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**EFFICACY OF A TWO-DOSE HEPATITIS B VACCINATION SCHEME.** Greet Boland, Toon van Bommel, UMC Utrecht, Utrecht, Netherlands; Annemarie van den Berg, Jan van den Berg, Foundation The Netherlands-Batam, Ede, Netherlands; Anton M van Loon, Jan van Hattum, UMC Utrecht, Utrecht, Netherlands

In Indonesia on the Isle of Batam we are currently performing a large hepatitis B vaccination campaign. Beside creating the infrastructure for large-scale vaccination and investigating the prevalence, incidence and transmission routes of hepatitis in this area, another aim is to investigate the efficacy of a two-dose hepatitis B vaccination schedule. A two-dose schedule of injections with a 6 month interval is much more practical for large-scale vaccinations. The study design is prospective, randomised and placebo-controlled. Two groups are made: group one is injected at 0, 6 and 12 months with respectively placebo, vaccine, vaccine and group two is injected with vaccine, placebo, vaccine at 0, 6 and 12 months. Also, at every time point blood is drawn. A final blood drawal is performed at 18 months in both schedules. The vaccines (Engerix-B, 20 ug recombinant HBsAg) are kindly given to us by SmithKline Beecham. By this design we can study the efficacy of one and two doses of the vaccine. At entry, from every subject the gender, birth date and location/socio-economic status is noted. In total about 9700 subjects were included in the study. About 30% was anti-HBc positive at entry and excluded for further follow-up of the vaccine efficacy, so 5945 subjects entered the vaccination study. At 6 months after one injection, serum from 3094 subjects (52%) was obtained, and 6 months after two injections, serum from 2149 subjects (36%) was obtained. In every serum sample, anti-HBs was measured (Elecsys system, Boehringer, Germany). To study the relation between vaccine response and age, the subjects were divided into 5 age groups: 5-20, 20-30, 30-40, 40-50 and >50 yrs old. The results after 2 injections with the vaccine are shown in the table. These result show that two injections with the recombinant hepatitis B vaccine give sufficient levels of protection in children and adolescents. The anti-HBs response is strongly age dependent, and adults should be given at least three injections. Protective efficacy of the two dose schedule is currently under investigation.

**Result of two-dose hepatitis B vaccination study in relation with age.**

| age (years) | 5-20 | 20-30 | 30-40 | 40-50 | 50 |
|---|---|---|---|---|---|
| n (subjects) | 1059 | 428 | 432 | 150 | 80 |
| GMT anti-HBs (IU/L) | 216 | 100 | 45 | 19 | 8 |
| %>10 IU/L | 90% | 82% | 73% | 63% | 55% |

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**VERTICAL TRANSMISSION OF HEPATITIS E VIRUS- A PROSPECTIVE STUDY.** Premashis Kar, Mona Beniwal, Ashok Kumar, Nishad Jilani, Maulana Azad Medical College, New Delhi, India

Background: Hepatitis E virus (HEV) is known to cause higher mortality in pregnant females as compared to non-pregnant females, but little is known about the vertical transmission of HEV from infected mothers to their infants. Aims and objectives: This study was designed to assess the obstetric outcome of pregnant women with HEV infection and vertical transmission of HEV from infected mothers to their infants. Materials and methods: Twenty-eight pregnant females with acute hepatitis due to HEV (IgM anti-HEV positive) were enrolled in the study. The patients were evaluated on the basis of history, clinical examination, liver function profile and serological markers for hepatitis A, B, C and E viruses. The serum samples were subjected to RT-PCR using oligonucleotide primers for amplification of HEV RNA in all the subjects. These subjects were followed up till delivery for the progression of the disease and development of any obstetric complications. At the time of delivery cord blood sample was taken and analyzed for IgM anti HEV antibodies and HEV RNA and vertical transmission was said to occur if either or both were positive. Results: Out of 28 cases, 19 were suffering from acute viral hepatitis and 9 from fulminant hepatitis. The average gestational period at the time of presentation was 35.3 weeks and there was seasonal variation in the occurrence of cases with maximum cases occurring from June to August. 7/28 (25%) patients died and all of them were suffering from fulminant hepatitis and 5 of them died undelivered. Of the 21 cases that delivered, 14 (66.6%) had preterm delivery and 3/28 (10.7%) had intrauterine death. 18 cord blood samples were analyzed for HEV infection and 6/18 (33.3%) had evidence of vertical transmission. 5/16 (31.25%) in the acute viral hepatitis group and 1 out of 2 (50%) in the fulminant hepatitis group had evidence of HEV infection in the cord blood. HEV RNA alone was positive in 3/6 (50%), IgM anti-HEV in 2/6 (33.3%) and both in 1/6 (16.6 %). Conclusion: Hepatitis E virus is associated with higher mortality in pregnant females and obstetric complications are also common in pregnant females suffering from acute hepatitis due to HEV. It is proposed that intrauterine vertical transmission of HEV infection is possible and factors responsible for increased risk of vertical transmission are to be studied in larger studies.

