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ALDO MORO

**CORSO DI IGIENE**

**Scuola  
di  
Medicina**

**Hepatitis A**



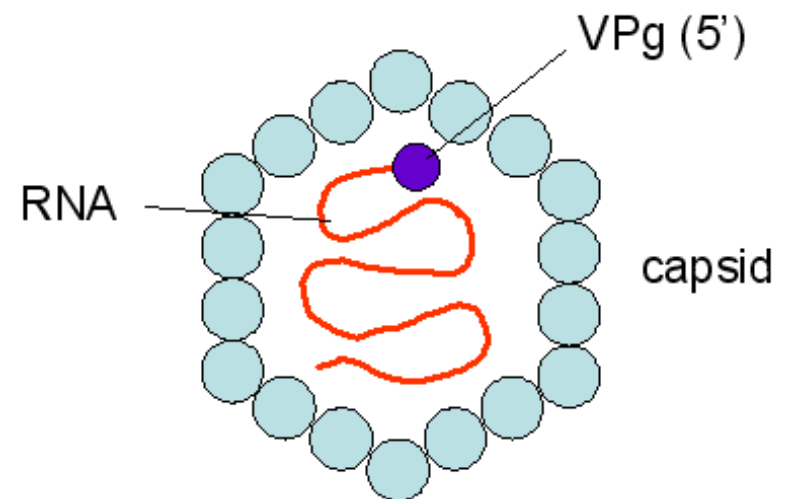
# Hepatitis A

- Epidemic jaundice attributed to Hippocrates
- Differentiated from hepatitis B in 1940s
- Serologic tests developed in 1970s
- Vaccines licensed in 1995 and 1996



# Hepatitis A Virus

- Picornavirus (RNA)
- Humans are only natural host
- Stable at low pH
- Inactivated by temperature of 185°F or higher, formalin, chlorine



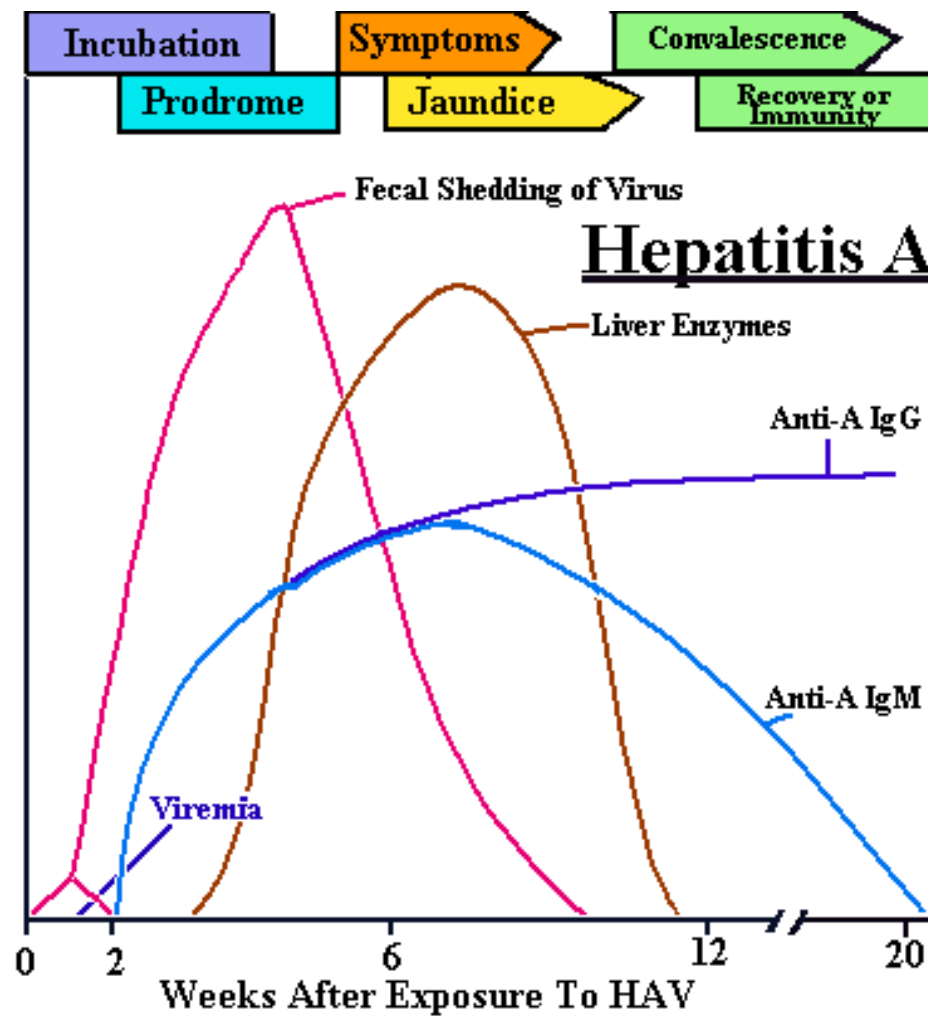


# Hepatitis A Pathogenesis

- Entry into mouth
- Viral replication in the **liver**
- Virus present in **blood** and **feces** 10-12 days after infection
- Virus **excretion** may continue for up to 3 weeks after onset of symptoms



