Application of Rejection Criteria for Stool Cultures for Bacterial Enteric Pathogens

KAILI FAN,1 ARTHUR J. MORRIS,1,2* AND L. BARTH RELLER1,2,3

Clinical Microbiology Laboratory,1 and Departments of Pathology2 and Medicine,3
Duke University Medical Center, Durham, North Carolina 27710

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Over 20 months, we prospectively assessed the yield of cultures for Salmonella, Shigella, and Campylobacter spp. from adults and children. In the first 10 months, 53% (567 of 1,097) of specimens from adults were from patients who had been in the hospital for >3 days. Overall, only 2.6% (29 of 1,097) of specimens contained pathogens, and all were from patients who had been in the hospital for ≤3 days. Over the second 10 months, specimens from adults in the hospital for >3 days were not cultured unless special reasons existed. Thirty percent (368 of 1,229) of specimens were rejected. Concurrently, 7.5% (51 of 677) of stool specimens from children were positive. Only one positive specimen came from a child who had been in the hospital for >3 days. Neither stool consistency nor fecal leukocytes were useful predictors for the presence of an enteric pathogen. We recommend that specimens from both adults and children in the hospital for >3 days not be cultured unless there are delineated plausible clinical or epidemiological reasons to do so.

Retrospective studies have shown that although Salmonella, Shigella, and Campylobacter spp. are causes of community-acquired diarrhea, they rarely cause nosocomial diarrhea (9, 15, 17). Yet stool cultures for these bacterial pathogens are commonly requested for patients who develop diarrhea during hospitalization (4, 5, 9, 15, 17). We have prospectively assessed the yield of stool cultures for Salmonella, Shigella, and Campylobacter spp. from adults and children over a 20-month period. On the basis of our findings, we established and monitored a rejection policy for stool cultures from adult patients hospitalized for more than 3 days and tested rejected specimens for Clostridium difficile toxin A. We also examined the usefulness of stool consistency and fecal leukocytes as predictors for the presence of enteric pathogens in our patient population.

Duke University Medical Center is a 1,125-bed tertiary care hospital that in fiscal year 1991 to 1992 had 308,048 inpatient hospital days and approximately 390,000 outpatient visits. All stool specimens for culture for enteric pathogens were inoculated onto Hektoen enteric agar, MacConkey agar, Selenite-F broth, and Campylobacter selective medium (all media were supplied by Becton-Dickinson Microbiological Systems, Cockeysville, Md.). Hektoen and MacConkey media were incubated at 37°C for 48 h. The Selenite-F broth was subcultured at 24 h onto Hektoen and MacConkey media. Campylobacter plates were incubated at 42°C for 72 h in a microaerophilic atmosphere. Stool was cultured for other pathogens on specific request. Potential pathogens were identified by standard laboratory methods (2).

From June 1991 through March 1992, we recorded the following details for each adult (>16 years old) patient: patient name, age, gender, and ward or clinic and whether the patient was an outpatient or inpatient. For inpatients, the day of hospitalization was also recorded. From June 1991 through January 1993, the same details were collected for each pediatric (≤16 years old) patient. The rejection policy described below was not applied to specimens from pediatric patients.

Once these results were analyzed, a circular detailing rejection criteria for stool cultures from adult patients for enteric pathogens was sent to all wards, clinics, and medical practitioners in the medical center. The circular stated that (i) almost half of the stool culture requests for enteric pathogens were for patients who had been in the hospital for more than 3 days; (ii) the yield from these cultures was minimal; (iii) stool cultures from adult patients who had been in the hospital for longer than 3 days would not be processed; and (iv) if clinical reasons existed for a stool culture outside this criterion, the clinician should contact the on-call Medical Microbiology Fellow or Clinical Pathology Resident. The rejection protocol was instituted in April 1992. Since then, a daily record has been kept of the number of specimens rejected and the number of specimens processed after a physician call to the laboratory.

Rejected stool specimens were tested for C. difficile toxin A with Bartel's C. difficile toxin A enzyme immunoassay (Baxter Diagnostics, Inc., Deerfield, Ill.) according to the manufacturer's recommendations.

From June through December 1991, all stools submitted for culture were examined for fecal leukocytes. A methylene blue mount was made from each specimen as previously described (11). Briefly, two-thirds of a drop of methylene blue was placed on a clear glass slide. A wooden stick was dipped into the specimen, and the material remaining on the stick was mixed with the methylene blue. The mixture was placed under a coverslip, and the entire mount was scanned under ×10 objective lens (100 magnification). Suspicious cells were examined under ×40 objective lens (400 magnification) (11).

