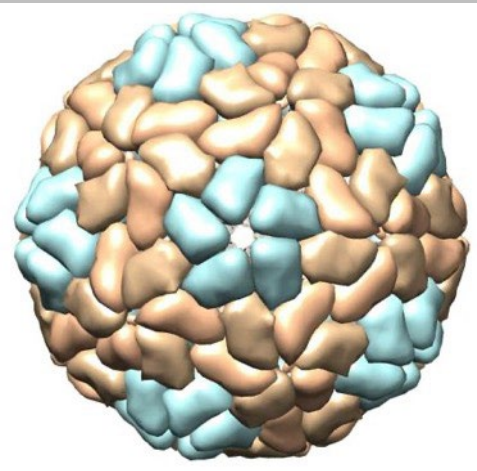# Hepatitis A outbreak in a refugee shelter in Kiel, northern Germany

VHPB Technical Meeting: Addressing Viral Hepatitis Among Europe's Migrant and Refugee Population, Antwerp, Belgium

26 March 2024 – 11:40–12:00

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Historic Milestones HAV

1923   G. Blumer: Study on 63 outbreals of infectious jaundice in the U.S.A (1812–1922)

1973   Electron-optical imaging (NIAID/NIH)
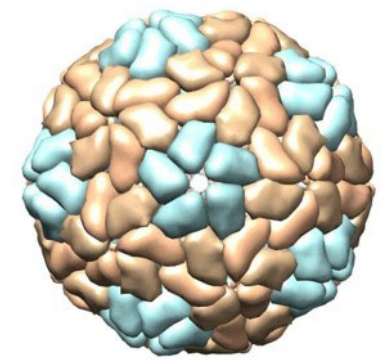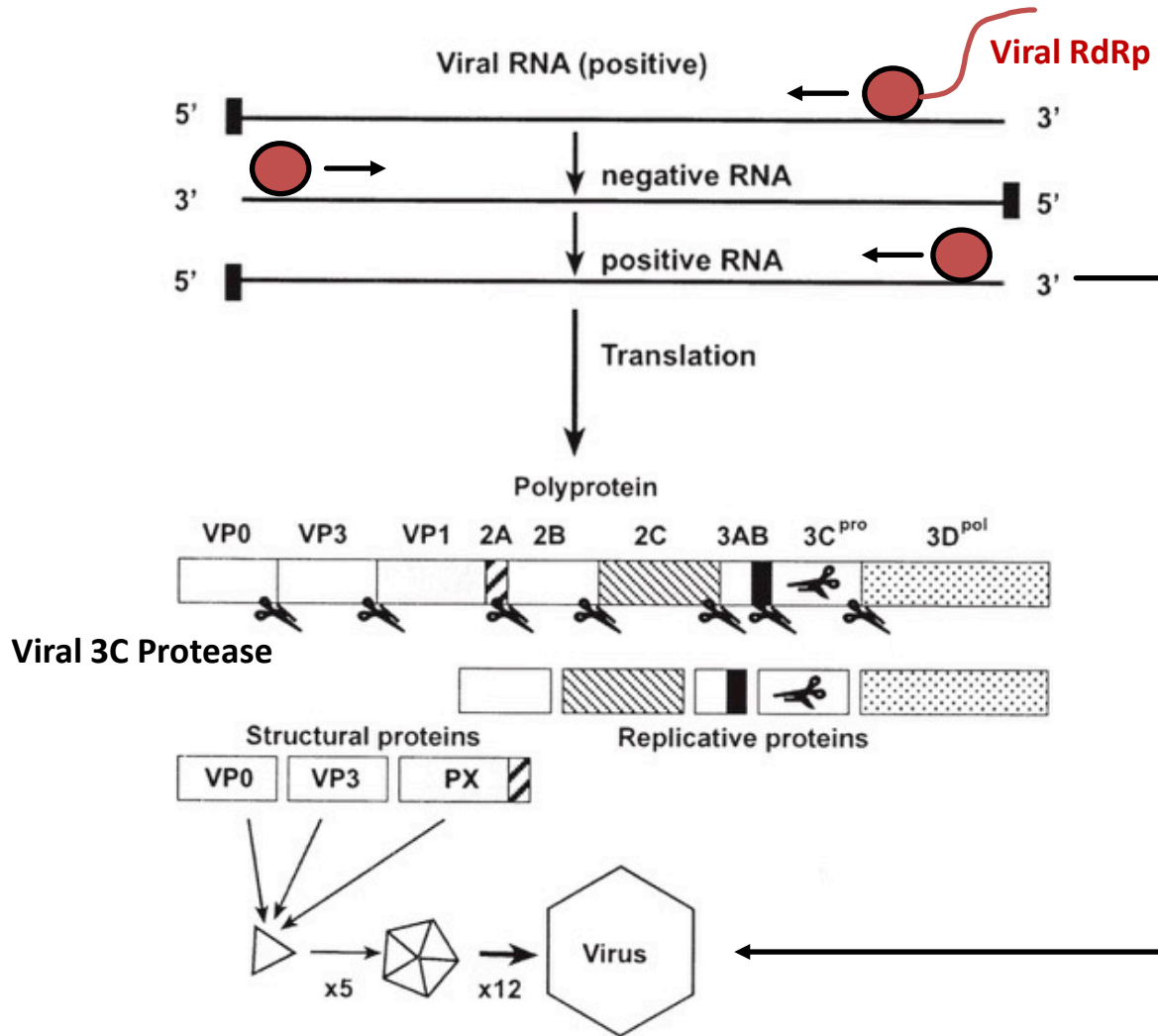
Feinstone et al, Science 1973; 182(116):1026–1028

