HEPATITIS A VIRUS

THE ORGANISM/TOXIN

- Hepatitis A virus (HAV) is a small, single-stranded RNA virus belonging to the *Picornaviridae* family and the only member of the genus *Hepatovirus* (1, 2, 3).
- There is a single HAV serotype and multiple genotypes. Genotypes I, II and III, further divided into subtypes A and B, infect humans. HAV subtypes are further divided into clusters or strains which have been associated with particular risk factors (2, 3, 4, 5, 6).
- HAV is the main cause of acute self-limiting hepatitis in humans worldwide. The virus is primarily transmitted by the faecal/oral route following exposure to infected people, or via contact with HAV-contaminated food, water, or surfaces (2, 3).

GROWTH AND ITS CONTROL

Growth:

- HAV cannot grow in food, water or the environment. Wild -type strains grow poorly in cell culture however, cell culture-adapted strains can be cultured easily and used for survival and inactivation studies (7).

Survival:

Temperature	• HAV is stable in the environment and can persist for prolonged periods (weeks or months) under normal, domestic food storage conditions (8, 9). • The virus remains intact and infectious for several years under freezing conditions (8, 10). HAV can survive for 90 days at -20°C on blueberries, raspberries, strawberries, basil and parsley (11). • HAV is stable under storage at 4°C in shellfish and produce with only 1.7 $\log_{10}$ reduction after 4 weeks (12) and 2 $\log_{10}$ reduction after 9 days respectively (13).
Drying	• The half-life of HAV ranges from more than 7 days at low humidity (25%) (5°C) to 2 hours at high humidity (95%) (35°C), demonstrating a greater resistance to inactivation at low humidity and temperatures (14).
pH	• Stable at acid pH. In tissue culture experiments, HAV remained infectious for up to 5 hours at pH 1.0 (25°C) (15). • Acidic fruits have been associated with HAV outbreaks due to the acid-resistance of this virus (10).

Inactivation:

Temperature	• The Ministry for Primary Industries and Food Standards Australia New Zealand recommend cooking food to 85°C for 1 minute to inactivate HAV (16). • The extent of virus inactivation is influenced by the food matrix. For example, complete inactivation of HAV has been observed in shellfish when heating to 85°C for 3 minutes (16, 17) however, heat stability is increased in foods (eg dairy) with a higher fat content. Heating cream or milk to 85°C for 30 seconds is sufficient to cause only a 5 $\log_{10}$ reduction in HAV titre (9, 16, 18). • HAV reduced by 6 $\log_{10}$ in natural berries after 4-6 minutes at 75°C. Addition of increasing concentrations of sucrose extended the time taken to achieve a similar reduction in virus titre (16).
***D* values**	• **A literature review suggests the following time/temperature (ºC/minutes) in "shellfish": D_{50} 54.2; D_{56} 9.3; D_{60} 3.3-6.5, "meat": D_{50} 42.1; D_{56} 20.6; D_{60} 5.9 and "spinach": D_{50} 34.4; D_{56} 8.4; D_{60} 4.6** (19).
Sanitisers /disinfectants	• Commercial disinfectants used in the food industry containing 2% glutaraldehyde, 0.4% quaternary ammonium compound and 6% sodium hypochlorite reduced virus particles on stainless steel by more than 4 $\log_{10}$ after one minute of contact time. Sodium hypochlorite at 3,000 ppm (5 minutes contact time at 22°C) reduced HAV on surfaces by > 5$\log_{10}$ (8). • Many chemical disinfectants used in institutional and domestic environments, including ethanol, chloroform, Freon, Arklone and perchloracetic acid, do not effectively inactivate the virus on hands or surfaces (8). • Chlorine disinfection of ready-to-eat (RTE) food reduced HAV on fresh produce including strawberries, cherry tomatoes and head lettuce (1.7 to 2.4 log reduction when exposed to 20 ppm solution of free chlorine for 5-10 minutes) (20).
Radiation	• Extremely resistant to ionising radiation compared with bacteria. • Nearly 3 kGy of gamma irradiation produced a 1 $\log_{10}$ reduction of HAV on lettuce and strawberries (21) and 3 kGy dose reduced HAV by less than 2 $\log_{10}$ in oysters and clams (10, 22).
Preservatives and other non-thermal processing technologies	• High pressure processing (350 MPa, 21ºC, 5 minutes) reduced HAV load in pureed strawberries and green onions by 4 $\log_{10}$ and in Mediterranean mussels (400 MPa, room temperature, 5 minutes) by 2.9 $\log_{10}$ (18, 23). • Modified atmosphere packaging is not a suitable strategy for reduction of HAV on food (10).

THE ILLNESS

Incubation: Range 10-50 days (average 28) (3, 8).

Symptoms:

- Most HAV infections are mild and self-limiting lasting up to two months. Many infections, particularly in children, are asymptomatic.
- When disease is evident, HAV usually presents as four classical phases: 1) hepatocyte viral replication in the absence of symptoms; 2) anorexia, nausea, vomiting,

headache, alterations in taste, abdominal discomfort and fatigue lasting 5 to 7 days; 3) darkening of the urine, light-coloured stools, jaundice and right upper quadrant pain with enlargement of the liver, jaundice and liver enzyme elevation. Faecal shedding and viraemia are maximal during this stage which occurs in fewer than 10% of children under 6, 40-50% of older children and 70-80% of adults; 4) symptoms resolve and liver enzymes return to normal (3, 8).

