PROBLEMS OF PROTEIN NUTRITION IN BURNED PATIENTS*

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Although the treatment of the burned patient is usually regarded as a surgical problem, numerous underlying physiologic, metabolic and clinical complications must be constantly borne in mind. Frequently, the success or failure of carefully planned and well executed surgical procedures, such as skin grafting, depends upon the early recognition and effective handling of these underlying disturbances. Infection,[1] shock, immediate or late,[2] anemia,[3] and disturbances of kidney or liver function[4] may occur as complications of burns. All these factors tend to delay healing.

The presence of any, or all, of these factors may also have a profound effect on the metabolism of the patient. An opportunity has been afforded to study some of the abnormalities of metabolism in a large series of burned patients. The details of the earliest of these investigations are given elsewhere.[5] The present communication deals with only one aspect of this very large problem, namely, the problem of protein metabolism in the burned patient.

Hypoproteinemia occurred frequently in a series of 63 patients upon whom a sufficient number of laboratory observations were made. In some patients, hypoproteinemia was fugitive, and was probably associated with early loss of plasma. In others, it persisted for some time, but was not severe and responded to high protein diets containing from 100 to 125 Gm. of protein per day. These diets were supplemented with 25 to 30 Gm. of brewers yeast† and other added vitamin supplements,‡ and contained approximately 3000 calories. Other patients did not respond to, or could not ingest, such diets. This group was composed of the most severely burned of all the patients studied, and in them the hypoproteinemia became progressive, and often reached the anasarca level. Simple loss of plasma in the form of persistent surface exudate could not alone account for the hypoproteinemia

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‡ Provided by the courtesy of Merck & Co., Rahway, New Jersey.

in these patients. But there is no doubt that this was an important contributing factor, although, unfortunately, one that cannot be studied quantitatively.

A detailed study of nitrogen metabolism has been made upon a patient with a burn of 55 per cent of his body surface. Similar studies have been made upon nine other patients. The data from these patients are not complete but are entirely confirmatory in essential details of the findings reported here. The important laboratory data are presented in Chart 1. All values have been calculated in terms of protein. They include protein intake from all sources.

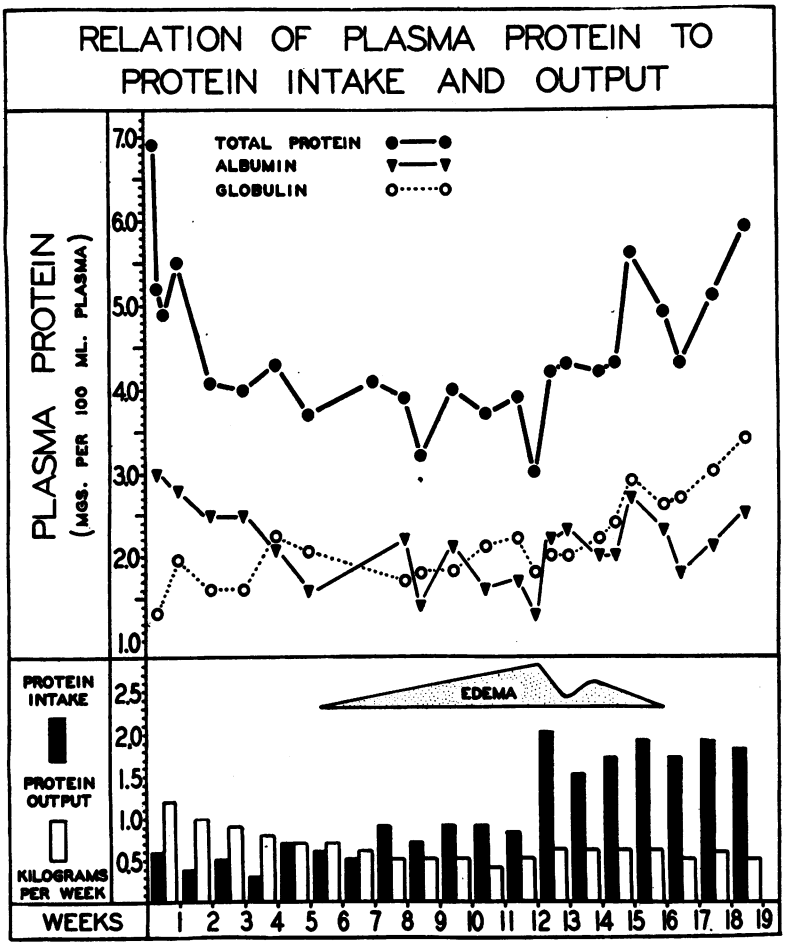

CHART I

CASE REPORT

C. J., age 22, a coast guardsman in excellent physical condition and with a noncontributory past history sustained flame burns shortly before entry to the hospital. On admission, a physical examination revealed a well-developed and well-nourished young man, with burns of such severity that it was later determined that approximately 45 per cent of his body area was involved in third degree burns and a 10 per cent further area with second degree burns. The burns were on the face, scalp, whole back, flanks, and large parts of all four extremities.

