

# Emerging viruses in organ transplant recipients - immune responses to H1N1/09 influenza vaccine and hepatitis E virus infection

## Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs Universitet offentlig kommer att försvaras i Sahlgrenska Aula, Blå Stråket 5, Sahlgrenska Universitetssjukhuset/Sahlgrenska, Göteborg,

Torsdagen den 6 april 2017 klockan 13.00

av

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## Avhandlingen baseras på följande delarbeten

- I. Marie Felldin, Marie Studahl, Bo Svennerholm, Vanda Friman. The antibody response to pandemic H1N1 2009 influenza vaccine in adult organ transplant patients. *Transplant Int.* 2012;25(2):166-71.
- II. Marie Felldin, Bengt Andersson, Marie Studahl, Bo Svennerholm, Vanda Friman. Antibody persistence one year after pandemic H1N1 2009 influenza vaccination and immunogenicity of subsequent seasonal influenza vaccine among adult organ transplant patients. *Transplant Int.* 2014;27(2): 197-203.
- III. Marie Felldin, Sanja Johansson, Jan Holgersson, Vanda Friman. HLA antibody responses in adult solid organ transplant recipients after AS03-adjuvanted influenza A (H1N1) vaccination. *In manuscript.*
- IV. Marie Felldin, Vanda Friman, Magnus Lindh, Heléne Norder. High prevalence of anti-HEV IgG in a Swedish solid organ transplant population. *Submitted.*

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INSTITUTIONEN FÖR MEDICIN**



# Emerging viruses in organ transplant recipients – Immune responses to H1N1/09 influenza vaccine and hepatitis E virus infection

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## Abstract

Solid organ transplant (SOT) recipients run the risk of serious infections. The pandemic influenza A H1N1/09 had unknown severity, so large-scale vaccination was needed. The AS03-adjuvanted vaccine (Pandemrix<sup>®</sup>) had unknown effects among SOT recipients. We aimed to explore the influenza-antibody (ab) response, ab persistence one year later and subsequent response to the seasonal influenza vaccine (TIV/10) among adult SOT recipients. Reports of narcolepsy and possible allo-sensitisation following the H1N1/09 vaccination necessitated an analysis of HLA abs and further follow-up. 80% of SOT recipients and 100% of controls had seroprotective H1N1/09 titre levels after 2 vaccine doses ( $p=0.003$ ). A significant loss of protection after 1 year was seen in all subjects. TIV/10 boosted a rise in seroprotection from 47% to 71% in the SOT group and 63% to 100% in controls. Non-responders were more often on triple immunosuppression and had lower renal function. No SOT recipient developed *de novo* HLA abs, but HLA abs with new specificities were detected in 7 patients. No acute rejection was seen within 2 years after vaccination. Two had chronic rejection within one year but a lower and mixed DSA response to the vaccine. The 4th study aimed to investigate the prevalence of hepatitis E (HEV) IgG, IgM and HEV infection, as chronic infection has been reported among SOT recipients. At transplantation, the anti-HEV IgG prevalence was significantly higher in SOT patients compared with blood donors, 30.6% and 16.8% respectively ( $p<0.0001$ ). The patients appeared to have been infected at an earlier age. Two cases of *de novo* and 2 chronic HEV infection were suspected but could not be verified by HEV-RNA.

**To summarise**, the AS03-adjuvanted H1N1/09 influenza vaccine was effective among SOT recipients but significantly less compared with controls. One third of all subjects lost their seroprotection after one year, but TIV/10 reproduced some of the former protection. No patient developed *de novo* HLA abs. The unexpected high prevalence of anti-HEV IgG among the Swedish SOT recipients highlights the possibility of hepatitis E as a new opportunistic infection in the immune compromised host.

**Keywords:** Solid organ transplant, SOT, Hepatitis E, Influenza, H1N1, AS03 adjuvant, HLA antibodies, DSA, rejection.