
THE SIGNIFICANCE OF CEVITAMIC ACID DEFICIENCY IN SURGICAL PATIENTS

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THE motive which led to the study of the problem to be presented was created over a period of years of close observation of postoperative complications. It must be apparent to every surgeon that frequently serious postoperative complications occur which demand some sort of explanation and perhaps prevention. Of these, non-healing of wounds as expressed by evisceration, postoperative hernia, or incomplete disruption of a wound, peritonitis from a leaking suture line, and non-union of fractures take a ranking position. Secondarily one may also allude to hemorrhage, wound infection, disturbances in function, such as delayed gastro-intestinal motility, loss of appetite with increasing weakness and prostration, nausea and vomiting, respiratory infections, and the like.

In a communication during 1935 attention was called to the nutritional status of the surgical patient and two elements of malnutrition were stressed, namely, protein deficiency and avitaminosis. An interexchange of ideas with Graham, of London, finally focused our attention on cevitic acid deficiency.

Scurvy is a disease which has been recognized for many centuries, although until quite recently its nature was a mystery. Hippocrates described it quite accurately. It is interesting to read an account of the ravages of scurvy in Lord Anson's fleet during a voyage around the world in 1740-44 as described by Richard Walter, chaplain on board the "Centurion" published in London in 1750. In writing of the disease he states:

"This disease is likewise attended with a strange dejection of the spirits, and with shiverings, tremblings and with a disposition to be seized with the

most dreadful terrors on the slightest accident. Indeed, it was most remarkable, in all our reiterated experience of this malady that whatever discouraged our people, or at any time damped their hopes, never failed to add vigor to the distemper; for it usually killed those who were in the last stages of it, and confined those to their hammocks who were before capable of some kind of duty; so that it seemed as if alacrity of mind and sanguine thoughts were not contemptible preservations from its fatal malignity. It often produced putrid fevers, pleurisy, the jaundice, and violent rheumatic pains, and sometimes it occasioned an obstinate costiveness, which was generally attended by a difficulty of breathing; and this was esteemed the most deadly of all scorbutic symptoms; at other times, the whole body, and more especially the legs, were subject to ulcers of the worse kind attended with rotten bones, and such a luxuriance of fungous flesh as yielded to no remedy. But a most extraordinary circumstance, and what would scarcely be credible upon a single evidence, is that the scars of wounds which had been for many years healed, were forced open again by this virulent distemper. Of this there was a remarkable instance of one of the invalids on board the 'Centurion' who had been wounded above fifty years before at the battle of the Boyne for though he was cured soon after, and had continued well for a great number of years past, yet, on being attacked by the scurvy, his wounds, in the progress of the disease, broke out afresh, and appeared as if they had never healed; nay what is still more astonishing, the callus of a broken bone which had been completely formed for a long time, was found to hereby dissolve and the fracture seemed as if it had never been consolidated."

This amazing report opens the door to some well chosen speculation such as the effect of excitation and fear upon cevitic acid metabolism especially as associated with the adrenal glands, also, wound healing. Further reference may be found concerning wound healing as associated with scurvy in the *Medical and Surgical History of the War of the Rebellion* in which in describing the clinical picture of scurvy it is written:

"This was further manifested by the indisposition of wounds to heal, slight scratches becoming converted into indolent ulcers or affected with erysipelas

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or gangrenous inflammation. . . . Doctor Jones refers to the ulcerations induced among the prisoners at Andersonville by slight injuries as the prick of a splinter or the scratching of a mosquito bite."

In the *Nashville Journal of Medicine and Surgery* of 1866 Eve stated:

"It certainly did complicate wounds and seriously interfered with surgical operations and was itself aggravated by erysipelas, syphilis, spurious vaccination. Secondary hemorrhage became more frequent from wounds and operations after the battles of Chickamauga and Missionary Ridge, September and December 1863; attributable justly to the increased scorbutic tendency in the soldiers as the war progressed."

Bizarre manifestations characterize scurvy, many of which are familiar; however, at the present time fully advanced cases are comparatively rare except among the children of the extremely poor. It is the incipient stage or latent scurvy which concerns us at the present time. McLester has stated that in the guinea pig a period of time elapses between the actual exhaustion of the vitamin C reserve and the appearance of scurvy, during which time pathological changes are taking place. He further believes that the same situation obtains in man and that there is constant need of a vitamin C supply because without appearance of actual scurvy, changes similar to those in the guinea pig occur which impair resistance for intercurrent infections. Moreover, different animals respond quite characteristically to vitamin C. Hart, Steenbock, and Smith report that cattle can be reared to maturity on a diet which will produce scurvy in guinea pigs in 4 or 5 weeks, and Hess, in *Scurvy, Past and Present*, states:

"We are confronted with the remarkable and inexplicable phenomenon, a fact concurred in by almost all investigators, that a diet induces either normal nutrition or malnutrition, according to the experimental animal employed. A diet of polished rice or other decorticated grain will lead to the development of scurvy in the guinea pig, to polyneuritis in the pigeon or fowl or according to Holst and Froelich, to a combination of these in the hog. . . . The nutrition of rats, mice, rabbits, hogs, pigeons, and fowls receiving a diet identical with that which regularly occasions scurvy in guinea pigs either progresses normally or a state of malnutrition develops which cannot be identified with scurvy."