# Hepatitis A Pathogenesis





# Hepatitis A Clinical Features

- **Incubation** period 28 days (range 15-50 days)
- Illness not specific for hepatitis A
- Likelihood of symptomatic illness directly related to age
- **Children generally asymptomatic**, adults symptomatic



# Case Definition

acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis

- fever
- headache
- malaise
- anorexia
- nausea
- vomiting
- diarrhea
- abdominal pain

and either

- Jaundice
- elevated serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels



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# Jaundice







# Complications

- autoimmune hepatitis
- subfulminant hepatitis
- fulminant hepatitis

**case-fatality rate among persons of all ages was approximately 0.3% but may have been higher among older persons (approximately 2% among persons 40 years of age and older)**

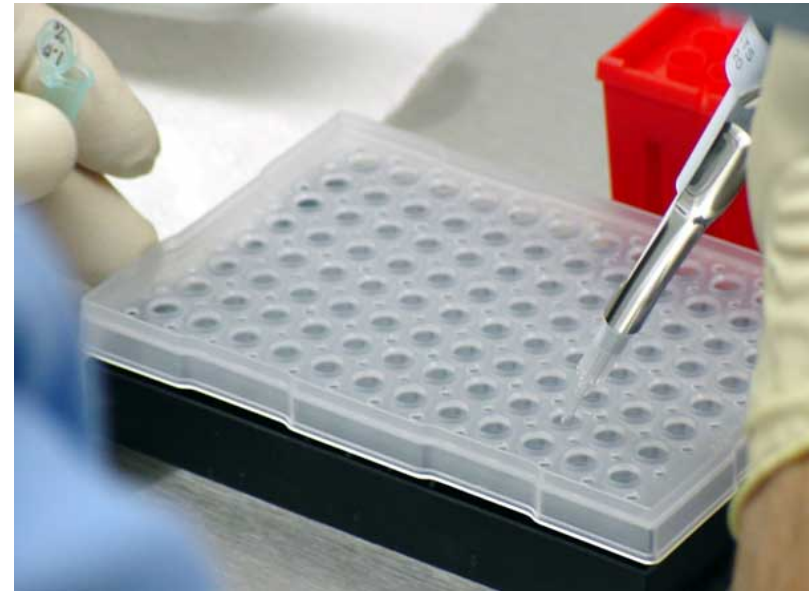


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# Laboratory Diagnosis

- Serologic testing (IgM anti-HAV)
- PCR on stools





# Hepatitis A Epidemiology

- **Reservoir**
  - human
- **Transmission**
  - fecal-oral
- **Temporal pattern**
  - none
- **Communicability**
  - 2 weeks before illness to 1 week after onset of jaundice



# Hepatitis A: source of infection

*Int J Food Microbiol.* 2002 May 5;75(1-2):11-8.

## Detection of hepatitis A virus in mussels from different sources marketed in Puglia region (South Italy).

Chironna M<sup>1</sup>, Germinario C, De Medici D, Fiore A, Di Pasquale S, Quarto M, Barbuti S.

### ⊕ Author information

#### Abstract

Hepatitis A virus (HAV) infection is endemic in Puglia (South Italy). Epidemiological studies have shown that consumption of shellfish, particularly mussels, is a major risk factor for HAV infection, since these products are eaten raw or undercooked. In this study, nested RT-PCR has been shown to be a sensitive technique for the detection of HAV in mussels. To detect the presence of HAV in a large sample of mussels by nested RT-PCR and to compare the results with those obtained by cell culture infection and RT-PCR confirmation. Two hundred and ninety samples of mussels were collected between December 1999 and January 2000. One hundred samples were collected before cooking and 100 were sampled in different seafood markets. HAV-RNA was detected in 20 (20.0%) of samples collected in the shellfish markets, without any positive samples collected in the seafood markets. No relationship between viral contamination and bacterial contamination was found (p > 0.05). The results of this study confirm the use of nested RT-PCR techniques in detecting HAV in shellfish and, thus, for the screening of a large sample of mussels. The results also suggest that decontamination and decontamination methods are needed to obtain virus-safe shellfish and reduce the risk for public health.

PMID: 11999400





# Hepatitis A: source of infection

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Eurosurveillance, Volume 20, Issue 29, 23 July 2015

**Research articles**

**FOOD-BORNE DISEASES ASSOCIATED WITH FROZEN BERRIES CONSUMPTION: A HISTORICAL PERSPECTIVE, EUROPEAN UNION, 1983 TO 2013**

L Tavošchi (Lara.Tavošchi@ecdc.europa.eu)<sup>1</sup>, E Severi<sup>1</sup>, T Niskanen<sup>1</sup>, F Boelaert<sup>2</sup>, V Rizzi<sup>2</sup>, E Liebana<sup>2</sup>, J Gomes Dias<sup>1</sup>, G Nichols<sup>1,3</sup>, J Takkinen<sup>1</sup>, D Coulombier<sup>1</sup>

+ Author affiliations

1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
2. European Food Safety Authority (EFSA), Parma, Italy
3. Current affiliation: Public Health England (PHE), Colindale, London, United Kingdom

