

DR. DAVID J. SANDWEISS (Detroit, Mich.): Dr. Reinhold stated that he found a low hemoglobin and low erythrocyte count in a certain number of his ulcer patients. Dr. E. A. Sharp (Director of the Anemia Laboratory, Harper Hospital) and I studied the hematopoietic system in 24 of the 63 ulcer patients reported by me this morning, who were treated with urine extracts. The blood studies were made before treatment was instituted, during treatment and after treatment was discontinued. Our data before treatment is apropos the subject under discussion.

Our studies consisted of red and white blood counts, hemoglobin determinations (Newcomer colorimetric method), capillary fragility test (Rumple-Leeds method), bleeding time (Ivy method), coagulation time (capillary tube method), and prothrombin time (A. J. Quick method). The mean diameter of the red blood cells was determined by the Bach Halometer. An indirect method was used for determination of the number of platelets. The total number was calculated from the number obtained by counting the platelets among 10,000 red blood cells.

We found no marked abnormal changes in the individual ulcer patients studied. On further study, however, of each hemogram and then in comparison with others in this group, we found that variations from the normal became more real than at first apparent. These changes will be described in a future publication.

With reference to the red blood count and hemoglobin determinations, our findings are as follows: in 54% of our 24 patients the hemoglobin was 100% or higher, the highest hemoglobin was 117% in two patients. In 62% of our 24 patients the red blood count was 5,000,000 or over, the highest 5,750,000. The lowest hemoglobin was 82% and the lowest red blood count was 4,150,000. These were found in a woman who six years before this study had an ulcer hemorrhage.

DR. T. T. MACKIE (New York, N. Y.): I should like to ask Dr. Reinhold at what season of the year these

studies were carried on. It has been our experience both in ulcer cases and in controls that there is a statistically significant difference in the mean blood level for both ascorbic acid and Vitamin A, comparing the winter months and the summer months.

DR. JOHN G. REINHOLD (Philadelphia, Pa.) (closing the discussion): To correct a possible misunderstanding, the protein intake of many of these patients was not normal, but there was no relationship between the protein intake in the relatively small number of patients whose diets were analyzed and the serum protein concentration. For example, in two patients who were taking 2 grams per kilo of protein per day, the concentration of serum protein was in the neighborhood of 6 per cent, which would put them low in the group.

In the studies described, there are either 50 or 52 cases represented, yet because of the fact that we had only fifteen controls, we used the Student method for comparison of means of small samples, as modified by Fisher, in arriving at our conclusions. That was the reason, also, for taking the limit of three times the standard deviation rather than twice the standard deviation, as is ordinarily done as a criterion of significance. If we had had more controls, possibly more of the results would have proven to be significant, although probably not.

It is interesting that one of the discussers found that capillary fragility was not altered. A large difference exists between low Vitamin C concentrations as seen both in our control groups and in our ulcer patients, and the occurrence of actual pathological changes as represented by increased capillary permeability.

We have, of course, drawn no conclusions concerning the etiologic importance of these findings at this time. The studies were carried out through the entire year and, with the exception of ascorbic acid concentration, there was no significant difference in the summer values as compared with winter, spring, or fall.

A Comparison of the Meulengracht and Sippy Therapies in the Care of Bleeding Peptic Ulcers

By

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ALTHOUGH there are several reports on the Meulengracht therapy of bleeding ulcer, none of them so far as I am aware, has compared the results with those obtained by complete alkalization as recommended by Sippy. The latter was the official treatment at the Peter Bent Brigham Hospital for fifteen years until January 1, 1940, at which time it was decided to try the Meulengracht treatment.

Our former regimen started patients on hourly doses of four grams of calcium carbonate or two grams of magnesium oxide throughout the twenty-four hours for 2-3 days and then transferred them to the regular Sippy regimen. If a hypersecretion or continuous secretion was suspected, powders were continued throughout the night for another 2-3 days after food was started. In the milder cases, the milk

feedings might be started from the very beginning. During the fifteen years in which this regime was in force we have treated approximately 450 ulcer patients with hematemesis or melaena, with a mortality of six per cent. This figure compares closely with the reports of various clinics throughout this country.

