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Epidemiology of hepatitis A, B and C among adults in Germany

Results of the German Health Interview and Examination Survey for Adults (DEGS1)

Background and purpose

Viral hepatitis A, B and C are contagious liver diseases that cause major public health problems worldwide. For hepatitis B and hepatitis C in particular, acute infection may progress to chronic disease, which can lead to cirrhosis of the liver and hepatocellular carcinoma. Hepatitis A virus causes only acute infections, but a fulminant course of infection with liver failure may rarely occur. The mortality of acute hepatitis A in people older than 60 years is 2%. According to the German Protection against Infection Act ("Infektionsschutzgesetz", IfSG), all suspected, diagnosed or deceased cases of viral hepatitis and all laboratory-confirmed cases of acute viral hepatitis (in case of hepatitis C: all newly diagnosed infections) in Germany must be notified to the local public health departments. Anonymised case reports are forwarded to the state public health departments in charge and electronically transmitted to the Robert Koch Institute (RKI). Assessment of hepatitis prevalence in the population based solely on data reported in accordance with the IfSG are subject to a range of limitations, as only newly diagnosed and acute infections are reported. In many cases viral hepatitis progresses without clinical symptoms and is not diagnosed in an early stage. Furthermore, information on immunity acquired through vaccination is not available from the national case reports. Therefore the information on the overall immunity of the population is incomplete. In order to develop targeted prevention strategies and to adapt vaccination recommendations, representative seroepidemiological surveillance is required. Ten years after the first seroepidemiological survey, the German National Health Interview and Examination Survey 1998 (GNHIES98), current and extensive data for hepatitis A, B and C are now available from the German Health Interview and Examination Survey for Adults ("Studie zur Gesundheit Erwachsener in Deutschland", DEGS).

Methods

The German Health Interview and Examination Survey for Adults (DEGS) is part of the health monitoring system at the Robert Koch Institute (RKI). The concept and design of DEGS are described in detail elsewhere [1, 2, 3, 4, 5]. The first wave (DEGS1) was conducted from 2008–2011 and comprised interviews, examinations and tests [6, 7]. The target population comprises the resident population of Germany aged 18–79 years. DEGS1 has a mixed study design, which permits both cross-sectional and longitudinal analyses. For this purpose, a random sample from local population registries was drawn to complete the participants of the German National Health Interview and Examination Survey 1998 (GNHIES98). A total of 8,152 persons participated, including 4,193 first-time participants (response rate 42%) and 3,959 revisiting participants of GNHIES98 (response rate 62%). There were 7,238 persons who attended one of the 180 examination centres, and 914 were only interviewed. The net sample (n=7,988) permits representative cross-sectional and trend analyses for the age range of 18–79 years in comparison with GNHIES98 (n=7,124) [2]. The data of the revisiting participants can be used for longitudinal analyses. The cross-sectional and trend analyses are conducted using a weighting factor, which corrects deviations in the sample from the population structure (as of 31 Dec 2010) with respect to age, sex, region and nationality as well as community type and education [2]. A separate weighting factor was generated for the examination part of the study. Calculation of the weighting factor also considered re-participation probability of GNHIES98 participants based on a logistic regression mod-

Tab. 1 Prevalence of antibodies against the hepatitis A virus (anti-HAV) by sex and age group from DEGS1 2008–2011 as percentages with 95% confidence intervals. $n_{unweighted}$=7,046

Age group	18–19 years	20–29 years	30–39 years	40–49 years	50–59 years	60–69 years	70–79 years	Overall
Sex								
Women	18.0 (10.8–28.3)	41.2 (35.8–46.8)	42.0 (36.3–47.9)	34.0 (29.3–39.1)	45.9 (41.4–50.5)	63.7 (58.5–68.5)	83.0 (78.5–86.7)	48.9 (46.7–51.1)
Men	24.1 (15.8–34.8)	40.3 (34.3–46.5)	39.0 (33.1–46.5)	41.9 (37.0–47.0)	42.0 (37.4–46.6)	63.9 (58.5–68.9)	83.9 (79.9–87.3)	48.3 (46.2–50.5)
Overall	21.5 (15.5–29.1)	40.7 (36.6–45.0)	40.5 (36.1–45.0)	38.1 (34.5–41.7)	44.0 (40.5–47.5)	63.8 (59.6–67.7)	83.4 (80.4–86.1)	48.6 (47.0–50.2)

el. For the purpose of conducting trend analyses, the data from the GNHIES98 were age-adjusted to the population level as of 31 Dec 2010. A non-response analysis and a comparison of selected indicators with data from census statistics indicate a high level of representativeness of the net sample for the resident population aged 18–79 years in Germany [2]. To take into account both the weighting as well as the correlation of participants within a municipality, the confidence intervals were determined using SPSS 20 procedures for complex samples. Differences are considered statistically significant if the respective 95% confidence intervals do not overlap.

Social status was determined using an index, which includes information on school education and vocational training, professional status and net household income (weighted by household needs) permitting classification into low, middle and high status groups [8].

