Hepatitis E – a “new” foodborne disease

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Abstract. Hepatitis E (HE) is a zoonosis caused by hepatitis E virus (HEV). The disease that used to be problematic only in developing regions with inadequate water supplies and poor sanitary conditions is now considered one of the foodborne diseases in industrialized countries as well. According to current knowledge, the main reservoir of the virus is linked to domestic swine and wild boar. Consumption of raw or undercooked pork meat and liver is considered as a risk factor for HE human infection, together with some other sources of infection like blood transfusion or organ transplantation. Although the number of cases has been rising in the last decade, HEV is still a generally unknown virus among the general public. Consumers need to be warned and educated about HEV and its potential sources of contamination within the food supply chain.

1. Introduction

Hepatitis E virus (HEV) is a non-enveloped virus with a single-stranded, positive sense RNA genome. The genome is 7.2 kb long and codes for three open reading frames [1]. It belongs to the Hepeviridae family, which is divided into the genera Ortohepevirus (species A-D) and Piscihepevirus. Ortohepevirus A has 7 genotypes [2]. Genotypes 1 and 2 infect only humans and are distributed mainly in Asia, Africa and North America. They can cause large waterborne epidemics due to insufficient hygiene. Genotypes 3 and 4 are zoonotic, their main reservoirs are swine and wild boar, and they can cause sporadic cases of hepatitis E (HE) in human. Genotype 3 is distributed worldwide [1, 3]. Genotype 4 is found mainly in Asia [1], but it has already been detected in swine populations in Italy, Belgium and Denmark [4]. HEV from genotypes 5 and 6 is found in wild boars and genotype 7 in camels [5].

2. Hepatitis E infection in human

HEV in humans causes acute icteric disease with a very variable clinical picture [6]. In most cases the infection is asymptomatic [3], while the symptomatic patient shows the following clinical signs: icterus with nausea, fever, abdominal pain, vomiting, hepatomegaly, pale stools and darkened urine [5]. The disease is mostly self-limiting [3]. In low levels, with immunosuppressed patients (organ transplant recipients, lymphoma/leukemia patients, patients with human immunodeficiency virus infection), it can develop into chronic infection and progress to severe fulminant liver failure with fatal outcomes [6]. The mortality is approximately 2% [3,5]. Besides typical symptoms, HEV infection has been associated with neurological disorders, such as Guillain-Barre and Parsonage Turner syndromes, neuralgic amyotrophy, bilateral brachial neuritis, peripheral neuropathy and encephalitis [7].
3. Animal reservoirs

Although domestic swine, wild boar and deer are the only animal species that have been directly linked to zoonotic hepatitis, viral RNA has been found in many other animal species such as rabbit, mongoose, moose, fox, chicken, rat, ferrets, mink and bats. Anti-HEV antibodies have been found in dogs, cats, cows, buffalo, goat, sheep and horses [8].

As domestic swine are considered the main reservoir of HEV, many facts about the dynamics of infection with HEV in pigs have already been discovered. After the level of maternal antibodies drop, young piglets become susceptible to infections, HE being one of them. When they come in contact with the virus, the infection occurs, which usually happens at around 8 weeks of age. Pigs start to shed the virus in feces between one and two weeks after the infection and the shedding lasts for up to 7 weeks [4,6,9]. The virus can be found in muscles and liver until 4 weeks after the onset of fecal HEV excretion, meaning that the risk of HEV-contaminated meat and entrails entering stores is greater when younger animals are slaughtered [4,10]. The age at which pigs are slaughtered varies slightly from country to country, but overall there are three age groups – around the age of 3 months, 6 months and sows/boars. Many countries have conducted an overview of the state of HE infections either on farms or in slaughterhouses and all of them came to the same conclusions: the percentage of viremic pigs in the acute stage of infection (meaning that the viral load in meat and organs is high and can cause an infection in human through consumption of such food) is significantly higher at the age of 3 months than at the age of 6 months [11,12,13,14,15,16,17,18].

A very important fact that strongly contributes to the foodborne nature of HE infection is that swine infected with HEV show no clinical symptoms at all. Only some microscopic lesions have been found in experimentally infected pigs – mild multifocal lymphoplasmatic hepatitis was observed in liver tissue [5].

4. Routes of transmission

HEV has many routes of transmission (Figure 1). In developing countries, the main source of infection is water contaminated by sewage. Poor sanitary conditions in connection with several environment settings (heavy monsoon rains and floods) lead to frequent waterborne epidemics [19]. In industrialized countries, the situation is different – two decades ago it was believed that HE infections occurred after trips to developing countries. When more information was gathered from these patients, it was clear that some people never travelled outside the country, which led to new findings about the possible sources of infection [20,21]. Now we know that autochthonous cases can be acquired through blood transfusion or organ transplantation, and even vertical transmission from mother to child has been observed, but the most important route is ingestion of infected raw or undercooked pork meat/liver. Besides meat products, HEV RNA has also been detected on leafy green vegetables and strawberries (probably caused by the use of contaminated irrigation water or contaminated manure) [22,23].