1979   P. Provost / G. Frösner: HAV-Isolation in cell culture

1996   Inactivated vaccine available

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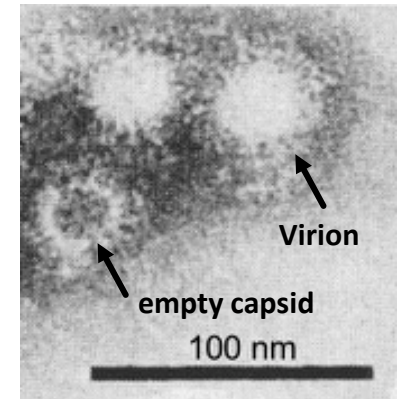**FAKULTÄT FÜR MEDIZIN**

NIAID/NIH, www.niaid.nih.gov

Left to right: **Robert Purcell**, M.D.; **Albert Kapikian**, M.D.; and **Stephen Feinstone**, M.D., first identified hepatitis A virus (HAV) in 1973. Their groundbreaking work led to development of the first licensed HAV vaccine

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Viral RNA (positive)

Viral RdRp

www.rcsb.org/structure/5WTE

Viral 3C Protease

Monomer   Pentamer   HAV-capsid

Virion

empty capsid

100 nm

Feinstone et al, Science 1973

Receptor: TIM-1/TIM-3 or IgA-receptor

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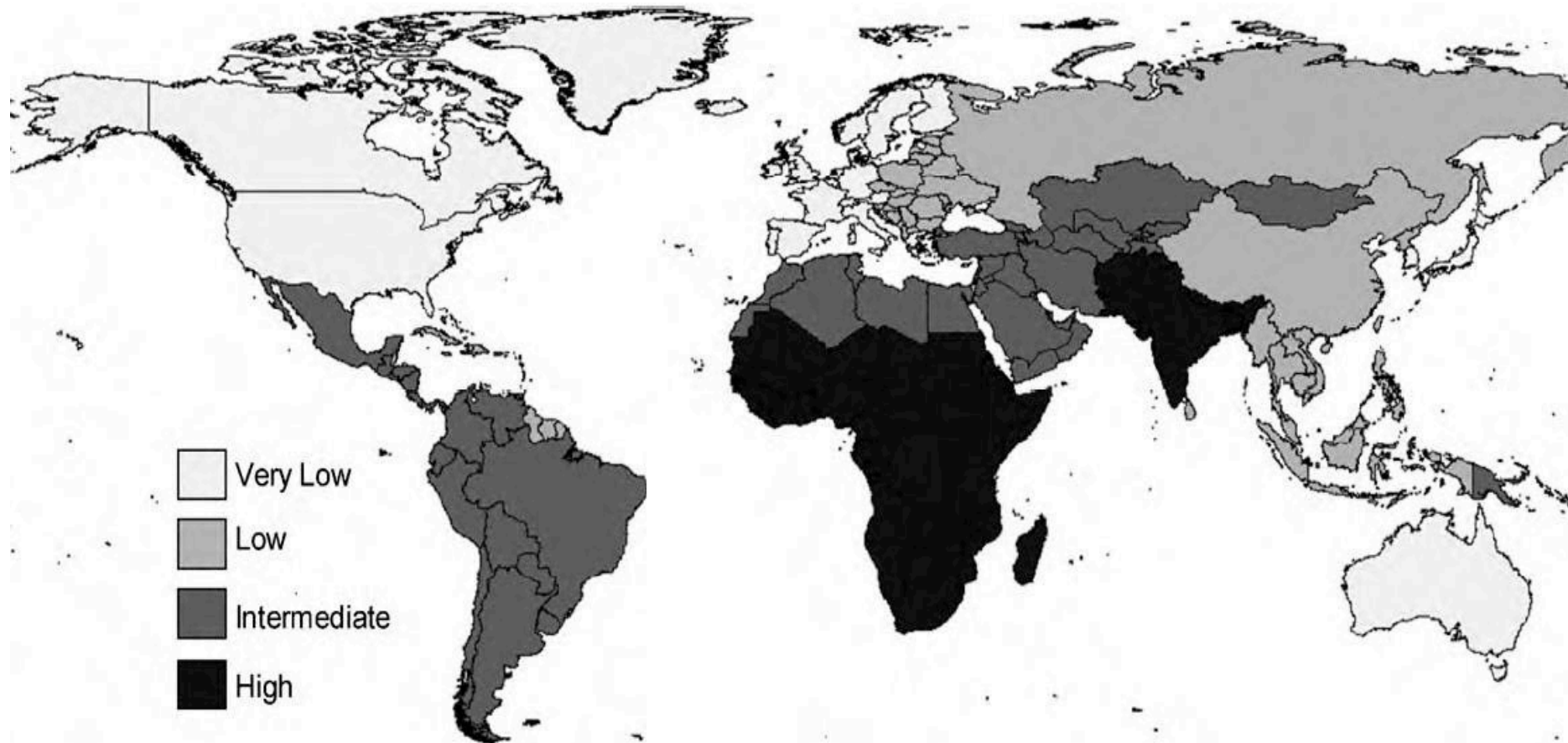**FAKULTÄT FÜR MEDIZIN**

Export of HAV from hepatocytes

1) HAV is exported into the blood via the basolateral membrane of the hepatocytes
2) and probably travels by "transcytosis" to the apical surface and finally into the bile duct
system => stool („faecal-oral-infection route")

