

Prevention of viral hepatitis in Germany and the Nordic Countries: lessons learnt and the way forward

Viral Hepatitis Prevention Board Meeting,
Berlin, Germany, October 13-14, 2003

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Executive VHPB Secretariat

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VIRAL HEPATITIS PREVENTION BOARD MEETING

BERLIN, GERMANY, OCTOBER 13-14, 2003

- MEETING PROGRAMME -

**PREVENTION OF VIRAL HEPATITIS IN GERMANY
AND THE NORDIC COUNTRIES:
LESSONS LEARNT AND THE WAY FORWARD**

Final meeting programme 2003-10-13 GF

Monday, October 13, 2003

SESSION 1 OPENING AND OBJECTIVES

Chair: Lars Rombo, Sweden, and Johannes Hallauer, Germany

09.00 - 09.30

- Welcome
Johannes Hallauer, Germany
- Introduction of the participants
- Objectives of the meeting:
 1. Update of the epidemiological situation on viral hepatitis in Germany and the Nordic Countries;
 2. Overview of surveillance systems for infectious diseases and adverse events following vaccination in Germany and the Nordic Countries;
 3. Evaluation of current prevention and control measures on viral hepatitis in Germany and the Nordic Countries;
 4. Lessons learnt from the experience in Germany and the Nordic Countries: successes, problems and barriers to overcome, and the way forward.
- Review of the meeting programme
- Epidemiology, prevention, and control of viral hepatitis in Germany and the Nordic Countries - Review/background document

SESSION 2 EPIDEMIOLOGY, PREVENTION, AND SURVEILLANCE OF VIRAL HEPATITIS IN THE NORDIC COUNTRIES

Chair: Lars Rombo, Sweden, and Johannes Hallauer, Germany

- 09.30 - 10.10 Hepatitis B epidemiology, surveillance, and prevention strategies in the Nordic Countries
Hans Blystad, Oslo, Norway
- 10.10 - 10.25 Epidemiology of hepatitis A in Sweden - the same old story?
Lars Rombo, Eskilstuna, Sweden
- 10.25 - 10.45 *Coffee break*
- 10.45 - 11.05 Problems associated with the introduction of HBsAg-positive children in day-care centres
Johan Struwe, Huddinge, Sweden
- 11.05 - 11.25 Investigation of a cluster of nosocomial HBV infections in Sweden - obstacles and efforts
Johan Struwe, Huddinge, Sweden
- 11.25 - 11.55 Hepatitis A and B outbreaks among intravenous drug users in the Nordic Countries
Hans Blystad, Oslo, Norway
- 11.55 - 12.25 Evaluation of a hepatitis B selective vaccination programme in Norway
Hanne Nøkleby, Oslo, Norway
- 12.25 - 14.00 *Lunch*

SESSION 3 EPIDEMIOLOGY OF VIRAL HEPATITIS IN GERMANY

Chair: Peter Grob, Switzerland, and Daniel Shouval, Israel

- 14.00 - 14.25 Hepatitis C virus infection in medical settings
Sergei Viazov, Essen, Germany
- 14.25 - 14.50 Follow-up of iatrogenous HCV infections related to anti-Rh prophylaxis
Anne-Sophie Endres, Berlin, Germany
- 14.50 - 15.15 Epidemiology of hepatitis A in Germany
Katharina Alpers, Berlin, Germany

15.15 - 15.30 *Coffee break*

15.30 - 15.55 Epidemiology of hepatitis B in Germany
Doris Radun, Berlin, Germany

15.55 - 16.20 HBV infection: always detectable, always preventable?
Wolfram Gerlich, Giessen, Germany

SESSION 4 THE HEALTH CARE SYSTEM IN GERMANY

Chair: André Meheus, Belgium

16.20 - 16.45 Organisation of the health care system in Germany
Johannes Hallauer, Berlin, Germany

SESSION 5 SURVEILLANCE SYSTEMS IN GERMANY

Chair: André Meheus, Belgium

16.45 - 17.10 Federal law on communicable diseases (*Infektionsschutzgesetz*) -
Reporting systems
Michael Kramer, Bonn, Germany

Conference dinner

Tuesday, October 14, 2003

SESSION 6 PREVENTION AND CONTROL OF VIRAL HEPATITIS IN GERMANY

Chair: Nicole Guérin, France, and Andrei Lobanov, France

09.00 - 09.30 Development of hepatitis B prevention in Germany - the first 10 years
Wolfgang Jilg, Regensburg, Germany

09.30 - 10.00 Screening pregnant women for hepatitis B: results from two studies
Wolfgang Jilg, Regensburg, Germany

10.00 - 10.35 Groups at risk for hepatitis B infection - who should be vaccinated
Ulrich Bienzle, Berlin, Germany

10.35 - 11.00 *Coffee break*

SESSION 7 EVALUATION OF VIRAL HEPATITIS PREVENTION AND CONTROL MEASURES IN GERMANY

Chair: Harold Margolis, USA, and Daniel Lavanchy, Switzerland

11.00 - 11.25 Universal vaccination against hepatitis B in Germany - a paediatrician's point of view
Uwe Büsching, Bielefeld, Germany

11.25 - 11.50 Monitoring system for adverse events following hepatitis vaccination
Johannes Hallauer, Germany, and round-table discussion

11.50 - 12.15 School-entry monitoring of vaccination status
Günter Pfaff, Stuttgart, Germany

12.15 - 12.40 Critical review of programme progress
Michael Kramer, Bonn, and Johannes Hallauer, Berlin, Germany

12.40 - 14.00 *Lunch*

SESSION 8 CONCLUSIONS OF THE MEETING

Chair: Mark Kane, USA, and Wolfgang Jilg, Germany

14.00 - 15.30 Presentation of the VHPB meeting conclusions, including discussion
David FitzSimons, Geneva, Switzerland

15.30 Close of the meeting

Part II The Nordic Countries

Almroth G, Ekermo B, Mansson AS, Svensson G, Widell A. Detection and prevention of hepatitis C in dialysis patients and renal transplant recipients. A long-term follow up (1989 - January 1997). *J Intern Med* 2002; 251:119-128.

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BACKGROUND: Hepatitis C is frequent problem in dialysis wards. **DESIGN:** A long time (1989-97) follow up of hepatitis C virus (HCV) infection in a Swedish nephrology unit was performed with anti-HCV screening, confirmatory antibody tests, viral RNA detection and molecular characterization. Case histories were reviewed with focus, onset of infection, liver morbidity and mortality. **RESULTS:** In October 1991, 10% (19 of 184) of the patients in the unit (haemodialysis, peritoneal dialysis and transplanted patients) were verified or suspected HCV carriers, whilst the number at the end of 1996 was 8% (13 of 157). Most patients were infected before 1991 but only in one case from a known HCV-infected blood donor. No new HCV infections associated with haemodialysis occurred during the study period. A total of 13 of 24 viremic patients had HCV genotype 2b, a pattern suggesting nosocomial transmission. This was further supported by phylogenetic analysis of HCV viral isolates in seven. HCV viremia was also common in patients with an incomplete anti-HCV antibody pattern as 8 of the 12 indeterminant sera were HCV-RNA positive. **CONCLUSIONS:** Awareness, prevention, identification of infected patients and donor testing limited transmission. Indeterminant recombinant immunoblot assays (RIBA)-results should be regarded with caution as a result of the relative immunodeficiency in uremic patients. Our data indicate nosocomial transmission in several patients.

Bottiger M, Christenson B, Grillner L. Hepatitis A immunity in the Swedish population. A study of the prevalence of markers in the Swedish population. *Scand J Infect Dis* 1997; 29:99-102.

Swedish Institute for Infections Disease Control, Stockholm, Sweden.

After a 20-year interval, the prevalence of seroimmunity to hepatitis A (HA) was again investigated in a statistical sample of the adult Swedish population. Sera from 3382 of the 4800 originally selected persons were tested. The prevalence of antibodies to HA had not changed since the 1960s when only the Scandinavian population was considered. In the oldest population born at the beginning of this century, the presence of antibodies amounted to 69%. It gradually declined to 6% in those born in the 1940s. In the population born after 1950, the percentage of seropositive individuals was only 2%. A slightly higher prevalence was seen in the big cities, compared with the rural areas (13% vs 9%). Persons of non-Scandinavian origin showed a different pattern. Those from other European countries showed a prevalence of about 70% in all the age-groups investigated. Among the young adults of Arabic or Asiatic origin, the figure was > 90%. The conclusion is that the native Swedish population has a low natural exposure to HA, which has not changed during the last 20 years. Prophylaxis before going to countries where the disease is endemic is strongly recommended.

Broholm KA, Sjödin L, Backlund I, Johansson B, Norder H, Magnus L. Hepatitis B outbreak in a day care center affected several families. It could have been prevented by vaccination of all children. *Läkartidningen* 2001; 98:2337-2238, 2341-2342. [Article in Swedish]

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An outbreak of hepatitis B originating in a family day nursery affected several children with Somali background. The transmission chain was confirmed by sequence analysis of the S gene. In Africa hepatitis B is often spread horizontally among children of pre-school age, a pattern of transmission that was retained in this outbreak. To limit the outbreak 126 children in the nursery and 50 members of staff had to be vaccinated. The total cost for this intervention was estimated to about 300,000 SEK. Considering the great number of immigrants in Sweden from areas highly endemic for hepatitis B the inclusion of vaccination in the general child immunisation program seems to be the most cost effective measure for long term prevention not only of hepatitis B transmission among children but also of venereal spread in early adulthood.

Christensen PB, Krarup HB, Niesters HG, Norder H, Schaffalitzky de Muckadell OB, Jeune B, Georgsen J. Outbreak of hepatitis B among injecting drug users in Denmark. *J Clin Virol* 2001; 22:133-141.

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BACKGROUND: The incidence of hepatitis B is low in Denmark, but injecting drug users (IDUs) remain a high-risk group for this infection. **OBJECTIVES:** The aim of the study was to describe a hepatitis B outbreak among IDUs by comparing existing registers. Additionally, we wanted to analyze the genetic variation of the hepatitis B virus involved in the outbreak. **STUDY DESIGN:** In the County of Funen, registers of laboratory diagnosis, hospital records and reports from clinicians to the Medical Officer of Health (MOH) were compared between 1992 and 1998. HBsAg-positive sera recovered from the epidemic were sequenced and compared to known HBV strains. **RESULTS:** We identified 648 cases of hepatitis B of which 51% (332) were acute infections. The laboratory database identified 96% (319/332) of these, 45% (150/332) were admitted to hospital and 38% (127/332) were reported to public health. By capture-recapture analysis based on MOH reports and hospital records the estimated total number of acute cases were 334 (95% CI 283-385). We sequenced 75 HBsAg-positive samples and identified two very similar strains of genotype D (serotype ayw3) among IDUs involved in the outbreak. **CONCLUSIONS:** The current surveillance system did not detect the majority of acute hepatitis B cases in County of Funen. We suggest laboratory-based surveillance of hepatitis B to be implemented at a national level as this may identify new outbreaks faster and more complete than the current surveillance system.

Christensen PB, Titlestad IL, Homburg KM, Georgsen J, Kristensen T. Hepatitis B core antibodies in Danish blood donors: a surrogate marker of risk behaviour. *Vox Sang* 2001; 81:222-227.