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Citation style for this article: Tavošchi L, Severi E, Niskanen T, Boelaert F, Rizzi V, Liebana E, Gomes Dias J, Nichols G, Takkinen J, Coulombier D. Food-borne diseases associated with frozen berries consumption: a historical perspective, European Union, 1983 to 2013. Euro Surveill. 2015;20(29):pii=21193. Article DOI: <http://dx.doi.org/10.2807/1560-7917.ES2015.20.29.21193>

Date of submission: 12 February 2015

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Epidemiological investigations of outbreaks of hepatitis A virus (HAV) and norovirus (NoV) infections in the European Union/European Economic Area (EU/EEA) have identified frozen berries as a vehicle of infection. Given this, we undertook a review of the existing evidence on this product. We searched the literature for outbreak/contamination events associated with frozen berries and evaluated the sources to identify areas of concern (i.e. outbreak, food contamination) in the EU/EEA. The identified pathogens were NoV, HAV and hepatitis E virus (HEV). A total of 27 events with over 15,000 cases reported overlapping sources for the period 2005–2013. Consumption of frozen berries is associated with 62% of the contamination events, particularly after 2005.







# Hepatitis A: source of infection

*Int J Food Microbiol.* 2002 Feb 25;73(1):29-34.

## The survival of hepatitis A virus in fresh

Croci L<sup>1</sup>, De Medici D, Scalfaro C, Fiore A, Toti L.

### ⊕ Author information

#### Abstract

Fresh produce has been repeatedly implicated as the objective of the present study was to evaluate the HAV and the persistence of the HAV. To this end, the authors sterile distilled water supplemented with an HAV suspension, the samples were stored at 4 degrees Celsius and analysed at 0, 2, 4, 7, and 9 days to detect the virus. For each vegetable, 100 g was used, positive samples were subjected to the quantitative determination using cell cultures. The three vegetables differed in terms of their adsorption capacity. The highest quantity of virus was consistently detected for lettuce, for which only a slight decrease was observed over time (HAV titre = 4.44 +/- 0.22 log TCID50/ml at day 0 vs. 2.46 +/- 0.17 log TCID50/ml at day 9, before washing). The virus remained vital through the last day of storage. For the other two vegetables, a greater decrease was observed, and complete inactivation had occurred at day 4 for carrot and at day 7 for fennel. For all three vegetables, washing does not guarantee a substantial reduction in the viral contamination.





## Groups at increased risk for hepatitis A

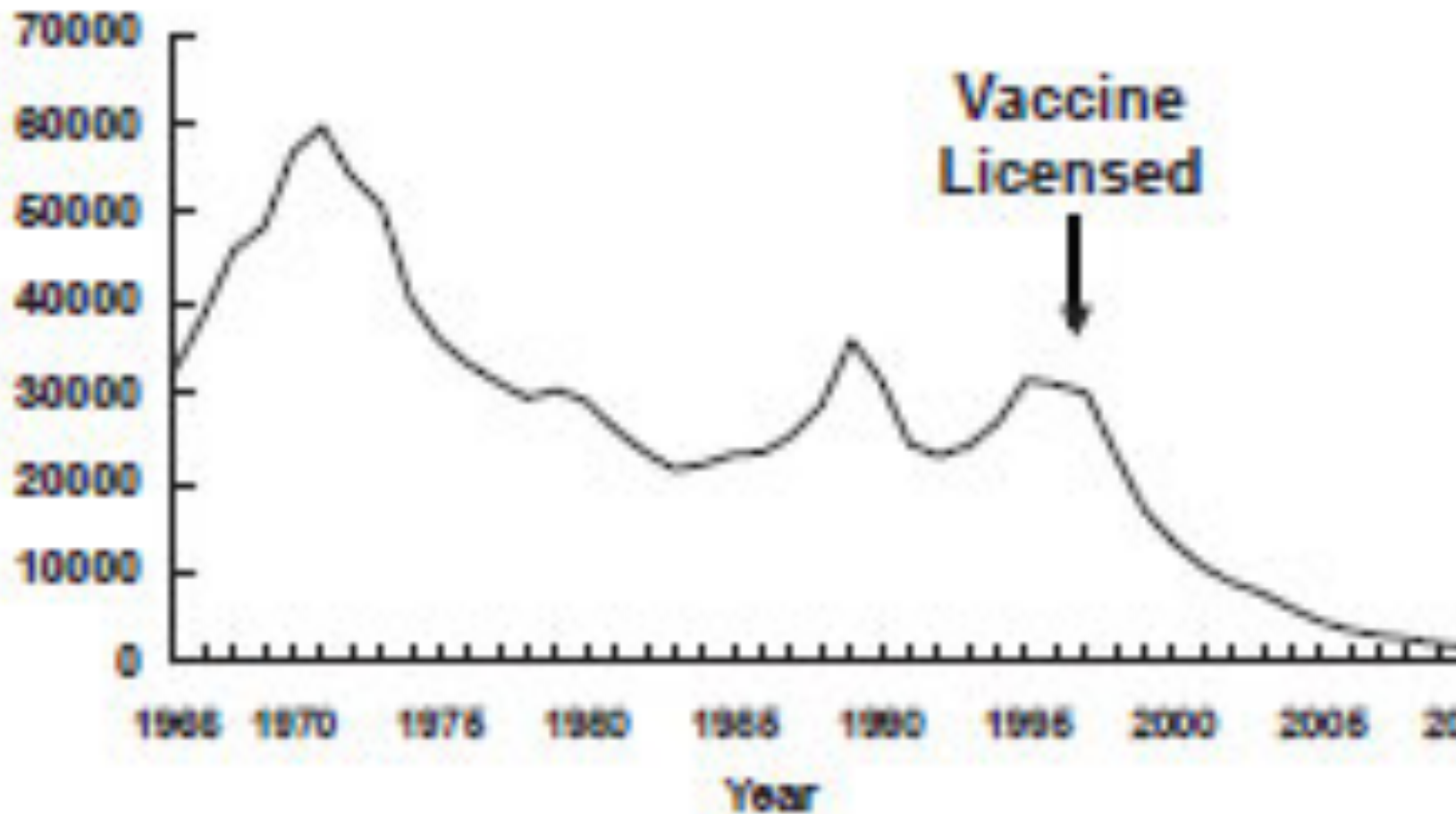
- international travelers
- contacts of recent international adoptees from HAV endemic countries
- men who have sex with men
- users of illegal drugs



