THESIS

ON

METABOLIC CHANGES AFTER SURGICAL OPERATIONS, WITH SPECIAL REFERENCE TO DISTURBANCES IN PROTEIN, CHLORIDE, SODIUM AND WATER METABOLISM AFTER PARTIAL GASTRECTOMY, AND TO THE USE OF PROTEIN HYDROLYSATES

SUBMITTED FOR THE DEGREE OF

Ch.M.

By

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INTRODUCTION

The work on protein hydrolysates to be described in this report was originally undertaken because of a request by the Protein Requirements Committee of the Medical Research Council for a clinical trial and assessment of the value of protein hydrolysates in surgical patients. The primary objects of this enquiry were to determine first the rate of administration of protein hydrolysates which would secure optimum utilisation; secondly, the effect on nitrogen balance of other nutrients given with the hydrolysates; and, thirdly, the form and rate of the excretion of nitrogen in the urine, particularly as to the loss of amino acid and peptide nitrogen, during hydrolysate infusion. In addition, as opportunities occurred, clinical trials with and without biochemical investigation were to be made in a number of selected states: after head injury or severe burns, in oesophageal obstruction, high intestinal obstruction, severe liver disease, etc.

The present report describes the investigations which were carried out on surgical patients by one of the groups which accepted the invitation of the Medical Research Council. It includes nitrogen balance studies of patients submitted to operations and fed on various diets, and of normal volunteer subjects; a comparison has also been made of the effects on nitrogen metabolism of casein hydrolysates administered by the oral and intravenous routes and of protein derived from other sources and given by various routes. In addition, a number of other patients to whom the hydrolysates were administered have been observed but

not /

not submitted to nitrogen balance studies; this group includes patients suffering from peritonitis, obstruction and fistula of the small intestine, obstructive jaundice and ulcerative colitis.

The first group of patients were submitted to operations such as those on the autonomic nervous system or on bones, and to gastrectomy, and were treated according to the post-operative methods used in the surgical unit in which the work was undertaken.

A number of control balances were done on normal volunteers who, in one experiment, were starved of protein, the calories being maintained, and in the other experiment were starved of both protein and calories. The food intake was arranged so as to be comparable with that of patients submitted to partial gastrectomy. In this way it was possible to estimate how much of the post-operative excretion of nitrogen might be related to starvation and how much to other effects of the operation. Attempts were then made to modify the nitrogen excretion after operation by various procedures, including oral administration of high protein high calorie diets before and after operation, with and without the addition of protein hydrolysates; the restriction of food intake after operation; intravenous administration of casein hydrolysate and plasma; and the instillation into the jejunum of a mixture of milk, milk powder and lactose.

It was believed that such a comprehensive investigation was necessary because of the wide differences in opinion recorded in published accounts of previous studies of post-operative protein metabolism. For example, Cuthbertson (1945) stated, "It is doubtful whether, during the early catabolic phase, any dietary measure /

measure can effectively suppress the catabolic destruction of protein," and, "The administration of a large excess of protein (more than 100-150 g.) for the first few days after injury is not at present indicated." On the other hand, Mulholland et al. (1943) have advocated the administration from the day of operation of 200 g. protein and 3000 calories per day through a jejunal tube, and others have recommended the parenteral administration of large quantities of protein hydrolysates. Behind these conflicting recommendations there appears to exist a wide divergence in opinion as to the disturbances produced by surgical operations of the severity of partial gastrectomy or by simple or compound fracture of the long bones of the limbs.

The most likely explanation of these differences of opinion seems to be that Cuthbertson's observations (1935-36) were made on well nourished subjects suffering from accidental injury, while the patients reported by Mulholland et al. (1943) were stated to be severely malnourished and suffering from protein depletion which was often of prolonged duration. While at present food is more abundant, though more expensive, and the general standard of intake probably higher in the United States of America than in Scotland, severe economic depression exists in some rural districts and in certain large cities of the U.S.A., and leads to more numerous instances of malnutrition, particularly in regard to protein, than is usual here. On the other hand, these patients when admitted to hospital meet different conditions and may there be fed more abundantly than would be the case here. So far as we were able to judge, few severely malnourished patients were encountered in the present series. /

series.

Nitrogen balance studies with all their disadvantages and limitations remain the most suitable method for the quantitative study of metabolism in man. The methods which have been used for many classical investigations in vitro (tissue slice and tissue culture) and in animals (regeneration of depleted plasma protein in plasmapheresed dogs, promotion of growth in immature animals, and quantitative or qualitative analysis of tissue) are of limited application in assessing the value of protein hydrolysates in human nutrition. In this connection mention will later be made of the possible effects of species difference in the origin of the protein hydrolysates employed.

Adult male animals in nitrogen equilibrium excrete an amount of nitrogen which is equivalent to that which they absorb from their food, and the total quantity of protein in their bodies and its composition remain constant. By careful measurement of the nitrogen ingested in food protein and of the nitrogen excreted in urine and faeces or lost by other routes, it is possible to establish the state of an animal or man in respect of nitrogen metabolism. The body excretes nitrogen chiefly in the form of non-protein nitrogenous compounds in the urine. It has long been known that the urinary nitrogen excretion rises in fevers, such as typhoid (Shaffer and Coleman, 1909), and that there is a contemporary loss of body tissue and weight.

Cuthbertson (1929, 1930, 1932, 1935, 1942) in a series of reports, described the increase in urinary nitrogen excretion which follows surgical operation or accidental injury in healthy men. He showed that in both man and animals the well nourished subject /

subject exhibits a profound metabolic disturbance after injury, and he suggested that this may be related to the processes of inflammation and repair after fractures of the long bones. Since his observations showed a simultaneous and proportionate change in nitrogen sulphur, phosphorus and potassium excretion, he suggested that the ratio of the quantities of nitrogen and phosphorus excreted indicated their common origin to be largely in skeletal muscle. The increased urinary excretion of nitrogen began within a day or two of injury, reached a maximum within ten days and then slowly declined. The maximum urinary nitrogen output commonly occurred between the fourth and eighth days after accidental fracture of the long bones, but it was sooner, generally on the second to fourth days, after osteotomy of the same bones; this was possibly due to less severe injury and more immediate immobilisation in surgical than in accidental fractures. Increases in basal oxygen consumption, temperature and pulse rate were proportional to the loss of nitrogen. While there appeared to be some relationship between the severity of the injury and the magnitude of the urinary loss of nitrogen, the loss of body substance was not proportional to the fever which usually followed on injury; moreover the reduction in body weight could not be wholly explained by the muscular wasting, due to immobilisation of fractured bones, though this was thought to be an important factor.

Some nitrogen excretion also normally occurs in the faeces, but stool nitrogen usually varies less than urine nitrogen even with changes in diet. It may, however, rise considerably when absorption of the products of protein digestion is impaired by excessive /

excessive rate of passage of bowel contents; this type of diarrhoea may occur when feeding is started after prolonged partial or complete starvation of food, or when excessive quantities of certain substances such as sodium chloride are ingested. True defects of protein digestion and absorption seem to be very rare in temperate climates.

Negative nitrogen balance exists when the excretion of nitrogen, or its loss in discharges from wounds, exceeds the absorption of nitrogen from the food. Negative balance may commonly result from restriction of food, increased protein catabolism, loss from wounds or a combination of these factors.

Positive nitrogen balance results when the amount of nitrogen derived from food exceeds that excreted; it implies that protein is being formed and retained in the body. Positive balance occurs during growth on an adequate diet and when abundant food is supplied after a period of depletion; it may even occur when depleted subjects are supplied with a diet which would be inadequate for them in normal circumstances of weight and nutrition, but which in their depleted state provides more than enough calories for their daily requirements, and more nitrogen than is being excreted; thus positive nitrogen balance may not imply optimum nitrogen intake.

The study of protein metabolism in human subjects, whether normal volunteers or surgical patients, is beset with variables of which can be learned or suspected only enough to make us view any conclusions with the greatest caution.

According to Folin's conception of endogenous and exogenous protein metabolism, the body proteins are in a static state and the /

the nitrogen excreted in the urine represents primarily that of degraded food constituents. Schoenheimer (1942), by feeding rats on diets which included small amounts of natural amino acids containing heavy nitrogen (N 15), has shown that the individual components of protein undergo rapid replacement in living plants and animals. In these experiments he found that instead of most of the labelled heavy nitrogen, incorporated in the amino acids administered as food, being excreted in the urine, at least half of the heavy nitrogen in the added amino acids was retained in the body. There was, however, no significant change in body weight. He concluded that substitution of dietary for tissue nitrogen had occurred. Analysis of the body tissue of the animal showed that about half the amino nitrogen ingested was retained as protein nitrogen and that there was a typical distribution common to the amino acids (leucine, glycine, glutamic acid, aspartic acid, tyrosine and lysine) which were studied. Schoenheimer concluded that his results indicated the general pathway of dietary nitrogen in the animal.

He also found that fixation of dietary nitrogen varied from organ to organ, but that tissue mass might compensate for low activity in this respect. Thus the muscles contained two-thirds of the deposited nitrogen but had a low unit activity, while there was only one-third in the combined internal organs which, however, might have high individual activities; the skin proteins showed least activity.

The isotopic nitrogen was shown to reach the tissue protein in several ways. An amino acid molecule from the food protein might replace a molecule of the same amino acid in a tissue protein, /

protein, or the nitrogen of one amino acid molecule might be transferred to another molecule of the same or another kind, either free or forming part of a protein molecule, and thus be incorporated in tissue. There was consequently continuous interchange of nitrogen atoms between different amino acids. Synthesis of amino acids, like that of fatty acids, occurred in the body even when dietary supplies were adequate and there was no apparent need for synthesis.

These isotope studies have shown the end results of protein metabolism in more detail, but there is still only limited information as to the exact mechanisms of the intermediate chemical processes involved. The nitrogen excreted by a normal animal in nitrogen equilibrium is of unknown origin: it may have come, more or less directly, from milk recently swallowed, or after many metabolic adventures it may have been derived from the amino acids of a bone. With these limitations constantly in mind, it is permissible to use the method of nitrogen balance study for the investigation of human subjects and to draw some general conclusions from the data obtained.

From the initial balance studies of the present series, it appeared that a daily intake of at least 70 g. protein (11.0 g. nitrogen) and 1800 calories was necessary for nitrogen equilibrium to be re-established after operations such as gastrectomy. This intake was therefore chosen as an arbitrary minimum for subsequent studies. It was reasoned that if such a level of intake was necessary for nitrogen equilibrium after the catabolic phase, then it was unlikely that the catabolic destruction of protein would be markedly reduced by lower intakes. An attempt

was /

was therefore made to achieve this intake during the immediate post-operative period, no matter what kind of protein or method of administration was employed. On most days the intravenous infusions of casein hydrolysate provided more than 11.0 g. of nitrogen but the daily calorie intake seldom greatly exceeded about 1000. The intravenous plasma infusions supplied more than 11.0 g. of nitrogen but even fewer calories than did the hydrolysate infusions. Only by jejunal instillation of a mixture of milk, dried skim milk and lactose, was it possible to achieve a sufficiently high intake of both protein and calories throughout the immediate post-operative period.

The provision of protein food in any form unaccompanied by at least an equal quantity of carbohydrate is wasteful and expensive, and it is probably most economical to provide protein and carbohydrate in the proportions of 1 to 4. The intravenous infusion of the equivalent of 70 g. protein and 280 g. glucose would require the injection of at least 4500 ml. of isotonic solution per day. Such large fluid intakes are undesirable and may be dangerous. They have been strongly recommended and have been commonly used in America, but the big climatic difference calls for caution in their adoption in this country. Even in America, with its continental extremes of climate, combined with the high average temperature and humidity of the hospital wards there, complications arising out of excessive administration of water and of sodium chloride are not uncommon. Since the time these studies were carried out, solutions containing a highly purified mixture of amino acids have become available in the U.S.A. These solutions can be given in a higher concentration and /

and at a faster rate than the relatively crude hyrdolysate preparations which were employed in the studies reported here.

Thus the value of intravenous hydrolysates is limited by the number of calories which can be supplied by the same route. At present these calories can be provided only as glucose, the daily quantity of which is limited by the tolerance of the body to intravenously injected water which in turn is dependent on several factors: the quantity of sodium chloride injected, the renal function, initial state of hydration, body temperature and certain as yet ill-defined effects of injury. Within the limits of water tolerance it was impossible in our cases to supply parenterally enough calories in the form of isotonic glucose solution to prevent wasteful metabolism of the protein.

It was not possible to relate the urinary nitrogen excretion and balance in terms of protein loss to body weight loss, since body weight changes were largely dependent on other factors of which the most likely seemed to be a disturbance of water and electrolyte metabolism. From an early stage in the investigations, observations were made on the daily total excretion of chloride in the urine before and after operation. During the first week after operation there was commonly a reduction of chloride excretion in the urine regardless of the amount of salt ingested, with consequent retention of chloride in the body. These observations led to a closer study of sodium, chloride and water metabolism after injury by operation. This has shown that sodium and chloride are retained after injury for a period which is of similar duration to the period of excessive protein catabolism and that water also is retained during this period.

