

IN BRIEF

INFECTION

Saliva — a new route for enteric viruses

Enteric viruses typically spread via the faecal–oral route of transmission. Now, research highlights a new transmission route: via saliva. Both murine norovirus and rotavirus were shown to infect and replicate in salivary glands, reaching comparable titres to those in the intestine. These enteric viruses were then released into saliva and it was demonstrated in mouse models that suckling infected pups could transmit these viruses from saliva to their mothers' mammary glands via backflow, leading to a rapid increase in maternal milk secretory IgA antibodies. Finally, enteric viruses replicated in salispheres (salivary gland-derived spheroids) and salivary gland cell lines.

ORIGINAL ARTICLE Ghosh, S. et al. Enteric viruses replicate in salivary glands and infect through saliva. *Nature* **607**, 345–350 (2022)

VACCINATION

No increased risk of acute liver injury after COVID-19 vaccination

The risk of acute liver injury (ALI) after COVID-19 vaccination (either the mRNA vaccine BNT162b2 or inactivated vaccine CoronaVac) was assessed in a case series analysis in Hong Kong of >2.3 million recipients of a COVID-19 vaccine who were at risk. The incidence of ALI after COVID-19 vaccination was very low and not increased compared with the non-exposure period; the majority of post-vaccination ALI was mild and self-limiting. The authors concluded that the potential benefits of mass vaccination for COVID-19 outweigh the risks of ALI from vaccination and SARS-CoV-2 infection.

ORIGINAL ARTICLE Wong, C. K. H. et al. Risk of acute liver injury following the mRNA (BNT162b2) and inactivated (CoronaVac) COVID-19 vaccines. *J. Hepatol.* <https://doi.org/10.1016/j.jhep.2022.06.032> (2022)

PAEDIATRICS

Positive phase III results for odevixibat for progressive familial intrahepatic cholestasis

The efficacy of odevixibat (an ileal bile acid transporter inhibitor) was assessed in a 24-week, randomized, placebo-controlled, phase III trial in paediatric patients with progressive familial intrahepatic cholestasis (PFIC). 62 patients with either PFIC1 or PFIC2 were randomly allocated to placebo ($n = 20$), 40 $\mu\text{g}/\text{kg}$ odevixibat daily ($n = 23$) or 120 $\mu\text{g}/\text{kg}$ odevixibat daily ($n = 19$). Compared with placebo, odevixibat significantly reduced pruritus and serum bile acids levels. The drug was generally well tolerated with the most common treatment-emergent adverse event being diarrhoea or frequent bowel movements.

ORIGINAL ARTICLE Thompson, R. J. et al. Odevixibat treatment in progressive familial intrahepatic cholestasis: a randomised, placebo-controlled, phase 3 trial. *Lancet Gastroenterol. Hepatol.* [https://doi.org/10.1016/S2468-1253\(22\)00093-0](https://doi.org/10.1016/S2468-1253(22)00093-0) (2022)

THERAPY

Fazirsiran shows promise for liver disease in AAT

An open-label phase II trial investigated the safety and efficacy of fazirsiran (an RNA interference therapeutic) in patients with liver disease associated with $\alpha 1$ -antitrypsin deficiency (AAT). Adults with the proteinase inhibitor ZZ genotype (who produce a mutant Z-AAT protein that accumulates in hepatocytes) and liver fibrosis received either 100 mg ($n = 4$) or 200 mg ($n = 12$) fazirsiran subcutaneously on day 1 and week 4 and then every 12 weeks. All patients had reduced accumulation of Z-AAT in the liver (median reduction of 83% at week 24 or 48) and in serum, with concurrent improvements in liver enzyme concentrations. Fibrosis regression was observed in 7 of 15 patients and fibrosis progression in 2 of 15 patients.

ORIGINAL ARTICLE Strnad, P. et al. Fazirsiran for liver disease associated with alpha-1 antitrypsin deficiency. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa2205416> (2022)

Journal Club

HEPATITIS



HEPATITIS D VIRUS: MORE ATTENTION NEEDED

A small proportion of patients with chronic hepatitis B virus (HBV) infection, estimated at 12–39 million people worldwide, are coinfecting with hepatitis D virus (HDV). HDV is the least common viral hepatitis, but it causes the most severe form of the disease. Chronic HDV infection progresses rapidly, with up to 80% of patients developing cirrhosis within 5–10 years, and it is associated with a higher risk of hepatocellular carcinoma and mortality than HBV monoinfection. In 1977, Mario Rizzetto and colleagues identified HDV by chance in liver biopsy samples of patients with chronic HBV infection. It was considered a novel agent and was referred to as “delta agent”. Further research characterized this agent as a new virus, hepatitis D, a defective virus that requires the presence of HBV, specifically the hepatitis B surface antigen (HBsAg), to infect humans.

Unlike HBV, there is no specific vaccine for HDV. However, preventing HBV infection also prevents HDV infection. Implementation of HBV vaccination programmes in the 1990s has undoubtedly had an effect on the prevalence of HDV, particularly in young populations.

Despite the 2017 European Association for the Study of the Liver (EASL) recommendations advocating HDV testing in all patients who are HBsAg⁺, HDV is usually underdiagnosed. This shortcoming is due to a lack of awareness, suboptimal screening programmes in individuals who are HBsAg⁺ and limited access to HDV RNA testing in some centres.

Since its identification >40 years ago, no effective treatment has been approved for HDV, with pegylated interferon- α (PEG-IFN α) being used as an off-label medication for this purpose. PEG-IFN α therapy is associated with considerable side effects and several contraindications, and only 25% of patients achieve sustained suppression of HDV replication. Nucleos(t)ide analogues, the drugs used to treat chronic

HBV infection, are ineffective against HDV.

“ identified HDV by chance in liver biopsy samples of patients with chronic HBV infection



Bulevirtide, an HBV entry inhibitor, is a synthetic N-acylated pre-S1 lipopeptide that blocks the sodium–bile acid cotransporter, the receptor responsible for entry of HBV and HDV into hepatocytes. This compound received conditional approval by the European Medicines Agency for the treatment of chronic HDV infection in June 2022, on the basis of the results of phase II studies. Bulevirtide has been evaluated in the real world as monotherapy or combined with interferon in >300 patients with chronic HDV infection, and the results are very similar to those observed in the phase II studies. In addition, other drugs such as lonafarnib, a farnesyltransferase inhibitor, and nucleic acid polymers are under investigation in patients with chronic HDV infection. New treatments can achieve maintained suppression of HDV and, in some cases, even clearance of HBsAg from the circulation, which is considered essential for functional cure of both HBV and HDV and for improving the disease prognosis.

Maria Buti

Liver Unit, Hospital Universitario Valle Hebrón, CIBEREHD del Instituto Carlos III, Barcelona, Spain.
e-mail: mbuti@vhebron.net

Competing interests

The author declares no competing interests.

ORIGINAL ARTICLE Rizzetto, M. et al.

Immunofluorescence detection of new antigen-antibody system (delta/anti-delta) associated to hepatitis B virus in liver and in serum of HBsAg carriers. *Gut* **18**, 997–1003 (1977)

RELATED ARTICLE Urban, S., Neumann-Haefelin, C. & Lampertico, P. Hepatitis D virus in 2021: virology, immunology and new treatment approaches for a difficult-to-treat disease. *Gut* **70**, 1782–1794 (2021)