It has been demonstrated that man, the monkey, and the guinea pig cannot form vita-

min C and must depend upon extraneous vitamin C for their needs while all other animals can apparently synthesize it. Therefore, it is practically impossible to produce a true vitamin C deficiency in most animals, while in man, the monkey, and the guinea pig, it is relatively common and can be induced by a low intake.

In this communication we wish to consider chiefly the relation or association of cevitamic acid deficiency with wound healing. We have considered the many vagaries of cevitamic acid metabolism, also we are conscious of the many other factors and conditions associated with the sick or injured individual.

Wound healing is effected by many intrinsic and extrinsic factors. Certainly the patient's nutritional status is one of the most important intrinsic factors. Proteins, carbohydrates, fats, water, minerals and vitamins all contribute to nutritional well-being. We immediately recognize, for instance, in many advanced gastrointestinal malignancies, cases in which all of these are partially depleted. Nevertheless, at the present time the preparation of such patients for operation consists only in the administration of fluids, carbohydrates, and salt, and then often in inadequate or poorly balanced amounts. If a transfusion is given, it is usually because of a frank anemia rather than because of a protein depletion. Rarely are any of the vitamins considered in planning the pre-operative regimen. The postoperative care is seldom more complete than the pre-operative in this respect. A wound cannot be expected to heal unless the essential building materials necessary to its repair are present, and we believe that vitamin C is one of these. Therefore the object of this communication is twofold: to increase interest and knowledge of vitamin C in wound healing, and to present a method of saturating the depleted patient and to note some phenomena in the course of saturation.

Although, the history of scurvy and even some evidence of its relation to wounds is very old, the history and work that lead directly to the present recognition of the relation of vitamin C to wound healing is not so old. During the World War Aschoff and Koch noticed constant pathological changes in the

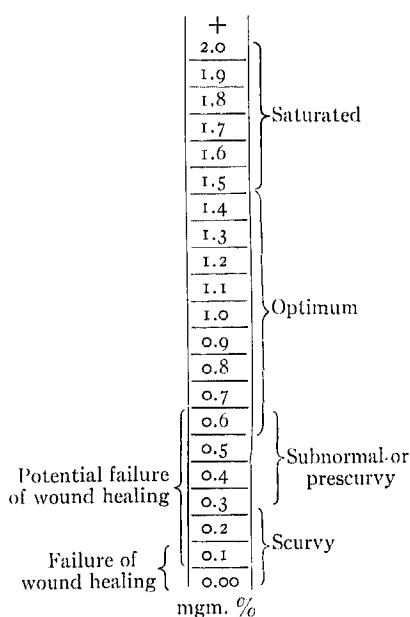


Chart 1. Significance of various blood levels.

| | Mgm. | Mgm. | |
|-----------|-------|-----------|-------|
| 1. W. Z. | -0.77 | 29. E. S. | -1.12 |
| 2. W. | -0.45 | 30. B. I. | -1.38 |
| 3. J. E. | -0.82 | 31. R. M. | -1.03 |
| 4. R. J. | -0.74 | 32. D. M. | -1.60 |
| 5. W. | -0.68 | 33. A. N. | -0.69 |
| 6. H. | -0.48 | 34. R. M. | -2.29 |
| 7. G. L. | -0.56 | 35. J. S. | -0.92 |
| 8. W. S. | -0.43 | 36. R. S. | -0.80 |
| 9. S. B. | -0.96 | 37. F. S. | -0.92 |
| 10. P. S. | -0.56 | 38. E. W. | -1.49 |
| 11. H. C. | -0.82 | 39. L. W. | -1.49 |
| 12. L. R. | -1.68 | 40. E. W. | -1.15 |
| 13. R. D. | -1.04 | 41. F. G. | -0.44 |
| 14. Z. S. | -0.48 | 42. O. A. | -0.60 |
| 15. C. | -0.80 | 43. R. A. | -0.96 |
| 16. S. | -0.22 | 44. P. B. | -1.04 |
| 17. R. Z. | -0.79 | 45. J. B. | -1.16 |
| 18. Y. | -0.62 | 46. W. B. | -0.68 |
| 19. W. M. | -0.74 | 47. C. C. | -0.92 |
| 20. M. | -0.13 | 48. W. C. | -0.64 |
| 21. C. S. | -0.97 | 49. J. C. | -0.44 |
| 22. B. J. | -0.81 | 50. F. C. | -0.28 |
| 23. R. H. | -1.35 | 51. G. D. | -0.88 |
| 24. F. B. | -0.64 | 52. E. G. | -0.60 |
| 25. D. W. | -0.68 | 53. J. G. | -0.88 |
| 26. J. M. | -0.76 | 54. D. F. | -0.60 |
| 27. P. G. | -1.32 | 55. L. F. | -1.24 |
| 28. B. H. | -2.08 | 56. B. L. | -1.29 |