There /

there is also evidence that some of the retained sodium, chloride and water is excreted during the second week after operation. It seems likely that the retention of sodium with chloride and water after injury is related to the inflammatory reaction to injury. This retention of chloride and sodium and its coincidence in time with the increased excretion of nitrogen and other elements during the first week or more after injury, seem to be but two large aspects of the response to injury by the mammalian body. The biological importance of such an association is immense. The clinical significance and applications also are great, because by the unspecific and too lavish use of intravenous infusions a new set of clinical disturbances may be created, while limited benefit is derived, and the original disturbance becomes lost amidst a host of secondary reactions. In man, these matters must be further studied at the bedside, in the surgical ward, by controlled experiments.

METHODS

A. CLINICAL

The nitrogen balance studies were begun at varying times before operation and were continued until the patient was discharged from hospital.

Diet

Food of a known caloric and nitrogen content was provided by the diet kitchen of the Royal Infirmary. The composition of the food was estimated from the standard tables of McCance and Widdowson (1946), check analyses being made from time to time. Unconsumed food was collected daily; the nitrogen content was estimated and deducted from the original issue. Certain difficulties deserve mention. The wards in which the studies were conducted were towards the end of the journey of the special diet waggon and the time of arrival of the food varied from day to day; usually this resulted in the service of meals after those of other patients in the wards, and additional delay might result at the ward because nurses were fully engaged when the food arrived. While the quality of the food was always high, at times patients chafed either because their choice had to be made in advance, or because the special diet did not appeal to them as much as the ordinary ward diet for the day. Some complaints and failure to eat the food provided were inevitable, but, by the consideration the dietitians gave to the tastes of the patients and by careful choice of patients, difficulties were minimised. In the early balance studies no restrictions were placed on consumption of water and tea, though /

though sugar and milk for the latter were taken from the daily ration. Later, however, two litres of water were provided each day and any remaining at the end of twenty-four hours was measured and deducted; all tea and fruit drinks were made from this water. Only in this way could accurate records be obtained of the daily consumption of water.

Collection of Urine, etc.

In a busy general surgical ward the collection of all the urine and faeces passed by a patient presents some difficulty. To avoid the complications introduced by menstruation and the difficulty of separate collection of urine and stools in women, men only have been studied. A number of methods and modifications were tried but the scheme finally adopted was as follows.

The purpose and the methods of study were explained to the patient who was asked if he would co-operate. If he agreed to do so, he was asked to pour all his urine, after voiding, from his glass urinal into a five-litre glass jar which was kept in a box hanging at the side of his bed. This jar was removed and replaced once daily at 9 a.m. and taken to the laboratory for measuring and sampling of the urine. To keep the urine and faeces separate, the patient was asked when defaecating to pass urine before using the bedpan. During the pre-operative period most of the patients went to the ward lavatory and defaecated there into a labelled bedpan, the faeces were then emptied into a labelled jar which was sent to the laboratory daily. After operation, the nursing staff were responsible for the preservation of the faeces and enema returns in the labelled jar. Since it is essential that all the faeces and urine be collected every day, /

day, the co-operation of the nursing staff must be secured. This is best obtained by short explanatory talks on the objects and methods of the investigation, and by the communication of such results as have been obtained.

The fluids obtained by gastric aspirations and from gastric lavage were also collected for analysis for nitrogen content. Blood loss at operation was estimated by comparison of the nitrogen content of the washings of the swabs and towels with that of a blood sample drawn shortly before operation. The nitrogen of blood transfused was also measured and the tissue removed at operation was digested with concentrated sulphuric acid and analysed for nitrogen content. In most cases, height and weight were recorded and daily weighings were carried out except for the day of operation and one or two days afterwards. A "Pollard" stretcher type bedside weighing machine, which is accurate to within two ounces, was employed. In a few cases repeated measurements of limb size were made. Twice a week, more often in some cases, venous blood was drawn for chemical analysis, the details being varied to cover a wide range of items.

B. BIOCHEMICAL

The following notes on the preparation of specimens for analysis and the analytical methods employed were prepared by my biochemical colleagues who were responsible for all the biochemical estimations in the present investigations.

Preparation of Specimens for Analysis

(1) Urine.- Unless otherwise stated, all analyses of urine were carried out on samples of urine taken from a complete twenty-four hour specimen, the volume of which was carefully measured. Suitable dilutions of the urine were made for the various estimations, which were performed immediately.

(2) Faeces.- Faeces and enema returns were collected in twenty-four hour specimens and were analysed daily in most instances. By using a Warburg blender, a relatively homogeneous solution was obtained, which was made up to 1000 ml. (sometimes 2000 ml.) in a volumetric flask with distilled water. Aliquots of this solution were then used for analysis.

(3) Gastric Aspirations and Vomitus.- The volume of the fluid was measured and, if necessary, put into the Warburg blender in order to obtain a more homogeneous solution. Aliquots suitably diluted were taken for analysis.

(4) Blood Lost during Operation.- All the swabs and towels used during the operation were collected. Immediately after the conclusion of the operation, the towels were rinsed thoroughly in cold water and wrung out at once and the washings preserved. The swabs were soaked for a longer period, sodium hydroxide being added to the water to make an approximately

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5 per cent. solution. On the next day the swabs were wrung out and resoaked in more dilute soda solution. The volume of the combined washings was measured and the nitrogen content of an aliquot of this fluid was determined. The nitrogen lost as blood at operation was then calculated. Total blood nitrogen was determined on a specimen of blood drawn just before operation. An approximate value was thus obtained for the volume of blood lost at operation.

(5) Stomach.- The portion of stomach resected was placed in a pyrex beaker, covered with A.R. sulphuric acid and left overnight. When the tissue had been completely dissolved by the acid, the solution was transferred to a volumetric flask and distilled water was added to make the volume up to 1000 (or 2000) ml. This solution was diluted 1/5 and a nitrogen determination carried out on a 1 ml. aliquot.

Analytical Methods

Total Nitrogen.- A micro modification of the Kjeldahl method was used. One millilitre portions of the fluid for analysis, diluted to contain not more than 2 mg. of nitrogen, were digested with 4 ml. of a modified Arnold Gunning digestion mixture (100 ml. A.R. sulphuric acid, 300 ml. A.R. phosphoric acid and 50 ml. of 5 per cent. w/v crystalline copper sulphate) until all charring had disappeared, and then for a further three minutes. The ammonia, formed by the conversion of the nitrogen, was released by the action of an excess of 40 per cent. sodium hydroxide solution and by means of steam distillation carried over into N/70 sulphuric acid. From back-titration with N/70 sodium hydroxide the amount of ammonia liberated and thus the

total nitrogen in the solution was calculated. By using this method, standard urea solutions gave recoveries of 98 to 100 per cent., and it was therefore decided not to use the method of digestion suggested by Chibnall et al. (1943), which, although more accurate, would have proved too time-consuming for the present purpose.

Plasma Proteins.- Plasma protein determinations were carried out by the micro-Kjeldahl technique, with magnesium sulphate as the fractionating agent. Popjak and McCarthy (1946) have shown that this method for the determination of the albumin-globulin ratio is reliable, the values obtained being in close agreement with those given by electrophoresis. Fibrinogen determinations were not made. In determinations of non-protein nitrogen, the plasma proteins were first precipitated with tungstic acid and then nitrogen was estimated by the micro-Kjeldahl method.

Urea.- On account of the simplicity and rapidity of the method, the urea concentrations of blood and urine were determined manometrically by the hypobromite reaction (Van Slyke, 1929), though as Peters and Van Slyke (1932) have pointed out, sodium hypobromite is a less specific agent than urease and errors of 1 to 4 per cent. may be expected.

Uric Acid.- Uric acid was determined colorimetrically both in blood (Folin, 1930) and urine (Benedict and Franke, 1922). The arsenophosphotungstic acid reagent used is specific for uric acid, and the blue colour produced is not normally affected by the other constituents of blood filtrates or urine.

Creatinine.- /

Creatinine.- The method of Folin (1914) was used to determine creatinine in urine, the red colour produced by the Jaffé reaction being compared with that produced by standard solutions using a Hilger Biochem Absorptiometer. A modification of this method was used for the blood analysis (Folin and Wu, 1919). There is some doubt as to the exact nature of the substances causing the Jaffé reaction in blood; Peters and Van Slyke (1932) have presented evidence which suggests that the colour is, for the most part, produced by substances other than creatinine though for convenience it is customary to treat the results as if the red colour was wholly due to creatinine.

Amino Acid Nitrogen.- The method of Frame et al. (1943, 1944) was employed. This method depends upon the combination of amino nitrogen groups with B-naphthaquinone sulphonate in alkaline solution to form highly coloured compounds. These compounds become orange-red in acid solution and were determined colorimetrically using a Gambrell Photoelectric Colorimeter, No. 549, with a blue filter O.B.2 (maximum light transmission 480 millimicrons). It has the advantage over the nitrous acid and ninhydrin manometric and titrimetric procedure of being suitable for determining 4 to 40 gamma of amino nitrogen per sample, whereas they require at least 40 gamma (preferably more). Chinard and Van Slyke (1947) compared the photometric and ninhydrin manometric methods and considered that the former method gave satisfactory, though in general slightly higher results (especially in cases of uraemia), due to the fact that B-naphthaquinone is not specific for amino nitrogen. Uric acid, the most concentrated of the interfering substances normally found /

found in blood, when it is present in a concentration of 1.0 mg. per 100 ml., yields a colour equivalent to 0.1 mg. per 100 ml. of amino nitrogen. However, as no abnormal blood uric acid values were encountered, no correction was applied. Urea does not interfere with the colour reaction. The procedure of Frame et al. (1943) was then followed with the exception that to produce a strong colour reaction, 0.4 ml. instead of 0.2 ml. of fluid was used. This method was also used for determining the amino acid content of urine. The urine was diluted 1 in 25 and shaken gently with permutit for five minutes to remove any ammonia, which is an interfering substance in the reaction. The supernatant fluid was decanted and filtered, and 1-ml. portions of this diluted urine were then treated in a manner similar to the plasma filtrate. Considerable individual variation in the daily excretion of amino acid nitrogen was encountered (0.1 to 1.4 g. per 24 hours), but the values for any particular individual were fairly constant. The daily figures given by the ninhydrin method (Van Slyke et al., 1943) correspond to 0.1 g. - 0.15 g. of amino nitrogen, whereas the nitrous acid method (Van Slyke and Kirk, 1933) and the copper titration procedure (Albanese and Irby, 1944) give higher results. The formol titration method (Northrop, 1926) gives figures averaging between 0.4 and 1.0 g. per day. The dependence of the results on the method employed is presumably due to differences in specificity for amino nitrogen.

Peptide Nitrogen.- The term "peptide nitrogen" was applied to the increase in amino acid nitrogen which resulted after hydrolysis of the urine. After treatment with permutit, 10 ml. of /

of the diluted urine were placed with 5 ml. of A.R. hydrochloric acid in a large pyrex tube. The tube was fitted with a glass stopper and placed in a boiling water bath for at least six hours. The hydrochloric acid was removed by vacuum distillation. The first residue obtained was dissolved in water and the procedure repeated. The final residue was washed into a 20-ml. flask with distilled water and made up to the mark. The solution was filtered and 1-ml. portions taken for analysis. In some instances it was found impossible to get a satisfactory reading on the colorimeter owing to cloudiness developing in the solution. It was thought that this unpredictable difficulty was due to some interfering substance in the urine.

Sodium.- Sodium was estimated gravimetrically as the uranyl zinc sodium acetate salt, which weighs 67 times as much as the sodium in it. The method is specific for sodium, unless the solution in which the precipitate is formed contains more than 50 mg. per ml. of potassium, which is unlikely in biological material. The urine received preliminary treatment with calcium hydroxide and mercuric chloride in order to remove phosphates and any protein which might be present; ashing was therefore unnecessary (Butler, 1931). Serum sodium estimations were performed according to the method described by Peters and Van Slyke (1932). This method was also employed for stool estimations, using 1-ml. portions of the stool solution; wet ashing was found to be more satisfactory than the more usual dry procedure.

Chloride.- Chloride estimations were carried out on 1-ml. specimens of blood, plasma, urine or stool solution, using a modification /

modification of the methods of Van Slyke and Sendroy (1923), whereby the chloride was precipitated by using 5 ml. of N/29.25 silver nitrate in concentrated nitric acid solution, and the excess silver nitrate was titrated against N/29.25 potassium thiocyanate, 5 per cent. ferric alum solution being used as the indicator.

Potassium.- For serum, the platinic chloride micro-titration method of Shohl and Bennet (1928), determining potassium as the iodo-platinate as described by Peters and Van Slyke (1932), was used. It is claimed that the accuracy of the method is such that with 0.4 mg. potassium (the amount in 0.2 ml. of serum) the error is within 12 per cent.

The same method was used for estimating urinary potassium as the dry ashing method gave inconsistent and low results. Recovery experiments with suitably diluted urine gave satisfactory results (95 to 100 per cent. recovery), but the high positive balances found before operation in well nourished patients raised doubts regarding the validity of the method. A variety of methods, using cobaltinitrate, either gravimetrically or colorimetrically, for the determination of urinary potassium, were also tried but were found unsatisfactory.

Analyses were also carried out on 10-ml. samples of stool suspension after dry ashing, the residue being dissolved in distilled water and 4N sulphuric acid, and made up to 50 ml. of which 4 ml. were used for analysis.

