STUDIES ON HYPOPROTEINEMIA. I. HYPOPROTEINEMIA IN PATIENTS WITH GASTRIC CANCER; ITS PERSISTENCE AFTER OPERATION IN THE PRESENCE OF BODY TISSUE REPLETION

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With the technical assistance of Iris Forbes, A.B.

INTRODUCTION

HYPoproteinemia occurs with greater frequency in patients with gastric cancer than in patients with other neoplasms or with benign lesions of the gastro-intestinal tract. This was noted earlier by various authors, and has been studied in this laboratory. Hypoproteinemia becomes more pronounced and resistant to therapy following surgical treatment for cancer of the stomach than following similar operations for benign lesions of the stomach or for cancers of other organs.

In previous studies from this laboratory, it was shown that the preoperative administration of large amounts of protein to patients with gastric cancer renders the postoperative hypoproteinemia less pronounced. The present study revealed that hypoproteinemia, once it is established in patients with gastric cancer following operation, is persistent in spite of the administration of large amounts of protein adequate to result in significant increase of body tissue protein.

CASE MATERIAL AND METHODS

GENERAL PLAN OF STUDY

Patients who underwent partial gastrectomies for benign gastric ulcers and patients undergoing similar operations or exploratory laparotomies for cancer of the stomach were given high protein, high caloric feedings as soon as possible following surgery. Nitrogen balances were recorded for from 7 to 108 days and potassium, calcium, sodium and phosphorus balances were studied as well. At regular intervals, plasma volumes, plasma protein concentrations and electrophoretic plasma protein fractions were determined. It was thus possible to evaluate nitrogen retention, body tissue repletion and plasma protein regeneration, to compare the changes occurring in patients with benign gastric lesions to those observed in patients with gastric cancer and to evaluate the utilization and distribution of nitrogen in both groups.

CASE MATERIAL

(Detailed case histories are given in the Appendix.) The initial plasma protein values of all patients are recorded in table 1.

Patients with Gastric Cancer

Three patients had cancer of the stomach which was operable, and underwent partial gastrectomy (cases 4, 5, and 6). These were 1 female, and 2 males, aged 60, 46, and 50 respectively.

Seven patients had inoperable cancer of the stomach. Six of these underwent exploratory laparotomy...
<table>
<thead>
<tr>
<th>Case no.</th>
<th>Days</th>
<th>Weight, Kg.</th>
<th>Plasma protein Gm./100 ml.</th>
<th>Plasma volume ml.</th>
<th>Total circulating protein Gm./day</th>
<th>Nitrogen intake Gm./day/ Kg.</th>
<th>Nitrogen output Gm./day/ Kg.</th>
<th>Nitrogen retained Gm./day/ Kg.</th>
<th>Intake %</th>
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<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>End</td>
<td>Average</td>
<td>Initial</td>
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<td>Inoperable cancers—long-term studies</td>
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</tr>
</tbody>
</table>

* Length of study, days.
† Beginning of study, days after operation.
‡ Nitrogen balance for 10 days only, plasma protein change in 14 days.
STUDIES ON HYPOPROTEINEMIA. I

(cases 7, 8, 9, 10, 11 and 13). These were two females and four males, aged 69, 47, 52, 49, 70, and 64, respectively.

One patient (case 12) was found to have a resectable cancer of the stomach which was removed, but firm, large lymph nodes were felt in the portal region and in the omentum and were not removed. This man was 65 years old.

Control Subjects

Three patients with benign gastric ulcers were studied (cases 1, 2, and 3). These were three males, aged 54, 45, and 53. This control group was kept small because previous work by Co Tui et al.8 had clearly shown that patients with gastrectomy for ulcers on a high nitrogen intake regenerate plasma protein within two weeks following operation and our findings confirmed this observation.