To assess the prevalence of seromarkers for hepatitis A, B and C, serum samples from 7,047 (7,046 for hepatitis A) of the 7,116 persons included in the cross-sectional survey were analysed (99%). Data from the current survey were compared with the results of GNHIES98.

Hepatitis A

Immunoglobulin G (IgG) antibodies against hepatitis A virus (anti-HAV) were qualitatively detected with the HAV chemiluminescence microparticle immunoassay (CMIA) on an ARCHITECT device (here and below: Abbott Diagnostics). Samples with an S/CO (sample/cut off) below 1.0 were considered not reactive, i.e. not detectable, and samples with an S/CO ≥1.0 were considered reactive, i.e. positive.

Hepatitis B

Each sample was first tested for antibodies against hepatitis B core (anti-HBc) and surface antigen (anti-HBs). Testing for anti-HBc was done qualitatively using the CMIA on an ARCHITECT device. Samples with an S/CO below 1.0 were considered not reactive, i.e. not detectable, and samples with an S/CO≥1.0 were considered reactive, i.e. positive.

Anti-HBs levels were determined quantitatively using the CMIA on an ARCHITECT device. In accordance with the criteria of the ARCHITECT anti-HBs assay, samples with an anti-HBs concentration of less than 10.0 mIU/ml were considered not reactive, i.e. not detectable, and samples with an anti-HBs concentration ≥10 mIU/ml were considered reactive, i.e. positive.

Test results reactive for Anti-HBc and non-reactive for anti-HBs (<10 mIU/ml) were re-tested with an independent anti-HBc test and for the presence of HBsAg. In accordance with the criteria of the ARCHITECT HBsAg assay, samples with a concentration <0.05 IU/ml were considered not reactive, and samples ≥0.05 IU/ml were considered initially reactive and were then tested again. Only if this additional test was reactive, the sample was considered positive. In samples tested anti-HBc positive and anti-HBs positive, the respective subjects were considered to have been exposed to hepatitis B virus with acquisition of immunity. These are persons who have had a hepatitis B infection and recovered from it. Anti-HBc positive and HBsAg positive participants were classified as suffering from hepatitis B (active acute or chronic hepatitis B infection). Subjects who tested positive for anti-HBc only generally can be assumed to have a history of resolved hepatitis B infection (with or without immunity). The presence of anti-HBc only can be explained by a waning of anti-HBs antibodies after a previous infection, by an occult chronic infection without measureable HBsAg or by false positive reactions [9]. A positive anti-HBs result (≥10.0 mIU/ml) without presence of other markers is interpreted as immunity acquired through vaccination.

Hepatitis C

Antibodies against hepatitis C virus (anti-HCV) were detected qualitatively using the anti-HCV CMIA on an ARCHITECT device. Samples with an S/CO below 1.0 were considered not reactive, i.e. not detectable, samples with an S/CO ≥1.0 were considered reactive, i.e. positive, in accordance with ARCHITECT anti-HCV assay criteria. Samples showing the same result in a second testing, were considered positive for anti-HCV and were then tested for the presence of HCV RNA by polymerase chain reaction (PCR). HCV RNA positive samples were classified as "active hepatitis C infection". If no viral RNA was found, the antibody test result was confirmed by immunoblot. An immunoblot-confirmed positive antibody-test without evidence of viral RNA was classified as cleared hepatitis C virus infection. RNA- positive and immunoblot-confirmed samples were summed up to calculate the overall prevalence of hepatitis C.

Initially, PCR was performed using the Cobas AmpliPrep/Cobas TaqMan Test (limit of detection 15 IU/ml) until September 2010, from then until October 2011 using the VERSANT HCV RNA qualitative TMA assay (limit of detection 10 IU/ml). Quantitative HCV RNA determination was performed with

the VERSANT HCV RNA 3.0 bDNA assay and from October 2011 onwards using the VERSANT HCVB RNA 1.0 kPCR assay (limit of detection 15 IU/ml) by Siemens Healthcare Diagnostics (Eschborn). The immunoblot was carried out using the Chiron Riba HCV 3.0 test until September 2010, using the recomBlot HCV IgG 2.0 test until October 2011, and using the recomLine HCV IgG test thereafter (both from Mikrogen Diagnostik, Munich).

Results

Hepatitis A

The average prevalence of antibodies against hepatitis A virus (anti-HAV) is 48.6% among adults aged 18–79 years and does not differ significantly between men and women. There are considerable differences between age groups. The prevalence of anti-HAV increases overall with age and for 70–79 year olds it exceeds 80%. Notable, however, are the relatively constant seroprevalences of around 40% for the age groups from 20–59 years. For the age group 30–49 years there is no increase in seroprevalence as compared to the next youngest age group. The largest rise in the prevalence of antibodies between consecutive age groups is only observed between the age groups 50–59 years and 60–69 years. This pattern is particularly evident among women aged 40–49 years. The antibody prevalence of 34.0% (95% confidence interval 29.3–39.1) in this age group is even statistically significantly lower than that in the next younger age group (**Tab. 1**).