Sulphur.- In urine, the total sulphur was determined gravimetrically by precipitation as barium sulphate (Benedict, 1909); 10-ml. portions of the stool suspension were similarly treated, /

treated, care being needed to avoid loss due to spurting while the suspension was drying.

Phosphorus.- Inorganic phosphorus (96 to 99 per cent. total urinary phosphorus) in serum and urine was determined colorimetrically, by measuring the intensity of the blue colour given with ammonium molybdate (Sumner, 1944). The urine was diluted so that the final solution for estimation contained between 0.01 to 0.2 mg. phosphorus (1/50 dilution being usually satisfactory); 10-ml. samples of the stool suspension were ashed overnight in a muffle furnace, dissolved in the minimum quantity of concentrated hydrochloric acid and then made up to 100 ml. with water. After being diluted 1/10, 10- or 20-ml. portions were used for analysis, thus enabling the total phosphorus content of the stool to be calculated. The colour determinations were made with a Hilger absorptiometer with red filter O.R.2

Carbon Dioxide Combining Power.- The carbon dioxide combining power of blood was estimated manometrically using Van Slyke's apparatus (Van Slyke and Gullen, 1917).

Blood Volume Determinations. (a) Packed cell volume.- Blood was withdrawn by venipuncture and 3 ml. of blood were placed in a tube containing the Wintrobe mixture of potassium and ammonium oxalate. Some of this blood was transferred to a graduated haematocrit tube and spun at 2,500 revolutions per minute for 30 minutes, the remainder of the blood being used for red cell enumeration. No allowance has been made for the plasma trapped in the red cells.

(b) /

(b) Plasma volume.- The method of Gibson and Evans (1937) was adopted. First, 20 ml. blood were withdrawn by venipuncture and then, through the same needle, a known amount of 0.24 per cent. T1824 dye was injected from a syringe calibrated for the 5 ml. mark. After periods of 10 and 30 minutes from the time of the injection of the dye, 15 ml. blood were withdrawn from a vein in the other arm. The blood specimens were allowed to clot. The clot was released and the specimens were then centrifuged at approximately 1000 revolutions per minute for 15 minutes. With a Pasteur pipette the serum was removed and was then again centrifuged for 15 minutes so as to remove any cells. The dye solution (0.24 per cent.) was diluted 1/500. Immediate readings of the colour intensity of the diluted dye solution and the serum samples withdrawn at 0, 10 and 30 minutes were made with a Spekker Photoelectric Absorptiometer, using a red filter O.R. 2 with distilled water as the reference liquid in all cases. Cells of capacity 3.5 ml. were used and the reading obtained with the 10-minute serum sample was used in the calculation:

$$\text{Plasma volume} = \frac{500 \times (\text{calibrated vol. of syringe}) \times (\text{reading of diluted dye solution})}{(\text{reading of serum at 10 minutes}) - (\text{reading of serum at 0 minutes})}$$

Serum was used for these determinations in preference to plasma as there was less likelihood of haemolysis occurring and also because of the necessity of avoiding anticoagulants which might affect the thiocyanate space determinations which were carried out simultaneously.

(c) Blood volume.- The blood volume was calculated from a knowledge of the plasma volume and the packed cell volume, using the /

the following formula:

$$\text{Blood volume} = \frac{\text{Plasma volume x 100}}{(100 - \text{packed cell volume per 100 ml.})}$$

(d) Extracellular fluid volume (thiocyanate space).- The method of Bowler (1944) was used to determine the thiocyanate space. These estimations were usually made at the same time as plasma volume determinations and, after the injection of the T1824 solution, a known amount of 5 per cent. sodium thiocyanate solution was injected from another syringe, calibrated for the 10 ml. mark. After precipitation of the serum proteins with 20 per cent. trichloracetic acid, ferric nitrate reagent was added to the filtrates and immediate readings of the red colour produced were made, using a Spekker Photoelectric Absorptiometer and a blue filter O.B.2. Readings were also made for the reagent solutions and for a 1/1000 dilution of the injected sodium thiocyanate solution. The thiocyanate space was calculated as follows:

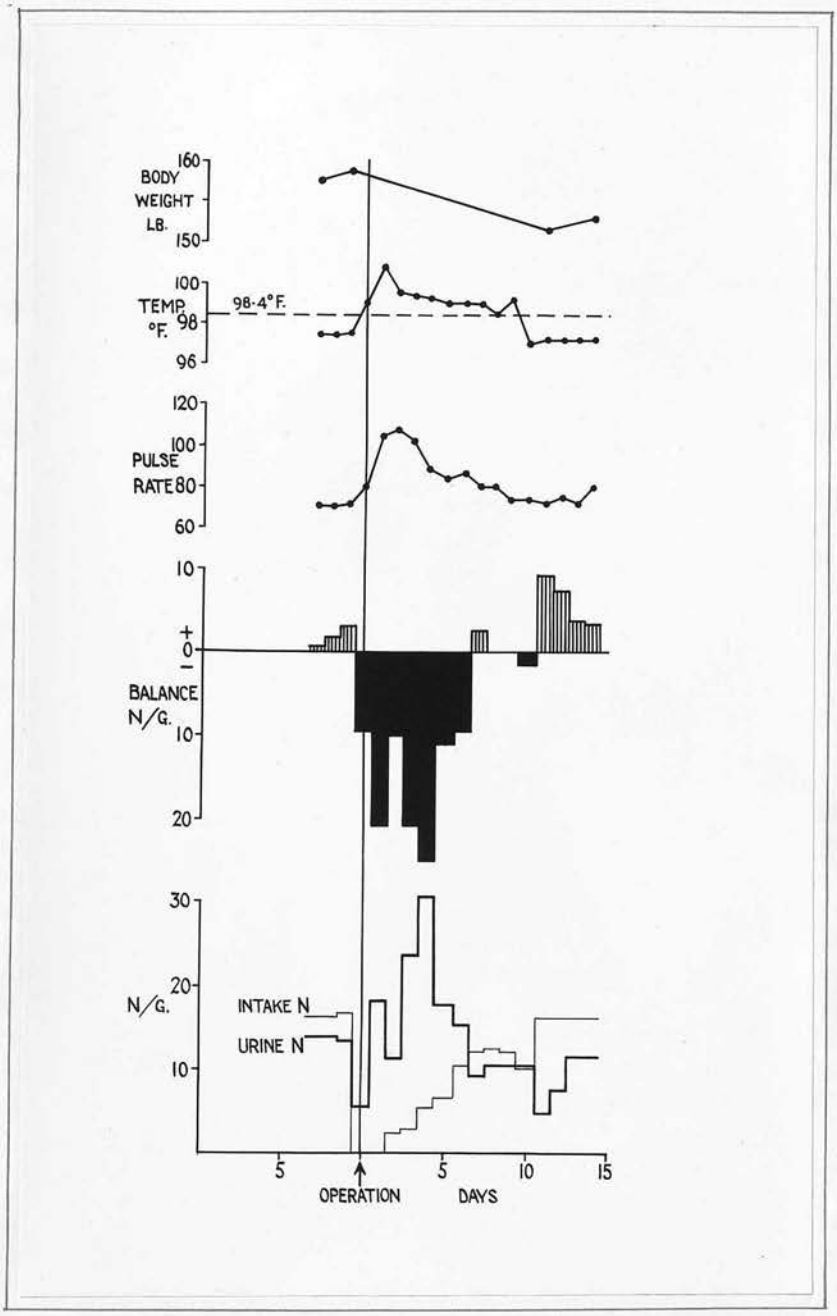
$$\text{Thiocyanate space} = \frac{1000 \text{ x (calibrated volume of syringe) x (reading of thiocyanate solution - reading of reagent blank)}}{\text{(reading of serum at 30 minutes) - (reading of serum at 0 minutes)}}$$

The faint red colour given by the ferric thiocyanate, resulting from the treated serum, gave maximum readings on the Spekker scale of about 0.1. Variations of 0.002 in the denominator and numerator reading may cause variations in the calculated thiocyanate space of 1000 ml., regardless of any errors arising from loss during the injection. Alterations in the thiocyanate space of less than 1000 ml. are therefore not significant.

CONTROLS

In spite of familiarity with such descriptions of the metabolic disturbances after injury and operation as those of Cuthbertson (1935-6), it seemed desirable to define these disturbances as they occurred after an operation such as partial gastrectomy for peptic ulceration. Indeed, if there was any substance in the suggestions that underlying the "catabolic phase" there might be a specific pattern of amino acid requirements and excretion for different types of injury, it was essential to establish the gross excretion and metabolic pattern to be commonly expected after partial gastrectomy. This normal pattern has been built up from the results of a number of balance studies, some of which have been included in other groups of this report. It is well exemplified by Case 1. In the first group, as well as this typical case others are quoted to exhibit the effects of food restriction after operation and of operations other than partial gastrectomy. After operation, differences in metabolism were observed which appeared to be related to food and calorie intake; it was therefore necessary to try to define the relative effects of starvation and operative injury. Originally it was planned also to carry out control observations on the effects of anaesthesia, either by subjecting volunteers to anaesthesia in addition to regulated starvation, or by nitrogen balance studies carried out on patients with peripheral vascular disease of the lower limbs, whose vascular function was to be studied during spinal analgesia. For various reasons, these additional investigations on the effects of anaesthesia had to be abandoned.

CHART I



Case 1.- To show typical response to partial gastrectomy in a fit subject, including increase in urinary nitrogen excretion (maximum on third and fourth days), rise in body temperature and in pulse rate.

Group 1. Control Patients Submitted to Operation

Nine patients are included in this group. Of these, two with chronic duodenal ulcers, one with a chronic gastric and one with a stomal ulcer were submitted to operations for partial gastrectomy and gastro-jejunostomy; on another man with a stomal ulcer vagotomy was performed. Lumbar sympathectomy was done for causalgia of the foot in one patient, and splanchnicectomy for hypertension in another patient. One patient was submitted to subtrochanteric osteotomy of the femur for unilateral arthritis of the hip joint. An extensive spinal fusion and bone grafting were carried out on a wasted youth, 18 years of age. These patients exhibit a number of interesting features and will be discussed in some detail.

Case 1 (Table 1, Chart I).- J.M., aged 35 years. Tram driver. For six years had had pain and flatulence after meals; perforation of duodenal ulcer 11 months previously; had been gaining weight for several months. On admission: a fit-looking man in good condition. At laparotomy: chronic duodenal ulcer; partial gastrectomy; gastro-jejunostomy. On day after operation, pain in chest but no physical signs; temperature raised to 99.6°F. for three days. Drip infusion and gastric suction for three days after operation. Superficial phlebitis following infusion. Up on 11th day, home on 16th day after operation.

In nitrogen equilibrium before operation on 100 g. protein, 2500 calories. Some urine lost on 7th post-operative day, but true positive balance not achieved until 10th day, after four days' intake of more than 70 g. protein and 2000 calories. Maximum urine nitrogen excretion 30 g. on 4th day after operation on intake of 5 g. nitrogen. Plasma albumin fell from 4.2 to 3.6 g. per 100 ml. 14 days after operation, globulin rising from 1.55 to 2.95 g. per 100 ml. No other significant changes.

This case exhibits a typical response to gastrectomy in a fit, well-nourished man. There was some prolongation of negative nitrogen balance perhaps due to the superficial phlebitis following /

following drip infusion. The marked positive balance on the 11th and 12th days is due to suspiciously low urinary nitrogen excretions on these days.

Case 2 (Table 2).- J.T., aged 35 years. Linoleum worker. Duodenal ulcer for many years; gastro-enterostomy 10 years ago. Six years and five years ago ulcer perforated, site not recorded. One month before admission severe haematemesis on way home after reporting at hospital. Appetite good; bowels regular; was on diet for ulcer; had not recently lost weight. Radiological examination showed functioning gastro-enterostomy with ulcer crater at stoma. At laparotomy: stomal ulcer; previous anastomosis undone; resection of jejunum with end-to-end anastomosis; partial gastrectomy; gastro-jejunostomy. Drip and suction for three days.

The dietary and urine nitrogen varied before operation but he was approaching equilibrium. Maximum urine nitrogen 17.02 g. on day after operation presumably related to large urine volume on this day, thereafter remained in region of 12.0 g. per day for four days, and later showed signs of stabilising below this level on an intake of 67 g. protein and 1800 calories. Nitrogen equilibrium reached on 8th day if the large stool on this day is spread over the preceding seven blank days.

All this evidence suggests that this man was accustomed to an intake of rather less than 70 g. protein with about 1800 calories, and he exhibited an unmistakable but mild catabolic response to an operation of considerable severity and duration.

Case 3 (Table 3).- W.L., aged 65 years. Fisherman. Perforated duodenal ulcer 18 years ago; hernia operation a year later. Three months ago had vomited blackish-brown watery material after every meal for a week; ate little food; no pain. One month later, for two days, had epigastric pain and passed black stools. Further attack of pain for two or three days a month later, just before admission. When no pain, had eaten well and continued at work. On admission: looked fit but thin. Radiological evidence of very large gastric ulcer on lesser curvature of pyloric antrum. At laparotomy: large gastric ulcer; partial gastrectomy; gastro-jejunostomy; only complication thrombosis of drip vein. Intravenous infusion and gastric suction for three days, 12 g. chloride (as NaCl) removed by suction in 48 hours.