Chart 2. Blood ascorbic acid on a group of students 19-30 yrs. of age.

supporting structures of scurvy victims. Höjer in 1924 duplicated this observation in guinea pigs in which he produced scurvy experimentally. He made the further significant observation that the changes noted were largely due to a collagen deficiency. Wolbach confirmed this observation in experiments upon guinea pigs, in which he controlled the formation of collagen and reticulum around isolated fibroblasts in wounds of animals varying from totally scorbutic to those with a normal vitamin C nutrition. Logically following are the experiments of Jeney and Törö in which they demonstrated a marked increase in collagen fibrils in *in vitro* cultures of fibroblasts following the addition of cevitic acid to the media.

Sir Reginald Payne reporting on the post-mortem findings after partial gastrectomy made the statement that in 12 of 16 patients who had died from peritonitis "the peritoneal infection appeared to have arisen as a bacterial leakage at the site of anastomosis following an almost complete absence of any fibrinous response along the suture line." Archer and Graham on the basis of this report and some work they had done on patients with scurvy reasoned that many patients with gas-

tric or duodenal ulcers were in a "subscurvy" state. Of 20 cases they checked, 90 per cent had definitely low levels and 60 per cent showed blood levels of 0.2 milligrams per cent or less.

Lanman and Ingalls and Taffel and Harvey studied groups of guinea pigs on normal and vitamin C deficient diets. All of the animals were subjected to upper abdominal and gastric incisions with suture and then sacrificed at selective postoperative intervals so that the tensile strength of the wounds might be tested. In all cases after the fifth postoperative day the normal animals showed greater wound strength. Gross examination of the ruptured wounds in the deficient animals showed changes strikingly resembling those found in non-infectious wound disruption in humans. Microscopically there was evidence of fibroblastic proliferation but marked decrease in intracellular material and a disorganized arrangement of the fibroblasts. There was also a consistent failure of the corium to unite in the deficient group.

Smith and McConkey added further similar evidence when they demonstrated that scari-

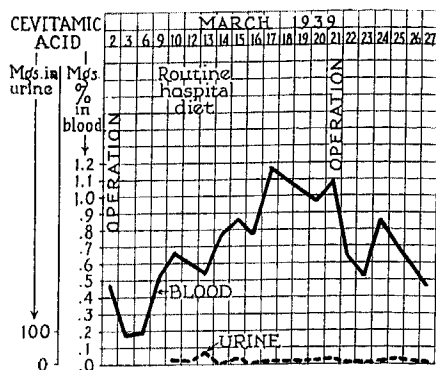


Chart 3. B. V. Male, aged 56 years. Diagnosis: carcinoma of the rectum. Bloody and watery stools for 1½ years and loss of 50 pounds of weight in past 2 years. Home diet balanced but meager. Colostomy on March 2, 1939, and closure of distal loop on March 21, 1939. He was on routine hospital diet while the cevitic acid studies were made.

fied duodenal mucosa failed to heal in vitamin C deficient guinea pigs but healed promptly in the control animals. They also demonstrated a marked tendency to spontaneous formation of peptic ulcers in the deficient animals as compared with an almost negligible tendency in the control animals.

We have checked the blood ascorbic acid levels on numerous patients and have had the opportunity to follow blood, urine, and feces levels on deficient patients who have come to surgery; to saturate these patients, and then to note their wound healing. In all of the



Fig. 1. Mr. C. A., aged 57 years. Gastric resection for perforating type of peptic ulcer. Appearance of wound 1 month after operation.

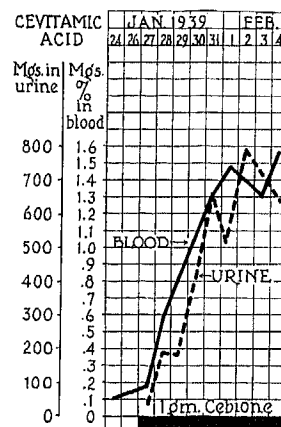


Chart 4. C. A. Male, aged 57 years. Diagnosis: peptic ulcer of the posterior gastric wall. History of pain and distress for 4 months with a weight loss of 35 pounds. Almost daily vomiting for 4 months. Restricted diet and frequent use of bicarbonate of soda to control pain. Gastric resection with anterior Pólya anastomosis on February 22, 1939. The observations and cebione administration were carried on until the patient was discharged but are not indicated in the chart because they were not of special interest. Total amount of vitamin C excreted in the stools on February 4, 1939, was 5.75 milligrams while the blood level was high, 1.575 milligrams per cent and the urinary excretion for the day was 631.35 mgs.

cases to be discussed the blood and urine determinations were made by titration with 2:6 dichlorophenolindophenol, the Farmer-Abt microblood technique being used for the blood determinations.