From June 1991 through March 1992, we received 1,097 specimens from adult patients, 567 (53%) of which were from adults who had been in the hospital for more than 3 days. Twenty-nine specimens (2.6%) contained an enteric pathogen: 10 Salmonella spp., 6 Shigella spp., and 13 Campylobacter spp. All positive cultures were from patients who had been in the hospital for ≤3 days. After introduction of the rejection policy, from April 1992 through January 1993, we
received 1,229 specimens for culture; 368 (30%) were rejected. Twenty-four of 861 (2.8%) cultured specimens contained an enteric pathogen: 9 *Salmonella* spp., 3 *Shigella* spp., and 12 *Campylobacter* spp. None of the 23 stool specimens cultured after physician contact with the laboratory contained an enteric pathogen. The first 182 rejected stools were tested for *C. difficile* toxin A, and 14 (8%) were positive. The mean duration of hospitalization for toxin-positive patients was 24 days (range, 5 to 93 days). The mean age was 53 years (range, 18 to 83 years).

From June 1991 through January 1993, 677 specimens were received from pediatric patients, 167 (25%) of which were from children who had been in the hospital for more than 3 days. Fifty-one specimens contained an enteric pathogen: 22 *Salmonella* spp., 22 *Shigella* spp., and 7 *Campylobacter* spp. Fifty of the 51 (98%) positive specimens were from children who had been in the hospital for less than 3 days.

The one positive specimen from a child who had been in the hospital for more than 3 days was not clinically relevant. The patient, a 3-year-old black female, was admitted for a 3-day history of abdominal pain and fever to 39.4°C. She had experienced diarrhea and vomiting. She had abdominal guarding and tenderness on deep palpation. Her peripheral leukocyte count was 36,400 x 10^9/liter, with 91% segmented neutrophils and 3% bands. Chest and abdominal radiographs were normal. Initial management included antimicrobial therapy for suspected intra-abdominal infection. By day 3 of hospitalization, a diagnosis of Kawasaki disease was made on the basis of her high fevers, strawberry tongue, conjunctivitis, hand and foot edema, trunk rash with perirectal desquamation, joint effusions, and axillary and inguinal lymphadenopathy. She received immunoglobulin intravenously. Diarrhea occurred on day 5 of hospitalization, and a stool specimen was sent for culture. *Salmonella newport* was isolated. The patient was discharged on day 8, before the final identity was known, her diarrhea having resolved.

From June through December 1991, all 1,031 stool specimens received were examined for fecal leukocytes. The presence of fecal leukocytes in relation to culture results is shown in Table 1. Fecal leukocytes were present in 64 specimens that did not contain an enteric pathogen. The presence of fecal leukocytes had sensitivity, specificity, and positive and negative predictive values for the presence of an enteric pathogen of 29, 93, 20, and 96%, respectively. Most positive stool specimens (71% [39 of 55]) would have been missed if fecal leukocytes had been used as a screening test. Although most positive stools were of either liquid or loose consistency, 38% (21 of 55) would have been missed if these criteria had been used as a screening test.

From June 1991 through March 1992, 1,416 stool specimens from both adults and children were cultured; 685 (48%) were from patients who had been in the hospital for more than 3 days. There were 61 (4.3%) positive specimens. At a charge of $55 a stool culture, the charge per positive result during this period was $1,276. If all specimens from both adults and children who had been in the hospital for more than 3 days had been rejected, the cost per positive result would have been $670. Total charges for cultures from all patients in the hospital for more than 3 days were $37,675, but these cultures only yielded one clinically unimportant *Salmonella* isolate.

Stool culture for the common enteric bacterial pathogens is one of the most costly microbiological tests, with cumulative laboratory charges per positive result being in the vicinity of $1,000 (6, 7, 9). It is, therefore, reasonable to try to identify those patient populations in which the yield of stool cultures is 0 or nearly so. Yannelli et al. observed that only 1 of 452 cultures from patients who had been in the hospital for more than 3 days contained an enteric pathogen (17). Siegel et al. found only 1 of 191 positive cultures to be from a patient in the hospital for more than 3 days, and this infection was not nosocomially acquired (15). Our results confirm these previous studies, which appear to have been conducted mostly on adult patients. Few data exist for pediatric populations, but Brady et al. did not observe a positive culture in 146 specimens sent from children who had been in the hospital for more than 3 days (5). Our findings confirm the low yield of such examinations in both age groups.