Pre-operative /

Pre-operative period too short for assessment of adequacy of diet for nitrogen equilibrium. After operation maximum urine nitrogen excretion was 16.19 g. on 4th day on an intake of 5.78 g. of nitrogen, not a marked catabolic phase. Intake rose to 60 g. protein and 1700 calories by 6th day, but remained at this level for five days before being increased to 80 g. protein and more than 2000 calories; during this time urine nitrogen was in region of 12.0 to 13.0 g.

The prolonged negative nitrogen balance was due rather to continued inadequacy of the food intake than to any increase in catabolism. This man was probably depleted to some degree before operation and therefore did not exhibit a typical increase in urine nitrogen excretion after operation.

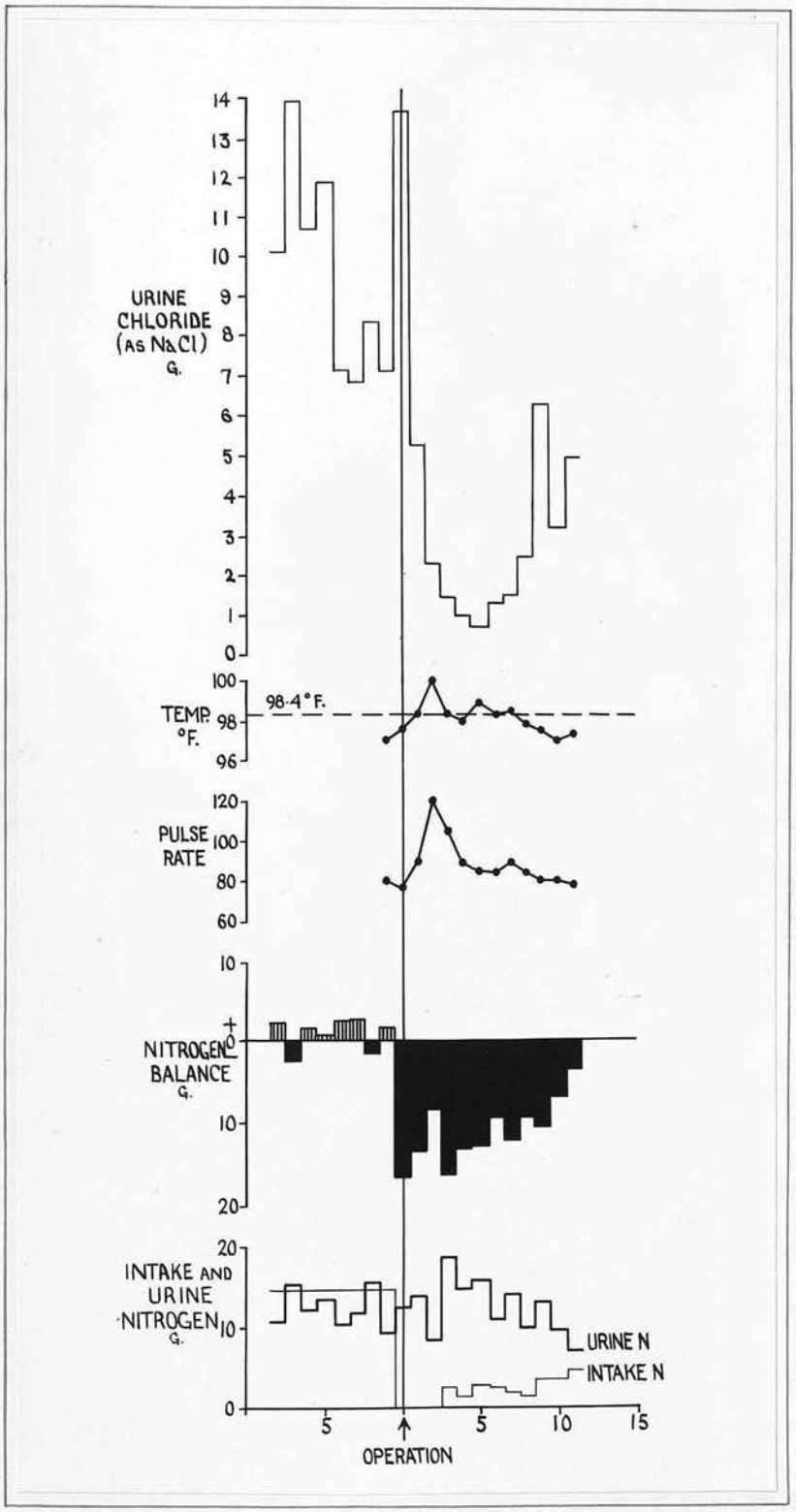
Case 4 (Table 4).- W.L., aged 33 years. Miner. Fourteen years ago began to have pain in abdomen when hungry; intermittent attacks of pain since then which are not now related to food and have been constant during past year. Seven weeks' medical treatment 10 months ago and three months ago, and while in convalescent home before admission here was free of pain and gaining weight. On examination: pale, poorly developed man in fair condition. Chronic duodenal ulcer shown on radiological examination. At laparotomy: chronic duodenal ulcer; partial gastrectomy; gastro-jejunostomy. Intravenous drip and gastric suction for four days. Temperature elevated for a week after operation. Blood chloride rose from 396 mg. on 3rd day to 460 mg. per 100 ml. on 7th day, and CO_2 combining power fell from 75 to 56 volumes per 100 ml.

In nitrogen equilibrium before operation on 80 g. protein and 2385 calories; feeding begun early but slow increase in diet after operation; nitrogen equilibrium achieved on 75 g. protein and 2000 calories 11 days after operation. Urine nitrogen not much raised after operation; maximum on 3rd day on intake of 4.0 g. nitrogen; urine nitrogen fell towards end of 1st week but rose again in 2nd week.

This man exhibited a poor catabolic response; he was probably depleted before admission, but after operation the negative nitrogen balance was prolonged by inadequate feeding.

Case /

CHART II



Case 5.- To show nitrogen intake and urinary nitrogen and chloride output during severe restriction of food after vagotomy.

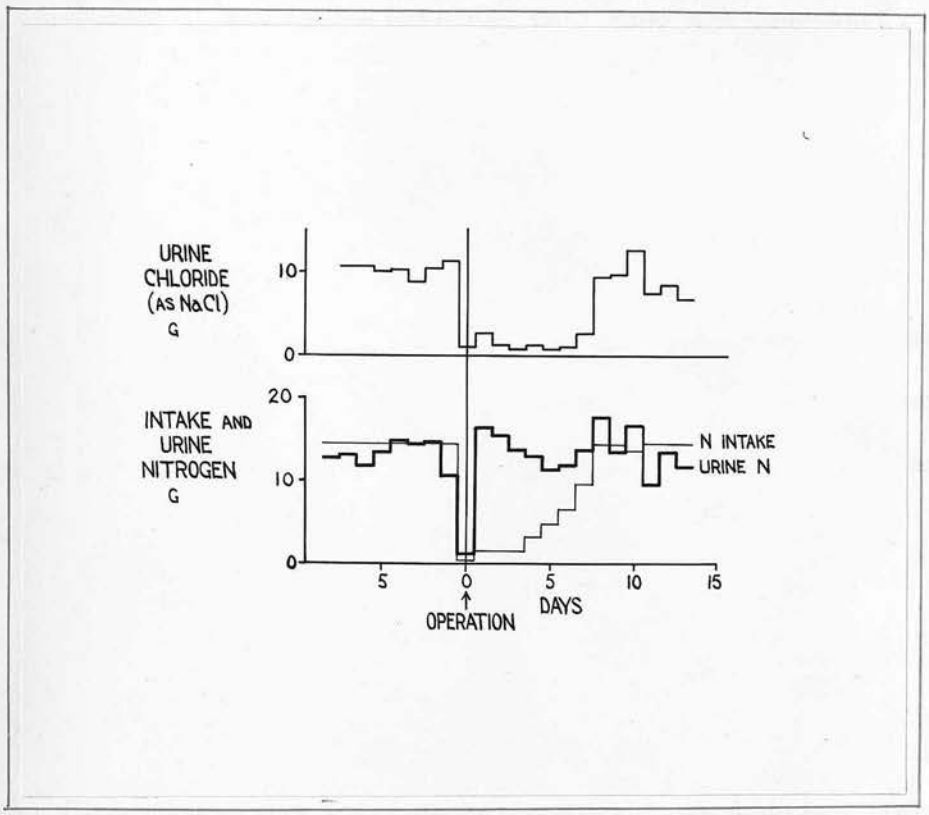
Case 5 (Table 5, Chart II).- J.K., aged 60 years. Thirty-five years ago perforated duodenal ulcer closed by operation, thereafter intermittent pain for 16 years when the ulcer perforated again. After three years' relief following this operation, ulcer perforated for third time, when perforation was closed and posterior gastro-enterostomy also done. Patient remained well until two years ago when pain began to recur; relieved by food and alkalis until recently. No loss of weight; on two occasions stools were black after acute pain. On admission: fit, stocky, heavily built man who does not look as though he had lost weight. On radiological examination stoma of gastro-enterostomy seen to function well but there was tenderness of stoma suggestive of ulcer; duodenum deformed but no active ulcer; good gastric emptying. At laparotomy: many adhesions; old duodenal and active stomal ulceration; vagotomy. Drip and gastric suction for three days. Diet increased at half usual rate; bowels moved spontaneously on 6th day. Some bronchitis; mild rise in temperature on second evening.

In nitrogen equilibrium before operation on 90 g. protein and 2500 calories. After operation, after two days' starvation, very slow increase in diet. On 11th day after operation still in negative nitrogen balance on 27.0 g. protein (4.4 g. nitrogen) and 517 calories. Maximum urine nitrogen 18.5 g. on 3rd day after operation. Urine nitrogen not related to urine volume.

The urine nitrogen in this exceptional case remained high on the day of operation and the next day, and then fell. There was then a rise for three days followed by a fall. This suggests that the catabolic phase really occurred on the 3rd, 4th and 5th days and that the nitrogen excretion on the day of operation and the next day is related rather to the pre-operative intake than to the operation and its consequences. There was a negative balance of 134 g. nitrogen from operation to the 11th day. There was no change in plasma albumin or globulin concentration and only a small rise in blood non-protein nitrogen concentration. The very slow increase in food intake was believed to be necessary because of the great reduction in gastric motility due to the vagotomy.

Case /

CHART III



Case 7.- To show increase in urinary nitrogen excretion and reduction in urinary chloride excretion after splanchnicectomy.

Case 6 (Table 6).- W.McI., aged 45 years. Railway labourer. Six years ago was wounded in left chest and right thigh. Made good recovery except for disabling causalgia of right foot. Operation: right lumbar sympathectomy. Mild rise of temperature in first three evenings, otherwise uneventful course. Lost 6 lb. in weight in first seven days after operation; no drip infusion.

Before operation in positive nitrogen balance of 1.0 to 5.0 g. per day on 90 g. protein (14.56 g. nitrogen) and 2500 calories. Urine nitrogen excretion of day of operation and next day pooled, no urine being passed within 24 hours of operation; urine nitrogen probably high on day after operation. The urine nitrogen fell from pre-operative level but was comparable to the unoperated controls starved in the same way. Urine nitrogen rose as food intake was increased; nitrogen equilibrium reached about 5th to 7th day after operation on 70 g. protein (10.48 g. nitrogen) and 1700 calories.

The tissue injury in this operation is of only mild or moderate severity and is comparable to that in appendicectomy or herniotomy. It is difficult to explain the absence after operation of an increase in the urinary nitrogen excretion and the loss of 6 lb. in weight.

Case 7 (Table 7, Chart III).- D.H., aged 36 years. Motor engineer. After a sudden impairment of vision while reading, hypertension diagnosed following discovery of albuminuric retinitis. Had some headache but was fit for heavy work. On admission: very well nourished, fat but not flabby muscular man; had lost 10 lb. in weight while being investigated in another hospital. Operation: left splanchnicectomy. After operation pleural effusion on left side for about 12 days. Fourteen days after first operation died during right splanchnicectomy. Cause of death intrapleural bleeding, collapse of left lung, respiratory embarrassment, circulatory failure.

In nitrogen equilibrium before operation on 90 g. protein and 2500 calories. Maximum urine nitrogen 16.32 g. on day after operation; thereafter gradually fell but rose again as intake increased to 90 g. protein. Intake uncertain on last three days before second operation as he did not feel very hungry; uneaten food was not estimated. Plasma albumin fell and globulin rose by 6th day but change reversed by 13th day. Packed cell volume fell from 57 per cent. before first operation to 41 per cent. on 10th day; creatinine consistently rose from 0.9 mg. to 1.7 mg. per 100 ml.

After /

After operation this man exhibited an obvious but not marked increase in urinary nitrogen excretion which persisted throughout the post-operative period and latterly was probably related to the pleural effusion. He was being studied in order to observe what happened after the second operation which would have resulted in bilateral renal and adrenal sympathetic denervation. It has not yet been possible to observe a similarly suitable male patient in good condition.

Case 8 (Table 8).- J.S., aged 62 years. Fruit merchant. For three years pain in right hip and in back. Increasing pain and disability; clinical and radiological evidence of severe osteo-arthritis of right hip. Fourteen months ago manipulation under pentothal anaesthesia. On admission: healthy man in good condition; looked younger than his age. Operation: subtrochanteric osteotomy right femur under general anaesthesia; immediate fixation in plaster. No rise in temperature after operation; no complications.