His pulse was rapid and thready. He was cold and clammy. His blood pressure was not taken because of his leg and arm burns. Marked hemoconcentration was present and the required 17 units* of plasma were administered based both on the extent of the burn and on hematologic data. The plasma and four liters of saline were administered over a period of 48 hours, all of the plasma being given in the first 24 hours. No débridement was attempted, and his burns were treated by triple dye.

His early complications were hemoglobinemia, hemoglobinuria, with oliguria and azotemia. His azotemia was of a reversible type. The blood nonprotein nitrogen returned to normal after a few days of normal urine output. At the end of 24 hours he was given sulfadiazine by mouth, with satisfactory blood levels and a normal kidney clearance of the drug.

Urine nitrogen data showed the presence of unusually large amounts of nitrogen in the urine, amounting on some occasions to 34 Gm. in a 24-hour period. He lost his appetite and, for a period of four weeks, the protein component in his diet did not exceed 80 Gm. per day. At the end of six weeks he had sustained a calculable net loss of over 2000 Gm. of protein. This deficit was occasioned by the negative nitrogen balance occurring during the first four weeks. These figures obviously do not take into consideration the very considerable loss of nitrogenous material from the burned area which, by clinical observation, persisted for 19 weeks, at which time the skin grafting was nearly complete. Therefore, the nitrogen deficit must actually have been much greater than the calculable 2000 Gm. would indicate.

The significance of a protein deficit of 2000 Gm. should be carefully examined. It represents an equivalent in terms of plasma of 40,000 Ml. Expressed as loss of muscle tissue, it represents a loss of ten kilograms, or approximately 22 pounds. The problem of balancing such a protein deficit in a severely burned patient by feeding a high protein diet was extremely difficult. By considerable persuasion, the patient was prevailed upon to take many supplementary feedings until his intake was approximately 130 Gm. of protein a day, and his caloric intake 3000 Gm. This represented in his case the absolute physical ability of the patient to ingest food by mouth. This diet was continued from the 7th to the 12th week of his hospital stay. From the end of the first week he also had another small source of protein intake in the plasma content of 6000 cc. of whole blood transfusions in 12 weeks. These were given in 300–1000 cc. doses at frequent intervals. The plasma proteins from this source is included in the values given in the chart. Nevertheless, in spite of cooperation on the part of the patient, and in spite of the fact that an *apparent positive nitrogen balance* was obtained throughout this period of high protein intake, his plasma protein fell and the edema, which became noticeable at the end of the fourth week, progressed. By the beginning of the 12th week the plasma proteins had fallen to 3.1 and the albumin to 1.6 mg. per Ml. of plasma, respectively, and the edema was massive.

His clinical condition at the beginning of the 12th week was desperate and heroic measures of alimentation were begun. Seventy-five Gm. of human albumin† and several units of desiccated plasma, reconstituted at ten per cent protein content, were administered and feeding commenced by vein and stomach tube. The details and

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* One unit of plasma is 250 ml. of therapeutic plasma with a protein content of approximately five per cent.

† Provided through the courtesy of Professor E. J. Cohn.

theoretic discussion of the alimentation used in this patient is given in another communication.[6] Only the essentials of the treatment will be given here. The protein intake was increased from 800 Gm. to between 1700 and 2000 Gm. per week. On some days his protein intake amounted to 500 Gm. Intravenous alimentation was carried out with amino-acids obtained from acid hydrolysis of casein with added water-soluble vitamins. By stomach tube, a high caloric, high protein, high vitamin diet in semifluid form were administered. The intubated food was supplemented with 30 to 40 Gm. of brewers yeast, 20,000 units of vitamin A, 1000 units of vitamin D, 200 mg. of asorbic acid, 20 mg. of thiamin, 10 mg. of riboflavin, and 200 mg. of nicotinamide per day. The nitrogen intake per week administered by vein was equivalent to 225 to 625 Gm. of protein, while by intubation over the same period of time from 1000 to 1200 Gm. of protein were administered.

The results were striking. Immediately following the administration of the albumin and concentrated plasma there was an abrupt delivery of the edema, which continued to diminish in degree throughout the first week of high protein intake. During the second week of forced alimentation the edema reappeared briefly, due, in part, to an error in making up the amino-acid solution in isotonic saline, instead of in distilled water. About 10,000 Ml. of saline solution were thus administered over a period of four days before the error was detected. However, the correct procedure was reestablished and the edema gradually decreased until, by the beginning of the 15th week, it disappeared. The forced alimentation was continued until the end of the 19th week.

In the 14th week his general appearance and the appearance of his granulating surface had improved to such an extent that for the first time since the burn it seemed possible to perform skin grafting operations. Because of the great area involved, Reverdin grafts were chosen as the only reasonable kind. During the next four weeks he underwent, in bed, four three-hour sessions of grafting. Novocain anesthesia was used. The growth of new skin between the grafts was exceptionally rapid.

The total plasma protein rose from the 12th to the 19th week to an almost normal level. Following the administration of albumin, there was an abrupt rise in the plasma albumin fraction. The loss of edema during the day following the administration of albumin was striking. It may also be mentioned that there was a slow rise of globulin from the 12th week on. The rise continued and resulted in an abnormally high globulin level. The cause of this rise is not at present known. Liver function tests at this time were normal although infection was present.

