

# HEPATITIS A

## The Most Common and Silent Viral Hepatitis in Children

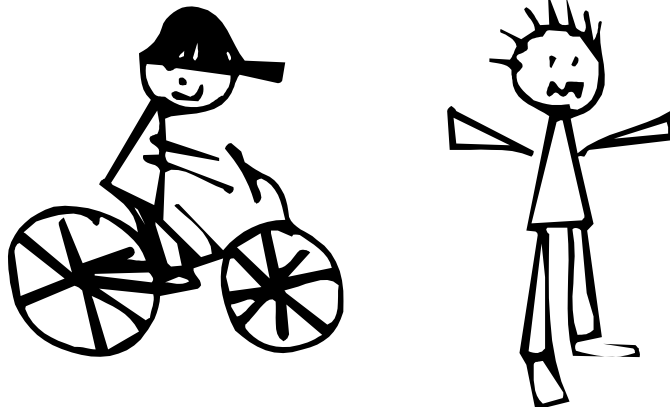
*Updated 2006*

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The hepatitis A virus is spread through food and water contaminated by the feces of people infected with the hepatitis A virus (HAV).

The virus is transmitted when the feces (stool) of an infected person reaches food or water that is ingested by a susceptible person. It is also transmitted through close, personal contact.

Those most commonly infected in the United States and around the world are children.



Hepatitis A virus infection continues to be one of the most frequently reported, vaccine-preventable diseases in the United States despite the introduction of a hepatitis A vaccine in 1995.

Children play an important role in spreading HAV. They are the ones most likely to become infected and because they rarely have symptoms, they are a silent source of infection for others.

When symptoms occur, usually in adults, they appear suddenly and may include fever, exhaustion, loss of appetite, nausea and abdominal discomfort, dark urine and jaundice (yellowing of the skin and eyes).

Children younger than age 6 usually have no symptoms.

Like all types of hepatitis viruses, HAV causes acute inflammation of the liver. If people with chronic hepatitis B or C or other liver diseases are infected by HAV, they risk

accelerated liver damage due to an additional virus infecting their inflamed and vulnerable livers. This is why it is important for all people at least 1 year of age with chronic hepatitis B or C to be vaccinated against hepatitis A.

### **Hepatitis A in the United States**

In May 2006, the CDC released the following data, a comprehensive look at hepatitis A in the United States:

#### **Disease Patterns**

##### **Prevaccine Era**

The incidence of hepatitis A in the United States has fundamentally changed since the hepatitis A vaccine was licensed and national Advisory Committee on Immunization Practices (ACIP) recommendations for its use were implemented.

Before vaccine licensure during 1995-1996, hepatitis A incidence was primarily cyclic, with peaks occurring every 10-15 years. In the United States, during 1980-1995, approximately 22,000-36,000 hepatitis A cases were reported annually to CDC, but incidence models indicate that the number of infections was substantially higher. One such analysis estimated an average of 271,000 infections per year during 1980-1999, representing 10.4 times the reported number of cases. Each year in the United States, an estimated 100 persons died as a result of acute liver failure attributed to hepatitis A.

The costs associated with hepatitis A are substantial. Surveillance data indicate that 11 to 22 percent of persons with hepatitis A are hospitalized. The average duration of work loss for adults who become ill has been estimated at 15.5 days for nonhospitalized patients and 33.2 days for hospitalized patients.

Estimates of the annual direct and indirect costs of hepatitis A in the United States have ranged from \$300 million to \$488.8 million in 1997 dollars. A recent analysis estimated

#### **Sources of Hepatitis A**

- A frequently reported source of infection transmission (13 percent) is household or sexual contact with a person with HAV infection.
- About 9 percent of reported cases occur among children or employees in daycare centers or among their contacts.
- About 13 percent of reported cases in the United States are attributable to international travel. Mexico is the most frequent (84 percent) destination, according to the National Centers for Disease Control and Prevention (CDC).
- Seventy-five percent of all travel-related cases are associated with travel to Mexico or to Central or South America.

economic costs of \$133.5 million during the lifetime of a single age group of children born in 2005, in the absence of vaccination (CDC, unpublished data, 2005).

### **Variation by Age, Race/Ethnicity, and Region**

During the prevaccine era, the reported incidence of hepatitis A was highest among children aged 5-14 years, with approximately one third of reported cases involving children aged 14 years or younger.

