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Editorial

Human metapneumovirus infection: An emerging problem in high-risk infants

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Viral infection is an important cause of upper and lower respiratory tract illness in infants and young children world wide, causing significant respiratory morbidity in affected children. Premature infants, especially those with bronchopulmonary dysplasia (BPD), chronic oxygen dependency and congenital heart disease are regarded as "high risk" infants because a higher proportion of such infants require hospitalization and admission to the pediatric intensive care units. Their problems often continue after discharge from hospital, as they may develop persistent symptoms such as cough and wheeze. This has significant impact on resource utilization, cost of care and quality of life for the infants and their families.

A number of viruses such as respiratory syncytial virus (RSV) and adenoviruses are well recognized to be implicated in the pathogenesis of serious lower respiratory tract illness, but in a substantial number of symptomatic children, no virus can be identified. This may be due to a variety of reasons including insensitivity of the specific diagnostic tests at individual hospitals, or the medical profession's unawareness of newly emerging pathogens. This was indeed the case when researchers in the Netherlands isolated human metapneumovirus (hMPV) from children for the first time in 2001 [1]. Since then, investigations in different countries have described a number of patients with acute respiratory tract infection due to hMPV [2]. Most of these published data suggest that the clinical spectrum produced by hMPV and RSV are similar but there may be important differences which we do not fully appreciate yet. For example, lower respiratory infection due to hMPV tends to occur mostly during late winter, between December to April with peak incidence in March, a pattern which coincides with the latter half of the RSV season. It is also known that hMPV infection can co-exist with other viral infections including RSV and severe acute respiratory syndrome (SARS) but we do not know what effect this has on the severity of illness [3].

In this issue of the Journal, Professor Greenough's group from London report their follow up findings on 112 children who were born premature and suffered from viral respiratory tract illnesses during the first year of life [4]. This was an observational study of a small cohort but all infants were diligently monitored for evidence of any lower respiratory tract infection if they presented with symptoms to either their hospital or general practitioners (GP). Nasopharyngeal aspirates (NPA) samples were obtained for all such cases and analyzed to identify causative pathogens including hMPV. Eighty-four out of 112 study infants suffered 126 lower respiratory tract illnesses (LRTIs); 94 viruses (41 RSV, 36 rhinovirus, 7 hMPV, 5 parainfluenza and 5 influenza) were identified from 82 of the 126 NPAs. Compared to the no viral LRTI group, infants with only RSV infection had more ($P = 0.038$) and longer

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($P = 0.045$) hospital admissions, more GP attendances ($P = 0.024$), more cough ($P = 0.030$) and wheeze at follow up ($P = 0.018$). If infants with dual infections were also considered, infants with a hMPV LRTI with or without other viral RNA being detected, compared to the no viral group had more hospital admissions ($P = 0.005$), longer admissions ($P < 0.001$), more GP visits ($P = 0.029$), more days of cough ($P = 0.008$) and more days of wheeze ($P = 0.004$). Based on their findings, authors calculated that lower respiratory tract illnesses caused by RSV and hMPV were associated with increase healthcare utilization due to increased respiratory morbidity in prematurely born infants. This has important implications, both for clinical practice and patient care planning because of significant burden on service provision and resource allocation, especially as they cause epidemics.

There is no safe and effective vaccine as yet developed to protect against these viruses. Immunoprophylaxis with Palivizumab does reduce RSV symptoms in prematurely born babies but its cost effectiveness as "routine" prophylaxis for all such infants has been questioned. Until this is resolved, it is important that we identify and selectively provide immunoprophylaxis to at least those babies who are at "high risk" for developing severe illness due to RSV. Naturally, the current information towards an effective antiviral strategy for hMPV is very limited because of scant data on pathogenesis of the virus. There are some indications that a monoclonal antibody could be used prophylactically to prevent lower respiratory tract disease caused by hMPV [5].

Thus, it seems that RSV is not the be-all and end-all of doing an NPA on a child suspected to have LRTI and there should be heightened surveillance and improved laboratory techniques to screen for other pathogens such as hMPV, particularly in a symptomatic child with negative RSV. Most of the hospitals, at least in the United Kingdom, do not consider inclusion of hMPV in their routine laboratory test, perhaps due to ignorance or cost. Certainly more information is needed about hMPV from population studies in order to establish or revise our diagnostic algorithm for investigation of viral respiratory infections in infants and children.

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