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Gastrointestinal tract and viral pathogens

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Abstract

Viral gastroenteritis is the most common viral illness that affects the gastrointestinal (GI) tract, causing inflammation and irritation of the lining of the stomach and intestines. Common signs and symptoms associated with this condition include abdominal pain, diarrhea, and dehydration. The infections commonly involved in viral gastroenteritis are rotavirus, norovirus, and adenovirus, which spread through the fecal-oral and contact routes and cause non-bloody diarrhea. These infections can affect both immunocompetent and immunocompromised individuals. Since the pandemic in 2019, coronavirus gastroenteritis has increased in incidence and prevalence. Morbidity and mortality rates from viral gastroenteritis have declined significantly over the years due to early recognition, treatment with oral rehydration salts, and prompt vaccination. Improved sanitation measures have also played a key role in reducing the transmission of infection. In addition to viral hepatitis causing liver disease, herpes virus, and cytomegalovirus are responsible for ulcerative GI disease. They are associated with bloody diarrhea and commonly occur in immunocompromised individuals. Hepatitis viruses, Epstein-Barr virus, herpesvirus 8, and human papillomavirus have been involved in benign and malignant diseases. This mini review aims to list different viruses affecting the GI tract. It will cover common symptoms aiding in diagnosis and various important aspects of each viral infection that can aid diagnosis and management. This will help primary care physicians and hospitalists diagnose and treat patients more easily.

Key Words: Virus diseases; Gastroenteritis; Enterocolitis; Rotavirus infections; Norovirus; Adenoviridae infections; Digestive system diseases

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Core Tip: Viral gastroenteritis is a common condition that affects the gastrointestinal (GI) tract. These viruses can affect people of all ages and are a significant public health concern. Dehydration resulting from the infection is the primary reason for emergency department visits in both children and adults. Our review discusses other GI viruses such as cytomegalovirus, herpes simplex virus, and hepatitis virus that cause manifestations such as hepatitis, gastritis, and bloody diarrhea. Both immunocompetent and immunocompromised individuals can be affected by these GI viral pathogens. Understanding the various viruses that cause GI manifestations can help with early diagnosis and appropriate management. This is a concise review of GI viral pathogens.

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INTRODUCTION

Viral pathogens cause gastrointestinal (GI) manifestations such as watery diarrhea, bloody diarrhea, and various other manifestations like hepatitis, ulcerative diseases, motility disorders, and neoplastic diseases of the GI tract in both immunocompetent and immunocompromised individuals. Infectious gastroenteritis is a major illness worldwide, especially in developing nations and viruses account for most of the illnesses. Globally, Norovirus is the leading cause of acute gastroenteritis outbreaks. Besides diarrhea, viruses are also responsible for causing diseases like hepatitis and ulcerative diseases. Asymptomatic and symptomatic co-infections with these pathogens listed are also mentioned in prior literature. Our paper is the first-of-its-kind mini-review summarizing most of the GI viral pathogens and their varied manifestations to update existing reviews[1,2]. We consolidated information on viruses that cause both diarrheal illness and non-diarrheal manifestations. Our paper will concisely summarize each entity to equip clinicians with accurate information and aid in correct diagnosis and management. As gastroenteritis is the most common disease caused by these viruses, we will be categorizing the paper based on this presentation. This categorization may also help with forming a differential diagnosis when patients present to health care centers and hospitals with the infection. We categorized the manuscript into: (1) Diarrheal illnesses further subdivided into non bloody diarrhea and bloody diarrhea; and (2) viruses associated with other non-diarrheal illnesses-hepatitis, ulcerative disease, and neoplasms (Table 1 shows common viruses that affect the GI system).

NON-BLOODY DIARRHEA FROM VIRAL GASTROENTERITIS

Norovirus

Norovirus is an RNA virus belonging to the *Caliciviridae* family and consists of forty-nine genotypes. According to Centers for Disease Control and Prevention (CDC), Norovirus is the leading cause of acute gastroenteritis among all age groups in the United States[3]. However, high-risk groups include young children, the elderly, travelers, military personnel, and the immunocompromised. On average, each year in the United States, Norovirus causes 109000 hospitalizations. Outbreaks usually occur in congregant environments like healthcare centers, cruise ships, and restaurants *via* fecal-oral transmission through food, water, or person-to-person contact. It is typically a self-limiting disease with symptoms like diarrhea, nausea/vomiting, and abdominal cramps that resolve within two to four days. It is primarily a clinical diagnosis. However diagnostic modalities include electron microscopy, polymerase chain reaction (PCR), enzyme-linked immunosorbent assay (ELISA), and immunochromatographic testing[4]. Diagnostic testing for Norovirus is rarely used given the short-lived nature of the disease. Currently, no drug has been clinically approved to treat norovirus infection owing to its mild state of disease. Complications of this illness include electrolyte imbalances, chronic gastroenteritis, irritable bowel syndrome, inflammatory bowel disease, convulsions, and encephalopathy (especially in children)[5]. Vaccinations are not currently licensed for norovirus infection prevention, but many trials are underway to assess the impact and efficacy of vaccines on disease prevention and transmission.

Rotavirus

Rotavirus, an RNA virus, and a member of the *Reoviridae* family is the major cause of diarrhea in children younger than five years. Reports from the Global burden of disease showed that 128530 deaths occurred due to Rotavirus infection alone[6]. Rotavirus contributed to 29.3% of total diarrheal deaths in 2015[6]. Younger age groups (< 5 years) and lower socioeconomic status seem to be the targets of the

Table 1 Common viruses affecting the gastrointestinal system

Virus	Route of infection	Population affected	Type of disease	Diagnosis	Treatment
Norovirus	Fecal-oral, fomites	Children < 5 yr	Gastroenteritis	Self-limited	Supportive
Rotavirus	Fecal-oral, fomites	Children < 5 yr	Gastroenteritis	Self-limited	Supportive
Adenovirus	Fecal-oral, fomites	Any age group, especially children	Gastroenteritis	Self-limited	Supportive
Hepatitis A	Fecal-oral, fomites	Any age groups; international travelers to endemic countries, IV drug users, men who have sex with men	Gastroenteritis, acute viral hepatitis, and fulminant liver failure	Serology	Supportive
Astrovirus	Fecal-oral, fomites	Children < 5 yr	Gastroenteritis	Self-limited	Supportive
Sapovirus	Fecal-oral, fomites	Children < 5 yr	Gastroenteritis	Self-limited	Supportive
Coronavirus	Fecal-oral, fomites	Any age group	Gastroenteritis; respiratory infection	Self-limited, viral rapid antigen, PCR can be performed	Supportive; for COVID-19-antivirals (nirmatrelvir/ritonavir, remdesivir), steroids, biologics (tocilizumab, baricitinib)
Hepatitis E	Fecal-oral, Fomites	15-40 yr	Gastroenteritis, acute hepatitis, and acute liver failure	Serology	Supportive
Cytomegalovirus	Contact with bodily fluids and organ transplantation	All ages	Colitis, toxic megacolon, and peritonitis	Viral PCR	Ganciclovir, valganciclovir, ganciclovir resistant-foscarnet, cidofovir
Herpes simplex virus	Sexual contact	MSM	Proctitis and anal ulcerations	Viral PCR	Acyclovir, valacyclovir, and famciclovir
HIV	Contact through bodily fluids like sexual contact, injection drug use, perinatal transmission	All ages	Acquired immunodeficiency syndrome, HIV enteropathy-diarrhea	2-step testing-combination antigen-antibody test followed by HIV 1/2 differentiation assay	HAART-combination therapy with Tenofovir, Emtricitabine, raltegravir, and bictegravir
Hepatitis B and D	Contact through bodily fluids like sexual contact, injection drug use, perinatal transmission	Usually adults, but all age groups can be affected	Hepatitis, cirrhosis, hepatocellular carcinoma	Serology, DNA load	Acute infections usually resolve; in some cases, tenofovir, entecavir
Hepatitis C	Contact through bodily fluids like sexual contact, injection drug use, transfusion, or perinatal transmission	Usually adults, but all age groups can be affected	Hepatitis, cirrhosis, hepatocellular carcinoma	Serology, RNA load	Combination therapy specific for genotypes; includes sofosbuvir/velpatasvir, glecaprevir/pibrentasvir
Varicella Zoster	Droplet, and contact infection	Commonly in children but can occur in any age group. Reactivation common in immunocompromised	Erosive disease of the stomach and intestines, motility problems	Clinical diagnosis, but RNA PCR is used for atypical presentations	Acyclovir, valacyclovir, and brivudin
Epstein-Barr virus	Contact with bodily fluids, especially saliva; sexual transmission, blood transfusion, organ transplantation	Individuals aged 15-24 yr	Gastritis, Enteritis, esophageal disorders, and gastric cancer	Mostly clinical diagnosis but can be diagnosed by serology	Symptomatic treatment, acyclovir in some cases
HHV-8	Sexual transmission, contact with saliva, blood transfusion, and organ transplantation	All age groups	Maculopapular and polypoid lesions of the GI tract	Endoscopy and biopsy	Radiation, intralesional chemotherapy, or systemic chemotherapy with liposomal doxorubicin and paclitaxel
HPV	Sexual transmission-oral, vaginal, anal sex	15-49 yr	Oropharyngeal, esophageal, gastric, colorectal, and anal cancers	Cytology and viral testing	Cancer-specific treatment

HIV: Human immunodeficiency virus; HPV: Human papillomavirus; HHV: Human herpesvirus 8; MSM: Men who have sex with men; PCR: Polymerase chain reaction; GI: Gastrointestinal.

disease[7]. Diarrhea caused by the virus is thought to be *via* two mechanisms: (1) Osmotic diarrhea due to malabsorption secondary to enterocyte damage; and (2) secretory diarrhea from activation of the enteric nervous system and non-structural protein-4[7]. The disease is transmitted through fecal-oral routes and fomites. Clinical manifestations include diarrhea, vomiting, and fever. Clinical morbidity is due to severe dehydration requiring hospitalization and can sometimes also lead to necrotizing enterocolitis[8]. ELISA can detect the virus until 1 wk after the onset of diarrheal illness whereas real time PCR (RT-PCR), being more sensitive can detect the virus until longer periods[7]. Fluid and electrolyte resuscitation remains the mainstay of treatment. Symptomatic management with Antiemetics and Antidiarrheal drugs decreases fluid losses thus fastening recovery and preventing death. Routine use of antivirals is not recommended for this infection. The advent of Rotarix and RotaTeq around 2006-2008 brought about a notable change in the morbidity and mortality of rotaviral disease. Mortality among children younger than 5 years of age has decreased by more than 45% since the mid-2000s[6]. It is prudent to say that, although there has been a shift from rotaviral illness being a fatal disease to a non-fatal disease, continued efforts are necessary to widen vaccination coverage and improve water and sanitation facilities.

