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Low positive results were somewhat easier to distinguish by EIA than LA, because the minimal color change produced in the EIA was more apparent than the few agglutinated latex particles in the LA test. However, some of the low positive Abbott Testpack Strep A and Cards Strep A plus and minus endpoints had an irregularly or partially filled vertical line that was neither clearly positive nor clearly negative, making interpretation difficult. The Icon Strep A tests resulted in the presence or absence of a clearly outlined central dot on a white background, giving unequivocal results, with only minimal experience required for interpretation.

DISCUSSION

Although there are many published clinical studies involving rapid GABHS ADTs, most compare only a single kit with the throat culture. Some studies used selective media or anaerobic incubation for their throat cultures, some used single or double swabs, some used hospital laboratory facilities, and others used small clinic offices and office personnel. With such a variety of settings and test conditions, it is difficult to compare one test with another, and as reported recently, there are widely differing results for the same GABHS ADT, depending on the circumstances under which it is tested.3,6

Despite the limitations of an in vitro study in making clinical assessments, this study does provide a common ground for comparing these eight commonly used ADTs under identical, simultaneous conditions. Such identical experimental conditions cannot be obtained from clinical specimens, making valid comparisons between ADTs difficult.

In addition to providing a useful means of comparing the accuracy of these various ADTs, this study also gave us the opportunity to try eight different streptococcal detection kits at one session. Thus we were also able to compare such characteristics as ease of performance, “user friendliness,” and manufacturer documentation and instructions. Hospitals or clinics considering adopting one of these newer kits would undoubtedly also find this approach useful in finding an ADT that best fits their needs. As a result of this study, we have selected the Tandem Icon Strep A for further clinical evaluation in our pediatric clinic.

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Rhinovirus in acute otitis media

Mikko Arola, MD, Thedi Ziegler, MS, Olli Ruuskanen, MD, Jussi Mertsola, MD, Kirsti Nanto-Salonen, MD, and Pekka Halonen, MD
From the Departments of Pediatrics and Virology, University of Turku, Finland

Respiratory virus infections predispose young children to acute otitis media; the risk is strongly associated with infections caused by respiratory syncytial virus, influenza virus, and adenoviruses.1-3 Rhinoviruses are considered to be the major etiologic agents of upper respiratory tract infections,4 but their role in the pathogenesis of acute otitis media is not fully understood. We studied middle ear fluid and nasopharyngeal secretions in 143 children with acute otitis media for the presence of rhinovirus and other respiratory viruses.

METHODS

The study was conducted at a private pediatric centre in Turku and at the Department of Pediatrics, Turku University Hospital, between September 1986 and December 1987. Children with acute otitis media were admitted to the study if tympanocentesis was done. No attempt was
Table I. Results of virus isolation in middle ear fluid and nasopharyngeal secretions of patients with acute otitis media

| Virus                     | Middle ear fluid (n = 143) | Nasopharyngeal secretions (n = 446) |
|---------------------------|-----------------------------|-------------------------------------|
|                          | n (%)                       | n (%)                               |
| Rhinovirus                | 11 8                        | 21 18                               |
| Adenovirus                | 4 3                         | 8 7                                 |
| Respiratory syncytial virus | 1 1                        | 4 3                                 |
| Total                     | 16 11                       | 33 28                               |

made to enroll all patients who were eligible for the study. The diagnosis of acute otitis media was based on signs and symptoms of acute infection and on the presence of fluid in the middle ear. Nineteen patients were receiving antibiotic therapy. The study population consisted of 84 boys and 59 girls. Twenty-five patients were younger than 6 months of age; 39 patients were between 6 months and 12 months; 30 were between 1 and 2 years of age; 29 patients were older than 2 years (mean age 1.5 years; range 19 days to 12.4 years). Middle ear fluid was obtained by tympanocentesis. After collection, a fraction of the fluid was used for routine bacterial culture (134 specimens were taken). For virus isolation a cotton stick was dipped in the middle ear fluid sample and placed in a vial containing 2 ml virus transport medium (0.5% bovine albumin in tryptose-phosphate broth containing antibiotics). Nasopharyngeal secretions for virus isolation were aspirated from the nasopharynx in 116 patients. The virus isolation specimens were frozen within 2 hours on dry ice or transported immediately to the laboratory and stored at -70 °C until processed.

Virus isolation was done as described earlier, with some modifications. One hundred microliters of each specimen was inoculated into duplicate roller-tube cultures of HeLa Ohio cells (donated by Dr. D.A.J. Tyrrell, MCR Common Cold Unit, Salisbury, England) and of human fibroblasts prepared in our laboratory. The cultures were stored in a roller apparatus (12 rev/hr) at 33 °C and examined microscopically every second day. After 6 days of incubation a blind passage was done of negative HeLa cultures and the passages were incubated for another week. On a few occasions a second blind passage was performed. Rhinovirus was identified by its typical cytopathogenic effect and lability to acid treatment.