The Sippy method of treatment differs from the usual starvation therapy in two important respects. It neutralizes the gastric contents if properly carried out. Although neutralization was the reason which led Sippy to instigate this treatment, it also introduces something continuously into the stomach and generally speaking, gives food somewhat sooner than the starvation method of treatment. Therefore, this method is more like the so-called Meulengracht treatment than Meulengracht himself was using before he started feeding his patients. One might well consider then whether other things being equal, one should ex-

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pect much greater improvement by the Meulengracht treatment over the Sippy as is found over the starvation treatment.

In January, 1940, we started treating all bleeding ulcer cases with the same diet as outlined by Meulengracht. Exactly the same foods and the same amount of alkali and belladonna have been given in order that there could be no question of diversion from Meulengracht's method. We did eliminate the use of iron.

TABLE I

Comparison of series treated by Meulengracht and Sippy

| | Meulen. | Sippy |
|---------------------------|-----------------------|-----------------------|
| No. Cases | 36 | 50 |
| Sex— Males | 83% | 80% |
| Age— Aver. Of ulcer | 44.3 yrs. 6.8 yrs. | 47.8 yrs. 8.3 yrs. |
| Prev. Hemorr. | 30% | 26% |

Thirty-six patients have been treated up to April 1, 1941, and these form the basis of this report. As a control I have taken fifty cases treated by the Sippy regimen during the years 1932 and 1933.

Table I shows that these two series are made up of a very similar type of patient. The incidence of sex is nearly the same. The Sippy patients were on the average three years older and had suffered from ulcers approximately 1½ years longer.

Table II shows that the severity of bleeding was about the same in the two groups, as judged by the average blood on admission and the patients' examination. A clinical evaluation, taking into consideration the degree of anemia and the reaction of the patient to the anemia suggested that a few more of the Sippy cases fell in the severe group than the Meulengracht. Approximately seventy-eight per cent of both groups appeared to have had an average hemorrhage. However, sixteen per cent of those placed on a Sippy had what could be termed severe bleeding, as compared with 8.3 per cent of those who were given the Meulengracht treatment. The groups are, nevertheless, sufficiently similar to make valid a comparison of the two forms of therapy.

The effectiveness of any treatment for bleeding may be considered under the mortality, the promptness with which bleeding stops and the rapidity with which the blood regenerates.

Table III gives a resume of these factors. Deaths on Meulengracht were 5.5 per cent as opposed to 8.0 per cent with the Sippy. However, the data show little to choose from as regards the drop in the blood after going on the regimen, the length of time required for the intestinal tract to free itself of blood and the rate of regeneration in the blood.

The figures of mortality are of the greatest importance and need careful evaluation. There were two deaths on the Meulengracht regimen.

The first was a 68 year old male, with no previous history of ulcer, who appeared to have suffered from

a severe loss of blood at the time of admission. The extremities were cold, he was drowsy and his blood pressure was 76/40. He was transfused four times in thirty hours and then transferred to surgery at which time his blood pressure was 150/90. At operation a resection was carried out and the patient died twenty-four hours later. It seemed to us that this case should be listed as a death against the Meulengracht, although Meulengracht might argue that perhaps he would have lived if surgery had not been resorted to because he states that he has given up surgery on all his bleeding ulcer cases.

The second case was a 43 year old female who had been troubled with an ulcer for two years. On entry she suffered from pallor and clammy extremities with a blood pressure of 118/72, a hemoglobin of 60 per cent and a red count of 3.18 millions. She did badly in spite of five transfusions of 2800 cc. of blood and finally died. Autopsy showed a perforation and an erosion through the pancreatico-duodenal artery.

Four patients died while on the Sippy treatment. The first was a seventy-one year old male who had gross bleeding four years and twelve years before. He showed no signs of shock on admission with a hemoglobin of 45 per cent and a red count of 2.1 millions. Later the blood dropped to 40 per cent hemoglobin and 1.4 million red cells and he died on the sixth day. Also, he suffered from chronic nephritis with hypertension and arteriosclerosis.