A multivariate logistic regression model adjusted for age and sex shows an association between the prevalence of anti-HAV and socioeconomic status (SES). The anti-HAV prevalence among adults with low or high SES is higher than among adults with middle SES (low versus middle SES odds ratio (OR) 1.22 (1.02–1.46), high versus middle SES OR 1.28 (1.08–1.52)).

Overall, the anti-HAV seroprevalence among men and women aged 18–79 is very similar to the figure obtained 10 years ago in GNHIES98 (**Tab. 2**). However, in GNHIES98 the seroprevalence rose continuously across all age groups, with a particularly large increase from age group 30–39 years to age group 40–49 years (**Tab. 2**). When considering the anti-HAV seroprevalence figures stratified by age, the current data from DEGS1 shows higher prevalence figures for the younger age groups from 18–39 years. In contrast, the seroprevalence figures for the age groups from 50–79 years are considerably lower than those obtained 10 years ago in GNHIES98 (**Fig. 1**).

Abstract · Zusammenfassung

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Epidemiology of hepatitis A, B and C among adults in Germany. Results of the German Health Interview and Examination Survey for Adults (DEGS1)

Abstract

Ten years after seroepidemiological data were obtained in the German National Health Interview and Examination Survey 1998 (GNHIES98), German Health Interview and Examination Survey (DEGS1) data contribute to a population-based, representative surveillance of hepatitis A and B immunity and of the serological markers for hepatitis C in Germany. The prevalence of antibodies against the hepatitis A virus is 48.6%. In comparison to the situation 10 years ago, seroprevalence is significantly higher among 18- to 39-year-old adults and is significantly lower in those aged 50–79 years. The association between age and seroprevalence has changed, indicating a decrease in naturally acquired hepatitis A immunity. Individual and population immunity has to be achieved through vaccination. Prevalence of hepatitis B antibodies indicates that 5.1% of adults have been exposed to the virus, significantly fewer than 10 years ago (7.9%). Prevalence of hepatitis B surface antibodies indicates that 22.9% of adults have been vaccinated against hepatitis B. Vaccination coverage has increased in all age groups and is highest in the younger age groups. These positive trends can be attributed to the general recommendation since 1995 to vaccinate against hepatitis B. For hepatitis C, the prevalence of antibodies in the general population is 0.3%. Germany thus remains a low-HCV-endemic country.

Keywords

Health survey · Hepatitis A · Hepatitis B · Hepatitis C · Seroepidemiology

Die Seroepidemiologie der Hepatitis A, B und C in Deutschland. Ergebnisse der Studie zur Gesundheit Erwachsener in Deutschland (DEGS1)

Zusammenfassung

Die Daten aus der Studie zur Gesundheit Erwachsener in Deutschland (DEGS1) ermöglichen 10 Jahre nach der seroepidemiologischen Erhebung im „Bundes-Gesundheitssurvey 1998" (BGS98) die Abschätzung der aktuellen Durchseuchung mit Hepatitis-A-, Hepatitis-B- und Hepatitis-C-Viren und der Immunitätslage gegen Hepatitis A und B sowie diesbezüglicher zeitlicher Trends in der Bevölkerung. Die Seroprävalenz von Antikörpern gegen das Hepatitis-A-Virus beträgt 48,6%. Im Vergleich zu den Werten vor 10 Jahren liegt sie bei den 18- bis 39-Jährigen signifikant höher, bei den 50- bis 79-Jährigen dagegen signifikant niedriger. Das veränderte Muster in der altersabhängigen Seroprävalenz zeigt einen Rückgang der natürlichen Durchseuchung mit dem Hepatitis-A-Virus. Ein individueller Schutz vor Hepatitis A und eine gute Immunität auf Bevölkerungsebene sind daher nur durch Schutzimpfungen zu erreichen. 5,1% der Erwachsenen weisen Marker für eine Hepatitis-B-Virus-Infektion auf; dieser Wert ist signifikant niedriger als vor 10 Jahren. Bei 22,9% der Frauen und Männer kann auf eine durch Impfung hervorgerufene Immunität gegen Hepatitis B geschlossen werden. Dieser Anteil sinkt mit dem Alter, ist aber über alle Altersgruppen hinweg signifikant gestiegen. Es zeigen sich bereits deutliche Erfolge der seit 1995 allgemein empfohlenen Hepatitis-B-Impfung. Die Durchseuchung mit Hepatitis-C-Viren liegt bei 0,3%; damit gehört Deutschland weiterhin zu den Ländern mit einer diesbezüglich niedrigen Prävalenz.

