O9 Epidemiology of respiratory coronaviruses (HCoV) in a Dutch university hospital

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Aim: The epidemiologic characteristics of HCoV-NL63, HCoV-HKU1 and HCoV-OC43 and HCoV-229e in adult and paediatric patients were investigated. Furthermore, the genetic variability of HCoV-NL63 and HCoV-OC43 strains was investigated.

Methods: Studies were performed on respiratory samples submitted to the Virology Laboratory of the Erasmus MC for routine respiratory virus detection between June 2004 and June 2005. Samples were analysed for the presence of human coronaviruses using real-time nucleic acid amplification. Patient records were reviewed for patients tested positive.

Results: 1376 Samples were submitted. 70 Coronavirus positive samples (5.1%) were detected from 54 patients: for HCoV-OC43 40 samples from 31 patients, for HCoV-229E 1 sample from 1 patient, for HCoV-NL63 27 samples from 23 patients and for HCoV-HKU1 2 samples from 2 patients. Three patients were positive for more than one coronavirus. Other respiratory viruses were found in seven HCoV-NL63 and 9 HCoV-OC43 positive patients, respectively 30% and 29%. Peak incidences appeared during winter and springtime. For HCoV-OC43 a left skewed age distribution was found with a peak detection rate in patients 0–9 years old: median age 2.5 years. HCoV-NL63 detection rates equalled for patients 0–9 years old and 50–59 years: median age 34.8 years. 40 Patients (74%) were admitted to the hospital, 14 patients visited an outpatient-clinic. Phylogenetic analysis revealed two major clusters for both HCoV-NL63 and HCoV-OC43.

Conclusion: HCoV-OC43 and HCoV-NL63 were detected in a significant number of paediatric and adult patients, in contrast to HCoV-229E and HCoV-HKU1. Screening for these viruses is warranted.

O10 Trent HCV study: mortality rates and ethnic differences in outcome

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Background: The Trent HCV cohort study was established in 1991 with the aim of characterising the natural history of chronic HCV (CHC) infection; over 2500 patients are enrolled, with a mean length of follow-up of >5 years.

Methods: CHC patients attending one of 7 sentinel clinics are invited to enlist with informed consent. Patient-derived data are stored in a centralised, anonymised database.

Mortality study: patients within the cohort are registered with the National Health Service Central Register. Death certificates and cancer registrations from Trent study patients are forwarded to the study group.

Ethnicity study: relevant data from all CHC patients within the cohort of Caucasian (n = 1700) and Indian sub-continent (n = 79) ethnic backgrounds were downloaded from the central database and compared.

Results: Of 228 cohort deaths, 87 were "liver related", 51 were related to injecting drug use, and 73 were "unrelated medical". Factors associated with all cause and liver-related mortality were increased age and male gender. Standardised mortality ratios were 6.4 (95%CI 4.6–10.3) and 2.1 (1.5–3.5) for males and females respectively. Compared with CHC in Caucasians, CHC in patients of Indian ethnicity was more likely to occur in females, in individuals with no clear history of risk factors, and presented at an older age with more severe liver disease.

Discussion: 5 year survival in our cohort is less than that reported in the literature; Mortality in HCV-infected patients is markedly increased compared to an age-matched population; CHC in different ethnic groups may have very different characteristics from that in Caucasian patients.

O11 Early evolution of hepatitis C virus (HCV) quasispecies after liver transplantation

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Background and Aims: Liver cirrhosis related to chronic infection by HCV is a main indication for liver transplantation (LT). Allografts are systematically re-infected with HCV yet prognosis of infection differs from patient to patient. A high rate of nucleotide mutations during HCV replication, a differential adaptation of viral strains to the liver graft and a variable efficiency of the immune response could explain HCV recurrence. In infected patients, HCV circulates as a mixture of closely related but distinct genomes called quasispecies. Little information is available on changes in HCV quasispecies early following transplantation.

Methods: Seventeen patients liver transplanted for HCV-related disease were included. HCV quasispecies were analyzed in plasma by cloning and sequencing the Hypervariable region 1 of E2 envelope gene before transplantation, after 7 days and one month later. NS3 was sequenced by studying three internal fragments with overlapping ends.

Results: HCV quasispecies tend to be more homogeneous at D7 than before transplantation (decrease in genetic complexity and diversity). Complexity and diversity at the amino-acid level were both diminished at day 7 after transplantation (4.7 and 6.9 respectively) compared to the time before transplantation (5.7 and 13.3 respectively). Mutations in NS3 could be observed in most patients: for one patient up to 11 non synonymous mutations were observed 3 and 6 months post-transplantation compared to HCV before transplantation.

Conclusion: Here we describe HCV genetic evolution during the early phase after LT, the best time to make an antiviral treatment optimal. Possible links between NS3 mutations and prognosis of recurrent hepatitis deserve to be analysed.

O12 Impact of targeted vaccination on HBV genotypes in Amsterdam

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Background and Aim: The Netherlands have adopted a policy of hepatitis virus (HBV) vaccination targeted towards high-risk groups, rather than universal vaccination. In 1998, a pilot program started in Amsterdam. We performed a retrospective molecular epidemiological cross-sectional survey covering 12 years (1992–2003).

Methods: Mandatory reported HBV cases were classified according to probable mode of transmission. Retrospective DNA sequencing was performed on 85 sera of patients with acute hepatitis B infections. We amplifyied the S-gene (nt 112–778) for phylogeny.

Results: The number of reported cases of acute HBV in Amsterdam declined from 214 before to 128 after the start of vaccination in 1998. An estimated 39–65% of those who should be vaccinated are presently still susceptible for HBV. Before 1998, phylogenetic analysis showed 3 main clusters: (I) men having sex with men (MSM, genotype A), (II) people from Morocco (genotype D), and (III) intravenous drug users (IDU) and heterosexual partners (genotype D). After 1998, the cluster with IDU and their heterosexual partners had disappeared. In the total 12-year study period the same HBV strain circulated among MSM in Amsterdam. Although the number of susceptible MSM in Amsterdam declined, the number of acute hepatitis B cases among MSM did not.

Conclusions: The decline of acute hepatitis B infections in Amsterdam was ascribed to a lack of reported HBV cases among IDU, probably due to a decline in injecting behavior. Increased sexual risk