<table>
<thead>
<tr>
<th>Time</th>
<th>Hydrolysate per feeding</th>
<th>Frequency of feeding</th>
<th>Water to be added</th>
<th>Remarks</th>
<th>Parenteral 9% dextrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of op.</td>
<td>cc.</td>
<td>hr.</td>
<td></td>
<td>Alternate as required</td>
<td>cc.</td>
</tr>
<tr>
<td>6 hrs. p.o.</td>
<td>—</td>
<td>—</td>
<td>30 cc. q 1 hr.</td>
<td>Same</td>
<td>1500</td>
</tr>
<tr>
<td>11 hrs. p.o.</td>
<td>30</td>
<td>q 2</td>
<td>30 cc. q 1 hr.</td>
<td>Same</td>
<td>1500</td>
</tr>
<tr>
<td>First day</td>
<td>Same</td>
<td>Same</td>
<td></td>
<td>To rinse tube</td>
<td>1500</td>
</tr>
<tr>
<td>Second day</td>
<td>Same</td>
<td>Same</td>
<td></td>
<td>To rinse tube</td>
<td>1500</td>
</tr>
<tr>
<td>Third day</td>
<td>30</td>
<td>q 1</td>
<td>30 cc. q 1 hr.</td>
<td>After hydrolysate</td>
<td>1000</td>
</tr>
<tr>
<td>Fourth day</td>
<td>60</td>
<td>q 2</td>
<td>75 cc. q 2 hrs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fifth day</td>
<td>60</td>
<td>q 2</td>
<td>45 cc. q 2 hrs.; 50 cc. boiled milk added.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sixth and seventh day as above. Reduce parenteral fluid according to patient's ability to swallow small amounts of water by mouth. Remove stomach tube on eighth day and start patient on routine seventh day gastrectomy diet.

Methods

1. Alimentation: Some of the patients had orojejunal feeding tubes inserted at operation and left in situ for as long as seven days postoperatively. Some had external jejunostomy tubes for feeding purposes. Unless otherwise specified, casein hydrolysate "Squibb" was used as a source of nitrogen in all cases. In general, the plan included the administration of 0.6 Gm. of nitrogen per day per Kg. of body weight in a mixture of the hydrolysate in a 10 per cent dextrose solution with 60 Gm. of "Amphojel." This feeding mixture was administered by the jejunal tube and/or by mouth and the total daily volume was adjusted to 750 ml. A feeding schedule given in table 2 was followed as closely as possible. After the first postoperative period this regimen was supplemented by the usual gastrectomy hospital diet in amounts measured in the metabolic kitchen and analyzed in the laboratory for nitrogen content. The caloric content of the total diet, including parenteral alimentation, was maintained at a level of approximately 1800 calories per day (except on the first, and sometimes, the second postoperative day when it was lower).

* The hydrolysate was provided by the courtesy of the Squibb Co.
Plasma and blood transfusions were given in all cases on the day of operation and thereafter as sparingly as possible to avoid interference with the observations on protein regeneration. Parenteral fluid intake was standardized as closely as possible, 1000 ml. of physiologic saline solution and 300 ml. of dextrose in water on the second and only rarely on the third postoperative day. All parenteral intake, as well as other alimentation, was carefully measured and recorded. The patients received a daily intramuscular injection of a vitamin B complex preparation* throughout the duration of the metabolic study. Other medication was given as indicated. The patients usually were allowed up on the second or third postoperative day, but this was not standardized. The 2 patients on whom long-term metabolic studies were carried out for 2.6 and 108 days were placed on a constant basic diet which was the same every day.

In addition, to maintain the desired high nitrogen content, these patients received part of their nitrogen intake in the form of protein hydrolysate (Casein Hydrolysate, "Squibb") and in the form of native protein (milk protein as "Delcos," Sharp and Dohme, and "Lactalbumin Squibb" in unhydrolyzed form).

2. Collection of specimens: Urines were collected in 24-hour specimens, preserved at pH 3 with acetic acid, and kept in the refrigerator without preservative. Vomitus and gastric aspiration fluid were collected in 4-hour samples and kept in the refrigerator without preservative.

3. Methods of Analysis:

Urine: Urinary nitrogen was measured by a micro-Kjeldahl method. Potassium and sodium were measured by flame photometry; phosphorus was determined by Fiske and Subbarow's method, and calcium by the method of Schohl and Pedley. Creatinine determinations were used to evaluate the accuracy of the collections.

Stools: A commercial homogenizer was used for the thorough mixing of stools which were then made up to a standard volume by the addition of distilled water. Nitrogen was measured by a micro-Kjeldahl method, and minerals were determined in dry ashed aliquots by the same methods used in the urine.

Blood: Plasma protein was measured by a micro-Kjeldahl method and corrected for nonprotein nitrogen. The plasma protein components were estimated by electrophoresis by Dr. M. L. Petermann. Plasma volumes were measured by the use of Evans' blue.

