Campden BRI
Station Road
Chipping Campden
Gloucestershire
GL55 6LD, UK

Tel: +44 (0)1386 842000
Fax: +44 (0)1386 842100
www.campdenbri.co.uk

Campden BRI
food and drink innovation

Foodborne viruses – what they cause, how they get into food, and what we can do about it.

Introduction

In recent years there has been an ever increasing awareness of the threat of foodborne viruses in the global food supply chain. In 2011, the US Centers for Disease Control and Prevention (CDC) estimated that each year roughly 48 million US citizens gets sick, 128 000 are hospitalized, and 3000 die from foodborne diseases. They report that almost 60% of domestically acquired foodborne illnesses were caused by norovirus, as compared to the other four of the top 5 pathogens of concern. This resulted in an estimated 5.5 million illnesses, of which nearly 15,000 infections required hospitalization and 149 died (http://www.cdc.gov/foodborneburden/2011-foodborne-estimates.html).

In the EU, data gathered in 2009 shows that enteric viruses were responsible for more than 1,000 outbreaks (19% of the total of all outbreaks), affecting nearly 9,000 people, with numbers on the increase since 2007 (EFSA 2011).

In the UK, the Food Standards Agency's (FSA) Strategic Plan for 2015-2020 has, as one of its main objectives, "to protect public health from risks which may arise in connection with the consumption of food (including risks caused by the way in which it is produced or supplied) and otherwise to protect the interest of consumers in relation to food. This would include the reduction of foodborne disease to ensure that food is safe." The Strategic plan has resulted in the FSA's commitment to gaining a better knowledge of the threat posed by foodborne viruses, through scientific projects aiming to identify the scale of the threat to the UK population and by identifying potential methods to help the food industry adopt appropriate control measures. The issues surrounding foodborne viruses were considered so serious that, in February 2016, the FSA alongside the European Food Safety Authority (EFSA) held an international workshop on foodborne viruses to identify key research priorities to help the industry, scientists and regulators to understand and manage the risk to consumers and thereby protect public health.

This white paper looks at the viruses concerned, how they get into food, and how we can detect and control them. For more information, contact:

Martin D'Agostino
+44(0)1386 842537
martin.d'agostino@campdenbri.co.uk

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The Viruses: Norovirus, Hepatitis A and Hepatitis E

There are three viruses of primary concern in food safety: Norovirus, Hepatitis A and Hepatitis E. Noroviruses (NoV) are transmitted via the faecal-oral route, and are highly contagious, with the infectious dose thought to be approximately 18 virus particles (Teunis *et al*., 2008). Noroviruses are non-enveloped, about 27 to 32 nm in size, and are single-stranded RNA enclosed in a capsid (outer protein shell), and belong to the *Caliciviridae* family. The incubation period of NoV in humans is around 12-72 hours, often with a rapid onset of symptoms which usually appear 20-30 hours after infection. Symptoms are generally mild, but include projectile vomiting and/or one to several days of diarrhoea; therefore dehydration is the biggest issue related to NoV infection. Once they are ingested they bind to histoblood group antigens in human intestinal epithelial cells, with the site of replication being considered to be the upper intestinal tract (Huang *et al*. 2005). The virus particles then pass through the gastrointestinal tract and are shed in the faeces at an average level of $10^5 – 10^9$/g. Shedding of the virus can last on average between 8 and 60 days (Teunis *et al*., 2015). They can be spread person-to-person and carried on the surfaces of foods. Foods may become contaminated with NoV by a variety of routes, including sewage contaminated irrigation water or wash water, infected handlers hands, or contaminated food preparation surfaces. A number of outbreaks have been reported on cruise ships, due to the isolated and highly populated environment. Care homes and nurseries are often affected also, where the illness may be more severe in the very young or elderly.

Hepatitis A virus (HAV) is a single-stranded, positive-sense, non-enveloped RNA virus belonging to the *Picornaviridae* family and is approximately 27-32 nm in diameter. HAV is usually transmitted via the faecal-oral route, and infection mainly occurs via person-to-person contact. However, as with NoV, it can be transmitted via contaminated foods and water. The incubation period for HAV is between 2 and 6 weeks, and on average around 28 days. Symptoms can include jaundice, fever, headaches and vomiting. The virus can be shed in large numbers - 10^6-10^8 viruses/g faeces from the final 2 weeks of the incubation period up to 5 weeks into the symptomatic phase. Some HAV infections occur without symptoms (asymptomatic), meaning the virus may be spread by otherwise healthy individuals.

Hepatitis E viruses (HEV) are non-enveloped single-stranded RNA viruses and are approximately 27 to 34 nm in diameter. HEV belongs to the *Hepeviridae* family. HEV infection has generally been thought of as being a travel related disease; however, reports have shown that there is a large increase in non-travel related hepatitis E cases, with hepatitis E recently having emerged as the most common cause of acute viral hepatitis in England and Wales. (Ijaz *et al*., 2014; PHE, 2015). Symptoms are similar to that of HAV, with an incubation period of 3-8 weeks with an average of about 40 days. Unlike genotypes 1 and 2, which are mainly spread by contaminated water in underdeveloped countries via the faecal-oral route and person to person, genotypes 3 and 4 are not spread person-to-person, but are considered to be zoonotic and can be foodborne with HEV RNA having been found in pork, dear and boar meat.