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# Hepatitis A — United States, 1966-2011



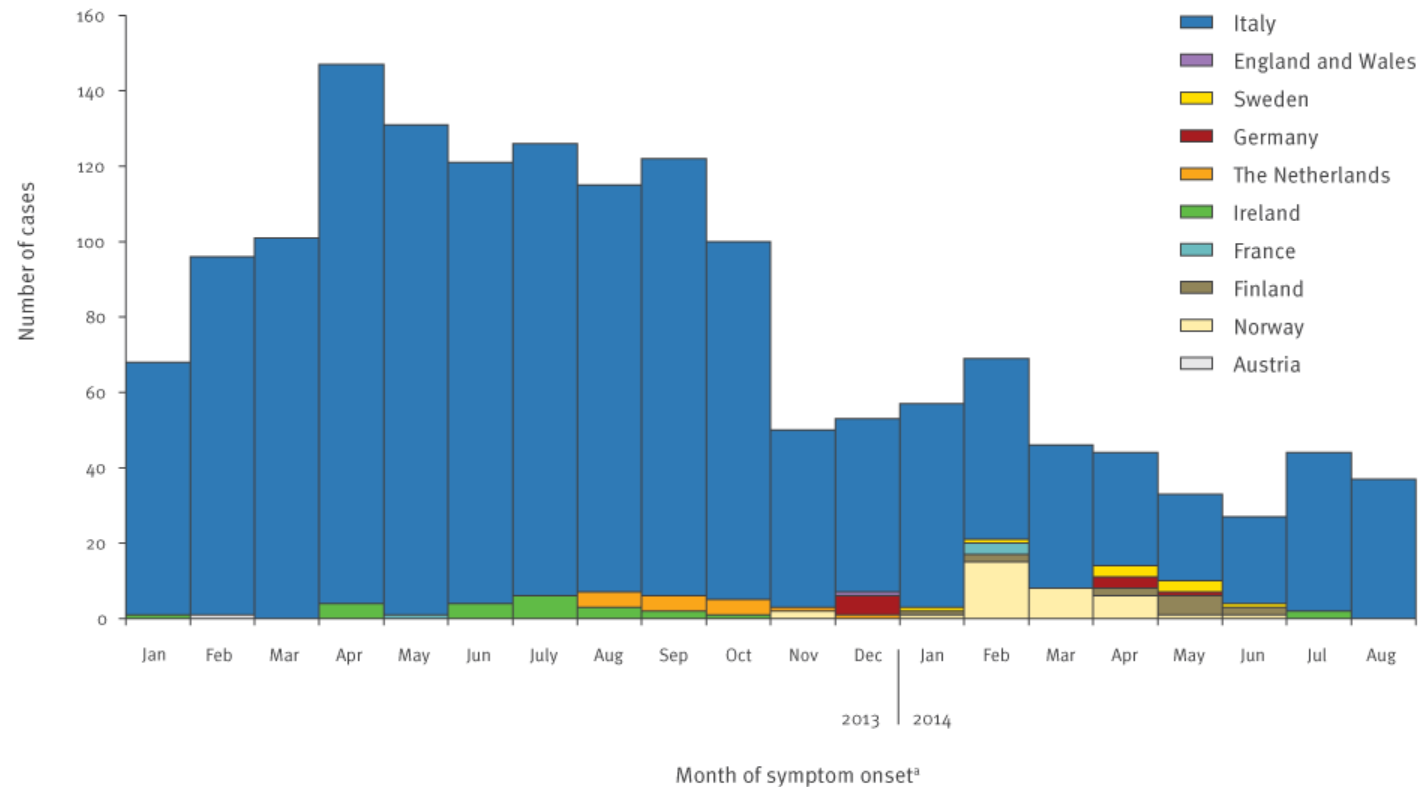




# Hepatitis A — Europe 2013-14

**FIGURE 2**

Hepatitis A cases by probable country of infection and month of symptom onset<sup>a</sup>, European Union/European Economic Area countries, 1 January 2013–31 August 2014 (n = 1,587<sup>b</sup>)



<sup>a</sup> Or month of testing when symptom onset date was unavailable.