**Liver cells are destroyed by cytotoxic CD8+ T lymphocytes, and not by the lytic activity of
the virus**

Anderson, DA & Counihan NA; 2011; ISBN 978-1-55581-463-2

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Hepatitis A prevalence

K.H. Jacobsen, S.T. Wiersma / Vaccine 28 (2010) 6653–6657

HAV sero-prevalence

Figure 70. Plot of Estimated Seroprevalence by Age in North Africa and the Middle East.
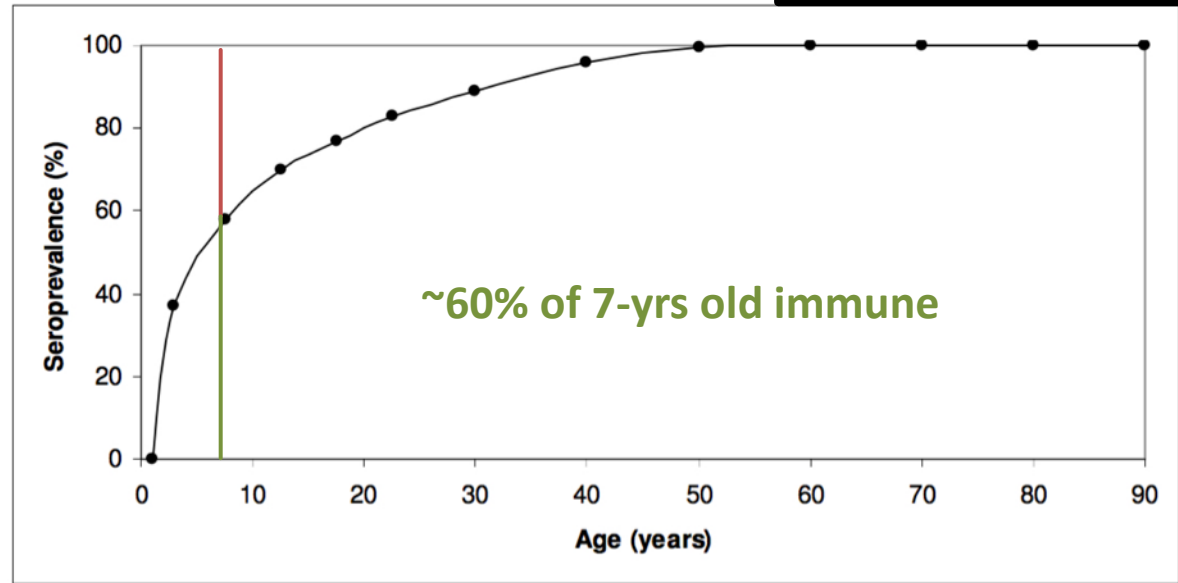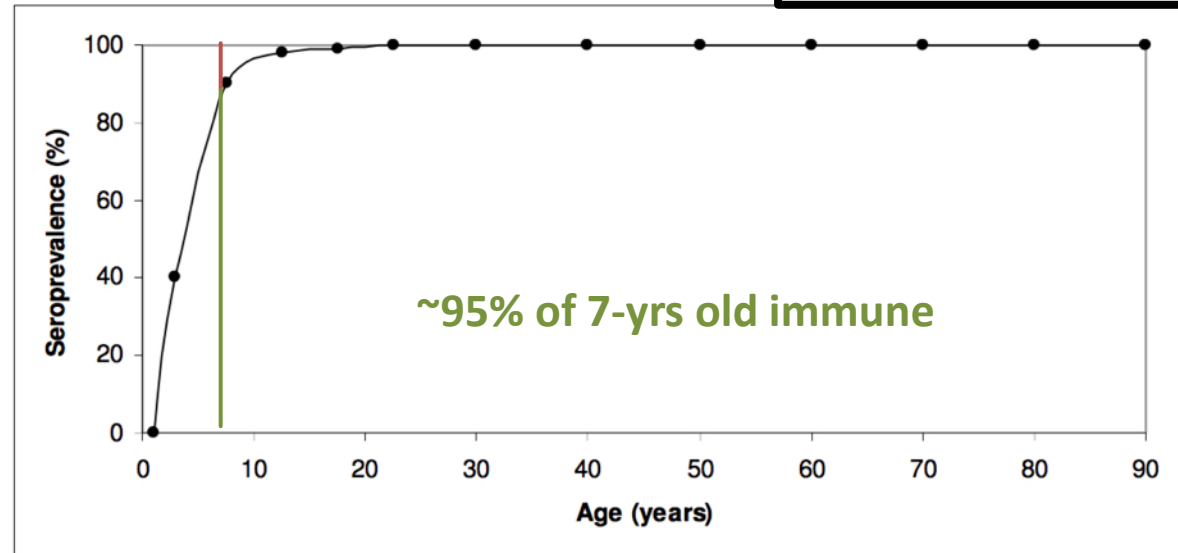
~60% of 7-yrs old immune

Figure 78. Plot of Estimated Seroprevalence by Age in Central sub-Saharan Africa.