Adenovirus

Adenovirus is a double-stranded DNA virus belonging to the Adenoviridae family. HAdV-F40 and F41 are the enteric serotypes implicated in causing acute gastroenteritis[9]. According to the re-analysis done by Global Enterics Multicenter Study, adenovirus was the second most common cause of diarrheal illness after Rotavirus in infants[9]. Infections caused by Adenovirus include febrile respiratory illness, pharyngoconjunctival fever, keratoconjunctivitis, and gastroenteritis. Transmission routes include aerosols, fecal-oral, and fomites. Adenovirus infections occur in congregate settings like daycare centers, summer camps, college campuses, and military camps. Symptoms of adenoviral gastroenteritis are like any other gastroenteritis including diarrhea, vomiting, and abdominal cramps. However, a multicenter study done in 8 Low-resource countries showed that fever was more commonly associated with adenoviral infection compared to other viral infections other than rotavirus[10]. Diagnostic methods are not often used but consist of antigen detection, PCR, and serology. No specific treatment is available for the infection but measures like rehydration, adequate food intake, and zinc supplementation are essential, especially in low to middle-income countries. Complications of adenoviruses include intussusception, hepatitis of unknown cause (adenovirus type 41), chronic lung disease, meningoencephalitis, and cystitis[11,12]. Currently, vaccination against Adenovirus type 4 and 7 is FDA-approved to prevent febrile acute respiratory disease for military populations aged 17 years to 50 years.

Astrovirus

Astroviruses are single-stranded RNA viruses belonging to the family of Astroviridae. Astroviruses are responsible for 0.5%-15.0% of diarrheal outbreaks across the world[13]. Transmission is through the fecal-oral route and fomites. Like any other gastroenteritis-causing virus, outbreaks happen in communal settings like schools, nursing homes, and swimming pools[14]. The incubation period is long (4.5 d) and it causes mild diarrhea lasting for about 2 d to 3 d associated with symptoms like fever, anorexia, and vomiting[15]. Diagnostics include electron microscopy, cell culture, immunoassays, and RT-PCR, with the latter being the most commonly used modality[16]. This infection is self-limited and usually resolves with fluid and electrolyte replacements. Immunocompromised adults and the elderly have longer-lasting symptoms with rare occurrences of complications like meningitis and encephalitis [17].

Sapovirus

Sapoviruses are single-stranded RNA viruses belonging to the same family as Norovirus, *Caliciviridae*. According to the Etiology, Risk Factors, and Interactions of Enteric Infection and Malnutrition and the Consequences for Child Health and Development (MAL-ED) study, sapovirus had the second-highest incident rate of acute diarrhea after Shigella. The study attributed an incidence rate of 22.8 cases per 100 child years to sapovirus with a 95% confidence interval ranging from 18.9 to 27.5[18]. Transmission occurs through fecal-oral contact, contaminated food/water, and fomites[19]. They are known to cause gastroenteritis in humans, specifically aged < 5 years, and animals[20]. Outbreaks occur in communal settings like daycare centers, hospitals, nursing homes, and schools[21]. While the usual clinical symptomatology is the same as any gastroenteritis-causing virus, it has also been implicated in causing chronic diarrhea, especially in immunocompromised populations. Definitive diagnosis by PCR detection, however, is not indicated due to the self-limiting nature of the disease and the cost considerations[21]. No antivirals are warranted, World health organization (WHO) guided treatment for diarrhea viz rehydration, zinc supplementations, and adequate nutrition is considered the treatment of choice[22]. Interestingly, Nitazoxanide has been tried in transplant patients with some benefits[23]. Cases of Sapoviruses causing septic shock and intestinal obstruction have been reported in the literature[24,25].

Enterovirus

Enteroviruses are single-stranded RNA viruses belonging to the Picornaviridae family. Enterovirus

genus consists of viruses like Poliovirus, Coxsackie virus, Echovirus, rhinovirus, and other enterovirus subtypes. According to the CDC, it is estimated that around 10-15 million non-polio-enterovirus infections occur annually[26]. They can be transmitted *via* the fecal-oral route or through respiratory secretions. Infants, children, and teenagers are more likely to get affected than adults[27]. They generally have a secondary tissue tropism and spread to other target tissues after they infect the GI system[28]. Non-Polio enteroviruses are known to cause diseases like aseptic meningitis, hand-foot-mouth disease, flaccid paralysis, myocarditis, pancreatitis, *etc*[28,29]. Some non-specific GI manifestations are less common but include abdominal pain, vomiting, and diarrhea and are self-limited. Enteroviruses can be detected in stool, pharynx, blood, and CSF using techniques like PCR, serology, and cell culture. Treatment is usually symptomatic care and no targeted therapies have been developed yet. Some of the dreaded complications of enteroviruses include meningitis, encephalitis, myocarditis, and acute flaccid paralysis[30,31]. The only enteroviral vaccine is the polio vaccine to prevent poliomyelitis.

Coronavirus

Coronaviruses are single-stranded RNA viruses belonging to the Coronaviridae family. SARS-CoV-1 emerged in 2002-2003 and caused a global outbreak that affected over 8000 people in 26 countries, with a case fatality rate of approximately 10%[32]. MERS-CoV emerged in 2012 and has since caused sporadic outbreaks in the Middle East and other regions, with a case fatality rate of approximately 34%[33]. Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 and has since spread globally, causing a pandemic that has affected millions of people worldwide. As of April 21, 2023, there have been over 435 million confirmed cases and over 5.8 million deaths reported globally[34]. Coronaviruses are transmitted through multiple routes, mainly through droplets, contact with infected persons, and contaminated surfaces.

Human Coronaviruses are known to cause respiratory infections, but they also cause GI symptoms including diarrhea, nausea, vomiting, and abdominal pain. The majority of HCoV infections like diarrhea occur in neonates, infants, and children. Also, they co-infect with other enteric viruses like norovirus and rotavirus. SARS-CoV and MERS-CoV, members of the coronavirus family have also been implicated in causing the above symptoms[35]. SARS-CoV2 causing COVID-19 also presents as diarrhea, nausea, vomiting, and abdominal pain along with respiratory symptoms and sometimes even in the absence of respiratory manifestations[36]. GI manifestations were speculated to be caused due to the high expression of ACE2 receptors in the gut which is the binding site for SARS-CoV-2[37]. Changes in the gut microbiota have also been observed in COVID-19-infected patients. Although they are respiratory viruses, interestingly, the GI transmission of this group of viruses has also been proven as many studies have mentioned the detection of RNA in stool samples[35]. Currently, no specific antivirals are indicated in SARS and MERS infections, whereas COVID-19 treatment entails various therapies like antivirals, steroids, biologics, *etc*. The most common complications of COVID-19, caused by SARS-CoV-2, include pneumonia and acute respiratory distress syndrome (ARDS), which can lead to respiratory failure and death in severe cases[38]. COVID-19 can also cause a range of other complications, including cardiovascular and neurological complications, blood clots, and multisystem inflammatory syndrome in children[39]. MERS-CoV infections are also associated with severe respiratory illness and complications such as pneumonia, ARDS, and septic shock[40]. SARS-CoV-1 infections can cause similar respiratory complications, as well as complications such as liver and kidney failure[41]. Currently, several vaccines against the COVID-19 have been developed. Pfizer-BioNTech and Moderna mRNA vaccines have reported efficacies of over 90% in preventing symptomatic COVID-19[42,43].

Hepatitis E virus

Hepatitis E virus is a single-stranded RNA virus belonging to the family Hepeviridae. According to the WHO, there are an estimated 20 million HEV infections worldwide every year[44]. hepatitis E caused approximately 44000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis)[44]. Hepatitis E is mainly transmitted through food and water contamination, also through perinatal transmission, and blood transfusions[45]. Pregnant women, especially those in their third trimester, and individuals with pre-existing liver disease are the most vulnerable groups for developing severe HEV infection[46-48]. Other groups that may be at increased risk of HEV infection include travelers to endemic areas, healthcare workers, and individuals who consume undercooked or raw pork[49]. It is usually a self-resolving illness but can sometimes occur with symptoms like fever, anorexia, jaundice, nausea, vomiting, hepatomegaly, and abdominal pain[50]. Diagnosis is by serology, enzyme immunoassay, or RNA detection by PCR. Acute hepatitis E does not require treatment, however, if liver failure occurs then liver transplantation is an option[51]. Chronic hepatitis E can be treated with Ribavirin for 12 wk[52]. In pregnant women, HEV infection can lead to fulminant hepatic failure, which has a mortality rate of up to 30%[46]. Other complications include acute liver failure, chronic HEV infection, and neurological complications like Guillain-Barre syndrome, myelitis, and neuropathy to name a few[53]. Vaccines are not yet commercially available for prevention except in China[54].

BLOODY DIARRHEA FROM VIRAL GASTROENTERITIS

Cytomegalovirus

Cytomegalovirus (CMV) is a double-stranded DNA virus and a member of the Herpesviridae family with a prevalence ranging between 40%-100% in the adult population[55]. Latent phase reactivation occurs in immunocompromised individuals, including transplant recipients, patients on immunosuppressive agents, and those with inflammatory bowel disease (IBD) treated with steroids[56]. CMV is transmitted by contact with infectious body fluids like saliva, urine, respiratory droplets, sexual contact, blood transfusion, and solid organ transplants. Symptomatology of CMV colitis could range from bloody diarrhea, abdominal pain, fever, weight loss, and lymphadenopathy to toxic megacolon. Few studies show that the severity of CMV is related to age and could cause Toxic megacolon and pan peritonitis in the elderly[57]. Although histology of tissue analysis is considered the gold standard for diagnosis, RT-PCR has the highest sensitivity and detection rate for infection. The most used antivirals are intravenous ganciclovir and valganciclovir. Foscarnet and cidofovir are used in ganciclovir-resistant cases. Some studies showed that although CMV is reactivated in IBD patients, it spontaneously disappears even without antiviral treatment[58,59]. Complications associated with CMV colitis may include ischemic colitis, perforation of the large bowel, toxic megacolon, and formation of pseudomembranous. Currently, there are no vaccines available for CMV. As per European Crohn's and Colitis Organization guidelines, if severe systemic CMV is detected, immunomodulators should be discontinued and screening for CMV is not routinely performed before starting immunomodulators in IBD[60].