RESULTS

Body Tissue Repletion: Table 1.

Repletion within one month after operation: In only 2 of the 3 ulcer cases studied were nitrogen balance studies done. The third case is included because, while nitrogen output was not measured, the nitrogen intake was known and was at least as high as in the two others. As previously shown by Co Tui et al. and by Reigel, positive nitrogen balance was obtained in both cases; the usual postoperative nitrogen loss, therefore, was offset by adequate nitrogen utilization. This was achieved on intakes of 0.26 and 0.49 Gm. of nitrogen per Kg. per day, or considerably less than had been planned originally. All patients with gastric cancer were in nitrogen balance or had positive nitrogen balance 7 to 20 days following operation. There was essentially no difference between those having undergone exploratory laparotomy and the one case with gastric resection in which nitrogen balance studies had been done (case 4). The least marked nitrogen retention actually occurred in the latter case. The nitrogen intake in the cases with cancer ranged from 0.2 Gm. per Kg. per day to 0.81 Gm. per Kg. per day, with an average of 0.43 Gm. per Kg.

* Beta Symplex was used (Winthrop) which has the following composition: thiamin, 10 mg.; riboflavin, 5 mg.; calcium pentothenate, 5 mg.; niacinamide, 50 mg.

† A patient is considered to be in nitrogen balance when the loss of nitrogen exceeds the intake by less than 0.01 Gm. per Kg. per day.
per day. An average of 26 per cent of the ingested nitrogen was retained as compared to 12 per cent (31 and −6 per cent) in the ulcer group.

Repletion more than one month after operation: Studies of nitrogen and mineral balances were made in 2 cases of gastric cancer following exploratory laparotomy (case 12) and following palliative gastrectomy (case 13) during periods of 26 and 108 days and starting 12 and 11 days after operation. These showed marked nitrogen retention: 402 Gm. or 0.065 Gm. per Kg. per day for 108 days, equal to 13 per cent of the intake; and, 264 Gm. or 0.15 Gm. per Kg. per day or 34 per cent of the intake.

**Table 3.**—Comparison between Theoretic and Actual Nitrogen Intake and Changes of Circulating Protein

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Type case</th>
<th>Theoretic nitrogen requirement</th>
<th>Nitrogen actually received</th>
<th>Protein, observed change</th>
<th>Protein, calculated change</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ulcer</td>
<td>313</td>
<td>158</td>
<td>+9.3</td>
<td>−1.1</td>
<td>+11.4</td>
</tr>
<tr>
<td>2</td>
<td>Ulcer</td>
<td>395</td>
<td>285</td>
<td>+9.1</td>
<td>+12.7</td>
<td>+36.1</td>
</tr>
<tr>
<td>3</td>
<td>Ulcer</td>
<td>421</td>
<td>—</td>
<td>+71.7</td>
<td>—</td>
<td>—</td>
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<td>4</td>
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<td>—</td>
<td>+13.0</td>
<td>−4.3</td>
<td>−8.7</td>
</tr>
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<td>Operable cancer</td>
<td>488</td>
<td>—</td>
<td>—</td>
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<td>—</td>
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<td>6</td>
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<td>473</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
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<td>7</td>
<td>Inop. cancer</td>
<td>473</td>
<td>133</td>
<td>+13.6</td>
<td>+41.0</td>
<td>+54.6</td>
</tr>
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<td>180</td>
<td>−10.3</td>
<td>+15.4</td>
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<td>−17.6</td>
<td>+4.4</td>
<td>−13.2</td>
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<td>192</td>
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<td>214</td>
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<td>−15.1</td>
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<td>3017</td>
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<td>+83.0</td>
<td>−93.0</td>
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<td>564</td>
<td>770</td>
<td>−7.1</td>
<td>+55.0</td>
<td>−62.1</td>
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</table>

* "Theoretic Nitrogen Intake" means the amounts of nitrogen required for correction of the plasma albumin deficit. (Assumed normal albumin 4.6 Gm./100 ml. All calculations are based on values obtained by the Howe method because this method was the one used in evaluating the proportion of albumin to the remaining body protein; ref. Elman, R.: Protein deficiency in surgical patients and its correction. J. Am. Dietet. A. 18: 141-144, 1944.) The total calculated nitrogen requirement includes 4 Gm. for daily maintenance during the period of study, the tissue protein loss calculated from the albumin lost and assumes a loss of 50 per cent of the ingested nitrogen (above the maintenance requirement of 4 Gm. per day).

