Reply to Ulloa-Gutierrez

To the Editor—We thank Dr. Ulloa-Gutierrez [1] for his interest in our recent article about the association of Streptococcus pneumoniae serotypes with necrotizing pneumonia in children in Utah [2]. Ulloa-Gutierrez [1] addressed parameters other than S. pneumoniae serotype that may be predictors of severity. Specifically, an elevated lactate dehydrogenase (LDH) level appears to be associated with severe necrotizing pneumonia caused by serotype 3 in the Hospital Nacional de Niños de Costa Rica (San José) [1]. An elevated LDH level likely represents cellular damage to lung parenchyma, and it is reasonable to hypothesize that the degree of elevation correlates with the extent of necrosis. If S. pneumoniae serotype 3 causes more extensive necrosis, it stands to reason that LDH levels will be more elevated in patients with pneumonia caused by serotype 3.

At the suggestion of Ulloa-Gutierrez [1], we retrospectively evaluated the pleural fluid LDH levels in the 14 patients with serotype 3 pneumonia in our study. Five of the 14 patients had pleural fluid LDH levels measured. The median LDH level was 49,460 U/L (range, 39,700–118,041 U/L). These values represent a 40–120-fold increase over the upper limit of normal for serum LDH level in our laboratory (975 U/L). These findings appear to be consistent with those of Ulloa-Gutierrez [1]. However, care should be taken when comparing pleural fluid indices from retrospective studies because of the variability in time to presentation and other clinical and laboratory factors.

Complicated pneumonia in children is a growing problem worldwide. We agree with Ulloa-Gutierrez [1] that pleural fluid indices might prove to be a useful adjunct in predicting outcomes and directing management. In a separate study, we demonstrated that among children with empyema, those with pleural fluid indices including higher WBC counts, lower glucose values, and the presence of bacteria on Gram stain or culture were more likely to require surgical intervention than were those without these findings [3]. The degree of LDH elevation, however, was not associated with the need for surgical intervention.

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References

This practice was abandoned when, in 1542, Ambroise Paré performed one of the first cohort studies to demonstrate that egg yolk and turpentine were better than boiling oil for treatment of gunshot wounds.

There are limited data on natural products, such as yogurt (which seems to help in controlling wound odor [2]), tea tree oil, and potato peeldings; however, there is a great interest in the use of honey for wound healing [3]. Indeed, honey kills staphylococci [4], including the fearsome community-acquired methillin-resistant Staphylococcus aureus [5], within a few hours; it has anti-inflammatory activity [6]; and its hypertonicity provides anti-septic activity. However, clinical data on the effect of honey on wound management are controversial [7, 8], often because of the low quality of some studies [9] and perhaps because of different antimicrobial activities of different honey types [10].

Although science and technology march ever forward, we must not fail to exploit the potential of natural products, because they may represent—as in ancient times—a hope for modern medicine.

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References


Antiviral Activity of Cidofovir and Ribavirin against the New Human Adenovirus Subtype 14a That Is Associated with Severe Pneumonia

To the Editor—Louie et al. [1] have described 3 cases of severe pneumonia caused by a new pneumotropic human adenovirus subtype 14a (HAdV-B14a). Moreover, several outbreaks of HAdV-B14a infection with a high mortality have been described in the United States, suggesting emergence of a highly pathogenic virus [2]. The emergence of HAdV-B14a as a respiratory pathogen has also been observed at US military training centers [3].

An experimental antiviral therapy with cidofovir for a single case of HAdV-B14a pneumonia was reported by Louie et al. [1], although it achieved limited clinical success. HAdV-B14a is a member of species B (subspecies B2) human adenoviruses. In vitro susceptibility of human adenoviruses to antiviral drugs is species dependent. Human adenoviruses of species C have been shown to be susceptible in vitro to both ribavirin and cidofovir, whereas the susceptibility of human adenoviruses of other species to ribavirin has been shown to be significantly lower [4, 5]. Nevertheless, testing the in vitro susceptibility of HAdV-B14a to ribavirin seems to be reasonable, because high concentrations of ribavirin (>1000 μM) can be achieved in respiratory secretions with use of high-dose aerosol therapy, which has been developed for treatment of respiratory syncytial virus infection [6].

Therefore, we tested the antiviral activity of cidofovir and ribavirin against HAdV-B14a (Portland isolate, generously provided by D. Erdmann, Centers for Disease Control and Prevention). A rapid quantitative PCR-based assay for testing antiviral agents against human adenoviruses on a lung cancer cell line (A549) was used as described elsewhere [5]. Human adenovirus type 5 of species C (HAdV-C5) served as a positive control. In vitro susceptibility of HAdV-B14a to cidofovir was high and in the same range as that of in vitro susceptibility of HAdV-C5. Peak plasma levels reported after intravenous

Table 1. Antiviral activity of ribavirin and cidofovir against human adenovirus type 5 of species C (HAdV-C5) and human adenovirus subtype 14a (HAdV-B14a) in a lung cancer cell line (A549 cells).

<table>
<thead>
<tr>
<th>Species</th>
<th>Ribavirin</th>
<th>Cidofovir</th>
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<tbody>
<tr>
<td></td>
<td>IC50 [μM]</td>
<td>IC90 [μM]</td>
</tr>
<tr>
<td>HAdV-B14a</td>
<td>2.6 (1.9–3.7)</td>
<td>734.3 (388.0–1557.4)</td>
</tr>
<tr>
<td>HAdV-C5</td>
<td>1.7 (1.1–2.8)</td>
<td>29.0 (15.1–64.4)</td>
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</tbody>
</table>

**Note.** Data are expressed as mean μM (95% CI). IC50, 50% inhibitory concentration; IC90, 90% inhibitory concentration.