5. Bockus, H. L.: Gastroenterology. Philadelphia, W. B. Saunders Co., 1944, vol. 1, p. 346.
6. Child, C. G., III: The Hepatic Circulation and Portal Hypertension. Philadelphia, W. B. Saunders Co., 1954.
7. Child, C. G., III, D. Barr, G. R. Holswade and C. S. Harrison: Liver Regeneration following Portacaval Transposition in Dogs. Ann. Surg., **138**:600, 1953.
8. Clarke, J. S., J. C. Hart and R. S. Ozeran: Increase in Heidenhain Pouch Secretion After Portacaval Transposition in the Dog. Proc. Soc. Exp. Biol. and Med., **97**:118, 1958.
9. Davis, M. D.: Portal Cirrhosis. A Study of 100 Consecutive Autopsied Cases. U. S. Armed Forces M. J., **9**:57, 1958.
10. Dixon, W. J. and F. J. Massey, Jr.: Introduction to Statistical Analysis. New York, McGraw-Hill Book Company, Inc., 1957, p. 280.
11. Dragstedt, L. R., E. R. Woodward, E. H. Storer, H. A. Oberhelman, Jr. and C. A. Smith: Quantitative Studies on the Mechanism of Gastric Secretion in Health and Disease. Ann. Surg., **132**:626, 1950.
12. Dubuque, T. J., Jr., L. V. Mulligan and E. C. Neville: Gastric Secretion and Peptic Ulceration in the Dog with Portal Obstruction and Portacaval Anastomosis. Surg. Forum, Am. Coll. of Surgeons, **8**:208, 1958.
13. Fainer, D. C. and J. A. Halsted: Sources of Upper Alimentary Tract Hemorrhage in Cirrhosis of the Liver. J. A. M. A., **157**:413, 1955.
14. Gerez, L. and A. Weiss: Über die Magensaftsekretion bei Eckscher Fistel. Ztschr. f. d. ges. exper. Med., **100**:281, 1937.
15. Gregory, R. A.: The Effect of Portal Venous Occlusion on Gastric Secretion. J. Physiol., **137**:76 P, 1957.
16. Grindlay, J. H. and F. C. Mann: Removal of the Liver of the Dog: An Experimental Surgical Technique. Surgery, **31**:900, 1952.
17. Hallenbeck, G. A. and E. Shocket: An Evaluation of Portacaval Shunts for Portal Hypertension. Surg., Gyn. & Obst., **105**:49, 1957.
18. Jahnke, E. J., Jr., E. D. Palmer, V. M. Sborov, C. W. Hughes and S. F. Seeley: An Evaluation of the Shunt Operation for Portal Decompression. Surg., Gyn. & Obst., **97**: 471, 1953.
19. Koide, S. S., E. C. Texter, Jr. and C. W. Borden: Perforation of Peptic Ulcer following Paracentesis in Patients with Cirrhosis. Am. J. Digest. Dis., **3**:24, 1958.
20. Lebedinskaja, S. I.: Über die Magensekretion bei Eckschen Fistelhunden. Ztschr. f. d. ges. exper. Med., **88**:264, 1933.
21. Linton, R. R. and D. S. Ellis: Emergency and Definitive Treatment of Bleeding Esophageal Varices. J. A. M. A., **160**:1017, 1956.
22. McDermott, W. V., Jr.: A Simple Discriminating Test for Upper Gastrointestinal Hemorhage. New Eng. J. Med., **257**:1161, 1957.
23. Ripstein, C. B.: Experiences with Portacaval Anastomosis in the Treatment of Portal Hypertension. Surgery, **14**:570, 1953.
24. Schnitker, M. A. and G. M. Hass: A Histologic Study of the Liver in Patients Affected with Peptic Ulcer. Am. J. Digest. Dis., **1**: 537, 1934.
25. Silen, W., D. L. Mawdsley, W. L. Weirich and H. A. Harper: Studies of Hepatic Function in Dogs with Eck Fistula or Portacaval Transposition. A. M. A. Arch. Surg., **74**: 964, 1957.
26. Swisher, W. P., L. A. Baker and H. D. Bennett: Peptic Ulcer in Laennec's Cirrhosis. Am. J. Disgest. Dis., **22**:291, 1955.
27. Whipple, A. O.: The Problem of Portal Hypertension in Relation to the Hepatosplenopathies. Ann. Surg., **122**:449, 1945.
28. Woodward, E. R., R. R. Bigelow and L. R. Dragstedt: Effect of Resection of Antrum of Stomach on Gastric Secretion in Pavlov Pouch Dogs. Am. J. Physiol., **162**:99, 1950.

Discussion

DR. LESTER H. DRAGSTEDT: Dr. Gilchrist, Ladies and Gentlemen: I have followed this work of Dr. Clarke and his associates with a great deal of interest. It seems to me that he has described and discovered a new clinical entity, and the scientific basis for it. It is additional evidence that peptic ulcers can be produced in an entirely normal mucous membrane by a hypersecretion of gastric juice.

The old idea of a local decrease in resistance is gradually receding, I think, into the background.