Department of Clinical Immunology, Odense University Hospital, DK 5000 Odense C, Denmark.
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BACKGROUND AND OBJECTIVES: The aim of this work was to determine the prevalence of antibodies to hepatitis B core antigen (anti-HBc) among Danish blood donors and to correlate this with risk factors for blood-borne and sexually transmitted diseases. **MATERIALS AND METHODS:** During a 5-month period, 10,862 consecutive donors in the County of Funen were screened for anti-HBc, and repeat-reactive samples were confirmed by supplementary testing. Information on risk factors was assessed by questionnaire in 585 consecutive anti-HBc-negative blood donors and compared with information obtained from confirmed positive donors. **RESULTS:** The prevalence of confirmed positive anti-HBc among donors was 0.70% (76/10 862, 95% confidence interval [CI]: 0.55-0.87). One donor was positive for anti-HBc immunoglobulin M (IgM); none tested positive for hepatitis B virus (HBV) DNA. In a logistic regression analysis, age, female gender, tattoos and commercial sexual relations, were independent predictive factors for the presence of anti-HBc. **CONCLUSION:** Anti-HBc is a surrogate marker for previous risk behaviour in the Danish blood donor population. We suggest that screening for anti-HBc may be used among new donors to supplement interviews on risk behaviour.

Christenson B, Bottiger M, Grillner L. The prevalence of hepatitis B in Sweden; a statistical serosurvey of 3381 Swedish inhabitants. *Epidemiol Infect* 1997; 119:221-225.

Department of Communicable Disease Control and Prevention, Stockholm County Council, Karolinska Hospital, Sweden.

The prevalence of hepatitis B virus markers in the adult Swedish population was investigated according to age, sex, origin and demographic stratum. Sera were collected from 3382 persons in 1990-1991. The sera were selected on a statistical basis considered to be representative of the Swedish population from adults aged \geq 18 years. Two of the sera (0.06%) were found to be hepatitis B surface antigen positive. The two hepatitis B carriers were of non-Scandinavian origin as were (8.9%) of those tested. A total of 90 persons had a marker of previous, hepatitis B virus infection, i.e. antibodies against hepatitis B core antigen. Of these, 66 (2.0%) were of Scandinavian origin and 24 (18.1%) from highly endemic areas. The overall hepatitis B virus marker prevalence was 2.7%. The highest age-specific prevalence of hepatitis B markers in those of Scandinavian origin was in those born in 1939 and earlier. In this age group, women had a significantly higher prevalence (3.6%) than males (1.9%). The lowest prevalence was found in those born in 1970 and later. No significant, age-related differences between younger or older persons, or between men and women, could be found in persons of non-Scandinavian origin. The results showed significant differences in exposure to hepatitis B virus among the indigenous population, compared with those of non-Scandinavian extraction. The results do not support the proposal to include hepatitis B vaccination in the Swedish immunization schedule.

Dalgard O, Jeansson S, Skaug K, Raknerud N, Bell H. Hepatitis C in the general adult population of Oslo: prevalence and clinical spectrum. *Scand J Gastroenterol* 2003; 38:864-870.

Medical Department, Aker University Hospital, Oslo, Norway. olav.dalgard@ioks.uio.no

BACKGROUND: The prevalence of hepatitis C in Northern Europe has not been well described. This study aimed to estimate the prevalence and spectrum of hepatitis C virus infection in the general adult population of Oslo, Norway. **METHODS:** The study was part of the Oslo Health Study 2000-2001 and included a random selection of individuals older than 30 years living in Oslo County. Sera from 11,456 participants were screened for anti-HCV (EIA-3), positive samples were

confirmed (RIBA-3) and examined for HCV RNA (PCR). All anti-HCV positive patients were offered clinical evaluation. Routine biochemical liver tests were performed. Candidates for HCV treatment were asked to undergo a percutaneous liver biopsy. RESULTS: Among 11,456 participants HCV RNA was detected in 62 (0.5%) and HCV RNA with raised serum alanine aminotransferase (ALT) in 46 (0.4%). Anti-HCV was detected in 78 (0.7%) with a peak prevalence of 1.5% among subjects 40 and 45 years old. Being anti-HCV-positive was associated with being unmarried, unemployed and having low education. Anti-HCV prevalence was higher among subjects with alcohol-related problems compared to those without (4.4% versus 0.6%, $P < 0.001$). It was also higher among smokers compared to non-smokers (2.0% versus 0.2%, $P < 0.001$). In 33 liver biopsies, bridging fibrosis was seen in 8 (24%) and cirrhosis in 1 (3%). The route of transmission was injecting drug use in 67%, transfusion in 6% and unknown in 27%. CONCLUSION: In this population-based survey the prevalence of chronic hepatitis C was 0.5% and ALT was raised in 80% of those with chronic infection.

Dickmeiss E, Christiansen AH, Smith E. Risk of disease transmission via donor blood in Denmark at the turn of the century. *Ugeskr Laeger* 2001; 163:2628-2632. [Article in Danish]

H:S Rigshospitalet, Klinisk immunologisk afdeling og epidemiologisk afdeling, Statens Serum Institut, København.

INTRODUCTION: Published results of donor blood screening in Denmark were used to calculate the risks of window phase donations. METHODS: The main parameter was the frequencies of a confirmed positive donation from regular donors per 100,000 donations are: 0.34, for HIV; 0.47 for hepatitis C virus; 0.53 for hepatitis B virus; and nil for HTLV I/II. The mean interdonation interval between donations from regular donors is six months year. Window phase duration were estimated to be 22 days for anti-HIV; 10 weeks for anti-HCV; and 56 days for HBsAg. Blood from candidate donors is not used in Denmark. Thus, the risk of a window phase donation equals the risk of a window phase donation in donations from regular donors. RESULTS: The risks of window phase donations in Denmark are: 1 in 2,000,000 for HIV; 1 in 500,000 for hepatitis C; 1 in 250,000 for hepatitis B; and immeasurably low for HTLV I/II. DISCUSSION: The measures taken nowadays to prevent infection from allogeneic blood transfusion have resulted in a risk reduction of HIV transmission by a factor 50 and of HCV transmission by a factor 400, compared with the risks prevailing in Denmark in the early 1980s. The present very low risk renders obsolete predeposited autologous blood solely on the indication to prevent infection. Zero risk of transmission of HIV and HCV might be approached by introducing NAT screening for these viruses.

Fisker N, Georgsen J, Stolborg T, Khalil MR, Christensen PB. Low hepatitis B prevalence among pre-school children in Denmark: saliva anti-HBc screening in day care centres. *J Med Virol* 2002; 68:500-504.

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Although Denmark has a low hepatitis B virus (HBV) prevalence, HBV transmission has been reported in Danish day-care centres. The aim of this study was to validate saliva anti-HBc testing as a method for HBV screening, the applicability of saliva sampling to pre-school children, and to determine the HBV prevalence in Danish day-care centres with a high proportion of immigrants.

For validation, paired saliva and plasma samples were obtained from blood donors and injecting drug users. Employees and children in day-care centres with a high proportion of immigrant children were offered saliva screening followed by blood test if positive. The specificity and sensitivity of anti-HBc tests on saliva was 100% (102 blood donors and four injecting drug users) and 85.9% (61 of 71 anti-HBc-positive injecting drug users), respectively. In all samples from HBsAg (n = 7) or anti-HBc IgM-positives (n = 9), anti-HBc was detected in saliva. Adequate saliva samples were obtained from 93% (588/634) of children and 100% (166/166) of employees participating in the day-care centre survey. Among children 55% were of non-Scandinavian origin and only one (0.2%, 95% CI [0.0; 1.0]) was HBV positive. Among employees the corresponding values were 22% and 7 (4.2%). The positive predictive value of the saliva test was 25% (1/4) among children and 88% (7/8) among adults. In conclusion, saliva testing is feasible for HBV screening among children in low prevalence populations, but any anti-HBc reactivity should be confirmed by plasma analysis. The HBV prevalence in pre-school children in Denmark is low even among immigrants from endemic areas.

Frederiksen JR, Ronne T. Selective screening for hepatitis B of pregnant women with previous acute hepatitis B. *Ugeskr Laeger* 2002; 164:187-190. [Article in Danish]

Epidemiologisk afdeling, Statens Serum Institut, København.

INTRODUCTION: The aim of this study was to examine the performance of the selective screening programme for hepatitis B (HB) in pregnancy. **MATERIAL AND METHODS:** Notifications of women with acute HB in the period 1981-1997 were traced in the National Birth Registry. For children born after the HB event, details of the records on the results of HB testing and other information about the previous HB disease were obtained from the maternity wards. **RESULTS:** The study group comprised 129 mothers and their 185 deliveries. Of the 185 deliveries, 31% took place without any information about the previous HB disease and 51% without testing for HB. When these results were related to the information on the notification form regarding the mode of transmission, it transpired that the proportion with an unknown mode of transmission was higher in those with no information about previous HB in the maternity records than in those with information (43% vs 18%). Of 18 infants delivered of 13 chronically infected mothers, four did not receive the proper immunoprophylaxis. **DISCUSSION:** The study shows that a selective screening programme as used in Denmark is not good enough to identify pregnant women at risk of chronic HB infection. The main problems are related to failure to identify risk factors of hepatitis B transmission. Screening and treatment failure in siblings delivered of chronically infected mothers was also found. As in most other western countries a general programme should replace the selective screening programme.

Gjeruldsen S, Myrvang B. Hepatitis B virus infection in drug addicts: no acute fatalities, no chronicity and could have benefits. *APMIS* 2002; 110:620-624.

Department of Infectious Diseases, Ullevål University Hospital, Oslo, Norway.

In a group of 159 drug addicts with acute hepatitis B in the 1970s there were no fatalities. During an observation period of about 25 years, 51 of the 159 died of various causes, but no deaths could be attributed to the hepatitis B infection. From 1998 to 2001, a follow-up examination of 53 of the 108 patients still alive, none of the 53 had a chronic hepatitis B virus infection. Fifteen out of

thirty-five patients who had completely stopped using narcotics claimed that hospitalisation for acute hepatitis B had been an important factor in their decision to quit drugs.

Gjorup IE, Skinhoj P, Bottiger B, Plesner AM. Changing epidemiology of HBV infection in Danish children. *J Infect* 2003; 47:231-235.

Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100, Copenhagen, Denmark

Hepatitis B continues to be a worldwide threat to human health, especially if infection occurs in childhood. Universal vaccination is recommended by WHO, but has not been implemented in the Scandinavian countries, Holland and UK, because of a low incidence rate. However, clinically overt infections are rare in childhood. We therefore performed a nation-wide serosurvey for HBV markers in 2428 children aged primarily 6-16 years from 16 primary schools in Denmark. Anti-HBc was found in altogether 20 children (0.8%), 12 of whom were among 144 immigrant children (8.3%) compared to 8 (0.4%) in those born in Denmark. Three of the children, all immigrants, were HBsAg-positive indicating chronic infection. At school level no relation of anti-HBc in Danish-born children was found to schools with high number of immigrant children or schools with HBsAg-positive children indicating a low risk of hepatitis B transmission in this setting. The results do not support implementation of general vaccination, but stress the need for HBV screening in immigrants as it provides a mean for immunization of close contacts at risk and information on prevention.