At the conclusion of the period of forced alimentation, it was calculated that a positive balance of 6000 Gm. of protein existed in this patient. However, partition of the blood and urine nitrogen showed no remarkable loss of amino-nitrogen when amino-acids were injected. Neither was the total nitrogen of the urine remarkably increased. In fact, on one day, when the intake was calculated as 500 Gm. of protein, the patient retained approximately 380 Gm. and the urine nitrogen excretion showed a 75 per cent conversion of all excreted nitrogen to urea. It would appear, therefore, that the loss of nitrogen through the granulating surface or the demand for tissue must have been very great, since, while the calculated nitrogen deficit based on intake and output studies was more than balanced by forced alimentation, he continued to metabolise and to retain large amounts of protein.

The clinical improvement of the patient under this regimen was striking. In the 19th week he was returned to a diet of 125 Gm. of protein without noticeable return of edema. In the 23rd week he was weighed for the first time since the accident. Although his health and appearance had improved greatly from his worst condition, he was still 55 pounds below his normal 167.

DISCUSSION.—The findings in this patient, and in the eight other patients studied, are confirmatory of the observations of Lucido.[7] In severely burned patients there appears to be an excessive loss of nitrogen into the urine in addition to large losses of nitrogen by exudation from the burned surface, and an increased nitrogen demand for the building of new tissue. These three factors can result in serious nitrogen deprivation, with consequent edema and general malnutrition. The causes of increased nitrogen loss are many. Tissue destruction, infection, increased metabolism and demand for protein for the repair process all play a part.

It must be emphasized that, while the majority of burned individuals may restore nitrogen balances on simple dietary regimens, severely burned patients may not. There was a direct relation between the extent and severity of burn and the amount of nitrogen loss in the present series of cases.

Nitrogen balance studies based upon urine and stool analyses, together with known nitrogen intake, cannot reveal the quite considerable nitrogen loss from the burned surface and the demand for building new tissue. On a high protein diet alone, this patient developed a protein deficit of 2000 Gm., based upon intake and output studies, which was eliminated and a final, apparent, positive balance obtained. In spite of this, the patient's edema increased and it was not until a total nitrogen retention estimated at over 6000 Gm. of protein had been obtained that the edema was completely delivered and a good nutrition obtained. In other words, at least 6000 Gm. of protein were required, over and above that indicated by balance studies by this patient, and this only after the net loss of 55 pounds of his original body weight.

These results suggest that an early appraisal of nitrogen losses in burned patients is necessary. When marked negative nitrogen balances appear, steps must be taken to provide an enhanced nitrogen intake. In some severely burned patients positive nitrogen balances will be found impossible to maintain from diets alone, due to the physical impossibility of ingestion of such diets. In such an event, it is suggested that forced alimentation by intubation or by the intravenous administration of amino-acids, with the precautions previously stated,[5] should be attempted as soon as possible.

With such protein deficits as shown here, replacement by whole blood or plasma transfusions are clearly impossible, since it would be necessary to administer 120 liters of plasma to accomplish the equivalent of the supplementary alimentation given. The only satisfactory way that can be considered at present is forced alimentation by intubation and amino-acid administration by vein with proper precautions.

SUMMARY AND CONCLUSION

1. Increased nitrogen excretion in the urine of some severely burned patients has been established.

2. Calculable nitrogen deficits, based upon intake and output studies alone, of some duration and great magnitude have been observed.

3. Correction of such a deficit by high protein feeding failed to bring a patient into true nitrogen balance because of incalculable losses which were probably from the burned and granulating surface.

4. Heroic intravenous and tube feeding apparently restored his true protein balance. This feeding reached a level of intake of the equivalent of 2000 Gm. of protein per week, and resulted in establishment of an apparent positive nitrogen balance of over 6000 Gm.

5. In spite of this apparent positive nitrogen balance, he is still more than one-third below his normal weight, so that even the calculation and considered deficits are much below the actual one.

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DISCUSSION.—DR. LELAND S. MCKITTRICK (Boston): Doctor Allen asked me if I would pinch-hit for him. I feel totally inadequate to discuss any one of these three papers. Doctor Allen felt, however, that it might be of some interest, as a part of this discussion, to summarize briefly the results at the Massachusetts General Hospital on the patients from the Cocoanut Grove disaster. When he found he had to leave town, he handed me this slip of paper on which were some figures given to him by Dr. Oliver Cope, who had taken a very active part in all the work of this group of patients.

There were 114 casualties brought to the Massachusetts General Hospital in the period of about an hour and a half. There were a few stragglers after that, but not very many. Fifty-five of those were dead on arrival, and within 15 minutes another 20 died, making a total of 75 deaths out of the 114 patients. Thirty-nine patients were admitted for treatment.

The hospital was particularly well suited to handle a group of this size. One surgical floor was completely evacuated, and these 39 patients were promptly sent to this floor.

These burns all followed a pretty uniform pattern—face, hands and trunk were