Schlüsselwörter

Gesundheitssurvey · Hepatitis A · Hepatitis B · Hepatitis C · Seroepidemiologie

Tab. 2 Prevalence of antibodies against the hepatitis A virus (anti-HAV) by sex and age group from GNHIES98 as percentages with 95% confidence intervals (age-standardised for state of population as of 31 Dec 2010). $n_{unweighted}$ =6,748

Age group	18–19 years	20–29 years	30–39 years	40–49 years	50–59 years	60–69 years	70–79 years	Overall
Sex								
Women	6.4 (2.3–16.5)	17.3 (13.3–22.2)	22.3 (18.5–26.7)	47.6 (43.0–52.2)	64.3 (59.9–68.5)	83.3 (78.8–87.0)	90.6 (86.3–93.7)	51.9 (49.5–54.4)
Men	9.6 (4.9–17.9)	21.1 (16.4–26.8)	26.2 (22.2–30.7)	38.3 (33.6–43.3)	63.1 (58.5–67.5)	82.7 (78.9–85.9)	88.0 (83.2–91.6)	49.1 (46.7–51.6)
Overall	8.0 (4.6–13.5)	19.2 (15.6–23.3)	24.4 (21.2–27.8)	42.8 (39.2–46.6)	63.7 (60.4–66.9)	83.0 (80.1–85.5)	89.4 (86.4–91.8)	50.5 (48.4–52.7)

Tab. 3 Prevalence of hepatitis B and hepatitis C seromarkers by sex and age group from DEGS1 2008–2011 as percentages with 95% confidence intervals. $n_{unweighted}$ =7,047

Age group	18–19 years	20–29 years	30–39 years	40–49 years	50–59 years	60–69 years	70–79 years	Overall
Hepatitis B								
Women								
Anti-HBc and HBs-Ag positive[a]	0	0.3 (0.0–2.1)	0.4 (0.1–2.8)	0	0.2 (0.0–1.4)	0.2 (0.0–1.2)	0	0.2 (0.1–0.4)
Anti-HBc and anti-HBs positive[b]	0	0.6 (0.1–2.8)	3.1 (1.6–6.2)	4.1 (2.4–6.9)	6.2 (4.3–8.8)	7.7 (5.1–11.4)	5.4 (3.4–8.7)	4.4 (3.6–5.4)
Only anti-HBc positive[c]	0	0	0.8 (0.1–5.2)	0	0.1 (0.0–1.0)	0.6 (0.2–1.6)	0.5 (0.1–1.9)	0.3 (0.1–0.7)
Only anti-HBs positive[d]	70.9 (59.6–80.1)	62.1 (56.5–67.3)	26.9 (22.3–32.1)	23.1 (19.4–27.2)	17.6 (14.2–21.5)	9.6 (7.0–12.9)	6.1 (4.1–9.0)	25.8 (23.8–27.8)
Men								
Anti-HBc and HBs-Ag positive[a]	0	0.2 (0.0–1.2)	0.8 (0.1–5.4)	0.2 (0.0–1.2)	0.8 (0.2–2.5)	1.0 (0.1–6.5)	0.2 (0.0–1.6)	0.5 (0.2–1.1)
Anti-HBc and anti-HBs positive[b]	0	1.1 (0.4–3.0)	2.9 (1.4–5.6)	3.8 (2.0–6.9)	5.4 (3.7–7.7)	5.7 (3.6–8.9)	6.1 (3.6–10.2)	3.9 (3.1–4.9)
Only anti-HBc positive[c]	0	0	1.2 (0.3–5.3)	0.2 (0.1–0.9)	0.8 (0.3–2.0)	2.6 (1.1–5.7)	1.8 (0.7–4.8)	0.9 (0.6–1.6)
Only anti-HBs positive[d]	61.6 (51.9–70.4)	51.8 (45.6–58.0)	20.0 (16.0–24.6)	14.1 (11.1–17.7)	11.0 (8.2–14.6)	7.4 (5.3–10.4)	3.3 (2.0–5.4)	20.1 (18.2–22.0)
Overall								
Anti-HBc and HBs-Ag positive[a]	0	0.2 (0.1–1.0)	0.6 (0.1–2.5)	0.1 (0.0–0.6)	0.5 (0.2–1.3)	0.5 (0.1–2.9)	0.1 (0.0–0.7)	0.3 (0.2–0.6)
Anti-HBc and anti-HBs positive[b]	0	0.8 (0.3–2.0)	3.0 (1.8–5.0)	3.9 (2.6–5.9)	5.8 (4.4–7.5)	6.8 (5.1–8.9)	5.8 (4.1–8.0)	4.1 (3.1–4.8)
Only anti-HBc positive[c]	0	0	1.0 (0.3–3.2)	0.1 (0.0–0.4)	0.5 (0.2–1.1)	1.5 (0.8–3.0)	1.1 (0.5–2.5)	0.6 (0.4–0.9)
Only anti-HBs positive[d]	65.5 (58.2–72.0)	57.1 (52.8–61.2)	23.4 (20.1–27.0)	18.5 (15.9–21.4)	14.3 (11.9–17.1)	8.5 (6.7–10.8)	5.4 (3.8–7.5)	22.9 (21.5–24.5)
Hepatitis C: anti-HCV confirmed positive and/or HCV-RNA positive								
Women	0	0	0	0.2 (0.0–0.8)	0.1 (0.0–0.9)	0.4 (0.1–1.9)	1.2 (0.3–5.6)	0.3 (0.1–0.8)
Men	0	0	0	0.6 (0.1–2.6)	0.5 (0.1–2.3)	0.2 (0.0–0.8)	0	0.3 (0.1–0.7)
Overall	0	0	0	0.4 (0.1–1.3)	0.3 (0.1–1.1)	0.3 (0.1–0.9)	0.7 (0.1–3.2)	0.3 (0.1–0.5)

[a]acute or chronic infection; [b]healed infection; [c]previous infection, immunity questionable; [d]immunity through vaccination.