~95% of 7-yrs old immune

KH. Jacobsen, S.T. Wiersma / Vaccine 28 (2010) 6653–6657

Very Low
Low
Intermediate
High

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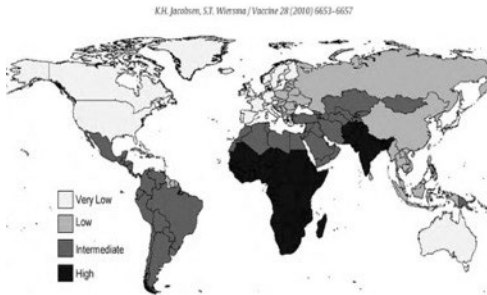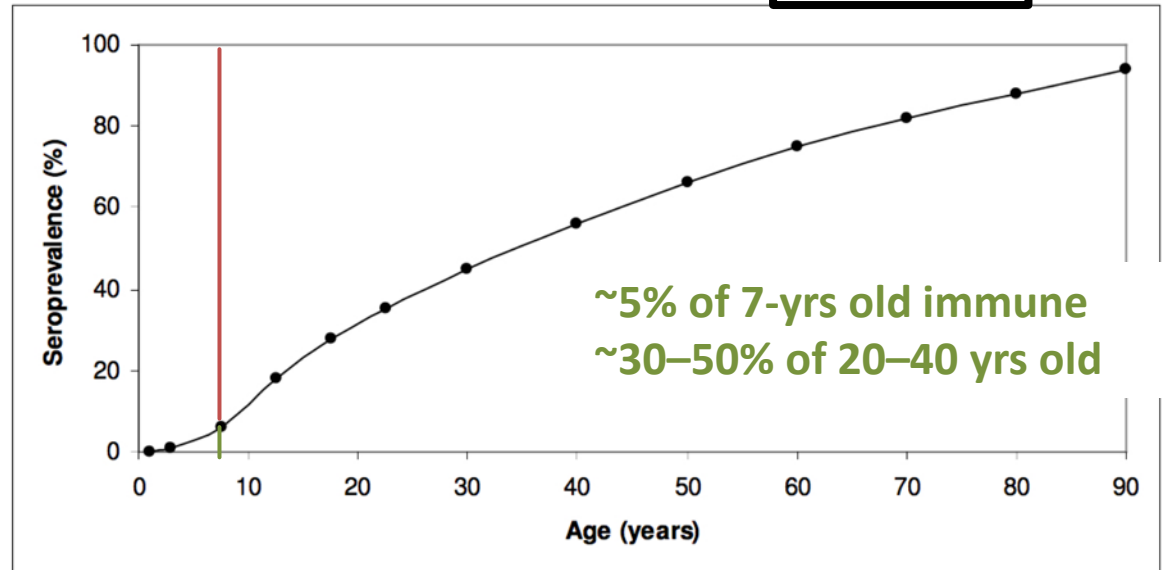
Figure 59. Plot of Estimated Seroprevalence by Age in Western Europe.

