Human Coronavirus Nomenclature

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To the Editor:

We are writing to express our concern about the nomenclature used to recently describe human coronaviruses in the *Pediatric Infectious Disease Journal*. In the November 2005 supplement, a review article by Kahn and McIntosh[1] and the Introduction by Johnston and Kahn[2] make reference to an apparently distinct coronavirus species, human coronavirus New Haven (hCoV-NH).

Using the available published data,[3] it is not possible to characterize this virus as significantly different from 2 other previously described viruses: hCoV-NL63[4] and hCoV-NL.[5] Fouchier et al acknowledged that hCoV-NL63 and hCoV-NL were "essentially the same virus."[5] However, Esper and colleagues claimed the discovery of a novel virus despite concluding in their article that HCoV-NH was closely related to HCoV-NL63 and that they "likely represent the same species."[3] Evidence to support that hCoV-NH is not "novel" comes from a companion paper to the original New Haven paper in which polymerase chain reaction primers used to identify hCoV-NH in a case–control study of Kawasaki disease were designed using sequence from hCoV-NL63 and hCoV-NL located on the GenBank database.[6]

Responding to early controversy about nomenclature, Esper et al stated "Until full genomic sequencing of HCoV-NH is complete, we believe that it is premature to state that HCoV-NH, HCoV-NL63, and HCoV-NL are the same virus."[7] It is a pity that more than 500 days after submission of the first New Haven articles,[3,6] the full sequencing data for hCoV-NH, and a comparison with those of hCoV-NL63, have not been published.

The classification and nomenclature of a new virus requires endorsement by the International Committee for Taxonomy of Viruses or an appropriate study group and this can be a slow process. The onus of proof in science has always been on the discoverer to demonstrate the novelty of their finding. Without clear evidence of uniqueness, the accepted interim format for publication is, and should remain, the use of the nomenclature proposed by the original study.

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Tuberculosis of Rib and Lung Presenting as Subcutaneous Emphysema

To the Editor:

A 9-year-old boy presented to us with progressively increasing swelling in the left posterior triangle of neck for 1 week. He also had associated pain, anorexia, malaise and occasional mild fever for last 2 months. There was a history of occasional nonproductive cough.

On examination, there was a diffuse swelling in the left posterior triangle of neck and on palpation, crepitation was felt. On auscultation, crepitus was present in the left upper chest.

On radiologic examination, there was evidence of subcutaneous emphysema in the left posterior triangle of neck, lytic lesion in left second rib with consolidation in the left upper zone. Computed tomography scan confirmed destruction involving the neck and angle of left second rib with surrounding abscess and associated lesion in the lung. There was no clinicoradiologic evidence of pneumomediastinum. Aspiration of the abscess of second rib revealed *Mycobacterium tuberculosis* by polymerase chain reaction. Anaerobic culture was negative. The patient had a bacille Calmette-Guerin vaccination scar.

A diagnosis of tuberculosis of the second rib and lung with localized subcutaneous emphysema was made, and the patient was treated with rifampin, isoniazid, pyrazinamide and ethambutol. Swelling slowly decreased in size and, after approximately 10 days, localized crepitus disappeared.

After 8 weeks, a chest radiograph revealed resolution of parenchymal lesion. Antitubercular therapy was continued for 6 months resulting in resolution of the rib lesion.

Tuberculosis of the rib is rare in endemic areas of Southeast Asia, occurring in only 2% of cases.[1] Associated pleuropulmonary tuberculosis has been reported in only a few cases.[7–9] In our case, contiguity of the rib and pulmonary lesion strongly suggests direct spread of the disease. A tuberculous rib lesion is usually involves the midshaft of rib or the parasternal area[10] and is associated with a fluctuant swelling on the chest wall,[11] absence of which makes the diagnosis difficult.[7,8] In our case, there was no fluctuant swelling on the chest wall and involvement of the rib was mainly posteriorly. A computed tomography scan can help demonstrate the skeletal lesion and any associated abscess or parenchymal involvement.[8,9,12]

Subcutaneous emphysema has been rarely reported in cases of pulmonary tuberculosis and is usually associated with pneumomediastinum.[2–6] Childhood tuberculosis usually presents with fever, cough, lymphadenopathy and loss of weight and appetite. Air leak is a very rare presentation and has been reported only associated with miliary tuberculosis.[4–6] Infections such as staphylococcal pneumonia, bronchial asthma, histiocytosis, trauma, rup-

ture of congenital lobar cyst, foreign body inhalation and toxin (ie, hydrocarbon inhalation), mechanical ventilation and invasive procedures are other causes of air leak in children.[13,14]

We believe that the pulmonary parenchymal lesion eroded into a peripheral airway, and because the parenchymal lesion and the rib lesion were in direct continuity, this resulted in localized subcutaneous emphysema.

In countries where tuberculosis is endemic, diagnosis is usually established clinically. This rare presentation with atypical clinical and radiologic findings can cause a diagnostic dilemma.