5. Foodborne disease

With increasing interest in HEV, and also more human cases in Europe revealed, it now appears that foodborne transmission is a major route of infection in Europe. The European Food Safety Authority (EFSA) reported that more than 21000 clinical cases with 28 fatalities have been reported in the last 10 years and a 10-fold increase in reported HE cases has been observed [7]. France, Germany and the UK are countries with the majority of reported cases. Austria, Czech Republic, Hungary, Italy and Spain have also reported outbreaks and/or sporadic foodborne cases [7]. However, it should be noted that the monitoring of HEV differs between EU countries and the overall number of cases is most likely even higher. Sometimes the source of infection is directly identified by detection of viral RNA, while other times it remains unknown or the suspected source is only epidemiologically determined. In reported outbreaks/sporadic cases, tripe sausages, undercooked pork meat, liver sausage, raw figatelli,
pig liver, wild boar meat and shellfish were the sources of infection. The most frequently reported food products causing HE infection are raw or undercooked pork meat or pork liver [7].

Figure 1. Different routes of hepatitis E virus transmission. Solid arrows indicate proven models of transmission, dashed arrows indicate the potential routes of spread [23].

6. Preventive measures – from stable to table

Hepatitis E, as many other foodborne diseases, should be treated comprehensively. Handling only one element of the whole issue will not make a drastic improvement. Responsible professionals involved in the pig chain should be aware of the critical control points that contribute to efficient management of this foodborne zoonosis (Table 1).

6.1. Hepatitis E virus on farms

Clear and focused measures for reducing HE infections should start at the farm level. Pigs shed the virus with feces and urine, so hygiene is of crucial importance. First, housing and equipment should always be disinfected before new animals are brought to the farm, otherwise the viral load in the environment can be high enough to cause infection in the new production batch of animals [10,24]. Secondly, farm workers have to understand biosecurity and practice it. If they follow the simple rules of changing clothes and shoes when entering the farm or when crossing from one part of the farm to another, the chances of spreading the infection between different age groups of animals will be reduced [25].

6.2. Hepatitis E virus in slaughterhouses

Even though ante and post mortem inspection in slaughterhouse is mandatory and samples are taken to monitor the zoonoses, this is not enough to detect pigs infected with HEV. As mentioned before,
animals show no symptoms at all and we have no way of knowing when HEV-positive animals come to slaughter. To avoid possible cross contamination, good practices should always be followed, not only at the slaughterhouse, but also during transport and lairage of the animals and processing and storage of pork meat. Cross contamination with feces has to be avoided at all times.

After stunning and bleeding, pigs are either scalded and dehaired or skinned. If the pig’s skin is removed without hot steaming or burning, viruses on the skin (if the pigs are contaminated with feces) can be transferred to the meat surface. If a scald tank (with water temperature of 64°C) is used, the chance of the virus on the skin surface surviving is probably lower, although it is still not clear what temperature and time of exposure to a particular temperature eliminates the virus in the technological environment.

Another critical control point on the slaughtering line is the removal of the intestines. If they are perforated, the feces can contaminate meat, organs and also the equipment used by workers. The same care should be taken when removing a gall bladder – bile has an even higher viral load than feces and perforation of the gall bladder can lead to cross contamination of liver and meat with HEV-laden bile [7].

6.3. Hepatitis E virus at home

In the end, the only efficient control for HE infection is the right heat treatment of food before eating. Pork meat, liver or meat products have to be thoroughly thermally processed (cooked, baked). The exact temperature and time period that should be used to efficiently eliminate the virus is still not clearly determined. Many experiments have been conducted and the results suggest that the heat resistance of HEV is variable – it depends on the strain or genotype and matrix as well. However, no matter how many experiments have been performed, there is a gap that still needs to be filled – a robust cell culture system for HEV that will allow the determination of HEV infectivity in laboratory circumstances with all practical parameters in real practice is urgently needed [26].

Table 1. Critical control points and preventive measures in pork chain production regarding hepatitis E virus (HEV)

| HEV Problem | Pig farm | Pig slaughter house | Pork consumption |
|-------------|----------|---------------------|-----------------|
| Circulation of HEV on the farm: | | Cross contamination of individual pigs and meat during slaughter and co-infection of meat/entrails via faces, bile or blood | Consumption of undercooked or raw pork meat, liver or pork meat products |
| 1. high viral load in the environment (feces and urine) | | | |
| 2. transmission through direct contact between the animals (mingling of animals from different pens) | | | |
| 3. cross contamination caused by workers on the farm | | | |
| | Preemptive measure | | |
| Biosafety: | | | |
| 1. hygiene measures (washing of the transport vehicles, housing disinfection) | | | |
| 2. protection of the herd from wild animals | | | |
| 3. showering and changing clothes before entering the farm | | | |
| | Education of slaughterhouse workers about good practices to help avoid cross contamination | | |
| | Education of consumers about the pork production chain HEV infection risk (importance of correct thermal treatment) and cross contamination risks during food preparation | | |
7. Conclusion

A lot of new information has been discovered about HEV in the last 20 years and this “new” foodborne disease is getting more attention from day to day. The implementation of these discoveries in the practical pork supply chain still needs a professional push. Also of crucial importance is the fact that consumers are still not familiar with HE; most of them have never heard of it. This issue needs to be addressed and people need to be educated, so they will have the knowledge to protect themselves from HEV when it occurs in foods coming from the pork production chain.

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