Hoffmann G, Berglund G, Elmstahl S, Eriksson S, Verbaan H, Widell A, Lindgren S. Prevalence and clinical spectrum of chronic viral hepatitis in a middle-aged Swedish general urban population. *Scand J Gastroenterol* 2000; 35:861-865.

Department of Medicine, Lund University, University Hospital, Malmö, Sweden.

BACKGROUND: Although abundant data are available regarding the prevalence of chronic hepatitis B or C virus (HBV, HCV) among both blood donors and patients with liver diseases, corresponding data for the general population are scarce. Accordingly, this study was designed to investigate the prevalence and clinical spectrum of HBV and HCV in a general Swedish middle-aged urban population. **METHODS:** Demographic data and blood samples were collected from subjects enrolled in a prospective study of cancer development in the city of Malmö (population 250,000). The participation rate in the preliminary examination was 46.2%. From 12,445 individuals born between 1926 and 1945 and included in the study, a statistically representative subsample of 6103 persons was selected. Blood samples were available from 5533 of these. The mean age of the subjects in the series was 58.5 +/- 5.9 years, and 59% were women. The HBV markers used were anti-HBc and HBsAg. HCV antibodies were detected with a third generation anti-HCV ELISA, followed by immunoblotting (RIBA 3) if the test was positive. Immunoblot-reactive samples were analysed for HCV-RNA by polymerase chain reaction and genotyped. In all patients with signs of chronic HBV or HCV, epidemiological data were evaluated and liver biopsies obtained. **RESULTS:** Of the series as a whole (n = 5533), 4.2% (n = 211) tested positive for anti-HBc and 0.2% (n = 10) for HBsAg. RIBA 3 analysis showed 0.37% (18/5533) to be anti-HCV-positive, of whom 83% (15/18) were HCV-RNA-positive. Apart from two (both from HBsAg carriers) with normal histology, all liver biopsies manifested various degrees of inflammation and fibrosis. Among anti-HCV-positives, median grade was 6 and median stage 1

(Knodell score). CONCLUSION: The prevalence of both chronic HBV and HCV is low in the Swedish general urban middle-aged population. Nonetheless, the long-term effects on the population and the health care system may be significant.

Iwarson S. Why the Scandinavian countries have not implemented universal vaccination against hepatitis B. *Vaccine* 1998; 16(Suppl):S56-S57.

Sahlgrenska University Hospital, Göteborg, Sweden.

Within the 50 member states of the WHO European region, HBsAg carriage rates vary from a high of approximately 20% to a low of 0.05%. The Scandinavian countries have the lowest carriage rates in the region (0.05%). The situation in Sweden is representative of the situation throughout Scandinavia: although a substantial number of immigrants to Sweden are HBsAg-positive, acute cases of hepatitis B continue to be seen mainly in drug addicts and their contacts and to a certain extent, in male homosexuals with multiple partners. Public health officials and governments in Scandinavia are unwilling to introduce universal vaccination of infants because hepatitis B infection is viewed as a limited public health problem that does not justify the expense and other efforts of universal immunization.

Jensen L, Heilmann C, Smith E, Wantzin P, Peitersen B, Weber T, Krosgaard K. Efficacy of selective antenatal screening for hepatitis B among pregnant women in Denmark: is selective screening still an acceptable strategy in a low-endemicity country? *Scand J Infect Dis* 2003; 35:378-382.

Department of Paediatrics, Hvidovre University Hospital, Hvidovre, Denmark. lise@dadlnet.dk

The prevalence of hepatitis B virus (HBV) carriage in Denmark is unknown, but expected to be low (0.1%). This study aimed to evaluate the efficacy of selective antenatal screening for HBV infection and the epidemiology of HBV and hepatitis C virus (HCV) among pregnant women. 4098 women were included in the study. Blood tests were examined for hepatitis B surface antigen (HBsAg), anti-hepatitis B core antigen (HBc) and anti-HCV. Case records were studied to evaluate whether patients at risk for HBV infection had been tested. Among the 4098 women, 18 (0.4%), 95% confidence interval (95% CI) 0.3-0.71, were HBsAg-positive. All had a risk factor for HBV infection. Only 13 (72%) were identified as HBsAg-positive in the selective screening programme. 115 women (2.8%, 95% CI 2.3-3.4) were anti-HBc-positive only. 95 (83%) were at risk for HBV. Only 72 of these (63%) were tested for HBsAg. The screening programme in this area of Denmark did not pick up one-third of pregnant women at risk of HBV.

Kaczynski J, Hansson G, Hermodsson S, Olsson R, Wallerstedt S. Minor role of hepatitis B and C virus infection in the etiology of hepatocellular carcinoma in a low-endemic area. *Scand J Gastroenterol* 1996; 31:809-813.

Department of Medicine, University of Göteborg, Ostra Sjukhuset, Sweden.

BACKGROUND: The etiologic role of hepatitis B (HBV) and C virus (HCV) for hepatocellular carcinoma (HCC) in a low-endemicity area is obscure. METHODS: Patients suspected of having primary liver cancer (PLC) in Göteborg, Sweden (n = 113), were tested serologically for HBV

surface antigen and antibodies to HBV surface and core antigens. The presence of HBV surface and core antigens in cancer and non-neoplastic liver tissue in HCC cases was investigated immunohistochemically. Antibodies to HCV were tested by third-generation tests. The prevalence of HBV and HCV infection was compared in 73 patients with HCC and 32 patients with a final diagnosis other than PLC. RESULTS: No patient had signs of chronic HBV infection. Seven of 64 (11%) HCC patients were anti-HCV-positive, compared with 1 of 31 (3%) without PLC. All seven patients with HCC and HCV infection had liver cirrhosis, and two were alcoholics. Alcoholism was judged the commonest (42%) cause of cirrhosis. CONCLUSION: Contrary to areas with a high incidence of HCC, chronic viral hepatitis, particularly HBV, seems to play a minor etiologic role for HCC in Sweden compared with alcohol-related cirrhosis.

Kidd-Ljunggren K, Broman E, Ekvall H, Gustavsson O. Nosocomial transmission of hepatitis B virus infection through multiple-dose vials. *J Hosp Infect* 1999; 43:57-62.

Department of Infectious Diseases, University Hospital, Lund, Sweden. karin.kidd@infek.lu.se

The source of acute hepatitis B virus (HBV) infection in two women (55 and 72 years old) was investigated. They displayed no risk factors for acquiring HBV infection, other than treatment with local anaesthetic injections some months previously. The HBV strains were sequenced and showed distinct homology to strains seen in Swedish intravenous drug users (IVDUs). Prior to these patients' acute infection, an outbreak of HBV had occurred among IVDUs in the same county. Analysis of the HBV strains from six of these IVDUs showed their core promoter, precore and pre-S sequences (679 nucleotides) to be identical to those from the two patients. Cross-contamination between samples was excluded and the most likely source of infection was thought to be multiple-dose vials of local anaesthetic that had been contaminated with the HBV strain circulating among the IVDUs population in the community. We believe that multiple-dose vials have no place in modern healthcare and recommend sequence homology analysis as an alternative or additional way to trace a source of HBV infection.

Lindh M, Horal P, Norkrans G. Acute hepatitis B in Western Sweden - genotypes and transmission routes. *Infection* 2000; 28:161-163.

Department of Clinical Virology, Göteborg University, Sweden. magnus.lindh@microbio.gu.se

A retrospective study of acute hepatitis B (AHB) during 1995-1996 in Göteborg, Sweden, was carried out to investigate whether the increasing number of hepatitis B virus (HBV) carriers due to immigration in northwestern Europe has influenced the incidence or genotype heterogeneity. 24 cases of AHB were identified, the probable transmission route of which was intravenous drug use (IVD use) in 11 (46%), heterosexual in six (25%), homosexual in one, hemodialysis in two and unknown in four cases. In no case was the source an immigrant with chronic HBV infection. Genotype D was seen in 12 patients, seven being anti-HCV-positive IVD users, two probably infected heterosexually and three with an unknown source. Genotype A was found in six patients: three IVD users, a sexual partner of an IVD user and two dialysis patients. Genotype B was found in one patient infected during travel to Vietnam, and genotype C in one patient, probably infected sexually from a previously identified chronic carrier. In conclusion, genotype D is the main genotype and IVD use still the major risk factor for AHB in Göteborg, while transmission from immigrants appears to be of minor importance despite the fact that this group comprises over 90% of the young, highly infectious carriers.

Ludviksdottir D, Skulason H, Jakobsson F, Thorisdottir A, Cariglia N, Magnusson B, Thjodleifsson B. Epidemiology of liver cirrhosis morbidity and mortality in Iceland. *Eur J Gastroenterol Hepatol* 1997; 9:61-66.

Department of Medicine, National University Hospital, Reykjavik, Iceland.

BACKGROUND: The mortality from liver cirrhosis in Iceland is the lowest in the Western world. **OBJECTIVE:** To study the epidemiology of liver cirrhosis mortality and morbidity in Iceland and to obtain a reliable separation between alcoholic cirrhosis (AC) and non-alcoholic cirrhosis (NAC) by using multiple data sources. **METHODS:** The study included the whole population of Iceland. Mortality was studied through death certificate data for the period 1951-90 and morbidity (clinical incidence) through hospital, autopsy and biopsy records for the period 1971-90. **RESULTS:** The average mortality for AC in age group 20 years and older was 8.6 and for NAC 19.2 per 10(6)/year and the average clinical incidence was 22.1 per 10(6)/year for AC and 25.9 per 10(6)/year for NAC. In the morbidity study 44% of cases were due to AC. In the mortality study 24% of cases were due to AC but the data suggested an underreporting of AC for males at a rate of 30%. There was a significant decrease in AC mortality with time but no change in NAC. Average alcohol consumption of inhabitants aged over 15 years increased from 2.1 to 4.9 litres per year (130%) during the period 1951-90. **CONCLUSION:** The incidence of cirrhosis in Iceland is very low for both AC and NAC, accounting for only 0.2% of total deaths. The reasons are unknown. The low incidence of AC in Iceland is probably partly due to low alcohol consumption. The decreasing incidence of AC despite 130% increase in alcohol consumption is thought to be due to intensive treatment of alcoholism. A low prevalence of hepatitis B and C probably contributes to the low incidence of NAC.

Mansson AS, Moestrup T, Nordenfelt E, Widell A. Continued transmission of hepatitis B and C viruses, but no transmission of human immunodeficiency virus among intravenous drug users participating in a syringe/needle exchange program. *Scand J Infect Dis* 2000; 32:253-258.

Department of Medical Microbiology, University of Lund, University Hospital, Malmö, Sweden.

The virological efficacy of a syringe/needle exchange program was evaluated in a cohort incidence study. Of 698 intravenous drug users (IVDUs) initially recruited, 15 (2.1%) were HIV-positive at baseline. Adequate follow-up was possible in 515 (74%) and showed no new cases of HIV infection during a median of 31 months. Most IVDUs had been previously exposed to HBV (anti-HBc-positive 70.1%) and HCV (anti-HCV-positive 90.7%). Of those 159 IVDUs negative at baseline for anti-HBc and/or anti-HCV, 56 (35%) seroconverted to one or both viruses during follow-up, corresponding to 11.7 seroconversions/100 y at risk for HBV and 26.3 seroconversions/100 y for HCV. Multiple logistic regression analysis showed hepatitis seroconversion to correlate with imprisonment during the study (OR 2.2; 95% CI 1.04-4.74), absence of drug-free periods (OR 5.7; CI 1.44-22.3) and frequent syringe/needle exchanges (OR 1.31; CI 1.02-1.7). The absence of HIV spread was probably partly due to the low prevalence of HIV-infected IVDUs in the city. Despite free syringes and needles, both HBV and HCV continued to spread at high rates. Nevertheless, syringe/needle exchange programs, coupled with monitoring of serostatus provide good surveillance and are valuable for further assessment of remaining risks.

