Review

Diagnosis of viral gastroenteritis: limits and potential of currently available procedures

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Abstract

The diagnostic approaches to viral gastroenteritis have evolved substantially over the past decades because of the advances in detection methods, the emergence of new pathogens, and the increase in diarrhea hospitalizations attributed to viruses, especially in young children in non-industrialized countries. Overall, these factors have lead to a relevant improvement of types and operating characteristics of diagnostic methods (including sensitivity and specificity), as well as turnaround time.

In this review, clinical and laboratory approaches to the diagnosis of viruses causing gastroenteritis are presented; in particular, specimen collection and detection methods are reviewed and discussed, taking into account performance and limitations.

Key words: diarrhea; gastroenteritis; virus; diagnosis.


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Introduction

Acute gastroenteritis (AGE) is a common cause of morbidity and mortality worldwide, with most cases occurring in young children in non-industrialized countries. In recent years, improvements in hygiene, sanitation, and water supply have led to a reduction of the cases of bacterial and parasitic infections, with a parallel increase in diarrhea-related hospitalizations attributed to viruses [1]. AGE is a major cause of illness in the United States, with an estimated 179 million episodes occurring annually [2]. Approximately 1.45 million deaths related to AGE occur worldwide every year [3-5]. AGE is estimated to be responsible for the deaths of 800,000 infants and young children each year [6,7]. Noroviruses are the leading cause of single-agent outbreaks (68% of cases), followed by Salmonella spp. (13%), Shigella spp. (4%), and Shiga toxin-producing Escherichia coli (4%) [8]. Low-income countries are affected by the most severe outcomes of AGE; more than 25% of deaths in children younger than five years of age are attributable to acute gastroenteritis in Africa and Southeast Asia [9,10].

Although at least 25 different bacteria and protozoa can cause childhood diarrhea, more than 75% of cases are caused by viruses; the most frequently detected viral agents of acute gastroenteritis are rotavirus, norovirus, enteric adenovirus, human astrovirus, and sapovirus. The main biological features of viruses associated with acute gastroenteritis in humans are shown in Table 1. Other viruses, such as Aichi virus, parechovirus, and bocavirus have been recently described in patients with diarrhea, but their association with AGE has not yet been established clearly [7,11-15]. Although rotavirus is reported to be the most common pathogen in children worldwide, the role of other enteric viruses is relatively less understood [1,16]. Three main types of manifestations are reported: (a) sporadic infantile gastroenteritis (GE) (mainly due to rotaviruses); (b) epidemic GE in adults and children (calicivirus: norovirus and sapovirus); and (c) sporadic GE of adults (calicivirus, rotavirus, astrovirus, adenovirus). Important epidemiological factors include history of contact, travel history (including cruise ships), eating history, and daycare history. Clinical presentation of AGE varies from
asymptomatic infections to severe diarrhea, vomiting, and dehydration, with an emerging risk of death. Typical presentations of viral AGE include a short prodromal phase, with mild fever and vomiting, followed by one to four days of non-bloody, watery diarrhea. However, the great majority of viral AGE is self-limiting, not leading to precise diagnosis and identification of the viral agent; these aspects limit further understanding of its physiopathologic and epidemiologic characteristics [7,16-19].

This paper is an update review on recent achievements in the field of diagnosis of viral gastroenteritis, and points out the main features of the licensed available assays and their clinical implications.

**Descriptions of the agents**

*Caliciviridae*

The *Caliciviridae* family comprises four genera: *Norovirus*, *Sapovirus*, *Lagovirus*, and *Vesivirus*; human norovirus and sapovirus are etiological agents of gastroenteritis.

*Norovirus*

Norovirus (NoV) is considered the major cause of AGE in both children and adults in community-based gastroenteritis; it is responsible for sporadic cases and several outbreaks in various epidemiological settings, including restaurants, schools, daycare centers, hospitals, nursing homes, and cruise ships. More than 267,000,000 annual infections have been reported worldwide [16].

The genus *Norovirus* is divided into six genogroups (G-I to G-VI). Viruses in genogroup I, II, and IV are known to infect humans, with most strains associated with human disease belonging to G-I and G-II. Transmission routes include contaminated food, water, environment, person-to-person contact, air, stool, and vomit of infected person. Waterborne outbreaks are more likely to be caused by G-I NoVs, whereas foodborne outbreaks or person-to-person transmission are mainly related to G-II strains [20,21]. Prolonged infections by norovirus and viral shedding have been observed in immunosuppressed hosts, in whom infections may occur year-round [20,22].

