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Chapter

# Hepatitis A: At-Risk Populations

*Rosa Coelho and Guilherme Macedo*

## Abstract

Hepatitis A virus (HAV) is transmitted mostly through exposure to contaminated food or water, or through exposure to infected persons. This infection can occur sporadically or in an epidemic form, confers lifelong immunity and it is preventable by a safe and effective vaccine. Therefore, prevention strategies are crucial and could eradicate the infection if they were successfully employed. In this chapter, authors summarize mode of transmission and preventive measures for HAV among the following population groups: travellers, health care workers, men who have sex with men, individuals who use illicit drugs, sewage workers, food handlers, military personnel, prisoners, blood transfusions recipients, haemophiliacs and patients with HIV and chronic liver disease. Moreover, authors describe which of these groups are eligible for HAV vaccination according to available data.

**Keywords:** hepatitis A, MSM, men who have sex with men, outbreak, sexually transmitted infections, viral infections, viral infections

## 1. Introduction

Hepatitis A virus (HAV) is a common cause of acute viral hepatitis and caused approximately 11 000 deaths in 2015 worldwide (accounting for 0.8% of the mortality from viral hepatitis) [1].

HAV infection can occur sporadically or in an epidemic form, confers lifelong immunity [2] and is preventable by a safe and effective vaccine. As a matter of fact, humans are the only known reservoir for HAV, so the successful employment of widespread prevention strategies could eradicate the infection.

In the literature, some risk groups for HAV infection were identified, such as travellers, healthcare workers (HCWs), men who have sex with men (MSM), individuals who use illicit drugs, sewage workers, food handlers, military personnel, prisoners, blood transfusions recipients and haemophiliacs [3].

## 2. Mode of transmission

HAV is usually transmitted by the faecal-oral route: primarily through close personal contact or by oral intake after faecal contamination of skin or mucous membranes. Less commonly, the transmission occurs due to consumption of contaminated food or water [4].

Regarding person to person contact, the transmission can occur within households, residential institutions and daycare centres, among military personnel and during sexual intercourse. HAV infection due to consumption of contaminated

food or water includes ingesting raw or undercooked foods, namely, shellfish and vegetables, or consumption of meals contaminated by infected food handlers.

Other modes of HAV transmission are due to blood transfusion and use of illicit drugs. Maternal-foetal transmission has not been described.

According to endemicity of hepatitis A (HA) disease, it can occur in three distinct ways [5]. In developing countries, with poor sanitary infrastructure, there are high infection rates occurring in childhood, and HA is endemic. Therefore, in these areas outbreaks are not frequent, and children develop immunity without ever being symptomatic [5]. In contrast, in developed countries with adequate sanitation and infrastructure, infection rates are low, and outbreaks are infrequent as long as the disease is not introduced into the population from an external source [5, 6]. Countries with intermediate levels of HA present increased numbers of susceptible adults and, occasionally, large outbreaks [5, 7]. In terms of HA endemicity, it is important to point out that exportation of food that cannot be sterilised, from countries of high endemicity to areas with low rates of infection, is a potentially important source of infection [5–7].

## 3. At-risk populations

### 3.1 Travellers to endemic countries

Travel is still one of the most important risk factors for HAV infection despite the improvement of socio-economic level considering the last decades [8]. The risk is varied and depends on the endemicity of visited countries and on the adherence of hygienic practices [3, 8].

Although the risk of infection may have slightly decreased in recent years, the incidence rate for non-protected travellers is estimated to be 3 cases per 1000 travellers per month of stay in developing countries [3].

A population-based study performed showed that the highest risk was associated with travel to East Africa followed by the Middle East, India and neighbouring countries [9]. The risk increases among young children visiting friends and relatives that accounted for a large proportion of cases and should be prioritised for vaccination [8, 10].

Few prevalence studies with contrasting and inconclusive data have been published regarding anti-HAV positivity and history of travel [3].

Considering prophylaxis for travellers in several countries, many recommendations and guidelines have been issued emphasising the importance of a correct information and prophylaxis for this at-risk group. Bearing in mind that vaccinated travellers still represent a small amount, it is crucial to promote this prophylaxis measure among physicians and this at-risk population [3].

### 3.2 Men who have sex with men

Since the 1980s, when an important decrease in HA incidence due to socio-economic improvements was evident, a peak in the incidence of HAV was noticed in males from 20 to 39 years old. These cases were attributed to sexually transmitted HAV and justified some outbreaks among MSM that have been described in Denmark, Sweden, the United Kingdom and the United States [3, 11, 12]. The predominant circulating HAV strains among MSM belonged to genotype IA [13].