<sup>b</sup> Information on month of symptom onset was unavailable for two cases.



# Hepatitis A Vaccines

- Inactivated whole-virus vaccines
- formulations
  - pediatric formulations approved for persons 12 months through 18 years
  - adult formulations approved for persons 19 years and older



# Hepatitis A Vaccine Immunogenicity and efficacy

- **Adults**
  - more than 95% seropositive after one dose
  - nearly 100% seropositive after two doses
- **Children and Adolescents**
  - more than 97% seropositive after one
  - 100% seropositive after 2 doses (in clinical trials)
- Efficacy among adults and children rounded 94-100%



# ACIP Recommendation for Routine Hepatitis A Vaccination of Children

- All children should receive hepatitis A vaccine at **12 through 23 months of age**
- Vaccination should be integrated into the routine childhood vaccination schedule
- Children who are not vaccinated by 2 years of age can be vaccinated at subsequent visits



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# ACIP Recommendation for Routine Hepatitis A Vaccination of Children

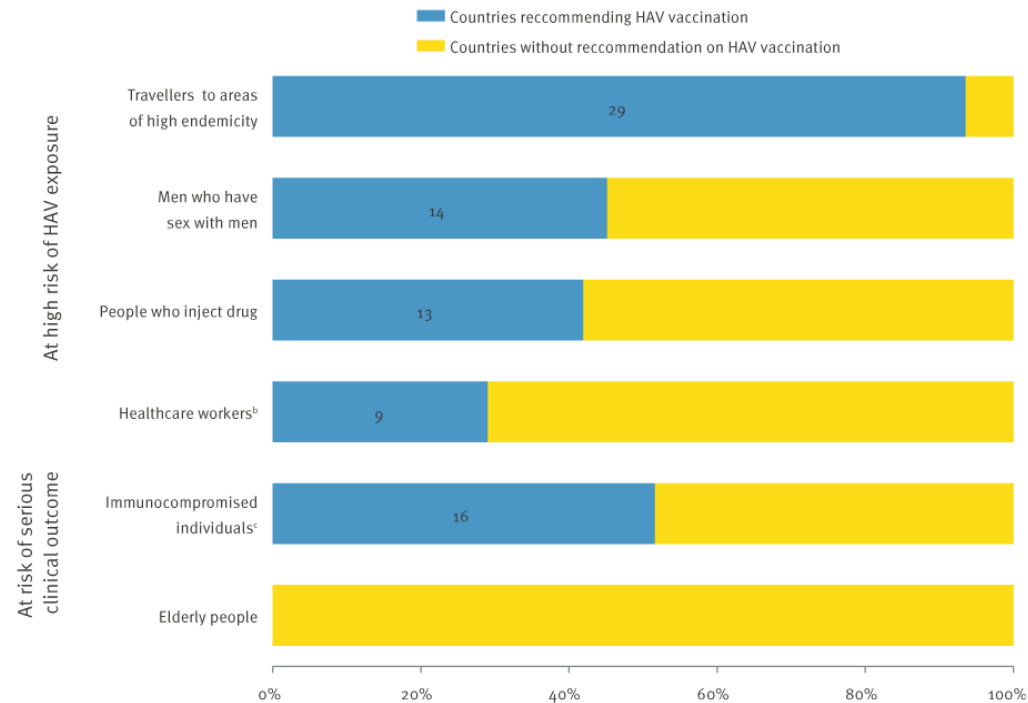
- States, counties, and communities with existing hepatitis A vaccination programs for children 2 through 18 years of age should maintain these programs
- New efforts focused on routine vaccination of children 12 months of age should enhance, not replace ongoing vaccination programs for older children
- In areas with without an existing hepatitis A vaccination program catch-up vaccination of unvaccinated children 2 through 18 years of age can be considered



# EU/EEA countries recommending hepatitis A virus vaccination to groups defined by the WHO as at high risk for exposure or at risk of serious clinical outcome, 2013

**FIGURE 2**

EU/EEA countries recommending hepatitis A virus vaccination to groups defined by the WHO as at high risk for exposure or at risk of serious clinical outcome, 2013 (n = 30<sup>a</sup>)



EEA: European Economic Area; EU: European Union; HAV: hepatitis A virus; HIV: human immunodeficiency virus; WHO: World Health Organization.

<sup>a</sup> Data from Cyprus were not available.

<sup>b</sup> Some countries recommend HAV vaccination only for specific groups of healthcare workers (e.g. laboratory staff).

<sup>c</sup> Countries recommending HAV vaccination to HIV patients and/or chronic liver disease patients have been included in this category.

Source: Epidemic Intelligence Information System for Vaccine Preventable Diseases, websites of National Public Health Institutes and Ministries of Health in the European Union and European Economic Area.