Herpes simplex virus

Herpes simplex virus (HSV) is a double-stranded DNA virus belonging to the Human Herpesviridae family. HSV proctitis is the second most common sexually transmitted cause of infectious proctitis in homosexual males and could be caused by HSV-1 or HSV-2, but 70% of cases are due to HSV-2[61,62]. Prevalence of HSV-1 and HSV-2 have decreased over time linearly from 59.4 % & 18.0% in 1999-2000 to 48.1% & 12.1% in 2015-2016[63]. HSV is transmitted by intimate person-to-person contacts like men who have sex with men (MSM), unprotected receptive anal, and oral sex. Clinical symptoms of HSV proctitis include rectal bleeding, tenesmus, anorectal pain, and mucous discharge. The absence of external HSV lesions should not diminish suspicion of HSV infection as only 32% of men with HSV proctitis have external anal ulcerations[64,65]. Due to the high seropositivity for HSV worldwide, serological analysis plays a minor role in the diagnosis. PCR has been used to accurately diagnose and quantify the HSV DNA from clinical biopsy specimens[66]. Immunofluorescence staining of colonic specimens with HSV-type specific monoclonal antibodies against glycoproteins is highly specific to confirm the diagnosis. CDC recommends antiviral treatment with acyclovir, valacyclovir, or famciclovir in acute proctitis if the HSV infection is suspected or confirmed. Complications of HSV proctitis can result in symptoms such as constipation, severe anorectal pain, difficulty urinating, sacral paresthesia's, and diffuse ulcerations of the distal rectal mucosa. Currently, there are no vaccines approved for the prevention of HSV. Infectious proctitis must be considered before starting immunosuppressant therapy for presumed IBD, as the immunosuppressive medications may result in a lack of improvement or symptomatic worsening of infectious proctitis. HSV-induced anogenital ulcers will lead to a 1.5 to 7.0-fold increase in human immunodeficiency virus (HIV) transmission due to associated mucosal barrier breach, hence HIV screening is important. Individuals with acute proctitis along with HIV and/or painful perianal ulcers should receive presumptive treatment for anogenital HSV[67].

VIRAL GASTROINTESTINAL PATHOGENS ASSOCIATED WITH DIARRHEA AND OTHER GASTROINTESTINAL MANIFESTATIONS

Hepatitis A virus

Hepatitis A virus (HAV) is an RNA virus and a member of the Picornaviridae family. According to a report published in 2017, the incidence of acute hepatitis A was 170 million cases globally[68]. It is commonly transmitted through the fecal-oral route *via* contaminated food and water consumption. Transmission through sexual contact, person-to-person contact, and illicit drug use also exist in the literature[69]. Case fatality was higher in males, older than 50 years, and coexisting chronic liver disease raised the risk of developing fulminant hepatitis after an HAV infection[69]. From prior literature, > 70% of children under six years of age do not develop symptoms whereas > 70% of adults manifest symptoms[70]. Symptoms include fever, malaise, nausea, vomiting, abdominal discomfort, and jaundice. Physical examination findings include hepatomegaly and jaundice[70]. Hepatitis A generally follows a benign course, however chronic relapsing hepatitis for as long as 1 year is a possibility. Diagnosis is through serology by measuring the IgM antibody. IgG detection is useful when the question of immune status arises. Owing to its self-limited nature, this infection does not require treatment. According to the CDC, Hepatitis A vaccination is recommended for all infants. It is also recommended for those at substantial risk of exposure to hepatitis A infection, those at risk of

progressing to fulminant hepatitis, those experiencing homelessness, and HIV-infected persons.

Human immunodeficiency virus

Human immunodeficiency virus (HIV) is an RNA virus, belonging to the family Retroviridae. According to recent statistics, around 1.5 million individuals acquired HIV in 2021[71]. High-risk groups include gay and bisexual populations of all races and ethnicities, African Americans, injection drug users, and transgender populations[72]. It is transmitted *via* body fluids through sexual contact, needle sharing, breast milk, and perinatal transmission. In addition to the wide range of clinical manifestations, it is interesting to note how this virus affects the GI system. A specific term, “HIV enteropathy” has been coined to define the GI manifestations caused by this virus[73]. It causes alteration of epithelial ionic balances and enterocyte apoptosis resulting in inflammation, change in permeability, and malabsorption[73]. Histologically, villous atrophy, crypt hyperplasia, and epithelial hyperproliferation ensue. All of this culminates in causing diarrhea secondary to HIV enteropathy. HIV also leads to other GI effects by the virtue of its immunodeficiency, thus paving the way for opportunistic infections. Antiretroviral therapy (ART), especially protease inhibitors itself, can also cause diarrhea in HIV[74]. GI complications range from Esophageal disorders, gastric illnesses to colitis, enteritis, and anorectal disease. Most of these are caused by secondary/opportunistic bacterial, fungal, and viral infections and HIV-induced neoplasia of the GI tract. Also, the GI tract is a favorable site for HIV replication and GI CD4 destruction[75]. Pancreatic and hepatobiliary complications include pancreatitis, exocrine pancreatic insufficiency, hepatitis, and non-alcoholic fatty liver disease[76]. Diagnosis is fourth generation antigen-antibody assay followed by HIV 1/2 differentiation assay. Stool samples for ova and parasite examination should be done to identify the causative pathogen given the high chance of opportunistic infections like *Cryptosporidium*, *Isospora*, *Giardia*, *etc*[74]. If a cause cannot be identified yet, endoscopy with biopsy is an option[74]. Highly ART (HAART) causes the reconstitution of peripheral circulating plasma CD4 cells, but studies have found that it is not successful in the replenishment of GI CD4 cells[77].

Hepatitis B and D virus

Hepatitis B virus (HBV) is a partially double-stranded DNA virus and belongs to the family of Hepadnaviridae. According to the CDC statistics, globally, 296 million people are infected with Hepatitis B. High-risk groups include veterans, healthcare professionals, MSM, injection drug users, persons with HIV, hepatitis C virus (HCV) co-infection[78]. hepatitis B can be transmitted perinatally, through sexual contact, percutaneous or person-to-person contact with infected body fluids[79]. The incubation period ranges from 1 mo to 4 mo. The acute phase of hepatitis B infection presents as a serum-sickness-like illness characterized by fever, rash, and arthralgia followed by jaundice, nausea and vomiting, and other constitutional symptoms[79]. It causes elevation of alanine aminotransferase (ALT) more than aspartate aminotransferase (AST) and bilirubin. Diagnosis is by serum viral biomarkers[79]. It is known that Hepatitis B is implicated in the causation of Hepatitis and its plethora of clinical manifestations including hepatocellular carcinoma (HCC). HCC contributes to 80% of global liver cancers in 2018[80]. Pathogenesis of HCC in hepatitis B is: (1) Direct-due to the oncogenic viral protein activating proto-oncogenes, transcriptional pathways (MAP kinase and JAK/STAT), and inhibition of tumor suppressor genes (p53); (2) chronic inflammation, cirrhosis, and regeneration[81,82]. It is also worth noting the other GI disorders caused by this virus. According to a cumulative analysis performed by Yang *et al*[83] involving 7027546 individuals across 13 studies-10 studies reported data on hepatitis and gastric cancer, and it was found that the risk of gastric cancer was 26 times higher in the hepatitis B population[83] (pooled HR, 1.26; 95%CI, 1.08-1.47; $P = 0.003$). This can be attributed to chronic inflammation, tumorigenesis, and alteration of the tumor suppression process due to oncogenic viral proteins [84,85]. Another study observed that Hepatitis B is associated with gut microbiota disturbance, especially in the cirrhosis population[86]. Acute HBV is self-limited and does not require treatment. Special cases like acute liver failure, complicated course (prolonged PT and marked elevation of jaundice are treated[87]. Treatment of chronic hepatitis B depends on factors like the presence or absence of cirrhosis, ALT level, and HBV DNA level. Therapy includes drugs like Tenofovir, Entecavir, and Interferon[87]. Complications of acute hepatitis B are mainly due to immune complex reactions occurring in various parts of the body manifesting as glomerulonephritis, polyarteritis nodosa, cryoglobulinemia[88], *etc*. Sequelae of chronic hepatitis B are well known including cirrhosis and HCC. Hepatitis B prevention is achieved with recombinant vaccines that require either three or two doses. Combined vaccination, along with diphtheria, pertussis, tetanus, and hepatitis A is also in use currently in the United States.

Hepatitis D virus (HDV) is a defective RNA virus requiring the presence of the Hepatitis B virus for its replication and assembly of virions. It belongs to the Kolmioviridae family. The global disease burden of hepatitis D/hepatitis B co-infection is 62-72 million[89]. HDV requires HBV to replicate and therefore the HBV population is the target group for this infection. The mode of transmission is the same as HBV infection. Hepatitis D infection can occur as a co-infection with hepatitis B occurring simultaneously which usually leads to spontaneous resolution[90]. On the other hand, superinfection in already infected HBV persons usually leads to conversion to chronic hepatitis D infection which is considered a severe form of chronic hepatitis. Symptoms of acute hepatitis D are indistinguishable from

other forms of viral hepatitis. However, superinfection with HBV can lead to fulminant liver failure[91]. In addition, the risk of progression to cirrhosis is 3 times higher in superinfection than in infection with HBV alone[92]. Diagnosis is through the detection of IgM and IgG Anti HDV antibodies and confirmed by testing for HDV RNA[93]. The current treatment strategy utilizes Pegylated interferon for at least 1 year[94]. However, several emerging therapies like myrcludex B and Sofosbuvir are gaining popularity in the treatment of hepatitis D.