Noroviruses possess highly infectious potential, with a small inoculum (as few as 10–100 virions) required for infection; furthermore, virions are relatively stable in the environment, with reported resistance to freezing, heating to 60°C, and disinfection with chlorine [16,23,24].

Noroviruses have been found to recognize specific histo-blood group antigens (HBGAs) as receptors for attachment in the gut; all three major HBGA families (ABO, secretor, and Lewis) are involved in the process of NoV recognition. Rotaviruses and other bacterial pathogens such as Helicobacter pylori, have also been found to recognize HBGAs [25].

*Sapovirus*

Sapovirus particles were first detected in human diarrheal stools in 1976 in the United Kingdom [26], and the prototype of human sapovirus was identified during an outbreak in Sapporo, Japan, in 1977 [27]. Sapoviruses cause acute gastroenteritis in humans and animals and are responsible for gastroenteritis in people of all ages in both outbreaks and sporadic cases worldwide [28]. They are the causative agents of AGE in only a minority of cases of sporadic gastroenteritis in children. However, the incidence of sapovirus-associated gastroenteritis in adults is steadily increasing, suggesting a rise in virulence and prevalence [29,30]. In general, the severity of sapovirus gastroenteritis is milder than that of norovirus, and mortality is rare. Sapoviruses are associated with more serious clinical complications in susceptible groups (e.g., premature neonates and immunocompromised patients) [22,28,31].

Sapoviruses can be divided into five genogroups (GI-GV), among which GI, GII, GIV, and GV are

| Table 1. General characteristics of the main viral agents responsible for gastroenteritis worldwide |
| --- | --- | --- |
| **Family** | **Genus** | **Biological characteristics** |
| *Caliciviridae* | Norovirus (genogroups I–VI) | Small, round, non-enveloped, positive-sense, ss-RNA, 27–35 nm diameter; 7,400–7,700 nt ss-RNA, 41–46 nm diameter; 7.1–7.7 kilobases |
| | Sapovirus (genogroups I–V; genogroups GVI to GXIV were recently proposed) [106] | Non-enveloped, linear ds-DNA; 70–100 nm in diameter; 26–45 kilobases |
| *Adenoviridae* | Mastadenovirus | Non-enveloped, ss-RNA, 28–30 nm in diameter; 6.1–7.3 kilobases |
| | Subgenera (A–G); at least 52 serotypes; 53 genotypes | Non-enveloped, dsRNA, 71 nm in diameter; approximately 18.5 kilobases |
| *Astroviridae* | Astrovirus (8 serotypes: HAstV1–HAstV8) | |
known to infect humans; sapovirus GIII infects porcine species. The infection is more common in young children than in adults, usually occurring by five years of age, especially at daycare centers and institutions [30].

Seroprevalence studies of human sapoviruses demonstrated a gradually increasing seroprevalence rate with age, which reached a high level (> 90%) in school-age children, and remained high (80%–100%) in sera collected from adults [32-35], suggesting that sapovirus infection is common during early childhood. Adults with serum antibodies to antigenically indistinguishable human sapoviruses did not show any clinical symptoms of reinfection [28].

Adenovirus

Human adenoviruses (ADV) are non-enveloped DNA viruses, belonging to the family Adenoviridae. They are the only DNA viruses among the most common viral pathogens in children, and have been associated with a spectrum of clinical presentations including respiratory, gastrointestinal, ocular, and urinary tract infections [1]. Adenovirus infections are largely asymptomatic, and only one-third of the 52 recognized human serotypes are associated with a specific human disease, including upper and lower respiratory tract manifestations, conjunctivitis, cystitis, and gastroenteritis. Enteric adenoviruses are second only to rotavirus as agents of AGE in infants and young children. Diarrheic manifestations can occur during infection by any type of ADV (especially serotypes 18, 31, 40, 41, and 52). Diarrhea is usually associated with fever, and can last for up to two weeks. Following the symptomatic phase, all ADV can remain in the gastrointestinal tract and potentially be excreted for prolonged periods of time (extended periods of time for subgenera C), being potentially reactivated in conditions of immune deficiency. Latency sites have been recognized in tonsils, lymphocytes, and adenoidal tissues [36,37]. However, specific subgenera (e.g., subgenera A and D) can be associated with large proportions of asymptomatic infections, and 0%–20% of asymptomatic people can shed adenoviruses [38].