# Twinrix

- Combination hepatitis A vaccine (pediatric dose) and hepatitis B (adult dose)
- Schedules
  - 0, 1, 6 months, or
  - 0, 7, 21 to 30 days and a booster dose 12 months after first dose
- Approved for persons 18 years of age and older



# Hepatitis A Serologic Testing

- Prevaccination
  - not indicated for children
  - may be considered for some adults and older adolescent
- Postvaccination
  - not indicated





# Hepatitis A Vaccine Contraindications and Precautions

- Severe allergic reaction to a vaccine component or following a prior dose
- Moderate or severe acute illness



# Hepatitis A Vaccine Adverse Reactions

- Local reaction
  - 20%-50%
- Systemic reactions (malaise, fatigue)
  - <10%
- No serious adverse reactions reported

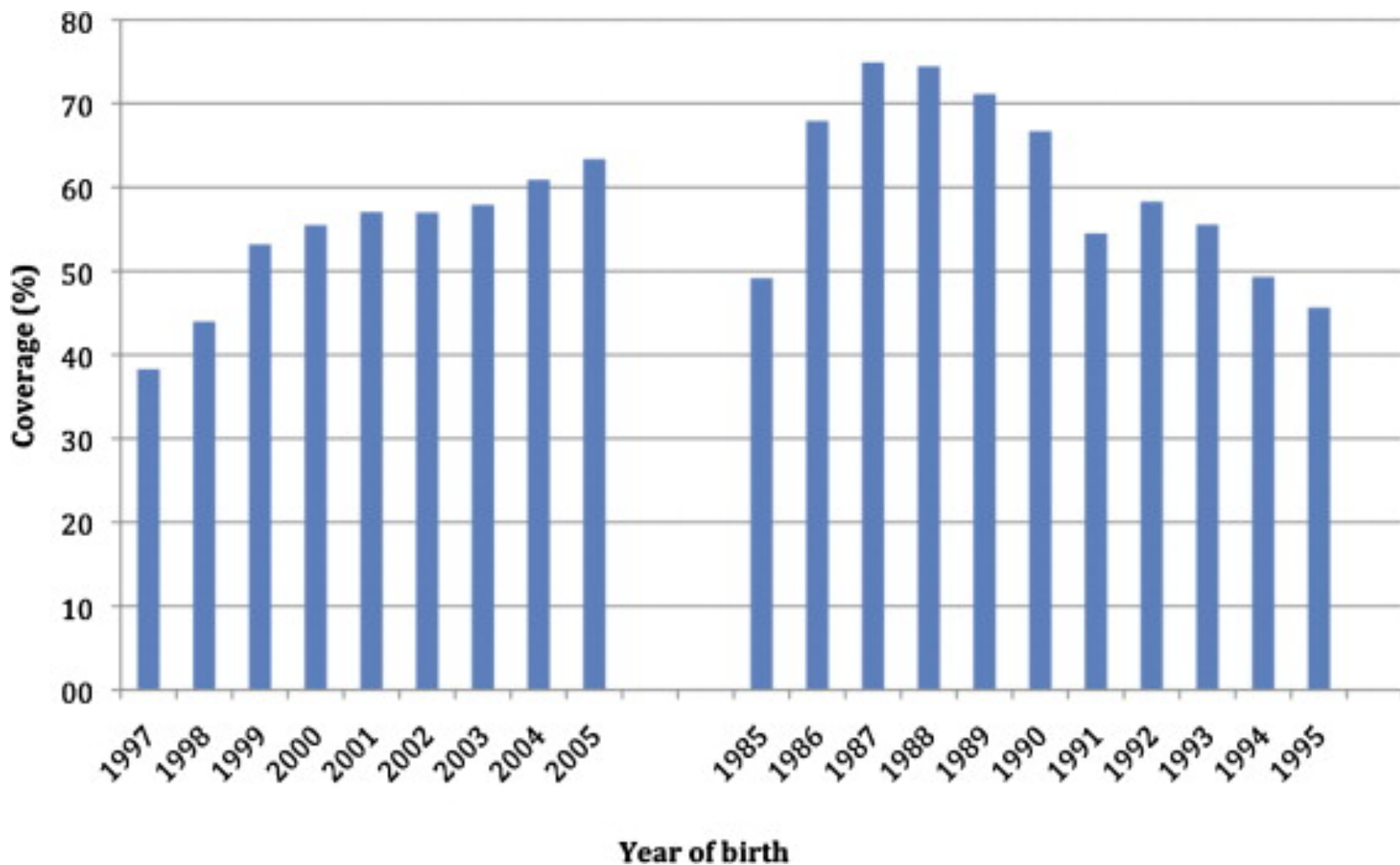


# Postexposure Prophylaxis

- Hepatitis A **vaccine** may be used for postexposure prophylaxis in healthy persons 12 months through 40 years of age
- **Immune globulin** is preferred for persons older than 40 years of age, children younger than 12 months of age, immunocompromised persons, and persons with chronic liver disease.