Young children frequently have unrecognized or asymptomatic infection, so a relatively smaller proportion of infections among children than adults are detected by routine disease surveillance.

Incidence models indicate that during 1980-1999, the majority of HAV infections occurred among children under age 10, and the highest incidence was among those aged 0-4 years.

Before the use of hepatitis A vaccine, rates among American Indians and Alaska Natives were more than five times higher than rates in other racial/ethnic populations, and rates among Hispanics were approximately three times higher than rates among non-Hispanics.

Since the 1960s, the highest hepatitis A rates and the majority of cases occurred in a limited number of states and counties concentrated in the western and southwestern United States. Despite year-to-year fluctuations, rates in these areas consistently remained above the national average. In 11 states (Alaska, Arizona, California, Idaho, Nevada, New Mexico, Oklahoma, Oregon, South Dakota, Utah, and Washington) with consistently elevated rates, representing 22 percent of the U.S. population, average annual hepatitis A incidence was twice the national average of approximately 10 cases per 100,000 population during 1987-1997; cases among residents of these states accounted for an average of 50 percent of reported cases.

An additional 18 percent of cases occurred among residents of six states (Arkansas, Colorado, Missouri, Montana, Texas, and Wyoming) with average annual rates above (but less than twice) the national average during this time.

Approximately 31 percent of the U.S. population had showed previous HAV infection, when measured in the Third National Health and Nutrition Examination Survey (NHANES-III) conducted during 1988-1994.

Anti-HAV (hepatitis A antibody, indicating the person had a previous infection) prevalence varied directly with age: among persons aged 6-11 years, prevalence was 9 percent; 20-29 years, 19 percent; 40-49 years, 33 percent; and more than 70 years, 75 percent.

Age-adjusted anti-HAV prevalence was considerably higher among Mexican-American participants (70 percent) compared with black (39 percent) and white (23 percent) participants, and among foreign-born participants (69 percent) compared with those born in the U.S. (25 percent).

### **Sources of Infection**

In the prevaccine era, the majority of U.S. cases of hepatitis A resulted from person-to-person transmission of HAV during communitywide outbreaks. The most frequently reported source of infection (in 12 to 26 percent of cases) was household or sexual contact with a person with hepatitis A.

Cyclic outbreaks occurred among users of injection and noninjection drugs and among men who have sex with men (MSM), and up to 15 percent of nationally reported cases occurred among persons reporting one or more of these behaviors.

Other potential sources of infection (e.g., international travel and recognized foodborne outbreaks) were reported among 3 to 6 percent of cases.

For approximately 50 percent of persons with hepatitis A, no source was identified for their infection.

### **Communitywide Epidemics**

During communitywide epidemics, infection was transmitted from person to person in households and extended family settings. These epidemics typically spread throughout the community, and no single risk factor or risk group could be identified that accounted for the majority of cases. Once initiated, epidemics often persisted for 1-2 years and proved difficult to control.

Because children often have unrecognized or asymptomatic infection, they played a key role in sustaining HAV transmission during these epidemics.

### **Vaccine Era**

In 2004, a total of 5,683 cases were reported, representing an estimated 24,000 acute clinical cases when underreporting is taken into account. This rate was the lowest ever

recorded and was 79 percent lower than the previously recorded low in 1992, in the prevaccine era.

Beginning in the late 1990s, national age-specific rates declined more rapidly among children than adults; as a result, in recent years, rates have been similar among all age groups.

Historic differences in rates among racial/ethnic populations also have narrowed in the vaccine era. For example, recent rates among American Indians and Alaska Natives represent a 99 percent decline compared with the prevaccine era and are now approximately the same or lower than those of other racial/ethnic populations.

Rates among Hispanics also declined 87 percent during this period, from 20.6 cases per 100,000 population during 1990-1997 to 2.7 per 100,000 in 2004, but remain higher than those for non-Hispanics.

Elimination of historic geographic differences in incidence rates has also occurred, and since 2001, rates in states where vaccination was recommended have been approximately equal to the rest of the United States.

In recent years, counties with higher rates have varied from year to year and have been distributed throughout the country.

Incidence declined sharply in states with historically consistent elevated rates. These states were included in the 1999 ACIP recommendations for routine hepatitis A vaccination of children. As a result, the majority of hepatitis A cases during recent years have been reported from states with historically low rates in which hepatitis A vaccination of children has not been widely implemented.