Astrovirus

Human astroviruses (HAstV) are the second-most common cause of gastroenteritis in children, after rotaviruses, with incidence varying from 4.3%–8.6%. Early studies indicated that HAstV1 is the most prevalent serotype worldwide, although there are increasing reports of the role of other serotypes in gastroenteritis [1,39,40]. Sporadic, community-acquired, and nosocomial infections have been described [41,42]. HAstVs are usually responsible for mild watery diarrhea lasting no more than three days, and vomiting, fever, anorexia, and abdominal pain are common. Persisting gastroenteritis due to astroviruses has been associated with HAstV3. Astrovirus-related deaths have been reported, though they are extremely rare [43,44].

Rotavirus

Rotaviruses (RVs) are the leading cause of acute childhood gastroenteritis, with 180,000–450,000 deaths occurring in children under five years of age, especially in developing countries [45,46]. Furthermore, rotavirus infection can sporadically be associated with neurologic manifestations, including benign convulsions, encephalitis, and encephalopathy; data exist on its plausible association with sudden infant death syndrome, intussusception, Kawasaki’s disease, and type 1 diabetes [47,48]. Rotaviruses also infect other mammalian and avian species, leading to diarrhea in calves, pigs, sheep, and poultry [49]. Two live-attenuated oral rotavirus vaccines (RotaTeq, Merck; Rotarix, GSK Biologicals) have been licensed, after the discontinuation of the quadrivalent RRV-based human reassortant vaccine Rotashield because of the severe adverse cases of gut intussusceptions. Both vaccines were found to reach protection rates of 70 to > 90% in developed countries. Interestingly, herd protection was observed in non-vaccinated children, probably related to reduced transmission of rotavirus in the community as a result of vaccination [48,50].

Laboratory diagnosis

Sample collection

Collection of an adequate specimen is fundamental for a correct diagnosis and to avoid costs and useless investigations. The specimen must be collected as early as possible in the presence of a suggestive clinical presentation, taking into account the acute phase and the duration of viral shedding. The specimen of choice for the diagnosis of the main viruses causing gastroenteritis is feces. Stool samples should be collected from affected individuals as soon as possible after the onset of acute gastroenteritis (between day 1 and 4 of the illness) because viral shedding is highest in the acute phase of the illness. Therefore, liquid diarrhea stool represents the more suitable sample for the detection of gastrointestinal viruses, particularly diarrheal stools defined as types 5
to 7 on the Bristol Stool Chart. Alternatively, a rectal swab can also be used if feces are not available. The specimen should be stored at 4°C until tested, and at -70°C for several months in suitable containers, though it should, ideally, be sent to the laboratory as soon as possible. It is good practice to contact the laboratory for information about specimen collection (time and temperature), conservation and to send information to and concur them, as well as to report complete information regarding the patient, such as age, underlying pathologies and co-morbidities, life habits, clinical suspect, therapies, and previous lab investigations. Time and temperature are critical issues for specimen collection; this is particularly relevant for viral isolation techniques and for detection of RNA viruses by molecular methods because of RNA degradation.

Diagnostic approaches to viral gastroenteritis include direct methods such as techniques to detect viral infectivity (e.g., viral isolation on cell cultures) and methods to detect virions or their components (e.g., electron microscopy, antigen detection, and nucleic acid detection), as well as indirect methods for the evaluation of virus-specific serological responses. In Table 2, a summary of the main features of diagnostic approaches is reported.

### Traditional diagnostic methods

#### Electron microscopy (EM)

Detection of gastroenteritis-producing viruses has traditionally been based on techniques of direct visualization using electron microscopy (EM) [51-53]. Direct EM can be used to screen fecal specimens for enteric viruses in public health laboratories. The turnaround time is rapid (same-day specimen submission and results), and EM has the distinct advantage of uncovering a diagnosis for a wide range of enteric viral pathogens. However, detection of enteric viruses in stool specimens using direct EM requires virus concentrations of at least 10⁶/mL of stool [54]. Therefore, airfuge techniques or immunoconcentration procedures are required to visualize most of the virions. In many laboratories, stool is mixed with phosphate-buffered saline (pH 7.4) or tissue culture medium to form a 10% to 20% suspension before being clarified by low-speed centrifugation (4,800 x g for 15 minutes) to eliminate larger debris. Subsequent concentration of virus may be achieved by ultracentrifugation or precipitation with ammonium sulphate. Virions are negatively stained using phosphotungstic acid, uranyl acetate, or ammonium molybdate [54]. The small numbers of viral particles present in fecal samples make direct EM, even after concentration, relatively insensitive. Moreover, this method requires highly skilled microscopists and expensive equipment, making it not feasible for large epidemiological or clinical survey studies.