HCV

HCV is a hepatotropic, single-stranded RNA virus belonging to the family of Flaviviridae. The prevalence of Hepatitis C is 0.5%-2.5% with the highest being in the eastern Mediterranean region and Europe[95]. It was recorded that 399000 individuals died in 2016 due to complications from chronic hepatitis C[95]. Injection drug users, HIV, healthcare professionals, prior recipients of blood products (before 1992), and hemodialysis patients are at risk of acquiring HCV[96]. Modes of transmission include injection drug use, blood transfusion, sexual contact, and perinatal transmission[97]. Acute hepatitis C infection is usually asymptomatic and can consist of symptoms like fever, abdominal pain, and jaundice[97]. Only 15%-20% resolve completely whereas the remaining percentage of infected patients go on to have chronic hepatitis C[97]. Chronic hepatitis C is characterized by the presence of HCV RNA for more than 6 mo. Sequelae of chronic hepatitis C are liver fibrosis, Cirrhosis, and Hepato-cellular Carcinoma. A decision analytical model done by Chen *et al*[98] predicted that the cumulative incidence of HCC among HCV-infected persons would be 583000 cases between 2012 to 2040. Several extrahepatic manifestations affect the quality of life in chronic hepatitis C like mixed cryoglobulinemia, glomerulonephritis, skin disease (porphyria cutanea tarda and lichen planus), thyroid disease (Hashimoto's disease and Grave's disease) to name a few[99]. Diagnosis is made by serology either by the presence of HCV RNA or anti-HCV antibody[100]. Guidelines suggest treatment with direct-acting antiviral agents (DAA) after acute infection to prevent progression to chronic infection and due to the high likelihood of loss to follow-up to test for spontaneous clearance of the virus[101]. Chronic hepatitis C is treated with DAA regimens based on the genotype and also the presence of advanced liver disease. Some of the pan-genotype regimens include Sofosbuvir and velpatasvir for 12 wk and glecaprevir and pibrentasvir for 8 wk[102]. Vaccination for hepatitis C is under development and prevention of hepatitis C solely depends upon the prevention of high-risk behavior like injection drug use and adopting safe sexual practices.

Varicella zoster virus

Varicella-zoster virus (VZV) is a double-stranded enveloped DNA virus belonging to the α -herpes-viruses subfamily. Adults, young children, and immunocompromised are at risk of developing the severe disease with primary varicella infection[103]. According to the CDC report, 4 million cases occurred annually in the United States during the pre-vaccine era. After the introduction of vaccines, incidence declined by around 97%[104]. Transmission is through droplets, aerosols, and direct contact with respiratory secretions or zoster lesions[105]. Reactivation of latent VZV from dorsal root ganglia leads to herpes zoster (shingles), which presents as localized cutaneous eruption associated with neuralgic pain. GI VZV lesions could present as multiple erosions occurring in the stomach, duodenum, and small and large intestines[106]. Skin findings often precede visceral involvement. In a study, 42 of 131 patients with herpes zoster [not specified as bone marrow transplant (BMT) or malignancy patients] progressed to visceral involvement[107]. The mortality rate from GI VZV ranges from 28.6% to 50.0% in BMT recipients despite antiviral therapy[108]. GI manifestations of herpes zoster are extremely rare. Constipation secondary to motility issues (visceral neuropathy) has been reported in some case reports [106,109]. Skin findings and concomitant GI symptoms should raise suspicion in predisposed patients. Elevated liver enzymes and abnormal imaging findings also aid in diagnosis. Diagnosis can be confirmed through immunohistochemical staining of biopsy specimens VZV. Although shingles is a clinical diagnosis, PCR (highly sensitive) and immunoassays are used for the diagnosis, especially in atypical presentations[110]. Treatment options include IV Acyclovir, valacyclovir, famciclovir, and brivudine. If clinical resistance to Acyclovir is suspected, foscarnet could be used. Complications of primary varicella infection are bacterial infections of the skin and soft tissues, pneumonia, and cerebellar ataxia[111]. Reactivation of VZV (Herpes zoster) is complicated by chronic pain, encephalitis, post-herpetic neuralgia, myelopathy, *etc*[112]. Varivax, a two-dose vaccine, is licensed for children above 12 mo of age to protect against chicken pox. Shingrix is an FDA-approved recombinant vaccine to reduce the risk of shingles in people aged 50 years or more.

Epstein-Barr virus

Epstein-Barr virus (EBV) is a double-stranded DNA virus belonging to the Herpesviridae family. It is estimated that more than 90% of the worldwide population has been infected with EBV[113]. It is associated with a wide range of clinical manifestations, the most common one being infectious mononucleosis (IM), prevalent among teens and adults[114]. It is spread through saliva and presents with fever, malaise, sore throat, and lymphadenopathy[114]. Chronic active EBV (CAEBV) is a condition where IM symptoms persist for more than 3 mo and is commonly seen in Asia[115]. EBV has also been

implicated in the pathogenesis of multiple sclerosis and rheumatoid arthritis[115]. Also, chronic EBV has been linked with gastritis, enteritis, and esophageal disorders, oral hairy cell leukoplakia[116-119]. A separate clinical subset of diseases EBV has been strongly associated with is lymphoproliferative cancers like Burkitt's Lymphoma, Hodgkin's lymphoma, Non-Hodgkin's lymphoma, and post-transplant lymphoproliferative disorder. Besides lymphoproliferative cancers, EBV has been implicated in causing other cancers like gastric cancer, nasopharyngeal cancers, and breast cancer. Some key features of EBV-associated gastric cancers are they can occur in the gastric fundus, cardia, and body, unlike non-EBV-associated gastric cancers which happen in the antrum. EBV-associated cancer starts as a lesser fibrotic nodular ulcer compared to the non-EBV type[119]. Microscopically, EBV-associated gastric cancer shows a monoclonal proliferation infected latently with EBV, suggesting the role of the virus in the early stages of tumorigenesis[119]. IBD patients on immunosuppressants like thiopurines have a high incidence of EBV and some studies also showed that patients taking these medications also have a higher incidence of lymphoproliferative disorders than those who are not on treatment for IBD [120,121]. EBV can be diagnosed by the detection of antibodies against various antigens like viral capsid antigens, EBNA; enzyme immunoassays, Western blot, PCR, heterophile antibody agglutination, *etc* [122]. There is no targeted therapy for EBV. Symptomatic treatment has been a cornerstone for the treatment of EBV. Several anti-viral drugs including acyclovir, and cidofovir have been tried with good invitro activity and with no clinical benefit[123].

Human herpesvirus 8

Human herpesvirus 8 (HHV 8) is a double-stranded DNA virus belonging to the Human Gamma herpesvirus family. It is also commonly known as Kaposi Sarcoma-associated herpesvirus due to the disease it causes, Kaposi's Sarcoma (KS). It is common in HIV, MSM, Mediterranean, Ashkenazi jews, and sub-Saharan African populations[124,125]. According to seroprevalence, Uganda has the highest seroprevalence worldwide where KS is endemic. No more than 6% seroprevalence has been reported in the United States[126]. KS is a low-grade vascular tumor that involves mucocutaneous sites and visceral locations, predominantly the respiratory and GI systems[125]. GI Kaposi sarcoma is usually asymptomatic but on progression, can present as abdominal pain, nausea, vomiting, and GI bleeding. Diagnosis is through endoscopy and biopsy[127]. It is most common in the stomach and small intestine and endoscopically appears as a maculopapular lesion to a nodular or polypoid mass which can sometimes bleed on touch[127]. In HIV Kaposi, HAART is the mainstay of treatment with or without chemotherapy. In classic Kaposi's sarcoma, treatment options include local therapy with radiation or intralesional chemotherapy; systemic chemotherapy with liposomal doxorubicin or paclitaxel[124]. Besides KS, HHV 8 is implicated in the causation of lymphoproliferative disorders like primary effusion lymphoma and multicentric Castleman's disease[128].

Human papillomavirus

Human papillomavirus (HPV) is a double-stranded DNA virus belonging to the Papillomaviridae family. It is estimated that around 13 million persons acquired HPV infection in 2018 in the United States and over 77 million had a prevalent infection during the same year[129]. It is primarily a sexually transmitted disease (vaginal, anal, and oro-genital) but can also be transmitted through skin-to-skin contact and vertical transmission[130]. High-risk sexual behaviors, multiple sexual partners, and previous history of STDs increase the risk of HPV acquisition. Clinical manifestations of HPV include cutaneous warts, anogenital warts, and respiratory papilloma's caused by HPV 6,11 *etc* genotypes along with cancer precursor lesions (intraepithelial neoplasia's) and cancers caused by HPV 16,18 genotypes. HPV is an oncogenic virus and has been associated with a multitude of cancers including GI cancers like esophageal cancer, stomach cancer, colorectal cancer, anal cancer, and liver cancer[131]. The other cancers to which it has been linked are cervical, penile, vulvar, vaginal, and oropharyngeal cancers [132]. HPV causes cervical cancer near the transformation zone where there is a transitional/transformational zone (squamocolumnar junction). In the same fashion, HPV also causes cancerous lesions in the anal region because of the presence of a squamocolumnar junction which is a site of multipotent embryonic cells. However, the incidence rates of cervical cancer and anal cancer are much different (17:1). Colposcopy, Biopsy, HPV DNA detection, PCR, and pap smear are some of the methods by which HPV can be diagnosed[133]. Treatment depends on the type of disease. Warts can be treated with topical medications like salicylate, imiquimod, trichloroacetic acid, cryosurgery, and electrocautery. Precancerous and cancerous lesions require detailed workup and surgical excision of lesions[134]. Current FDA-approved vaccines are Bivalent (for types 16 and 18), quadrivalent (for types 6, 11, 16, and 18), 9 valent (for types 6, 11, 16, 18, 31, 33, 45, 52, and 58) protect against genital warts, precancerous lesions of vulva, cervix and anus, oropharyngeal cancers and are approved for males and females aged 9-45.

CONCLUSION

After conducting a comprehensive review of the literature on viruses and the GI tract, these pathogens

play a significant role in both acute and chronic GI diseases. While many viruses can cause mild symptoms, such as diarrhea and vomiting, some can lead to severe and even life-threatening conditions. The importance of early detection and appropriate management of viral gastroenteritis cannot be overstated.

Several studies have highlighted the need for better prevention and control measures, including improved hygiene practices and the development of effective vaccines. It is crucial to continue researching the relationship between viruses and the GI tract to better understand how these pathogens operate and to develop more targeted treatments.

Overall, this review provides clinicians with a differential diagnosis when they encounter patients with GI manifestations. It emphasizes the importance of recognizing the different presentations of viruses on the GI tract and understanding the prevention, diagnosis, and treatment of these illnesses.

