infants are able to recover today on supportive therapy alone, careful observation for one or two months is essential since some reports suggest that as many as 10% of patients may develop strictures,[1] although our experience does not indicate that the percentage is this high.

Intravenous nutritional support continues to be one of the mainstays of care in the postoperative period. Since most patients have significant malabsorption problems for periods varying from two weeks to three months, initial provision of total parenteral nutrition with a gradual advance to partial parenteral nutrition with small supplements of enteral feedings has proven to be the most effective method of management thus far available. An additional dividend obtained has been the ability to support early nutrition without being forced to push enteral feedings which might potentiate the recurrence of enterocolitis. Not a single patient in this series had recurrence of NNE during the period of follow-up.

The long-term follow-up of infants who have been followed through the period of gastrointestinal tract reconstruction, even in the case of subtotal colectomy, has been gratifying in the long run. All eventually resumed normal growth and development. Even though some patients have had prolonged periods of malabsorption and diarrhea, this has eventually responded to therapy and adaptation. A limitation perhaps is the realization that a certain number of these very tiny, critically ill infants will be brought through a long and difficult illness only to end up with varying degrees of neurologic impairment. However, this is a factor in the care of low-birth-weight infants in general and must be evaluated as further experience is gained in long-term follow-up.

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Discussion

Dr. H. Biemann Othersen, Jr. (Charleston, South Carolina): Dr. O'Neill has presented an elegant protocol for diagnosis and treatment and management of these children, and his results are certainly to be applauded. I agree with all of the data and the method of management which he has presented. I would just like to ask two questions.

Why do we see such an incidence difference in various parts of the country?

In Charleston, we rarely see infants with NNE, and I don't know why. I have talked to our pathologist about it, and he doesn't know why. Shortly after we talked about it, we had three cases come in, but I expected that. Subsequent to that, we have seen very few.

And if anyone knows of a reason why there is such a difference in incidence around the country and around the world, I don't think it's been brought out. But I'd like to know if Dr. O'Neill knows that.

And the second question is: Did you use intraluminal antibiotics, as well as systemic antibiotics?

Dr. Anthony Shaw (Charlottesville, Virginia): It is curious how the differences from one region to another are so marked. Almost all of the infants in whom the diagnosis of neonatal necrotizing enterocolitis was made in our neonatal nursery at the University of Virginia required surgical treatment; and I think we're perhaps as astute at diagnosing it as anyone.

Our criteria are clinical and radiographic. Those who had radiographic evidence of the disease we would treat with parenteral and enteral antibiotics, withdrawal of early feedings—we even gave them dextran intravenously, which some people recommend—and almost all of them progressed downhill. Their acidosis got worse, and all the bad things that Dr. O'Neill indicated on his slide occurred, and almost all of them required an operation.

Our findings at surgery were similar to his. The severest involvement was in the distal small bowel, the terminal ileum, and the right bowel. This was managed with resection, a cutaneous enterostomy, and oversewing of the distal end. We usually would perform a gastrostomy as well.

Our major problem lay in those children who seemed to have involvement from stem to stern. There were some in whom the

whole bowel was actually falling apart in our fingers. But there were a number where it was difficult to determine viability: There appeared to be skip areas, some areas, perhaps, potentially gangrenous, others in between that seemed to be pretty good.

I wonder how Dr. O'Neill manages these.

Let me just show you how we have managed a few of these in our series.

(slide) This shows the kind of thing I mean, with dilatation of the bowel from one end to the other, areas of hemorrhage, areas with pneumatosis, a lot of gas bubbles very often replacing the blood in the mesenteric circulation.

We usually can find an area that looks normal quite proximal in the bowel. We divide the bowel at this point, pass a catheter distally, and completely aspirate the bowel contents.

(slide) This is proximal, and going all the way down into the colon, completely decompressing this. Sometimes after decompressing it, it doesn't look quite so bad, but usually it's just about as bad.

We bring out a proximal enterostomy, and defunctionalize the entire midgut by bringing out several more stomas, so that the end result looks like this.

(slide) This is the proximal stoma. This is the proximal enterostomy of the midgut. And this is the distal end, the defunctionalized midgut segment. So this comes out at two sites, and antibiotics can be instilled into this segment. The proximal end of divided colon has been oversewn and dropped in.

We have done about half a dozen babies this way, where we weren't certain as to the degree of necrosis of the midgut. They all survived the operation, but as time went by we re-explored many of them. Some of them had essentially no bowel; it was all decomposed. Others had various segments of bowel left which were salvagable. The adhesions were formidable. Some of them never functioned quite well. About half of this small group survived in the long term.