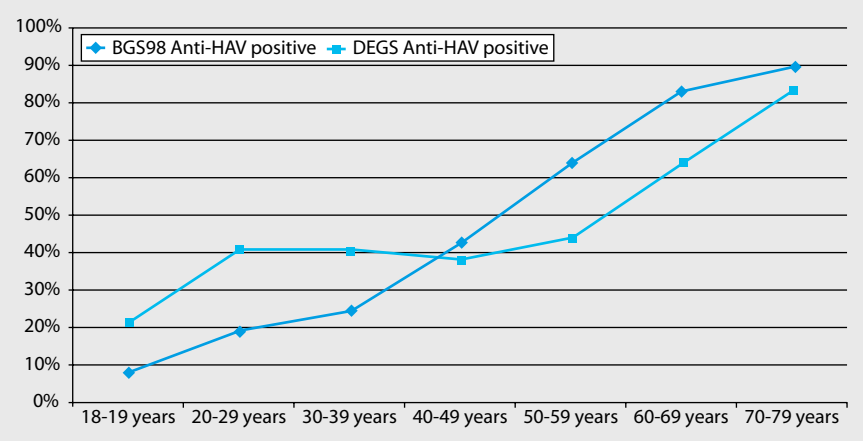

Fig. 1 ▲ Seroprevalence of antibodies against the hepatitis A virus as percentages by age group in DEGS1 and in GNHIES98 (weighted for state of population as of 31 Dec 2010), n=7,046

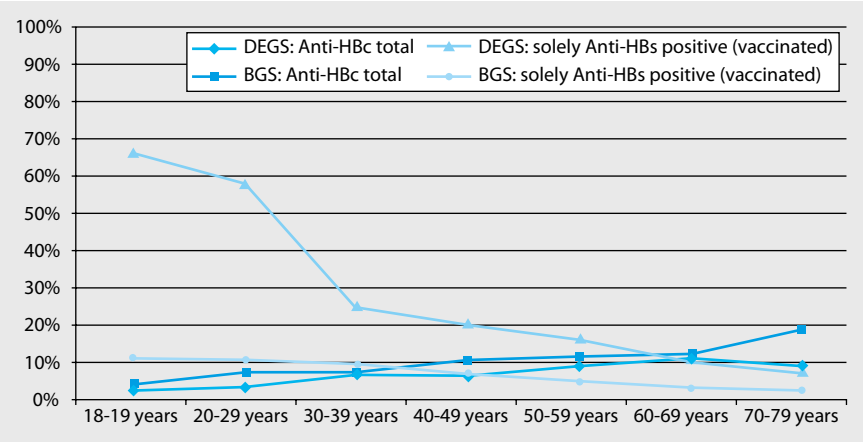

Fig. 2 ▲ Prevalence of hepatitis B seromarkers as percentages by age group in DEGS1 and in GNHIES98 (weighted for state of population as of 31 Dec 2010), n=7,047

Hepatitis B

The results of for hepatitis B seromarkers are listed in **Tab. 3**. A total of 5.1% of adults were positive for antibodies against hepatitis B core antigen (anti-HBc) and thus markers for hepatitis B infection (women 4.8% (4.0–5.8), men 5.3% (4.3–6.5)). The prevalence of acute or chronic HBV infection (anti-HBc positive and HBsAg positive) is 0.3%. The relatively high prevalence among men (0.5%; 0.2–1.1) as compared to women (0.2%; 0.1–0.4) is statistically not significant. Age-stratified analyses were not performed due to low case numbers. The prevalence of anti-HBc/anti-HBs positive samples as serological evidence for resolved hepatitis B infection is 4.1% and is higher for the elder age groups as compared to younger ones. It does not differ between women and men. The prevalence of anti-HBc only in the study population is 0.6%. This serological result, classified as exposure to HBV without evidence of acquired immunity, was slightly more frequent in men than in women, but without statistical difference. A multivariate logistic regression model adjusted for age and sex shows a correlation between hepatitis B infection and socioeconomic status (SES) (low versus high SES: OR 3.82 (2.57–5.66), middle versus high SES: OR 1.76 (1.20–2.58)). The lower the social status, the higher is the risk of hepatitis B infection.