In addition, the narrowing or elimination of national differences in age, race/ethnicity, and state-specific rates can be attributed largely to changes that occurred in the states in which routine hepatitis A vaccination of children was recommended and implemented.

In 2004, for example, approximately two thirds of the nearly 6,000 cases were reported from states without childhood vaccination recommendations.

The 2004 rate among all Hispanics in these states remained four times higher than among non-Hispanics and was seven times higher among Hispanic compared with non-Hispanic children. The highest rate in any demographic subgroup occurred among

Hispanic children in states for which routine hepatitis A vaccination of children is not recommended.

### **Sources of Infection**

In recent years, sexual or household contact with a person with hepatitis A has been reported in a smaller proportion of cases but continued to account for 13 percent of cases during 2002-2004.

The proportion of persons with hepatitis A reporting exposure to child care centers also has declined to approximately 9 percent.

The number of international travel-associated cases has remained approximately the same, but as overall incidence has declined, the proportion of cases attributable to this exposure has increased, accounting for an average of 13 percent of cases during 2002-2004. During this time, more than 25 percent of cases among children under age 15 could be attributed to international travel.

Approximately 75 percent of all travel-related cases were associated with travel to Mexico or to Central or South America. Outbreaks among MSM and users of illicit drugs also continue to occur.

### **Groups at Increased Risk for Hepatitis A**

#### **Travelers**

Persons from developed countries who travel to developing countries are at substantial risk for acquiring hepatitis A. Such persons include tourists, immigrants and their children returning to their country of origin to visit friends or relatives, military personnel, missionaries, and others who work or study abroad in countries with a high or intermediate hepatitis A presence.

Hepatitis A remains one of the most common vaccine-preventable diseases acquired during travel. The risk might be higher among travelers staying in areas with poor hygienic conditions, varies according to the region and the length of stay, and appears to be increased even among travelers who reported observing protective measures and staying in urban areas or luxury hotels (CDC, unpublished data, 2005).

In the United States, children account for approximately 50 percent of reported travel-related cases. In one study of Hispanic children in San Diego with hepatitis A, two thirds reported international travel (to Mexico) during the incubation period; travel was the only exposure associated with infection in a case-control study.

Travelers who acquire hepatitis A during their trips also might transmit to others on their return.

### **MSM**

Hepatitis A outbreaks among MSM (Men who have Sex with Men) have been reported frequently. Cyclic outbreaks have occurred in urban areas in the United States, Canada, Europe, and Australia and can occur in the context of an outbreak in the larger community.

Since 1996, ACIP has recommended hepatitis A vaccination of MSM. Although precise data are lacking, vaccine coverage appears to be low.

### **Users of Injection and Noninjection Drugs**

During the preceding 2 decades, outbreaks have been reported with increasing frequency among users of injection and noninjection drugs in Australia, Europe, and North America.

In the United States, outbreaks have frequently involved users of injected and noninjected methamphetamine, who have accounted for up to 48 percent of reported cases during outbreaks. Since 1996, ACIP has recommended hepatitis A vaccination of users of illicit drugs, but vaccine coverage data are not available.

### **Persons with Clotting-Factor Disorders**

During 1992-1993, outbreaks of hepatitis A were reported in Europe among persons with clotting-factor disorders who had been administered solvent-detergent—treated, “high-purity” factor VIII concentrates that presumably had been contaminated from plasma donors incubating hepatitis A.

In the United States, data from one serologic study suggested that persons with hemophilia might be at increased risk for HAV infection.

HAV is resistant to solvent-detergent treatment, and during 1995-1996, one study identified six patients with clotting-factor disorders who had hepatitis A after having been administered solvent-detergent—treated factor VIII and factor IX concentrates. However, changes in viral inactivation procedures, high hepatitis A vaccine coverage, and improved donor screening have decreased the risk for HAV transmission from clotting factors.

During May 1998 through July 2002, no new cases of HAV infection attributed to blood products were identified in an analysis of serosurveillance data from 140 participating hemophilia treatment centers.

### **Risk for Severe Adverse Consequences of Hepatitis A Among Persons with Chronic Liver Disease**

Although not at increased risk for HAV infection, persons with chronic liver disease are at increased risk for fulminant (coming on suddenly and with great severity) hepatitis A. Death certificate data indicate a higher prevalence of chronic liver disease among persons who died of fulminant hepatitis A compared with persons who died of other causes.