In nitrogen equilibrium before operation on 80 g. protein and 1960 calories. Maximum urine nitrogen excretion 19.92 g. on 5th day. Apart from this peak, slight evidence of catabolic phase, but prolonged small negative nitrogen balance from 5th to 14th days after food had reached an adequate level (above 70 g. protein and 1800 calories).

The short duration of the "catabolic" increase in urinary nitrogen excretion after operation is perhaps related rather to the small degree of operative injury and immediate immobilisation, than to previous protein depletion. The failure to achieve nitrogen equilibrium until the 14th day may be related to the wasting of the right lower limb which was immobilised in plaster after the operation.

Case /

Case 9 (Table 9).- A.M., aged 17 years. Brewery labourer. Congenital dysplasia of spine and ribs; severe mid-thoracic kyphoscoliosis with marked angulation causing cord compression and paraparesis. Ten months ago, antero-lateral decompression of spinal cord, followed by skeletal traction through skull and tibiae on anterior plaster shell. Admitted for stabilisation of spine. On admission: thin, sallow youth with severe wasting of whole body. When turned on to anterior shell before operation there was severe upset, dizziness and vomiting; operation delayed.
Operation: bilateral spinal fusion from 2nd to 9th thoracic vertebrae; grafts derived from tibiae; blood loss moderate; two pints blood given after operation.

In nitrogen equilibrium before operation on over 60 g. protein and 1700 calories; average urine nitrogen excretion 8.6 g. per day. After operation, urine nitrogen fell during first four days and then rose to a level approximately that of intake nitrogen level; from 11th day onwards nitrogen equilibrium achieved. Food intake varied a good deal, 70 g. protein and 1700 calories reached on 6th day; at end of balance study 2 to 3 g. nitrogen per day retained on 60 g. protein and 1780 calories. Wounds healed normally; bones fused satisfactorily.

This was a wasted youth still in growing period with extensive bony anomaly of spine who was submitted to severe and extensive operations on his bones. After operation there was a reduction rather than an increase in urine nitrogen excretion. There was no rise in temperature except once to 99°F., and no complications.

Comment

In the present series it was found that after partial gastrectomy in well-nourished men there was an increase in the urinary nitrogen excretion which lasted for from five to eight days, the maximum loss of urine nitrogen being on the second to fifth days. Coupled with this increased output of nitrogen, there was a reduction in the intake of nitrogen as protein food which was most marked during the first week after operation, but might /

might be severe for up to 14 days. The result of these two factors was a period of negative nitrogen balance lasting about five to eight days or more after operation, the minimum period of five to six days being found in those patients whose protein and caloric intake was rapidly increased and reached an adequate level within five or six days of operation; the duration of negative nitrogen balance beyond the minimum, while related closely to protein and caloric intake, appeared to be dependent to some extent also on complications, such as wound infection, broncho-pneumonia and other pulmonary disturbances, superficial phlebitis, etc. The most consistent changes in the blood analyses were reduction in packed cell volume, red cell count and haemoglobin concentration. Elevation of serum globulin and reduction in albumin concentration were common but not invariable changes (Table 63).

There is an important exception to this sequence. Instead of the usual big increase in urine nitrogen on the second day or so after operation, there may be no increase or perhaps an additional output of only one or two grams of nitrogen per day; the so-called catabolic increase either does not occur or occurs only to a slight extent. This minimal reaction was observed in several patients submitted to gastrectomy and to other procedures. When related to severe operative trauma, this small nitrogen increase is suggestive of severe depletion of protein tissue, but when the injury is of mild degree it may be due to insufficient stimulus to protein destruction. It seems important to recognise also that a combination of these two factors may be the basis of a slight response to operation in this respect.

Some /

Some of these features are exhibited by Case 1 (Table 1, Chart I), a fit man in good condition who was in nitrogen equilibrium before operation on an intake of 104 g. protein and 2587 calories per day. The maximum urine nitrogen excretion (30.0 g.) occurred on the fourth day and negative nitrogen balance lasted for six days after operation; by this time the daily urine nitrogen was in the region of 10.0 g. per day and the intake of nitrogen was 11.0 g. or more, with 1850 calories.

Case 2 (Table 2) is an example of a very severe operation for stomal ulcer producing only a moderate increase in urinary nitrogen excretion in a man whose diet had been restricted before operation but who had not recently lost weight. A large amount of nitrogen was lost in the stools before operation, probably because of the activity of his stomal ulcer. By the eighth day, nitrogen equilibrium was regained on 67 g. protein and 1800 calories. After operation there was a loss of weight of only 3 lb.

In Cases 3 and 4 (Tables 3 and 4), there was a delay in restoring the intake of food. In Case 3 there was evidence suggestive of some depletion before operation, and urinary nitrogen excretion did not increase markedly after operation. Feeding was started on the day after operation but was increased only slowly, and the diet remained at 60 g. protein (9.6 g. nitrogen) and 1680 calories from the sixth to the tenth days. Following a further increase in diet, equilibrium was soon achieved. There was a large loss of nitrogen in the stools. The steady loss of about 12.0 g. of nitrogen in the urine from the sixth day onwards is unexplained, unless it represents catabolism /

catabolism of protein because of an inadequate food intake. In Case 4, feeding was again started on the day after operation, but increased slowly and reached 75 g. protein (12 g. nitrogen) and 2000 calories only on the eleventh day after operation. There was a smaller increase in urinary nitrogen than in Case 3, in spite of the rise of body temperature during the first five days. The negative nitrogen balance after operation was interrupted by a reduction in urine nitrogen on the sixth day which seemed to indicate the end of the catabolic phase.

After vagotomy for stomal ulceration following gastro-enterostomy in Case 5 (Table 5, Chart II), severe restriction of food and fluid intake by mouth was enforced for fear of gastric and jejunal stasis and distention. After two days' starvation only small quantities of food were provided. There was a rise in urinary nitrogen excretion on the third, fourth and fifth days. When the study was stopped on the eleventh day after operation, the daily food intake was only 27.5 g. protein and 500 calories and there was still marked negative nitrogen balance. Subsequently the patient was allowed more food and made an excellent recovery. This case exhibits the degree to which negative nitrogen balance may be due to restriction of intake of food, and is in strong contrast to Case 1.

Following right lumbar sympathectomy under spinal analgesia in Case 6 (Table 6), there was a reduction in urine nitrogen excretion to about 9.0 g. per day during the immediate post-operative period, when food intake was also low. There was an increase from the eighth day following the increased food intake. There is little operative injury in this operation, and this

case probably indicates the minimal response to injury in a healthy man. Comparison with subjects of Group 2 makes it clear that there was no true catabolic increase in nitrogen but merely a period of negative nitrogen balance attributable to the reduction in food intake.

In Case 7 (Table 7, Chart III), a left splanchnicectomy was carried out under high spinal analgesia and light general anaesthesia. Although there was a more severe tissue injury than in Case 6, it was considerably less than is involved in partial gastrectomy. After this operation there was a rise in nitrogen excretion and later a slow fall, but excretion exceeded intake for 10 days although the intake reached 90 g. protein and 2500 calories on the eighth day, presumably because of the complication of pleural effusion. Unfortunately this patient died during the second operation.

In spite of a rapid increase in food intake after a subtrochanteric osteotomy of the femur in Case 8 (Table 8), a well-nourished man aged 62 years, there was a negative nitrogen balance due to a small but unusually prolonged increase in urinary nitrogen excretion for 12 days after operation. This is surprising because there were no infective or other complications and the limb was fixed in plaster immediately after operation; it has been ascribed to the wasting of muscle due to immobilisation of one limb in plaster. In Case 9 (Table 9), however, there was a reduction rather than an increase in urine nitrogen excretion after an extensive exposure of a kyphotic thoracic spine, and the insertion of bone grafts taken from the tibiae. This youth was in a very poor physical state, thin and wasted, and appeared to lose little tissue after operation; yet his wounds healed and he made a satisfactory recovery.

Group 2. Control Subjects not Submitted to Operation

Following gastrectomy in the surgical charge in the wards of which these studies were made, it was the usual practice for food intake to conform to a common pattern similar to that shown in Case 1 and Chart I, unless some disturbance compelled modifications. In order to define more clearly that part of the catabolic phase which may be fairly attributed to operative trauma, certain control experiments were done. Four healthy male medical students volunteered to act as subjects, none was actively growing, all were well-nourished though varying widely in physical type, and all were younger than most of the patients submitted to operation.

Case 10 (Tables, 10, 11, 49).- D.P., aged 20 years. Height, 68.5 in. (173.9 cm.). Weight, 158 lb. Short, stocky, thickset, heavily-muscled, very well-nourished; normally ate considerably more than best diet provided during balance studies; keen and active athlete.

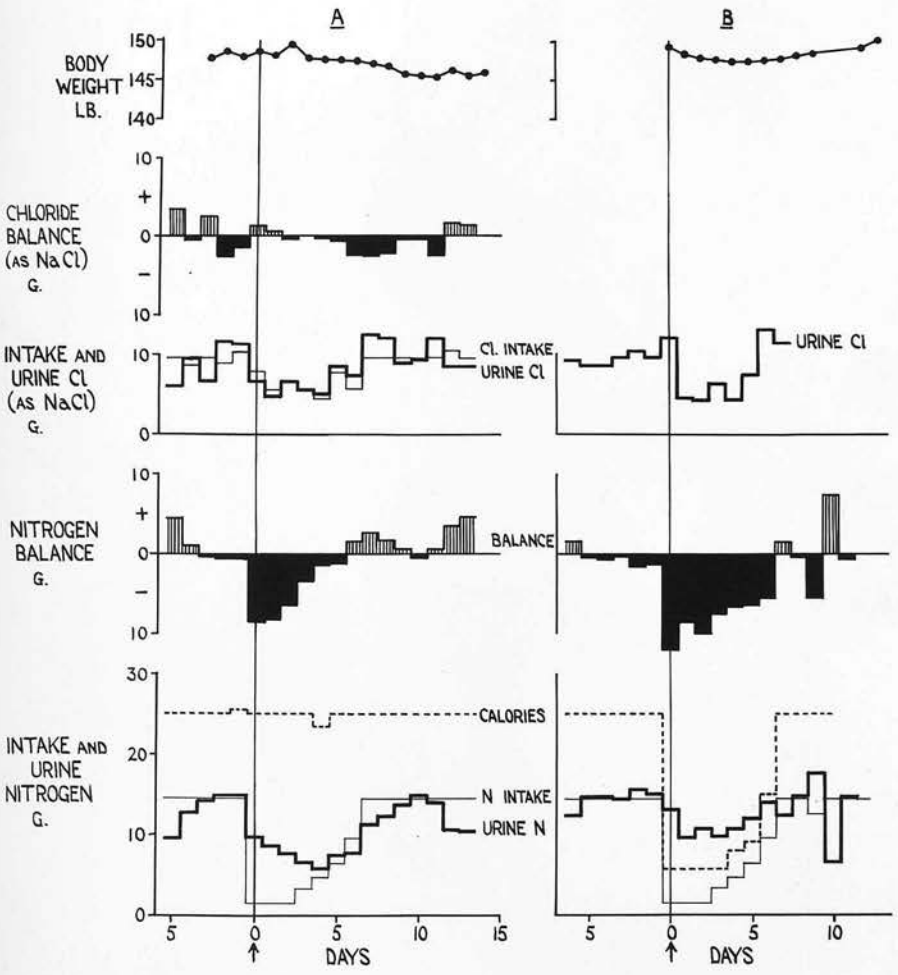
Case 11 (Tables 12, 13, 50; Chart IV).- L.M., aged 19 years. Height, 73 in. (185.5 cm.). Weight, 149 lb. Tall and slim with heavy bones. Normally ate a good deal of carbohydrate.

Case 12 (Table 14).- R.R., aged 20 years. Height, 68 in. (172.7 cm.). Weight, 120 lb. Rather lightly built; not a big eater.

Case 13 (Tables 15, 51).- A.M., aged 20 years. Height, 69 in. (175.27 cm.). Weight, 150.6 lb. Thickset but not as heavily muscled as Case 12 and taller; good appetite and ate well but not largely.