The usual method of saturation was to give 1 gram of cebione (Merck) daily. This was given intravenously to avoid errors in absorption as might be the case in vomiting, gastric stasis, and the like. The cebione was mixed with one-half gram of soda bicarbonate and diluted with distilled water to a volume of approximately 30 cubic centimeters *just before* administering, in order to reduce irritability in the venous system.

Our impression of the significance of the various blood levels is depicted in Chart 1. The highest figure we have found recorded on a patient with scurvy symptoms was 0.35 milligrams per cent. Therefore, this figure must delimit the scurvy from the subnormal group at least for the present. On the other hand, it is entirely possible for an individual to have a blood level considerably below this figure and not show symptoms of scurvy, the most likely explanation being that a lowered

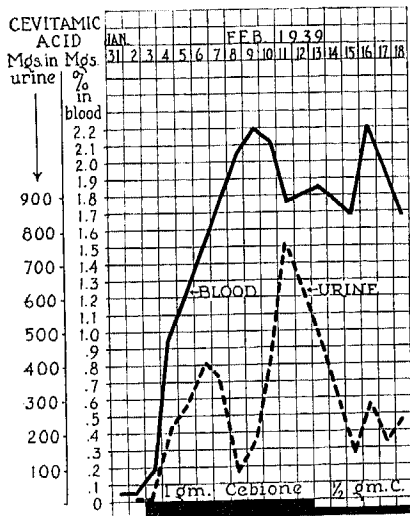


Chart 5. J. R. Male, aged 54 years. Diagnosis: extensive peptic ulcer of the lesser curvature of the stomach. The first ascorbic acid estimation was made 1 month after admittance to the hospital during which time he had extensive alkaline therapy and restricted diet. No operation was performed. He excreted 7.03 milligrams of vitamin C in his stools on February 3, 1939, at which time the blood level was 0.18 milligrams per cent and the urinary excretion for the day was 2.82 milligrams.

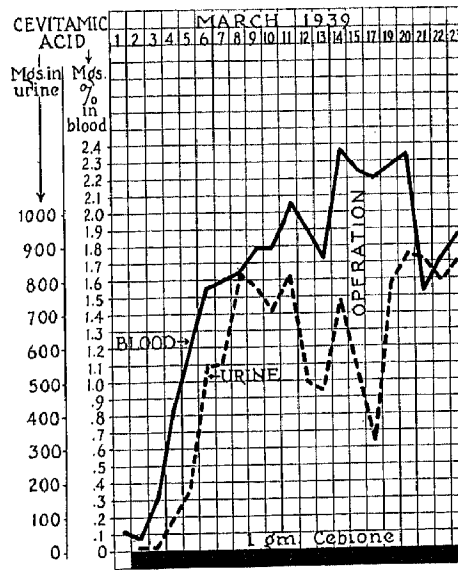


Chart 6. W. H. Male, aged 47 years. Diagnosis: colloid carcinoma of the stomach. History of abdominal discomfort for 1 year with frequent use of bicarbonate of soda. Only occasional vomiting. The patient took an average amount of fruit juice and did not restrict his diet notably. Posterior gastro-enterostomy was performed on March 15, 1939.

blood level is followed at a considerably later period by tissue changes.

This latter fact again is important in attempting to define an optimum level which we indicate as varying from 0.6 to 1.5 milligrams per cent. The optimum and pre-scurvy groups actually overlap more than is indicated. A vitamin C balanced person, who because of an operative procedure or infection utilizing more vitamin C, or who is deprived of a vitamin C intake for several days, may have a low blood level, but will respond quickly to an intake of orange juice or pure cevitamic acid. Conversely, a truly subnormal person given a large dose of cevitamic acid will have a sudden elevation in the blood ascorbic acid level but he cannot maintain this level unless the intake remains high while the tissues are becoming saturated.

Chart 2 illustrates the blood ascorbic acid levels on a group of students from 19 to 30 years of age. In several instances markedly low values are indicated and histories of C deficient diets were obtained. Otherwise, the list is quite representative of any group of

average normal individuals upon fairly balanced diets. The several low values are of note because they illustrate the tendency to eliminate the vitamin C containing foods when under economic stress.

The following case illustrates what may be considered the average cevitamic acid levels of the ordinary surgical case and indicates that a well balanced hospital or home diet will maintain an individual.

B. V., a male clinic patient, 56 years of age, entered Passavant Memorial Hospital with a diagnosis of carcinoma of the rectum. His home diet was not restricted except as was necessarily due to a meagre family budget. His original blood level was 0.4 milligrams per cent (Chart 3) and therefore in the subnormal group as we should expect, but studying the chart we find he responded well to the vitamin C content of the average hospital diet so we feel that he did not have a tissue depletion. His urinary output of vitamin C was very low at all times illustrating that he was using most of his intake to maintain his blood and tissue levels. There is shown the typical postoperative depression in the blood level and urinary output.