Among MSM population, some risk factors for HAV infection were identified, such as oro-anal sexual practices and digital-rectal intercourse, history of sexual contacts with anonymous sex partners, group sex and sexual promiscuity [3].

As a matter of fact, in this at-risk group, the widespread availability and use of mobile-accessible, especially geosocial networking apps for MSM facilitate anonymous sexual activities being potential drivers of recent outbreaks of HAV [13–16]. On the other hand, dating apps and websites can be an important and effective tool to promote HAV infection prevention campaigns in outbreaks, with the advantage of a range of hard-to-reach MSM seeking anonymous sex [17].

Although MSM with sexual behaviour risks are responsible for HAV infection outbreaks, several prevalence studies do not demonstrate significant differences in anti-HAV positivity between MSM and control groups (general population/persons who use illicit drugs) [3].

Since the mid-1990s, HAV vaccine has been licenced and recommended for MSM. However, the emergence of HAV infection has continued to constitute a health threat to MSM in several developed countries [13].

### 3.3 Persons who use illicit drugs

Since the 1970s, as the numbers of injecting drug users (IDUs) increased, several outbreaks of acute HAV infection among IDUs' communities have been reported in several developed countries of low endemicity for HAV infection [13].

HAV acute infection in this at-risk group is strongly associated with the changing prevalence of this viral infection in the general population, usually in whom natural immunity was reduced in countries with low incidence.

Most of the outbreaks were described in Europe and the United States in the 1980s and 1990s but were seldom described after the early 2000s [13]. Some prevalence studies described an increased antibody prevalence among IDUs [3].

Transmission can occur via faecal-oral contact through poor personal hygiene and living conditions or percutaneously through contamination of illicit drugs or injecting equipment by faecal materials or blood [13, 18].

In the literature the most important risk factors identified for HAV infection in this group are scarce personal hygiene, socio-economic factors, sexual promiscuity, syringe exchange and contamination of instruments used to prepare drug consumption [3].

Prevention of HAV is important, and vaccination programmes should be implemented as occurred already in some European countries, such as the United Kingdom, Norway and Italy [13].

### 3.4 Food handlers

In the HAV transmission chain, food handlers can be involved in two different ways: they can become infected via contaminated food (principally shellfish and raw seafood), and, once infected, they may be the source of outbreaks [3].

Despite numerous HAV epidemics having been described [3], since the introduction of the HAV vaccine, the incidence of HAV infection has decreased, including those among food handlers [19].

However, due to their occupation, food handlers are not considered an at-risk group for HAV infection, as it can be easily avoidable if the most common hygienic precautions are taken. Some studies described a very slight increase in prevalence in food handlers under the age of 30 years versus the general population of the same age. Also higher anti-HAV antibody seroprevalence was detected in the personnel employed in the kitchen than in medical personnel, but socio-economic factors are not taken into account [3]. Nonetheless, this group may belong to demographic groups, such as young people and people with lower socio-economic status, who have a higher incidence of HAV than the general population [20].

Mandatory food handler vaccination is unlikely to be cost-effective. However, based on local needs, health departments of each country should make decisions about requiring vaccination for this group [21].

### 3.5 Healthcare workers

Data regarding the mode of HAV transmission show that personal contact with an infected person is the most common risk factor for developing the infection. Thus, healthcare workers are at potential risk of exposure to contagious patients infected with HA, particularly in paediatric wards [22–24].

The analysis of several studies regarding outbreaks in hospital settings indicates the main risk factors are eating and drinking in hospital divisions and inadequate hand cleaning [3].

The seroprevalence studies did not show consistent findings, and there were wide variations in the proportion of seropositive HCWs, taking into account different countries and professional groups [24].

As a matter of fact, studies comparing anti-HAV antibody seroprevalence between paediatric divisions' nurses and nurses of other hospital departments did not show any difference [3].

It is interesting to point out that one study comparing the hospital laundry workers with nurses suggested that the former group was more exposed to HA occupational risk, probably due to contact with handling dirty linen prior to washing them [25].

However, considering that universal precautions should be implemented in healthcare centres, some authors might argue that HCWs do not constitute an at-risk group for HAV [3, 24].

Nonetheless, considering that HA vaccines provide a safe, immunogenic and efficacious prevention tool, some authors recommend vaccination considering that HCWs are exposed to a higher risk infection than the general population [24].

It is crucial to implement general precautionary measures at the workplace that could reduce the transmission of HAV. Moreover, it is crucial that hospitals have an effective infection control of HA outbreaks which means early recognition, including awareness of atypical presentations of HAV infection, and strict adherence to universal infection control measures [24].