FOOTNOTES

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REFERENCES

- 1 Goodgame RW. Viral infections of the gastrointestinal tract. *Curr Gastroenterol Rep* 1999; **1**: 292-300 [PMID: 10980963 DOI: 10.1007/s11894-999-0112-5]
- 2 Makimaa H, Ingle H, Baldrige MT. Enteric Viral Co-Infections: Pathogenesis and Perspective. *Viruses* 2020; **12** [PMID: 32824880 DOI: 10.3390/v12080904]
- 3 Burke RM, Mattison CP, Pindyck T, Dahl RM, Rudd J, Bi D, Curns AT, Parashar U, Hall AJ. Burden of Norovirus in the United States, as Estimated Based on Administrative Data: Updates for Medically Attended Illness and Mortality, 2001-2015. *Clin Infect Dis* 2021; **73**: e1-e8 [PMID: 32291450 DOI: 10.1093/cid/ciaa438]
- 4 Kirby A, Iturriza-Gómara M. Norovirus diagnostics: options, applications and interpretations. *Expert Rev Anti Infect Ther* 2012; **10**: 423-433 [PMID: 22512752 DOI: 10.1586/eri.12.21]
- 5 Lu MC, Lin SC, Hsu YH, Chen SY. Epidemiology, Clinical Features, and Unusual Complications of Norovirus Infection in Taiwan: What We Know after Rotavirus Vaccines. *Pathogens* 2022; **11** [PMID: 35456126 DOI: 10.3390/pathogens11040451]
- 6 Troeger C, Khalil IA, Rao PC, Cao S, Blacker BF, Ahmed T, Armah G, Bines JE, Brewer TG, Colombara DV, Kang G, Kirkpatrick BD, Kirkwood CD, Mwenda JM, Parashar UD, Petri WA Jr, Riddle MS, Steele AD, Thompson RL, Walson JL, Sanders JW, Mokdad AH, Murray CJL, Hay SI, Reiner RC Jr. Rotavirus Vaccination and the Global Burden of Rotavirus Diarrhea Among Children Younger Than 5 Years. *JAMA Pediatr* 2018; **172**: 958-965 [PMID: 30105384 DOI: 10.1001/jamapediatrics.2018.1960]
- 7 Crawford SE, Ramani S, Tate JE, Parashar UD, Svensson L, Hagbom M, Franco MA, Greenberg HB, O'Ryan M, Kang G, Desselberger U, Estes MK. Rotavirus infection. *Nat Rev Dis Primers* 2017; **3**: 17083 [PMID: 29119972 DOI: 10.1038/nrdp.2017.83]
- 8 Bernstein DI. Rotavirus overview. *Pediatr Infect Dis J* 2009; **28**: S50-S53 [PMID: 19252423 DOI: 10.1097/INF.0b013e3181967bee]
- 9 Lynch JP 3rd, Kajon AE. Adenovirus: Epidemiology, Global Spread of Novel Types, and Approach to Treatment. *Semin Respir Crit Care Med* 2021; **42**: 800-821 [PMID: 34918322 DOI: 10.1055/s-0041-1733802]
- 10 Guga G, Elwood S, Kimathi C, Kang G, Kosek MN, Lima AAM, Bessong PO, Samie A, Haque R, Leite JP, Bodhidatta L, Iqbal N, Page N, Kiwelu I, Bhutta ZA, Ahmed T, Liu J, Rogawski McQuade ET, Houpt E, Platts-Mills JA, Mduma ER. Burden, Clinical Characteristics, Risk Factors, and Seasonality of Adenovirus 40/41 Diarrhea in Children in Eight Low-Resource Settings. *Open Forum Infect Dis* 2022; **9**: ofac241 [PMID: 35854993 DOI: 10.1093/ofid/ofac241]

- 11 **Shieh WJ.** Human adenovirus infections in pediatric population - An update on clinico-pathologic correlation. *Biomed J* 2022; **45**: 38-49 [PMID: 34506970 DOI: 10.1016/j.bj.2021.08.009]
- 12 **Ilic I, Ilic M.** Multi-country outbreak of severe acute hepatitis of unknown origin in children, 2022. *Acta Paediatr* 2023 [PMID: 36705335 DOI: 10.1111/apa.16685]
- 13 **Mattison CP, Vinjé J, Parashar UD, Hall AJ.** Chapter 19-Rotaviruses, astroviruses, and sapoviruses as foodborne infections. In: Morris JG, Vugia DJ, editors. *Foodborne Infections and Intoxications*. 5th ed. Academic Press, 2021: 327-344 [DOI: 10.1016/b978-0-12-819519-2.00033-5]
- 14 **Moser L, Schultz-Cherry S.** Astroviruses. *Encyclopedia of Virology*. 2008. [cited 3 March 2023]. Available from: <https://www.sciencedirect.com/topics/neuroscience/astrovirus>
- 15 **Bosch A, Pintó RM, Guix S.** Human astroviruses. *Clin Microbiol Rev* 2014; **27**: 1048-1074 [PMID: 25278582 DOI: 10.1128/CMR.00013-14]
- 16 **Pérot P, Lecuit M, Eloit M.** Astrovirus Diagnostics. *Viruses* 2017; **9** [PMID: 28085120 DOI: 10.3390/v9010010]
- 17 **Cortez V, Meliopoulos VA, Karlsson EA, Hargest V, Johnson C, Schultz-Cherry S.** Astrovirus Biology and Pathogenesis. *Annu Rev Virol* 2017; **4**: 327-348 [PMID: 28715976 DOI: 10.1146/annurev-virology-101416-041742]
- 18 **Rouhani S, Peñataro Yori P, Paredes Olortegui M, Lima AA, Ahmed T, Mduma ER, George A, Samie A, Svensen E, Lima I, Mondal D, Mason CJ, Kalam A, Guerrant RL, Lang D, Zaidi A, Kang G, Houpt E, Kosek MN.** The Epidemiology of Sapovirus in the Etiology, Risk Factors, and Interactions of Enteric Infection and Malnutrition and the Consequences for Child Health and Development Study: Evidence of Protection Following Natural Infection. *Clin Infect Dis* 2022; **75**: 1334-1341 [PMID: 36094137 DOI: 10.1093/cid/ciac165]
- 19 **Kitajima M, Oka T, Haramoto E, Katayama H, Takeda N, Katayama K, Ohgaki S.** Detection and genetic analysis of human sapoviruses in river water in Japan. *Appl Environ Microbiol* 2010; **76**: 2461-2467 [PMID: 20190080 DOI: 10.1128/AEM.02739-09]
- 20 **Diez Valcarce M, Kambhampati AK, Calderwood LE, Hall AJ, Mirza SA, Vinjé J.** Global distribution of sporadic sapovirus infections: A systematic review and meta-analysis. *PLoS One* 2021; **16**: e0255436 [PMID: 34411109 DOI: 10.1371/journal.pone.0255436]
- 21 **Becker-Dreps S, González F, Bucardo F.** Sapovirus: an emerging cause of childhood diarrhea. *Curr Opin Infect Dis* 2020; **33**: 388-397 [PMID: 32796163 DOI: 10.1097/QCO.0000000000000671]
- 22 **World Health Organization.** The treatment of diarrhoea: a manual for physicians and other senior health workers, 4th rev. 2005. [cited 3 March 2023]. Available from: <https://apps.who.int/iris/handle/10665/43209>
- 23 **Ghussón N, Vasquez G.** Successfully Treated Norovirus- and Sapovirus-Associated Diarrhea in Three Renal Transplant Patients. *Case Rep Infect Dis* 2018; **2018**: 6846873 [PMID: 30538873 DOI: 10.1155/2018/6846873]
- 24 **Landa E, Javaid S, Won JS, Vigandt E, Caronia J, Mir P, Thet Z.** Septic Shock Secondary to Severe Gastroenteritis Resulting From Sapovirus Infection. *Cureus* 2022; **14**: e24010 [PMID: 35547467 DOI: 10.7759/cureus.24010]
- 25 **Model L, Burnweit CA.** Sapovirus Gastroenteritis in Young Children Presenting as Distal Small Bowel Obstruction: A Report of 2 Cases and Literature Review. *Case Rep Surg* 2016; **2016**: 6302875 [PMID: 27891287 DOI: 10.1155/2016/6302875]
- 26 **Centers for Disease Control and Prevention.** National Center for Immunization and Respiratory Diseases (NCIRD) DoVD. 2020. [cited 3 March 2023]. Available from: <https://www.cdc.gov/ncird/index.html>
- 27 **Midgley CM, Jackson MA, Selvarangan R, Turabelidze G, Obringer E, Johnson D, Giles BL, Patel A, Echols F, Oberste MS, Nix WA, Watson JT, Gerber SI.** Severe respiratory illness associated with enterovirus D68 - Missouri and Illinois, 2014. *MMWR Morb Mortal Wkly Rep* 2014; **63**: 798-799 [PMID: 25211545]
- 28 **Wells AI, Coyne CB.** Enteroviruses: A Gut-Wrenching Game of Entry, Detection, and Evasion. *Viruses* 2019; **11** [PMID: 31117206 DOI: 10.3390/v11050460]
- 29 **Lugo D, Krogstad P.** Enteroviruses in the early 21st century: new manifestations and challenges. *Curr Opin Pediatr* 2016; **28**: 107-113 [PMID: 26709690 DOI: 10.1097/MOP.0000000000000303]
- 30 **Khetsuriani N, Lamonte-Fowlkes A, Oberst S, Pallansch MA; Centers for Disease Control and Prevention.** Enterovirus surveillance--United States, 1970-2005. *MMWR Surveill Summ* 2006; **55**: 1-20 [PMID: 16971890]
- 31 **Kühl U, Pauschinger M, Seeborg B, Lassner D, Noutsias M, Poller W, Schultheiss HP.** Viral persistence in the myocardium is associated with progressive cardiac dysfunction. *Circulation* 2005; **112**: 1965-1970 [PMID: 16172268 DOI: 10.1161/CIRCULATIONAHA.105.548156]
- 32 **Donnelly CA, Fisher MC, Fraser C, Ghani AC, Riley S, Ferguson NM, Anderson RM.** Epidemiological and genetic analysis of severe acute respiratory syndrome. *Lancet Infect Dis* 2004; **4**: 672-683 [PMID: 15522679 DOI: 10.1016/S1473-3099(04)01173-9]
- 33 **Zumla A, Hui DS, Perlman S.** Middle East respiratory syndrome. *Lancet* 2015; **386**: 995-1007 [PMID: 26049252 DOI: 10.1016/S0140-6736(15)60454-8]
- 34 **World Health Organization.** Weekly epidemiological update on COVID-19-20 April 2023. World Health organization. April 6, 2023. [cited 3 March 2023]. Available from: <https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---6-april-2023>
- 35 **Luo X, Zhou GZ, Zhang Y, Peng LH, Zou LP, Yang YS.** Coronaviruses and gastrointestinal diseases. *Mil Med Res* 2020; **7**: 49 [PMID: 33054860 DOI: 10.1186/s40779-020-00279-z]
- 36 **Zeng W, Qi K, Ye M, Zheng L, Liu X, Hu S, Zhang W, Tang W, Xu J, Yu D, Wei Y.** Gastrointestinal symptoms are associated with severity of coronavirus disease 2019: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol* 2022; **34**: 168-176 [PMID: 33470700 DOI: 10.1097/MEG.0000000000002072]
- 37 **Chen F, Dai Z, Huang C, Chen H, Wang X, Li X.** Gastrointestinal Disease and COVID-19: A Review of Current Evidence. *Dig Dis* 2022; **40**: 506-514 [PMID: 34510032 DOI: 10.1159/000519412]
- 38 **Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, Cereda D, Coluccello A, Foti G, Fumagalli R, Iotti G, Latronico N, Lorini L, Merler S, Natalini G, Piatti A, Ranieri MV, Scandroglio AM, Storti E, Cecconi M, Pesenti A; COVID-19 Lombardy ICU Network.** Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020; **323**: 1574-1581 [PMID: 32250385 DOI: 10.1001/jama.2020.10438]