† The calculated change of plasma protein is based on the amounts of nitrogen retained or lost, assuming that plasma protein represents one thirtieth of the total body protein.

in 26 days. There was concomitant retention of phosphorus and potassium in the proportions in which these minerals are known to exist in protoplasm. In these two instances, the ability of these patients to build body tissue is thus well demonstrated.

**Plasma Protein Regeneration:** Table 3.

Regeneration within one month after operation: In all patients with gastrectomy for benign ulcers, an increase in circulating plasma protein occurred promptly. The extent of this increase varied widely in these 3 patients and was predominantly in
the globulin fraction in one. The increase of the circulating plasma protein was of
the same order of magnitude as that observed by Co Tui under similar conditions
and not to be ascribed to changes of plasma volume alone (table 1). In all patients
with gastric cancer except two (case 10 and case 7), there was a decrease of circu-
lating plasma protein during the period of study. In case 10, the increase observed
follows a rise of the plasma volume more marked than in most of the other cases
and thus may be only illusory. In case 7, there was an actual increase, entirely
caus ed by a rise of plasma globulin.

Regeneration more than one month after operation. The changes of circulating plasma
protein in these two cases following 16 and 108 days of postoperative high protein
feeding were insignificant and probably within the range of technical errors.

Comparison of Theoretic and Actual Plasma Protein Increases: Table 4.

Studies by Weech'6 in dogs showed that the plasma albumin represents 0.6 of
the body protein and by transferring this assumption to man, one can estimate the
amounts of circulating albumin which theoretically should be formed from a given
amount of retained food protein. Applying these relationships, Elman'7 has de-
vised a calculation to evaluate the nitrogen need of a depleted individual from his
plasma albumin concentration. The further assumption may be made that albumin
represents most of the plasma proteins lost in protein depletion and that thus, the
total protein may be substituted for albumin in such cases. These rough theoretic
figures demonstrate that on the whole the discrepancy between the actual and the

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**Table 4.** Changes in Globulin and Albumin as Determined by Electrophoresis and Plasma Volume Measurement. (Initial Values at Beginning of Study. Final Value at End of Period—Stated in Last Column)

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Type case</th>
<th>Change of plasma volume</th>
<th>Albumin</th>
<th>Globalin</th>
<th>Days</th>
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</thead>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>Initial</td>
</tr>
<tr>
<td>1</td>
<td>Benign ulcer</td>
<td>-11.5</td>
<td>80.0</td>
<td>81.5</td>
<td>+2.0</td>
</tr>
<tr>
<td>2</td>
<td>Benign ulcer</td>
<td>-13.0</td>
<td>69.5</td>
<td>78.9</td>
<td>+13.5</td>
</tr>
<tr>
<td>3</td>
<td>Benign ulcer</td>
<td>16.2</td>
<td>46.4</td>
<td>40.0</td>
<td>-15.3</td>
</tr>
<tr>
<td>4</td>
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<td>-1.4</td>
<td>57.2</td>
<td>43.6</td>
<td>-13.8</td>
</tr>
<tr>
<td>5</td>
<td>Operable cancer</td>
<td>-15.5</td>
<td>74.7</td>
<td>57.5</td>
<td>-13.0</td>
</tr>
<tr>
<td>6</td>
<td>Operable cancer</td>
<td>-17.6</td>
<td>106.0</td>
<td>91.9</td>
<td>-13.3</td>
</tr>
<tr>
<td>7</td>
<td>Inoperable cancer</td>
<td>-2.7</td>
<td>70.2</td>
<td>64.5</td>
<td>-8.1</td>
</tr>
<tr>
<td>8</td>
<td>Inoperable cancer</td>
<td>12.7</td>
<td>*</td>
<td>*</td>
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</tr>
<tr>
<td>9</td>
<td>Inoperable cancer</td>
<td>+12.7</td>
<td>53.3</td>
<td>37.4</td>
<td>-15.4</td>
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<td>10</td>
<td>Inoperable cancer</td>
<td>+14.6</td>
<td>86.5</td>
<td>101.8</td>
<td>+17.7</td>
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<tr>
<td>11</td>
<td>Inoperable cancer</td>
<td>0</td>
<td>83.1</td>
<td>65.2</td>
<td>-18.7</td>
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<td>+11.0</td>
<td>81.9</td>
<td>90.8</td>
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<td>Inoperable cancer</td>
<td>-18.4</td>
<td>112.5</td>
<td>119.0</td>
<td>-2.85</td>
</tr>
</tbody>
</table>

* Only total protein was determined.
† Refers to total circulating fractions.
calculated figures is much wider in the group of cancer patients than in the two ulcer cases and that it becomes extreme in the long-term studies.