The second case was a 27 year old male who had an ulcer for one year. He entered with a hemoglobin of 25 per cent and a red count of 1.2 million. He was

TABLE II

Relative severity of bleeding on admission of patients treated by Meulengracht and Sippy

| | Meulen. | Sippy |
|----------------------|---------|-------|
| Admission hemoglobin | 65.0 | 61.5 |
| Admission red cells | 3.2 | 3.3 |
| Pallor | 67.2% | 68% |
| Coldness of skin | 5.5% | 2.0% |
| Restlessness | 5.5% | 2.0% |
| Apprehension | 2.2% | 2.0% |
| Weakness | 2.2% | 10.0% |
| Air hunger | 0 | 6.0% |
| Severe | 8.3% | 16.0% |
| Mild | 13.8% | 6.0% |
| Average | 77.7% | 78.0% |

transfused after two days and seemed to improve temporarily. During the night his temperature began to rise, he became drowsy and comatose and expired 18 hours later. His death was attributed by those who saw it, to a transfusion reaction.

The third case was a 50 year old female whose ulcer dated back 12 years. She entered with a hemoglobin of 44 per cent and a red count of 2.1 millions. Her stools became free of occult blood after eight days, with the passage of her seventh stool. An autopsy re-

vealed that death occurred from a coronary closure. The ulcer showed no sign of recent bleeding.

The last case was a 71 year old male who had had ulcer symptoms for four years. Although he entered with a hemoglobin of 95 per cent and a red count of 5.3 millions he continued to bleed and was transferred to the surgical service. At operation two spurting vessels were found in the base of the ulcer. Ligation was performed but the patient died twenty-four hours later. No autopsy was obtained.

DISCUSSION

Interest has centered particularly in Meulengracht's reports that feeding his patients has dropped the mortality from around 7-8 per cent to approximately 1.5-2 per cent. As previously reported, our mortality has been six per cent which has included all deaths from bleeding ulcers irrespective of the condition or treatment. Considered in this way, the mortality under the Meulengracht was 5.5 per cent as opposed to 8.0 per cent under the Sippy. Of the two cases which died in our series treated with the Meulen-

TABLE III

Figures to show comparative results of treatment

| | Meulen. | Sippy |
|-----------------------|---------|-------|
| Av. drop in Hgb. | 13.0 | 19.0 |
| Av. drop in RBC | 0.8 | 1.1 |
| Av. number of days | 4.0 | 5.0 |
| Av. regeneration Hgb. | 13.0 | 15.0 |
| Av. regeneration RBC | 0.78 | 1.2 |
| Av. number of days | 16.0 | 18.0 |
| Guaiac-free stools: | | |
| Av. number | 11.0 | 10.0 |
| Av. number of days | 11.0 | 11.0 |
| % deaths | 5.5 | 8.0 |

gracht regimen, one had a perforation and eroded artery which obviously could not be relieved by any medical treatment. If this case is eliminated the mortality becomes 2.7 per cent, a figure which approximates closely Meulengracht's findings. Turning to the Sippy patients, two should be eliminated because of death from a coronary occlusion and a transfusion reaction. Of the remaining two cases it seems unlikely that one would have died if it had not been for the associated nephritis, hypertension and arteriosclerosis. However, it must be retained as a death on the Sippy regimen. The other of the two had two spurting vessels as a result of erosion and must be eliminated for the same reason that one of the patients on the Meulengracht regimen has been dropped. This leaves a mortality of one out of 50 patients or 2 per cent, a figure comparable to the Meulengracht treatment. The number of cases in these series is obviously too small from which to draw definite conclusions. However, their close similarity is of interest.

