Rotavirus gastroenteritis places a heavy burden on European hospitals


Rotavirus (RV) gastroenteritis places high demands on European healthcare systems, accounting for a substantial proportion of hospitalizations and emergency department (ED) visits due to community-acquired acute gastroenteritis in children under the age of 5.

Dr. Johannes Forster, St. Josefskrankenhaus, Freiburg, Germany, and multicentre colleagues assessed the burden of RV gastroenteritis in children under 5 years of age in France, Germany, Italy, Spain and the UK. The burden of disease was assessed using data provided by Surveillance for Hospitalized Rotavirus Infections in Kids (SHRIK). The survey was undertaken immediately before the introduction of new RV vaccines in Europe and data were collected from 12 hospitals overall. “Among the 3734 children aged <5 with acute gastroenteritis retained in the per protocol analysis, 55.1% were recruited via the ED, 41.8% were hospitalized because of community-acquired acute gastroenteritis and 3.1% had nosocomial RV gastroenteritis,” investigators reported.

Stool samples were available for 2928 cases of community-acquired acute gastroenteritis, of which 43.4% tested positive for RV by ELISA. The proportion varied between countries, however, from a low of 29.8% in Spain to a high of 57.6% in France. Overall, over 56% of community-acquired acute gastroenteritis cases requiring hospitalization—and almost one-third of children seen in the ED—tested positive for RV. Predictably, over 80% of the cases occurred in children under the age of 2, while over 82% of children requiring hospitalization for acute gastroenteritis were also under 2. More children who tested positive for RV had severe acute gastroenteritis and RV-positive children were also more likely to present with vomiting, severe dehydration and fever, and to require intravenous rehydration therapy, than RV-negative children. The median duration of hospitalization did not, however, differ at 4.0 days between RV-positive and RV-negative disease.

“Most RV gastroenteritis cases [89%] occurred between December and May, corresponding to the RV season in Europe,” the authors observed. G1P(8) was the most prevalent RV type, accounting for 40.3% of all cases, followed by G9P(8) (31.2%), G4P(8) (13.5%) and G3P(8) (7.1%).

“Results confirm that RV is a major cause of acute gastroenteritis among European children aged <5 years, accounting for 43.4% of all cases,” researchers concluded, “and based on our findings, it is reasonable to expect RV vaccination to have a major impact in reducing the burden of RV gastroenteritis in the region, lessening ED and hospital overcrowding because of winter acute gastroenteritis.”

HZ vaccine immunogenicity not inferior in a younger cohort


According to an American study, the immunogenicity of the herpes zoster (HZ) vaccine in patients between the ages of 50 and 59 years is not inferior to that elicited in patients ≥60 years of age and vaccinating a younger cohort could potentially prevent approximately half of all HZ episodes.

Dr. Santosh Sutradhar, Upper Gwynedd, Pennsylvania, and colleagues compared varicella-zoster virus (VZV) antibody titres in 50- to 59-year-olds who received the HZ vaccine in one of two multicentre clinical trials to those of adults ≥60 years of age. In one study, 135 vaccine recipients were between the ages of 50 and 59 years while in the second study, 259 were between 50 and 59 years of age. In the first study, approximately half of the recipients received the refrigerated formulation of the HZ vaccine while the other half received the frozen formulation. In the second study, recipients received the frozen formulation only but half received the vaccine at the same time as the inactivated influenza vaccine while the other half received both vaccines given 28 days apart.

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Cross-protection seen against oncogenic non-vaccine HPV types in both HPV-naive and sexually-active women


Wheeler et al. The impact of quadrivalent human papillomavirus (HPV; types 6, 11, 16, and 18) L1 virus-like particle vaccine on infection and disease due to oncogenic nonvaccine HPV types in sexually active women aged 16-26 years. J Infect Dis 2009;199(7):936-44.

A significant degree of cross-protection against oncogenic human papillomavirus (HPV) types not incorporated in the quadrivalent vaccine has been demonstrated in both HPV-naive and sexually-active women between 16 and 26 years of age, all of whom participated in the FUTURE HPV studies program.

Dr. Darron Brown, Indiana University School of Medicine, Indianapolis, and multicentre colleagues evaluated the impact of the quadrivalent HPV vaccine on infection rates and subsequent disease associated with 10 non-vaccine HPV types in women who were both seronegative and DNA-negative to HPV 6, 11, 16 and 18 on enrolment. A total of 9296 subjects (53%) of those enrolled in the FUTURE trials program were included in their analyses for cervical disease. Cross-protection was evaluated for HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59, which are associated with >20% of cervical cancers. Study participants were followed for an average of 3.6 years.

