ORIGINAL ARTICLE

The Microbiology of Secondary and Postoperative Pancreatic Infections

Implications for Antimicrobial Management

Stephen W. Behrman, MD; Michael H. Bahr, MD; Paxton V. Dickson, MD; Ben L. Zarzaur, MD

Hypothesis: We reviewed our experience with secondary pancreatic infections with a focus on preemptive intervention and the potential alteration of the recovered microbial flora. The pathogens associated with postoperative pancreatic infections were analyzed with respect to nonenteric organisms, if any, that were recovered. We hypothesized that our findings might alter the antimicrobial management of these patients.

Design: Retrospective review.

Setting: Hospitals affiliated with the University of Tennessee Health Science Center, Memphis.

Patients: Patients developing secondary and postoperative pancreatic infections following severe acute pancreatitis.

Methods: Factors examined relative to secondary pancreatitis included preoperative antibiotic use and antecedent extrapancreatic infections potentially implicated in seeding the pancreatic bed. Patients who had elective resection received 24 to 48 hours of antibiotic prophylaxis.

Results: Twenty-two patients required surgery for secondary infections following severe acute pancreatitis, with 29 pathogenic isolates being recovered. Of these 22 patients, 14 received vancomycin hydrochloride prior to surgical intervention. Of those 14 patients, 6 had isolates recovered at the time of surgery that were positive for *Enterococcus faecalis* and 5 of these isolates were vancomycin resistant. Eight of the 22 patients received antifungal prophylaxis with no fungi recovered from intraoperative culture. However, 2 of the 14 patients who did not receive empiric therapy had isolates that were positive for fungi. Five patients who required an urgent operation for sepsis had pathogenic isolates that were similar to those recovered from central lines. Postoperative infections occurred in 40 of 225 patients (17.8%) who had an elective pancreatic resection, with 72 pathogenic isolates being recovered. Of these 40 patients, 22 (55.0%) had polymicrobial infections. Of the 72 pathogenic isolates recovered from patients, 34 (47.2%) were gram-positive organisms, 15 (20.8%) were fungal organisms, and 17 (23.6%) were drug-resistant bacteria.

Conclusions: Prolonged vancomycin use in patients with severe acute pancreatitis is associated with the acquisition of vancomycin-resistant enterococci. Empiric antifungal therapy may reduce the incidence of secondary fungal pancreatic infections. Systemic bloodstream infections at extrapancreatic sites can lead to seeding of pancreatic pseudocysts. Postoperative infections frequently include gram-positive, fungal, and drug-resistant organisms, and empiric therapy directed at these pathogens should be utilized until definitive culture results are obtained.

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SEPSIS WITHIN THE PANCREATIC bed following severe acute pancreatitis (SAP) and after elective resection remains common. These secondary and postoperative infections prolong hospital length of stay, require therapeutic intervention, and are associated with significant morbidity and mortality.[1-6] Secondary pancreatic infections have historically been associated with enteric pathogens.[1,7] However, more recent management schemes (including use of prophylactic antibiotics) have led to an alteration in the bacterial flora recovered from patients.[8-11] Furthermore, extrapancreatic bloodstream infections have the potential for seeding an otherwise sterile pancreatic bed with nonenteric bacteria. Postoperative sepsis following pancreatectomy occurs in up to 16% of patients.[12-15] The microbial flora associated with these infections has received sparse attention. We reviewed our experience with secondary infections with a focus on preemptive intervention and the potential alteration of the recovered microbial flora. The

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Author Affiliations:
Department of Surgery, University of Tennessee Health Science Center, Memphis.

pathogens associated with postoperative infections were analyzed with respect to nonenteric organisms, if any were recovered. We hypothesized that our findings might alter the antimicrobial management of these patients.