RESULTS

Rhinovirus was isolated from the middle ear fluid in 11 (8%) of 143 children with acute otitis media; adenovirus was found in the middle ear fluid in four patients, and RSV in one (Table I). Rhinovirus was first isolated in the middle ear fluid in a 19-day-old infant; no bacterial growth was found. Rhinovirus was isolated from nasopharyngeal secretions in 21 (18%) of 116 patients, adenovirus in eight patients, and RSV in four. Altogether, evidence of viral infection in the middle ear fluid or nasopharyngeal secretions was found in 38 (27%) of 143 patients with acute otitis media. Rhinovirus infection accounted for 24 (63%) of the cases. Of the 33 patients with virus in nasopharyngeal secretions, 11 (33%) also had virus in the middle ear fluid.

Of the 116 children without antibiotic therapy in whom middle ear fluid was cultured for bacteria, 62 (53%) had a bacterial pathogen. *Streptococcus pneumoniae* was found in 23%, *Haemophilus influenzae* in 11%, *Branhamella catarrhalis* in 9%, *Staphylococcus aureus* in 8%, and *Haemophilus parainfluenzae* in 3% of patients.

In seven of 13 patients with virus in the middle ear fluid the virus was the only pathogen detected (three children with antibiotic therapy and negative bacterial culture were excluded; two had rhinovirus and one adenovirus; Table II). In the rhinovirus-positive group, no bacterial growth was found in six of nine middle ear fluid samples. Correspondingly, no bacterial growth was found in 47 of 103 samples in the virus-negative group. The difference was not statistically significant.

DISCUSSION

Our results indicate that rhinovirus may play a more prominent role in the etiopathogenesis of acute otitis media than has been suggested earlier. We isolated rhinovirus in the middle ear fluid of 11 of 143 patients. Gwaltney isolated rhinovirus from one of 16 middle ear fluid sam-
pies, and Chonmaitree et al. found rhinoviruses in the middle ear fluid in three of 84 patients. According to Henderson et al., acute otitis media is more closely associated with infections with RSV, adenovirus, and influenza virus than with infections with rhinovirus.

Why the role of rhinoviruses in acute otitis media has not been shown earlier can be explained in several ways. The three studies that have reported rhinovirus infections in patients with otitis may have been made during a season when no major rhinovirus outbreaks occurred in the community. Henderson et al. diagnosed rhinovirus infection in only 48 of 2406 acute episodes of infection, and Chonmaitree et al. in four of 84 patients with acute otitis. Rhinovirus causes about 30% to 50% of all acute respiratory illness. We detected rhinovirus infection in 17% of patients with acute otitis media.

In addition to epidemiologic explanations, technical differences may explain some of the differences between the results of our study and earlier studies. The virus isolation samples were frozen at −70 °C within 2 hours after sampling. A blind passage was done of negative HeLa Ohio cell cultures, which increased the sensitivity of virus isolation. Furthermore, secretions were aspirated from the nasopharynx through the nostrils and a large amount of mucus was usually obtained, from which a swab was taken for virus isolation. We suggest that this collection method may have contributed to the relatively high frequency of rhinovirus infections detected.

In addition to rhinovirus we found adenovirus and RSV in middle ear fluid, in agreement with our earlier studies and with those of others. The low rate of RSV isolation can be explained by the facts that the epidemic was only beginning at the end of the study and the direct detection of RSV antigen was not attempted. Virus as a sole pathogen was found in the middle ear fluid in seven (6%) patients who had received no antibiotic treatment. This observation is in agreement with the studies of Sarkkinen et al. and Klein et al., who found viruses as sole pathogens in 9% and 13%, respectively, of patients with acute otitis.

We conclude that rhinovirus infection is associated with acute otitis media. In some patients rhinovirus may be the only pathogen detectable in middle ear fluid.

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Early coagulopathy in severe iron poisoning

Milton Tenenbein, MD, FRCP, and Sara J. Israels, MD, FRCP

From Winnipeg Children's Hospital, the Departments of Pediatrics and Pharmacology, University of Manitoba, and the Manitoba Poison Control Centre, Winnipeg, Manitoba, Canada

Hepatotoxicity with resultant coagulopathy is a well-known complication of severe iron poisoning and usually occurs at least 24 hours after ingestion. Early gastrointestinal hemorrhage related to mucosal injury occurs within hours of overdose. Any coincident coagulopathy would aggravate the gastrointestinal hemorrhage. Our observations support the presence of an early, reversible coagulopathy dependent on the serum iron concentration in poisoned patients.

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