A total of 22.9% of participants tested positive for anti-HBs exclusively, indicating a vaccination-acquired HBV-immunity. Immunity due to vaccination differs significantly between women and men, with women having a considerably higher anti-HBs-seroprevalence. Although the differences in individual age groups are not statistically significant, the prevalence of anti-HBs is clearly higher among younger women below 30 years of age as compared to men in the same age-group: Among 18- to 19-year-old persons, women had a prevalence of anti-HBs of 70.9% compared to 61.6% in men, and in 20- to 29-year-old persons, anti-HBs prevalence in women was 62.1% compared to 51.8% in men. A multivariate logistic regression model adjusted for age and sex shows an association between vaccination-acquired immunity against HBV and SES (high versus low SES: OR 3.53 (2.62–4.76), middle versus low SES: OR 2.08 (1.60–2.69)). Low SES thus is associated with the lack of vaccination-acquired immunity. The risk of HBV infection (current infection or history of infection) is higher for adults with low SES than for persons with middle SES, and it is also higher for persons with middle SES as compared to those with high SES.

The proportion of exclusively anti-HBs positive samples for men and women across all age groups is considerably higher in the current survey (**Fig. 2**) as compared to the results from GNHIES98 (**Tab. 4**). This increase in the proportion of vaccinated subjects is greatest for the age group 18–29 years. The overall proportion of anti-HBc positive adults as marker for HBV infection is 5.1% (4.4–5.8) significantly lower than 10 years ago (7.9% (6.9–9.1)). Prevalence figures from GNHIES98, age-adjusted for the current population structure (**Tab. 4**), indicate an even more important decrease of HBV infection in the German population from 8.7% (7.7–9.9) to 5.1% (4.4–5.8). This difference is most distinct in the oldest age group of 70–79 years.

Hepatitis C

The average prevalence of antibodies against the hepatitis C virus (anti-HCV) among the study population is 0.3%. Evidence of HCV RNA was found in two thirds of HCV positive samples (overall 0.2%). In one third (overall 0.1%) antibodies against HCV were present, but no viral RNA was detected. Thus markers for infection with HCV are present in a total of 0.3% (0.1–0.5) of adults (**Tab. 3**). Multivariate logistic regression did not reveal differences in prevalence by sex or SES

Tab. 4 Prevalence of hepatitis B seromarkers by sex and age group from GNHIES98 as percentages with 95% confidence intervals (age-standardised for state of population as of 31 Dec 2010). $n_{unweighted}$ =6,747

Age group	18–19 years	20- 29 years	30–39 years	40–49 years	50–59 years	60–69 years	70–79 years	Overall
Sex								
Women								
Anti-HBc and HBs antigen positive[a]	0	0	0	0.6 (0.2–2.4)	0.3 (0.0–2.2)	0.6 (0.2–2.4)	0.8 (0.1–5.7)	0.4 (0.2–0.9)
Anti-HBc and anti-HBs positive[b]	1.6 (0.2–10.7)	3.3 (1.5–7.2)	3.6 (2.2–5.9)	6.7 (4.5–9.8)	5.5 (3.6–8.5)	9.9 (7.2–13.4)	13.6 (9.5–19.1)	6.7 (5.6–8.1)
Only anti-HBc positive[c]	0	1.8 (0.6–5.5)	0.5 (0.1–3.8)	0.5 (0.2–1.7)	0.2 (0.0–1.2)	0.7 (0.2–2.2)	1.2 (0.4–3.6)	0.8 (0.4–1.4)
Only anti-HBs positive[d]	13.2 (7.5–22.2)	12.3 (9.3–16.1)	9.6 (7.5–12.1)	6.0 (4.4–8.2)	4.4 (2.7–7.2)	1.0 (0.3–2.7)	0.4 (0.1–1.8)	5.9 (5.0–7.0)
Men								
Anti-HBc and HBs antigen positive[a]	0.9 (0.1–6.3)	0.4 (0.1–2.0)	2.1 (0.9–4.6)	1.4 (0.6–3.2)	2.0 (0.9–4.3)	0.5 (0.1–2.5)	0.3 (0.0–2.2)	1.2 (0.8–2.0)
Anti-HBc and anti-HBs positive[b]	1.1 (0.2–4.9)	4.3 (2.4–7.7)	3.0 (1.8–5.0)	6.5 (4.4–9.4)	7.6 (5.4–10.5)	5.6 (3.7–8.3)	15.5 (10.7–21.9)	6.5 (5.4–7.8)
Only anti-HBc positive[c]	0	0.6 (0.1–4.0)	1.3 (0.5–3.4)	0.8 (0.3–2.0)	2.8 (1.5–5.3)	2.3 (0.9–5.6)	3.6 (1.5–8.3)	1.7 (1.1–2.5)
Only anti-HBs positive[d]	5.3 (2.5–10.9)	4.9 (3.1–7.9)	5.1 (3.5–7.4)	3.1 (2.0–4.9)	1.1 (0.4–2.6)	0.5 (0.2–1.8)	0	2.7 (2.2–3.4)
Overall								
Anti-HBc and HBs antigen positive[a]	0.5 (0.1–3.3)	0.2 (0.0–1.0)	1.1 (0.5–2.4)	1.0 (0.5–2.0)	1.2 (0.6–2.4)	0.5 (0.2–1.6)	0.6 (0.1–2.8)	0.8 (0.5–1.2)
Anti-HBc and anti-HBs positive[b]	1.4 (0.4–4.8)	3.8 (2.4–6.0)	3.3 (2.3–4.7)	6.6 (4.9–8.8)	6.5 (4.9–8.7)	7.8 (6.0–10.0)	14.5 (11.0–18.8)	6.6 (5.7–7.6)
Only anti-HBc positive[c]	0	1.2 (0.5–3.1)	0.9 (0.4–2.3)	0.6 (0.3–1.3)	1.5 (0.8–2.8)	1.5 (0.7–3.1)	2.3 (1.2–4.5)	1.2 (0.9–1.7)
Only anti-HBs positive[d]	9.2 (5.6–14.7)	8.6 (6.9–10.7)	7.3 (5.9–9.0)	4.6 (3.5–6.0)	2.8 (1.8–4.2)	0.8 (0.3–1.6)	0.2 (0.1–1.0)	4.3 (3.8–5.0)