The efficacy of the vaccine against cervical intraepithelial neoplasia (CIN) 1-3, or adenocarcinoma in situ (AIS) caused by the 10 non-vaccine types was 23.4%. Efficacy against high-grade lesions (CIN 2-3/AIS) attributable to the 10 tested HPV types was 32.5%. More individually, vaccination reduced the incidence of HPV 31/45-related CIN 1-3 by 43.6% and of HPV 31/33/45/52/58-related CIN 1-3/AIS by 29.2%. "Efficacy was driven primarily by reductions in HPV 31, 33, 52 and 58," investigators noted, "[while] no efficacy for disease was observed with respect to HPV 45." Of the 10 non-vaccine HPV types examined, type 45 was the least likely to be detected in CIN lesions, the authors added. "Over the course of follow-up, reductions in the incidence of disease became increasingly apparent for the 10 tested non-vaccine HPV types," investigators noted. "These findings are the first demonstration of cross-protection for any HPV vaccine against CIN2-3/AIS disease end points that are cervical cancer precursors and that formed the basis of vaccine licensure."

In a separate analysis, Dr. Cosette Wheeler, University of New Mexico, Albuquerque, and multicentre colleagues examined the impact of the same quadrivalent vaccine on infection and cervical disease related to the same 10 non-vaccine HPV types in a cohort of HPV-naive women and women with pre-existing HPV infection and/or HPV-related disease on study enrolment. In this cohort, vaccination reduced the rate of HPV 31-, 33-, 45-, 52- and 58-attributable infection by 17.7% and CIN 1-3/AIS by 18.8%. Vaccination also reduced the rate of HPV 31-, 58- and 59-related CIN 1-3/AIS by 26%, 28.1% and 37.6%, respectively, investigators added. "These cross-protection results complement the vaccine’s prophylactic efficacy against disease associated with HPV 6, 11, 16 and 18," they concluded.

Pneumococcal vaccine effectiveness confirmed in matched case-control study


The effectiveness of the 23-valent pneumococcal polysaccharide vaccine (PPV) against pneumonia in middle-aged and older adults has been confirmed in a matched case-control study.

Dr. Angel Vila-Corcoles, Primary Care Service of Tarragona-Valls, Spain, and multicentre colleagues assessed the clinical
effectiveness of the 23-valent PPV in preventing pneumococcal pneumonia—with and without bacteremia—in patients ≥50 years of age. The study included 304 patients with pneumococcal pneumonia and 608 outpatient controls. Among the 304 patients with pneumococcal pneumonia, 30.9% presented with bacteremia and 69.1% were non-bacteremic cases. The case fatality rate was 18.1% for patients with bacteremia and 8.6% for those without. Crude vaccine effectiveness against overall pneumococcal pneumonia was 46% while crude effectiveness against all bacteremic cases was 60%. Vaccine effectiveness against non-bacteremic cases was 38% but against bacteremic infections due to vaccine types, crude effectiveness reached 74%.

“The adjusted vaccine effectiveness against all pneumococcal pneumonia was 60%... during the influenza period and 49%... during the non-influenza period,” the authors added. As they pointed out, the effectiveness of the PPV has been controversial. “In this study, a significant adjusted vaccine effectiveness of 48% against overall pneumococcal pneumonia has been found. This effectiveness was on the basis of the effect of the vaccine in preventing bacteremic cases [66%] as well as non-bacteremic cases [42%].”

Researchers concluded that the benefit of vaccination against nonbacteremic cases, as shown in this study, means that the vaccine has a greater level of cost-effectiveness than has been suggested in the past and thus supports its use, even if protection against pneumococcal pneumonia is not entirely complete.

**New CMV vaccine may decrease maternal, congenital CMV infection**


According to a multicentre randomized phase II trial, a new vaccine against cytomegalovirus (CMV) has the potential to decrease maternal and congenital CMV infection.

Dr. Robert Pass, University of Alabama, Birmingham, and colleagues tested the efficacy of a CMV glycoprotein B vaccine in a population of women of childbearing age who had a high rate of incident CMV infection. “Subjects who were negative for antibody to CMV [seronegative] were invited to participate in the 42-month clinical trial if they were in good health, between the ages of 14 and 42, not pregnant and not nursing,” the authors noted. A total of 234 subjects were assigned to receive the vaccine, while 230 received placebo.