### 3.6 Sewage workers

Wastewater plant workers may be exposed to various infectious agents. However, at the moment it is unclear whether sewage workers have an increased risk of contracting HA or not, especially if the disease is preventable by using a vaccine [26].

Actually, sewage workers can be exposed to aerosols and direct contact with potentially contaminated materials such as raw wastewater, which means that a plausible biological risk to acquire HA in this group of employees exists [3, 26]. However, studies regarding anti-HAV antibody seroprevalence and risk of acquiring the disease are conflicting [26]. A recent systematic review [27] concluded that the incidence of clinical HA does not show an increased risk in sewage workers. Nonetheless, it found a moderately increased risk of subclinical HA infection when seroprevalence studies are considered. Results of seroprevalence studies may be flawed by several methodological factors.

Considering these discrepant results, there is no consensus on the need to vaccinate sewage workers. On the one hand, some authors recommend a systematic vaccination because of the increased risk. On the other hand, some authors do not

consider vaccination necessary, and some authors consider that vaccination programmes can be discussed for those workers heavily exposed to sewage [27].

Some specialists in occupational health just recommend immunisation in order to "maintain labour peace", to prevent litigation costs, or only after evaluating the specific epidemiological situation [27].

However, these conclusions may not be generalisable to populations with different natural immunity as they are based mostly on investigations from Europe and North America [27].

### 3.7 Military personnel

Control of HA has been an important concern for US military forces in war and peace mostly in the past. However, nowadays due to the improvement of the sanitation level with better hygienic sanitary conditions, the risk of HA in this group is mainly attributed to activities in high endemic areas. As a matter of fact, this group usually works in difficult areas characterised by poor hygienic conditions and scarce control on food sources and drinking water supplies. Moreover, in remote areas, soldiers can be exposed to parenterally transmitted infections in case of injuries, hospitalisations and transfusions [3, 28]. In fact, most studies reporting HA epidemics among military personnel were published before 1990 showing numerous HA outbreaks that devastated whole army forces during the world wars, conditioning the military strategies [3].

Almost all the studies published later analysed the vaccine effectiveness and suggest different vaccination programmes considering soldiers as an at-risk group for HA [3].

However, in several papers military personnel is considered just as a sample of the general population, and as it has been recently occurring in other groups, a decrease in seroprevalence is evident. Moreover, only a few studies analyse the correlation between HA infection with epidemiologic factors such as overcrowding and consumption of contaminated food and water in military activities [3].

A recent and large multicentric cross-sectional study (11 training centres) conducted within the Indian Armed Forces during 1 year (2010–2011) showed a high seroprevalence of HAV (93%) among healthy young adults [29]. In contrast, HA was found to be a cause of acute viral hepatitis in 30% of 102 cases seen in an Armed Forces hospital from southern India [30]. So, even in the same countries, data are not consistent, and therefore, it can be difficult to justify the economic cost of universal HAV vaccination.

### 3.8 Prisoners

Prison is considered to be an environment where many risk factors for HA can be easily identified, such as overcrowding, frequent prison relocation, sexual promiscuity, drug abuse and poor sanitation.

As a matter of fact, prison facilities in which inmates live in close proximity and engage in high-risk behaviours for HAV transmissions may diminish the effectiveness of strategies of infection control based on universal adoption of hygienic practices [31].

Data regarding HAV prevalence among prisoners are few, conflicting and not conclusive [3]. Epidemiological investigations concluded that HA among prisoners have been introduced mainly by newly arrived prison entrants who were incarcerated during their incubation period who subsequently developed acute HA [31].

A recent cross-sectional survey undertaken after a multicentre outbreak of HAV infection in the Queensland prison system, following a community-based HAV epidemic among users of illicit drugs, identifies the determinants for recent and past HAV infection [31]. The authors concluded that the common factor among recently acquired and past infection of HA was due to the use of illicit drugs. In contrast, there was no evidence that IDUs were associated to higher rates of HAV-IgG seropositivity (past infection) [31].

In prison settings, routine vaccination of all susceptible inmates with inactivated HA vaccine may be considered as an important strategy in order to prevent transmission of HAV infection especially during periods of higher incidence among the incoming prisoner population [31].

### 3.9 Blood transfusion recipients

HAV infection is not a significant complication of blood transfusion due to the short-lasting viremic period [3]. As a matter of fact, considering the sporadic nature of the HAV acute infection among blood donors and the lack of HAV chronic carriers, antibody screening tests for HAV for serological screening of blood donors are not recommended in any country [32]. However, even if it is rare, HAV parenteral transmission is possible, and many countries recommend vaccination for polytransfused patients [33, 34].