[a]acute or chronic infection; [b]healed infection; [c]previous infection, immunity questionable; [d]immunity through vaccination.

(data not shown). Anti-HCV-positive results were found exclusively in age groups 40–79 years.

Overall HCV prevalence in the current survey does not differ from results obtained 10 years ago in GNHIES98 (confirmed anti-HCV 0.4%, (0.2–0.6)). However, in contrast to GNHIES98, where 20- to 29-year-old persons and older individuals tested positive for anti-HCV, in DEGS1 no persons below the age of 40 years showed evidence for HCV infection.

Discussion

Hepatitis A

Hepatitis A is an acute inflammation of the liver, whose symptoms typically include jaundice and which typically is of relatively short duration and completely resolves. However, mortality increases with age (approx. 2% among over 60 year olds). The hepatitis A virus is excreted with the faeces and is transmitted from person to person and via contaminated food. In countries with low standards of hygiene the incidence of infection is very high already among children. In Europe and North America the incidence has declined steadily over the last 10 years, so that ever fewer adolescents and adults have naturally acquired immunity to the hepatitis A virus. Vaccination is available in Germany and since 1993 has been recommended by the Standing Committee for Vaccination ("Ständige Impfkommission", STIKO) for travellers to regions with a high prevalence of hepatitis A and for persons with increased risk of infection due to occupational exposure or sexual behaviour [10].

Almost 50% of adult men and women in Germany have antibodies against the hepatitis A virus. These were acquired either naturally (previous infection) or as a result of hepatitis A vaccination. Antibodies against the hepatitis A virus are found in a smaller proportion in adults with middle SES than in adults with low or high SES. Taking into account the low hepatitis A vaccination rates for adults with low SES and the high vaccination rates for adults with high SES shown in another publication in this issue [11], this result indicates that immunity was more often acquired naturally among people with low SES and more often via vaccination among people with high SES.

The overall prevalence of anti-HAV does not differ from the data gathered in the years from 1997–1999 [12]. In both surveys the overall seroprevalence considerably increases by age. However, the current DEGS1 pattern of age-dependency clearly differs from the steady rise of anti-HAV seroprevalence with age in the GNHIES98. Currently the seroprev-

alence figures for anti-HAV in the age groups from 18–39 years are higher than 10 years ago, while in the groups from 50–79 years, on the other hand, they are lower. This means that the proportion of older men and women with no immunity to the hepatitis A virus has risen sharply over the last 10 years. Taking into consideration the continuous decrease of hepatitis A incidence across all age groups based on the case notifications according to the German Protection against Infection Law (IfSG) [13], the considerably higher anti-HAV seroprevalence in age groups 18–39 years are most likely due to an increased hepatitis A vaccination coverage (for example before travelling abroad). While well over 2,000 cases of hepatitis A infection were notified in 2001 (2,271 in 2001), since 2009 there have been fewer than 1,000 annually notified cases. The DEGS1 results are also consistent with the data based on IfSG notifications regarding distribution by sex, i.e. anti-HAV seroprevalence is not different between males and females.

Two large, representative seroepidemiological surveys were carried out in the Netherlands from 1995 to 1996 and over 2006/2007 on the anti-HAV prevalence. They found an increase in the prevalence of anti-HAV from 34 to 39.3%, which was attributed to increasing vaccination coverage and a higher proportion of immigrants [14]. Anti-HAV prevalence in the Netherlands is thus lower than the prevalence observed in Germany. However, it is also highly age-dependent. In the Dutch surveys also conducted at 10-year intervals, an increase in the proportion of older men and women who are not immune to the hepatitis A virus is also evident.

Conclusion

The data available from DEGS1 on the seroprevalence of anti-HAV provides an up-to-date, population-based and valid estimate of immunity to the hepatitis A virus. Anti-HAV antibodies indicating protection against hepatitis A can be detected for a long time after vaccination [15] and even longer after previous infection [16, 17]. Currently younger age groups are better protected, while older age groups are less protected against infection with the hepatitis A virus than 10 years ago. Better hygienic conditions have led to a reduction in the incidence of HAV infection. Individual protection against the hepatitis A virus and good immunity at a population level can therefore only be achieved in Germany by vaccination. Generally it is important to ensure that the vaccination recommendations made by the STIKO are properly implemented in practice. This is particularly important for older people travelling to high-prevalence regions, since hepatitis A can be particularly severe in these age groups and prevalence of natural immunity is decreasing.