Roll M, Norder H, Magnius LO, Grillner L, Lindgren V. Nosocomial spread of hepatitis B virus (HBV) in a haemodialysis unit confirmed by HBV DNA sequencing. *J Hosp Infect* 1995; 30:57-63.

Department of Medicine, Danderyd Hospital, Sweden.

An outbreak of hepatitis B virus (HBV) infection in a haemodialysis unit is described. Four patients in the unit contracted subclinical HBV infection within three months. DNA sequence analysis of the S gene of HBV isolates from chronic carriers and newly infected patients in the unit aided in tracing possible transmission pathways. Three newly infected patients had received partial or complete HBV vaccination previously. HBV was rapidly cleared from all three although the anti-HBs titre had not reached 10 IU/l in any of them at the time of infection.

Samdal HH, Blystad H, Eskild A, Fjaerli HO, Nordbø SA, Stray-Pedersen B, Torvik HP. Hepatitis C virus infection among pregnant women and their children in Norway. *Tidsskr Nor Laegeforen* 2000; 120:1047-1050. [Article in Norwegian]

Avdeling for virologi, Statens institutt for folkehelse, Oslo.

Estimates indicate the births of 6 to 78 children vertically infected with hepatitis C virus infection each year in Norway. There is insufficient knowledge of the magnitude of this health problem and the National Institute of Public Health commissioned the authors to approach issues relating to vertical transmission of hepatitis C virus (HCV) infection in Norway. The risk of vertical transmission of HCV appears to be associated with the titre of the maternal viral load. Vertical transmission from nonviraemic mothers has not been demonstrated. No postexposure prophylaxis exists. There is a lack of association between vertical HCV transmission and delivery mode and no association with breast feeding. Universal screening for HCV infection among pregnant women is not recommended. Children born to women known to be HCV-positive should be followed up with antibody and polymerase chain reaction investigations in order to clarify their HCV status. More studies of HCV infection among pregnant women and their children in Norway are needed.

Sangfelt P, Reichard O, Lidman K, von Sydow M, Forsgren M. Prevention of hepatitis B by immunization of the newborn infant - a long-term follow-up study in Stockholm, Sweden. *Scand J Infect Dis* 1995; 27:3-7.

Department of Infectious Diseases, Karolinska Institute, Danderyd Hospital, Sweden.

In order to assess the present hepatitis B immunization program in Stockholm, Sweden, 212 children of HBsAg carrier mothers were followed up 2-9 years after birth. In babies of HBeAg-positive mothers a combined passive and active immunization schedule with hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine was used. Among 25 children to such mothers, 1 HBsAg carrier and 5 children with asymptomatic seroconversion were found. To newborns of HBeAg-negative/anti-HBe-negative mothers, only vaccine was given. Among 15 such children, no HBsAg carrier (but 1 child with an asymptomatic seroconversion) was found. In babies of HBeAg-negative/anti-HBe-positive mothers, immunization was withheld between 1983 and 1987. Among 90 such children, 1 HBsAg carrier and 8 asymptomatic seroconversions were detected. After 1987, newborns in this group were vaccinated whereafter 3 asymptomatic seroconversions were found among 82 children. We conclude that in low prevalence areas a screening program for HBsAg

should be offered to pregnant women originating from hepatitis B endemic regions, since immunoprophylaxis gave long-term protection to most children at risk. Children born to HBeAg-positive mothers should receive vaccine in combination with HBIG, whereas for children of mothers lacking HBeAg, vaccination only seems sufficient, at least if a rapid vaccination schedule is used.

Söderström A, Lindh M, Eriksson K, Horal P, Krantz M, Kristiansson B, Lindberg J, Norkrans G. Chronic hepatitis B in children in Gothenburg, Sweden. *Scand J Infect Dis* 1999; 31:109-114.

Department of Infectious Diseases, Sahlgrenska University Hospital, Ostra, Göteborg, Sweden.

Sweden is a low-prevalence area for hepatitis B, but the number of chronic carriers has increased during the last decade due to immigration. Out of a total of 120 children with identified chronic hepatitis B in Gothenburg, Sweden, 93 were investigated during the 2-year period 1994-95. The children had a mean age of 10.9 years and originated from 21 different countries. Most infections were discovered during various screening programmes after arrival in Sweden. A total of 90 of the 93 children were HBV-DNA-positive by Amplicor HBV Monitor (Roche Diagnostics) and 58% (54/93) were HBeAg-positive. All children either originated from areas with a high or medium prevalence of HBV infection (81/93, 87%) or were born in Sweden to mothers originating from high or medium prevalence countries (12/93, 13%). Three of these 12 children were vertically infected in spite of adequate immunoprophylaxis and 8 were born to mothers with undiscovered chronic HBV infection. In all, 34 children had mothers who were HBsAg-positive. No overt case of transmission was notified in day-care centres or schools, or from a child to a non-immune parent. None of the children reported any symptoms of liver disease, but 38% (35/93) had elevated aminotransferases. Therefore, screening programmes are essential to identify chronic HBV infection in children in order to prevent transmission and to find individuals at risk of progressive liver damage who should be considered for treatment.

Stene-Johansen K, Jenum PA, Hoel T, Blystad H, Sunde H, Skaug K. An outbreak of hepatitis A among homosexuals linked to a family outbreak. *Epidemiol Infect* 2002; 129:113-117.

Department of Virology, National Institute of Public Health, Oslo, Norway.

Several outbreaks of hepatitis A occurred in Norway in 1995-1998. Molecular epidemiology was used to follow the spread of hepatitis A virus in the population. Distinct strains of hepatitis A virus (HAV) were detected by reverse transcriptase-polymerase chain reaction (RT-PCR) and subsequent sequencing in serum from patients in different communities at risk of infection. Two HAV strains were detected in an outbreak among 26 men having sexual contact with other men. One of these strains was also detected in a geographically limited family outbreak. The family outbreak was first believed to be acquired abroad. The sequence information linked the two outbreaks, and epidemiological and serological analyses revealed the transmission route. This study demonstrates the importance of molecular epidemiology in outbreak investigation, surveillance and monitoring of hepatitis A in the population.

Stene-Johansen K, Skaug K, Blystad H. Surveillance of hepatitis A by molecular epidemiologic studies. *Tidsskr Nor Laegeforen* 1999; 119:3725-3729. [Article in Norwegian]

Avdeling for virologi, Statens institutt for folkehelse, Oslo.

Hepatitis A virus was studied by molecular epidemiology in connection with an outbreak of hepatitis A associated with intravenous drug users (IVDU) in Norway. Hepatitis A virus was characterised by sequencing 114 of 1,242 notified cases of hepatitis A from January 1995 to July 1998. One hepatitis A variant (IVDU variant I) was detected among IVDU during an outbreak of hepatitis A, as well as among 19 out of 49 cases with no apparent association to this outbreak. During the autumn of 1997, a new variant (IVDU variant II) was detected in the IVDU communities. Genotyping of virus from imported cases associated with travel to endemic regions, revealed that they were distinct from the two other IVDU variants. Hepatitis A has disseminated among IVDU over years; this indicates that hepatitis A is endemic in these communities. At the turn of the year 1997/98, there was a smaller outbreak of hepatitis A among homosexual men in Oslo, distinguished by genotyping from the outbreaks in the IVDU communities. By molecular epidemiology we have been able to identify individual outbreaks of hepatitis A and distinguish them from the IVDU outbreak.

Struwe J, Giesecke J. Cost of acute hepatitis B infection in Swedish adults. *Scand J Infect Dis* 1993; 25:693-697.

Department of Infectious Diseases, Huddinge Hospital, Sweden.

In order to register data on costs for episodes of acute hepatitis B virus (HBV) infection in adults, the medical records from 70 adults with acute HBV infection seen at Roslagstull's Hospital in Stockholm, Sweden, were reviewed. All cost-consuming events due to medical treatment, absence from work, and secondary prophylaxis were registered. The average cost was 1,230 pounds for medical treatment, 570 pounds for work loss and 290 pounds for secondary cases and prophylaxis, a total of 2,090 pounds in 1992 prices. This figure is considerably lower than that reported in 3 previous European studies. Accurate estimates of the costs for a case of HBV infection, as well as those of different vaccination strategies, are essential when economic aspects of HBV vaccination programmes are discussed.

Sylvan S. WHO spearheads global initiative to eradicate hepatitis B. *Läkartidningen* 2000; 97:3738-3740. [Article in Swedish]

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It is estimated that over 350 million people live with a chronic hepatitis B virus (HBV) infection, claiming over one million deaths per year due to progress of the chronic disease to cirrhosis and/or hepatocellular carcinoma (HCC). An extended program of immunization including hepatitis B vaccine for children under one year of age has been launched in more than 110 countries. Recent studies conclude that mass hepatitis B immunization is effective in preventing HBV infection and has resulted in a decrease in the occurrence of HCC in children living in countries where hepatitis B is endemic. However, the vast majority of infected children live in the poorest developing countries in Africa and Asia that currently cannot afford the vaccine or lack the basic infrastructure necessary to deliver a national immunization service. The Global Alliance for Vaccines and Immunization (GAVI) was established in 1999 as an alliance of WHO, UNICEF, the World Bank, industry, foundations, and other partners to reinvent immunization for the 21st century, by forging

a common vision and new ways of working together at global, regional and national levels. WHO recommends global elimination of hepatitis B by universal infant and/or adolescent immunization, but health planners in Sweden and the other Scandinavian countries, the Netherlands and UK have not yet been convinced of the cost-effectiveness of HB-prevention through routine childhood immunization with HB-vaccine. The inclusion of hepatitis B vaccine in already available multivalent vaccines may alter this situation in the future, but until then an intensified vaccination strategy aimed at those groups of individuals that are particularly at risk for hepatitis B should be adopted in accordance with the recommendations of The Swedish National Board of Health (SOSFS 1991:2) and local instructions from the County Medical Officer for Communicable Disease Control.

Wandall DA, Christiansen AH, Samuelsson IS. Hepatitis A in Denmark. Notified cases 1996-1999. *Ugeskr Laeger* 2000; 162:6233-6236. [Article in Danish]

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INTRODUCTION: The aim of the study was to describe the incidence of hepatitis A in Denmark with the emphasis on the role of immigrants in relation to transmission and prevention of the disease. **METHOD:** A retrospective study of notified cases of hepatitis A during the period, 01.01.1996 - 31.12.1999. **RESULTS:** A total of 398 notified cases were examined, 45% of which occurred in immigrants. The average incidence per year was 13.2 per 100,000 for immigrants and 1.1 per 100,000 for Danes. The incidence for immigrants from Pakistan and Turkey was 4-5 times that for immigrants as a whole. The median age in immigrants was eight years and in Danes 29 years. Immigrants were hospitalised in 35% of the cases. Of children below ten years of age 31% were admitted. Danes were hospitalised in 43% of the cases, and of children below ten years of age 44% were admitted. Infection was acquired abroad for 71% of immigrants, 49% of whom visited Pakistan or Turkey. Of those infected in Denmark, person-to-person transmission was the most common mode of infection for both groups. Immigrants who had been travelling to endemic areas were involved in 21 of 34 outbreaks. **CONCLUSION:** The incidence of hepatitis A in Denmark seems to relate highly to the children of immigrants, who come from high endemic areas. Vaccination of those above one year of age is recommended when travelling abroad if anticipated. Economic compensation could be considered.