Patients with gastric disease in the majority of instances use alkalis and a very restricted

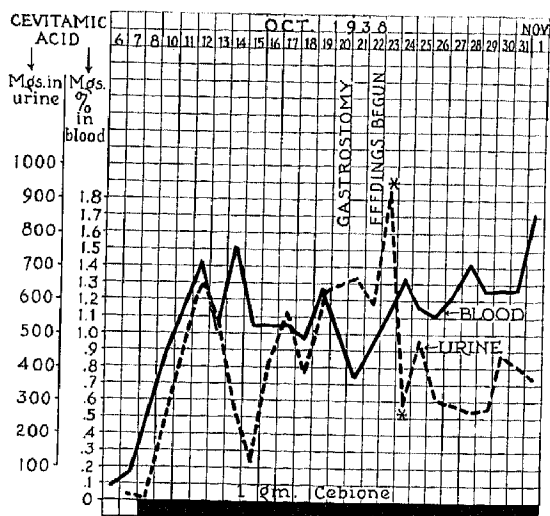


Chart 7. A. S. Male, aged 72 years. Diagnosis: carcinoma of the middle third of the esophagus. History of substernal distress after eating, dysphagia growing progressively worse, and a loss of 40 pounds in 3 months previous to entrance to the hospital. On October 10, 1938, 4.53 milligrams of vitamin C were excreted in the stools and on October 14 only 0.94 milligrams with a blood level of 1.50 milligrams per cent and a urinary excretion of 281.18 milligrams. On the 17th, 18th, and 19th of October the stools contained 1.7, 1.04 and 0.25 milligrams of vitamin C. During this time the blood levels were high and the maximum daily urinary excretion was 626.45 milligrams. Asterisk indicates error in the separation of the specimens of October 23 and 24.

diet, both because they find that they are more comfortable on that regimen and also because the use of alkalies is the basis of most peptic ulcer therapeutics. Therefore, in this type of case the blood ascorbic acid levels are low and there is often present a tissue depletion. The following case reports are illustrative:

C. A., a male clinic patient, 57 years of age, entered Passavant Memorial Hospital with a diagnosis of peptic ulcer. There was a history of epigastric pain and distress for 4 months and a weight loss of 35 pounds. His diet was voluntarily limited to very soft bland foods and he used soda bicarbonate frequently during the day. His first blood ascorbic acid levels were 0.1 and 0.13 milligrams per cent (Chart 4). He was given a gram of cebione intravenously every day and in 3 days the blood level rose to normal and he excreted a large percentage in the urine. He was operated upon because of a suspicion that carcinoma was present and approximately two-thirds of the stomach was resected and an anterior Pólya anastomosis was done. The clips were removed on the fourth postoperative day and his course while in the

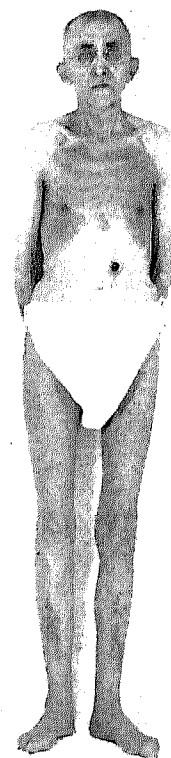


Fig. 2. Mr. A. S., aged 72 years. Gastrostomy for carcinoma of the esophagus. Appearance of patient 5 months after operation. Note the tanning of chest from deep x-ray therapy, appearance of gastrostomy, and emaciation despite gain of 15 pounds in weight since operation.

hospital was quite without event. The wound healed promptly (Fig. 1).

J. R., a male clinic patient, 54 years of age, entered Passavant Memorial Hospital with an extremely large lesser curvature ulcer. When first seen he had a history of having taken, on advice of a friend, a teaspoonful of mustard seeds daily for 2 weeks, as a "cure" for rheumatism. Such violent spasms of epigastric pain ensued that he had to take several teaspoonfuls of soda bicarbonate every 10 to 20 minutes for 10 days previous to admittance to the hospital. His diet had been restricted to milk, much of which he vomited. In the hospital he was placed on a bland diet and continuous Amphojel drip through a gastric Levine tube. One month later the blood ascorbic acid determination was 0.045 milligrams per cent (Chart 5). After a single dose of 1 gram of cebione the blood level rose to a normal—0.9 milligrams per cent—and remained above optimum limits during the remainder of the period of observation. The urinary output on the fourth day after cebione was started was 405 milligrams for the 24 hours. However, the urinary excretion of vitamin C again

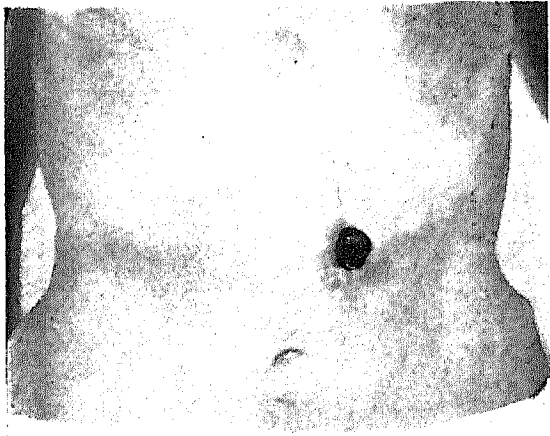


Fig. 3. Close up of wound and gastrostomy shown in Figure 2 to show character of wound healing.