~5% of 7-yrs old immune
~30–50% of 20–40 yrs old

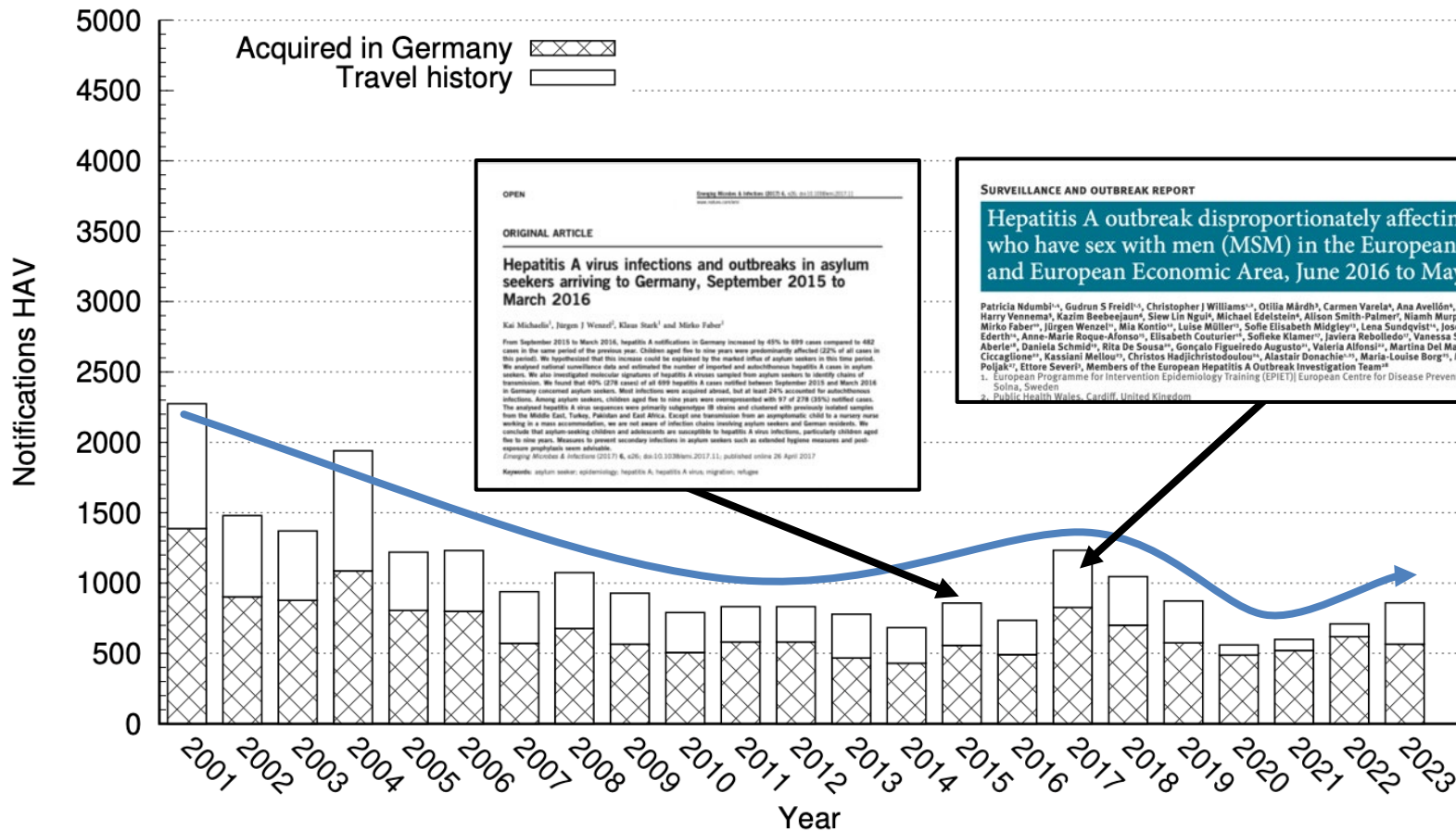*Jacobsen KH. World Health Organization; 2009*

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People greet refugees as they arrive at the main train station in Munich, Germany, 2015

Source: Corbis; http://i.telegraph.co.uk/multimedia/archive/03431/refugee_germany06_3431198b.jpg

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HAV-Notifications, Germany, 2001–2023

Data source: Robert Koch-Institute

Current HAV-"risk factors"
in Western countries

- **Travel** to HAV endemic areas without vaccination (or contact to travellers)

- Contaminated **imported food** (e.g. frozen berries, dates)