Weiland O. Give all children vaccine against hepatitis B! *Läkartidningen* 2001; 98:3780-3784. [Article in Swedish]

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The number of individuals with chronic hepatitis B in Sweden has increased, mainly due to new immigrant groups. A safe and effective hepatitis B vaccine exists which allows a flexible dosing schedule. Most countries in the world adhere to the WHO recommendations to include this vaccine in the childhood vaccination regimen. This has led to a substantial drop in morbidity and mortality from hepatitis B virus infections in high-endemic regions such as Taiwan. Sweden should consider changing its vaccination policy, including the vaccination of high-risk groups only, and consider vaccination of all infants.

PART III GERMANY

Angele S, Philippi B. National development of health targets in Germany - Forum Health Targets Germany. *Z Ärztl Fortbild Qualitätssich* 2003; 97:59-65. [Article in German]

Health targets.de is a co-operation between the German Federal Ministry of Health (BMG) and the Association for Social Security Policy and Research (GVG) and is funded by the Ministry. Health targets.de unites numerous players in the field of health care and establishes a round table to put the development and implementation of some exemplary health targets to the test by the players themselves. The players are required to reach consensus about health targets and strategies and propose them collectively to health policy makers. Herewith, health targets.de aims to establish this 'health targets' tool in order to supplement existing instruments of German health policy. Furthermore, its aim is to strengthen the idea of target setting at all levels of the health care system. Health targets.de was started in December 2001 and will present results at the beginning of 2003. Interim results are made accessible on the Internet. Since December 2001 health targets.de has so far been developing five specific health targets concerning diabetes; breast cancer; reduction in tobacco consumption; nutrition, physical activities and stress reduction in children and adolescents; and the improvement of the patients' and citizens' competence in health-related issues. Further topics will be dealt with later. For additional information see www.health-targets.de.

Diekamp U, Kamutzky K, Windel CD. Anti-hepatitis C prevalence and incidence in 2.8 million blood donors in Lower Saxony - residual transfusion-associated HCV infection risk. *Beitr Infusionsther Transfusionsmed* 1997; 34:5-10. [Article in German]

Blutspendedienst der DRK-Landesverbände NSOB, Springe, Germany.

561 out of 2,777,021 blood donations from 582,655 donors tested confirmed positive for anti-HCV (RIBA II or Matrix Dot), 549 of them at their first donation, in their first HCV test ever, or in the first HCV test with a new, more sensitive test generation. Thus, our anti-HCV prevalence is 0.037% or 1 in 2,679 donations; among first-time donations it is five times higher than among repeat donations. Twelve repeat donors seroconverted, yielding an anti-HCV incidence of 0.0008% or 1 in 122,570 repeat donations and a seroconversion rate of 2.32 per 10(5) repeat donor person-years. The residual risk associated with transfusion of blood for repeat donors amounts to 5.2 per 10(6) repeat donations. We estimate a risk reduction from introduction of direct virus genome testing after PCR to be at 3.7 per 10(6) repeat donations. Look-backs among recipients of the last seronegative blood products from 12 donors with subsequent seroconversion revealed no recipient infection. Thus, today the residual risk for HCV transmission through transfusion of blood components obtained from Lower Saxony blood donors is quite low. The added safety from direct virus genome testing after PCR is considered extremely low, which casts doubt on the cost-effectiveness of such a measure.

Diel R, Schneider S. Transmission of hepatitis A in Hamburg, Germany, 1998-1999 - A prospective population based study. *Eur J Epidemiol* 2001; 17:175-182.

School of Public Health, University of Düsseldorf, Germany. rol.diel@t-online.de

To study the pattern of transmission of HAV in a large urban community a prospective cohort study was conducted in Hamburg between 1 January 1998 and 31 December 1999. Four hundred and eleven patients were classified as hepatitis A cases comprising 144 foreign and 267 German persons. Univariate analyses were carried out to examine differences between socio-demographic, clinical and behavioural characteristics. To determine independent predictors for HAV infection a multiple logistic-regression model was used. The principal risk factor was travel to areas where hepatitis A is endemic, with 32.6% (n= 134/411) of all documented cases of hepatitis A. Foreign patients who had acquired the infection abroad, mostly children, accounted for the majority of these cases. Of all 411 cases, 42 (10.2%) were associated with parenteral drug, followed by day-care or school contact (8.3%; n = 34). Outbreaks contributed to 11.4% of cases (n = 47), but only 7.1% (n = 29) were household contacts. The low incidence rate among exposed persons in the households of those infected was similar in the groups of foreign and German nationals (17/384 = 4.4% and 12/231 = 5.2%, respectively), which may demonstrate a good hygienic level in general. Our findings suggest that preventive measures such as the improvement of hygienic conditions in a defined general population may contribute to a reduced incidence of hepatitis A. Nevertheless, because hygienic standards may change with time, this policy should be supplemented by targeted vaccination of groups at risk.

Erhardt A, Theobald I, Petry W, Rohrborn A, Heintges T, Wettstein M, Haussinger D. Hepatocellular carcinoma: rising incidence of hepatitis C virus-associated cases at a university clinic in Germany. *Dtsch Med Wochenschr* 2002; 127:2665-2668. [Article in German]

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BACKGROUND AND OBJECTIVE: Hepatocellular carcinoma (HCC) ranks eighth among malignant tumors worldwide. Western countries belong to areas of low HCC prevalence, but incidence of HCC is rising. The aim of the present, retrospective study was to determine changes in the incidence rates and risk factors for HCC in Germany based on the data of a single center. **PATIENTS AND METHODS:** Epidemiological data of 205 consecutive patients with HCC (163 males, 42 females, mean age 64 +/-1 years), admitted to the University clinic Düsseldorf between January 1988 and December 2001, were evaluated. For comparison this time period was divided into two equal intervals (1988 - 1994 and 1995 - 2001). **RESULTS:** The number of newly diagnosed HCC has more than doubled in the years 1995 - 2001 compared to the years 1988 - 1994. Chronic hepatitis C (HCV), hepatitis B (HBV), and chronic alcohol abuse accounted for almost 80 % of HCC. The number of HCV-associated HCC increased from 31.0 % in the years 1990 - 1995 to 44.6 % (p < 0.04) in the years 1996 - 2001, whereas the proportion of HBV-associated HCC decreased. There were no changes in the Okuda tumor stage, tumor diameter and alpha-fetoprotein levels at the time of HCC diagnosis throughout the years 1988 - 2001. More than 65 % of HCC were non-resectable at the time of HCC diagnosis due to tumor diameter or number of tumor lesions. **CONCLUSION:** Screening for HCC, possibly rising in its incidence, should be further improved, taking into account that chronic HCV infection is the major risk factor for HCC in Germany.

Fischer F, Nauert T. Nosocomial transmission of HBV and HCV by public health workers. *Gesundheitswesen* 2003; 65:270-274. [Article in German]

Abteilung Gesundheitsschutz der Volkswagen AG, Wolfsburg, Germany.

Transmission of HBV and HCV from people who work in medical professions to their patients is still an unsolved hygienic and legal problem. In Germany, cases of nosocomial hepatitis virus infection in health care units have received great public interest. Medical examinations of the employees according to occupational safety regulations aim at the employees only. Legal regulations including regulations of the European Union limit the purpose of these examinations on safety and health of the employees. These examinations do not serve the safety of patients. Protection against infections is regulated by the relevant German public health law, however regulations - especially those that concern the protection of the public - are incomplete. In Germany it is mandatory to inform the public health departments only in cases of acute hepatitis. Doctors do not need to give information about chronic liver infections. This may lead to the situation that a health care worker is unaware of a chronic, potentially infectious condition and his immunological status may remain unknown for a long period. Examinations in occupational medicine cannot solve this problem. In order to improve the protection of the public, there is a need to extend the regulations concerning the notification of chronic hepatitis and to implement solutions for this difficult and sensible problem in Germany.

Gürtler L. Hepatitis C in Germany. More than 5000 new infections annually. *MMW Fortschr Med* 2002; 144:26-28. [Article in German]

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The number of people infected with HCV in Germany is estimated to be 300,000. New infections total 5100 every year, with drug consumption playing a major transmission role. Since the introduction of routine tests, the risk of contracting HCV infection from donated blood has now decreased to less than 1 in 1 million. For diagnostic purposes, antibody screening assays, confirmation assays to exclude false positive results (immunoblot), core antigen assay and nucleic acid testing are employed. An effective vaccine against HCV infection is still not available, so that prevention of transmission must continue to be the main aim of prophylaxis. In this connection, every practicing physician is expected to know his infection status for HCV, HIV and HBV.

Harbarth S, Szucs T, Berger K, Jilg W. The economic burden of hepatitis B in Germany. *Eur J Epidemiol* 2000; 16:173-177.

Department of Epidemiology, Harvard School of Public Health, Boston, USA.

Despite the widespread distribution of Hepatitis B virus (HBV) infection and the ongoing controversy about HBV immunization, surprisingly few published studies examined in detail the economic impact of HBV infection in Europe. Therefore, we investigated a cohort of 180 patients throughout Germany to evaluate the economic burden of HBV-associated disease. In 58 patients with acute and 122 patients with chronic HBV infection, cost-consuming events including direct medical costs and work-loss costs were documented. The direct costs were DM 7702 (95% confidence interval (CI): 5473-9931) for each acute HBV infection and DM 4247 (CI: 1601-6893) per patient-year of chronic HBV infection, with marked differences between different stages of HBV disease. The derived overall costs (1997 price levels) per year were DM 10,018 (CI: 7613-12,421) and DM 4860 (CI: 2185-7536), respectively. Based on crude population-based estimates

(30,000 acute and 420,000 chronic HBV cases), we calculated the total HBV-related costs in Germany to exceed DM 1200 millions in 1997 (CI: 924.2-1536.7), with the treatment of patients with chronic active HBV disease as the major cost determinant. Previously published data from Germany probably overestimated the financial impact of acute HBV infection. In summary, our results illustrate the ongoing economic importance of this potentially life-threatening, but preventable disease and support the call for more accurate HBV surveillance and control in Germany.

Hartmann K, Keller-Stanislawski B. Rekombinante Hepatitis-B-Impfstoffe und Verdachtsfälle unerwünschter Reaktionen - Eine Bewertung der Spontanerfassungsdaten des Paul-Ehrlich-Instituts 1995 bis 2000. *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz* 2002; 45:355-363. [Article in German]

Paul-Ehrlich-Institut, Langen, Germany.

In October 1995, after realising that the strategy of immunising only individuals at high risk for hepatitis B infections did not influence the incidence, the STIKO (Permanent Committee on Vaccination at the Robert Koch-Institute) recommended the general immunisation of all infants and children. The number of paediatric doses of recombinant vaccine sold between 1995 and 2000 shows that HBV vaccination is widely accepted by paediatricians. The cases of suspected adverse reactions reported from the German spontaneous pharmacovigilance system are summarised and discussed.