In the past, some epidemic cases of HA were reportedly caused by children who received infected blood or plasma. However, none of the prospective studies, conducted in the 1970s and 1980s to establish incidence and agents of posttransfusion hepatitis, identified cases of HAV infection [3]. In fact, no data showing higher prevalence of HAV in subjects receiving blood transfusion are available, which means that there is no evidence to consider polytransfused patients as a risk group.

Nonetheless, recently two cases of HAV transmission to blood recipients from a healthy donor that later presented to the blood bank with jaundice were published [32]. Actually, one of the cases was fatal and the patient died from fulminant HA. It is important to highlight that the patient was immunocompromised due to bone marrow transplantation and had also hepatitis C [32]. This case report points out the importance of timely identification of post-donation symptoms and notification to blood banks and also that specific groups of immunocompromised patients may benefit from a HAV vaccination programme [32].

### 3.10 Haemophiliacs

Some outbreaks of HAV infection among haemophilia patients have been reported due to transfusions of factors VIII/IX concentrates treated with the solvent/detergent method used to inactivate blood-borne viruses [3]. In fact, in these studies a causal relationship was found between the injection of blood clotting factors and an outbreak of HA among haemophilia patients.

Clotting factor concentrates manufactured from large pool may be contaminated by HAV, which can be present even in a single highly viremic blood donor.

The solvent/detergent method used to inactivate HAV virus seemed to be not effective to ensure the safety of clotting factor concentrates [35]. Therefore, Guilaume TA et al. proposed a new method using a terminal 100°C dry-heat sterilisation in order to destroy also non-lipid-enveloped viruses [36].

However, case–control papers and studies regarding seroprevalence of HAV in this group did not show an increased risk of contracting HA among haemophiliacs [3], and therefore at present haemophiliacs are not included as an at-risk group to acquire HAV.

### 3.11 Other populations

HA results in acute liver failure in less than 1%, age superior to 50 years old and those with underlying liver disease being important risk factors, especially with chronic hepatitis B and C virus infections [37, 38]. As a matter of fact, HAV superinfection in patients with underlying chronic liver disease is not also associated with a high risk of liver failure but also of death [37, 38].

Besides, patients with pre-existing liver disease (i.e. non-alcoholic fatty liver disease or alcoholic steatohepatitis) present a higher risk of developing an acute-on-chronic liver failure in cases of HAV infection [38, 39].

Therefore, it has been recommended to vaccinate against HAV in patients with chronic liver disease [40]. Nonetheless, studies show HAV testing and vaccination rates were low in clinical practice. Public health programmes are needed in order to increase awareness about HAV vaccination in patients with pre-existing liver damage [41–43].

HAV infections among older individuals continue to pose public health and clinical challenges because HA illness severity increases with age, presence of liver disease and other comorbid medical conditions [42]. In fact, the increased number of HAV infection in hospitalised patients with hypertension, ischemic heart disease, disorders of lipid metabolism and chronic kidney disease may also reflect increasing age. Older age (over 65 years old) and any liver disease are independent risk factors to being hospitalised more than 5 days, suggesting that these factors increase the severity of HA illness [42]. Therefore, more studies are needed to guide recommendations for HA vaccination in adults with other chronic diseases other than chronic liver disease.

Considering HIV-positive individuals, only very few studies with a limit number of patients address the risk of HA in these populations [3]. Even though the direct evidence on the correlation between contracting HIV and HAV was scarce, observational data suggested that HIV-positive individuals, especially MSM and IDUs, are at increased risk of acquiring HAV [3]. Moreover, Ida et al. published a study of 15 HIV-positive individuals that showed that the duration of HAV viremia in HIV-seropositive individuals with acute HA was prolonged compared to that in HIV-negative individuals, which may increase the probability of HAV transmission to others [44].

Considering HIV-seropositive patients, two independent risk factors associated with seropositivity for HAV were recognised: older age and injecting drug use. However, HAV seroprevalence was lower in HIV-positive MSM despite the at-risk sexual behaviours [13].

Regarding prophylaxis in HIV-positive patients, HAV vaccination is not universally recommended but specifically for those with increased risks of exposure (such as from injecting drug use, oral-anal sex, travel to or residence in endemic areas, frequent clotting factor or blood transfusions) or with increased risks of fulminant disease (such as those with chronic hepatitis) [45, 46].

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