One obtains the impression from Meulengracht's writings that he attributes much of the improvement

in the mortality rate to the fact that feeding his patients has prevented death from inanition rather than that the bleeding necessarily stopped earlier or was less profuse. This is an important concept, but one which cannot necessarily be checked by all clinics because of the possible differences in the social and economic status of patients seen in different places. Because I have not analyzed the cases at the Peter Bent Brigham Hospital sufficiently from this point of view, I can only give as my impression that we do not see many patients dying from this cause. It so happens that the ward cases are on a comparatively high economic level with the result that our statistics are different and our attitude on treatment can differ from the clinic that treats a large proportion of "down and outers." Radical surgery is not so necessary for the patient who is intelligent enough and able to follow a good medical regimen as for those who cannot or will not. Similarly, one should not expect that the incidence of death from inanition will be as great among those who were well-nourished and in better health before bleeding occurred. My present belief is that a definite decrease in the mortality rate at the Peter Bent Brigham Hospital will come only by determining earlier and more accurately which patients need surgery to stop their bleeding.

Meulengracht has reported that the stools became free of occult blood on the average of 3 days sooner under feeding than on starvation (13.4 days with 4.5 defecations under his former regimen to 10.2 days with 4.8 defecations on his present regimen). We were unable to demonstrate any real difference in this regard between the Meulengracht regimen and the Sippy form of treatment. The stools became free of occult blood on an average of 11 days with both methods of therapy. The number of stools averaged 11 on both regimens. I can account for this difference between our figures and Meulengracht's only by a difference in the way of performing the test.

Again, Meulengracht and Schiodt report a more rapid regeneration of the blood under the feeding method. Our figures show little to choose from between our two series. Regeneration averaged to be somewhat more rapid at the end of 15 days on the Sippy than at the end of 16 days on the Meulengracht. However, it should be noted that we did not prescribe iron as Meulengracht advises. It seems possible that if we had done so our results might have been similar to his. Our data suggest that perhaps the prescribing of iron from the beginning is the important factor in the more rapid regeneration of the blood under the Meulengracht regimen.

We have found that patients enjoy the Meulengracht more than the Sippy. Moreover, they appear to retain their strength better and seem to be better in general. This is a very desirable accomplishment and leads us to continue feeding our patients from the beginning as Meulengracht advises insofar as we have not demonstrated that this method increases the mortality over the figures obtained on the Sippy.

CONCLUSION

In conclusion, therefore, we have found that the mortality on the Meulengracht regimen closely approximates the Sippy treatment insofar as we can determine from a small series of cases. It surpasses the

Sippy in being pleasanter for the patients and in maintaining their strength. We could not obtain evidence that bleeding stopped any quicker on the Meulengracht or that the extra food increased the rate of blood regeneration.

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DISCUSSION

DR. LEON SCHIFF (Cincinnati, Ohio): Mr. President, and Members and Guests: We have been using the Meulengracht regimen for a little over three years at the Cincinnati General Hospital where we admit many severe cases of bleeding peptic ulcer with average red cell counts considerably below those shown by Dr. Emery. Since we have adopted the Meulengracht regimen our mortality has decreased from 24 per cent to about 6 per cent. I realize that our patients are receiving closer attention now than they did formerly due to our increased interest in the general problem of hematemesis and melena, but I do not believe that this factor alone can account for our improved statistics.

Like Dr. Emery, we have seen bleeding continue and even prove fatal on a Meulengracht regimen, and we believe that an important problem which still confronts the clinician is to be able to pick out early enough that patient who is going to bleed to death unless some measures other than medical are taken to stop the hemorrhage.

Perforation occurred in one of our patients twenty-four hours after he was taken off the Meulengracht regimen because of persistence of pain and placed on a Sippy diet.

I should like to mention one point showing the unreliability of the presence of occult blood in the stools as an indication of duration of hemorrhage. If one gives blood orally to normal individuals, he will find that they may continue to pass occult blood in the stools for many days afterwards and the duration of the positive test for occult blood will vary with different individuals and to a certain extent with the amount of blood administered at a given time.

DR. JOHN L. KANTOR (New York, N. Y.): Mr. Chairman, Ladies and Gentlemen: May I make the following comments on Dr. Emery's very interesting study?

First, as he himself has stated, the total number of cases was rather small. Second, a chemical test is not the best way to prove the persistence of bleeding. It would be better to use the presence of melena as a guide, and even that is far from perfect. Third, iron should have been administered as an integral part of the Meulengracht procedure. Fourth, the comparison should not have been made with the Sippy diet, which is one of the early feeding plans, but rather with the old starvation procedure, which is the essentially new point brought out by Meulengracht.