METHODS

The medical records of patients who underwent surgery for secondary pancreatic infections and patients who developed postoperative infections following elective pancreatectomy, at hospitals affiliated with the University of Tennessee Health Science Center in Memphis during the period from 1997 to 2009, were retrospectively reviewed. Patients who had secondary pancreatic infections that were managed by nonoperative means were not included. Of 22 patients identified, 6 were transferred from other facilities at a mean of 6 days (range, 2-16 days) following initial presentation. Other than medical support, no therapeutic intervention was performed prior to arrival at our hospitals. The majority of patients (16 of 22) were alimented by total parenteral nutrition prior to surgical intervention. The indication for surgery for those patients with computed tomographic evidence of pancreatic necrosis included fever, persistent end-organ failure, and bandemia, either in isolation or in combination beyond 2 weeks of initial presentation in most cases. Three patients with infected necrosis had a drain placed preoperatively prior to surgical consultation. Pancreatic pseudocysts were presumed infected and drained operatively when patients had fever exclusive of other sources, bandemia, or computed tomographic evidence of gas within the cyst. Percutaneous sampling of the pancreatic bed to assess for infection was not used. Factors analyzed relative to secondary infections included use of preoperative prophylactic antibiotics and preoperative instrumentation of the pancreatic bed and antecedent extrapancreatic bloodstream infections potentially responsible for seeding a sterile pancreatic process.

The incidence and microbiology of postoperative infections were recorded. Factors potentially implicated in the pathogens recovered included the use of preoperative biliary decompression and a preexisting immunocompromised state. All patients who had elective pancreatectomy received 24 to 48 hours of prophylactic antibiotics only. In addition, rigid glucose monitoring during the perioperative period was maintained during the last 5 years, as previously described.[15]

Methicillin or vancomycin hydrochloride resistance of recovered organisms was noted. Extended-spectrum β-lactamase–producing organisms were defined as gram-negative bacteria resistant to antibiotics and lacking a β-lactamase inhibitor moiety that are typically effective against these microbes. For the purposes of our study, resistance was defined as a minimal inhibitory concentration level of 8 μg/mL or higher. No specific extended-spectrum β-lactamase testing was performed. The incidence of fungal infections was noted relative to the prophylactic antifungal therapy that may have been used.

Comparisons between patients who developed postoperative infections and those who did not were made using the *t* test for continuous variables and χ^2 analysis for categorical variables. Significance was assessed at the 95th percentile.

RESULTS

Twenty-two patients required operative intervention for secondary pancreatic infections, including 10 patients with necrosis and 12 with pseudocysts. The mean age was 47 years (range, 32-76 years). It was possible to calculate Ranson criteria in 14 patients with a mean score of 5 (range, 3-8). The etiology of SAP was gallstones for 15 patients, alcohol for 4 patients, unknown for 2 patients, and hypertriglyceridemia for 1 patient. For those patients with infected necrosis following the onset of SAP, operative intervention took place at a mean of 22 days (range, 13-33 days). For those patients with pseudocysts following the onset of SAP, operative intervention took place at a mean of 38 days (range, 15-55 days). Of these 22 patients, all but 1 received antibiotics prior to surgery for a duration of 3 to 27 days. Sixteen patients received carbapenems prophylactically as either monotherapy or in combination with other agents. Fourteen patients received vancomycin prior to surgical intervention as either prophylaxis or as treatment for extrapancreatic infection. Eight patients received prophylactic antifungal therapy (7 received fluconazole, and 1 received caspofungin).

Table 1. Data on 29 Isolates Recovered From 22 Patients With Secondary Pancreatic Infections

Type of Organism	Isolates, No.	Comment
Gram positive		
Enterococcus faecalis	6	5 Isolates were vancomycin resistant
MRSA	3	
Staphylococcus epidermidis	3	
Streptococcus viridians	1	
Clostridium perfringens	1	
Lactobacillus	1	
Gram negative		
Escherichia coli	6	Isolates were ESBL-producing organisms
Enterobacter cloacae	1	
Enterobacter aerogenes	1	
Psuedomonas aeruginosa	1	
Klebsiella ozaenae	1	
Citrobacter freundii	1	
Bacteroides fragilis	1	
Fungal		
Candida albicans	2	

Abbreviations: ESBL, extended-spectrum β-lactamase; MRSA, methicillin-resistant *Staphylococcus aureus*.