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Nasal Continuous Positive Airway Pressure and Gram-Negative Sepsis in Low-Birthweight Infants

To the Editors:

We read with great interest the article by Graham et al[1] on risk factors for late-onset Gram-negative bloodstream infection (GN-BSI) in low-birthweight infants. In this case-control post hoc analysis, the authors established significant associations between GN-BSI and the duration of central venous catheterization, nasal cannula continuous positive airway pressure (NC-CPAP) use, H2 blocker use, and gastrointestinal tract pathology. The study could not establish any association between BSI and birthweight or use of mechanical ventilation. We would like to add some comments on these issues.

There is a tight association between low birthweight and NC-CPAP. The majority of low-birthweight infants (75% of control and 81% of cases) are supported with NC-CPAP from birth. The order of ranking of variables in the logistic model is critical for interpretation of the results and may explain why birthweight was not found to be a significant variable. Further, the identification of NC-CPAP and not mechanical ventilation as an independent risk factor for GN-BSI is curious, given the univariate data presented in Table 1 of that article (case/control, NCPAP 81% versus 75%; mechanical ventilation, 71% versus 44%).

The model that was established in this article is counter to previous literature indicating that mechanical ventilation and birthweight are known risks for infections.[2] Neither variable was associated with sepsis in the provided model.

The reported rate of infection in the 2 nurseries was 298 episodes of BSIs in 548 VLBW infants (54%). Some infants may have had more than 1 infection (data not reported), but this is still a rate about twice the national average.[2] Whether these data would apply to NICUs with better infection-control practices is questionable.

The authors' speculation about pathogenesis includes deep suctioning, which seems unlikely on NCPAP and, if so, would more likely to be associated with endotracheal intubation and suctioning.

We recently reported a new strategy to control BSI in the NICU.[3] At the George Washington University, we observed only 8 positive cultures that were all Gram-positive. We did not have a single Gram-negative infection during the 36-month study, despite the fact that we use the same "bubble CPAP" used at Columbia Presbyterian. The new line-care strategy was adopted from the NICU at Connecticut Children's Hospital, a unit also using bubble CPAP and not experiencing significant GN-BSI.

There is a strong link in the literature between late-onset BSI and the use of mechanical ventilation.[2] Both can lead to increased incidence of CLD. It is difficult to understand how the use of CPAP, an alternative to mechanical ventilation, is associated with more infections but still less CLD. In fact, the NICU at Columbia Presbyterian (one of the 2 NICUs in the study) has traditionally had the lowest CLD reported among NICUs in the NICHD consortium. This record would be surprising if GN-BSIs were so prevalent.

One of the concerns in the authors' analysis is using CPAP and mechanical ventilation as a categorical variable. These 2 variables should be analyzed as continuous variables, similar to central line days.

NC-CPAP may lead to nasal mucosal erosion and predisposition to systemic infection. As the authors point out, such infection would not likely be Gram negative because newborns usually have Gram-positive colonization of the nasal mucosa. We have seen occasional babies with *Staphylococcus aureus* sepsis thought to be caused by nasal mu-

cosal erosion from NC-CPAP. Following a cluster of 3 such infants, we began using Bactroban (mupirocin) in the nasal mucosa for babies on NC-CPAP with either *S. aureus* colonization or significant mucosal breakdown and have not had a subsequent case.

Finally, we suggest that reduction in all nosocomial BSIs (including GN-BSIs) in VLBW infants is best achieved by careful infection-control practices, particularly those related to insertion and care of central venous lines, rather than limiting the use or duration of NC-CPAP or central lines.

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Reply

To the Editors:

I thank Drs. Aly and Herson for their comments on our article regarding risk factors for late onset Gram-negative bloodstream infection (GN-BSI) in very-low-birthweight (VLBW) infants[1] and congratulate them on the reductions in bloodstream infections in their respective NICUs.

I agree that the association between nasal-cannula CPAP and GN-BSIs is unexpected and present possible reasons for this association in the discussion section beyond the one commented on in the letter. This matter clearly deserves prospective investigation. Like the letter's authors, I would have preferred to analyze nasal-cannula CPAP and mechanical ventilation as continuous variables; unfortunately, this was a secondary analysis of existing data and information was not available in that form.

I also agree that the lack of an association between low birthweight and GN-BSI is interesting. The authors cite Stoll et al's NICHD study as showing that birthweight is inversely correlated with infection. Although this is true in a broad sense, our aim was to examine specific risk factors for GN-BSIs in VLBW infants that have not previously been well established outside of outbreak investigations. Our lack of detection of an association between birthweight and GN-BSI may have been because we examined 217 subjects, all of whom were VLBW. It may be that an increased risk of lower birthweight within this already at-risk population is difficult to discern without a very large sample size.

The comment that reduction in all nosocomial BSIs is best achieved by careful infection control practices is one I wholeheartedly agree with. We did not actually suggest limiting nasal-cannula CPAP; rather, we noted an association between its use and GN-BSI and suggested further study. Limiting the duration of central venous catheter use to when absolutely necessary and being aware of the increased risk of infection that accompanies increased duration of catheterization should be part and parcel of "careful infection control practices."

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