In one experiment (A) (using Cases 10, 11 and 13), the caloric intake was maintained at 2500 per day throughout; an initial protein intake of 90 g. (14.5 g. nitrogen) per day was reduced to 10 g. protein (1.6 g. nitrogen) on the day of hypothetical /

CHART IV

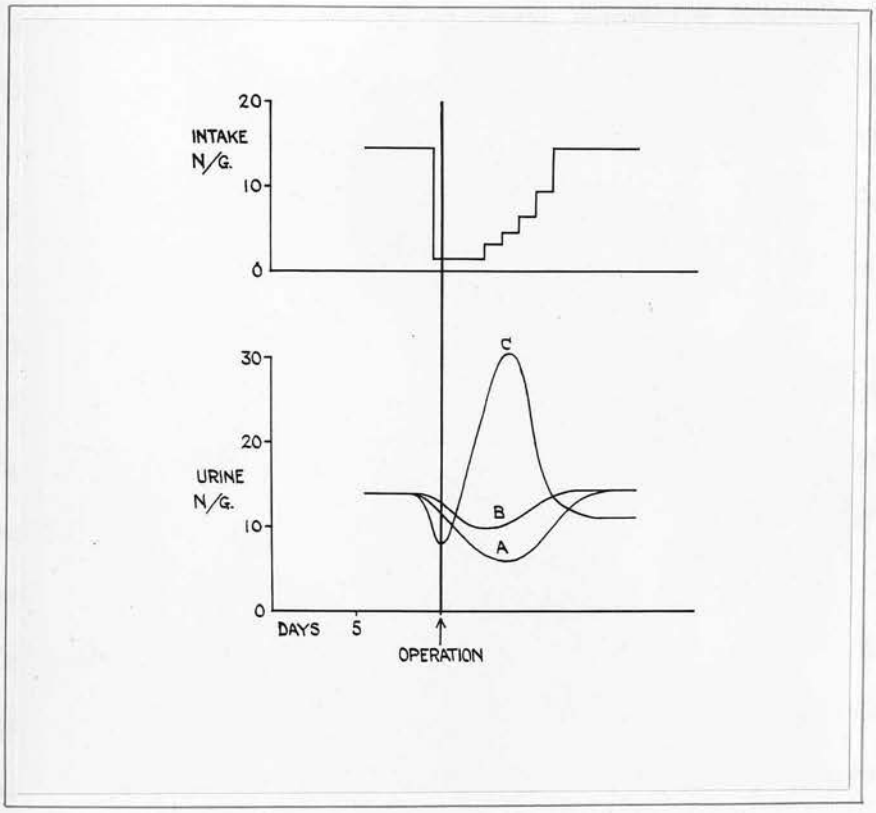


Case 11.- To show the effect of restriction at (A) of protein, and at (B) of protein and calories, on urinary nitrogen and chloride excretion and on body weight in a normal subject.

hypothetical operation and for the succeeding two days; this was done rather than complete starvation of protein to make the experiment less rigorous and unpleasant and also to allow greater variety and palatability in the supply of carbohydrate. From the fourth day onwards protein intake was increased as closely as possible at the same rate as in Case 1. A somewhat higher level of both protein and caloric intake was achieved and maintained regularly in the controls than in many of the patients after operation. In the other experiment (B), using Cases 10, 11 and 12, the preliminary period was similar but at the same time as the protein restriction, caloric intake also was reduced to 500 per day and maintained at this level for three days, when calories were increased step by step with the protein (at the same rate as before) until the original level of intake was regained. The amount of 500 calories per day was chosen because this is the equivalent of the glucose which might be administered in 2500 ml. 5 per cent. glucose solution or glucose saline solution in a day, 2500 ml. being the commonly accepted maximum desirable daily volume of fluid to be given by the intravenous route. A free but measured daily intake of water was allowed. Activity was limited only during the period of the fast when they spent most of the day in bed but got up to defaecate. After this, activity was gradually returned to normal.

The results of both experiments were fairly constant in the groups, and those of Case 11 are shown in Chart IV. When both calories and protein were restricted, the urine nitrogen fell from the previous level of 13.0 to 14.0 g. per day to about 8.0 to 10.0 g. per day, but rose again towards the initial level as /

CHART V



To show the three levels of urinary nitrogen excretion on the same intake of protein, but at (A) with calories maintained at 2500 per day, at (B) calories 500 only per day, and at (C) calories 500 per day plus operation for partial gastrectomy.

as food intake was increased from the third day onwards. When protein alone was restricted, there was a more marked reduction in urinary nitrogen excretion to about 5.0 or 6.0 g. per day. In one case the lowest daily quantity of nitrogen was excreted after protein intake had been increased. In the other cases, as protein intake was increased, there was a gradual and almost equivalent increase in urinary nitrogen excretion towards the initial levels before starvation. In no case in either experiment was there an increase in urinary nitrogen above the preliminary daily quantities. In both groups on starvation there was a reduction in urinary nitrogen excretion which was greater when the caloric intake was maintained at 2500 per day.

In Chart V the urinary nitrogen excretion is shown before and after gastrectomy in Case 1 and during the two kinds of starvation in Case 11. It is clear that in either kind of starvation there was a reduction at a time when partial gastrectomy combined with starvation for protein and calories caused an increase in urinary nitrogen excretion. The maintenance of a calorie intake of 2500 per day appears to prevent the destruction of body protein containing up to 5.0 g. nitrogen per day. It is emphasised that the most important feature so far as the present investigation is concerned is the quantity of nitrogen excreted in the urine; this is a closer and clearer index of nitrogen metabolism than nitrogen balance, for the latter is affected to a larger degree by the nitrogen intake. There was no significant alteration in blood chemistry (Table 63).

Comment /

Comment

These observations on starvation and on the effects of operative injury are not original but in their close resemblance to similar findings in the well-known and classic researches of the past they helped to establish the validity of the methods of the present study. They confirm Cuthbertson's findings (1932, 1935) that there is an increase in urinary nitrogen excretion following injury. He found that after injuries to bones or other accidental injuries there was a rise in urinary nitrogen excretion which might last for 10 days or more. The maximum daily excretion which might exceed 23.0 g. nitrogen, occurred usually between the fourth to eighth days; after osteotomy, however, the maximum excretion might occur earlier, usually between the second and fourth days, and the total excretion was less than after accidental injuries. In the present series, the day of maximum urinary nitrogen output was usually between the second and fifth days after operation, and there was an increased output for six to eight days only after operation, except when complications developed.

Discussion

Lusk (1928) defined starvation as deprivation of any or all of the elements of nutrition. He said it was complete only when all the required elements were inadequate. For example, the dog deprived of all food does not starve in this strict sense, for metabolised tissue provides enough water for urine formation and for loss as water vapour in respiration and through the skin.

Nor /

Nor does the dog starve for water when fed only on meat, for this contains enough water when metabolised by the dog to dissolve the products of the animal's total metabolism in the urine. True water hunger in the dog results when dry meat powder mixed with fat is fed; for several days water is withdrawn from the tissues, chiefly the muscles, but then the flow of digestive secretions diminishes and the food is regularly vomited and food as well as water starvation results. Similar definition of the conditions must be aimed at in studying metabolic changes in man.

In the early days of a fast, two factors control the amount of protein catabolised (Lusk). The first is the glycogen content of the individual. Prausnitz (1892) fasted 15 normal subjects for 60 hours and found that there was less nitrogen in the urine from 12 to 36 hours than in that from 36 to 60 hours; this he claimed was due to the reduction of protein breakdown in the first 24 hours of the fast by the utilisation of glycogen. Benedict (1907) believed that up to 5.0 g. nitrogen was spared by glycogen in the first day of starvation. The second factor is the quantity of protein which has been ingested in the period before the fast. This was first shown for the dog by Voit (1866, 1881) who found a direct relation between the urinary nitrogen excretion and the protein intake in the period immediately before fasting; during the first five or six days there was a gradual fall in nitrogen output to a fairly constant daily quantity.

This has been amply confirmed in man in a normal subject on a protein-free diet, which provides sufficient calories to prevent the use of protein tissue of the body for energy requirements. /

requirements. The urinary nitrogen falls very rapidly in the first three to five days. There is then a slow further reduction to a minimum reached after a varying period, the total amount of nitrogen excreted in this process being related to the previous protein intake (Thomas, 1910; Wilson, 1931). Thomas also noticed that, after a period on a protein-free diet, an adequate intake of protein resulted in nitrogen retention; this retained nitrogen was given up only very slowly when a protein-free diet was resumed. He therefore suggested that, when protein is presented to a protein-depleted subject, it is retained in the reverse order to that in which protein was lost during deprivation. An alternative explanation based on the law of mass action might be that the rate of loss depends on the total mass available; the more complete the replenishment, the less true is Thomas's observation on the rate of secondary loss. Martin and Robison (1922) also observed that the nitrogen excretion on a protein-free diet decreases in a regular manner, and found that the logarithmic curve of the daily differences in nitrogen excretion was a straight line; they concluded that the daily excretion of nitrogen was proportional to the amount remaining in the body. Lusk quoted a fast of long duration in a dog in which, in the first four days, the nitrogen loss per day was 6.23 g. or 0.23 g. per kg. In the last four days of a fast of 117 days on 700 g. of water per day, the daily nitrogen loss was 2.44 g. or 0.23 g. per kg. The body weight fell from 26.3 kg. to 9.76 kg. Again the law of mass action applies.

In the present series, in the patients submitted to operation there was often a marked reduction in urinary nitrogen excretion /

excretion on the day after operation, as well as on the day of operation (this being probably chiefly due to lack of urine formation). No such sharp fall in nitrogen excretion occurred after starvation either of protein or of protein and calories, except in Case 10, Experiment B, and Case 13, Experiment A. It was not observed in Case 14. In all these control subjects carbohydrate and fat equivalent to 500 or 2500 calories were being provided. There is no sign, except in Case 10, Experiment B, of the increase in nitrogen output in the second half of a 60-hour fast described by Prausnitz. To spare as much as 5.0 g. nitrogen required 2000calories in the form of glucose and fat in these subjects. If Benedict's belief is true, that 5.0 g. nitrogen are spared by glycogen in the first day of starvation, then very large quantities of glycogen must be mobilised. Another explanation may be that the conditions in the present experiments are not sufficiently similar to those of Benedict and Prausnitz. There remains to be explained the difference in nitrogen excretion in the first two days after operation and after simple restriction of diet to a similar degree, but without the intravenous infusions of glucose solution, saline or blood which followed the majority of the operations in this series. This reduction, noted also by Cuthbertson (1932), Howard (1944) and Peters (1944), seems to be as essential a part of the disturbance due to operation as is the later increase in nitrogen output. It might be explicable on the grounds that the nitrogen is in part related to the previous day's intake, and that after operation there is also a disturbance of renal function which does not occur in simple starvation, unless the water /

water intake, as well as that of protein, is changed.

Rubner (1883) showed that if enough carbohydrate was provided, the protein metabolism of the fasting dog could be reduced until only 4 per cent. of the total calories were derived from protein. In prolonged starvation, there may be, as Rubner (1911) suggested, a further application of the law of mass action; the less the total mass of protein remaining the less there will be consumed no matter what the diet; also metabolism as a whole, and not merely that of protein, becomes diminished in intensity. To some extent the property of sparing protein is vested in carbohydrate, for example Landergren (1903) showed that although on a diet composed of fat and carbohydrate, the daily urinary nitrogen excretion was reduced to 4.0 g. per day; if fat alone was provided, the daily nitrogen excretion was the same, 10.0 g. per day, as in starvation of all food. Ample carbohydrate was provided in the present studies and for the diet of the patients after operation carbohydrate was always in excess of fat.

In the conduct of experiments on protein metabolism it is therefore essential that certain conditions be fulfilled. The total daily intakes of protein, fat and carbohydrate must be individually recorded throughout. The preliminary period before operation or other serious disturbance should be long enough to enable an accurate estimate of the level of protein metabolism to be made. The length of the periods at the different rates of intake also should be as long as possible. These last two conditions are particularly difficult to fulfil and more so in the case of men than women. The patients who submitted /

submitted to study in the present investigation were all men admitted to hospital for necessary treatment, and they all wanted to leave as soon as they could. The additional stay of a week before operation imposed an important financial burden on these men and their families and relations in loss of earnings, additional expenses for fares, etc. In most cases the studies covered a period of five or more days before operation and 14 days after operation. This period of study has limited the scope of the observations especially after operation; it has the important advantages, however, that, first, it includes a pre-operative period from which some idea can be gained of the basal level of protein metabolism for any particular individual, and, secondly, it includes also the day of operation and the whole of the next week. It is unfortunate that many of the reports concerning post-operative protein metabolism that have been published do not include either the pre-operative period or the first few days after operation. This objection applies with rather less force to the studies of accidental injuries in well-nourished, previously normal, subjects, and did not prevent Cuthbertson and others from making fundamental observations. It is important, however, in relation to claims to have abolished or prevented the "catabolic phase" in patients who previously, for months or years, have suffered from severe upper gastro-intestinal disease and have for various reasons restricted their food intake.

Comparison of the data from a typical subject submitted to gastrectomy with one of Cuthbertson's patients with accidental fractures, shows certain differences. After gastrectomy, there

was /

was a smaller fluid intake, other than by the intravenous route, and a more prolonged reduction in urine volume, but urinary nitrogen excretion rises much earlier, in spite of the diminished urinary volume, than after fractures. Cuthbertson found a relative or absolute anuria, occasionally lasting for 24 hours followed by a retention of water for several days after fractures. There was then a compensatory increase in urine volume, which usually occurred after the nitrogen excretion had reached a maximum. It was difficult, in his cases, to exclude such complicating factors as variable consumption of water and pulmonary disturbances. In the present cases, intravenous saline and blood transfusions are additional complications which render any but general conclusions undesirable; however, there is evidence of similar retention of water after operation which will be mentioned again later.

When a large number of the present cases and of those which have been previously reported from Canada and the United States of America were studied, it was seen that, in a proportion, nitrogen equilibrium was regained only when and as soon as the intake of protein and calories exceeded 70 g. (11 g. nitrogen) and about 1800 calories. This was especially noticeable when there had been a prolonged period of negative nitrogen balance or when food had been restricted for an unusually long period after operation. It appeared that this order of intake of protein and calories was a critical one for nitrogen equilibrium. Examination of the cases of the present series has shown that while the above statement is in general true, there are a number of patients who achieved nitrogen balance on rather smaller /

smaller intakes of both protein and calories, while others, in the absence of complications, required somewhat larger daily quantities. This is what would be expected from our knowledge of the wide individual variations in protein consumption and excretion. This daily intake of 70 g. protein (11 g. nitrogen) and 1800 calories is the basal requirement for a patient in bed who is not suffering from active inflammation of any kind or from malignant disease. When there is an active inflammatory reaction both protein and caloric requirements increase. There is little information regarding the general metabolic disturbances in malignant disease, although the difficulty of achieving nitrogen equilibrium seems to be well recognised.