### **Risk for Hepatitis A in Other Groups and Settings**

#### **Food-Service Establishments and Food Handlers**

Foodborne hepatitis A outbreaks are recognized relatively infrequently in the United States. Outbreaks typically are associated with contamination of food during preparation by an HAV-infected food handler; a single infected food handler can transmit HAV to dozens or even hundreds of persons. However, the majority of food handlers with hepatitis A do not transmit HAV.

Food handlers are not at increased risk for hepatitis A because of their occupation. However, among the approximately 40,000 adults with hepatitis A reported during 1992-2000 for whom an occupation was known, 8 percent were identified as food handlers, reflecting the large number of persons employed in the food service industry.

Outbreaks associated with food, especially green onions and other raw produce, that has been contaminated before reaching a food-service establishment have been recognized increasingly in recent years. Low attack rates are common, and outbreaks often have been recognized in association with a single restaurant in which no infected food handler was identified on subsequent investigation.

#### **Child Care Centers**

Outbreaks among children attending child care centers and persons employed at these centers have been recognized since the 1970s, but their frequency has decreased as overall hepatitis A incidence among children has declined in recent years.

Because infection among children is typically mild or asymptomatic, outbreaks often are identified only when adult contacts (typically parents) become ill. Poor hygiene among children who wear diapers and the handling and changing of diapers by staff contribute to the spread of HAV infection; outbreaks rarely occur in child care centers in which care is provided only to children who are toilet trained.



Although child care centers might have been the source of outbreaks of hepatitis A in certain communities, disease in child care centers more commonly reflects extended transmission from the community.

Despite the occurrence of outbreaks when HAV is introduced into child care centers, there is no substantially increased prevalence of HAV infection among staff at child care centers compared with prevalence among those not working in child care centers.

### **Institutions for Persons with Developmental Disabilities**

Historically, HAV infection was highly endemic in institutions for persons with developmental disabilities. As fewer children have been institutionalized and as conditions in institutions have improved, the incidence and prevalence of HAV infection have decreased, although outbreaks can occur in these settings.

### **Schools**

In the United States, the occurrence of cases of hepatitis A in elementary or secondary schools typically reflects disease acquisition in the community. Child-to-child disease transmission in the school setting is uncommon; if multiple cases occur among children at a school, the possibility of a common source of infection should be investigated.

### **HAV Infection Worldwide**

Globally, the number of clinical cases of HAV infection as of 2003 is estimated to be approximately 1.5 million per year with most cases occurring in children, with an average fatality rate of less than 0.4 percent, according to the World Health Organization.

The highest rates of HAV infection occur in Central and South America, Africa, the Middle East, Greenland and Central, Southeast and Eastern Asia.

In developing countries, some epidemiologists predict the infection rate in children ages 12 and younger is about 100 percent. In countries with prolific childhood infection, hepatitis A in adults is virtually non-existent due to near universal infection during childhood.

Once infected with HAV, a person enjoys life-long immunity against re-infection.

### **The Hepatitis A Virus**

The hepatitis A virus is a single-strand RNA (ribonucleic acid) virus that belongs to the Picornavirus family. This viral “family” includes viruses that cause polio and the

common cold.

This virus has no outer coating or envelope. The hepatitis A genome has a single strand of RNA. The virus binds to a receptor on a liver cell and then enters the cell and replicates in the cytoplasm, the area outside the cell's nucleus. The virus exits the liver through bile into stool.

This is a hearty virus. It is able to survive the body's highly acidic digestive tract, and at room temperature it can live for more than a week. In water, it can survive from three to 10 months, which is why it could be found in shellfish in sewage-contaminated water bodies.

HAV has only one serotype or viral strain. No other "strains" or "genotypes" of this virus exist around the world. This means the hepatitis A vaccine will work worldwide to prevent HAV infection.

### **How the Virus Affects People**

The symptoms of hepatitis A are similar to those of other acute viral infections of the liver. Following an incubation period (the time between infection and when symptoms appear), ranging from 15 to 50 days, patients—usually adults—experience exhaustion, loss of appetite, nausea and abdominal discomfort. Darkening of the urine, whitish stool and yellowish staining of skin and the whites of the eye (jaundice) are evidence of liver problems.

