

DISCUSSION

DR. PAUL NEMIR, JR. (Philadelphia): Dr. Creech, Members and Guests: I would like to congratulate Dr. Gurd and his colleagues for this important contribution.

By eliminating the toxic breakdown products of ingested protein, a real measure of protection has been afforded.

Our studies on shock and intestinal ischemia have been concerned also with the toxic effect of incomplete breakdown products of protein digestion intrinsic in nature rather than extrinsic or ingested, and more specifically blood and its derivatives.

Enzymically digested blood is highly lethal on intravenous injection into recipient animals. Denatured globin hemochromogen, a substance yielding a similar absorption spectrum to that obtained upon enzymically digested blood or hemoglobin, is also highly lethal. A hemochromogen-like pigment is present in the plasma of animals in the late stages of hemorrhagic shock.

We have studied the site of origin of this pigment, and its possible relationship to hemorrhagic shock, using a modified Wiggers preparation and maintaining the blood pressure at 30–35 mm. of mercury for 4 to 7 hours. Between 2 and 3 hours after the onset of hypotension, absorption spectra identifiable as hemochromogens appeared in superior mesenteric or portal blood samples, and subsequently in the systemic circulation. The appearance coincided with, or preceded, the earliest histological alteration of the mucosa, and occurred considerably before the development of hemorrhagic enteritis.

A quantitative increase in circulating hemochromogens occurred as time progressed, and in late stages approached levels previously noted when highly toxic amounts of denatured globin hemochromogen were ingested.

(Slide) Here are serial plasma hemochromogen concentrations in a group of animals receiving lethal amounts of denatured globin hemochromogen by slow intravenous drip over a period of hours, and here are average concentrations in a group of animals subjected to hemorrhagic shock for up to 5 hours. In late stages, concentrations were in the same range in both groups.

It is likely that the lethal factor resides in the globin fraction rather than the hemochromogen. If heme is combined with a simpler nitrogenous base, such as nicotine amide, the resulting nicotine amide hemochromogen is essentially innocuous. On the other hand, denatured globin has been found to be just as lethal, or even more so, than globin hemochromogen.

Our studies, therefore, support those of the authors with respect to the central importance of the breakdown products of protein digestion in the genesis of shock or conditions in which there is intestinal ischemia.

My question to Dr. Gurd: How much of a factor is the depression of the bacterial flora in the protection of the mucosa? In other words, is it not possible that the elemental diet does not

necessarily reduce the intraluminal toxic factor, but rather by decreasing the bacterial flora, preserve the integrity of the mucosa, which is then able to contain intraluminal toxic factors for a longer period of time? Thank you. (Applause)

DR. JERE W. LORD, JR. (New York): Dr. Creech, this beautifully conceived and carefully executed experiment by Dr. Gurd and his associates may have some important clinical implications, and I would like to mention one of them.

Over the past 12 years we have carried out some two hundred operations on the abdominal aorta for aneurysms and for obstructive lesions of the aorta and iliac arteries. It has been my custom in these 12 years to employ a preoperative preparation which was carried out for purposes of better exposure by eliminating as far as possible the content of the small and large intestines, and also to lessen the chances of paralytic ileus postoperatively. These patients have been treated for a 36-hour period with a clear liquid diet—no food—and given a cocktail 24 hours preoperatively of citrate of magnesia, 4 ounces, and the evening before operation a tap water enema.

There may be, therefore, some reason to believe, in view of the fact that there has been no intestinal necrosis or clinically evident ischemia, that this has been helpful. As the incidence of this complication with this type of surgical intervention is only 1 to 4%, a small series of 200 patients may be meaningless. However, I think there may be not only in this area but in others important clinical implications of Dr. Gurd's beautiful study. Thank you. [Applause]

DR. FRASER N. GURD (Closing): Mr. President, Dr. Nemir's question regarding the bacterial flora is, of course, uppermost in all our minds, and we did incorporate in the study an attempt at quantitation of the microorganisms in a segment of ileum and a segment of colon. The massive stool is largely eliminated by 3 days on this type of diet, so that certainly as far as the lower colon is concerned, the total mass of bacteria is reduced.

However, in the more functional levels higher in the small bowel we were surprised at the small order of magnitude of the reduction of bacteria in a cubic centimeter of washings from the ileum. There was a reduction across the board in all organisms, but it was not great. The coliforms were not reduced appreciably. With regard to the whole place of bacteria in the syndrome, we doubt that it is of prime importance. The evidence for this doubt is detailed in the published paper.

Dr. Lord's preoperative preparation, 36 hours on clear fluids, is something that all of us have used for various types of work, particularly colonic surgery, and we have not had reason to doubt its value clinically. On the other hand, in our animals, we have found that starvation beyond an 18-hour fast is detrimental, and seems to sensitize in some way the mucosa to damage. It seems as if a balanced nutritional recipe is best, and is best administered by the enteric route.

I would like to thank the discussors very much.