- 10.1001/jama.2020.5394]
- 39 **Menter T**, Haslbauer JD, Nienhold R, Savic S, Hopfer H, Deigendesch N, Frank S, Turek D, Willi N, Pargger H, Bassetti S, Leuppi JD, Cathomas G, Tolnay M, Mertz KD, Tzankov A. Postmortem examination of COVID-19 patients reveals diffuse alveolar damage with severe capillary congestion and variegated findings in lungs and other organs suggesting vascular dysfunction. *Histopathology* 2020; **77**: 198-209 [PMID: 32364264 DOI: 10.1111/his.14134]
 - 40 **Assiri A**, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, Flemban H, Al-Nassir WN, Balkhy HH, Al-Hakeem RF, Makhdoom HQ, Zumla AI, Memish ZA. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *Lancet Infect Dis* 2013; **13**: 752-761 [PMID: 23891402 DOI: 10.1016/S1473-3099(13)70204-4]
 - 41 **Lew TW**, Kwek TK, Tai D, Earnest A, Loo S, Singh K, Kwan KM, Chan Y, Yim CF, Bek SL, Kor AC, Yap WS, Chelliah YR, Lai YC, Goh SK. Acute respiratory distress syndrome in critically ill patients with severe acute respiratory syndrome. *JAMA* 2003; **290**: 374-380 [PMID: 12865379 DOI: 10.1001/jama.290.3.374]
 - 42 **Polack FP**, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW Jr, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med* 2020; **383**: 2603-2615 [PMID: 33301246 DOI: 10.1056/NEJMoa2034577]
 - 43 **Baden LR**, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Khetan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham BS, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Ivarsson M, Miller J, Zaks T; COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med* 2021; **384**: 403-416 [PMID: 33378609 DOI: 10.1056/NEJMoa2035389]
 - 44 Acute unexplained hepatitis in children. *Bull World Health Organ* 2022; **100**: 530-531 [PMID: 36062241 DOI: 10.2471/BLT.22.020922]
 - 45 **Mirazo S**, Ramos N, Mainardi V, Gerona S, Arbiza J. Transmission, diagnosis, and management of hepatitis E: an update. *Hepat Med* 2014; **6**: 45-59 [PMID: 24966702 DOI: 10.2147/HMER.S63417]
 - 46 **Kamar N**, Bendall R, Legrand-Abravanel F, Xia NS, Ijaz S, Izopet J, Dalton HR. Hepatitis E. *Lancet* 2012; **379**: 2477-2488 [PMID: 22549046 DOI: 10.1016/S0140-6736(11)61849-7]
 - 47 **Gérolami R**, Moal V, Colson P. Chronic hepatitis E with cirrhosis in a kidney-transplant recipient. *N Engl J Med* 2008; **358**: 859-860 [PMID: 18287615 DOI: 10.1056/NEJMc0708687]
 - 48 **Aggarwal R**. Diagnosis of hepatitis E. *Nat Rev Gastroenterol Hepatol* 2013; **10**: 24-33 [PMID: 23026902 DOI: 10.1038/nrgastro.2012.187]
 - 49 **Dalton HR**, Kamar N, van Eijk JJ, Mclean BN, Cintas P, Bendall RP, Jacobs BC. Hepatitis E virus and neurological injury. *Nat Rev Neurol* 2016; **12**: 77-85 [PMID: 26711839 DOI: 10.1038/nrneuro.2015.234]
 - 50 **Harun-Or-Rashid M**, Akbar SM, Takahashi K, Al-Mahtab M, Khan MS, Alim MA, Ekram AR, Khan MM, Arai M, Mishiro S. Epidemiological and molecular analyses of a non-seasonal outbreak of acute icteric hepatitis E in Bangladesh. *J Med Virol* 2013; **85**: 1369-1376 [PMID: 23703666 DOI: 10.1002/jmv.23601]
 - 51 **Wedemeyer H**, Pischke S, Manns MP. Pathogenesis and treatment of hepatitis e virus infection. *Gastroenterology* 2012; **142**: 1388-1397.e1 [PMID: 22537448 DOI: 10.1053/j.gastro.2012.02.014]
 - 52 **Khuroo MS**. Hepatitis E: an emerging global disease - from discovery towards control and cure. *J Viral Hepat* 2016; **23**: 68-79 [PMID: 26344932 DOI: 10.1111/jvh.12445]
 - 53 **Webb GW**, Dalton HR. Hepatitis E: an expanding epidemic with a range of complications. *Clin Microbiol Infect* 2020; **26**: 828-832 [PMID: 32251845 DOI: 10.1016/j.cmi.2020.03.039]
 - 54 **Zhang J**, Zhang XF, Huang SJ, Wu T, Hu YM, Wang ZZ, Wang H, Jiang HM, Wang YJ, Yan Q, Guo M, Liu XH, Li JX, Yang CL, Tang Q, Jiang RJ, Pan HR, Li YM, Shih JW, Ng MH, Zhu FC, Xia NS. Long-term efficacy of a hepatitis E vaccine. *N Engl J Med* 2015; **372**: 914-922 [PMID: 25738667 DOI: 10.1056/NEJMoa1406011]
 - 55 **Cannon MJ**, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. *Rev Med Virol* 2010; **20**: 202-213 [PMID: 20564615 DOI: 10.1002/rmv.655]
 - 56 **Zhang C**, Krishna SG, Hinton A, Arsenescu R, Levine EJ, Conwell DL. Cytomegalovirus-Related Hospitalization Is Associated With Adverse Outcomes and Increased Health-Care Resource Utilization in Inflammatory Bowel Disease. *Clin Transl Gastroenterol* 2016; **7**: e150 [PMID: 26963000 DOI: 10.1038/ctg.2016.10]
 - 57 **Kuwabara A**, Okamoto H, Suda T, Ajioka Y, Hatakeyama K. Clinicopathologic characteristics of clinically relevant cytomegalovirus infection in inflammatory bowel disease. *J Gastroenterol* 2007; **42**: 823-829 [PMID: 17940835 DOI: 10.1007/s00535-007-2103-3]
 - 58 **Matsuoka K**, Saito E, Fujii T, Takenaka K, Kimura M, Nagahori M, Ohtsuka K, Watanabe M. Tacrolimus for the Treatment of Ulcerative Colitis. *Intest Res* 2015; **13**: 219-226 [PMID: 26130996 DOI: 10.5217/ir.2015.13.3.219]
 - 59 **Malhi NS**, Bhasin DK, Gupta NM, Vaiphei K, Singh K. Exacerbation of ulcerative colitis by cytomegalovirus infection in an immunocompetent Indian patient. *Trop Gastroenterol* 2002; **23**: 88-90 [PMID: 12632977]
 - 60 **Rahier JF**, Magro F, Abreu C, Armuzzi A, Ben-Horin S, Chowers Y, Cottone M, de Ridder L, Doherty G, Ehehalt R, Esteve M, Katsanos K, Lees CW, Macmahon E, Moreels T, Reinisch W, Tilg H, Tremblay L, Veereman-Wauters G, Vigeat N, Yazdanpanah Y, Eliakim R, Colombel JF; European Crohn's and Colitis Organisation (ECCO). Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis* 2014; **8**: 443-468 [PMID: 24613021 DOI: 10.1016/j.crohns.2013.12.013]
 - 61 **Cone MM**, Whitlow CB. Sexually transmitted and anorectal infectious diseases. *Gastroenterol Clin North Am* 2013; **42**: 877-892 [PMID: 24280405 DOI: 10.1016/j.gtc.2013.09.003]
 - 62 **Lavery EA**, Coyle WJ. Herpes simplex virus and the alimentary tract. *Curr Gastroenterol Rep* 2008; **10**: 417-423 [PMID: 18627656 DOI: 10.1007/s11894-008-0078-8]
 - 63 **McQuillan G**, Kruszon-Moran D, Flagg EW, Paulose-Ram R. Prevalence of Herpes Simplex Virus Type 1 and Type 2 in Persons Aged 14-49: United States, 2015-2016. *NCHS Data Brief* 2018; **1**-8 [PMID: 29442994]

