Human metapneumovirus – why the poor cousin of RSV?

LONDON, UK----27th May 2015----ExpertREACT. According to latest research by **VacZine Analytics**, there is no compelling reason why the vaccine industry should not consider developing an hMPV vaccine. RSV appears to have stolen the limelight from its similarly dangerous cousin – but it could help its cause.

Human metapneumovirus (hMPV) is a RNA virus member of the *Metapneumovirus* genus in the *Pneumovirinae* subfamily of the *Paramyxoviridae* family (1). Despite only being discovered in the Netherlands in 2001, serologic studies have indicated the virus has been circulating in humans, globally for at least 50 years. The virus is transmitted via direct or close contact with contaminated secretions, which may include saliva, droplets or large particle aerosols. Similar to its cousin, Respiratory syncytial virus (RSV), which is also a *Pneumovirinae*, and influenza, hMPV has a seasonal distribution similar to with most cases occurring in late winter/early spring (2).

The main issue associated with hMPV is that the virus is believed to be the second most common cause of lower respiratory tract infection after RSV in young children (1). Characteristic symptoms in this age group are cough and bronchitis, which can cause hospitalization with a pneumonia outcome. Not all children exhibit serious symptoms with hMPV infection, Seropositivity for hMPV approaches 100% by 5–10 years of age (3). However, prevalence rates in hospitalised children are high and range from ~5 to 10%. Children hospitalised with hMPV are more likely to have pneumonia or asthma, require supplemental oxygen and have a longer stay in the ICU than those without hMPV (3). In this subset, mortality occurs in 5–10% of hMPV-positive children - which is of grave concern considering there is no specific treatment for the virus.

hMPV also affects adults (prevalence 2.2-10.5%)(4), through a process of reinfection. Reinfection generally causes a mild illness, including fevers/shivers, most commonly in the greater than 60 yrs age group. However, again reinfection of hMPV can cause severe symptoms e.g. pneumonia and even death in immunocompromised groups. Mortality from hMPV occurs in 3.4–6.6% of hospitalised adults (4,5).

hMPV has some distinct differences from its closely related cousin, RSV. hMPV infected children tend to be older than RSV-infected children and are more likely to have a fever; however, other clinical signs and the need for ICU admission were not different between the diseases (6). Risk factors for severe infection with both viruses tend to be similar in both infants and adults. For infants severe disease tends to occur in <6 months, more than three children in the household, prematurity and presence of comorbidity. In adults, severe infection occurs in those with advanced age, COPD, asthma, immunocompromised and transplant recipients. Coinfection with both viruses does occur in 5 to 14% of cases, and 70% of infants with severe bronchiolitis (7,8).

Given the substantial burden of disease related to hMPV, especially in infants/younger children. It is somewhat surprising that the number of current efforts to develop an hMPV vaccine dwarf in comparison to RSV. For example, an analysis by PATH updated (March 2015) indicated that there were at least 10 RSV vaccine programs in full clinical development, the most advanced of which remains the glycoprotein F Nanoparticle approach by U.S. Novavax (9). To complement this, the preclinical RSV vaccine pipeline is substantial, with >40 approaches across a wide range of approaches. In comparison, our latest analysis suggests there is only one active clinical development program for a hMPV vaccine, namely rhMPV-PA (live attenuated approach), which is being developed by NIAID (10). This vaccine, which is composed of a chimeric approach containing avian N or P proteins inserted into the hMPV genome, is being tested in healthy adults, infants and children (Phase I) study - with completion June 2015 (NCT01255410). At present, no major vaccine company appears to be explicitly involved in hMPV development.

Our recent analysis (11) has assessed the commercial potential of a monovalent hMPV vaccine and a bivalent hMPV vaccine, which also would target RSV. Our modeling would suggest both putative vaccines are commercially attractive.

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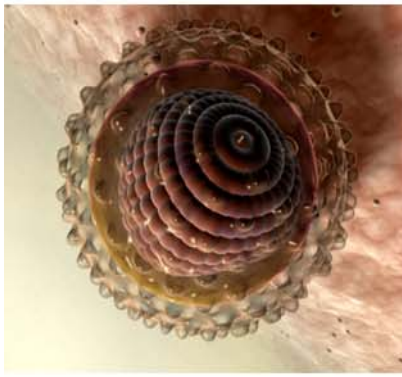

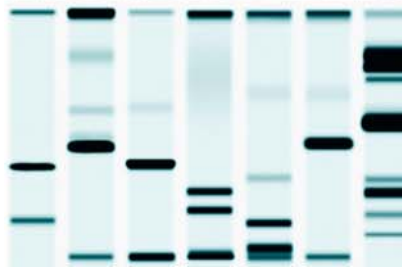

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Any developer wishing to consider hMPV vaccine development will be aware that much investigation has already been conducted at the preclinical level (11). Similar to RSV, hMPV vaccine development has also been tainted with the prospect of vaccine induced pulmonary disease enhancement observed by one antiquated approach (formalin inactivated) in the cotton tail rat reported by Hamelin et al 2007; Yim et al., 2007. These data shouldn't deter any manufacturer. Instead the real challenges are 1) whether to couple hMPV vaccine development with RSV, 2) choosing an appropriate vaccine approach that in turn 3) is most suited for the target group(s) in question. Maternal immunization – is an important discussion area.

Coupling RSV to hMPV vaccine development could be an advantage in that significant research momentum already exists in the segment. However, at the same time the prospect of a bivalent approach could significantly raise the hurdle of technical feasibility. AZ/Medimmune stands out as a company with a good fit to hMPV vaccine development should live-attenuated approaches be considered – but the need to protect the very young infant may favour alternative strategies.

References and Notes:

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