# Post marketing evaluation of Hepatitis A UVM: the Apulian case

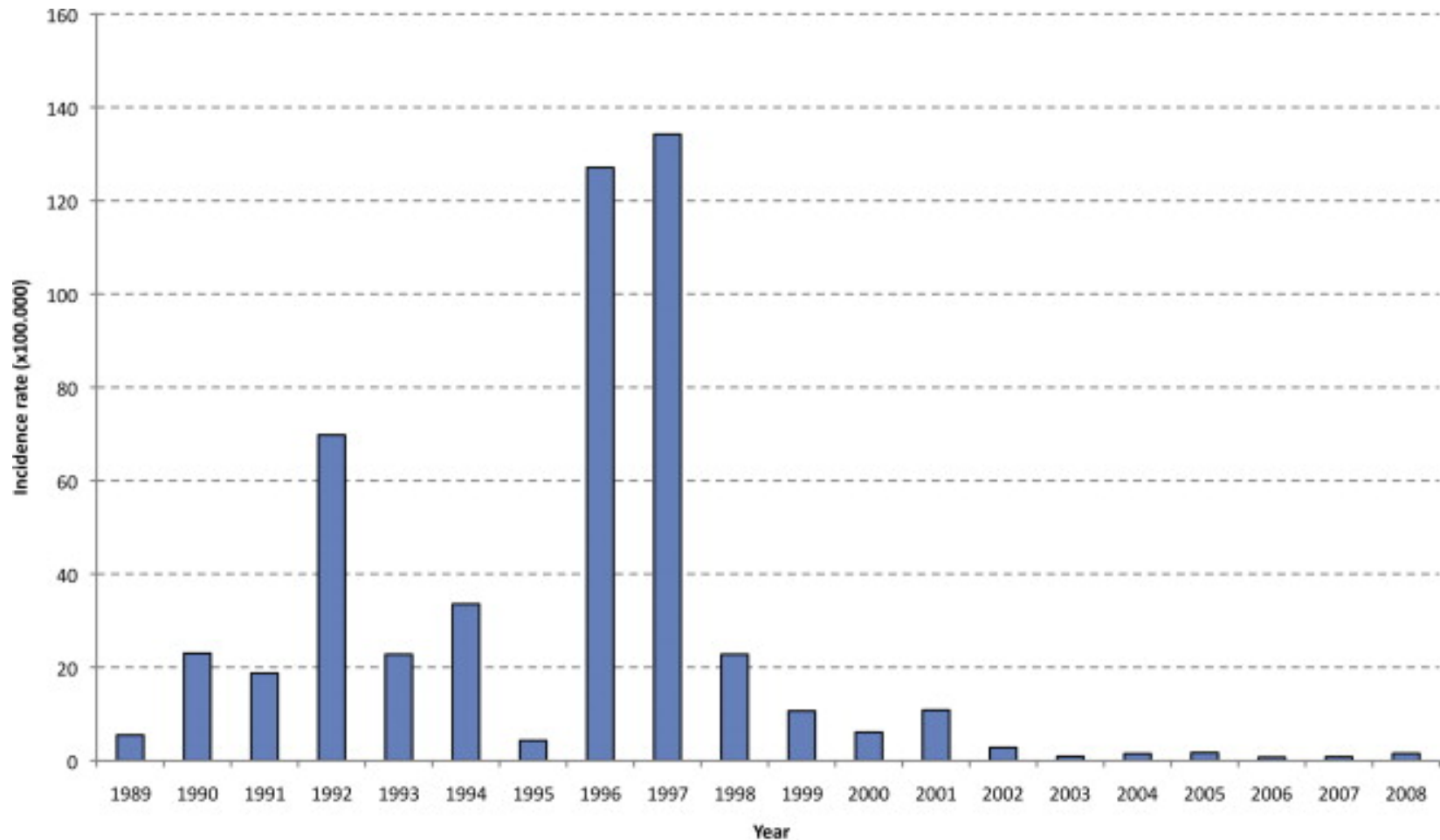


Hepatitis A vaccine coverage in Puglia. Routine data, 1998–2007

*Martinelli D et al, Vaccine 2010*



# Post marketing evaluation of Hepatitis A UVM: the Apulian case



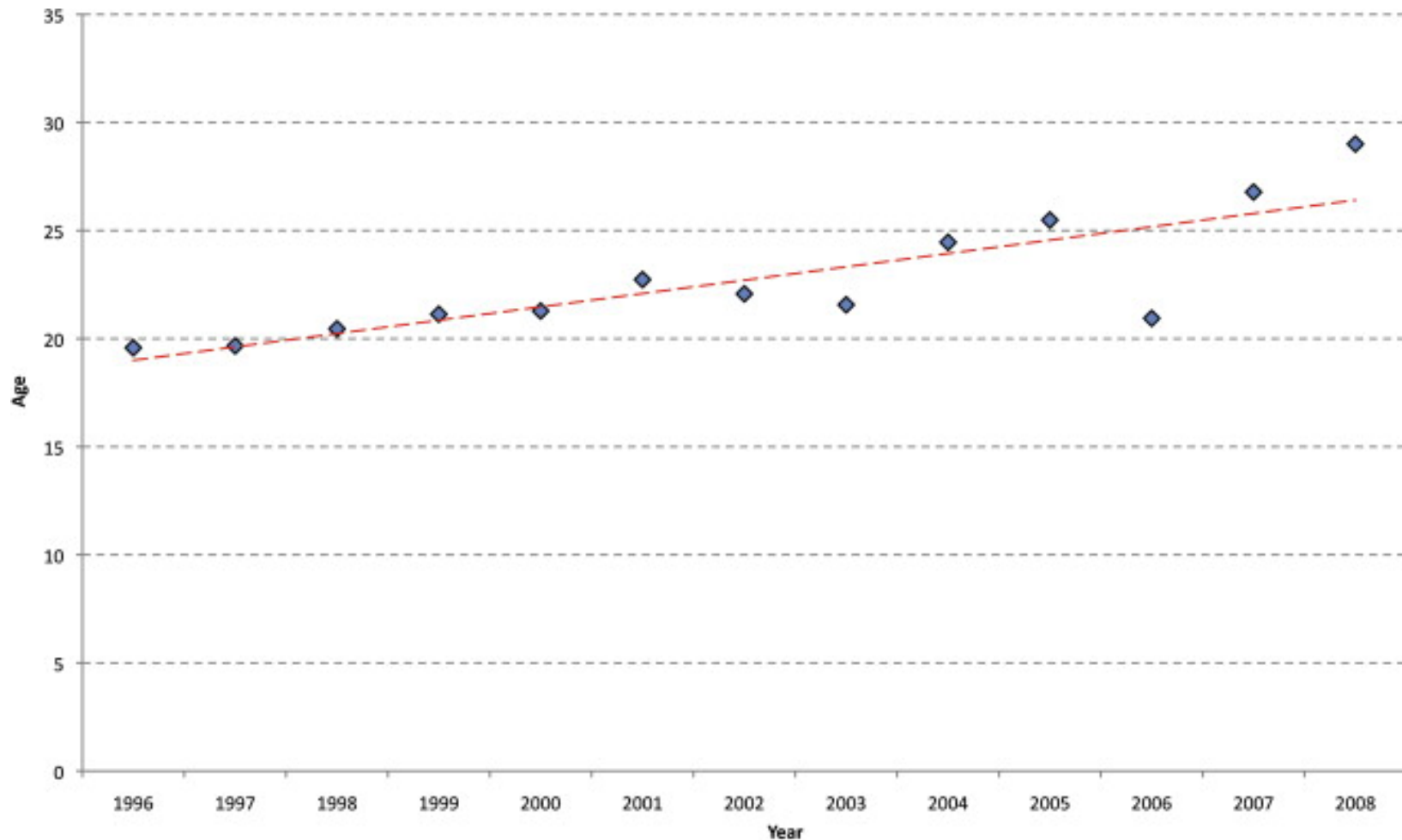
Hepatitis A incidence rate in Puglia, 1989–2008



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# Post marketing evaluation of Hepatitis A UVM: the Apulian case



Average age at infection of Hepatitis A cases in Puglia, 1996–2008