- 64 **Bissessor M**, Fairley CK, Read T, Denham I, Bradshaw C, Chen M. The etiology of infectious proctitis in men who have sex with men differs according to HIV status. *Sex Transm Dis* 2013; **40**: 768-770 [PMID: [24275725](#) DOI: [10.1097/OLQ.0000000000000022](#)]
- 65 **Lamb CA**, Lamb EI, Mansfield JC, Sankar KN. Sexually transmitted infections manifesting as proctitis. *Frontline Gastroenterol* 2013; **4**: 32-40 [PMID: [23914292](#) DOI: [10.1136/flgastro-2012-100274](#)]
- 66 **Harel L**, Smetana Z, Prais D, Book M, Alkin M, Supaev E, Mendelson E, Amir J. Presence of viremia in patients with primary herpetic gingivostomatitis. *Clin Infect Dis* 2004; **39**: 636-640 [PMID: [15356775](#) DOI: [10.1086/422643](#)]
- 67 **Workowski KA**, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015; **64**: 1-137 [PMID: [26042815](#)]
- 68 **GBD 2017 Disease and Injury Incidence and Prevalence Collaborators**. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1789-1858 [PMID: [30496104](#) DOI: [10.1016/S0140-6736\(18\)32279-7](#)]
- 69 **Zeng DY**, Li JM, Lin S, Dong X, You J, Xing QQ, Ren YD, Chen WM, Cai YY, Fang K, Hong MZ, Zhu Y, Pan JS. Global burden of acute viral hepatitis and its association with socioeconomic development status, 1990-2019. *J Hepatol* 2021; **75**: 547-556 [PMID: [33961940](#) DOI: [10.1016/j.jhep.2021.04.035](#)]
- 70 **Shin EC**, Jeong SH. Natural History, Clinical Manifestations, and Pathogenesis of Hepatitis A. *Cold Spring Harb Perspect Med* 2018; **8** [PMID: [29440324](#) DOI: [10.1101/cshperspect.a031708](#)]
- 71 **Global Health Policy**. The Global HIV/AIDS Epidemic. 2023. [cited 15 April 2023]. Available from: <https://www.kff.org/global-health-policy/fact-sheet/the-global-hiv-aids-epidemic/>
- 72 Populations at greatest risk. *AIDS Alert* 2011; **26**: 111 [PMID: [22096789](#)]
- 73 **Crum-Cianflone NF**. HIV and the Gastrointestinal Tract. *Infect Dis Clin Pract (Baltim Md)* 2010; **18**: 283-285 [PMID: [21547005](#) DOI: [10.1097/IPC.0b013e3181f1038b](#)]
- 74 **Dikman AE**, Schonfeld E, Srisarajivakul NC, Poles MA. Human Immunodeficiency Virus-Associated Diarrhea: Still an Issue in the Era of Antiretroviral Therapy. *Dig Dis Sci* 2015; **60**: 2236-2245 [PMID: [25772777](#) DOI: [10.1007/s10620-015-3615-y](#)]
- 75 **Brenchley JM**, Douek DC. HIV infection and the gastrointestinal immune system. *Mucosal Immunol* 2008; **1**: 23-30 [PMID: [19079157](#) DOI: [10.1038/mi.2007.1](#)]
- 76 **Chu C**, Selwyn PA. Complications of HIV infection: a systems-based approach. *Am Fam Physician* 2011; **83**: 395-406 [PMID: [21322514](#)]
- 77 **Serlin MH**, Dieterich D. CHAPTER 23-Gastrointestinal Disorders in HIV. In: Volberding PA, Sande MA, Greene WC, Lange JMA, Gallant JE, Walsh CC, editors. *Global HIV/AIDS Medicine*. Edinburgh: W.B. Saunders, 2008: 251-260 [DOI: [10.1016/b978-1-4160-2882-6.50027-7](#)]
- 78 **Lim JK**, Nguyen MH, Kim WR, Gish R, Perumalswami P, Jacobson IM. Prevalence of Chronic Hepatitis B Virus Infection in the United States. *Am J Gastroenterol* 2020; **115**: 1429-1438 [PMID: [32483003](#) DOI: [10.14309/ajg.0000000000000651](#)]
- 79 **Burns GS**, Thompson AJ. Viral hepatitis B: clinical and epidemiological characteristics. *Cold Spring Harb Perspect Med* 2014; **4**: a024935 [PMID: [25359547](#) DOI: [10.1101/cshperspect.a024935](#)]
- 80 **Rumgay H**, Ferlay J, de Martel C, Georges D, Ibrahim AS, Zheng R, Wei W, Lemmens VEPP, Soerjomataram I. Global, regional and national burden of primary liver cancer by subtype. *Eur J Cancer* 2022; **161**: 108-118 [PMID: [34942552](#) DOI: [10.1016/j.ejca.2021.11.023](#)]
- 81 **Di Bisceglie AM**. Hepatitis B and hepatocellular carcinoma. *Hepatology* 2009; **49**: S56-S60 [PMID: [19399807](#) DOI: [10.1002/hep.22962](#)]
- 82 **Zhang X**, Guan L, Tian H, Zeng Z, Chen J, Huang D, Sun J, Guo J, Cui H, Li Y. Risk Factors and Prevention of Viral Hepatitis-Related Hepatocellular Carcinoma. *Front Oncol* 2021; **11**: 686962 [PMID: [34568017](#) DOI: [10.3389/fonc.2021.686962](#)]
- 83 **Yang Y**, Jiang Z, Wu W, Ruan L, Yu C, Xi Y, Wang L, Wang K, Mo J, Zhao S. Chronic Hepatitis Virus Infection Are Associated With High Risk of Gastric Cancer: A Systematic Review and Cumulative Analysis. *Front Oncol* 2021; **11**: 703558 [PMID: [34307172](#) DOI: [10.3389/fonc.2021.703558](#)]
- 84 **He Y**, Mao M, Shi W, He Z, Zhang L, Wang X. Development and validation of a prognostic nomogram in gastric cancer with hepatitis B virus infection. *J Transl Med* 2019; **17**: 98 [PMID: [30909980](#) DOI: [10.1186/s12967-019-1841-3](#)]
- 85 **Shalapour S**, Lin XJ, Bastian IN, Brain J, Burt AD, Aksenov AA, Vrbanc AF, Li W, Perkins A, Matsutani T, Zhong Z, Dhar D, Navas-Molina JA, Xu J, Loomba R, Downes M, Yu RT, Evans RM, Dorrestein PC, Knight R, Benner C, Anstee QM, Karin M. Inflammation-induced IgA⁺ cells dismantle anti-liver cancer immunity. *Nature* 2017; **551**: 340-345 [PMID: [29144460](#) DOI: [10.1038/nature24302](#)]
- 86 **Chen Z**, Xie Y, Zhou F, Zhang B, Wu J, Yang L, Xu S, Stedtfeld R, Chen Q, Liu J, Zhang X, Xu H, Ren J. Featured Gut Microbiomes Associated With the Progression of Chronic Hepatitis B Disease. *Front Microbiol* 2020; **11**: 383 [PMID: [32265857](#) DOI: [10.3389/fmicb.2020.00383](#)]
- 87 **Terrault NA**, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, Brown RS Jr, Bzowej NH, Wong JB. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology* 2018; **67**: 1560-1599 [PMID: [29405329](#) DOI: [10.1002/hep.29800](#)]
- 88 **Kappus MR**, Sterling RK. Extrahepatic manifestations of acute hepatitis B virus infection. *Gastroenterol Hepatol (N Y)* 2013; **9**: 123-126 [PMID: [23983659](#)]
- 89 **Chen HY**, Shen DT, Ji DZ, Han PC, Zhang WM, Ma JF, Chen WS, Goyal H, Pan S, Xu HG. Prevalence and burden of hepatitis D virus infection in the global population: a systematic review and meta-analysis. *Gut* 2019; **68**: 512-521 [PMID: [30228220](#) DOI: [10.1136/gutjnl-2018-316601](#)]
- 90 **Mentha N**, Clément S, Negro F, Alfaïate D. A review on hepatitis D: From virology to new therapies. *J Adv Res* 2019; **17**: 3-15 [PMID: [31193285](#) DOI: [10.1016/j.jare.2019.03.009](#)]
- 91 **Farci P**, Niro GA. Clinical features of hepatitis D. *Semin Liver Dis* 2012; **32**: 228-236 [PMID: [22932971](#) DOI: [10.1016/j.sld.2012.03.009](#)]