When we first learned about this work of Dr. Clarke, Dr. Kohatsu and Dr. Gwaltney repeated the experiments which Dr. Clarke has described, and in each case confirmed them. Hypersecretion continued even after the antrum was removed, which is a very interesting phenomenon.

Now, it is quite possible that when the blood from the intestinal tract is diverted away from the

CHART 1. *Association of Cirrhosis and Peptic Ulcer*

(From Liebowitz and Rousselot: Bleeding Esophageal Varices. Charles S. Thomas, 1958.)

Author	No. Cases of Cirrhosis	No. Cases with Peptic Ulcer	Percentage Incidence
Ratnoff and Patek**	386	13	3.6
Schnitker and Haas*	72	14	19.4
Swisher *et al.**	417	58	13.9
Lipp and Lipsitz*	302	15	5.0
Dagradi *et al.**	92	12	13.1
Sullivan *et al.**	94	3	4.2
Palmer and Brick*	150	22	14.6
Fainer and Halsted**	94	16	17.0
Lipp and Lipsitz**	130	15	11.5

* Clinical studies.
** Postmortem studies.

liver that there are substances in that portal blood that are normally detoxified in the liver, that gain access to the circulation and stimulate gastric secretion. It is a most interesting and new piece of physiological research.

DR. CHARLES GARDNER CHILD III: I consider it a privilege to congratulate Dr. Clarke and his associates on a beautiful bit of physiologic experimentation. In this connection I am reminded of what Dr. Harkins said earlier today—about the man who took something to the laboratory and did not leave it there. I am afraid I am guilty of devising portacaval transposition and leaving it in the laboratory after having proved but a single point with regard to hepatic regeneration. Needless to say I am gratified at the number of experiments for which this preparation has been used and chagrined that I have not been able to put it to greater use.

As far as the problem of ulcer after portacaval shunt is concerned, I looked up, at Dr. Clarke's suggestion, my own experience with some 100 patients with end to side shunts. I discovered five who developed either a duodenal or gastric ulcer in the postoperative period.

I had not paid any particular attention to this complication until the reports of hyperacidity after Eck fistulae came to my attention (American College of Surgeons, Forum, Volume VII, 208–211, 1957). I then looked up all our patients and found one had died of hemorrhage proved to have come from a duodenal ulcer, and another from hemorrhage thought to have come from a duodenal ulcer. Another patient had to have a gastric resection. The remaining two patients have done well on a dietary program. Interestingly enough both patients who bled rather promptly went into coma from which they could not be aroused. We believed them to be advanced cirrhotics in whom operation was not justified.

Certainly Dr. Clarke's paper points up the fact that when a patient whose shunt is opened bleeds and whose varices have disappeared, he may well be suffering from one form or another of peptic ulceration. Although the final significance of this important observation cannot be determined at this time, I am sure we are indebted to Dr. Clarke for focusing our attention upon this potentially important problem.

DR. LOUIS M. ROUSSELOT: Dr. Gilchrist, Members and Guests: I likewise wish to rise and compliment the authors, Dr. Clarke and his associates, on this most provocative group of physiologic studies, and on reading the abstract I was interested enough to look up a variety of clinical data which I think are pertinent to the subject.

I think that the association of peptic ulcer following portocaval shunt may not necessarily be an association that is greater than occurs in cirrhotics without portocaval shunts (Chart 1).

A study of the assembled statistics on the association of peptic ulcer and cirrhosis reveals certain differences in incidence and also discrepancies between clinical and postmortem observations. Such disparity in findings is inherent in the nature of the study because the material is selective and not picked at random. Validity of the necropsy assay of combined incidence depends on the meticulous care with which the tissues are examined and the interest of the prosector.

Again, many ulcers heal without residual scarring, leaving no mark of their former presence. Accuracy of the clinical survey, by the same token, rests on the skill of the radiologist in the hunt for an ulcerative lesion. The discordant reports of the incidence of peptic ulcer at necropsy is a well known point in order.

Fainer, subjecting his findings to statistical analysis, reported that "the incidence of peptic ulcer in patients with cirrhosis has been found to

be significantly greater than the incidence in those without cirrhosis."

On the basis of this and other reports shown on the slide now projected, one may conclude that gastro-duodenal ulcers exist more frequently in patients with cirrhosis, in whom at least 85% of portal blood flow is already deviated via collaterals.

Wangensteen found that gastro-duodenal ulceration provoked by histamine occurred more readily after ligation of the portal vein in rabbits, as compared to control animals. The mucosal congestion and hyperemia engendered by portal pooling and stasis as occurrs in cirrhosis facilitates the development of peptic ulcer and similarly increases the susceptibility to bleeding from the lesion.

Portocaval shunt in portal hypertension diverts the static pool, reduces portal tension, empties collateral veins and diminishes mucosal congestion. One would, therefore, expect a reduction in the post-shunt vulnerability of duodenal mucosa to either acid or humoral influence.

Finally, post-shunt studies on liver function have shown no deleterious effect on liver function ascribable to the operation per se.

