Diversity of Pathogens Responsible for Acute Diarrheal Disease in China

To the Editor—Acute diarrheal disease causes approximately 2.8 billion episodes and 1.3 million child deaths annually worldwide [1, 2], hampering the achievement of Millennium Development Goal 4 [3]. Now, multidrug-resistant and enhanced-virulence diarrheal pathogens are emerging to cause serious public health problems [4–7]. In China, >10 000 diarrheal deaths occur annually and China remains one of the countries with the highest mortality rates among children due to diarrhea [3, 8]. However, the distribution and contribution of specific pathogens for acute diarrheal disease in China are not well known [3], significantly impacting its effective prevention and control measures. Here, through analyzing 22,817 diarrheal specimens between 2009 and 2012 collected from 32 nationwide sentinel hospitals, we found the diversity of types, populations affected, and temporary and spatial distribution of diarrheal pathogens.

At least 1 pathogen was detected in 5783 of the 22,817 samples (25%); in total, 6155 pathogens were isolated. Rotavirus was the most commonly detected pathogen (28%), followed by *Shigella* species (17%), caliciviruses (15%), diarrheagenic *Escherichia coli* (11%), *Salmonella* species (9.4%), and others (Figure 1). The specimens that most frequently yielded pathogens (88%) were collected at outpatient clinics or emergency departments. Analysis of the age distribution of diarrheal pathogens revealed that bacterial pathogens were more common among...
Figure 1. Distribution of bacterial and viral-associated diarrhea with respect to patient age (A), onset time (B), isolation department, geographic division, and others (C); age categories from top to bottom are 0–12 mo, 1–4 y, 5–14 y, 15–49 y, 50–64 y, and ≥65 y, respectively) in China from 2009 to 2012. Abbreviation: O/E, outpatient clinic or emergency department.
15- to 49-year-olds (43%; Figure 1A). In comparison, viral pathogens were more common in children aged <5 years (77%), among whom rotavirus infections were more common (84%).

Overall, diarrheal pathogens were detected most commonly in August (16%), whereas the fewest were in April (3.2%; Figure 1B). Bacterial-associated diarrheal pathogens were most commonly observed in August (22%), with the fewest cases in February (0.6%), and viral diarrhea showed a varied distribution with the highest frequency (14%) in November and the lowest frequency (3.7%) in April. Diarrheal pathogens across China are geographically diverse. Eastern China had the greatest (27%) and southern China (5.3%) the lowest overall burden (Figure 1C).

In China, most patients with a diarrheal illness (65%) are still treated with antibiotics without identification of the causative pathogen [9]. Given the large number of inpatients with viral-associated diarrhea, many patients receive antibiotic therapy with no benefit, potentially accelerating the emergence of an enhanced-virulence or multidrug-resistant microorganism. Our diarrheal surveillance program detected 316 isolates (of 3122 [10%]) of novel serotypes of Shigella, E. coli, and other bacteria with enhanced virulence or multidrug resistance in developed areas in China, including novel serotypes of Shigella flexneri 4cv, 4s, 2x, and 1c; these Shigella serotypes have shown increased virulence and antimicrobial resistance.

The emergence of novel strains with enhanced virulence or multidrug resistance and documented changes of dominant strains over different regions and time periods in developed areas in China causes difficulties in clinical treatment. Because developed, high-density population areas have novel diarrheal pathogens, there is an increased risk for spread across China and internationally due to the increased propensity of the Chinese population to travel. Strengthening of the diarrheal surveillance network, to monitor the distribution and variation in bacterial and viral pathogens as well as antimicrobial resistance and virulence changes, is necessary to reduce the burden of diarrhea in China or other countries.

Notes

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