- 10.1055/s-0032-1323628]
- 92 **Buti M**, Homs M, Rodriguez-Frias F, Funalleras G, Jardi R, Sauleda S, Tabernero D, Schaper M, Esteban R. Clinical outcome of acute and chronic hepatitis delta over time: a long-term follow-up study. *J Viral Hepat* 2011; **18**: 434-442 [PMID: 20546496 DOI: 10.1111/j.1365-2893.2010.01324.x]
 - 93 **Lee AU**, Lee C. Hepatitis D Review: Challenges for the Resource-Poor Setting. *Viruses* 2021; **13** [PMID: 34696341 DOI: 10.3390/v13101912]
 - 94 **Shah PA**, Choudhry S, Reyes KJC, Lau DTY. An update on the management of chronic hepatitis D. *Gastroenterol Rep (Oxf)* 2019; **7**: 396-402 [PMID: 32494363 DOI: 10.1093/gastro/goz052]
 - 95 **Brunner N**, Bruggmann P. Trends of the Global Hepatitis C Disease Burden: Strategies to Achieve Elimination. *J Prev Med Public Health* 2021; **54**: 251-258 [PMID: 34370938 DOI: 10.3961/jpmph.21.151]
 - 96 **Gupta E**, Bajpai M, Choudhary A. Hepatitis C virus: Screening, diagnosis, and interpretation of laboratory assays. *Asian J Transfus Sci* 2014; **8**: 19-25 [PMID: 24678168 DOI: 10.4103/0973-6247.126683]
 - 97 **Millman AJ**, Nelson NP, Vellozzi C. Hepatitis C: Review of the Epidemiology, Clinical Care, and Continued Challenges in the Direct Acting Antiviral Era. *Curr Epidemiol Rep* 2017; **4**: 174-185 [PMID: 28785531 DOI: 10.1007/s40471-017-0108-x]
 - 98 **Chen Q**, Ayer T, Adey MG, Wang X, Kanwal F, Chhatwal J. Assessment of Incidence of and Surveillance Burden for Hepatocellular Carcinoma Among Patients With Hepatitis C in the Era of Direct-Acting Antiviral Agents. *JAMA Netw Open* 2020; **3**: e2021173 [PMID: 33206188 DOI: 10.1001/jamanetworkopen.2020.21173]
 - 99 **Spearman CW**, Dusheiko GM, Hellard M, Sonderup M. Hepatitis C. *Lancet* 2019; **394**: 1451-1466 [PMID: 31631857 DOI: 10.1016/S0140-6736(19)32320-7]
 - 100 **Modi AA**, Liang TJ. Hepatitis C: a clinical review. *Oral Dis* 2008; **14**: 10-14 [PMID: 18173443 DOI: 10.1111/j.1601-0825.2007.01419.x]
 - 101 **Martinello M**, Hajarizadeh B, Grebely J, Dore GJ, Matthews GV. Management of acute HCV infection in the era of direct-acting antiviral therapy. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 412-424 [PMID: 29773899 DOI: 10.1038/s41575-018-0026-5]
 - 102 **American Association for the Study of Liver Diseases**. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis. 2022. [cited 3 March 2023]. Available from: <https://www.hcvguidelines.org/treatment-naive/simplified-treatment>
 - 103 **Pergam SA**, Limaye AP; AST Infectious Diseases Community of Practice. Varicella zoster virus (VZV) in solid organ transplant recipients. *Am J Transplant* 2009; **9** Suppl 4: S108-S115 [PMID: 20070670 DOI: 10.1111/j.1600-6143.2009.02901.x]
 - 104 **Harpaz R**, Leung JW. The Epidemiology of Herpes Zoster in the United States During the Era of Varicella and Herpes Zoster Vaccines: Changing Patterns Among Older Adults. *Clin Infect Dis* 2019; **69**: 341-344 [PMID: 30496358 DOI: 10.1093/cid/ciy953]
 - 105 **Marin M**, Leung J, Lopez AS, Shepersky L, Schmid DS, Gershon AA. Communicability of varicella before rash onset: a literature review. *Epidemiol Infect* 2021; **149**: e131 [PMID: 33958016 DOI: 10.1017/S0950268821001102]
 - 106 **Hsu CC**, Hsu CC, Rosenberg RM. Gastrointestinal Manifestations of Disseminated Varicella. *Gastroenterol Hepatol (N Y)* 2014; **10**: 682-683 [PMID: 27540342]
 - 107 **Schwarczmann P**. The visceral manifestations of herpes zoster. *Munch Med Wochenschr* 1964; **106**: 1033-1038 [PMID: 14221312]
 - 108 **David DS**, Tegtmeier BR, O'Donnell MR, Paz IB, McCarty TM. Visceral varicella-zoster after bone marrow transplantation: report of a case series and review of the literature. *Am J Gastroenterol* 1998; **93**: 810-813 [PMID: 9625133 DOI: 10.1111/j.1572-0241.1998.230.a.x]
 - 109 **Kim ED**, Kang BG, Kim JH, Roh M, Jo DH. Abdominal distention and constipation followed by herpes zoster infection. *Korean J Anesthesiol* 2013; **65**: S143-S144 [PMID: 24478851 DOI: 10.4097/kjae.2013.65.6S.S143]
 - 110 **Sauerbrei A**. Diagnosis, antiviral therapy, and prophylaxis of varicella-zoster virus infections. *Eur J Clin Microbiol Infect Dis* 2016; **35**: 723-734 [PMID: 26873382 DOI: 10.1007/s10096-016-2605-0]
 - 111 **Lo Presti C**, Curti C, Montana M, Bornet C, Vanelle P. Chickenpox: An update. *Med Mal Infect* 2019; **49**: 1-8 [PMID: 29789159 DOI: 10.1016/j.medmal.2018.04.395]
 - 112 **Nagel MA**, Gilden D. Complications of varicella zoster virus reactivation. *Curr Treat Options Neurol* 2013; **15**: 439-453 [PMID: 23794213 DOI: 10.1007/s11940-013-0246-5]
 - 113 **Womack J**, Jimenez M. Common questions about infectious mononucleosis. *Am Fam Physician* 2015; **91**: 372-376 [PMID: 25822555 DOI: 10.1056/NEJM198507043130111]
 - 114 **Tian S**, Westbrook LM, Xiao SY, Zhang Y, Huang Y, Wang HL. The Morphologic Features of Primary Epstein-Barr Virus Infection in the Gastrointestinal Tract: An Approach to Correct Diagnosis. *Am J Surg Pathol* 2019; **43**: 1253-1263 [PMID: 31283632 DOI: 10.1097/PAS.0000000000001319]
 - 115 **Fugl A**, Andersen CL. Epstein-Barr virus and its association with disease - a review of relevance to general practice. *BMC Fam Pract* 2019; **20**: 62 [PMID: 31088382 DOI: 10.1186/s12875-019-0954-3]
 - 116 **Jha HC**, Pei Y, Robertson ES. Epstein-Barr Virus: Diseases Linked to Infection and Transformation. *Front Microbiol* 2016; **7**: 1602 [PMID: 27826287 DOI: 10.3389/fmicb.2016.01602]
 - 117 **Zhang B**, Wang X, Tian X, Cai Y, Wu X. Chronic Active Epstein-Barr Virus-Associated Enteritis: CT Findings and Clinical Manifestation. *Biomed Res Int* 2020; **2020**: 2978410 [PMID: 32685462 DOI: 10.1155/2020/2978410]
 - 118 **Patel J**, Patel P, Vanar V, Yong S, Srinivas P, Dhillon S. The Epstein Barr Virus: An Unusual Source of Gastritis: 2342. *The American Journal of Gastroenterology* 2016; **111**: S1139 [DOI: 10.14309/00000434-201610001-02342]
 - 119 **Ayee R**, Ofori MEO, Wright E, Quayle O. Epstein Barr Virus Associated Lymphomas and Epithelia Cancers in Humans. *J Cancer* 2020; **11**: 1737-1750 [PMID: 32194785 DOI: 10.7150/jca.37282]
 - 120 **Xu S**, Chen H, Zu X, Hao X, Feng R, Zhang S, Chen B, Zeng Z, Chen M, Ye Z, He Y. Epstein-Barr virus infection in ulcerative colitis: a clinicopathologic study from a Chinese area. *Therap Adv Gastroenterol* 2020; **13**: 1756284820930124 [PMID: 32913442 DOI: 10.1177/1756284820930124]

- 121 **Zhang H**, Zhao S, Cao Z. Impact of Epstein-Barr virus infection in patients with inflammatory bowel disease. *Front Immunol* 2022; **13**: 1001055 [PMID: 36389673 DOI: 10.3389/fimmu.2022.1001055]
- 122 **Hess RD**. Routine Epstein-Barr virus diagnostics from the laboratory perspective: still challenging after 35 years. *J Clin Microbiol* 2004; **42**: 3381-3387 [PMID: 15297472 DOI: 10.1128/JCM.42.8.3381-3387.2004]
- 123 **Pagano JS**, Whitehurst CB, Andrei G. Antiviral Drugs for EBV. *Cancers (Basel)* 2018; **10** [PMID: 29899236 DOI: 10.3390/cancers10060197]
- 124 **Infections Diseases Society of American**. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. 2022 [cited 3 March 2023]. Available from: <https://www.idsociety.org/practice-guideline/prevention-and-treatment-of-opportunistic-infections-among-adults-and-adolescents/>
- 125 **Radu O**, Pantanowitz L. Kaposi sarcoma. *Arch Pathol Lab Med* 2013; **137**: 289-294 [PMID: 23368874 DOI: 10.5858/arpa.2012-0101-RS]
- 126 **Rohner E**, Wyss N, Trelle S, Mbulaiteye SM, Egger M, Novak U, Zwahlen M, Bohlius J. HHV-8 seroprevalence: a global view. *Syst Rev* 2014; **3**: 11 [PMID: 24521144 DOI: 10.1186/2046-4053-3-11]
- 127 **Lee AJ**, Brenner L, Mourad B, Monteiro C, Vega KJ, Munoz JC. Gastrointestinal Kaposi's sarcoma: Case report and review of the literature. *World J Gastrointest Pharmacol Ther* 2015; **6**: 89-95 [PMID: 26261737 DOI: 10.4292/wjgpt.v6.i3.89]
- 128 **Ablashi DV**, Chatlynne LG, Whitman JE Jr, Cesarman E. Spectrum of Kaposi's sarcoma-associated herpesvirus, or human herpesvirus 8, diseases. *Clin Microbiol Rev* 2002; **15**: 439-464 [PMID: 12097251 DOI: 10.1128/CMR.15.3.439-464.2002]
- 129 **Lewis RM**, Laprise JF, Gargano JW, Unger ER, Querec TD, Chesson HW, Brisson M, Markowitz LE. Estimated Prevalence and Incidence of Disease-Associated Human Papillomavirus Types Among 15- to 59-Year-Olds in the United States. *Sex Transm Dis* 2021; **48**: 273-277 [PMID: 33492097 DOI: 10.1097/OLQ.0000000000001356]
- 130 **Kombe Kombe AJ**, Li B, Zahid A, Mengist HM, Bounda GA, Zhou Y, Jin T. Epidemiology and Burden of Human Papillomavirus and Related Diseases, Molecular Pathogenesis, and Vaccine Evaluation. *Front Public Health* 2020; **8**: 552028 [PMID: 33553082 DOI: 10.3389/fpubh.2020.552028]
- 131 **Baj J**, Forma A, Dudek I, Chilimoniuk Z, Dobosz M, Dobrzyński M, Teresiński G, Buszewicz G, Flieger J, Portincasa P. The Involvement of Human Papilloma Virus in Gastrointestinal Cancers. *Cancers (Basel)* 2022; **14** [PMID: 35681587 DOI: 10.3390/cancers14112607]
- 132 **Bucchi D**, Stracci F, Buonora N, Masanotti G. Human papillomavirus and gastrointestinal cancer: A review. *World J Gastroenterol* 2016; **22**: 7415-7430 [PMID: 27672265 DOI: 10.3748/wjg.v22.i33.7415]
- 133 **Dixit R**, Bhavsar C, Marfatia YS. Laboratory diagnosis of human papillomavirus virus infection in female genital tract. *Indian J Sex Transm Dis AIDS* 2011; **32**: 50-52 [PMID: 21799579 DOI: 10.4103/0253-7184.81257]
- 134 **Stern PL**, van der Burg SH, Hampson IN, Broker TR, Fiander A, Lacey CJ, Kitchener HC, Einstein MH. Therapy of human papillomavirus-related disease. *Vaccine* 2012; **30** Suppl 5: F71-F82 [PMID: 23199967 DOI: 10.1016/j.vaccine.2012.05.091]



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