Hasselhorn HM, Hofmann F. Transmission of HBV, HCV and HIV by infectious medical personnel - presentation of an overview. *Chirurg* 2000; 71:389-395. [Article in German]

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This report analyzes 46 cases of personnel-to-patient transmissions of hepatitis B (HB), hepatitis C (HC) and HIV in health care settings. Similar circumstances were found for transmission of HB (40 cases, 404 infected patients), HC (4 cases, 224 infected patients) and HIV (2 cases, 7 infected patients). Cases with the highest number of transmissions (one anesthesiologist with 217 HC transmissions, and one EEG technologist with 75 HB transmissions) were attributed to poor infection control practices. As long as infected health care workers (HCW) adhere to general infection control measures, a risk for transmission to patients exists only from infected surgeons who perform 'exposure-prone invasive procedures.' Whether changes in duties of infected HCW are necessary should be decided on an individual basis. Often, the infected personnel were assumed to have acquired the disease occupationally. Medical practices and devices bearing a risk of infection should constantly be reviewed with regard to risk for patients and personnel.

Jilg W. Hepatitis B vaccination of children and adolescents. *Fortschr Med* 1997; 115:26, 29-32, 33. [Article in German]

Institut für Hygiene und Mikrobiologie der Universität Regensburg, Germany.

In the 14 years that have passed since its introduction, the hepatitis B vaccine has proved to be highly immunogenic, effective and very well tolerated. The vaccination, previously performed only in persons at high risk of contracting hepatitis B, in particular medical personnel, has appreciably reduced the incidence of hepatitis B in this group. The incidence of the disease in the general population, however, has been reduced only marginally. Thus, the sole possibility of resolving the hepatitis B problem is to introduce general vaccination. To this end, the *Ständige Impfkommision* (STIKO) has included hepatitis B vaccination in the catalog of vaccinations for children and adolescents. The greatest importance must probably attach to vaccination of young children, in whom hepatitis B vaccination is carried out along the same lines as the diphtheria, pertussis and tetanus vaccination, within the framework of which it can therefore be administered, thus making possible a wide application. However, the 12-15 year-old age group should also be involved in the vaccination program, for this is the group on the threshold of the periods of greatest danger of infection, which begins with the initiation of first sexual relationships.

Jilg W. Preventive vaccination for viral hepatitis. *Z Gastroenterol* 1997; 35:585-590. [Article in German]

Institut für Medizinische Mikrobiologie und Hygiene, Universität Regensburg, Germany.

Viral hepatitis A-E belong to the most important infectious diseases worldwide. Viral hepatitis is highly endemic in most developing countries in Africa, South East Asia, and southern America; however also in industrialized countries as Germany hepatitis A, B and C represent a threat that should not be underestimated. In Germany, there are about 20,000 to 40,000 hepatitis A infections every year, most of them acquired abroad; about 50,000 new hepatitis B infections and about 5,000 to 8,000 infections with hepatitis C virus occur every year. About 500,000 individuals are chronic carriers of hepatitis B virus and roughly the same number is supposed to be chronically infected with hepatitis C virus. As possibilities for therapeutic intervention in chronic hepatitis B and C are still limited, immunoprophylactic measures are of particular importance. Passive and active immunization is available for hepatitis A and B but so far not for hepatitis C. Passive immunization by application of specific immunoglobulins gives protection which is effective within a few hours but is limited according to the amount of immunoglobulin to six to twelve months. Active immunization on the other hand induces a specific immune response starting after a delay of usually days or sometimes weeks but nevertheless lasting for at least several years. The combination of both methods, passive-active immunization, has the advantage of immediate protection due to the immunoglobulin which lasts until the active immunization induces an endogenous antibody production.

Jilg W. Epidemiology, diagnosis and prevention of viral hepatitis. *Chirurg* 2000; 71:374-380. [Article in German]

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Viral hepatitis is one of the most important infectious diseases worldwide. It is frequent in tropical and subtropical areas, but also plays still a significant role in the industrialized countries of Northern and Western Europe and the USA. In Germany more than 100,000 people are infected by viral hepatitis each year. Whereas hepatitis A and E are transmitted fecal-orally, hepatitis B, C and D are transmitted by the parenteral route. Most hepatitis A infections seen in Germany are

acquired abroad. Hepatitis B is still a nosocomial disease; the majority of infections in Germany, however, seems to be transmitted sexually. For the serological diagnosis of viral hepatitis a battery of sensitive tests for specific antibodies and antigens is available; usually testing of one serum sample allows an unambiguous diagnosis. Prophylaxis of hepatitis A and B is possible using safe and efficient vaccines.

Jilg W. Adults tired of vaccines. Ask your patients about vaccine protection! *MMW Fortschr Med* 2001; 143:30-35. [Article in German]

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In general, vaccinations can be divided into standard and indication-related vaccinations. The former, which are mandatory for adults too, include tetanus and diphtheria, and those against influenza and pneumococci in people older than 60. The term indication vaccinations is used to describe those that are recommended in certain situations, for example, in the presence of a particular occupational risk, in certain underlying diseases, or particular situations, e.g. women of childbearing age, people living in regions endemic for meningoencephalitis, and drug addicts. Since the vaccination rate in the case of adults leaves much to be desired, all physicians should be required to ensure that 'gaps' are closed and immunization protection is maintained.

Jilg W, Hottentrager B, Weinberger K, Schlottmann K, Frick E, Holstege A, Scholmerich J, Palitzsch KD. Prevalence of markers of hepatitis B in the adult German population. *J Med Virol* 2001; 63:96-102.

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The prevalence of hepatitis B virus markers was investigated in 5305 individuals considered to be representative for the adult German population. After adjustment of the data according to the age and sex distribution in the whole German population an anti-HBc prevalence of 8.71% (95% confidence interval, 7.94-9.48%) and an HBsAg carrier rate of 0.62% (95% confidence interval, 0.40-0.84%) were calculated. Anti-HBc prevalence increased with age from 4.12% in the youngest group to 15.66% in the 61-70-year-old. The percentage of HBsAg carriers showed a maximum of 1.12% in the 41-50-year-old individuals and decreased significantly in the older age groups. 1.40% (95% confidence interval, 1.08-1.72%) of individuals had anti-HBc only. There was a trend to higher rates of this pattern in males than in females; a significantly higher percentage of persons with anti-HBc only was found in anti-HBc-positive individuals below 31 years than in older individuals. Five participants with anti-HBc only (7.7%, or about 0.1% of the whole population) showed HBV-DNA despite the absence of HBsAg. 3.1% of anti-HBc positive individuals were also positive for anti-HCV, that was significantly higher than the percentage of anti-HCV-positives among persons without any HBV marker (0.46%). This study provides a comprehensive picture of the current hepatitis B situation in Germany, showing new data especially on the distribution of HBsAg in the general population and on the subgroup of individuals with anti-HBc only.

Kallinowski B, Knoll A, Lindner E, Sanger R, Stremmel W, Vollmar J, Zieger B, Jilg W. Can monovalent hepatitis A and B vaccines be replaced by a combined hepatitis A/B vaccine during the primary immunization course? *Vaccine* 2000; 19:16-22.

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A combined hepatitis A/B vaccine (Twinrix Adult) has been licensed in Germany since 1997. We investigated possible differences in immunogenicity and safety when changing over from vaccinations with monovalent vaccines made by different manufacturers to vaccinations with the combined hepatitis A/B vaccine in an open, randomized, multicenter trial. We therefore compared four different schemes changing over from concomitant vaccinations with monovalent vaccines against hepatitis A and B (Havrix 1440+Engerix-B or Vaqta+Gen H-B-Vax) to combined vaccination against hepatitis A+B with three injections of the combined hepatitis A/B vaccine (0, 1, and 6 month schedule). Local and general symptoms were mostly mild in all five groups. With complete three-dose course using the combined vaccine or an early changeover from monovalent vaccines to the combined vaccine, higher overall anti-HBs seroprotection rates and geometric mean concentrations (GMCs) against hepatitis B could be achieved as early as after 2 months as compared to those groups switching later to the combined vaccine. This study demonstrated for the first time that switching from monovalent hepatitis A and B vaccinations to the combined hepatitis A and B vaccination has no negative influence on the tolerability and improves the immunogenicity.

Keller-Stanislawski B, Hartmann K. Auswertung der Meldungen von Verdachtsfällen auf Impfkomplicationen nach dem Infektionsschutzgesetz. *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz* 2002; 45:344-354. [Article in German]

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The German Protection against Infection Act (*Infektionsschutzgesetz*) came into action on January 1, 2001. Reporting of complications after vaccination became mandatory according to Article 6 No. 3. From January 1, 2001 to October 19, 2001 a total of 236 reports were registered in a central database and analyzed. Age distribution revealed the following pattern: 44.1% of the notifications concerned children from 0 to 11 years of age, 6.8% concerned adolescents and 48.7% concerned adults. Two deaths and nine lasting health damages were reported. For none of the latter adverse events a causal link to vaccination was evident. Compared to other sources of reporting (pharmaceutical companies, drug commissions) a considerable underreporting has to be considered. Efforts to improve the reporting compliance of physicians according to the requirements of the Protection against Infection Act are therefore necessary.

Knöll A, Helmig M, Peters O, Jilg W. Hepatitis C virus transmission in a pediatric oncology ward: analysis of an outbreak and review of the literature. *Lab Invest* 2001; 81:251-262.

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Hospital-related hepatitis C virus (HCV) infections continue to occur even after the introduction of blood donor screening. We report an outbreak of HCV in nine patients of a pediatric oncology

ward in 1996/1997. Sequencing of the hypervariable genomic region 1 (HVR1) of the E2/NS1 region showed near identity between HCV isolates from these patients as evidence for infection with the same virus. Despite a detailed and careful investigation, the source of infection and the mode of virus transmission could not be established. Based on a review of the current literature about nosocomial HCV infection and HCV infection in children, hypotheses for possible means of transmission in this outbreak are discussed.

Körner K, Cardoso M, Dengler T, Kerowgan M, Kubanek B. Estimated risk of transmission of hepatitis C virus by blood transfusion. *Vox Sang* 1998; 74:213-216.

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OBJECTIVE: The risk of transmitting hepatitis C (HCV) by transfusion of anti-HCV-negative screened blood was estimated for the blood donor population of Baden-Württemberg (southwestern Germany). **METHODS:** The data from the blood donors screened for anti-HCV and for HBsAg during 1990-1995 were analyzed. **RESULTS:** The prevalence of confirmed anti-HCV - positive blood donations decreased continuously during the last 5 years, reaching 121 per 100,000 blood donations. A higher anti-HCV prevalence rate was found in female than in male blood donors ($p < 0.05$). The estimated risk of transmitting HCV during the window period is 1:200,000 (1:97,000-1:1,400,000) for repeat donors. In 1995, the calculated risk for first-time donors was 1:20,000 (1:15,000-28,000). The incidence for HCV was 1.2 per 100,000 blood donations. **CONCLUSION:** The risk of transmitting hepatitis C by blood transfusion is low. Additional tests to shorten the window period to detect antibodies to HCV might increase the safety of blood transfusion.