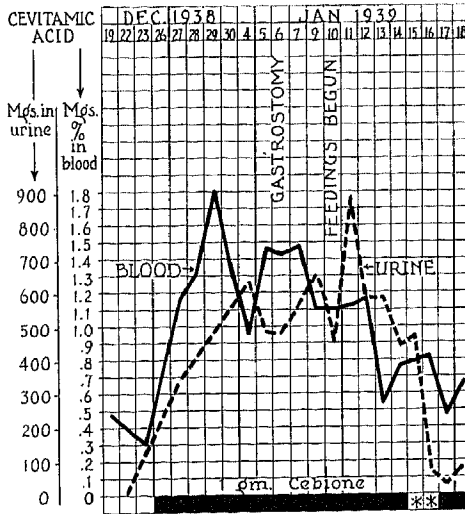


Chart 8. S. K. Male, aged 69 years. Diagnosis: advanced carcinoma of the cardiac end of the esophagus. Symptoms of esophageal obstruction for 8 weeks. Loss of 25 pounds of weight in past year. Stools on January 18, 1939, contained 0.37 milligrams vitamin C. Asterisk indicates error in computing dosage.

was lower than in the preceding case. Also in this case is well illustrated the fallacy of taking the first high blood level to indicate saturation.

dropped as low as 87 milligrams per 24 hours and finally reached a normal excretory level for a daily dose of 1 gram of cebione (744 mgm. excreted per 24 hours) on the ninth day after cebione was begun. When the daily dose of cebione was cut to 1/2 gram daily the total excretion dropped sharply whereas the computed absorption of vitamin C and the blood ascorbic acid level remained constant.

In this case the alkaline therapy was more rigorous and as a result the original blood level

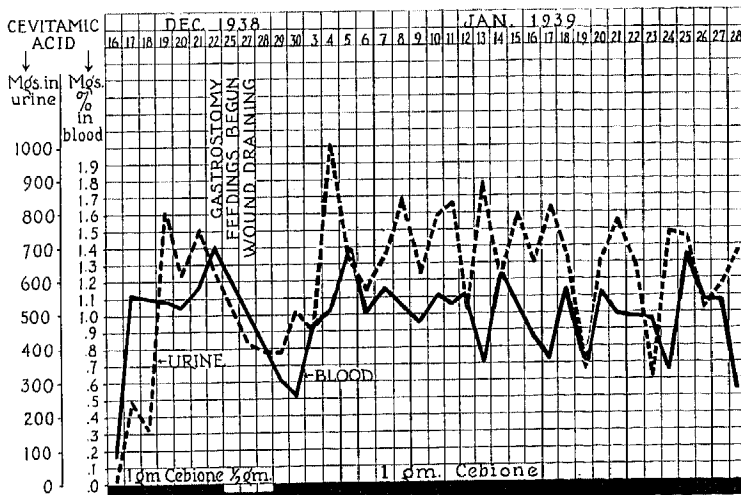


Chart 9. S. L. Male, aged 50 years. Diagnosis: carcinoma of the middle third of the esophagus. History of substernal pain, vomiting of food, and coughing for 3 months. Had deep radiation therapy over site of lesion and had had x-ray evidence of spread of the lesion into the hilus of the left lung. Estimation of amounts of vitamin C in the stools showed on December 20, 1938, 1.01 milligrams, on January 6, 1939, 1.0 milligrams and on January 23, 1939, 1.01 milligrams.

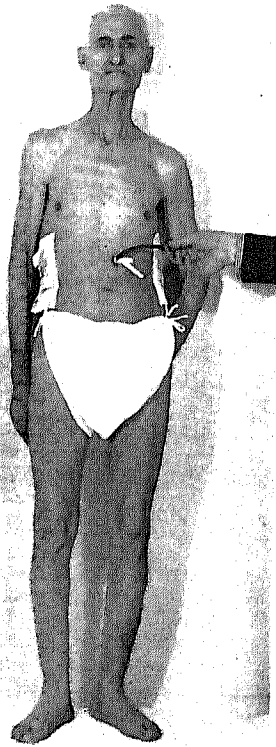


Fig. 4. Mr. L. C., aged 70 years. Jejunostomy for carcinoma of lower third of esophagus and cardia. Appearance of patient 1 month after operation.

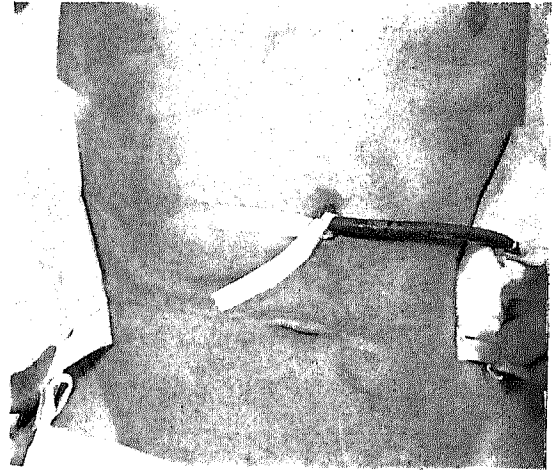


Fig. 5. Close up of wound in Figure 4 to show character of healing.