**DISCUSSION**

Hypoproteinemia continues in gastric cancer patients after operation in spite of adequate body tissue repletion.

Causes of hypoproteinemia are: (1) inadequate formation; (2) increased utilization or destruction; or (3) abnormal distribution of circulating proteins. Inadequate formation may be due to (a) insufficient protein intake, (b) excessive nitrogen loss, or (c) specific defect in serum protein synthesis. In patients with gastric cancer who show hypoproteinemia before operation, insufficient intake and excessive loss of nitrogen have been eliminated by earlier studies. The present investigation supplies evidence that inadequate intake and excessive loss of protein are not responsible for the persistence of the hypoproteinemia in gastric cancer patients after operation.

One concludes that either inadequate fabrication or distribution is responsible for hypoproteinemia in gastric cancer. The defect is probably nonspecific, as similar observations have been made in patients with tuberculosis. It may be related to the gastro-intestinal tract, to the liver, or to the adrenal cortex.

Further studies are in progress to determine if the hypoproteinemia is due to decreased synthesis, to increased utilization or destruction, or to abnormal distribution of proteins.

**APPENDIX**

*Summaries of Clinical Histories of the Patients Studied*

**CASE 1**

**History:** Anorexia for 2 years. Pain in midepigastrium for 4 months before admission. 13 lbs. weight loss in 2 years. No vomiting, no tarry stools.
**Physical examination:** Tenderness in epigastrium on deep pressure; no other findings.
**X-ray examination:** Gastric ulcer, lesser curvature.
**Laboratory data:** Hemoglobin 82%, RBC 4,800,000. WBC 6,100; normal differential count. Urine negative. Serum chlorides 95-105 meq./l. Serum bilirubin 1.0-1.4 mg./100 ml. Blood urea nitrogen 11.2-30.4 mg./100 ml.
**Gastric analysis:** Free HCl 0, 0, 22, 14, 15.
**Total HCl** 12, 18, 35, 36, 30.
**Operation:** Partial gastrectomy 6-24-46.
**Pathology:** Chronic peptic ulcer.
**Course:** Uneventful postoperative recovery. Discharged 15 days postoperatively; asymptomatic since.

**CASE 2**

**History:** Preprandial pain 7 years ago, successfully treated by dietary measures. Recurrence one year ago, unrelieved by diet. In the 4 months before admission, frequent vomiting. Only 4-5 lbs. weight loss.

* Data included in the paper are not repeated in the appendix.
† First samples before 0.5 mg. of histamine, following samples every 15 minutes thereafter. Acid in ml. of N/10 NaOH.
Physical examination: Negative.

X-ray examination: Duodenal ulcer.

Laboratory data: Hemoglobin 89-103%, RBC 4,100,000-4,600,000, WBC 4,000-8,300; normal differential count. Urine negative. Serum chlorides 94-102 meq./l. Serum bilirubin 1.1 mg./100 ml. Fasting blood sugar 89 mg./100 ml. Blood urea nitrogen 16.3-26.4 mg./100 ml.

Gastric analysis: Free HCl 35, 40, 60, 55, 50
Total HCl 44, 48, 64, 66, 60.

Operation: Partial gastrectomy, 5-21-46.

Pathology: Gastric ulcer, scars in duodenum, fibrous adhesions.