DR. C. ROLLINS HANLON: Dr. Gilchrist, Members of the Association and Guests: I should like also to compliment Dr. Clarke and his co-authors on this fine presentation. I wish to comment on work at St. Louis University by Mulligan and Dubuque concerning the incidence of ulcer in patients with portocaval shunts and their experimental study of the mechanism by which these ulcers occur. Some of this work was presented in the 1957 Fundamental Forum.

In their group of patients with portocaval shunts, there were 43 out of 58 who survived beyond 4 weeks, and left the hospital with a satisfactory result. Of these 43 patients, 8 developed gastric or duodenal ulcers in a follow up period of a year or more. Two of the 8 were demonstrated radiologically only; two were demonstrated at the time of gastrectomy for gastro-intestinal hemorrhage, and 4 were found at autopsy. I might say that all 8 of these patients had been studied preoperatively without demonstration of an ulcer, nor was there any evidence of ulcer at the time of the shunt.

(Slide) This is a normal upper gastro-intestinal series in a patient just preceding a portocaval shunt.

(Slide) Fourteen months later, one can see a series of lesions in the barium filled stomach. These were interpreted initially as diverticula; they turned out at autopsy to be massive gastric ulcerations from which the patient exsanguinated.

Another patient developed a very large duodenal ulcer from which he bled massively. He had a high subtotal gastrectomy with relief for 2 months following which he exsanguinated from a jejunal ulcer.

(Slide) This slide indicates some of Mulligan and Dubuque's studies on gastric secretion and portal hypertension. Eighteen dogs are represented, all with portal hypertension and Heidenhain pouches. These animals resemble those of Dr. Clarke and his group with the exception that portal hypertension was produced not by portal transposition but by Popper's technique of near total occlusion by ligation of the portal vein. The restriction of flow through the portal vein regularly progresses to complete occlusion with this technic.

In a control group of three dogs with Heidenhain pouches, studied over an average of about 2 weeks, the average daily output of gastric acid was 30 mEq. and after a sham operation there was very little change.

In another group of 8 animals with portocaval shunts, the total daily secretion before the shunt was comparable to that in the control animal; after a portocaval anastomosis you can see the tremendous increase in daily acid output due in large part to volume increase rather than in increase in acidity per unit.

(Slide) In the third group portal ligation was done with a subsequent high daily output of acid. After about a month of steady high acid secretion, a portocaval anastomosis was done, which, as you see, did not modify the hyperacidity at all. In other words, there is hyperacidity with portal obstruction and it remains high even with adequate portocaval shunt.

Now, in addition to these studies, 38 dogs were stimulated by histamine in beeswax and observed for gastroduodenal ulcer. In a control group of 11 animals, the incidence of ulcer was about 55%, whereas in the remaining groups with histamine stimulation plus portocaval shunts, or histamine stimulation plus portal ligation and portocaval shunt, the incidence was 90%. The two animals who did not develop ulcer were found at autopsy to have incomplete portal obstruction. Thus experimental portal obstruction regularly makes the dog more prone to peptic ulcer.

DR. ROBERT R. LINTON: Mr. President, Members and Guests: This has been an interesting presentation of what is considered a complication following a portocaval shunt, but actually the incidence that the authors have reported does not equal the reported incidence of peptic ulceration in cirrhotic patients without portocaval shunts. I think it is of interest that in the general population the incidence of peptic ulceration has been reported to be about 10% and in patients with cirrhosis of the liver, it runs between 15 and 20%. It would appear, therefore, that in order to incriminate portocaval shunts, as a causative factor in the production of peptic ulceration, one would expect a much higher incidence than has been reported here today. I certainly do not think that this should deter us from performing portacaval shunts. There has been considerable skepticism in the last few years in regard to shunting procedures and it disturbs me to think of the possibility that a peptic ulceration may develop after one of these

has been performed, may deter internists and surgeons still further. I would like to state that in my own experience in approximately 200 cases with portacaval and splenorenal shunts, there have been only four instances of peptic ulceration develop in the postshunt period or an incidence of 2%. I think it is important to remember that this condition can develop following shunting procedures and one should not jump to the conclusion that the shunt has not been effective in controlling bleeding from the esophageal varices. In my opinion the usual treatment for peptic ulceration in these cases should be carried out, including gastric resection if necessary.

DR. JAMES S. CLARKE (closing): I appreciate the discussion by Drs. Dragstedt, Child, Rousselot, and Hanlon.

With regard to Dr. Child's and Dr. Hanlon's comments, we chose portacaval transposition specifically because we wanted to be as sure as possible that if a change in secretion was found, it would not be due to anoxia or diminution in blood flow to the liver. Clearly, this preparation is less enlightening with reference to the clinical problems of end-to-side portacaval shunt than Eck fistula, but it yields some additional information of a physiological character.

Dr. Rousselot pointed out very clearly the fact that it is extremely hard statistically to show exactly what the incidence of ulcers is in these groups of patients, and I think that we can't say that ulcers are more frequent in portacaval shunt patients than in patients with cirrhosis. We can say that ulcers do occur after shunt and they occur in significant numbers. Certainly, portal decompression does not alleviate the ulcer tendency very much, as we would expect if the ulcers were due to vascular congestion from portal hypertension. Thank you very much.