Role of Proteae in Diarrheal Disease

The recent paper by H. E. Müller (3) on the role of the Morganella-Proteus-Providencia group in diarrheal disease raises some important points. Previous reports have speculated on the role of these organisms in gastrointestinal disease (1, 2, 4). To date, no specific mechanism of pathogenicity has been described which links the Proteae with infectious diarrhea. The prevalence study reported by Dr. Müller is important in that it surveys a large population for the carriage of members of the Proteae; however, a more complete investigation would include comprehensive screening of diarrheal stools for all known agents of infectious diarrhea: bacterial, viral, and parasitic. It is possible that infection with well-documented enteropathogens allows these organisms to establish colonization and grow in the fecal flora. Only by ruling out other etiologic agents can conclusions be drawn as to the role of the Morganella-Proteus-Providencia group in gastrointestinal pathology.

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We read with interest the recent report by Dr. Müller on the occurrence and pathogenicity of Proteae in human feces (8). The concluding remark that Proteus penneri was probably previously identified as an atypical Proteus vulgaris rather than a species that has recently appeared in the human fecal flora is supported by the literature.

In their description of P. penneri, Hickman and her colleagues refer to three earlier reports of indole-negative P. vulgaris (two from the United States and one from the United Kingdom, but none earlier than 1968; 4). We find the earliest report of indole-negative P. vulgaris was made in 1941 when Rustigan and Stuart found 4 of 69 P. vulgaris strains to be indole negative (10). There are also reports of significant episodes of nosocomial urinary tract infection being caused by indole-negative P. vulgaris in the United Kingdom in the mid-1950s (1, 6, 7). One of these episodes was carefully documented, indole-negative P. vulgaris being found as the most common species of Proteus (37 of 59 strains isolated; 6). In another of these reports, 10% of 50 patients were infected by indole-negative P. vulgaris (7). Indole-negative P. vulgaris has also been reported from Australia (5). A total of 224 Proteus strains from clinical specimens yielded 52 indole-negative P. vulgaris; interestingly, these strains showed greater resistance to chloramphenicol (typical of P. penneri) than indole-positive P. vulgaris isolated at the same time. Colistin-sensitive, indole-negative P. vulgaris has also been reported from clinical specimens (3). There are few reports of indole-negative P. vulgaris from animals, but in one study single isolates were obtained from bird and bovine feces (9). It seems that P. penneri has not been associated with substantial episodes of nosocomial urinary tract infection since the 1950s; however, it is a species which both colonizes and causes sporadic episodes of disease (predominantly urinary tract infection) in hospital patients (manuscript in preparation).

The assertion that only Proteus mirabilis and Morganella morganii "have a role in diarrheal disease" seems to be a case of guilt by association. There has long been discussion about the ability of Proteae to cause diarrhea, and it is now the custom for diagnostic laboratories to disregard them as a cause of diarrhea. We feel there is a need for a detailed examination of examples of all of the Proteae for the genes associated with enterotoxin production, and we are undertaking such a study. With regard to P. mirabilis and diarrhea, a recent study looking for enterotoxigenic Escherichia coli in the feces of patients with diarrhea also examined 35 examples of P. mirabilis with gene probes for the presence of LT, ST-H, and ST-P toxin genes and failed to find any (2).

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Author's Reply

In reply, I would like to thank Dr. Swiatlo and Dr. Hawkey et al. for sharing their thoughts about my article on the role of *Proteae* in diarrheal disease. The discussion of this problem shows that there are two different interpretations of the role of the *Morganella*-Proteus-Providencia group in gastrointestinal disease. I agree with Dr. Swiatlo that my paper showed a statistical correlation of the occurrence only of *Morganella morganii* and *Proteus mirabilis*, but not of other *Proteae*, with diarrhea. Similar findings were published previously by Moffet et al. (1) and simultaneously by Senior and Leslie (4). Of course, these observations do not necessarily imply a biological significance; additional studies are needed to bridge the gap between statistical observations and clinical relationships. The proposal of Dr. Swiatlo may be a helpful step to reach this goal.

The absence of toxic genes in *P. mirabilis*, cited by Hawkey et al., does not mandate that these bacteria do not cause diarrhea. Hawkey et al. suggest that earlier descriptions of indole-negative *Proteus vulgaris* indicate the existence of *Proteus penneri*. That is not necessarily true, for there is an indole-degrading enzyme(s) in all species of the *Morganella*-Proteus-Providencia group that can lead to erroneous identification (2). However, *P. penneri* is not only indole-negative, but strains freshly isolated and incubated for 3 days show a typical green color reaction with Kovac's indole reagent (3). It is surprising that this striking reaction has not been observed previously.

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