CASE 3

(F. H. 81072-17) white male of 53 years. Admitted 6-15-46; discharged 7-17-46.
History: From 18 months to 1 year before admission pain after eating. Weight loss in that period 25 lbs. Vomiting for about 4 weeks.
Physical examination: Negative.
X-ray examination: Crater of 1 inch in lesser curvature, probably benign ulcer.
Laboratory data: Hemoglobin 81%, RBC 3,700,000-4,500,000. WBC 5,000-15,000. Urine negative.
Serum chlorides 96-102 meq./l. Serum bilirubin 0.7-1.3 mg./100 ml.
Fasting blood sugar 87 mg./100 ml.
Blood urea nitrogen 11.9-20.4 mg./100 ml.
Gastric analysis: Free HCl 32, 38, 35, 35.
Total HCl 28, 30, 32, 34, 36.
Operation: Partial gastrectomy, 7-1-46.
Pathology: Chronic peptic ulcer (gastric).
Course: Patchy pulmonary infiltration on eighth postoperative day with moderate elevation of temperature. Responded well to penicillin. Asymptomatic since then.

CASE 4

History: Abdominal pain of 3 months' duration and weight loss of 30 lbs. in 4 months before admission.
X-ray examination: Advanced gastric carcinoma of the body of the stomach and the pyloric region.
Laboratory data: Hemoglobin 63-88%, RBC 3,800,000-4,200,000. WBC 4,400-16,800.
Serum chlorides 93-106 meq./l. Serum bilirubin 0.6-1.1 mg./100 ml. Fasting blood sugar 87 mg./100 ml.
Blood urea nitrogen 11.9-20 mg./100 ml.
Gastric analysis: Free HCl = 0.
Total HCl 5, 4, 4, 6, 6.
Operation: Subtotal gastrectomy (4/3), Hoffmeister anastomosis 7-1-46. No liver metastasis or peritoneal implants found.
Pathology: Diffuse gelatinous adenocarcinoma, extension to the fat about nodes. Lymph nodes proper were clear.
Course: Uneventful recovery. Patient has left town; no follow-up recorded.

CASE 5

History: 3 months' persistent epigastric pain following fall from horse. Lost 60 lbs. in 4 months and noticed progressive weakness.
Physical examination: Essentially negative.
X-ray examination: No gastro-intestinal examination.
Laboratory data: Hemoglobin 64-86%, RBC normal. WBC 9,000-15,000, normal differential count.
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Urine negative, except for occasional i+ albumin. Serum chlorides, 97–103 meq./l. Serum bilirubin 0.6-4.8 mg./100 ml. Serum cholesterol: total 141, free 52., esters 89 mg./100 ml. Fasting blood sugar 99 mg./100 ml.

**Gastric analysis:** Free HCl = o. Total HCl 26, 10, 7, 10, 15.

**Operation:** No metastasis seen in liver, lymph nodes or peritoneum. A large tumor involving the greater gastric curvature and extending into the transverse colon and the omentum was found. Subtotal gastrectomy and resection of the medial portion of the transverse colon and a large portion of the omentum was performed. A Mikulicz colostomy was done (7-19-46). On 8-8-46, patient developed acute intestinal obstruction and a number of fibrous adhesions were dissected at an emergency laparotomy. The patient recovered and was discharged. On 10-4-46, colostomy was closed.

**Pathology:** Adenocarcinoma, Grade III, invading entire thickness of gastric wall and extending into serosa of colon.

**Course:** Patient now in good health.

CASE 6

(M. S. 8116-33) white male of 50 years. Admitted 6-30-46; discharged 7-12-46.

**History:** Midepigastic pain for 7 months, with 11 lbs. weight loss.

**Physical examination:** Negative.

**X-ray examination:** Carcinoma of lesser curvature, near cardia.

**Laboratory data:** Hemoglobin, 48-87%, RBC 2,300,000-3,000,000. WBC 3,700-9,600; normal differential count. Urine negative. Serum chlorides 98-108 meq./l. Blood urea nitrogen 11.1-36.8 mg./100 ml.

**Gastric analysis:** Free HCl 10, 25, 30, 55, 60. Total HCl 20, 40, 38, 75, 80.

**Operation:** No metastasis seen in liver, lymph nodes or peritoneum. Subtotal gastrectomy.

**Pathology:** Adenocarcinoma of stomach.

**Course:** Uneventful recovery.

CASE 7

(B. J. 80928-8) white male of 69 years. Admitted 3-21-46; discharged 4-8-46.