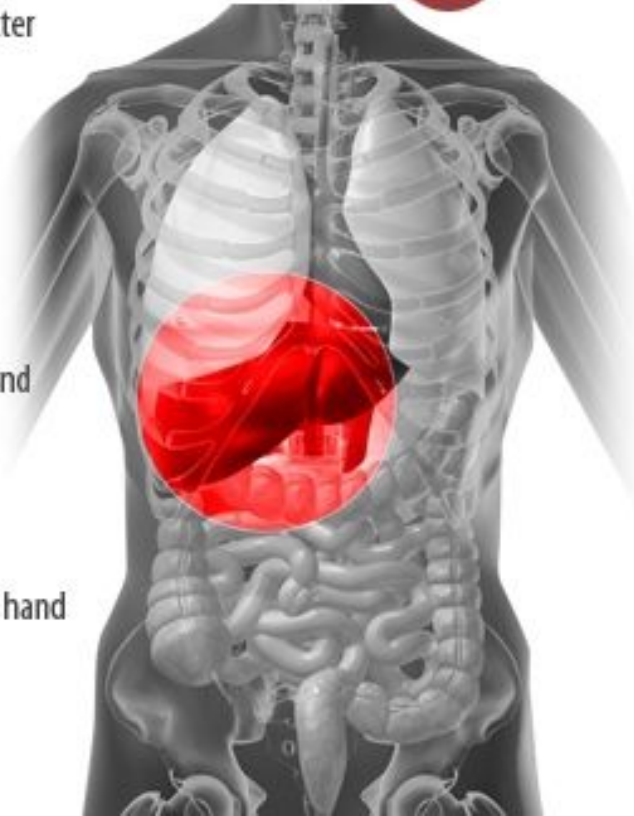
# HEPATITIS **A** FACTS

- 1** Is a viral infection of the liver spread when faecal matter enters the mouth



- 2** May last several weeks and can be debilitating but most people recover completely

- 3** Preventable with careful hand washing, keeping toilets and bathrooms clean, avoiding infected water sources



## SYMPTOMS INCLUDE

nausea



vomiting



## SPREAD BY



direct  
contact



food &  
beverages



cups &  
spoons

and any other objects handled by  
the infected person