Immune EM (IEM) can be used to increase the sensitivity of EM by using specific antibodies or immune sera added to the sample. In this technique, immune sera are used to enhance the detection of the virus by aggregation of viral particles in stool suspensions. The virus clumping that occurs in the presence of specific antibody enables its detection and improves diagnostic capability. IEM has been used to differentiate between the morphologically identical groups A, B, and C rotaviruses. However, the technique is useful only for samples collected during the early stages of gastroenteritis, and is laborious, cumbersome, and time-consuming [55]. The lack of detection of viral particles in positive specimens probably reflects the very low concentration of viruses in many stool samples and the lack of first early diarrheal stool samples.

Modifications to the IEM method have been made to improve the detection of viral particles and to simplify the performance of the test. Solid-phase IEM (SPIEM) has been used to capture viral particles directly onto the grid [54,56,57]. A SPIEM method

Table 2. Main features of diagnostic approaches to viral gastroenteritis

<table>
<thead>
<tr>
<th>Viruses detected</th>
<th>Electron microscopy</th>
<th>Viral isolation</th>
<th>Antigen detection</th>
<th>Nucleic acid testing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wide range</td>
<td>Wide range (except calciviruses)</td>
<td>Wide range</td>
<td>Very wide range, including identification of novel pathogens</td>
</tr>
<tr>
<td>Turnaround time</td>
<td>24 hours</td>
<td>5–10 days</td>
<td>30 min</td>
<td>2–6 hours</td>
</tr>
<tr>
<td>Technical expertise</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Good (virus concentrations of at least 10⁶/mL of stool)</td>
<td>Good (specimen collection and storage important)</td>
<td>Good (higher in pediatric patients)</td>
<td>High</td>
</tr>
</tbody>
</table>

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that uses protein A, goat anti-human immunoglobulin M (IgM), and human serum has been described for serotyping of noroviruses [57].

**Immune adherence hemagglutination assay (IAHA)**

The immune adherence hemagglutination assay (IAHA) has been used successfully to detect antibody levels to norovirus in large numbers of sera. In particular, Kapikian et al. used the IAHA to perform epidemiological studies of Norwalk agent seroprevalence in children and adults [58]. Purified viral particles from stool samples are used as an antigen, and antigen-antibody complement interactions are detected in a microtiter plate format by agglutination of sensitive human O erythrocytes. Comparative studies between the IAHA and the conventional complement-fixation (CF) test revealed that, in most cases, the IAHA was more sensitive than the CF test. Furthermore, diagnosis on the basis of a fourfold change in antibody titer was made more rapidly by the IAHA test. The IAHA test was found to be a very simple and practical technique, requiring only a few hours for completion, compared with the conventional CF test, which required up to 24 hours. Although the IAHA has the advantage of requiring less antigen for its performance than CF, it was soon replaced with another test, the radioimmunoassay (RIA), which uses even less antigen and is more sensitive [52,59,60].

**Radioimmunoassay (RIA)**

Radioimmunoassay (RIA) was developed as an alternative method to IEM for the detection of norovirus antigen in stool [59,60]. Convalescent sera from a volunteer experimentally infected with norovirus are used to capture virus antigen. Immunoglobulin G (IgG) purified and radiolabeled with gamma-radioactive isotopes of iodine, such as 125-I, is used as a detector system. Although the RIA technique is extremely specific and 10 to 100 times more sensitive than IEM, it requires special precautions since radioactive substances are used [60-62]. RIA assays have been modified to detect virus-specific antibodies using a blocking format. Several RIA blocking techniques have been developed for the detection of antibodies to noroviruses; these assays appeared to be 10 to > 200 times more sensitive than the IAHA [60-62].