Condition: Hepatitis A

At Risk Groups:

- All age groups. The disease is milder in children under 6, compared to older children and adults. Complications are more likely to occur in older and immunocompromised people (8).
- In developing/endemic countries, primary infection at a young age confers life-long immunity, hence outbreaks are unusual. In developed countries, HAV infections are less common, due to increased standards of living, but the majority of adults remain susceptible to infection leading to the occurrence of outbreaks amongst the general population (2, 3, 24)..
- Risk factors include consumption of contaminated RTE food and/or water, travel to HAV- endemic areas and contact with infected persons. Increased risk is linked with exposure to blood or blood products (for example, injection-drug use) (2).

Long-term effects:

- Long or recurring illness, lasting up to 6 months, can occur in approximately 3-20% of clinical cases (8).
- Extra-hepatic disorders rarely occur but may include haemolysis, acute renal failure, reactive arthritis, pancreatitis, fulminant hepatitis and neurological syndromes (8, 25).

Dose: Highly infectious. As few as 10-100 virus particles appear to be able to cause disease (26).

Incidence:

- New Zealand incidence rate of 0.7/100,000 (2016). Notifications for HAV have remained relatively stable at 0.6-2.1 during the last 10 years. There have been fluctuations due to outbreaks in 2008, 2012 and 2013 (27). Updates can be found on the ESR website *https://surv.esr.cri.nz/surveillance/annual_surveillance.php*
- New Zealand incidence rates are slightly lower than the EU (2.6/100,000 (2010)) (28), slightly higher than the USA (0.43/100,000 (2015)) (29) and similar to Australia (1/100,000 (2014)) (30).

Treatment:

- Treatment rarely required. Supportive care with treatment for specific complications as appropriate (31).

Prevention and control strategies:

- Most effective way to prevent HAV infection is to improve sanitation, food safety and immunisation practices (3, 31).
- HAV is a vaccine-preventable disease (inactivated HAV vaccines are approved for use in New Zealand although are not routinely recommended for children). The vaccine is recommended for certain at-risk groups including transplant patients, people with chronic liver disease, close contacts of hepatitis A cases, travellers, health care workers and food handlers when situations warrant it (3, 31, 32, 33).
- Post-exposure prophylaxis (within 2 weeks) and prophylactic administration of human immunoglobulins may be recommended for short-term protection against HAV for certain groups including day-care centre, military and food industry staff (31, 33, 34).

SOURCES

Human:

- Humans are the major reservoir of natural HAV infection (3).

Animal:

- No animal vectors. Chimpanzees and several small, non-human primates are also susceptible to HAV but the disease is milder (3).

Food:

- Contaminated shellfish, salads, fruits and vegetables and any manually-prepared RTE foods (2).
- Poor hygiene practices, poor sanitation and contamination of fresh produce, with e.g. HAV-contaminated irrigation water during production, are major risk factors for the transmission of HAV to humans (2).

Environment/Water:

- HAV can survive, but not multiply, in the environment. Many factors will influence virus stability including relative humidity, temperature, type of suspending medium and type of surface contaminated (8).
- Survival of HAV in environmental sources (fresh and seawater, wastewater, marine sediments, soils and shellfish) is prolonged (>12 weeks) at 25°C (2, 8).
- Faecal pollution, from infected individuals, can contaminate shellfish beds, recreational, irrigation and drinking water (2).

Transmission Routes:

- Directly, via person-to-person contact, or indirectly via consumption of contaminated food or water or contact with fomites (2, 8).
- On rare occasions, HAV may also be transmitted via blood transfusion or blood products originating from infected donors (35).

OUTBREAKS AND INCIDENTS

Outbreaks:

New Zealand

- Since 2008, the number of outbreaks of HAV has ranged from 0 to 5. The number of associated cases has ranged from 2 to 54.
- The number of foodborne outbreaks has remained at 1 or less for the past 10 years (36).
- The remainder of the annual outbreaks/cases may be sporadic or can be attributed to other sources including person-to-person and travel (36).

New Zealand

Notable foodborne outbreaks in recent years are included below (36).

Year	Foodborne outbreaks (cases)	Suspected foods
2008	1 (2)	No identifiable source
2009	0 (0)	N/A
2010	1 (3)	No identifiable source
2011	0 (0)	N/A
2012	0 (0)	N/A
2013	0 (0)	N/A
2014	0 (0)	N/A
2015	1 (7)	Fruit (imported frozen, mixed berries)

Worldwide

Notable foodborne outbreaks in recent years are included below.

Year	Cases (deaths)	Suspected foods	Country	Control measure failure
2004	269	Raw beef	Belgium	HAV-infected food handler (37).
2009	562	Semi-dried tomatoes	Australian (multistate)	Contamination of raw ingredients and manufacturing environment (38).
2012-2013	107	Strawberries/mango	EU (multistate)	Contaminated Egyptian produce. Cases among EU travellers returning from Egypt associated with exposure to strawberries or mango. Transmission likely to have occurred on hotel premises (39).
2013	165	Frozen pomegranate arils	USA (multistate)	Poor hygiene during food production for exportation the likely cause (40).
2013-2014	1589 (2)	Imported mixed, frozen berries	EU (multistate)	Consumption of various products containing contaminated berries. No point source of contamination identified (41).
2016	143	Frozen strawberries	USA (multistate)	Contaminated produce imported from Egypt (42).

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