- Contaminated food due to **infected food handlers**

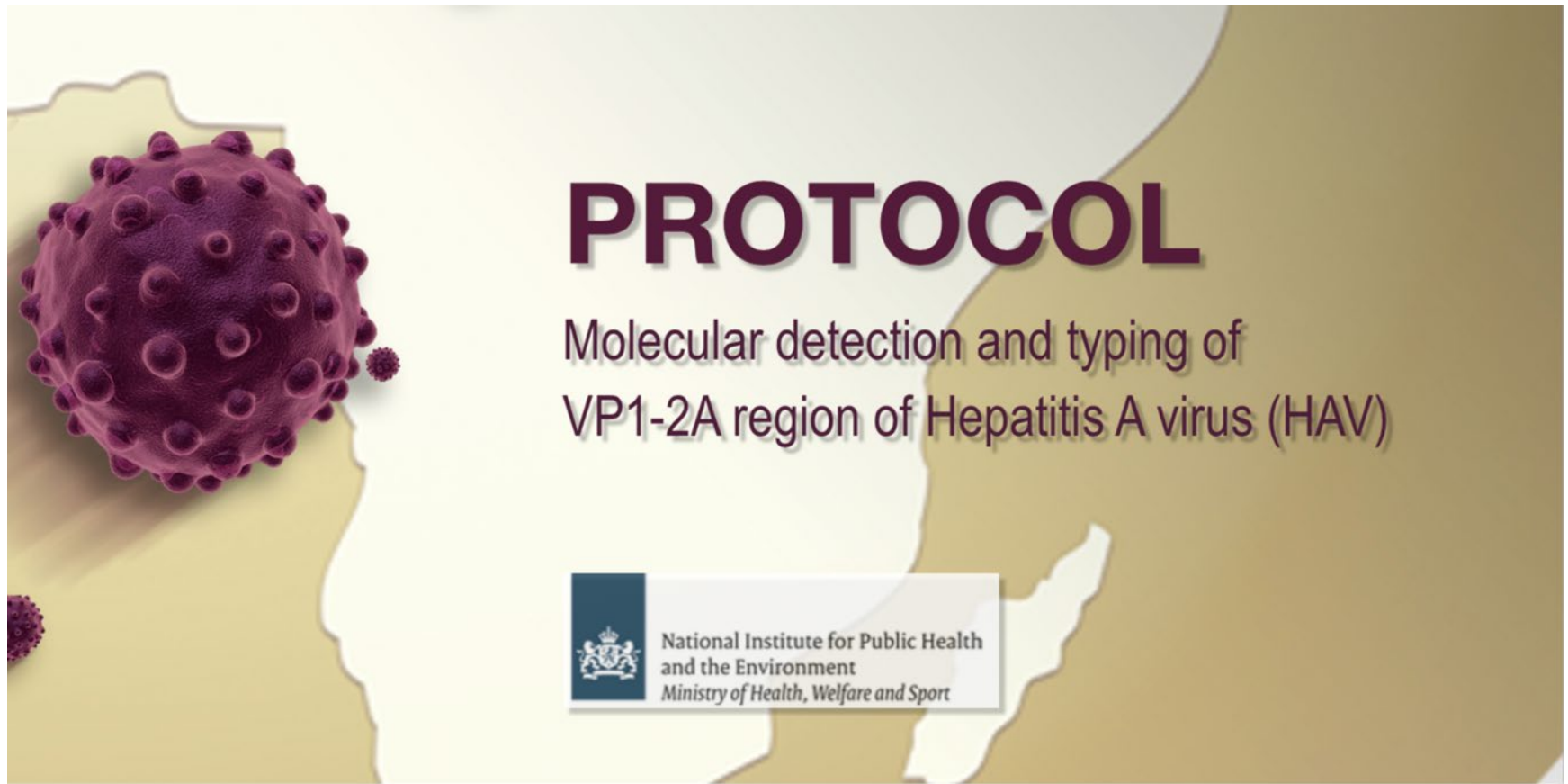- Transmission from **person to person** (e.g. MSM-outbreak 2017)

Amit Bhargava/Associated PressA sewage pipe in Varanasi, India, in 2001 that moves waste to the Ganges River.

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What tools do we have to identify HAV outbreak-strains in the lab?

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HAVnet Typing Protocol

Source: RIVM, http://www.rivm.nl/en/Topics/H/HAVNET

Sequencing of the VP1-2A-region

Unique genetic fingerprints of HAV outbreak-strains

349 nt Gaude etol 1997 (VP1 inner)