**History:** Weight loss of 6 lbs. in 3 months and loss of appetite.

**Physical examination:** Negative.

**X-ray examination:** Large mass in pars media of stomach.

**Laboratory data:** Hemoglobin 75-85%, RBC 3,700,000-4,600,000. WBC 6,100-10,200. Normal differential count. Urine negative. Serum chlorides 100-108 meq./l. Serum bilirubin 0.7 mg./10 ml. Serum cholesterol: total 197, free 61, esters 136 mg./100 ml. Fasting blood sugar 88 mg./100 ml. Blood urea nitrogen 13.4-13.2 mg./100 ml.

**Gastric analysis:** Free HCl 0, 0, qns,* qns, 0. Total HCl 24, 7, qns, qns, 8.

* Insufficient quantity.

**Operation:** Laparotomy 3-28-46. A large mass was found involving the stomach, extending along both curvatures. Numerous metastatic nodules in liver, gall bladder, and nodes along aorta. Inoperable case.

**Pathology:** Metastatic adenocarcinoma.

**Course:** Complicated by hypoproteinemia (hypochloremia and edema). Patient was discharged, no follow-up notes.

CASE 8

(G. Y. 80364-96) white male of 47 years. Admitted 1-17-46; discharged 1-27-46.

**History:** Past history of glycosuria. Negative urine at time of admission. Weight loss of 60 lbs. in 18 months. Epigastric fullness and anorexia for 12 months.
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Physical examination: Evidence of weight loss, large abdominal mass.

X-ray examination: Large mass in region of cardia and larger curvature.

Laboratory data: Hemoglobin 58-95%, RBC 3,000,000-4,600,000. WBC 5,000-9,400. Normal urine. Serum chlorides 101-105 meq./l. Serum bilirubin 0.5-0.8 mg./100 ml. Serum cholesterol: total 121-230, free 42-71, esters 79-179 mg./100 ml. Blood urea nitrogen 12.0-28.4 mg./100 ml.

Gastric analysis: Free HCl = 0.

Total HCl 10, 10, 12, 8, 10.

Operation: Laparotomy 1-5-46. Large tumor mass, involving gastric cardia and greater portion of fundus, as well as mesentery, spleen, pancreas, and lymph nodes. Inoperable. External jejunostomy.

Pathology: No biopsy material taken.

Course: Patient died 3-26-46. No necropsy.

CASE 9

(B. L. 89091-6) white female of 52 years. Admitted 3-19-46; discharged 4-9-46.

History: Dull abdominal pain for 4 months, small weight loss.

Physical examination: Negative.

X-ray examination: Polypoid infiltrating cancer of distal segment of stomach.

Laboratory data: Hemoglobin 65-81%, RBC 3,103,000-3,500,000. WBC 7,200-7,600, normal differential count. Urine negative. Serum chlorides 91-103 meq./l. Serum bilirubin 0.7 mg./100 ml. Fasting blood sugar 91-103 mg./100 ml. Blood urea nitrogen 8.5-10. No gastric analysis reported.

Operation: Laparotomy and external jejunostomy 3-26-46. Large mass involving stomach, extension into lesser and greater omenta, multiple metastases in liver (biopsy material taken).

Pathology: Metastatic adenocarcinoma.

Course: No follow-up notes.

CASE 10

(S. S. 8172.6) white male of 49 years. Admitted 5-2-46; discharged 6-2-46.

History: Weakness of 3 months’ duration and postprandial epigastric pain and tarry stools of one month duration. No evidence of weight loss.

Physical examination: Abdominal mass 8 cm. in diameter.

X-ray examination: Carcinoma of antrum of stomach.

Laboratory data: Hemoglobin 51-81%, RBC 3,500,000-3,800,000. WBC 7,200-7,600, normal differential count. Urine negative. Serum chlorides 95-103 meq./l. Serum bilirubin 0.6 mg./100 ml. Fasting blood sugar 91-103 mg./100 ml. Blood urea nitrogen 8.5-10. No gastric analysis reported.

Operation: Laparotomy and exclusion gastroenterostomy, 6-7-46. Large tumor of gastric antrum adherent to pancreas, and meso-sigmoid and colic vessels. Numerous metastases in liver. Firm lymph nodes.

Pathology: None reported.

Course: No follow-up notes.

CASE 11

(G. G. 81240-21) white female of 70 years. Admitted 6-2-46; discharged 7-20-46.

History: Nocturia due to cystocele. Marked weight loss (70 lbs.) in 5 months before admission. Anorexia and "heart burn" for one year prior to admission. Negative gastro-intestinal x-ray examination some months before admission.

