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Discussion

DR. CHARLES F. FREY (Sacramento, California): Dr. Bradley a number of years ago brought to our attention the open packing method of treating patients with infected necrosis of the pancreas and peripancreatic tissues. He has now accumulated a large experience and has achieved the lowest mortality reported for this otherwise lethal complication of pancreatitis. I believe Dr. Bradley's technique of dealing with infected necrosis represents a significant advance.

It is important to emphasize one semantic point that bears on this. That is, a well-loculated walled-off collection, whether it is called an abscess or an infected pseudocyst, is a different entity from infected pancreatic necrosis. Reports lumping the two together are mixing apples and oranges. Infected pancreatic necrosis occurs earlier after the onset of symptoms than an abscess. It consists of large segments of intact or infected particulate matter involving the pancreas and/or pancreatic tissues. It is usually associated with signs of gram-negative sepsis and can only be effectively managed by debridement or excision of particulate matter, and as Dr. Bradley is teaching us, by open packing and repeated debridement. The latter is made necessary by the fact that the combination of bacteria and enzymatic destruction of the pancreas and peripancreatic tissue continues after the initial debridement, creating new areas of necrosis. Abscesses, on the other hand, are easily managed by operative or percutaneous drainage as no new necrosis occurs after drainage.

I support the use of the open packing technique, which we use in our patients, as we believe it reduces the mortality and the length of hospitalization.

I would like to show two slides, and I would like comments from Dr. Bradley, which are little variations in technique.

Before we put in the open packing technique, we use a large Davol drainage catheter from one side of the abdomen to the other for irrigation purposes. (Slide) Then we place the adaptic gauze and packed over it.

The other thing I would like to ask Dr. Bradley about is that we have encountered patients in whom there has been hemorrhage at the time of the debridement with extension of infection into the spleen. We have found splenectomy should be performed under these circumstances to avoid further bleeding.

I would also like to ask the question of Dr. Bradley as to whether he has follow-up information on his patients after they have been discharged from the hospital. Dr. Braasch, a number of years ago, pointed out that many of the patients who had recovered from their pancreatic infections returned with complications of chronic pancreatitis.

Finally, I do not believe we can attribute all of the reductions in mortality to the open packing technique. The importance of other factors such as improved surgical intensive unit care, including monitoring, ventilator care, fluids and electrolytes, antibiotics and TPN, cannot be discounted and are, in my opinion, significant contributors to the reduction in mortality we are seeing in this disease.

DR. ANDREW L. WARSHAW (Boston, Massachusetts): I rise in admiration of Dr. Bradley's continuing efforts to deal with these very ill patients, but I must say that I have to disagree with him on a number of points.

He and Dr. Frey have made the point that infected necrosis is different from an abscess. There is an element of difference in that some of these patients are more ill than others, but I submit that infection is not the primary difference, but whether or not there is ongoing necrotizing pancreatitis.

The infected necrosis patients do present earlier, at an average of about 10 days. The so-called pure pus collections are several weeks later, and they are often less ill but not always. At the time of operation the difference between infected necrosis and noninfected necrosis may be absolutely indistinguishable to the naked eye. It, therefore, may make little difference in terms of the treatment.

In terms of toxicity, Beger, whom Dr. Bradley quoted, has shown that the hemodynamic changes of necrotic tissue, whether or not infected, are virtually identical, and therefore, the toxic effects on the organism as a whole may be indistinguishable.

On the contrary, the patient with infected necrosis may be completely nontoxic. Percutaneous needle aspiration studies have shown in fact that a patient may have no signs of toxicity: no fever, leucocytosis or hemodynamic instability, and yet have bacteria present in the pancreatic necrosis. I remind you that Ranson's criteria are prognostic signs developed in the first 2 days of illness. They are not signs of what goes on 2 weeks later at the time of pancreatic abscess or infected necrosis.

The infection can set in as early as the fourth or fifth day, much earlier than we had previously suspected. This indicates that there may be a long indolent phase before it is clinically apparent. It would seem that the effects of infection and the ongoing enzymatic and necrotizing effects of pancreatitis combine early in some patients to generate a particularly fulminant course.

I find it difficult as well to accept the bland statement of how much of the pancreas is involved. Much of the lucent areas seen in these CAT scans is not pancreatic but peripancreatic fat. Since the tissue that is debrided is unidentifiable necrotic debris, I find it difficult to know how much of the pancreas is involved no matter how big the glob of swamp muck you pick out. In fact, as Bradley's figures show, few of these patients turn out to be diabetic in the long run. Although up to 80 or 90% has to be lost before producing diabetes, long-term studies do not show much pancreatic insufficiency after severe necrotizing pancreatitis.

