The study by Bresheer et al in this issue of the Journal on identification of etiologic agents in acute gastroenteritis (AGE) raises a number of important issues for clinicians and public health authorities. Although most persons presenting with acute diarrhea do not undergo stool studies, and only a very small proportion of routine stool cultures that are performed identify a pathogen, a substantial proportion of patients are treated with antimicrobials [1]. It is imperative that data-driven differential diagnoses and improved diagnostics inform guidelines and practices regarding testing and treating patients with AGE to optimize management.

Overall, a potential pathogen was detected in one-fourth of the subjects in this study under conditions that do not reflect common clinical practice. For example, serologic testing (which even now is available only in rare circumstances) identified a substantial proportion of norovirus cases. Although it is not uncommon to submit swab specimens in transport media, this study demonstrated a >5-fold higher yield from whole stools. Unfortunately, prompt submission of whole stools is sometimes impractical. There are few recent studies comparing the utility of swab specimens versus whole stools for identification of a variety of pathogens; this is an important area for additional study as the number of commercially available transport media [2] and different diagnostic tests grows. As this study demonstrates, even intensive testing has limited yields, and all of the laboratory technology in the world cannot help if adequate specimens are not collected.

It is notable that even a decade ago these investigators identified an etiologic agent in half of all whole stools collected, which is higher than in many other intensive studies. Not surprisingly, the majority of these were viruses, which are generally not tested for in most clinical laboratories. This study did not test for many less common bacterial and viral causes of diarrhea, some of which were not even identified at the time this work was done. In recent years, new, more virulent strains of norovirus and Clostridium difficile, for example, have become widespread and may drive the proportion of AGE caused by these pathogens even higher. The proportion of adult patients with AGE in this study with rotavirus was surprisingly high, and monitoring how that incidence changes with the increasing use of vaccine in children will be important.

Since this study was performed, the number and types of diagnostic tests available for diarrheal pathogens have increased dramatically [3–5]. With the increasing commercial availability of antigen detection tests and improved polymerase chain reaction (PCR) methods and other molecular diagnostics, it is likely that even in clinical practice, the yield from stool studies will continue to increase. Even in more recent studies performed in a research context, however, 20%–40% of stool specimens failed to yield a potential pathogen [5]. There are a variety of possible explanations for this, including inadequate test sensitivity, failure to test for the correct pathogens, presence of as-yet-unknown etiologic agents, or a noninfectious cause.

In this study, approximately 9% of whole stools yielded >1 potential pathogen. A number of recent studies using newer diagnostic methods have reported even higher rates. For example, in 2007, using PCR analysis to retest >4600 specimens from a large European case-control study a decade earlier increased detection of ≥1 pathogen from 53% to 75%. Importantly, the yields from controls also increased, from 19% to 40% [6]. Many common potential pathogens can be carried by asymptomatic persons, and in symptomatic patients with mixed infections, a clinician is faced with the challenge of having to decide whether any of them warrants antimicrobial therapy. At present, few data are available to help support those decisions, although recent studies have begun to look at the utility of pathogen quantitation to explore this issue.

Approximately 10% of the subjects in this study had respiratory symptoms...
concurrently with AGE. Data were not presented on the proportion of these patients with an identified etiologic agent, compared with those without respiratory symptoms. Further exploration of this issue may provide insight into whether such clinical observations can help clinicians determine the usefulness of stool studies in individual patients.

In addition to direct benefit to the patient, identifying the etiologic agent for AGE can have important public health implications. Most of the improved diagnostic tests being developed are based on molecular methods. One of the consequences of the increasing use of nonculture diagnostic testing for AGE is that these tests do not provide isolates for additional testing by public health laboratories. Public health has traditionally relied on cultured organisms for serotyping, subtyping, and antimicrobial resistance testing for epidemiologic purposes. Currently the Centers for Disease Control and Prevention requests concurrent culture and nonculture testing in many cases [7], but with the inexorable shift away from traditional laboratory methods in the clinical world, such an approach is probably unsustainable in the long term. Public health laboratories will increasingly have to develop the capacity to routinely perform testing such as sequencing in order to gather the subtyping information on which epidemiologists have become so dependent.

Ultimately, studies such as this highlight several important questions: what is the utility of stool studies, and how does testing help the clinician or the patient with AGE? This study was performed on only a small subset of persons seeking care in emergency rooms, apparently during only selected hours, which may be a cohort with more serious disease than commonly presents to an outpatient clinic. Even so, the large majority of subjects were relatively young and otherwise healthy, and most identified pathogens were viral. Based purely on probabilities, it is likely that only a very small number of these persons would require antibiotics for their infections. This study did not identify any clinical features that help physicians predict a particular etiologic agent. In an era of increasing pressure to contain costs and increasing rates of antibiotic resistance, additional work is critical, to identify inexpensive, effective ways to guide practice. In the meantime, it is important that guidelines for the judicious use of testing and treatment are followed [8, 9]. No matter how good laboratory tests become, clinical judgment will continue to be important in optimizing the utility of stool studies. Few of us have time to formally consider Bayes’ theorem and “pretest probabilities” during a busy clinic, but it is often not appropriate to order a test that is highly unlikely to show anything useful or have to decide whether a surprising positive test result is clinically meaningful. Unfortunately, it is not uncommon to forget until too late the dictum, “Don’t test if the result isn’t going to affect your treatment.”

**Note**

Potential conflict of interest. Author certifies no potential conflicts of interest.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

**References**