Twenty-nine isolates were recovered at the index operation in 18 patients (**Table 1**). Four patients had sterile cultures despite clinical signs of sepsis, including 3 patients with pseudocysts and 1 with necrotizing pancreatitis. These 4 patients clinically improved following surgical intervention. Eight of the 18 patients (44.4%) with positive culture results had polymicrobial infections. Fifteen of the 29 isolates (51.7%) were gram positive in nature. Of note, 6 of these 15 gram-positive pathogenic isolates were *Enterococcus faecalis,* 5 of which were vancomycin resistant. All patients who were positive for *Enterococcus* on culture had received vancomycin preoperatively for at least a 1-week course. There were no fungal isolates recovered from 8 patients who received empirical antifungal therapy. In contrast, 2 patients who did not receive prophylaxis had cultures that were positive for fungi in addition to other bacterial pathogens. Five patients with previously stable pseudocysts re-

Table 2. Risk Factors for Postoperative Pancreatic Infections

Risk Factor	Patients, No. (%) With Infection (n = 40)	Patients, No. (%) Without Infection (n = 185)	*P* Value
Mean age, y	59.2	58.3	
Carcinoma	24 (60.0)	92 (49.7)	.30
Mean operating time, min	375	387	
Whipple procedure	31 (77.5)	131 (70.8)	.44
Immunocompromised	7 (17.5)	38 (20.5)	.83
Placement of biliary stent	6 (15.0)	48 (25.9)	.20
Placement of surgical drain	20 (50.0)	112 (60.5)	.30
Postoperative hemorrhage	4 (10.0)	5 (0.03)	.06
Development of pancreatic fistula	7 (17.5)	9 (0.05)	.01
Management of soft pancreatic remnant	28 (70.0)	79 (42.7)	.002
Use of fibrin glue sealant	31 (77.5)	112 (60.5)	.05
Placement of pancreatic stent	26 (65.0)	93 (50.3)	.12
Use of octreotide acetate	38 (95.0)	130 (70.3)	<.001

quired an urgent operation for worsening abdominal pain and sepsis and had pathogenic isolates recovered from samples that were similar to those recently obtained from central lines, concurrent blood cultures, and, in 1 case, a knee aspirate (3 patients had methicillin-resistant *Staphylococcus aureus*, 1 patient had *Escherichia coli*, and 1 patient had *E faecalis* isolated). Positive culture results (from samples of catheters and blood) preceded by 2 to 4 days the deterioration of a patient's condition (which was determined by abdominal examination) and prompt surgical exploration. Two patients acquired β-lactam–resistant *E coli,* neither of whom received carbapenems as a prophylactic agent. Three patients, all with necrotizing pancreatitis, had a preoperatively placed percutaneous drain. Bacterial isolates recovered at the time of surgery within 1 week of drain placement correlated with those isolates recovered following surgical debridement. Three patients died, 2 of whom had isolates recovered during surgery that were positive for vancomycin-resistant *Enterococcus* (VRE).

During the study period, 225 patients had elective pancreatectomy, with 169 (75.1%) having the procedure performed because they had periampullary carcinoma. Of these 225 patients, 40 (17.87%) developed postoperative infections, 22 (55.0%) of whom had polymicrobial isolates. The potential risk factors contributing to the development of postoperative infections are presented in **Table 2**. Although the use of fibrin glue sealant and perioperative octreotide acetate were associated with infection, it is doubtful whether these adjuncts contributed to sepsis. Only the management of a soft pancreatic remnant and the development of a postoperative pancreatic fistula were significantly associated with the development of a postoperative infection. Implementation of rigid glucose control during the perioperative period did not decrease the incidence of these infections (**Figure**).

Seventy-two isolates were recovered from these 40 patients (**Table 3**). These infections were diagnosed a mean

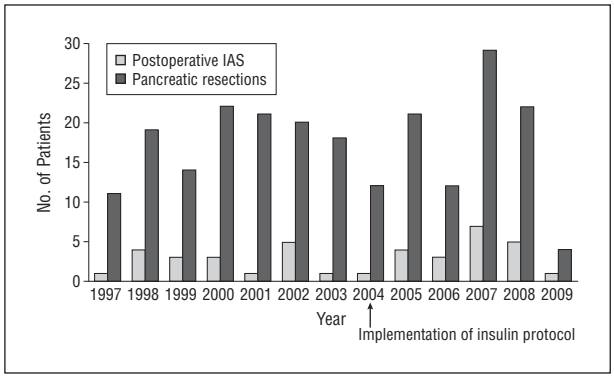

Figure. Number of patients with pancreatic resections and number of patients with intra-abdominal sepsis (IAS), per year, at hospitals affiliated with the University of Tennessee Health Science Center, Memphis.