**Virus isolation**

Cell culture of gastrointestinal viruses is not considered to be useful for diagnostic purposes, as it is technically cumbersome and slow. Among the viruses that have been shown definitively to be causes of gastroenteritis, only caliciviruses cannot be grown in cell culture. The study of rotaviruses, enteric adenoviruses, and astroviruses has been facilitated greatly by the ability to propagate these viruses in cell culture. The ability to cultivate these viruses has allowed the production of reagents for use in diagnostic studies, a better understanding of factors correlated with immunity to infection, and elucidation of each virus’s life cycle. In particular, astroviruses were reported to be cultivable in a variety of human and monkey cell lines, although the number of cell lines that are permissive for all eight serotypes is lower [63]. Adenoviruses (subgenera A-E) can be cultured in a variety of cell lines (HeLa, HEP-2, 293, Chang conjunctival, CaCo-2, and PLC/PRF/5 cells), albeit slowly, and thus may be overgrown by other faster-growing viruses [64-68]. Cell-culture isolation of astroviruses and adenoviruses is often combined with immunofluorescence detection by using specific antibodies. However, the maintenance and the use of cell cultures are time consuming and expensive.

**Development and application of newer diagnostic tests**

**Antigen detection**

Recently, a wide variety of tests for the detection of antigen in fecal specimens have been developed. These are based on enzyme immunoassay (EIA), agglutination with latex particles (LA), immunochromatography (IC) and, more recently, chemiluminescent immunoassay (CLIA), all of which are available commercially for human calicivirus, rotavirus, adenovirus, and astrovirus [53,69]. Rapid antigen assays are widely used, as they are able to provide results at the point of care in less than 30 minutes. Moreover, the low cost represents an advantage in the evaluation of the diagnostic work-up. In clinical laboratory practice, rapid and reproducible antigen detection methods seem to be superior among the conventional techniques. The sensitivity of rapid antigen detection is generally higher than that of conventional methods (e.g., EM and IAHA) although lower than that of molecular methods [70-72]. However, these assays are particularly useful in the pediatric setting; the sensitivity is higher in this population because children often shed gastrointestinal viruses at higher titers and for longer time periods than do adults.

Enzyme immunoassay has been proven to be very sensitive and specific for the detection of group A and
C rotaviruses in fecal specimens, especially if monoclonal antibodies are used [73,74]. Immunoassay techniques are also available for the detection of astroviruses, due to the development of monoclonal antibodies against these viruses [75-78]. Various formats of astrovirus antigen detection EIAs have been developed for diagnostic purposes. Some of these have been marketed, and have good specificity and sensitivity compared with EM and molecular assays (e.g., IDEIA Astrovirus, Dako Diagnostics, Ltd., Ely, UK, able to detect all eight astrovirus serotypes) [79,80]. Several EIA methods using monoclonal and polyclonal antibodies have been developed for the detection of calicivirus. In particular, EIA techniques that use monoclonal antibodies have been evaluated for their ability to detect noroviruses in stool samples. These assays were reported to have a twofold greater sensitivity than assays using polyclonal antibodies [81]. These methods appear promising, although their use currently seems to be limited to research laboratories [51,82]. With respect to adenoviruses, most of these immunoassay techniques detect the common group antigen, and many studies have shown that about 45%–95% of positive specimens for the group antigen correspond to enteric serotypes 40 and 41 [83-86].

The LA technique is used clinically in the identification and typing of most gastrointestinal viruses. Latex particles coated with virus antibodies are agglutinated in the presence of virus antigen to produce the visible aggregates. Although the agglutination test is a more rapid method than EM or EIA, it is relatively less sensitive [53,74].

IC assay is rapid, technically very simple, and showed results comparable to those achieved with EIA [87,88]. Given that these tests have a high sensitivity and specificity (90%–95%), they are widely used in clinical laboratory practice. Most recently, rapid detection strip tests by IC kits have become commercially available for testing for astroviruses and noroviruses in stool specimens (IP Astro V Kit, ImmunoProbe Co. Ltd., Saitama, Japan, and RIDAQUICK Norovirus, R-Biopharm AG, Germany) [89].

The CLIA method is a diagnostic chemiluminescent immunoassay in which the virus antigen is captured by antibodies coupled with a molecule capable of emitting light during a chemical reaction. Light emission is used to measure the formation of the antigen-antibody complex. A CLIA test able to detect rotavirus in stool specimens (LIAISON Rotavirus, DiaSorin, Saluggia, Italy) has been marketed recently.