Kralj N, Hofmann F, Michaelis M, Berthold H. Current hepatitis B epidemiology in Germany. *Gesundheitswesen* 1998; 60:450-455. [Article in German]

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Hepatitis B (HB) is the most common occupational hazard for health care workers. On the other hand 90% of the notified HB cases in Germany are observed among the general population (including other high-risk groups like i.v. drug abusers etc.). About 350 million persons all over the world are carriers of the hepatitis B virus (HBV). The availability of effective HB vaccines since 1982 made a control of HB possible. In this communication we report on epidemiological changes due to hepatitis B vaccination in a large university hospital in Germany. Health care workers and non-health care workers occupied at Freiburg university hospital were tested for HBV markers in 1984/85 ($n = 4218$), 1989/90 ($n = 4081$) and 1994/95 ($n = 4022$) during routine occupational health check-ups. Vaccinations were performed using a plasma-derived vaccine (1984/85) or a vaccine obtained by genetic engineering, respectively (1989/90, 1994/95). In 1984/85 prevalence of anti-HBs/HBc in German health care workers (12.4%) was 2.5 times higher than the one in non-health care workers (4.9%), in 1994/95 anti-HBs/HBc prevalence in both groups (4.4 vs. 4.5%) was comparable. On the other hand HBV carriage in persons occupied in professions without blood contact increased from 1984/85 (0.5%) to 1994/95 (1.1%). Therefore, the number of HBV carriers (ca. 1.1 millions) in Germany can be roughly estimated. Our data indicate a high degree of effectiveness of hepatitis B vaccines. Vaccination programme for the general population in accordance with German (STIKO) and WHO recommendations are necessary for the control of HBV infection.

Krämer A, Prufer-Krämer L. Experience with the new German hepatitis B vaccination strategy since 1995. *Int J STD AIDS* 2002; 13(Suppl 2):35-37.

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In Germany general hepatitis B (HB) vaccination for newborns and adolescents was introduced in all federal states following the recommendation of the STIKO (Permanent Vaccination Commission) of 1995. In 1998 serological studies of the German National Health Survey showed that at least 9.8% in the age group of 18 to 19 years had been vaccinated against HBV infection. By 1996 the vaccine doses sold for children rose dramatically and started to reach a plateau of approximately five million per year in 1997. Data from the *kassenärztliche Vereinigung* of the Oberpfalz region in Bavaria also indicate that the new policy started to be implemented in 1996. At school entry, however, in 1997 only 10% of the children in seven West German states showed serological evidence of HB vaccination coverage. According to observations of virologists, paediatricians and public health experts the current acceptance of the HB vaccination recommendations is 80%-90% in children below the age of six years but only 30% to 40% in adolescents. To achieve high HB vaccination coverage rates in Germany more rapidly a modern surveillance system providing detailed data about vaccination coverage in the different age and population groups is needed. Based on those data additional targeted vaccination strategies for those that can only be contacted by the traditional health care system, such as teenagers and vulnerable groups, should be developed, involving the public health service, local communities and other agencies.

Krause G, Altmann D, Claus H, Hellenbrand W, Buchholz U, Hamouda O, Breuer T, Ammon A, Kramer M; Arbeitsgruppe IfSG; Arbeitsgruppe Infektionsschutz der Arbeitsgemeinschaft der obersten Landesgesundheitsbehörden. First evaluation of the surveillance systems of notifiable diseases under the infectious disease control law in Germany. *Gesundheitswesen* 2003; 65(Suppl 1):S8-S12. [Article in German]

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INTRODUCTION: The implementation of the infectious disease control law (IfSG) on 01.01.2001 standardised the German surveillance system for notifiable diseases. For management and transmission of reports health departments use either the software programme Surv Net@RKI, which was developed by the Robert Koch-Institut (RKI), or one of five commercially offered disease-reporting software. After more than one year of its existence, we investigated the success of the implementation of the new surveillance system with the aim to identify possibilities for further improvement. **METHODS:** Based on 2001 data available to the RKI, we evaluated the criteria simplicity (standardisation of legal regulation and of software systems), acceptability (number of reporting regional counties), time (period from data entry at the health department to entry at the RKI) and data quality (information on immunisation status among reports of hepatitis A cases). **RESULTS:** For electronic processing 5 versions of Surv Net@RKI and 47 versions of the 5 commercial products are used. Additional rules of individual states expand the legal obligation for notification of the IfSG, by adding new diseases, different definitions or different reporting channels. Within the first quarter after implementation of the IfSG, 393 (90 %) of the

425 counties transmitted data weekly. The median transmission time from data entry at the health department and entry at the RKI was 5 to 7 days after the fourth reporting week. The proportion of hepatitis A case reports with information on immunisation status was 58 % (1323 of 2277); among the 1052 reports by health departments using Surv Net@RKI the proportion was 82 % (n = 858); among the 1225 reports from health departments using other programmes the proportion was 38 %. CONCLUSION: Implementation of the new surveillance system is successful. Electronic data systems should be standardised to improve data quality and simplicity. The deadlines for transmission should be shortened to allow earlier detection and control of multi-state outbreaks. State-specific rules on notifiable diseases should be standardised to avoid conflicting or redundant reporting channels.

Meisel H, Reip A, Faltus B, Lu M, Porst H, Wiese M, Roggendorf M, Krüger DH.

Transmission of hepatitis C virus to children and husbands by women infected with contaminated anti-D immunoglobulin. *Lancet* 1995; 345:1209-1211.

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In 1978-79 a single-source outbreak of hepatitis C occurred in 2533 women who had received virus-contaminated anti-D immunoglobulin. Children and husbands of 74 women with self-limited, and of 86 women with chronic, hepatitis C were followed up for over 10-15 years. In 3 of 231 investigated children (1.3%) serological evidence for HCV infection was found. However, none of the children developed an apparent or chronic hepatitis. Serum samples of the 94 husbands investigated showed no HCV antibodies or HCV RNA. We consider the risk of intrauterine or perinatal transmission of HCV, as well as that of transmission through close family contacts, to be low. No evidence was found for sexual transmission from women to men.

Meyer C, Rasch G, Keller-Stanislawski B, Schnitzler N. Anerkannte Impfschäden in der Bundesrepublik Deutschland 1990-1999. *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz* 2002; 45:364-370. [Article in German]

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The decrease in infectious diseases preventable by immunisation and the absence of complications caused by these diseases leads to an increased awareness of vaccine-associated adverse events. The analysis of a survey of the vaccine injury compensation data from the German Bundesländer shows the decrease in accepted and demanded compensation from 1991 to 1999. From 1976 to 1990 1139 of 4569 demands were accepted, whereas from 1991 to 1999, acceptance of only 389 of 2543 demands was reported. In all, 38% of the accepted compensations refer to the smallpox vaccine which is not longer recommended by the STIKO (Permanent Vaccination Commission in Germany) since immunisation against smallpox was stopped in the 1980s. Regional differences show that process elements of the German healthcare system as well as political and social reasons express most of the differences in rates and prevalence of vaccine associated adverse events. Epidemiological questions and questions of causality cannot be answered by the analysis of data collected in vaccine injury programs. Valid analysis needs a register of individual documented cases of vaccine adverse events. The surveillance of adverse events following immunisation will make progress by the analysis of data reported according to the Protection against Infection Act (IfSG) and by further surveillance systems that should be implemented in the near future. A

centralised commission with expert opinion concerning causality could increase transparency and homogeneity within judgement and documentation of vaccine-associated adverse events.

Neubauer G. Wishes and possibilities in the face of limited resources. *Zentralbl Gynakol* 2002; 124:493-496. [Article in German]

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The main intention of health economic studies is to find out how to cope with the prevailing scarcity of resources. But scarcity is comparable to morbidity. As morbidity can not be finally cured by medical intervention, the problem of scarcity can only be solved relatively by economic research. It is evident, that the sensation of scarcity even aggravates with increasing prosperity. That is because human demands do in fact outrun economic potentials. The scarcity of resources therefore demands for setting of priorities. That is what economics in general and health economics in particular has set rules for. Priorities can be set by the state, the market or joint associations. The prevailing system in Germany is based on associations, the so called self-governing body. The scarce financial resources are divided into budgets and allocated to service suppliers following predefined negotiation mechanisms within the joint self-administration. In recent years an increasing paternalism of the German government on the joint self-administration can be observed. Although Germany spends more on healthcare than ever before, the scarcity is noticed as threatening. The government currently interferes to cope with this problem. In opposition to that approach critics postulate more individual freedom in decisions for insurance holders, patients, health insurances and suppliers. The principal of subsidiarity intends to strengthen self-responsibility in the health care sector while in return the principle of solidarity within the legal health insurance is reduced.

Oppermann H. The status of vaccine-preventable diseases in Germany. *Gesundheitswesen* 2001; 63:102-106. [Article in German]

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The European members of the World Health Assembly (WHO) adopted the goal of eliminating poliomyelitis by the year 2000 (certification 2003), tetanus of the newborn by 2005 and measles by 2007 (certification 2010). Regarding the reduction by 2010 diphtheria, hepatitis B, pertussis and rubella syndrome are in the foreground of discussions. As WHO member Germany looks after these aims with growing acceptance, too. The current situation of the specific target illnesses is differentiated in the eastern and western part of Germany. While the final stage of certification for a polio-free region in the whole of Germany has been reached and there have only been single illnesses of diphtheria and tetanus for years, there are reported more than 5,000 illnesses of hepatitis B every year with an estimated number of unknown cases of at least 15,000 clinically manifested illnesses and a high age specific incidence rate for people who are 20-40 years old. The incidence rate in the eastern federal states is lower than in the western federal states owing to a smaller portion of endangered risk groups in the population. The trend on the whole is declining. Useful epidemiological data of measles and pertussis are currently only available in the eastern federal states of reunited Germany. To control measles a national intervention programme 'measles, mumps, rubella' was started. The aim of this programme is to reduce the illnesses of measles in Germany from currently 50 to at first 5 illnesses per 100,000 inhabitants. In the eastern German federal states the situation is still better than in the western federal states. However, a

permanent lower incidence rate of less than 1/100,000 inhabitants has not been reached after 1990. Pertussis is an example for the consequences of different vaccination strategies in East and West. The estimated illness rates in the western federal states are at 80-100/100,000 inhabitants. In the eastern federal states a continuous increase of incidence rates of more than 5 per 100,000 inhabitants has been noticed since 1991. For a permanent reduction of incidence rates of infectious diseases which are preventable by vaccination, provable high vaccination coverage and an effective epidemiological control are necessary.

Palitzsch KD, Hottentrager B, Schlottmann K, Frick E, Holstege A, Scholmerich J, Jilg W. Prevalence of antibodies against hepatitis C virus in the adult German population. *Eur J Gastroenterol Hepatol* 1999; 11:1215-1220.