The dietary restriction which commonly follows surgical operations varies widely and depends on many factors. It is, however, probably less often conditioned by the ability of the patient to consume food and by his appetite and desire for food than by other factors. That the severity and duration of dietary restriction after operations is often unnecessarily great is evident from some of the cases which have been described.

It was concluded, therefore, that after surgical operations such as gastrectomy, there is an increase in urinary nitrogen excretion which lasts from five to eight days and reaches its maximum between the second and fifth days. There is an associated reduction in food intake and the two disturbances result in a negative nitrogen balance. The duration of the period of negative nitrogen balance could be prolonged by restriction of food intake; it remained to be seen whether a reduction could be effected in the quantity and duration of the increase in urinary nitrogen /

nitrogen excretion.

In the belief that the excess urinary nitrogen was derived from the breakdown of protein tissue, or stores of protein or protein components in the body, it seemed worth while to find out whether this response to injury in man could be modified by variations in the intake of protein and calories before and after surgical operations.

HIGH PROTEIN HIGH CALORIE DIET BEFORE AND AFTER OPERATION

Cuthbertson (1935) reported that the ingestion of diets very rich in first class protein and of high caloric value by persons suffering from fracture of one or more of their long bones as the result of direct violence, resulted in considerable modification of the normal marked loss of body protein. The possible applications of this observation to patients suffering from peptic ulceration seemed to be two: first, that the common dietetic regime imposed after operation in such cases was deficient in both calories and in protein and an increase in the post-operative food intake should be of value if it was tolerable, and, secondly, it might be possible to reduce the post-operative requirements for protein and therefore for calories by abundant consumption of both in the immediate pre-operative period.

The chief object in this group of studies was the observation of the effects of a period of pre-operative high protein high calorie feeding on the general condition of the patients and on the post-operative disturbances. In addition, observations were made on the effect after operation of rapid increase in oral food intake and on the effects before and after operation of oral administration of a casein hydrolysate, pronutrin.

In this group there are five patients and one control subject. Three of the patients were suffering from gastro-jejunal ulceration following previous gastro-jejunostomy for duodenal ulceration; another had a chronic gastric ulcer; and the fifth had a chronic duodenal ulcer. Extensive surgical procedures were necessary in each case, these operations being amongst /

amongst the most severe encountered in this series. The control subject was recovering from popliteal nerve suture carried out three weeks before the balance study was begun, the affected limb having been immobilised in plaster.

Case 14 (Table 16).- R.S., aged 20. Soldier. Injury, while jumping, eight months before admission: lesion of lateral popliteal nerve and rupture of lateral ligament of knee. Balance started 32 days after admission and 22 days after operation on nerve. Balance study began with an intake of 96 g. protein, 2500 calories; after four days 160 g. pronutrin added and two days later total protein raised to 278 g. and calories to 3400 per day. Seven days later diet reduced for one day to 165 g. protein and 1000 calories, and then for two days to 3 g. protein and 500 calories. Thereafter he was fed, as a patient would be after gastrectomy, on routine diet except that in response to his demands for food the intake was increased more rapidly than usual.

He retained a little nitrogen on the first level of intake, but when the protein intake and calories were fully raised, he retained nearly 8.0 g. nitrogen a day. When the nitrogen intake fell after the imaginary operation of the experiment, the urine nitrogen excretion fell also with a delay of only one day to approximately the initial level. The subsequent increase of nitrogen intake was too rapid to allow the urine nitrogen excretion to fall far. There was, however, a striking negative nitrogen balance. Judging by the balance figures, it seemed as if the post-operative catabolic phase was due to starvation. The urine nitrogen level, however, rises in the catabolic phase but does not do so in starvation. In this case, chloride excretion in the urine fell, lagging a little behind the urine nitrogen, and rose again when the food intake once more was near normal. There was no significant change found in the blood chemistry. There was some variation in /

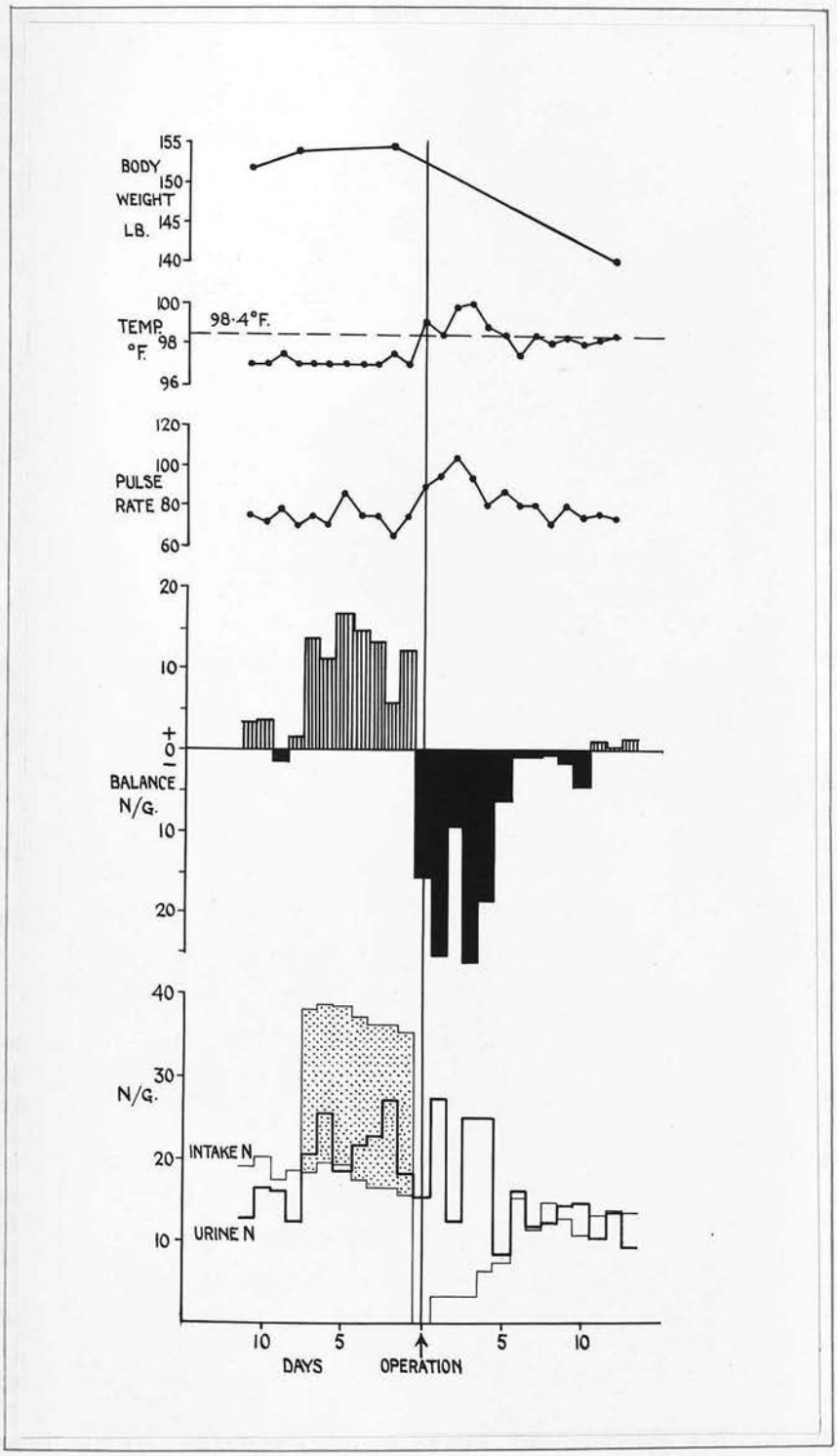
in weight on the high intakes and a steady loss of 10 lb. after the imaginary operation, for which no cause has been ascribed. As he had been in bed and immobilised in plaster for 22 days before the balance study was begun, the loss of weight could hardly be due to these factors. He noticed the loss of flesh himself and was worried by it; subsequently weight was regained, but only slowly.

Case 15 (Tables 17, 65).- R.M., aged 45 years. Commercial traveller. For past six years upper abdominal pain usually after meals. Four years ago gastro-enterostomy for chronic duodenal ulcer; nine months ago perforation of stomal ulcer. Active tuberculous lesion of apex of right lung, sputum negative. Radiological examination showed functioning gastro-jejunostomy with ulcer crater in jejunum distal to stoma and associated jejunitis. Well-nourished but flabby man. At laparotomy: gastro-jejunostomy undone; resection of jejunum with end-to-end anastomosis; three-quarters of stomach stump resected; gastro-jejunostomy. After operation intravenous infusion for three days; thrombosis of internal saphenous vein to mid-thigh on third and fourth days; gastric aspiration for four days; temperature and pulse rate raised for four days. Discharged home on 25th day after operation; laparotomy wound not yet healed.

For over a fortnight before operation a high protein high carbohydrate diet was provided, containing 119 g. protein (19 g. nitrogen) and 2900 calories. Weight rose by 2 lb. during this period and there was also a slight rise in plasma protein concentration. During these two weeks, 49 g. nitrogen were retained, the daily retention increasing in the 2nd week. Stool nitrogen varied from less than 1.0 g. to 3.6 g. per day. After operation oral feeding was begun on the 2nd day and by the 7th day an intake of over 80 g. protein and 1800 calories had been reached, and nitrogen equilibrium was regained. The diet supplied was too abundant for him and he was unable to consume all of it. On the 9th day after operation 160 g. of pronutrin per day were added to the diet and marked positive nitrogen balance followed and lasted as long as the pronutrin was taken; this was, however, for only five days as he was nauseated by the hydrolysate and refused to take any more. After the pronutrin was stopped there was a four-day period of negative nitrogen balance followed once more by positive balance.

After /

CHART VI



Case 16.- To show the effect of a high protein high calorie intake before operation. Dotted area: nitrogen derived from pronutrin.

After operation the urinary nitrogen excretion rose to a maximum of 22.46 g. on the 3rd day but stabilised at about 10 g. per day from the 6th to 8th days. There was another increase as soon as pronutrin was ingested, reaching over 25 g. on the 4th day of this supplementary feeding, but subsiding within three days after the hydrolysate was stopped. There was a gain in weight of just over 2 lb. before operation and a loss of 9 lb. in the 10 days immediately after operation which was not modified by the pronutrin supplement.

Before operation total plasma protein concentration rose. After operation albumin concentration fell while that of globulin rose. There was reduction in packed cell volume, haemoglobin concentration and red cell count after operation (Table 65).

The impression of several observers, and of the patient himself, was that before operation his condition was improved by the high protein high calorie diet, though the objective evidence in support of this impression is slight. The additional attention and fuss contingent upon a nitrogen balance study undoubtedly impressed the patient who was a rather critical and observant man.

Case 16 (Tables 18, 65; Chart VI).- A.S., aged 40 years. Canteen chef. For over 10 years had suffered from abdominal pain. Ten years ago, gastro-jejunostomy. Eight months ago, haematemesis and melaena from bleeding stomal ulcer; treated by laparotomy and gastrotomy. Good recovery, put on 2 st. in weight in six months, but two weeks ago haematemesis after recurrence of pain. On admission, anxious but fit-looking, well-nourished man. Radiological examination showed evidence of stomal ulcer in distal limb of jejunum with jejunitis and deformity of duodenal cap. At laparotomy: stomal ulcer; resection of stoma and adjacent jejunum and three-quarters of stomach; end-to-end anastomosis of jejunum; gastro-jejunostomy. After operation, temperature and pulse rate raised for four days; intravenous infusion and gastric aspiration for three days; up on 14th day; home on 16th day.

In the pre-operative period a diet containing more than 120 g. protein (19 g. nitrogen) and 2600 calories was provided at first, but after four days 160 g. pronutrin were added and this intake of over 280 g. protein (39 g. nitrogen) and 3300 calories was maintained for seven days before /

before operation. During this period faecal nitrogen was about 1.0 g. per day but about 2.0 g. nitrogen per day was lost in the vomitus and gastric washout fluid. Some nitrogen was retained in the initial four days, but the addition of 160 g. pronutrin resulted in a daily retention of 12 g. nitrogen; in the whole pre-operative period, 89 g. nitrogen were retained and there was a gain in weight of 2.7 lb. After operation the food intake was so increased that on the 6th day 97 g. protein (15.2 g. nitrogen) were ingested with 1500 calories; thereafter protein intake fell because as the calories were increased the bulk of the meals was too great for his limited gastric capacity. However, 11 g. nitrogen were taken with over 2200 calories per day from the 8th day onwards. There was nitrogen equilibrium from the 6th day, except on the 9th and 10th days when there were unexplained increases in urinary nitrogen excretion. A large volume of urine containing 15 g. nitrogen was excreted on the day of operation; presumably this was related to the high dietary intake of nitrogen on the day before operation. The maximum urinary nitrogen excretion (27.5 g.) was on the day after operation, but 25 g. were excreted in the urine on each of the 3rd and 4th days and these days are probably the true maximal days rather than the 2nd day, when the high pre-operative protein intake may still have been responsible for some of the large quantity excreted. After operation he lost 14 lb. in weight in 12 days, and in the same period there was a negative nitrogen balance of 82 g.

