Discussion

Dr. John D. Stewart: It's a pleasure to accept Dr. Dennis' invitation to discuss this interesting study.

As far as I know, this is the first systematic effort to determine the preferable method of treatment of the acutely bleeding ulcer in the same clinic, and as a continuing study through a period of time. The authors rightly point out that one of the reasons for confusion on this subject is that results are often compared in cases which are not truly comparable, and controls have not been properly observed.

I think the plan of this study is excellent. I am sure that the essayist would agree that the study needs to be carried longer, however, and that a larger body of statistics is needed before final opinions can be drawn.

For example, I was somewhat interested in the point that, as reported in the Group I management, there were 58 cases; in the Group II, 37; and in Group III, 35 cases. Theoretically, with random selection, or systematic selection, the numbers should be approximately the same, I should think, in the three groups.

One type of control which is almost impossible to achieve in this study, however, is in the case of the patient who has serious concurrent disease. As you all know, most of these patients who are seriously bled out fall in the older age group. In many instances, the patients have grave disease apart from the ulcer. We have found that the patients who come in massively bled out from an ulcer and who have cirrhosis or who have a history of previous myocardial infarction or cardiovascular accidents are serious risks. We know when we operate on such patients the results are going to be less good than average.

However, the question is whether the results would be any better if the patients were not operated on. That kind of control is extremely difficult to establish, and some clarification on that point will come, I'm sure, from this study, with a larger body of evidence.

I would like, in closing, to ask two questions. I would like to ask, first, whether the essayist has any data at hand regarding the time interval in dealing with the Group II cases before operation was carried out.

Secondly, I would like to ask whether he has encountered any of the interesting acute, superficial ulcerations which comprise, in our series, about 10% of the whole.

Finally, he might be interested to know that, in our series of patients managed as in the Group II category, and comprising now over 250 cases, the operative mortality rate is approximately what he reports in this present study.

Thank you.

Dr. John Englebert Dunphy: I would like to congratulate Dr. Dennis and his group on this challenging and important study.

When I saw the abstract, which lists the method of Hoerr and Dunphy as having a mortality of 18%, I was inclined to take the attitude that we see in *The New Yorker,* of "How's That Again?" But the final figures seem to me to be a little more reassuring.

We have no comparable study, Dr. Dennis, but during the period 1933 to 1945, at the Brigham Hospital, all patients were treated by a modified Andresen regimen. They were fed milk and a Sippy diet. They were not transfused except in very small quantities when they were exsanguinating, and the attitude of the physicians was that the mortality at that time, which was around 15%, was considerably less than the mortality, or risk, of a gastric resection.

We were struck by two young patients who died of exsanguination from duodenal ulcers, having no other major lesion at postmortem. One of these had been treated for 10 days on this regimen, and it seemed to us that if surgery has any role in the treatment of hemorrhage, this is an example in which it should be applied. It was then that Dr. Hoerr and I became interested in trying to select from the bleeding group those most apt to bleed to death.

Dr. Dennis' study, I think, shows the great difficulty of selection, and, at the present time, I would presume that the figures which he has presented to us are not really statistically valid to confirm any of the 3 approaches. It indicates again how difficult it is to evaluate clinical problems statistically. It takes a long period.

Yet when one sees a patient who is bleeding to death, it takes a courageous surgeon to let him exsanguinate! If I get anything from this study, it is that in Group I the cause of death was exsanguination primarily, and so I would conclude by saying that until more data is available, I think we should regard bleeding ulcer in general as an exsanguination syndrome best treated in the selected patient by operation.

Thank you.

Dr. Claude E. Welch: Dr. Gilchrist, I have had the privilege of reading Dr. Karlson's paper. It is so convincing that I thought I'd better get up here and say that it troubles me.

First, there is the factor of selection. To use a Goldwynism, I think the big question is: shall we include the cases in or include them out?

For example, there are some cases who are sent in to the hospitals who have had previous transfusions. Whichever group they fall into, they are going to weigh the mortality rates heavily since they probably represent the worst cases. They fell into the nonoperative group, but were excluded because they had had previous transfusions, and three out of four died. If they had been included in the nonoperated group in the statistics, obviously they would have changed the mortality significantly.

The second factor is that of age, which is ex-

tremely important. In our own figures, we have found that at the present time there is essentially no variation in mortality despite the method of treatment below age 50, and that the difference appears only in the 60's and 70's. This seems to be true in this series as well. For example, in the 60's, without operation, there was a 32% mortality; with an immediate operation, a 21% mortality. In the 70's, the figures are not statistically accurate because there are so few, but still there was quite an improvement when immediate operation was carried out. This factor of age must be studied more thoroughly with a larger series of patients.

In the third place, there is another factor which was mentioned, but only alluded to, and that is: what happens to these patients when they have recovered from a hemorrhage? We have found that the results are so poor afterwards that our main question with a massive hemorrhage is not whether or not to operate, but when to operate. That is the only question.