During the acute or symptomatic stages of hepatitis A, there are marked increases of liver enzymes (such as alanine aminotransferase or ALT) in the bloodstream. These enzymes are released when liver cells are damaged or die. There may also be increases in aspartate aminotransferase (AST) levels, alkaline phosphatase and bilirubin levels in the bloodstream.

The period of acute illness may last as long as a few months. ALT levels typically return to normal before bilirubin levels fall. In some cases, ALT levels may remain abnormal for several months, but usually return to normal within a year.

In young children, HAV infection rarely causes symptoms, and it may only be detected through laboratory tests. In adults and in elderly persons, the disease is frequently more severe, but rarely fatal.

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Usually, diagnosis of HAV infection is made when HAV antibodies are found in the blood. There is a significant rise in the level of HAV-specific antibodies during the first few weeks of infection.

IgM (Immune Globulin Class M) antibodies are present and indicate an acute HAV infection. HAV IgM antibodies are necessary to diagnose the acute stage of HAV infection. The presence of IgM antibodies in the blood indicates a current or very recent infection, usually within six months. After the initial onset of an HAV infection, the concentration of IgMs in the blood declines over a six-month period.

However, low levels of another type of HAV antibody, the IgG (Immune Globulin Class G) antibody is also present. The IgG antibodies persist for years in the body and confer life-long immunity against future re-infection by HAV.

### Viral Hepatitis A Tests

<b>Hepatitis A IgM Antibody</b> (Anti-HAV IgM or HAV IgM Ab)	<ul style="list-style-type: none"><li>• A positive result indicates a recent infection.</li><li>• This antibody is present for up to six months after infection.</li></ul>
<b>Hepatitis A Antibody</b> (Anti-HAV or HAV Ab)	<ul style="list-style-type: none"><li>• This does not help in diagnosing the timeline of an infection.</li><li>• A positive result indicates a past or present infection and life-long immunity to hepatitis A.</li><li>• Individuals given serum immune globulin for hepatitis A might test positive for this antibody for at least six months.</li></ul>

### How Does the Virus Spread?

HAV is transmitted through the fecal-oral route. For instance, Sally is infected with hepatitis A. She goes to the restroom but fails to wash her hands. She then prepares a salad for Mary and herself. Mary eats the salad, which has trace amounts of fecal matter on it due to Sally's unwashed hands, and then Mary becomes infected with hepatitis A.

The virus is also spread through close, intimate contact such as during sexual intercourse. Though rare, it can be spread through blood transfusions. Since 2002, nucleic acid amplification tests such as polymerase chain reaction (PCR) have been applied to the screening of source plasma used for the manufacture of plasma-derived products.

HAV is known to be transmitted among injecting illegal drug users.

Casual contact, including kissing or the sharing of utensils, does not transmit the virus. Transmission might occur by drinking water or eating ice or uncooked fruits or vegetables grown with or washed in water contaminated by fecal matter from infected people.

HAV accumulates in high concentrations in raw or uncooked shellfish, such as oysters, clams or mussels that absorb the virus in sewage-polluted marine environments.

There are rare, periodic outbreaks of hepatitis A in restaurants or other institutions when a food handler or server is infected and fails to adequately wash his or her hands.

Peak infectivity, when the concentration of virus in feces is highest, is approximately a week before and a week after the onset of symptoms or elevation of liver enzymes. As a result, people who are able to transmit the disease often do not yet know they are infected. In infected people, HAV replicates in the liver, is excreted in bile and shed in the stool.

Fecal shedding of HAV usually lasts for only a few weeks, and with the possible exception of infection in people whose immune systems are compromised by another infection, chronic excretion of this virus has never been reported.

Children and infants can shed the virus through their stool for longer periods than adults, up to several months after the onset of clinical illness.

Because most children have unrecognized infections, they play critical roles in transmitting HAV. Studies of adults without identified sources of infection found about 50 percent of infected persons had household contact with young children who had been infected with HAV.

### **Treating Hepatitis A**

Currently, there is no specific treatment for people with hepatitis A. Physicians treat the symptoms caused by hepatitis A infection. Severely ill patients are hospitalized to ensure appropriate diet and rest. All drugs that are toxic to the liver, including alcohol, should be avoided until after the illness is over.

When a person has been exposed to HAV, immune globulin must be administered within two weeks after exposure to the virus for maximum protection.

The hepatitis A vaccine is not approved for use in a postexposure situation.

