging them to drink fluids. An additional intervention that has been used is administration of *Lactobacillus* spp bacteria to shorten the duration of diarrhoea.[112,113] Although seldom used in children, codeine, loperamide, and diphenoxylate can help with symptom relief and control of the volume of diarrhoea.[114] Bismuth salicylate, in a placebo-controlled double-blinded trial, was efficacious in treating the symptoms of rotavirus diarrhoea.[115] Trial use of bismuth salicylate can be considered in adults when other coexistent infectious causes have been ruled out.

If symptoms cannot be controlled and the patient becomes dehydrated, administration of intravenous fluids and hospital admission might be necessary. Rarely, extraordinary measures have been attempted to help resolve rotavirus infections. For example, human breastmilk has been provided to immunodeficient infected children to help resolve chronic diarrhoea.[59] This option, however, is not practical in adults. Several groups report oral administration of human serum immunoglobulins possessing antirotavirus activity to bind free rotavirus antigen. Guarino and colleagues[116] noted a mean duration of diarrhoea of 76 h in children who received one oral dose of 300 mg/kg human serum immunoglobulin, compared with 131 h in children who did not. In a study involving three immunocompromised children with chronic rotavirus diarrhoea, oral administration of human serum immunoglobulins (IgG 150 mg/kg) cleared rotavirus antigen in all three, but rotavirus antigen recurred in two.[117] Among adults, oral immunoglobulin administration of 5–6 g daily for 5 days to bone-marrow-transplant recipients has been successful.[118]

Prevention

Prevention of rotavirus infection can be facilitated by avoiding exposures and faecal-oral spread. Contact with sick children and potentially contaminated food and water should be avoided. Since 43% of rotavirus virions placed on human fingers survive for 60 min, thorough hand washing is critical in prevention.[119] Contact isolation for patients diagnosed with rotavirus infection is necessary, generally for the duration of hospital stay, because of sustained faecal shedding of low concentrations of virus.[120] Gloves, gowns, isolation, and rigorous hand washing should be used in the care of individuals infected with rotavirus.[121]

Sattar and colleagues[122] reported that rotavirus survives best in low humidity on non-porous surfaces at room temperature or cooler. Phenolic disinfectants do not inactivate rotavirus; instead hypochlorite or sodium dichloroisocyanurate tablets with a free chlorine concentration of at least 20 000 parts per million are recommended.[110] A 70% ethanol solution is also effective in inactivation of rotavirus and can help to prevent environmental spread.[120] Rotavirus infection in adults has been successfully prevented by use of a commercially available

disinfectant spray on rotavirus contaminated fomites under experimental conditions.[123]

Given the substantial disease-related morbidity and mortality associated with rotavirus, the development of an effective vaccine is a priority. Although multiple vaccines were under development, the tetravalent rhesus-human reassortant rotavirus vaccine (RRV-TV) seemed to produce the best results. The RRV-TV vaccine prevented about half of rotavirus infections, but was much more effective in preventing severe disease.[124,125] Shortly after the vaccine was approved, the vaccine adverse-event monitoring system noted by mid-1999 an excess of cases of intussusception among recently vaccinated infants, eventually prompting the vaccine to be withdrawn. Two sharply differing perspectives on the risk and benefits of the RRV-TV vaccine and the Advisory Committee on Immunization Practices' confirmation of its decision to withdraw its recommendation for the vaccine have been put forward.[126,127] Other vaccines are under development.

Vaccines have been primarily developed to attempt to decrease the severity of rotavirus infections in children. Although vaccines seem to be fairly safe in adults from the vaccine trials, we are unaware of any plan to consider vaccination in adult patients. Vaccination could theoretically be used in adult patients considering travel to Central America or the Caribbean or among immunocompromised patients to prevent or lessen the severity of rotavirus diarrhoea.

Salient points
Despite recognition as an important cause of gastroenteritis in children, rotavirus's role in adult gastroenteritis is underappreciated. Immunity to rotavirus is incomplete and most people have multiple infections over their lifetime. Adults with rotavirus can be asymptomatic, but the most common symptoms are nausea, malaise, headache, abdominal cramping, diarrhoea, and fever. Adults at particular risk of rotavirus infection are travellers, adults exposed to infected children, and immunocompromised people. Group A rotavirus, the most common human pathogen, can be diagnosed with many different commercial assays, but all have limited sensitivity. Rotavirus testing might be beneficial in certain clinical settings if detecting rotavirus would change management of patients or prevent nosocomial spread. Treatment is primarily symptomatic. Rotavirus should be considered in the differential diagnosis of adult infectious gastroenteritis.

Conflicts of interest
We have no conflicts of interest.

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Clinical picture

Nasal tuberculosis in an elderly patient

Ana María Bravo Blanco, Carmen Santos, and Quintairos Manuel Blanco Labrador

A 73-year-old woman presented with a 2-year history of persistent ulcerous nasal injury that had progressed slowly and without fever, respiratory, or any general symptoms, until the upper lip was affected. A painless ulcero-vegetating injury was seen but the patient was otherwise normal; chest radiographs did not show abnormalities. Further examination showed soft tissue attenuation and an ulcered mass lesion in the nasal cavity (figure). The definitive diagnosis was made by isolating *Mycobacterium tuberculosis* from tissue removed during biopsy and antituberculous therapy was started. The lesion had resolved at completion of treatment.

Tuberculosis of head and neck occurs infrequently and involvement of the nose is rare. Granulomatous lesions within the nasal cavity may represent either local disease or a manifestation of a systemic disorder and the differential diagnosis must include tuberculosis. Although almost forgotten in industrialised countries, this unusual form of tuberculosis can appear mainly in females and the elderly. It is not thought to be contagious, or to produce noticeable symptoms or physical signs.

All authors are at the Department of Internal Medicine and Otorhinolaryngology, Complexo Hospitalario de Ourense, Ourense, Spain.

Correspondence: Dr Ana María Bravo Blanco, Rua Nuño de Ousende 13B, 32004, Ourense, Spain. Tel +34 988 240805; email anabravob@yahoo.es