(slide) In reoperating, we would find strictures of this sort, which were amenable to resection.

One last question. I don't believe we have had any infants who have developed neonatal necrotizing enterocolitis who have been on breast milk since they were in our nursery. We know that breast milk seems to have a protective effect in these infants, and I wonder whether Dr. O'Neill knows whether any of the infants who developed neonatal necrotizing enterocolitis were fed breast milk alone.

DR. H. HARLAN STONE (Atlanta, Georgia): This is indeed a unique condition, where bowel is gangrenous and yet there is no aroma to the infection. In adults such extensive gangrene carries a mortality rate of not less than 80%; but the mortality rate in these infants is somewhere between 20 and 40%.

We wondered about the participation of anaerobes in this form of sepsis. Over a period of twelve years, 64 infants were noted to have perforated their necrotizing enterocolitis out of 170 where the diagnosis had been made, a 38% perforation rate. Aerobic and anaerobic cultures were taken prior to operation of the blood as well as from the peritoneal cavity at the time of laparotomy. Of these 64 patients, 49 (or 77%) had positive blood cultures. The average was 1.3 species per patient. No blood culture contained an anaerobe.

The presence of bacteria in the blood did not in any way influence survival; that is, except for two species being present, Pseudomonas and hemolytic Streptococcus. If either were present, the infant died. Otherwise, a positive blood culture did not seem to predict an ominous outcome.

With respect to peritoneal cultures, at least 1 g negative rod grew from the peritoneal cavity of each infant. The average was 2.3 species per patient. Anaerobes were identified in six infants, yet these in no way adversely affected future outcome. There were two Clostridia, three gram positive anaerobic cocci, and one Bacteroides fragilis. No anaerobic bacteria were cultured unless perforation had occurred beyond the eighth day of life.

I wonder what has been your experience with respect to the presence of anaerobes in this particular type of newborn sepsis. In addition, have any bacterial species been uniformly associated with a fatal outcome?

DR. JAMES A. O'NEILL (Closing discussion): Dr. Otherson, I have no idea why the incidence of neonatal necrotizing enterocolitis in Nashville appears to be different from that over the Blue Ridge Mountains. On the other hand, this is a phenomenon which has been pointed out very well in the literature by Vernig and others in studies of the epidemiology of this illness. They have tried to account for it with specific populations of bacteria in neonatal intensive care units. They have also shown that the incidence is different from time to time and from place to place.

Dr. Shaw, we do not use intraluminal antibiotics. It has not made sense to me to use them in patients who have a severe ileus and gastric retention, and in whom intestinal decompression appears to be vital in terms of preventing the extension of necrosis in bowel which already has diminished vascularity because of distention. While I am aware that some use intraluminal antibiotics, I am also aware that there is not one bit of evidence to show that they do any good.

I cannot explain why most of your patients seem to need operation. We do use a central venous catheter very clearly, and try to accomplish rapid repletion of volume and cardiovascular support. I would like to think that makes the difference.

Your mention of distal bowel involvement makes a great deal of sense. That happens to be the area where flow is most peripheral and where gastrointestinal flora exist in the highest concentrations, so perhaps those two factors are influential. Also, intestinal transit time in that area is delayed.

Dr. Shaw, we have noted that with decompression, skip areas of necrosis in small bowel have improved. We have been able to plicate small areas of necrosis with success in every instance except one, and we have not had a single leak in that particular group, so we have tended to prefer that. There may be an individual patient who needs multiple enterostomies as you describe, but they should be rare.

The question of breast milk and IgA is interesting. As you know, it is important for the baby to receive milk from its own mother. Somebody else's breast milk is not as good. Also hyperosmolar feeding does appear to be detrimental. In our group of babies, 16 had received feedings and 17 had not. The 16 which had received feedings had received conventional, elemental formulas. They were too small and too weak to be with their mothers, and breast milk was simply not available in that group.

Dr. Stone has alluded to some fascinating information regarding bacteriology. (slide) He has alluded to his findings relative to the phenomenon of anaerobic bacterial growth in patients such as these. These are the culture characteristics of our group of patients. We had positive cultures from the peritoneum in all but one of the acute patients. In 16, or approximately half, there were positive blood cultures, which correlated; and, similarly, cultures from some other place, all of which were sampled regularly, also correlated. I think what this indicates is that this is a phenomenon of generalized colonization, rather than an indication that a particular bacterium is a primary etiologic agent. Our experience would be much like yours in that some Gram negative organisms existed in just about every patient. The majority had Aerobachter and Klebsiella. We have had one resistant Klebsiella organism unfortunately. We have had deaths where Strep has been present, but we have not had a problem with respect to Pseudomonas being uniformly lethal.