### **Preventing HAV Infection**

As with most all germs, the best way to prevent hepatitis A infection is to wash your hands—a lot. Also, don't eat raw or undercooked seafood or shellfish and if traveling in developing countries, don't drink untreated water or ice cubes. Vegetables and fruits should be cooked or peeled before eating. Make sure you're vaccinated.

Improved sanitary conditions and personal hygiene reduce the spread of HAV. However, given the circumstances under which these infections occur most frequently around the world, short-term improvements are difficult, particularly where there is extreme poverty and substandard drinking water sources and sewage treatment facilities.

Immune globulin against HAV infection is costly and short-lived. However, the hepatitis A vaccines represent an efficient way to achieve long-term protection against hepatitis A worldwide.

Adults and children 1 year of age and older with chronic liver disease who have never had hepatitis A should be vaccinated, as there is a higher rate of fulminant hepatitis (rapid onset of liver failure, often leading to death) among persons with chronic liver disease who are infected with HAV.

Immune globulin is recommended for travelers younger than one because the vaccine is currently not licensed for use in this age group. The safety of the vaccine during pregnancy has not yet been determined.

### **Hepatitis A Vaccines**

Currently, there are hepatitis A vaccines commercially available in the United States. They are administered in two doses at least six months apart.

There are no live viruses in hepatitis A vaccines. The virus is inactivated or killed during production of the vaccines, similar to Salk-type inactivated polio vaccine. The currently available cell culture-derived, inactivated vaccines are highly effective in preventing HAV infection and are well tolerated and without significant side effects, according to CDC and the World Health Organization.

According to CDC, clinical trials show the vaccines will protect 94 to 100 percent of those vaccinated against HAV infection. The long-term protection is still unknown but estimates from kinetic models predict protection will last 20 years.

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There is also a combination vaccine for hepatitis A and hepatitis B available for persons 18 years of age and older. The combination vaccine is administered in a three-injection regimen over six months.

### **Hepatitis A vaccines are recommended for:**

- All children 1 year (12 through 23 months) of age.
- Persons 1 year of age and older traveling to or working in countries with high or intermediate prevalence of hepatitis A, such as those located in Central or South America, Mexico, Asia (except Japan), Africa, and eastern Europe. For more information see [www.cdc.gov/travel](http://www.cdc.gov/travel).
- Children and adolescents through 18 years of age who live in states or communities where routine vaccination has been implemented because of high disease incidence.
- Men who have sex with men.
- Persons who use street drugs.
- Persons with chronic liver disease.
- Persons who are treated with clotting factor concentrates.
- Persons who work with HAV-infected primates or who work with HAV in research laboratories.

Other people might get hepatitis A vaccine in special situations:

- Hepatitis A vaccine might be recommended for children or adolescents in communities where outbreaks of hepatitis A are occurring.

*Hepatitis A vaccine is not licensed for children younger than 1 year of age.*

### **Hepatitis A Vaccine Side Effects**

Among children, the most frequently reported side effects occurring after vaccine administration were:

- Pain or tenderness at the site of injection
- Headache
- Feeding problems

### **Complications of Hepatitis A in Patients with Hepatitis B or C**

Like all forms of viral hepatitis, hepatitis A causes acute inflammation of the liver. If people with chronic hepatitis B or C or other liver diseases are infected by HAV, they face serious liver damage due to the additional virus infecting their inflamed or

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vulnerable livers. This is why it is important for all people at least 1 year of age with chronic hepatitis B or C to be vaccinated.

“Acute hepatitis A doesn't necessarily make chronic hepatitis B disease worse, but you have a new disease affecting an already damaged, sick and compromised liver,” explained Dr. Philip Rosenthal, director of Pediatric Hepatology and the Pediatric Liver Transplant Program at the University of California, San Francisco.

Unlike hepatitis B or C, this common form of hepatitis is short-lived and never develops into a chronic or long-term condition. It shares many similarities with the hepatitis E virus, which is also transmitted through contact with the feces of infected people.

In a report in *The New England Journal of Medicine*, a group of adults with chronic hepatitis C infection were studied. Of 17 patients with hepatitis C, six who subsequently contracted hepatitis A died of sudden liver failure. The study, conducted by researchers at the University of Verona, also followed 10 adult patients with chronic hepatitis B virus infection who contracted hepatitis A. None of these chronic hepatitis B patients died as a result of their exposure to the hepatitis A virus.

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