Although several groups have shown that it is rare to recover such pathogens from patients who have been in the hospital for more than 3 days (3, 4, 5, 9, 15, 17), no prospective data have been published to show what savings can be realized if these specimens are not cultured. Siegel et al. noted that 51% of stool specimens were from patients who had been in the hospital for more than 3 days. For our laboratory, 48% of our previous workload would be eliminated if the policy were applied to adult and pediatric patients. It is important to note that after application of our rejection criterion, the proportion of stools sent from adults who had been in the hospital for more than 3 days decreased from 53 to 30%, suggesting that the policy had an effect on ordering behavior. A similar decrease occurred after application of rejection criteria for ovum and parasite examinations (12).

While it is clear that culturing for the above pathogens is wasteful of resources, investigation for *C. difficile*-associated disease is not. We found that 8% of stools rejected for culture because the patient had been in the hospital for more than 3 days contained *C. difficile* toxin. Others have found that 17 to 22% of the stools submitted for toxin testing from this group of patients contained *C. difficile* toxin (5, 15, 17). This is similar to the 23% observed by Bowman et al. when both culture and toxin tests were performed (4).

Fecal leukocytes are often found in specimens containing common enteric pathogens such as *Campylobacter* spp. (70 to 85%), *Salmonella* spp. (36 to 90%), and *Shigella* spp. (69 to 100%) (1, 8, 10, 11, 13, 14). Fecal leukocytes were only present in 11 to 50% of our patients with these pathogens. Recently Tarr et al. observed fecal leukocytes in 42 to 72% of patients with these three pathogens (16). Although the presence of fecal leukocytes may increase the likelihood of recovering a common enteric bacterial pathogen (3), their absence cannot be used to screen out specimens for culture. A more rational use of the fecal leukocyte test could be to

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**TABLE 1.** Stool culture result, day of hospitalization, stool consistency, and presence of fecal leukocytes in stool specimens containing an enteric pathogen

<table>
<thead>
<tr>
<th>Enteric pathogen (n)</th>
<th>No. (%) of stool cultures taken:</th>
<th>After ≤3 days of hospitalization</th>
<th>With liquid or loose stools</th>
<th>With fecal leukocytes present</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Salmonella</em> spp. (19)</td>
<td>18</td>
<td>12 (63)</td>
<td>2 (11)</td>
<td></td>
</tr>
<tr>
<td><em>Shigella</em> spp. (20)</td>
<td>20</td>
<td>13 (65)</td>
<td>10 (50)</td>
<td></td>
</tr>
<tr>
<td><em>Campylobacter</em> spp. (16)</td>
<td>16</td>
<td>9 (56)</td>
<td>4 (25)</td>
<td></td>
</tr>
<tr>
<td>Total (55)</td>
<td>54 (98)</td>
<td>34 (62)</td>
<td>16 (29)</td>
<td></td>
</tr>
</tbody>
</table>
pursue less commonly encountered pathogens, such as _Yersinia enterocolitica_ or _E. coli_ 0157:H7 (16), with selective techniques for patients with persistent diarrhea, fecal leukocytes, and stools negative for _Salmonella_, _Shigella_, and _Campylobacter_ spp.

Rejecting stool specimens from patients who have been in the hospital for more than 3 days should not be taken as a statement that infections with the common enteric pathogens do not occur in this patient group, although they rarely do (3, 9), but rather that the yield is so low that stool cultures should only be performed when there are plausible clinical or epidemiological reasons to do so. Moreover, we believe that the laboratory should have an integral role in deciding how the specimen should be worked up. Situations which may be considered for workup would include a delay in specimen collection, elucidation of the history of diarrhea sometime into the admission, epidemiological evidence of nosocomial acquisition, and specimens collected by an invasive procedure, e.g., colonoscopy. No policy can be expected to cover all situations. We feel that it is important, therefore, for the ordering physician to be able to speak to the laboratory and to have the facility to get the test performed when the situation is appropriate. Apart from this, many unnecessary tests can be prevented by applying this and a similar policy for ovum and parasite examinations (12).

In summary, reasonable rejection criteria coupled with clearly delineated lines of communication and responsibility can decrease unproductive diagnostic practices, maintain quality of care, and reduce the costs of health care.

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REFERENCES