Fifth, the real value of the Meulengracht method should be appraised, to my mind, on the basis of the total length of the convalescent period and not so much on the incidence of these very bad bleeding cases, because the "spurters" will probably occur no matter what method of treatment is used.

DR. WALTER L. PALMER (Chicago, Ill.): I had not meant to discuss the subject of hemorrhage, but rather to ask two questions of Dr. Emery. Dr. Schiff's comment with regard to the 20 per cent mortality rate, however, leads me to comment on that. My first thought was that a mortality rate of 20 per cent in the treatment of massive hemorrhage is inexcusable. That is a pretty harsh state-

ment. I realize that conditions in different hospitals vary. Dr. Schiff is dealing with a large general hospital, and the patients probably come in in very bad condition indeed, but when the mortality rate drops from 20 per cent to 6 per cent, it makes me wonder if a good deal of the improvement may not be due to the increased care with which the patients are watched. Certainly if a patient with massive hemorrhage is given careful attention, the mortality rate under any form of treatment, to my mind, should not be 20 per cent.

Now, I should like to ask Dr. Emery, first, how many blood transfusions were given in these two series.

Secondly, how many patients were referred for operation in the two groups?

Thirdly, if you calculate your results on the basis of the number of patients who bled to death in the two groups, how does it come out?

It seems to me, as you indicated, that death from coronary occlusion should not be included. You have one or two other causes of death which I didn't hear. If you compute the results purely on the basis of exsanguination, that is, the number of cases actually bleeding to death, how do you come out in the two groups?

DR. HENRY A. RAFSKY (New York, N. Y.): In appraising mortality statistics of any method of treating bleeding ulcer, three factors should be taken into account: (1) severity of the hemorrhage, (2) age distribution and (3) complicating diseases. It is these factors which vary the statistics reported by different authors even at times, when the same method of treatment is employed. Another point which should be emphasized is that we are inclined to brush aside too freely and explain away the deaths due to complicating diseases. Dr. Weingarten and I compared the results of the treatment of a series of patients with bleeding peptic ulcers treated by the Sippy and Meulengracht plans. The mortality rate was about the same in each group. Four of the 39 patients treated with the Meulengracht diet succumbed. One was operated upon for a perforation. Three had a recurrence of the bleeding; two of these patients had arteriosclerosis. Notwithstanding the complications, these fatalities must be charged to the Meulengracht regimen. Severity of the hemorrhage should be taken into account in analyzing mortality statistics. If you read Meulengracht articles you will note that this clinician thought that the bleeding had stopped in most of his patients before they came to the hospital. Another point which should be stressed in connection with the treatment of bleeding peptic ulcer is the question of age distribution. It makes a difference if the patient is above or below fifty years of age. Meulengracht, to the best of our knowledge, did not stress the factor of age distribution in his series.

DR. DONALD T. CHAMBERLIN (Boston, Mass.): The present policy at the Lahey Clinic is based on a theory that a stomach with an acute ulcer in it tolerates food poorly, and that a hemorrhaging ulcer is an acute ulcer. We feel that to change a regimen which works well would be hazardous and we doubt whether in certain arteriosclerotic cases with vessels that continue to bleed, any form of medical treatment can stop the hemorrhage more effectively than the conservative method; while in the younger individuals with mild hemorrhage both radical and conservative medical treatments would be effective.

The chief criticism of the Meulengracht regimen is the difficulty in early segregation of those cases who will require surgery. It is our belief that forty-eight to seventy-two hours without food, provided supportive measures, including parenteral fluids and transfusions, are used, will do no harm to the patient. The starvation period should not be prolonged, however, beyond this, as an extended period is unnecessary, dangerous, and indicates that medical management is inadequate. Our main principle

of treatment in the presence of active hemorrhage is haemostasis by medical management if possible, and, if not, by whatever surgical procedure is required.

The Meulengracht diet as described by the originator, is not, in our opinion, a good regimen for the ordinary ulcer patient to have in the early days of his hospitalization; therefore, it seems unrealistic to prescribe it for the bleeding ulcer patient who is in a more serious state at the onset.