Hepatitis B

Hepatitis B is a contagious liver inflammation of worldwide significance, caused by HBV and is transmitted primarily sexually or via blood. Among adults the infection usually resolves, but in up to 10% of cases, the virus can cause chronic liver infection that can later develop into cirrhosis of the liver and hepatocellular carcinoma. Since 1982 (West Germany) and 1984 (East Germany) vaccination has been recommended for groups with increased risk of infection. In 1995, the general recommendation for HBV-vaccination of all neonates and non-vaccinated older children and adolescents was implemented by the Scientific Secretariat of the Standing Committee on Vaccination at the Robert Koch Institute (STIKO) [18].

The overall prevalence of infection with hepatitis B virus is 5.1% and does not differ between men and women. The serological findings most frequently indicate previous hepatitis B infection with acquired immunity. However, compared with the seroprevalence figures obtained in GNHIES98 10 years ago the DEGS data indicate a decrease in HBV infection. This positive development is most clearly seen in the young age groups. At the same time, the proportion of persons who have been vaccinated has increased considerably, particularly in the young age groups. It can therefore be assumed that the general vaccination for children recommended by the STIKO is already showing an impact. A positive trend is also evident in the prevalence of current acute or chronic HBV infection. The HBsAg prevalence of 0.8% measured in GNHIES98 10 years ago has decreased to 0.3%. The positive trend observed in the seroprevalence figures can also be seen in the national surveillance data for HBV. Reported case numbers of acute HBV infection are steadily decreasing and stable since the year 2007. The decrease is particularly pronounced among young age groups. However, a similar reduction is also evident among older age groups, indicating that, in addition to the success of HBV vaccination, general prevention measures (for example hygiene regulations in healthcare, improved safety of blood and blood products) seem to be having an effect. The annual incidence figures of hepatitis B (IfSG), however, continue to show a distinct difference between men and women (in 2010, 0.6 cases per 100,000 women, 1.3 cases per 100,000 men). Starting from the age group 25–29 years there was a consistently higher incidence among men than among women of the same age [19]. In contrast, the seroprevalence figures from DEGS1 show virtually no difference between men and women with respect to the seromarkers indicating acute or previous hepatitis B infection. This discrepancy can be explained by the fact that the higher incidence of hepatitis B among men is probably attributable to high-risk sexual behaviour and to more frequent intravenous drug use among men. The true prevalence tends to be underestimated in population-based surveys.

Fifteen years after the introduction of the general hepatitis B vaccination, trends appear to be positive given the decrease in the total percentage of persons infected with hepatitis B and in the incidence of hepatitis B in particular among young adults and children in Germany. Similar trends have also been described in Italy, where vaccination was generally recommended in 1991 [20].

Conclusion

The seroprevalence figures obtained in DEGS1 give a measure of the situation regarding HBV infection and immunity in the population at large. Today, particularly the younger age groups are considerably better protected against hepatitis B than 10 years ago. Overall, lifetime prevalence of HBV infection has decreased. The risk of infection decreases with high-

er social status. On the one hand the observed reduction in overall prevalence is due to the fact that the age group with the highest rate of HBV infection 10 years ago, the then 70–79 year olds, did not participate in the current survey for age-related reasons. On the other hand there is also a lower rate of infection among the younger age groups. This can be attributed to the introduction of the general vaccination against hepatitis B for infants. In the age groups investigated here, however, the declining rate of infection is primarily the result of vaccination of older children and adolescents. Since all study participants were born before the recommendation for general vaccination was made, and as the vaccination coverage is higher in younger than in older age groups, it is likely that the positive trend will continue.

Hepatitis C

Hepatitis C is a contagious inflammation of the liver affecting people worldwide that is caused by the hepatitis C virus. HCV is transmitted parenterally. Without treatment the infection becomes chronic in 50–85% of cases [22, 23] and after decades can result in cirrhosis of the liver or hepatocellular carcinoma. There is no vaccine against hepatitis C. The available diagnostic markers at present do not allow any assessment of the duration of infection, so that in general it is not possible to differentiate between acute and chronic infections. In comparison to the findings from GNHIES98, the overall prevalence of hepatitis C in Germany remains unchanged. However, no hepatitis C positive results were found in the younger age groups 18–39 years in the current survey. Important preventative measures, including routine hepatitis C screening as part of blood donor monitoring, were introduced in 1991. This may explain the decrease in HCV infection among the younger population. A further reduction in the number of chronic HCV infections can be expected as antiviral treatment options improve [24].

Conclusion

With a prevalence of HCV infection of 0.3%, Germany ranks among European nations as one of the countries with a low prevalence of hepatitis C [25]. The true prevalence of HCV antibodies may, however, be greater than indicated by DEGS1, since hospitalised patients, persons in psychiatric care and prison-inmates were excluded from the survey and other risk groups such as intravenous drug users and other populations at higher risk of HCV infection were not included representatively.

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