of 10.9 days following the index procedure. Nearly one-half of these isolates were gram-positive organisms, including 12 drug-resistant pathogens (11 methicillin-resistant *S aureus* isolates and 1 VRE isolate). Twelve isolates were either *E coli* or *Klebsiella pneumonia* on final culture, 5 of which were extended-spectrum β-lactamase–producing organisms. Fifteen patients (20.8%) had fungal isolates, and these infections were monomicrobial in 5 patients. Of the 15 patients who developed fungal infections, 3 (20.0%) died; of the 17 patients who had bacterial isolates recovered, 2 (11.8%) died.

COMMENT

Our study supports the work of others who demonstrated a shift from enteric flora to gram-positive organisms in patients receiving prophylactic antibiotics for SAP. We further note a striking trend in vancomycin-resistant organisms in patients receiving this antibiotic during the preoperative period. Our data suggest that prophylactic antifungal therapy in patients with SAP may prevent the development of invasive infection. Finally, we documented rapid seeding of previously sterile pseudocysts from bloodstream infections most commonly originating from central line–associated infections. Postoperative infections following elective pancreatectomy were noteworthy for the recovery of unanticipated gram-positive, drug-resistant, and fungal organisms despite only a short period of antibiotic prophylaxis perioperatively. The limitations of our study are that we did not attempt to identify those patients with SAP who may have avoided surgery because they received prophylactic antibiotics and/or underwent percutaneous catheter drainage.

The use of prophylactic antibiotics in patients with SAP has been the subject of much debate. Because secondary infections require operative intervention, antimicrobial prophylaxis, in theory, might prevent the progression from a sterile to an infected process and ultimately reduce morbidity and mortality. Randomized controlled trials addressing this issue have been difficult to perform, interpret, and assess owing to the inherent heterogeneity of the patient population studied, the lack of a consistent definition of SAP, and the relatively small number of patients ulti-

Table 3. Data on 72 Isolates Recovered From 40 Patients With Postoperative Pancreatic Infections

Type of Organism	Isolates, No.	Comment
Gram positive		
Staphylococcus aureus	14	11 Isolates were methicillin resistant
Enterococcus faecalis	10	1 Isolate was vancomycin resistant
Streptococcus viridians	4	
Staphylococcus epidermidis	2	
Staphylococcus hominis	1	
Enterococcus faecium	1	
Group A beta-hemolytic *Streptococcus*	1	
Clostridium	1	Not *Clostridium perfringens*
Gram negative		
Escherichia coli	8	4 Isolates were ESBL-producing organisms
Enterobacter cloacae	3	
Klebsiella pneumoniae	4	1 Isolate was an ESBL-producing organism
Haemophilus parainfluenzae	2	
Klebsiella oxytoca	1	
Citrobacter freundii	1	
Proteus mirabilis	1	
Pseudomonas aeruginosa	1	
Bacteroides fragilis	2	
Fungal		
Candida albicans	9	
Toulopsis glabrata	2	
Candida tropicalis	1	
Aspergillus	1	
Yeast	2	Not *Candida albicans*

mately requiring surgical intervention.[16-18] These studies have yielded conflicting results regarding the need for prophylaxis, although the 2 most recent randomized clinical trials[17,18] failed to show any advantage. Because the morbidity and mortality rate associated with operative intervention for secondary infections remains substantial, many health care facilities continue to use antimicrobial prophylaxis without firm data proving its benefit.

Prior to antibiotic prophylaxis for SAP, the microbiology of secondary infections comprised predominantly enteric flora, with approximately 50% of these infections being polymicrobial in nature.[1,19] Several recent studies have documented a shift from gram-negative to gram-positive isolates in patients receiving prophylaxis.[8,20,21] Büchler and colleagues[20] reported 86 patients with necrotizing pancreatitis, including 27 with infected necrosis who underwent necrosectomy. All patients received imipenem–cilastatin sodium for a 14-day course. More than 60% of the isolates recovered during surgery were polymicrobial in nature, and 55% of the organisms were gram positive. In a follow-up report from this institution using similar prophylaxis, 33 of 103 patients had surgical necrosectomy.[21] Of note, 43% of patients received other unspecified antibiotics in addition to imipenem–cilastatin. Fifty-eight percent of patients had polymicrobial infections, and 55% of isolates were gram positive in nature. Three of the 33 patients had drug-resistant, gram positive organisms recovered from samples, and 2 of these 3 patients died. Seven of the 33 patients had bacteria recovered that were resistant to antimicrobial agents that were used for prophylaxis, and 3 of these 7 patients died.