DR. EDWARD S. EMERY, JR. (Boston, Mass.) (closing the discussion): In regard to Dr. Chamberlin's comments, I agreed with the feelings he expresses before we started this theory. I believed that it was questionable whether or not the Meulengracht treatment could be superior to the other on purely theoretical reasoning; however, it seemed to me Meulengracht had presented a very clear-cut picture in a very adequate way, and it was only fair to test it out for ourselves.

In regard to some of the other points brought out, I think we must all remember that different hospital clinics differ tremendously in the type of patient they have; for example, it so happens that the Peter Bent Brigham Hospital, in Boston, has a relatively high social and economic status of clinic patients, as opposed to the Boston City Hospital, where they have a great many down-and-outers.

Their treatment so far as surgery or medical treatment are concerned, has to be different, I think, from the treatment we use.

With regard to Dr. Kantor's point about the stool, I agree with him; on the other hand, I don't know of any other method of obtaining the desired information.

In regard to Dr. Palmer's questions. I cannot answer him exactly. I have forgotten just how many, but both groups did have a certain number of transfusions. There were about six patients on the Meulengracht who were transfused at one time or another, and about two on the Sippy.

We have been using transfusions more often in the last year or two than we did before.

In regard to the number of cases that went to surgery, there were two patients in each of the two groups.

In regard to the evaluation of deaths, as I think I tried to point out before, one of the two patients on the Meulengracht died from a perforation and an erosion of the pancreatic duodenal artery. The other patient died from the effects of the hemorrhage.

Of the Sippy cases, one died of a coronary occlusion after the bleeding had entirely stopped, as was proven by autopsy. One of the patients died following an operation, but at the time showed two spurting vessels.

One of our Meulengracht cases was sent to surgery and died twenty-four hours later.

Gastrosopic and Histologic Studies of the Stomach with Gastric and Extra-Gastric Disease During Life and at Autopsy

By

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and

(by invitation)

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THIS study of 40 cases is offered as a preliminary attempt to understand better the underlying pathology existing in gastritis. It is an extraordinary fact that although several hundred publications have appeared on the gastrosopic aspects of gastritis, no satisfactory examination has been made of the actual histologic changes occurring in the gastric mucosa. The need for studying non-operative biopsy mucosa from the stomach and correlating it with the gastrosopic appearance of the same stomach, has been urged by all students of the gastritis problem, and especially by Schindler, Henning, Crohn and ourselves. To quote Schindler, "A method to harmonize anatomic and gastrosopic findings, is urgently needed." It is true that several investigators have attempted to correlate the gastrosopic appearance of the stomach with a histologic study of surgically resected stomachs, but it is now known that this method of approach is fallacious for the following reasons. Schindler et al, Necheles and others have shown that the trauma of surgical clamping, dissecting, etc., of the operation, creates a marked gastritis. Schindler, Necheles and Gold, have shown conclusively that when the stomach

is partially or wholly deprived of its blood supply, a definite gastritis is set up within two hours, consisting of ulcerations, erosions and inflammatory tissue reaction. This depends on the presence of gastric acidity during the operation. Since most of the surgically resected stomachs, studied histologically, have been for peptic ulcer, the gastric acidity can be regarded as the usual finding; this questions the accuracy of the existence of previous gastritis from such histologic studies. We have accumulated data from a number of interesting cases in which gastrosopic studies were compared with subsequent histologic findings in the surgically resected stomach. Despite this fact, we are not presenting this material, since (a) it is subject to the criticism stated above, (b) it does not add to the histologic conclusions in studies arrived at from surgically resected stomachs, and (c) these gastritis cases, are complicated by a peptic ulcer, which has been so intractable or serious as to necessitate surgical resection of a stomach. Likewise, the cases of gastric carcinoma, are not comparable to gastritis cases, not involved by such a severe lesion.

The obvious reasons for this great lack in laying a more solid foundation in the gastritis conception, are (1) the dangers of carrying out such biopsy studies with particular reference to the danger of perforation

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