The use of contrast-enhanced CT scanning is being suggested. This is a bandwagon that many are jumping on now. As far as I am aware, it has yet not been validated in any long-term study in Europe or here.

Finally, the statement that this is the best series in terms of reduction of mortality from this very difficult problem is a slight overstatement. Beger's own large study is reported as achieving about a 5% mortality rate with closed debridement and drainage. Although he does add local lavage catheters into the pancreatic bed, it is closed drainage, not packing. In our own series presented before this society 2 years ago, now up to 60 patients, the mortality over the past 7 years, and about 40 patients is also 5%. Our historical controls like Dr. Bradley's had a 40% mortality rate in the previous 5 years.

Therefore, what we are seeing in a number of different centers is a much improved survival rate resulting from a variety of different techniques: open packing, closed debridement and drainage (which is what we use), and Beger's closed debridement and drainage with addition of local lavage. Since all are accomplishing the same thing, it is probable that the common element is adequate debridement. Whatever else you do is probably less important and camouflages the basic issue.

I would like to ask Dr. Bradley at what point would he use needle aspiration techniques to determine whether or not there is infection, and would he use that information once he had it to decide whether or

not to debride a patient who had extensive necrotic tissue? Do we really know the natural history of that dead gangrenous material well enough to sit back on any of them? Perhaps when the amount is small, but with large areas I am doubtful.

DR. JOHN M. HOWARD (Toledo, Ohio): I recently summarized 30 patients with massive pancreatic necrosis treated by external (closed) drainage. Debridement is the thing that I should like to emphasize as did Dr. Bradley. Repeated debridement was often required.

I would like to say that of the 30 patients, there was one death, a mortality rate of 3%. I should like to challenge my colleagues by saying that I believe in 1987, the mortality rate of acute pancreatitis should approach that of acute appendicitis. The mortality rate of pancreatic abscess should approach that of appendiceal abscess. The figures quoted in the past no longer are acceptable.

Could I show you a slide? (Slide) I would like to ask Dr. Bradley if this is a pancreatic abscess. Here is a woman 2 months into her illness. She has been receiving hyperalimentation, and is off and on antibiotics. She has been on a ventilator off and on for 2 months. The indication for operation was failure to thrive and delayed gastric emptying. Her temperature was 99–102 F over 2 months.

The lesser cavity is approached by laparotomy. A needle is inserted, and you see the pus exuding from the retroperitoneal tissue. The culture is negative. The gram stain is negative. There are many polymorphonuclear cells present.

The debridement continued with the hemostat inserted along the needle track and the massive retroperitoneal adipose tissue removed.

It is my belief that this may or may not be an abscess. The consistency and color suggests liquefying retroperitoneal adipose tissue. Perhaps we are looking at liquifaction of adipose tissue more than an exudate of infection.

I would like to show one other slide, (Slide) a patient who was operated on 11 months after the acute attack. The retroperitoneal tissue was debrided, and you see that over 11 months, this tissue had not liquefied.

It is my impression that the retroperitoneal tissue constitutes the majority of the necrotic tissue and that liquefaction in this relatively ischemic, more or less encapsulated space, proceeds very slowly.

DR. JOHN H. C. RANSON (New York, New York): I also would like to congratulate Dr. Bradley on the results he has achieved with this difficult problem using open drainage. Like the previous discussants, I agree that patients with infected necrosis require radical surgical debridement and that a readiness to reoperate and redebride necrotic tissue is an essential feature of their management. However, in evaluating the results reported today, it is critical to remember that major advances in diagnosis and supportive care have occurred in recent years and that the 40–60% mortality rate that Dr. Bradley ascribes to closed drainage is from an earlier era.

The report this morning prompted me to review our own experience with 29 consecutive patients managed over the past 4 years by debridement and wide, but closed section, drainage. The overall mortality rate in this group of patients was 17%, which, although not as good as that reported this morning, is much better than we had heard ascribed to this type of treatment. Among the patients who died, two deaths were cardiac without any residual sepsis, two deaths were related to hepatic failure in patients with associated cirrhosis, and one death was due to pulmonary embolism, in the only patient who died with uncontrolled sepsis. One third of the surviving patients required reoperation and redebridement, but two thirds required only one operative procedure for control of sepsis. In short, I believe that open packing may be a valuable approach for selected patients, but it is not needed for most patients.

Dr. Bradley reported in his abstract that his patients had more than 30% glandular necrosis, and like Dr. Warshaw, I would like to ask him how this was quantified. Certainly, contrast-enhanced computed tomography may not reliably differentiate, I believe, fluid from necrotic tissue, and certainly was not available, as Dr. Bradley said, for the whole period of his study. Measurement of weight of debrided tissue may be a valuable index of the extent of necrosis but cannot, I believe, reliably differentiate pancreatic from peripancreatic tissue necrosis.