Physical examination: Mass of 10 cm. diameter in mid-abdomen.

X-ray examination: Gastric carcinoma.

Laboratory data: Hemoglobin 61-94%, RBC 2,500,000-3,800,000. WBC 5,300-14,000, normal differential count. Serum chlorides 95-104 meq./l. Serum bilirubin 0.6 mg./100 ml. Serum cholesterol: total 141, free 52, esters 89 mg./100 ml.

Gastric analysis: Free HCl = 0.

Total HCl 15, 8, 10, 12, 12.

Operation: Laparotomy and exclusion gastroenterostomy, 6-7-46. Large tumor of gastric antrum adherent to pancreas, and meso-sigmoid and colic vessels. Numerous metastases in liver. Firm lymph nodes.

Pathology: None reported.

Course: No follow-up notes.
Operation: Laparotomy, 6-28-46. Extensive carcinoma with metastasis to nodes and liver.
Pathology: Adenocarcinoma, Grade III.
Course: Convalescence complicated by bronchial pneumonia.

CASE 12
History: Weight loss during one year preceding operation of about 30 lbs. Several bouts of dark black stools and rectal bleeding.
Physical examination: Negative.
X-ray examination: Filling defect involving almost the entire pyloric portion.
Laboratory data: Hemoglobin 8.4-54%, RBC 1,190,000-5,000,000. WBC 4,700-8,800, normal differential count. Urines negative. Serum chlorides 92.-104 meq./l. Serum bilirubin 0.62. mg./100 ml. Thymol turbidity 1.8 ml. Cephalin flocculation 24 hours, negative. Hippuric acid excretion 1.5 Gm. Bromsulfalein retained in blood, 30 minutes, 5%; 45 minutes, 2%. Serum cholesterol: total 104, free 36, esters 68 mg./100 ml. Blood urea nitrogen 16.2-34 mg./100 ml.
Gastric analysis: Free HCl = 0.
Total HCl 20, 28, 30, 34.
Operation: On 11-28-46, a large bulky lesion was found in the greater curvature of the stomach, a few nodes were palpated in the gastro-hepatic ligament. The tumor was removed, and a gastro-jejunostomy was done. Liver and peritoneum free of metastases.
Pathology: Gelatinous adenocarcinoma, Grade III, extensive lymphatic permeation, metastases to nodes.
Course: Essentially uneventful postoperative course. This study was continued up to the 205th postoperative day.18b. The patient died of carcinomatosis 66 weeks after operation. Reviews of additional articles bearing on this subject, which have appeared since this paper was submitted, are noted in the references.18a,b

CASE 13
(S. J. 109337-4) White male of 64 years. Admitted 8-28-46; discharged 10-14-46.
History: Weight loss of 40 lbs. in 4 months before admission. Hematemesis one month before admission, epigastric fullness.
Physical examination: Mass in epigastrium.
X-ray examination: Polypoid carcinoma of stomach (fundus and body).
Laboratory data: Hemoglobin 46-76%, RBC 2,100,000-3,400,000; Hematocrit 18-37%. WBC 4,500-10,600, normal differential count. Normal urine. Serum chlorides 108 meq./l. Serum bilirubin 1.1 mg./100 ml. Fasting blood sugar 107 mg./100 ml. Blood urea nitrogen 15.9 mg./100 ml.
Gastric analysis: Free HCl = 0.
Total HCl 14, 14, 14, 10.
Operation: 9-9-46. Large tumor from cardia through antrum among lesser curvature. Liver studded with metastases. Exploratory laparotomy, biopsy from liver metastases.
Pathology: Gelatinous adenocarcinoma.
Course: Died Dec. 1946.

Summary and Conclusions
1. The existence of hypoproteinemia in patients with gastric cancer has once again been observed.
2. The intractability of this type of hypoproteinemia in the postoperative phase to treatment with high protein diets and in the presence of positive nitrogen balance has been demonstrated.
3. Long-term studies in two patients, for 28 and 108 days respectively, suggest that the persistence of hypoproteinemia in patients with gastric cancer in positive
nitrogen balance is probably not due to a marked degree of depletion of tissue protein stores alone. These patients retained more protein than would have been necessary to replenish depleted tissues.

4. It seems more likely that while such patients are capable of tissue protein synthesis, they fail to shift new protein into the blood stream.

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