Comments on the Review of a Book Entitled Bacterial Pathogenesis: A Molecular Approach

Str—I read with interest Dr. Schwartz’s review of Bacterial Pathogenesis: A Molecular Approach [1] because I use this book as my textbook for a graduate student course of the same name. I, too, find the volume both highly readable and factually correct. Therefore, I do not lightly take issue with the rationale given by its authors (Abigail A. Salyers and Dixie D. Whitt) for why antibiotic resistance among isolates of Streptococcus pneumoniae is so closely linked to the occurrence of otitis media among children who attend day care centers in the United States. On page 286, the authors state that

Physicians still routinely treat earache in children with antibiotics. The reason is that parents demand antibiotics. Parents may be motivated not just by their own desire to have the child become symptom-free as quickly as possible, but also by the fact that some day care centers require a child with an ear infection to be taking an antibiotic before the child can return to day care. Opponents of day care like to portray parents who place children in day care as selfish adults who value their own commitments, income and advancement over the well-being of their children. The more accurate image is of a desperate parent (often a single mother, who can barely afford day care) who is facing the loss of a job that supports herself and her child. It is not easy for a physician to withstand that kind of pressure [1].

As can be seen from the passage above, the authors believe that the persons who are primarily responsible for use of antibiotics to treat pneumococcal otitis media are single parents, who (it is implied) pressure physicians to prescribe antibiotics so that their children may return to day care as quickly as possible. The available data simply do not support such an assertion.

The salient conclusion from a study published in 1998 by the National Center for Infectious Diseases was that “increasing proportions of penicillin-nonsusceptible [pneumococcal] isolates were associated with higher median household incomes” [2, p. 1212]. Higher socioeconomic status is itself highly correlated with the mean number of parents in the home, as well as with the sex of the head of the household (see [3] for extensive information concerning, for instance, the Washington, D.C., area). Moreover, in a recent review, Butler and Schwartz [4] of the Centers for Disease Control and Prevention (Atlanta, GA) concluded that antibiotic use is more common with increasing affluence, and that nearly 25% of all antibiotic prescriptions are written for treatment of otitis media. Unfortunately, ∼15% of the population of the United States have little or no access to health care, such that children of single parents are at substantial risk of not even being seen by a physician. Children of more-affluent parents are indeed more likely to receive antibiotics and to transmit antibiotic-resistant pneumococcal strains to their fellow day care attendees than are children of less affluent households, where there is often only a single caregiver.

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A Regimen Containing Rifabutin for the Treatment of Tuberculosis in Patients Intolerant to Rifampin

Str—When rifampin (Rif) cannot be used because of intolerance, current recommendations for the treatment of tuberculosis are administration of isoniazid (INH) and ethambutol (Eth) for 18 months or administration of INH, pyrazinamide (PZA), and streptomycin for 9 months [1]. However, prolonged regimens are associated with diminished adherence and a higher risk of recurrence among patients with tuberculosis due to multiple drug-resistant strains [1]. We used rifabutin (Rib) as a substitute for Rif in the treatment of 2 consecutively seen patients with tuberculosis who were unable to tolerate Rif.

Patient 1 was an 80-year-old woman with pulmonary tuberculosis. After receiving treatment with INH, Rif, Eth, and PZA for 1 week, she developed a hypersensitivity reaction (flulike syndrome, pruritus without rash, and deep thrombocytopenia), which resolved with the discontinuation of Rif. The reintroduction of Rif 1 week later was immediately followed by a recurrence of the hypersensitivity reaction.

Patient 2 was a 35-year-old woman with tuberculous lymphadenitis. She was unable to tolerate Rif and experienced intractable vomiting after each uptake of the drug.

For both patients, Rib was used as a substitute for Rif because of intolerance. The patients received INH, Rib, Eth, and PZA daily for 8 weeks, followed by INH and Rib administered daily for 18 weeks. Rib was well tolerated, and the symptoms
of tuberculosis disappeared with no evidence of recurrence at 1-year follow-up.

Drug interactions between Rif and protease inhibitors have prompted clinical studies of HIV-infected patients that have documented the efficacy of Rib as a substitute for Rif in the 6-month antituberculosis regimen [2–4]. Intolerance to Rif is not rare and could be another indication for Rib. The tolerance profile of Rib is distinct from that of Rif, and there is no indication that cross-toxicity is of concern [5]. In conclusion, a regimen that contains Rib could be the first-choice alternative for the treatment of patients with tuberculosis who are intolerant to Rif.

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Association of TT Virus Primary Infection with Rhinitis in a Newborn

Str—TT virus (TTV), which was discovered in 1997, is the first identified circovirus-like virus that infects humans. To date, TTV has not been formally associated with any disease in humans, even when highly divergent TTV isolates that belong to the SEN family are present, as reported by Chamberland in a recent review [1]. In the general population, reported prevalences of TTV infection are up to 80% [2], and the virus is most often detected in serum and saliva [3]. Transmission of the virus is suspected to occur through multiple pathways and, in particular, through saliva droplets. Mother-to-infant transmission of TTV is uncertain and is not well documented [4, 5]. We report the findings of early follow-up of a full-term female newborn, along with the findings for both parents.

Oral swabs were used to obtain saliva samples from the mother (M) and father on days –25, –19, and +28 (with respect to the newborn’s delivery date) and from the newborn (N) on days +3, +4, +6, +9, +11, +13, and +28. A total of 10 μL of a Chelex-100 (Bio-Rad)–extracted DNA solution [6] was amplified using highly conserved primers located in the viral untranslated region and a standard PCR protocol [7]. First-round primers were COM1sens (5’-CRSWKCMGGATGGYWGAGTTTYW-3’) and COM-2rev (5’-GCCCGAATTGCCCCTWGAC-TKCG-3’), and second-round primers were COM1sens and TTSPErev (5’-HCG-GCACCACGCWCCGGGACG-3’). Control PCR consisted in β-globin gene amplification.

TTV genome was detected in all samples obtained from the mother and in none of those obtained from the father. Very high virus loads were transiently present in the samples obtained from the newborn on days +4, +6, and +9 only. PCR products M(–25), M(+28), and N(+4) were cloned and, for each 15 clones, were sequenced. Phylogenetic analysis of these clones as well as the reference sequences confirmed the specific amplification of TTV genome. Each group of sequences (M(–25), M(+28), and N(+4)) constituted an independent evolutionary cluster (genetic heterogeneity, 28.3%–30.4%). However, PCR primers specifically designed from N(+4) sequences permitted amplification of a sequence from the M(–25) sample, which showed 100% identity with the N(+4) sequence.

This finding strongly suggests that the strain that infected the newborn was acquired from the mother during delivery or during the postpartum period. That the transmitted strain appears to be distinct from the dominant strain that infected the mother suggests that all TTV strains do not have the same potential for interhuman transmission.

Follow-up of the newborn’s natural history was performed in parallel to TTV DNA detection. Of interest, the newborn experienced clinical symptoms of a benign “viral” rhinitis from days +4 to +10, including clear nasal discharge; no fever, diarrhea, or cutaneous rash; and a spontaneous recovery. Neither the mother nor the father harbored corresponding clinical signs. This episode corresponded exactly to the period of positive detection of TTV in saliva and is suggestive of the etiological implication of TTV infection. Therefore, this report might be the first to describe the clinical symptoms associated with primary infection with TTV, and it should permit the association of TTV with extrahepatic disorders to be envisaged, despite its initial suggested implication.

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References