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**CYTOKINE POLYMORPHISMS AND THEIR ROLE IN THE SUSCEPTIBILITY TO UVB-INDUCED IMMUNOMODULATION AFTER HEPATITIS B VACCINATION IN HUMAN VOLUNTEERS.** Greet Boland, Annemarie Sleijffers, UMC Utrecht, Utrecht, Netherlands; B Yucescoy, National Institute for Occupational Safety and Health, Morgantown, WV; Johan Garssen, National Institute of Public Health and the Environment, Bilthoven, Netherlands; Frank R de Gruijl, Jan van Hattum, Willem A van Vloten, UMC Utrecht, Utrecht, Netherlands; M I Luster, National Institute for Occupational Safety and Health, Morgantown, WV; Henk van Loveren, National Institute of Public Health and Environment, Bilthoven, Netherlands

Exposure to ultraviolet (UV) radiation can modulate immune responses in animal and humans. Remarkably, the UV-induced immunosuppression is not restricted to the exposed skin but is also found at other body sites, i.e. systemic immunosuppression. Effects of UV radiation on infections cannot be determined by experimentation on humans, but the effects of UV on vaccination may serve as a model. Moreover, it is important in its own right whether UV radiation affects vaccination responses. In the present study, the effect of UVB exposure on the development of immune responses after hepatitis B vaccination in human volunteers (n=191) was investigated. Volunteers were exposed to UVB on 5 consecutive days (1 MED/day) followed by a standard hepatitis B vaccination protocol. Although the UVB exposure regime was sufficient to suppress cutaneous hypersensitivity responses and NK activity, antigen-specific humoral (anti-HBs) and cellular immunity (proliferation induced by HBsAg) were not significantly affected. For all volunteers single nucleotide polymorphisms (SNPs) have been determined for the following interleukines: IL-1RA (+2018), IL-1α (+4845), IL-1β (+3953), TNF-α (-308) and TNF-α (-238). These polymorphisms, and most importantly for IL-1RA, IL-1α and IL-1β, affect quantitatively the production of the corresponding interleukines, and may thereby play a role in the susceptibility to UVB-induced immunomodulation. Taking into account these polymorphisms, it was demonstrated that humoral and cellular immune responses to the hepatitis B vaccine as well as the susceptibility to UVB-induced immunomodulation depends on the type of polymorphism. We conclude therefore that UVB exposure prior to hepatitis B vaccination does not affect either humoral nor cellular responses at a population base. However, when study objects are subdivided according to their interleukin polymorphism profile, differences in vaccination responses as well as in UVB-induced immunomodulation of these responses can be observed.

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**RAPID DETECTION AND QUANTIFICATION OF HEPATITIS G VIRUS RNA BY A NOVEL ONE-STEP REAL TIME RT-PCR.** Hans-Dieter Nischalke, Jacob Nattermann, Universitaetsklinikum Bonn, Bonn, Germany; Bernd Kupfer, Institut fuer Mikrobiologie Bonn, Bonn, Germany; Juergen Rockstroh, Tilman Sauerbruch, Ulrich Spengler, Universitaetsklinikum Bonn, Bonn, Germany

INTRODUCTION: Hepatitis G virus (HGV) has not unequivocally been associated with any known disease. Thus, only few diagnostic tools have been developed. However, recent data suggest improved survival and delayed progression to AIDS in HIV-positive patients co-infected with HGV (Xiang et al., 2001; Tillmann et al., 2001). Therefore, HGV infection has regained scientific interest. At the moment, research on HGV is hampered by the lack of commercially available assays for detection and quantification. Here, we describe an easy and rapid one-step reverse-transcription PCR (RT-PCR) for detection and quantification of HGV. METHODS: To develop a one-step RT-PCR for detection of HGV RNA, a total of 8 different primers from the 5'UTR were tested in various combinations using lightcycler real time PCR technology. Specifity and sensitivity were analysed with a panel of sera classified as HGV RNA positive or negative by conventional reverse-transcription nested PCR. To analyse, if HGV RNA quantification can be simplified by using a post PCR product (HGV DNA) as external standard, gauge curves were measured by 10-fold dilutions ($10^2$-$10^7$copies) of 6 different post-PCR products and their slopes compared to the slopes obtained with 6 serially diluted high titre HGV RNA-positive sera (RNA standard). RESULTS: Sensitivity of the one-step RT-PCR was comparable to the conventional nested PCR, as all sera tested positive for HGV RNA by nested RT-PCR were also positive by the one-step real time RT-PCR. The slopes measured with the DNA post-PCR product as a standard were identical to the slopes of the RNA standard curves (-3,292 ±0,035 versus -3,309 ±0,064). The detection limit of the RT-PCR was below 10 copies of template RNA, and the linear range of quantitative HGV RNA measurements was between $10^2$ and $10^7$ copies. CONCLUSION: We have developed an easy single step RT-PCR protocol, which enables not only a reliable but also fast quantitative detection of hepatitis G virus RNA in human sera by using HGV post-PCR DNA as external standard. This PCR technique is a useful tool to study further the effects of HGV infection on the course of other disease.

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