If we did use this last criterion, our one death with uncontrolled sepsis would have been classified as having 100% necrosis, and, in this particular patient, this was combined with duodenal and colonic necrosis, which brings up my last question for Dr. Bradley.

Three, or about 10%, of our recent group of patients, have had necrosis of a portion of the duodenum in addition to their other infected necrosis. I would like to ask him if he has observed this problem, and if so, how does he approach it in his patients managed by open packing?

DR. J. PEMBERTON (Rochester, Minnesota): Thank you for allowing me to read the manuscript and for extending an invitation to discuss this fine paper.

You are to be congratulated for achieving such an enviable mortality rate for one of the most devastating complications facing patients with pancreatitis.

I would like to lend support from our institution to you and to others who are attempting to define precisely the pathologic process of pancreatic abscess. Your term "infected pancreatic necrosis" is a good one, aptly descriptive and accurate. Such a term qualitatively describes a group of patients with pancreatic abscess who have the most aggressive form of this lethal complication.

Further understanding of this particularly difficult problem will be helpful in classifying such patients in the future. Moreover, you have nicely documented the severity of the predisposing episode of pancreatitis. The severity scores in your patients were high and consistent with an expected mortality of greater than 50%.

That the surgical procedure used achieved the desired goal is illustrated by the fact that no patient in your series had sepsis after operation. At Mayo, the persistent sepsis rate after operation was 47%, even after open drainage. We defined sepsis, however, based on both laboratory and clinical parameters, and I wonder if your definition and ours were the same? Nevertheless, we need to do better.

Your technique for open drainage deserves comment. As you might remember, in commenting on our report in 1985, you suggested protecting the base of the lesser sac and the abdominal viscera with Adaptic® gauze and/or Silastic® sheeting to decrease fistula and rebleeding rates. Indeed, the incidence of enteric fistula reported today is commendably low. I and others at our institution have heeded your advice, and in addition, in some cases have used a heavy plastic zipper, described by Stone, to prevent drying of those packs and subsequent debridement of the viscera.

Your report stimulated us to update the Mayo series of 81 consecutive patients with this problem. Eight additional patients were identified between 1985 and 1986. Of the five patients treated by controlled open drainage, one patient, or 20%, died. Of the three patients treated by closed drainage, all died. These most recent results, therefore, continue to support the use of open drainage in most patients with severe pancreatic abscess and necrosis.

I have two brief additional questions. Do you ever use a zipper?

Your 28 patients had 28 organisms cultured. Apparently no patient, therefore, had a polymicrobial infection. Typically, between 10 and 66% of such patients will have multiple organisms cultured from the retroperitoneum. Such polymicrobial infections may be more difficult to treat than monomicrobial infections. Although your patients had severe pancreatitis and therefore were at high risk of death, were they less difficult to manage because most of their infections were monomicrobial?

DR. DAVID A. DREILING (New York, New York): I have three brief questions: (1) How long was the follow-up? (2) How many of the patients treated stopped drinking because this leads to the third question? (3) Have you observed any patients who were diabetic who lost their diabetes, and have you observed any patients who showed a malabsorption who lost that dysfunction? Many of these patients do regenerate, and I have had a patient whose total pancreas was necrotic and I could see the duodenal curve, etc., and within 18 months, his pancreatic function returned to normal. I am very interested in the possibility of pancreatic regeneration even in these severely ill patients.

DR. GEORGE H. A. CLOWES, JR. (Boston, Massachusetts): I want to make a brief report on a carefully studied series of pancreatic necroses

in which we looked at the protein metabolism in 10 patients. Two of these patients, who were cirrhotic, died. On the other hand, we had a number of patients who had liver failure associated with the presence of pancreatic septic process. You have heard me talk about the "central plasma clearance rate" of amino acids. I simply want to report that those who survived had an average value of 195 mL/m^2/min, and that those who died were in the range of 100 mL/m^2/min, which is significantly lower.

The importance of this is that Dr. Bradley is applying a real surgical principle of removing the stimulus that causes the trouble throughout the rest of the body, and I would just ask him to tell us whether with his procedure, he did not see a fairly rapid improvement in other systems. Did the patients get off the ventilator promptly? Did their liver function improve by whatever method of assessment you used?

DR. EDWARD L. BRADLEY, III (Closing discussion): I am most grateful to the discussants not only for their perceptive but also stimulating questions. I wish, indeed, I had all the answers for you this morning. Surgery in acute pancreatitis is still in its infancy. I believe over the next 10–15 years we will improve our indications and procedures. Having said that, let me address the specific questions.