Howard and Temple[8] studied 95 patients who underwent surgery for necrotizing pancreatitis. They compared the microbiology of recovered organisms both before and after the institution of prophylaxis (imipenem-cilastatin for 14 days) in those patients with SAP. Isolates of gram positive flora were more commonly recovered from patients who received imipenem-cilastatin than from patients who did not receive antibiotics (52% vs 23%). Carbapenem prophylaxis was not associated with a greater incidence of β-lactam resistance or fungal superinfection.

Twenty-one of our 22 patients received antibiotics preoperatively. In all but 2 of these 21 patients, antimicrobial therapy was given prophylactically for severe SAP, and 15 of these 19 patients had a regimen that included carbapenems as either monotherapy or in combination with other agents. In common with others, 52% of our isolates yielded gram-positive organisms. We did note 2 isolates of β-lactam–resistant *E coli* from 2 different patients, although neither of these patients received prophylactic carbapenems. The data reported herein as well as the data of others support the relative safety of using carbapenems prophylactically in patients with SAP. Although a shift from gram-negative to gram-positive flora has occurred, this has not been associated with an increase in morbidity and mortality and, to date, has not led to the development of drug-resistant organisms.

We found a correlation between prolonged vancomycin therapy and the recovery of *E faecalis* isolates during surgery, findings not observed in patients who received other antimicrobial agents. Of particular concern was the high incidence of vancomycin-resistant *E faecalis* isolates in this cohort. Similar observations noting the relationship between vancomycin use and the development of nosocomial VRE infections has been previously reported.[22,23] Rubin et al[24] performed a case-control study of 8 patients colonized with VRE on a pediatric oncology ward. The control group without VRE colonization was matched with respect to tumor type and age. Medical records were reviewed for the 60 days preceding the first stool or throat culture positive for VRE. All 8 patients with VRE colonization (100%) had received vancomycin for a mean of 16 days compared with 15.3% of patients who did not receive similar therapy. Vancomycin was subsequently used only for documented invasive infection. The 68 patients followed thereafter demonstrated no VRE on surveillance cultures, and no child was treated for an invasive infection.

Mainous and colleagues[25] studied 134 nosocomial bacteremic episodes in a surgical intensive care unit during a 3-year period. Thirty percent of the 134 isolates were enterococcal species, approximately 25% of which were VRE. Seventy percent of patients with VRE septicemia

had received vancomycin compared with only 10% of patients who did not. Stosor et al[26] analyzed 53 patients with *Enterococcus faecium* bacteremia, 43% of whom also had VRE bacteremia. Eighty percent of patients who developed VRE sepsis received vancomycin prior to invasive infection compared with 34% of patients who had vancomycin-sensitive *E faecium* bacteremia. Mortality and hospital costs were higher for patients with VRE bacteremia.

Invasive VRE infections commonly occur during debilitating illnesses requiring prolonged hospitalization, often in the intensive care unit (not unlike patients with SAP).[25-27] These infections have been associated with an increase in mortality in some but not all studies, and it is unclear whether VRE infection in and of itself causes death or is a marker for severity of illness. In our study, 2 of the 3 patients with secondary pancreatic infections who died had cultures that grew VRE. Regardless of whether VRE is a direct cause of mortality, it seems reasonable to take all measures possible to reduce the incidence of these infections, including the use of isolation techniques. Cumulative data would suggest that vancomycin should not be used prophylactically in patients with SAP; rather, its use should be limited to documented invasive infections and only when other antimicrobial agents are ineffective.