460 nt HAVNet

349 nt CDC

VP1-2A

Source: German Consultant Lab for HAV and HEV

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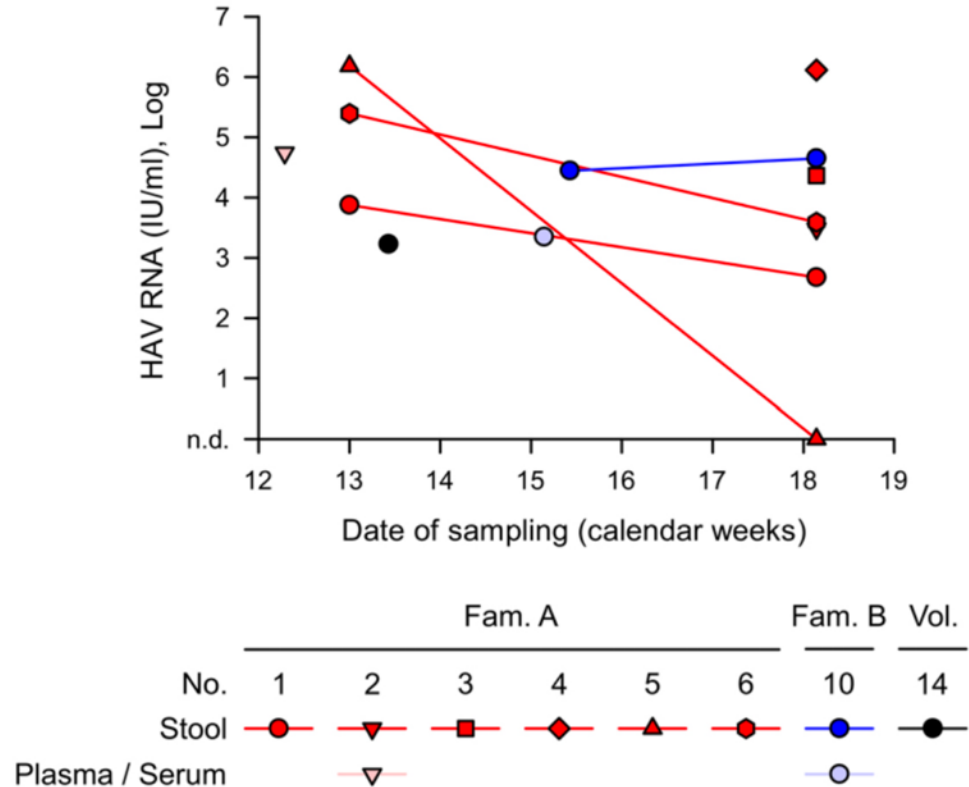# Hepatitis A outbreak in a refugee shelter in Kiel, northern Germany

FIGURE 1 Hepatitis A virus (HAV) ribonucleic acid (RNA) concentration quantified by one-step reverse transcription and quantitative PCR in plasma/serum and stool of affected individuals

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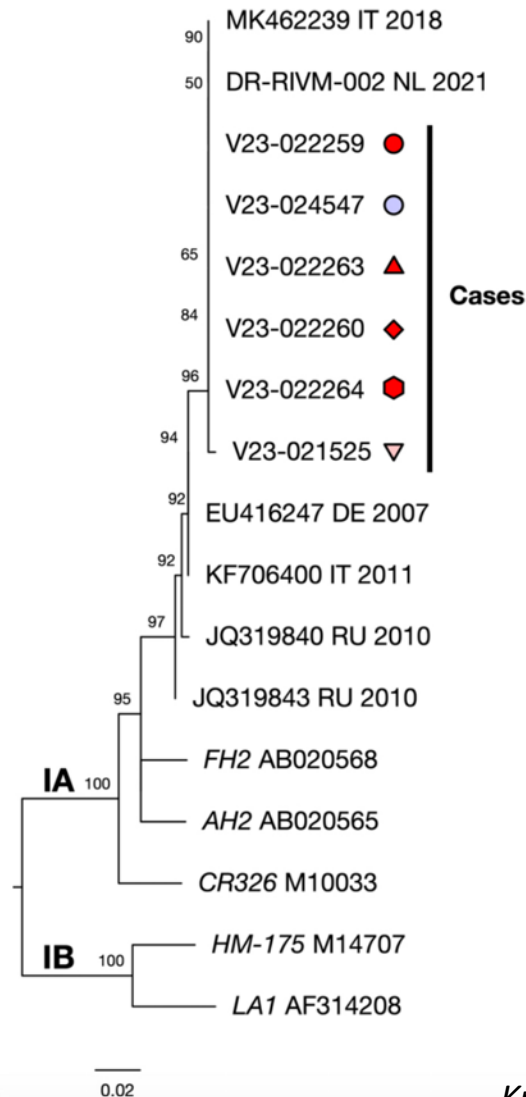# Hepatitis A outbreak in a refugee shelter in Kiel, northern Germany

FIGURE 2 Rooted maximum likelihood phylogenetic consensus tree for viral protein 1 and protease 2A partial nucleotide sequences of hepatitis A virus (HAV) strains, hepatitis A outbreak Kiel, February–May 2023. All sequences of the outbreak-related strains cluster in HAV subgenotype IA. Sequences from five cases are 100% similar to a recent European outbreak sequence (strain HAV/Netherlands/DR-RIVM-002/2021). The sequence of case V23-021525 is 99.7% similar (one nucleotide difference in a 349-nt