Contamination of foods

The foodstuffs mainly at risk from contamination with NoV, HAV and HEV are those which are either lightly processed or those which are eaten raw, and ready-to-eat foods. For NoV and HAV these foods mainly include salad vegetables, soft berry fruits and shellfish (bivalve molluscs). Salad vegetables and soft berry fruits can be at risk from contamination due to sewage contaminated irrigation water and washing water or by being handled by infected humans, whilst shellfish are at risk of contamination via sewage entering the waters in which they are grown. The risk, however, is not just limited to the primary production sites of these foods. Contamination could potentially occur anywhere along the

supply chain. As mentioned previously, workers who are ill or who have been ill may be shedding the viruses at very high levels for a number of days or possibly weeks, and the virus particles may then spread from these infected individuals to food surfaces and food contact surfaces, thereby introducing a secondary source of contamination. It is known that HEV is endemic in the UK pig population (as is also the case in some other European countries) and a recent small-scale study performed by the Animal and Plant Health Agency (APHA) suggested that 10% of retail UK pork sausages contained Hepatitis E virus (Berto *et al.* 2012), although it should be noted that this was not representative of the UK market and should be interpreted only as an indication of prevalence.

Epidemiological studies have also backed up the association between consumption of undercooked pork products and Hepatitis E cases (Said *et al*. 2013). As a consequence, Hepatitis E has emerged as a foodborne risk in the pork supply chain. These findings highlight that HEV contamination within the pork supply chain needs to be investigated further. Unsurprisingly, Government, consumers, the media and the pig industry have shown an increased interest in this virus. As a consequence of this increased awareness, the FSA has a focus on identifying an infectivity assay which is suitable for differentiating between infectious and non-infectious HEV in foods.

Detection of viruses in foods.

If foods do become contaminated with viruses, there are several challenges involved with their detection. This is mainly due to the fact that viruses do not multiply in or on foods, they can often be present in very low numbers and they cannot readily be cultured. This means that the viruses have to be extracted directly from the foodstuffs, followed by sensitive molecular detection techniques - a much more involved process than the traditional culture based detection of bacterial contaminants. In addition, because it is the viral nucleic acid which is being detected, the issue of whether or not the virus is infective or not is a major issue. At the moment, none of the viruses can be grown in culture routinely, hampering the development of effective control measures and assessing its potential infectivity. If, however, one of the viruses is detected in a foodstuff it can indicate that somewhere along the food production process, a procedural or physical control may have failed. There is an ISO Technical Standard (ISO15216 1/2) which can be followed to detect NoV and HAV in certain foods. In the case of HEV, it is not necessarily just the surface of the product which may be contaminated. In such cases, a different extraction procedure is required and as yet there is no standard method available for its detection; however, some laboratories perform their own in-house methods to detect HEV.

How can we control these viruses?

Inadequate controls can pose a real risk when it comes to viral contamination of foods, but this is where things can get difficult. Importation of fresh or frozen products from countries where control measures may not be as strict as other countries, and the lack of traceability to the source of the foods (such as bags of mixed frozen berries) can make the task of sourcing the origin of contamination very difficult. Although viruses cannot multiply on foods, they can persist for long periods on the surfaces of foods. Due to the lack of effective, validated risk management strategies to eliminate viral contamination in bivalve molluscs and fresh produce prior to consumption without changing the characteristics of the food, prevention should be focussed primarily at the pre-harvest level (e.g. bivalve molluscs, raw fresh produce), at the harvest level (fresh fruits and salad vegetables) and at the post-harvest level for other foods (such as prepared, ready-to-eat foods). This can be done by means

of both physical and procedural controls, e.g. following good hygienic practices and virus-specific recommendations and guidelines. For further information on specific guidelines and standards, see the Codex Alimentarius Commission Guidelines on the Application of General Principles of Food Hygiene to the Control of Viruses in Food (CAC/GL 79-2012).

Work being carried out at Campden BRI

Although there are no readily available culturing systems available for human norovirus, hepatitis A virus or hepatitis E virus, the use of culturable surrogate viruses (those which are reported to be closely related to the target viruses) can provide a way of providing information on the effect of control measures, such as differing pH, A_w, and disinfectant parameters. A member funded research project is investigating the efficacy of these control measures along with potential virucidal treatments such as fogging, pulsed light, pressure and heat, using bacteriophage and a culturable norovirus (murine norovirus). We can also carry out analysis of soft berry fruit and salad leaves for the detection of norovirus and hepatitis A with a programme of work in place to gain UKAS accreditation for this.

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Contact:

Martin D’Agostino
+44(0)1386 842537
martin.d’agostino@campdenbri.co.uk