Dr. Frey, thank you very much for your kind words. We do not use catheters as part of our open drainage technique. We had significant trouble when we were using the large-bore closed drainage catheters with erosion into blood vessels and into various pieces of intestine.

Dr. Frey also asked about whether we have seen hemorrhage; yes, we have. We have seen if from the splenic vein and from the superior mesenteric vein, and it certainly got our attention on both occasions. However, it does respond well to packing, part and parcel of our technique. However, we do recommend that you place Adaptic® gauze over any exposed vessels.

Dr. Frey asked for follow-up information. We have an average 5-year follow-up for this group. Within that period we did not see any of the typical changes of chronic pancreatitis.

Dr. Howard, you are to be congratulated for your low mortality rate with closed drainage in patients with pancreatic abscess. With regard to the slide you showed us, we could consider that to be liquified fat necrosis, possibly in a patient who had peripancreatic necrosis.

Dr. Ranson also has experienced low morbidity and mortality from his patients with closed drainage, and has suggested that recent changes in intensive care may have accounted for a significant portion of that result. I have no doubt that we are much smarter than we used to be in this regard, and certainly I believe patients are being better taken care of in our institution than they were 5–10 years ago. However, if you look at this particular question from a more critical viewpoint, such as the people from Mayo Clinic did when they reported their experience with open drainage in 1984, you may reach a different conclusion. They divided their data into three periods. The most recent period included all of the recent modalities such as CT scans, ICU support, and needle aspirations, and they did not find any change in mortality that they could attribute to earlier diagnosis or improved survival through better care in the intensive care unit. Accordingly, the question of why we are achieving these low mortality rates with this technique is open for further study. It is our belief that we are achieving these results because of the repetitive removal of persistent or recurrent infected necrosis.

Dr. Ranson has questioned whether we need to do open drainage if we are prepared to reoperate. In the abstract, the answer is no. However, as I told you, three quarters of the deaths in *postoperative* patients with infected pancreatic necrosis have been from sepsis. Clearly, that means that there has been reluctance to re-explore these patients in the past. Today, if one wishes to debride and close a patient with infected necrosis, one must observe these patients much closer than they have been observed in the past, and be willing to reoperate at a relatively frequent level.

Dr. Pemberton, thank you for updating the Mayo Clinic series. I am pleased that you are continuing your good results. We have not used the zipper and have not found it necessary.

The particular bacterial floral was predominantly monomicrobial, although we did have anaerobic bacteria in some of the patients along with the aerobic bacteria.

Dr. Dreiling, our follow-up, as mentioned, is 5 years. We have seen malabsorption in these patients, which probably reflects the degree of pancreatic necrosis.

Several of the questioners asked how we could tell whether the necrosis was pancreatic or peripancreatic. It is not always easy. In situations where one can visualize the splenic vein or the superior mesenteric vein, after you have done the debridement, I believe you can be reasonably certain that the pancreas is missing. Furthermore, we have had the opportunity to do ERCP on nine of these patients after operation, and in eight of the nine, at least half of the pancreatic duct was not visualized. I believe we can be sure in the that group of patients that we certainly have pancreatic necrosis.

Dr. Warshaw, has asked a series of stimulating questions. He specifically asked about necrosis *versus* infected necrosis, and, whether in fact, they are different. The only data that I know that bear on this question are the data from Dr. Beger's study. Mortality rate for noninfected necrosis was 8%, and was 32% for infected necrosis. This is a significant clinical difference.

He asked us about our classification system and reminded us that Dr. Ranson's classification is one that is done in the first 48 hours. We also classified these patients with Banks' criteria, which, of course, are continuing criteria. In both classification systems, the mortality rate should have exceeded 50%.

We agree that dynamic pancreatography is not yet validated, and we are currently conducting a prospective study to investigate whether it is going to be useful in the management of the timing of operation in these patients.

We use needle aspiration only when we see an avascular area on our dynamic pancreatogram. We do not advocate doing needle aspirations in every patient with acute pancreatitis, but only if the patient shows evidence of what we consider to be focal necrosis and clinical sepsis.

Your results in patients with pancreatic abscess, like those of Dr. Ranson's and Dr. Howard's, are to be commended because they are equally low. However, patients with infected pancreatic necrosis have a higher mortality rate and a greater incidence of multiorgan failure than do patients with pancreatic abscess. In our opinion, infected necrosis requires open drainage.

(Slide) This, ladies and gentlemen, is an apple. (Slide) And that is an orange.