Molecular methods

A wide variety of diagnostic techniques are currently applied for the detection of gastrointestinal viruses. Traditional diagnostic methods such as electron microscopy, serology, and virus isolation have been the mainstay of clinical laboratories, especially in the past two decades. However, these traditional tests lack sensitivity. To overcome the shortcomings of traditional diagnostic methods, molecular techniques have been developed. Several nucleic acid amplification techniques (NAATs), particularly polymerase chain reaction (PCR), real-time PCR, and multiplex PCR, are currently used in routinely in clinical laboratories. Such approaches have allowed rapid diagnosis with a high degree of sensitivity and specificity. Moreover, NAATs have offered additional advantages over traditional methods by production of easily standardized protocols, thus resulting in a potential for automation with a range of options for real-time detection chemistries. The advent of fully automated systems with faster turnaround times has given clinical laboratories the tools necessary to report out accurate and sensitive results to clinicians.

By the end of the decade, a new generation of isothermal amplification techniques will gain wide popularity as diagnostic tools due to their simple operation, rapid reaction, and easy detection. Today, these new techniques, including loop-mediated isothermal amplification (LAMP) and NASBA, are starting to be used routinely in clinical laboratories to detect gastrointestinal viruses. Recently, an astrovirus-specific NASBA assay and a RT-LAMP for the identification of norovirus was developed for rapid detection of vital RNA in large numbers of stool specimens [90].

Conventional molecular methods (end-point PCR, nested PCR)

PCR has become the method of choice in the epidemiologic survey of gastrointestinal viruses. Currently, PCR is widely employed as a tool for the routine diagnosis of astrovirus, norovirus, sapovirus, rotavirus, and adenovirus infections. These PCR assays are highly sensitive, specific, and easy to perform. The most reliable marker for diagnosis of virus infection is the presence of viral nucleic acid in stool specimens. Therefore, the specimen of choice is stool samples from patients with diarrhea. To facilitate
the molecular analysis, the amplification of the viral genome and sequencing of the amplification products should be performed, and virus genotypes can be identified based on their sequence analysis. Therefore, PCR assays and nucleic acid sequence analysis are widely used for the detection and genotype identification of viruses causing gastroenteritis [91-95]. Gradually, these techniques have replaced the traditional immunological tests and have become the gold standard for diagnosis of gastrointestinal viruses for almost two decades. Nested PCR assays were also developed to increase both sensitivity and specificity. At last, multiplex RT-PCRs have been widely described. In particular, multiplex RT-PCRs for the detection of groups A, B, and C rotaviruses and identification of G and P genotypes of group A rotaviruses have been developed.

Real-time PCR

Real-time PCR technology provides results more quickly than conventional PCR assays and shows improved sensitivity and specificity. Although reagent and instrument costs are higher for real-time PCR technology compared to conventional molecular methods, real-time PCR requires less hands-on time per specimen than traditional PCR, particularly nested PCR, which is labor intensive. Automation of the extraction process and the use of real-time PCR further reduce the hands-on time in the clinical laboratory. Moreover, real-time PCR technology offers advantages over conventional PCR by providing lower risk of false-positive results due to amplicon contamination and quantification of viral load. Real-time PCR assays that detect the most common gastrointestinal viruses in large numbers of stool specimens have been developed [96-105].

Conclusions

Viral gastroenteritis is second only to viral respiratory diseases as a cause of morbidity and mortality worldwide, with most cases occurring in young children in non-industrialized countries. Diagnosis of viral gastroenteritis was previously based on conventional methods such as electron microscopy or indirect methods for the evaluation of virus-specific serological response. However, even when these methods were combined, some clinical specimens resulted negative despite clinical or epidemiological evidence of gastrointestinal infection. In this context, antigen detection and especially molecular approaches have greatly improved the ability of the clinical laboratory to diagnose viral gastroenteritis. NAATs have been shown to be more specific and sensitive compared to non-nucleic-acid-based methods. Thus, infected patients will be diagnosed more accurately and much more quickly during the course of viral infection when they are shedding low levels of virus, by using NAATs rather than non-molecular tests. Moreover, an accurate diagnosis provides more accurate information to public health authorities regarding the epidemiology of viruses causing gastroenteritis.

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