lowering the intermediate range to include isolates with MICs of 4 μg/mL, or, perhaps, to consider all staphylococcal isolates with vancomycin MICs of ≥4 μg/mL to be nonsusceptible.

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References


Epidemiologic versus Genetic Relatedness to Define an Outbreak-Associated Uropathogenic Escherichia coli Group

Str—France et al. [1] reported that a recently described clonal group of uropathogenic Escherichia coli appears to be distantly clonal and is not an outbreak-related group. They used a variety of strain-typing methods (enterobacterial repetitive intergenic consensus sequence 2 [ERIC 2] PCR, fumC C288T single-nucleotide polymorphism [SNP] analysis, PFGE, virulence profile, and mechanism of resistance) to show that a group of E. coli strains defined as clonal group A (CGA) by ERIC 2 PCR analysis was considerably more diverse than would be expected for an outbreak-related clone. Their conclusion, based on the analysis of their collection of 45 trimethoprim-sulfamethoxazole–resistant CGA isolates obtained from patients with cases of urinary tract infection (UTI) from 1996–1999, is valid and not surprising. However, their conclusion may lack external validity.

We feel that a collection of only 45 isolates spread over 3 years, by definition, is not likely to reveal any UTI outbreak. E. coli O157:H7 that causes outbreaks of hemorrhagic colitis is also distantly clonal [2, 3]. If PFGE analysis were applied to a small collection of E. coli O157:H7 strains from a single geographic site over a 3-year period, they would also be found to be diverse, even though this E. coli serotype is implicated in well-recognized outbreaks. The authors cannot generalize from a single collection of CGA that CGA does not constitute an outbreak-associated group.

The earlier study suggesting that CGA constituted an outbreak-related group was based on a collection of 55 trimethoprim-sulfamethoxazole–resistant isolates obtained over a 3.5-month period at 1 college campus [4]. Their genetic relatedness was assessed by multiple techniques, including ERIC 2 PCR, virulence factor profiling, serotyping, and PFGE. With use of the most discriminating method—PFGE—several of the isolates were indistinguishable. The conclusion that these genetically related strains comprised an outbreak group was based on the observation that they clustered in time at 1 geographic site.

We agree with France et al. [1] that ERIC 2 PCR is a highly condition-dependent typing method. ERIC 2 PCR should not be used to define a clone. However, it is an excellent tool with which to screen a large number of isolates to provisionally identify a clonal group. Once such a provisional group is identified, other, more-discriminating methods can be applied to define a clone. However, one cannot then go on to conclude that the strains within a clonal group do not constitute an outbreak group. Outbreaks of diarrhea caused by mixed Salmonella serotypes, phage types, drug-resistance types, or genotypes do occur. In the report by Manges et al. [4], geographic comparison isolates obtained from 2 other college campuses did not identify E. coli isolates that belonged to the same serogroup and had the same ERIC 2 PCR pattern, but those isolates had distinct PFGE patterns. However, the difference in PFGE patterns does not necessarily exclude the possibility that some of the comparison strains belonged to an outbreak-related group.

The conclusion that a collection of strains constitutes an outbreak group is based on epidemiologic information, which, in diseases like community-acquired UTI, may not be easily obtained. This is why, in performing molecular epidemiologic studies, strain typing techniques must be applied to isolates that were appropriately collected with regard to place and time. Genotype data do not define an outbreak. They are only used to support the epidemiologic data that ultimately define an outbreak.

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References

Escherichia coli Clonal Group A

Sir—Certain conclusions of France et al. [1] regarding Escherichia coli clonal group A (CGA) warrant comment. First, the authors documented diverse virulence profiles and antimicrobial-resistance phenotypes and genotypes among the 28 isolates that exhibited enterobacterial repetitive intergenic consensus sequence 2 (ERIC2) profile A but lacked CGA’s hallmark C288T single-nucleotide polymorphism (SNP). This contrasts with the considerable homogeneity they observed among the 16 isolates that exhibited both of these CGA-defining characteristics. Given the unreliability of PCR fingerprinting [2], the precise correspondence of this SNP with CGA status demonstrated previously within a diverse validation set [2], and the considerable uniformity of virulence profiles among human-source CGA isolates from around the world [3–6], the possibility must be considered that the authors’ discrepant isolates actually were not from CGA. Before the isolates are accepted as representing CGA and conclusions regarding CGA (or limitations of the SNP assay) are drawn from them, it would be important to confirm their CGA status with use of an alternative phylotyping method, such as random amplified polymorphic DNA (RAPD) analysis, multilocus sequence typing (MLST), or phylo-PCR [7]. Likewise, it would be important to confirm that, in the authors’ laboratory, ERIC2 PCR is specific for CGA (a concern underscored by the authors’ silence regarding use of negative control strains) [1].

Second, the observed diversity (despite an overall similarity) of PFGE profiles among isolates that exhibited both ERIC2 profile A and the CGA SNP is presented as a significant finding, supported by a gel image [1]. However, this actually has been observed in every previous PFGE analysis of CGA, with the exception of a cluster of indistinguishable-profile isolates from 1 locale in 1 study [3]. Thus, that CGA usually does not behave in a typical point-source outbreak fashion is well established. Still, geographically and temporally dispersed sampling limits the strength of this conclusion. As for the supposed absence of clonality among trimethoprim-sulfamethoxazole–resistant isolates from Cook County Hospital, as inferred by others from PFGE analysis and cited by France et al. [1], a reexamination of these isolates showed that 29% actually represented CGA, exhibited the stereotypical CGA virulence profile, and had largely similar PFGE profiles [6].

Third, the proposition that horizontal transfer of accessory traits underlies the nonuniformity of PFGE profiles observed among CGA isolates is misleadingly linked by the authors to the diversity of virulence profiles and resistance genotypes observed among SNP-negative putative CGA members [1]. However, the diversity of PFGE profiles actually was documented among SNP-positive CGA members, most of which exhibited identical virulence profiles, resistance profiles, and integron content. Diversity of PFGE profiles is characteristic of E. coli clonal groups in general, such as E. coli O18:K1:H7 (OMP 6 subclone), within which independent isolates typically exhibit unique PFGE profiles despite their homogeneity for accessory traits [8]. An equally or more plausible explanation for this phenomenon is the ongoing occurrence of point mutations within the genomic backbone, involving sites not sampled by ERIC2 PCR, RAPD analysis, or MLST. Further genetic analysis would be needed to resolve this point.

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Reply to Riley and Manges and to Johnson

Sir—We thank Riley and Manges [1] and...