W. H., a male clinic patient, 47 years of age, entered Passavant Memorial Hospital with a diagnosis of carcinoma of the pyloric end of the stomach. He had symptoms of gastric distress for 1 year, but had vomited only on several occasions. He had not restricted his diet and on the basis of his history we had reason to believe that he had a better intake of orange juice than the first patient with carcinoma of the rectum who had a blood ascorbic acid level of 0.4 milligrams per cent. However, his original blood

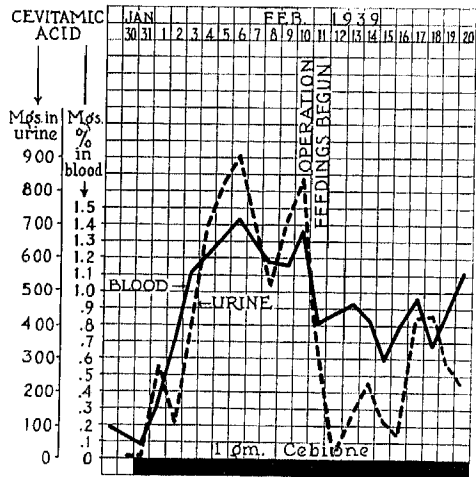


Chart 10. L. C. Male, aged 70 years. Diagnosis: carcinoma involving the cardiac end of the stomach and lower end of the esophagus. Progressive dysphagia and vomiting of 8 months' duration. Weight loss of approximately 40 pounds. Urinary retention upon admission to the hospital. Jejunostomy was done on February 10, 1939.

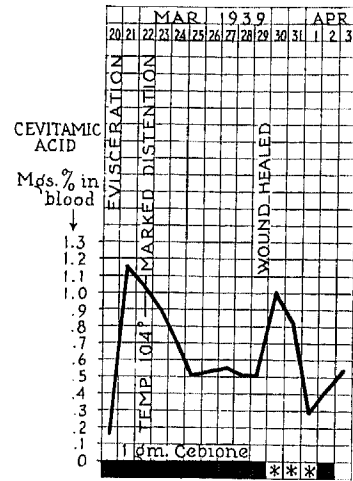


Chart 11. C. L. Female, aged 4 years. Diagnosis: exstrophy of the bladder. Implantation of ureters into the colon. Lower midline incision. Eviscerated on the sixth postoperative day. Resutured on March 20, 1939. Patient later developed intestinal obstruction and on April 18, 1939, the abdomen was again opened through a left lower rectus incision to free adhesions. Healing again occurred promptly and without event. Asterisk indicates that no cebione was given because of error.

ascorbic acid level was 0.12 milligrams per cent (Chart 6). Investigation revealed that he had taken a total of about a pound of soda bicarbonate weekly to control his pain. Two days after starting cebione the blood reached a normal level and on the seventh day the urinary output indicated a probable tissue saturation. After operation there was a slight drop in urinary excretion of ascorbic acid, probably indicating a slight increase in utilization of cevitic acid.

In a recent communication on the subject of wound disruption and postoperative hernia, Singleton and Blocker state: "It is common knowledge that wound healing is delayed in patients showing emaciation, general debility, or old age, and this is especially noticeable in patients with cancer." They further point out that of the 160 cases of disruption they reviewed, 22 per cent were not accompanied by the local contributing factors of infection or hematoma but there was merely a non-union of the wound margins.

The next few cases reported, therefore, should have been ideal candidates for failure of wound healing and disruption.

A. S., a male clinic patient, 72 years of age, entered Passavant Memorial Hospital with a diagnosis of carcinoma of the middle third of the esophagus. He was emaciated having lost 40 pounds in the 3 months before entering the hospital. His original blood ascorbic acid levels were 0.08 and 0.16 milligrams per cent (Chart 7).

He was prepared with cebione in the usual manner and was also given what liquids high in protein and carbohydrate that he could still swallow, supplemented by intravenous glucose and salt solution. A Spivack type gastrostomy was done through a left upper rectus incision. He wished to be up in a wheel chair the next day and was allowed to do so. Feedings were started through the gastrostomy tube on the third postoperative day, the wound edges did not separate, and no herniation or keloid formation has occurred 7 months after operation (Figs. 2 and 3).

S. K., a male clinic patient, aged 69 years, entered Passavant Memorial Hospital with a diagnosis of advanced carcinoma of the inferior end of the esophagus (Chart 8). He had symptoms of 8 weeks' duration and a loss in the past of at least 25 pounds of weight. He was similarly prepared and a Spivack gastrostomy was done. He left the hospital on the eleventh day after operation. One week later he became irrational, comatose, and died 2 weeks after being discharged.