“After a minimum of one year of follow-up, there were 49 confirmed infections, 18 in the vaccine group and 31 in the placebo group,” researchers reported. Infection was confirmed by the detection of CMV in body fluids by culture, PCR or both in all but two subjects. Congenital CMV infection was detected in one of 81 infants born to mothers in the vaccine group and in three of the 97 infants born to mothers in the control arm, all of which were the result of maternal infection during pregnancy.

Further analysis revealed that the women assigned to the vaccine group were more likely to remain uninfected during the 42-month trial than those assigned to placebo. On the basis of infection rates per 100 person-years, vaccine efficacy was 50%, investigators noted. Arthralgias occurred significantly more frequently in the vaccine group but only after the third dose of the vaccine. Otherwise, no significant differences in rates of adverse events were seen between the two treatment groups.

As reported by the investigators, “The prevention of congenital CMV infection and its sequelae is the ultimate goal of a CMV vaccine. If future studies, such as a phase III clinical

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**Novel intradermal influenza vaccine elicits superior immune responses than intramuscular vaccine in elderly patients**


A novel intradermal influenza vaccine has been shown to elicit superior immune responses than those achieved by conventional intramuscular (i.m.) vaccination, a response that is expected to enhance patient protection against influenza in those over the age of 60.

Dr. David Holland, Centre for Clinical Research and Effective Practice, Middlemore Hospital, Auckland, New Zealand, and multicentre colleagues compared the immunogenicity and safety of two doses of an intradermal trivalent inactivated influenza vaccine with that of a conventional licensed i.m. control vaccine in 1107 participants between the ages of 60 and 85. The intradermal vaccinations were given using a new microinjection system containing either 15 or 21 µg of hemagglutinin per strain. The primary end points of the study were the strain-specific hemagglutination inhibition geometric mean titres (GMTs) noted 21 days after vaccination.

“After vaccination, GMTs against each strain increased in all groups and were higher in the intradermal groups,” the authors reported. Both doses of the intradermally-administered vaccine were superior to the i.m. control vaccine in terms of the GMT noted 21 days after vaccination, and post-vaccination GMTs in each intradermal group were 48% to 70% higher than those in the control group. “For each strain and for each intradermally-administered vaccine, the seroprotection rate, the rate of seroconversion or significant titre increase, and the GMT ratio were significantly higher than those associated with the i.m.-administered control vaccine,” the authors added, with the exception of seroprotection rates against one strain following the administration of the 15-µg intradermal dose.

Local injection-site reactions, particularly erythema, were more common following the intradermal vaccination, investigators observed. Nevertheless, it was achieved with an easy-to-use, reliable microinjection system, suggesting that this system is likely to provide increased protection against influenza infection and its associated complications in elderly adults, the authors concluded.
trial, continue to demonstrate reasonable efficacy, safety and an acceptable level of reactogenicity, then this vaccine may be useful in preventing CMV infection in young women and congenital CMV in their infants.”

**MMR vaccination does not increase risk of invasive infections 90 days later**


The measles-mumps-rubella (MMR) vaccine does not increase the risk of invasive infection within 90 days of vaccination, according to a UK study, negating the hypothesis that there is an induced immune deficiency due to overload from multi-antigen vaccines.

Dr. Julia Stowe, Protection Agency Centre for Infections, London, UK, and multicentre colleagues had previously tested the hypothesis that the MMR vaccine induces significant immunosuppression, thereby leading to increased hospitalization from bacterial infections in the three months following MMR vaccination. Having found no evidence for such an effect, they proceeded to update findings with an additional 10 years of hospital admission data in children between the ages of 12 and 23 months.

A total of 2077 admissions in 2025 children were linked to an MMR record. Analyses were carried out using the self-controlled, case-series method and separately for bacterial and viral infection cases, using risk periods of 0 to 30 days, 31 to 60 days and 61 to 90 days’ post-MMR vaccine. In the 0 to 30-day period following MMR vaccination, the authors observed a reduced risk for both bacterial infection (relative incidence = 0.68) and viral infections (same relative incidence).

“There was also no increased risk in any period when looking at combined viral or bacterial infections or for individual infections with the single exception of an increased risk in the 31 to 60 days’ post-vaccination period for herpes infections,” researchers added. For those children who were given the meningococcal group C (MCC) vaccine concomitantly with the MMR vaccine, there was again no increased risk in either bacterial (relative incidence = 0.54) or viral infections (relative incidence = 0.46).