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OBJECTIVE: The prevalence of anti-HCV in Germany has been determined for blood donors and certain risk groups, but the burden of disease in the general population remains unknown. The aim of this study was to determine the prevalence of anti-HCV in a study group representing the normal adult German population. **DESIGN:** A total of 5312 individuals aged 18-70 years were randomly selected from small, middle-sized and big cities in five different German states. Sera were tested for anti-HCV by enzyme immunoassay and immunodot assay, as well as for anti-HBc and, in the case of a positive result, for anti-HBs and HBsAg. Serological typing was performed in anti-HCV-positive persons. **RESULTS:** Thirty-nine individuals were anti-HCV positive; indeterminate results (with antibodies against the viral core protein only) were obtained in 20. There was a tendency to higher prevalence rates with increasing age as well as to a higher prevalence in women. Serological typing revealed the presence of genotype 1 in the vast majority of participants (82%); only a minority showed genotype 3 (7.2%) or other genotypes (7.2%). Markers of HBV were seen in 43.6% of the anti-HCV positive individuals, with nearly one third (29.4%) of the double-infected showing anti-HBc as the only marker for HBV. **CONCLUSIONS:** According to our data, an anti-HCV prevalence of 0.63% (95% confidence interval, CI, 0.42-0.84%) can be assumed in the general adult German population, with higher values in older people and women. Nearly half of the anti-HCV positive individuals also show markers of hepatitis B virus.

Riemer-Hommel P. The changing nature of contracts in German health care. *Soc Sci Med* 2002; 55:1447-1455.

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The flexibility inherent in the German health care system is fairly limited. The contracting environment itself is characterized by bilateral cartels negotiating the terms covering their respective members. Looking at some recently implemented reforms, namely structural contracts and experimental settings, the paper assesses the potential for sickness funds to take on a more active role. The paper also evaluates the implications for the contracting relationships between the statutory sickness funds and provider associations. Furthermore, the potential effect of selective contracting on the health care system is studied. A look at the reforms recently enacted in other countries illustrates the difficulties contractual reform has to cope with in an environment

characterized by strong informational asymmetries. It is postulated that both private and public choices are needed for a successful reform effort.

Ross RS, Viazov S, Renzing-Kohler K, Roggendorf M. Changes in the epidemiology of hepatitis C infection in Germany: shift in the predominance of hepatitis C subtypes. *J Med Virol* 2000; 60:122-125.

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Hepatitis C virus (HCV) subtype distribution was studied in 395 chronically infected patients from Germany. HCV genotype 1 was most frequent (80.5%). One hundred forty-three individuals (36.2%) were infected with subtype 1a and 175 (44.3%) were suffering from subtype 1b infection, respectively. HCV subtype 3a was found in 53 (13.42%) persons. Subtypes 2a, 2b, and 2c have been detected in 5 (1.27%), 10 (2.53%), and 4 (1.01%) individuals. Genotypes 4 and 5a accounted for HCV infections in 4 (1.01%) and 1 (0.25%) subjects. There was a notable variation in the distribution of the prevalent subtypes 1a and 1b in different age groups. Subtype 1a was detected in 53.3% and 68.0% of patients aged 1-10 and 11-20 years, whereas subtype 1b in the same groups was present only in 33.3% and 28.0% of patients, respectively. In contrast, in individuals older than 50 years subtype 1b was most frequent. Thus, subtype 1b has been gradually substituted for subtype 1a during the last 20 years. Logistic regression analysis with adjustment for sex and different modes of HCV acquisition demonstrated that age of the infected subjects was a direct explanatory variable for subtype 1a and 1b distribution. Therefore, the observed shift in HCV subtype prevalence could not be attributed to changes in the epidemiological relevance of different known risk factors of HCV transmission, as had been assumed in previous studies. The altered subtype pattern reported here may have a profound influence on the future epidemiology of HCV infection.

Schosser R, Keller-Stanislawski B, Nübling CM, Löwer J. Causality assessment of suspected virus transmission by human plasma products. *Transfusion* 2001; 41:1020-1029.

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BACKGROUND: Causality assessment of reports on suspected virus transmission is crucial for early detection of infectious plasma products. Commonly used algorithms, such as the WHO criteria, do not meet the specific requirements for causality assessment of suspected virus transmission. **STUDY DESIGN AND METHODS:** A special algorithm, based on nucleic acid amplification and gene sequencing technology, effectiveness of validated virus-inactivation methods, empirical data concerning the safety record of the product, and information on batch-related infection clusters, was developed. The algorithm is focused on laboratory test results or otherwise standardized data, with few clinical data being required. To facilitate practical application, the algorithm has been converted into a graphical decision tree. **RESULTS:** The feasibility of the algorithm is shown by causality assessment of sample cases. Three cases are presented with the details of each case used in the 12-question checklist. The answers provided by the checklist led to the causality classification. **CONCLUSION:** The algorithm is a tool for evaluating reports of suspected virus transmission in a standardized manner. It thus has the

potential to improve early signal detection in pharmacovigilance of plasma products by confirmation or exclusion of suspected infectivity in most cases.

Stark K, Bienzle U, Vonk R, Guggenmoos-Holzmann I. History of syringe sharing in prison and risk of hepatitis B virus, hepatitis C virus, and human immunodeficiency virus infection among injecting drug users in Berlin. *Int J Epidemiol* 1997; 26:1359-1366.

BACKGROUND: Injecting drug users (IDU) are at risk of parenterally transmitted diseases such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infection. We investigated whether a history of syringe sharing in prison is a risk factor for these infections. In the longitudinal part of the study, HBV, HCV, and HIV seroincidence rates were determined. **METHODS:** The participants were recruited by multisite-sampling at different agencies for IDU. Data on risk behaviour were obtained by a standardized questionnaire. Serological markers for HBV, HCV, and HIV were determined. Logistic regression analysis was performed to adjust for confounding effects. **RESULTS:** A history of syringe sharing in prison was significantly associated with HBV (adjusted prevalence odds ratio [POR] = 3.9, 95% confidence interval [CI]: 2-10), HCV (POR = 9.7, 95% CI: 3-33), and HIV infection (POR = 10.4, 95% CI: 4-29). The HIV seroincidence rate was 5.9 per 100 person-years. None of the IDU receiving methadone maintenance treatment (MMT) seroconverted whereas the HIV incidence was 8.5 among IDU not in MMT (P = 0.01). **CONCLUSIONS:** The increased risk of HBV, HCV, and HIV infection among IDU who had shared syringes in prison warrants specific preventive action. The longitudinal data suggest that IDU in MMT have a lower risk of HIV infection.

Szucs T. Cost-effectiveness of hepatitis A and B vaccination programme in Germany. *Vaccine* 2000; 18(Suppl 1):S86-S89.

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A recent study in Germany analysed the epidemiological and economic impact of combined hepatitis A and hepatitis B vaccination of all 1-15-year-olds or of all 11-15-year-olds projected over three periods of 10 years compared with a strategy of non-vaccination. Vaccination of all 1-15-year-olds will achieve a reduction of 57,596 new hepatitis A cases with 7555 new infections remaining over 30 years. Vaccination of all 11-15-year-olds will reduce the number of new hepatitis A cases by 19,826, with 45,325 new cases remaining over 30 years. Vaccination of all 1-15-year-olds will reduce the number of new hepatitis B cases by 45,820 with 7484 new cases remaining over 30 years, compared with vaccination of all 11-15-year-olds, which will reduce the number of new hepatitis B cases by 21,905 with 31,339 new cases remaining over 30 years. This significant reduction in the number of new cases will lead to savings in treatment costs of DM 2.9 billion for vaccination of 11-15-year-olds and of DM 5.1 billion for vaccination of 1-15-year-olds. The cost-effectiveness of vaccination ranges from costs of DM 90,000 for each infection avoided to savings of DM 50,000 for each case avoided. If unreported cases are also taken into account and are equally distributed between all age-groups, the savings per infection avoided over 30 years are DM 69,796 for vaccination of 11-15-year-olds and DM 55,850 for vaccination of 1-15-year-olds. Although the strategy of vaccinating 11-15-year-olds is the more cost-effective, it leaves a large percentage of the population at high risk of hepatitis A virus infection. The use of an initially more expensive combined hepatitis A and B vaccine represents a cost-effective alternative to monovalent hepatitis B vaccination and is more beneficial in terms of its epidemiological impact.

Thierfelder W, Hellenbrand W, Meisel H, Schreier E, Dortschy R. Prevalence of markers for hepatitis A, B and C in the German population. Results of the German National Health Interview and Examination Survey 1998. *Eur J Epidemiol* 2001; 17:429-435.

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The prevalence of serological parameters indicative of infection with hepatitis A, B and C was determined using sera collected from representative population samples in the former East German (new) federal states and the West German (old) federal states during the German National Health and Examination Survey in 1998. Sera were tested for antibodies to hepatitis A virus (HAV), to hepatitis B core antigen (HBc) and to hepatitis B surface antigen (HBsAg), hepatitis C Virus (HCV), as well as for the presence of HBsAg and HCV-RNA. The mean weighted prevalence of anti-HAV was 46.5% (95% CI: 45.3-47.7) and increased markedly with age. The mean weighted prevalence of past infection with hepatitis B was 7.7% (95% CI: 7.0-8.4) in the old federal states and 4.3% (95% CI: 3.2-5.3) in the new federal states, corresponding to an overall prevalence of 7.0% (95% CI: 6.4-7.6). The mean weighted prevalence of HBsAg carriage was 0.6% (95% CI: 0.4-0.8), while the prevalence of HCV antibodies was 0.4% (95% CI: 0.2-0.5).

Thierfelder W, Meisel H, Schreier E, Dortschy R. Prevalence of antibodies to hepatitis A, hepatitis B and hepatitis C viruses in the German population. *Gesundheitswesen* 1999; 61(Spec No):S110-S114. [Article in German]

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Representative random samples were tested for hepatitis A, hepatitis B and hepatitis C infections within the framework of the German National Health Interview and Examination Survey. The laboratory parameters included determination of anti-HAV, anti-HBc, anti-HBs, HBsAg, anti-HCV and hepatitis C virus RNA. The prevalence rate for anti-HAV was 46.5% with a definite age-dependence. The infection rates for hepatitis B of 7.7% in former West Germany and of 4.3% in former East Germany were obtained. This is equivalent to a total of 7% prevalence rate. The HBsAg carrier rate was 0.6%. Hepatitis C virus antibodies showed a prevalence rate of 0.4%.

von Kondratowitz HJ, Tesch-Römer C, Motel-Klingebiel A. Establishing systems of care in Germany: a long and winding road. *Aging Clin Exp Res* 2002; 14:239-246.

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Since 1995/1996 a long-term care insurance (LTCI), which promised to develop new support structures, in particular for the group of potentially frail elderly people, has been implemented in Germany. It will be shown that this LTCI has undoubtedly improved the social situation of the persons in need of care, even if its scheme is only providing basic support with a ceiling in cash-benefits and benefits in-kind, and privileging home care by informal caregivers. But certain misdevelopments in the LTCI have shown that the present scheme requires further effort to cope with these negative effects and to elaborate new integrated models of care that bridge the still existent gap between medical and social support. This article points to long traditions of separating the social and medical dimensions in Germany which have also resulted in divided institutional

arrangements. The current scheme of the LTCI, its organizational principles and its entitlements and benefits are outlined, which gives the opportunity to point out certain deficiencies, e.g., the still inappropriate provision for dementia care which is due to the dominant IADL-orientation of the medical assessment procedure and its implicit negligence of social care elements. The public debate about necessary improvements in benefits for the demented aged has already led to slight revisions of the LTCI, and will develop into a more comprehensive movement to path-bridging models of social and medical care in which the quality dimension will play a decisive role.

PART IV ADDITIONAL BIBLIOGRAPHY

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Annex

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