Nosocomial fungal infections (the vast majority of which are due to *Candida* species) remain prevalent in the critical care setting.[28] These infections prolong hospitalization, increase disease-related costs, and, in some studies, have been associated with an increased mortality rate. Intra-abdominal and invasive fungal infections are not uncommon in surgical populations, especially in patients who are critically ill and/or require a second operation for tertiary peritonitis. In a prospective study, Clandra and colleagues[29] noted that risk factors for intra-abdominal candidiasis included recurrent gastrointestinal perforations, anastomotic leakage, surgery for acute pancreatitis, and splenectomy.

Vege et al[30] analyzed the incidence of fungal infection in 207 patients with SAP, with tissue assessed by either operative or nonoperative means. Fifty-two patients received prophylactic antibiotics, but only 19 received antifungal therapy. Ninety-nine patients had sterile cultures. Thirty patients (~28% of those with positive culture results) had fungal isolates, all *Candida* species. These infections were associated with longer intensive care and hospital length of stay, and patients were more likely to undergo operative intervention when compared with those with bacterial infections or sterile cultures. Gloor et al[21] noted a 24% incidence of fungal organisms recovered from 33 patients who underwent surgical debridement for infected necrotizing pancreatitis and were treated a median of 14 days with imipenem-cilastatin as monotherapy (53% of patients) or in combination with other antimicrobial agents. Fungal infection within the pancreatic bed did not correlate with an adverse outcome in their study.[21] We noted 2 fungal infections, both of which were due to *Candida albicans*, which is similar to the findings of Vege et al.[30] These infections were not associated with an increase in mortality.

He and colleagues[31] randomly assigned 70 patients with SAP to antifungal prophylaxis or placebo. When compared with the control group, the patients receiving prophylaxis had a statistically significant reduction in the incidence of deep-seated fungal infections as well as hospital length of stay. Small numbers precluded direct conclusions with respect to the effect of prophylaxis on the reduction in mortality. Our findings reveal trends similar to those reported by He and colleagues[31]. Specifically, antifungal prophylaxis for patients with SAP seems to prevent the development of fungal infections within the pancreatic bed. Whether this therapy ultimately leads to an improvement in patient outcome remains uncertain. Nonetheless, these results suggest that antifungal prophylaxis should be considered for patients with SAP, especially those receiving concurrent antibacterial agents.[31,32]

Five patients with stable pseudocysts developed sepsis quickly and required urgent surgical drainage following an antecedent episode of central line–associated sepsis with concurrent positive blood culture results and the recovery of identical pathogenic isolates from pseudocyst fluid samples. Although it is possible that the reverse occurred (ie, that an infected pseudocyst led to septicemia and secondary infection associated with the use of a central access catheter), the microbial flora identified in these patients (as well as in patients in other reports in the literature) would favor a septicemia-to-infected pseudocyst sequence. Gloor and colleagues[21] recognized the potential for the hematogenous spread of extrapancreatic infections to the pancreatic bed. Of the 33 patients who underwent surgical necrosectomy, 14 (42%) had pathogenic isolates recovered that were similar to those recovered from other types of samples, including the biliary tree and venous catheters. Of these 14 patients, 2 had fungal infections, and 12 had bacterial infections. Seeding of a previously sterile pseudocyst by a contaminated venous catheter was also noted by Olivero et al.[33] All 5 infections in their series[33] were bacterial and similar to the infections in the study by Gloor and colleagues[21] (ie, monomicrobial in nature). This suggests that bloodstream infections are particularly prone to seed pancreatic pseudocysts. Given that most patients with SAP will have central venous access, we recommend particular vigilance of catheter sterility and early consideration of replacing the catheter if infection is suspected.

Four patients had sterile cultures. We did not routinely perform needle aspiration of the pancreatic bed to confirm infection but relied on clinical parameters suggestive of sepsis to proceed with surgical intervention. We are not unique in this approach, and the improved clinical status of these patients following operative intervention, despite the sterile cultures, has been previously described by others.[34-36]

The microbial flora responsible for postoperative infections following elective pancreatectomy was not studied prior to our initial report in 2008, and this finding has not changed in this updated series.[15] In contrast to the enteric organisms that would predictably be anticipated, our results were noteworthy for the high incidence of gram-positive, fungal, and drug-resistant or-

ganisms. Nearly one-half of the isolates were gram positive, and fully one-fifth were fungal in nature. Furthermore, nearly 25% of the isolates recovered were drug-resistant organisms, including methicillin-resistant *S aureus* and extended-spectrum β-lactamase–producing gram-negative bacteria. Because these patients received only prophylactic perioperative antibiotics, there would seem to be little selection pressure for the nonenteric flora identified. Only 15% of patients who developed a postoperative infection had placement of a preoperative biliary stent, suggesting that potential colonization of the bile could not in and of itself explain the flora identified in these infections. We were particularly concerned with the mortality associated with fungal infections (20%). Reports from other institutions would be extremely valuable to support or refute the results reported herein.