I hope the authors' further studies will not confirm what they say here. Their paper has been a convincing study of the special groups of patients as they were set up. The groups were small and if defined in a different way, would change the conclusions drastically. If many people accept their conclusions without a critical review of the cases, I believe the calendar could be turned back about 25 years in the treatment of gastro-intestinal hemorrhage.

DR. STANLEY HOERR: Dr. Gilchrist, Members and Guests: I have also enjoyed this interesting paper.

The principle of randomization is undoubtedly a very valid one, and constitutes the "new look" in statistics. I have not had the opportunity to examine the manuscript before hand, and as I sat here I wondered whether a question also arose in the minds of some of the rest of you concerning these three groups of patients.

There was the first group, a nonoperated group selected by randomization; a second group where an immediate operation was performed, selected by randomization; and a third group where the operation was done on a selective basis.

Now, in the third group, there will be three or four patients not operated on for every one that is operated. Are these nonoperated patients included in Group III? Were they all operated, or were they a mixture?

Thank you very much. I enjoyed the paper very much, and I look forward to further illumination on this difficult problem.

DR. C. DENNIS (closing): Mr. Chairman, Members and Guests: My associates and I wish to express our thanks to Drs. Stewart, Dunphy, Welch, and Hoerr for the excellent discussions which have been given.

If one is going to undertake a study such as this, it requires an immense amount of coordination and collaboration. I don't think that I would be fair in permitting this moment to go by without expressing the appreciation of all of us to Dr. Perrin Long, Chairman of the Department of Medicine, who made possible this collaborative study between the two departments, and to Dr. Andresen, who is always available for consultation when questions with regard to interpretation appear. Finally, a large house staff and the whole surgical staff were concerned, but are not listed among the authors of the paper, because of limitations of space.

I would like to try to answer some of the questions which have been posed.

Dr. Stewart asks about why there were not identical numbers of patients in the three groups. Frankly, I don't know. We have tried to run this down on many occasions. I think that when one takes a random sample such as this, one is very likely to find that there are differences in numbers. These differences are enough to distress me somewhat, but I would add quickly that one of the things that distressed me most was that I found that my associates were beginning to become convinced that perhaps if one had a bleeding ulcer himself, the best thing to do was to keep the surgeons out of the room and go to bed with a bottle of milk. This is a dangerous conviction to develop when one is trying to run a precisely controlled study, and we have endeavored to rule it out as much as possible.

In regard to Dr. Stewart's question about associated diseases, we did not exclude patients with associated diseases.

In regard to the question of time in Group II patients until operation was performed, those patients included in the statistical study are the cases in which operation was performed according to the recommendation of Stewart—that is, within 12 hours of reaching the hospital.

With regard to Dr. Dunphy's questions, the young patient, I think, is no safer with conservative management than is the old. The one patient which Dr. Karlson mentioned, who bled down to shock levels 4 times under Dr. Andresen's method of management, was in his middle 40's. This patient ultimately died, and, I think, most of us were convinced that he would not have died if he had happened to fall into an operative group.

With regard to Dr. Dunphy's question about the statistical significance of the conclusions that we have drawn, I think the conclusion that we have drawn is that there is no statistically significant difference among the 3 types of therapy which were employed.

In the last analysis, Dr. Dunphy, in regard to your last question, in Group I, most mortality was due to exsanguination. In Groups II and III, most mortality was due to complications of operation. What we are trying to do in our study is balance the one against the other as best we can.

With regard to Dr. Welchs question of previous transfusions, including patients in Group I but not Groups II or III, previous transfusions excluded

patients from the study, so we tried to make the matter identical for all three types of therapy.

The matter of follow up, with regard to which Dr. Welch made mention, is a distressing one to us. In the municipal hospitals of New York City, patients are required to pay for their hospitalization if they are able to do so, and we find that a very substantial percentage of the patients who come into the hospital deliberately give false names and false addresses. I am not permitted to fingerprint them, and it is very difficult to get a good follow up. [Laughter] We have tried to get a good follow up, but it has not been possible; we do feel that the patient who is treated by Andresens regimen does run a much higher risk of subsequent massive hemorrhage than does the patient who has a gastric resection successfully.

In answer to Dr. Hoerr's question, those patients not subjected to operation in Group III all recovered.

I would like to add just one final comment, if I may, and that has to do with some experimental work which my associate, Dr. Hans Roth, has just gotten under way in the experimental laboratory. This is related to the contention that the plug will be blown out of the artery if one transfuses and raises the patient's blood pressure above the shock level.

In the experimental animal this is not true, provided the bleeding has ceased for at least a half hour prior to the replacement of the blood; but if bleeding is still persisting slowly, or if bleeding has ceased within less than a half hour of the time that the blood is replaced, or if one drips gastric juice onto the end of the vessel which has been occluded by a clot, then bleeding usually recurs in vigorous fashion. There does seem to be some excuse for the contention that transfusing these people will lead to fresh hemorrhage.

The likelihood that we should be using fresh blood with platelets intact in transfusing these patients is a very real one. The troubles in the way are gradually diminishing now, and we may go over to this pattern of management.

I wish to thank the discussers again. Thank you kindly.