This case is interesting because, although his general condition from the time we first saw him was that of a rapid downhill course

of an advanced malignancy, his wound healed as rapidly as did that of the previous case, and the gastrostomy functioned perfectly up to the time of his death.

S. L., a male patient, aged 50, entered Passavant Memorial Hospital with an advanced carcinoma of the middle third of the esophagus. He had received radiation therapy and had early evidence of spread of the carcinoma into the mediastinum and hilus of the left lung. He was prepared in the same manner as the previous cases (Chart 9). On the third postoperative day a temperature elevation and chill indicated infection and the next day the wound was opened inferior to the gastrostomy and foul pus was evacuated. Several days later gastric secretion was evident in the wound. The patient had persistent paroxysms of coughing which became slowly but progressively worse. Despite these handicaps the infection cleaned up and the wound granulated in with remarkable rapidity. Such is entirely contrary to the usual course of gastrostomy wounds with the three complicating factors of infection, gastric secretion in the wound, and paroxysms of severe coughing.

L. C., a male clinic patient, 70 years of age, entered Passavant Memorial Hospital with a diagnosis of carcinoma of the lower end of the esophagus and cardia. He had lost 40 pounds of weight in the several months preceding hospitalization. On the first day in the hospital he developed urinary retention due to an enlarged prostate and thereafter had a mild urinary sepsis. Preparation was as in the previous cases plus a retention catheter (Chart 10). When his temperature leveled off below 100 degrees F, a jejunostomy was performed because a gastrostomy was not feasible in face of the extensive involvement of the cardiac end of the stomach by carcinoma.

Besides the ease with which the wound healed (Figs. 4 and 5), this case is also interesting because of the sharp drop in the blood ascorbic acid levels and the urinary excretion of vitamin C beginning with the time that jejunal feedings were started, this despite intravenous cebione. Experiments upon guinea pigs have shown that at least in that animal the upper intestine is one of the main sites of storage of vitamin C. Did the disturbance of jejunal physiology attendant upon feedings directly into its lumen cause this drop in blood ascorbic acid level?

The question may arise as to whether any cases of wound disruption have been checked for blood cevitic acid levels. One case that we know of is reported in the literature in which evisceration occurred and although the blood ascorbic acid level had not been deter-

mined, the autopsy findings showed other early evidences of scurvy. We may also add one case of carcinoma of the esophagus with gastrostomy in which there was a mild wound infection followed by a slow but complete dissolution of the wound. The blood ascorbic acid level taken after wound separation was 0.03 milligrams per cent.

The second case, C. L., a female patient 4 years of age, entered Passavant Memorial Hospital with an exstrophy of the bladder for the second stage of the procedure of implanting the ureters into the pelvic colon (Chart 11). She eviscerated on the sixth post-operative day. A blood ascorbic acid taken at the time of evisceration was 0.16 milligrams per cent. One gram doses of cevione were started immediately and the blood responded promptly. There was a secondary drop which was due either to high temperature, the infection in the wound, or to the distention causing disturbances of the intestinal physiology. However, the wound healed firmly despite marked distention and stitch abscesses to complicate the process.

CONCLUSIONS

1. Although, at present, there is no absolute proof of the relation of vitamin C deficiency to non-union of wounds in humans there is considerable evidence, historical, pathological, experimental, and clinical, to give strong support to the theory that a relationship exists and to encourage further study, particularly in the clinical field.

2. If the blood ascorbic acid is low and is accompanied by a history of deficient or defective alimentation of foods containing vitamin C, the patient may be considered to have also a tissue depletion.

3. Patients deficient in vitamin C may be saturated by large doses of synthetic cevitamic acid administered either by mouth or intravenously, or by adequate feedings of foods rich in vitamin C.

4. The deficient patient cannot be considered saturated until the blood level has been maintained at optimal or above for a sufficient period. These should be verified by a high urinary excretion. The latter can be determined only when the daily intake of vitamin C is known.

When such determinations are not available the deficient patient should be saturated with doses of 1 gram of cevitamic acid daily for a

period of 9 to 10 days and then maintained on doses of about 300 to 500 milligrams of cevitamic acid daily until the wound is healed. The patient may then be kept saturated on a diet including adequate vitamin C containing foods.

5. The excretion by way of feces of vitamin C is negligible except in the presence of hypermotility of the small intestine or in alcoholics.

6. Vitamin C deficiency should be thought of and determinations made in the following types of patients: (a) Those with a deficient diet—voluntary, because of low income, or because of a doctor's dietary orders; (b) those taking large doses of alkalis by mouth; (c) those with obstructive gastro-intestinal lesions, particularly at the pylorus or above; (d) those with a history of vomiting over long periods; (e) those with hypermotility of the small intestine; and (f) syphilitics and alcoholics.

7. After operation normal patients may show a drop to scurvy levels because of long periods of intravenous therapy without food by mouth, because of abnormal bowel physiology, and because of the increased utilization of vitamin C that apparently accompanies infections and operative procedures.

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