Given the results reported to date and until definitive culture results are obtained, we recommend the use of broad-spectrum antibiotics, including agents directed at methicillin-resistant *S aureus* and extended-spectrum β-lactamase–producing organisms, as well as antifungal therapy in patients with postoperative pancreatic infections.

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Correspondence: Stephen W. Behrman, MD, Department of Surgery, University of Tennessee Health Science Center, Memphis, 910 Madison Ave, Ste 208, Memphis, TN 38163 (sbehrman@uthsc.edu).
Author Contributions: *Study concept and design:* Behrman, Bahr, Dickson, and Zarzaur. *Acquisition of data:* Behrman, Bahr, Dickson, and Zarzaur. *Analysis and interpretation of data:* Behrman, Bahr, Dickson, and Zarzaur. *Drafting of the manuscript:* Behrman, Bahr, and Dickson. *Critical revision of the manuscript for important intellectual content:* Behrman, Bahr, Dickson, and Zarzaur. *Administrative, technical, and material support:* Behrman, Bahr, Dickson, and Zarzaur. *Study supervision:* Behrman, Bahr, Dickson, and Zarzaur.
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INVITED CRITIQUE

Pancreatic Infections

Infections in and about the pancreas are difficult to manage and result in increased morbidity and mortality. For patients with severe acute pancreatitis or those undergoing pancreatic resections, there are no defined antimicrobial regimens to address secondary infections. Behrman et al have written a thoughtfully planned article that gives a review of the pertinent literature and details their own, retrospectively collected data. Their data are an invaluable addition to ongoing debates about antimicrobial therapy for pancreatic infections.

Pancreatic infections occur in 2 very different, clinical settings: with severe acute pancreatitis and after elective pancreatic resections. Empirical antibacterial and/or antifungal medications are routinely used in treating patients with severe acute pancreatitis, although, with the exception of carbapenem therapy, the literature does not clearly indicate efficacy.[1] Prophylactic antibiotics are given to the majority of patients undergoing pancreatic resections. This antibiotic use is implicated in the shift from gram-negative to gram-positive flora isolated from infected pancreatic beds as well as the emergence of drug-resistant strains.[2,3]

The mechanism of secondary infections with severe acute pancreatitis is thought to be translocation and inoculation of necrotic pancreatic tissue. After elective pancreatic resections, infections occur with the development of a pancreatic fistula and/or anastomotic leak. With both disease processes, infections are now more polymicrobial, with a predominance of gram-positive organisms. This is falsely attributed to an increase in prophylactic antibiotic use, because the majority of prophylactic antibiotics have satisfactory gram-positive coverage.

Gram-positive drug-resistant strains such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* are nosocomially acquired and are associated with worse outcome. The association between pancreatic infections due to vancomycin-resistant *Enterococcus* and long-term vancomycin use was observed by Behrman et al and others.[4,5]

In conclusion, pancreatic infections are associated with a high morbidity and mortality. Empirical treatment should include carbapenems, antifungal medication,[6,7] and quinupristin-dalfopristin (Synercid) or linezolid (Zyvox) for patients requiring antecedent vancomycin therapy for extrapancreatic infections.

Farhaad C. Golkar, MD
Alexander S. Rosemurgy, MD

Author Affiliations: Tampa General Medical Group, Tampa General Hospital (Drs Golkar and Rosemurgy), and Division of Digestive Disorders, Department of Surgery, University of South Florida (Dr Golkar), Tampa.
Correspondence: Dr Golkar, MD, Tampa General Medical Group, Tampa General Hospital, 409 Bayshore Blvd, Tampa, FL 33606 (fgolkar@health.usf.edu).
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