Apart from the reduction in packed cell volume, haemoglobin concentration and red cell count, there was no significant alteration in the blood analyses after operation (Table 65).

This man thought he had been improved by the pre-operative diet though he seldom ate all he was given and the wastage was even greater after operation. He was a chef and was critical of the quality, nature and service of his food. Some of his criticism was well founded and undoubtedly contributed to improvements in the methods employed in the balance studies. Other observers thought benefit was derived from the abundant pre-operative diet, but little objective support for this impression has been obtained. The increase of food intake after operation was too rapid. At first it was easier to achieve a relatively /

relatively high protein intake than to provide adequate calories because of the bulk of the food necessary; as the total caloric intake was raised, the consumption of protein fell.

Case 17 (Table 19).- T.M., aged 40 years. Bus driver. Abdominal pain for about 20 years. Seventeen years ago, gastro-jejunostomy and appendicectomy; two years later perforated duodenal ulcer followed by subphrenic abscess. Six years later perforated gastric ulcer closed at operation; duodenal ulcer still present. When admitted, was in fair condition; no marked loss of weight. At laparotomy: partial gastrectomy; gastro-jejunostomy. Intravenous infusion and gastric aspiration for four days. No complications.

Before operation, on an intake of 126 g. protein (20.1 g. nitrogen) and 2600 calories per day, was in positive nitrogen balance of about 4.0 g. per day. When 160 g. promutrin were added and calories raised to 3330 per day, 114.2 g. nitrogen were retained in nine days, an average of over 12 g. nitrogen per day. Urine nitrogen rose sharply following the increase in protein and caloric intake. After operation food intake was rapidly restored, 74 g. protein (11.8 g. nitrogen) and 1380 calories being consumed on the 5th day, but it was not until the 7th day, when intake was 99 g. protein (15 g. nitrogen) and 2455 calories, that nitrogen equilibrium was regained. The urinary nitrogen excretion was 10.38 g. on the day of operation, no doubt due to the high intake on the previous day; it then fell, partly because of very low urine volume on the first day. The maximum output was 24.25 g. on the 3rd day. On the 8th day the patient took 120 g. promutrin by mouth, and another 85 g. on the 9th day but was then nauseated, vomited, and refused to take any more. These quantities were sufficient to put him into strong positive nitrogen balance; they also caused a reduction in food consumption. Even before the promutrin was given, the diet had proved too abundant for his gastric capacity. In spite of retaining 114 g. nitrogen during the pre-operative period, this man gained only 2 lb. in weight while in the first 10 days after operation he lost 4 lb. in weight and 40 g. nitrogen.

Having regard to the large quantity of nitrogen which was retained before operation, the catabolic excretion after operation seems of a particularly mild degree and suggests that he was suffering from protein depletion. The consensus of opinion

was /

was that his condition had been improved by the pre-operative feeding; he was a most co-operative patient who took the pronutrin supplements without fuss and even acquired some liking for the hydrolysate. After operation he was asked to indicate at once when he felt able again to consume pronutrin and it was restarted on the eighth day. However, he was nauseated within 24 hours, in spite of his previous good tolerance towards the supplement.

Case 18 (Table 20).- W.F., aged 40 years. Undertaker. Twenty-three years ago severe abdominal pain; gastric ulcer found during operation for appendicectomy; two months later gastro-enterostomy performed which resulted in relief of pain for 10 years when pain recurred; intermittent pain since then; haematemesis two years ago after two weeks' continuous pain. Repeated attacks of pain in last two years; appetite good but had lost 28 lb. in weight. On admission, well built, healthy-looking man. Radiological examination showed ulcer near stoma of gastro-enterostomy, jejunitis and pyloric stenosis. At laparotomy: large stomal ulcer; gastro-jejunostomy undone; jejunum closed; partial gastrectomy; gastro-jejunostomy. After operation, intravenous drip and gastric suction for three days, temperature and pulse rate raised for three days. Stitches out and patient up on 13th day, home on 17th day.

Before operation was in strong positive balance of over 11 g. nitrogen per day on intake of 297 g. protein (41.16 g. nitrogen), of which 160 g. were pronutrin, and 3380 calories per day; this diet was wholly consumed and well tolerated. About five hours after operation, as almost nothing had been obtained by gastric aspiration, an intragastric infusion of pronutrin and glucose was started (100 g. pronutrin and 174 g. glucose in 800 ml. water). Two hours later, after 400 ml. had been run in, he complained of distention and nausea; 250 ml. fluid withdrawn from stomach. Infusion continued more slowly; one hour later patient vomited tube and 240 ml. fluid. Tube replaced and infusion restarted at very slow rate but only another 100 ml. had been given 12 hours later, when milk was given as a drink. It was very difficult to regulate the drip rate which varied with posture and respiration and ran too fast or too slow or stopped. Twenty-four hours after operation 140 ml. aspirated. Two hours later vomited because of nausea due to pronutrin; his breath smelled of pronutrin and every time he swallowed a drink of water the taste or odour of pronutrin came up from his stomach. One hour later, 641 ml. thin brown fluid were aspirated containing milk /

milk, sputum and blood clot and smelling strongly of pronutrin; gastric drip infusion was therefore stopped. In the next seven hours 1340 ml. thin, brown fluid smelling strongly of pronutrin were aspirated from stomach.

On the morning of the 2nd day after operation his abdomen was distended and there were windy pains; it was not tense or tender. Fluid was aspirated in large quantity from stomach, was no longer smelling of pronutrin but was acid and wholesome and greenish-brown in colour. Milk mixture was still being given to drink but was rather heavy for him. Large volumes of fluid were aspirated until the morning of the 3rd day when change for better began.

There was again a high urinary nitrogen excretion on the day of operation; the maximum daily urinary nitrogen output (21.05 g.) was on the 2nd day after operation but the nitrogen excretion was raised for seven days after operation. The nitrogen content of fluid aspirated from the stomach was high. Nitrogen equilibrium was regained on the 8th day on 94 g. protein (15 g. nitrogen) and 1880 calories. Subsequently the intake was raised to 127 g. protein (20 g. nitrogen) and 2700 calories, and on this there was a marked daily nitrogen retention. During the six days of the pre-operative treatment there was a loss in weight of 1.5 lb. in spite of the retention of nearly 70 g. nitrogen. After operation 9.5 lb. were lost in 12 days during which there was a loss from the body of 76 g. nitrogen. In the last four days of the study there was an increase in weight of 6 lb. During the whole period of the balance study there was a loss of 6 lb. in weight and a gain of 9 g. nitrogen.

The pronutrin seemed to be largely responsible for the post-operative disturbance in this patient; certainly it was responsible for the nausea, and might, by its hypertonicity, have caused an increase in gastric and intestinal secretion. On the other hand, neither transient ileus, mechanical obstruction of the distal limb of the jejunal anastomosis, nor the retention of water resulting from somewhat excessive intravenous infusion, can be entirely excluded.

Case 19 (Table 21).- W.H., aged 43 years. Surface worker. Five years ago, while working underground, began to have upper abdominal pain eased by food, recurring at intervals of several months. Ten months ago, haematemesis; off work two months; returned to light surface work. Four /

Four months ago, pain became more severe. For five years had been on a diet, mostly fish and milk but when meat was eaten it did not cause pain. On admission, looked fit and well fed. Almost complete absence of acid in test meal juice. Radiological examination showed large ulcer crater on lesser curvature of stomach. At laparotomy: large gastric ulcer; partial gastrectomy; gastro-jejunostomy. After operation, four days' gastric aspiration, six days' intravenous infusion. In first six hours after operation gastric aspiration produced only 150 ml. so intragastric infusion of pronutrin (100 g. pronutrin, 174 g. glucose in 800 ml. water) was started and run for 10 hours; no pain, no distention, but some discomfort from Ryle's tube. Volume of fluid obtained by suction increased after start of infusion and remained large. On morning after operation was well and drinking water eagerly; further 800 ml. pronutrin and glucose solution started 25 hours after operation, but two hours later patient was flushed in face, and hiccough which had been occasionally present for six hours, became persistent and severe. An hour or so later patient was euphoric, muddled, wandering or jovial in speech. Hiccough increased in severity during night and next day and resisted treatment. On 3rd day patient vomited twice and eight litres of fluid in all were removed by aspiration; he had been drinking large quantities of water; 450 ml. blood and 400 ml. plasma transfused. On 5th day in spite of avertin, morphine and hyoscine by intravenous injection, hiccough continued. Phrenic nerve block produced transient relief on two occasions. On 6th morning both phrenic nerves crushed under local analgesia, with partial relief of hiccough. Intravenous infusion stopped on 7th morning. Temperature elevated until 8th day; up on 12th day; occasional hiccough persisted until discharge on 16th day.

During the six days before operation on daily intake of 297 g. protein (41.16 g. nitrogen), of which 160 g. were pronutrin, and 3380 calories; average nitrogen retention was 12 g. per day. After operation urinary nitrogen excretion fell on day of operation but rose to maximum of 24.25 g. on 3rd day and remained high for 11 days. Nitrogen equilibrium regained only about 13th day in spite of provision of 80 g. protein and 1700 calories from 8th day, and 87 g. protein and 1900 calories from 11th day. Faecal nitrogen higher than usual after operation. In the pre-operative period 72 g. nitrogen were retained but there was no change in body weight. In the first 12 days after operation 9.25 lb. in weight were lost and there was a negative nitrogen balance over the same period of over 150 g. nitrogen.

A striking feature in this case was the rapid increase in food intake from almost complete starvation to 80 g. protein and /

and 1700 calories in two days in a patient who for five days, after an extensive partial gastrectomy, had had a severe disturbance of the upper small intestine. This disturbance was ascribed to the stimulation of intestinal secretion by the instillation of a hypertonic solution of pronutrin and glucose.

Comment

During the period of high protein and caloric intake the control subject (Case 14) retained over 80 g. protein but there was no significant change in body weight. The daily nitrogen retention was increased to an average of 6.0 g. per day by the addition to the diet of 160 g. pronutrin per day. At the time this study was made, the nitrogen of transfused and lost blood was being included in balance computations; for this reason 165 g. protein and 14.8 g. fat were provided on the day of imaginary operation to represent the equivalent of transfused blood. In addition, the carbohydrate equivalent to the glucose given by the intravenous route in an ordinary patient was provided. There was a slower rate of reduction of urinary nitrogen excretion than in the unoperated controls already described. This was presumably due to the high protein intake on the day of operation and before operation as food and pronutrin. Otherwise the urinary nitrogen excretion during starvation in Case 14 resembles that found in these earlier control studies with low calorie intakes (Group 2, Experiment B) in that it was reduced to about 10 g. per day. There is the difference, however, that later in Case 14 the daily urinary nitrogen output stabilised at a somewhat lower level: between

9.0 /

9.0 and 11.0 g. per day even on an intake of over 90 g. protein (15 g. nitrogen) and 2500 calories. While some of the difference was accounted for by a higher faecal nitrogen, there was a daily retention of nitrogen of 2.0 to 3.0 g. per day. Whether the subjects had been fed on a high protein and caloric diet, or, as in the case of the other controls, fed on ordinary diets, there was a reduction rather than an increase in urinary nitrogen excretion following the reduction of the protein and caloric intake. During and after the starvation period in Case 14, there was a loss of about 10 lb. in weight and of 40 g. nitrogen in eight days; later there was some restoration of weight and retention of nitrogen.

In just over two weeks Case 15 retained 49 g. nitrogen and gained 2 lb. in weight; his general condition appeared to improve. In this case the excretion of 22.46 g. nitrogen in 1010 ml. urine on the third day after operation, compared with 9.34 g. nitrogen in 950 ml. on the day after operation, appears to support the belief sometimes expressed that there is retention of nitrogenous products by the kidney in the first 48 hours or so after operation. Such a striking difference deserves further consideration and it seems desirable to study in more detail the changes in renal function in the first 100 hours or so after severe surgical operations.

Pronutrin before Operation.- Before operation in four cases (Nos. 16, 17, 18 and 19), 160 g. pronutrin per day were administered as a supplement to a diet containing more than 120 g. protein and 2600 calories per day. In two patients (Cases 16 and 17), there was retention of 3.0 and 4.0 g. nitrogen per /

per day on the high protein high calorie diet. When 160 g. pronutrin per day were added, the daily nitrogen retention rose in each case to over 12 g. Yet although in Case 16, 89 g. nitrogen, and in Case 17, 114 g. nitrogen, were retained, the weights of each patient increased only by 2 lb. In the two remaining patients (Cases 18 and 19), a diet containing a total of 297 g. protein (of which 160 g. were pronutrin) and 3380 calories, was provided for six days. During this period both patients retained 70 g. nitrogen, but one patient (Case 18) lost 1.5 lb. weight, and in the other (Case 19), there was no change in weight. If the retained nitrogen is expressed in terms of protein tissue (according to Rubner's equation), in these patients the nitrogen retentions are equivalent to 8.3, 6.4, 5.0 and 5.0 lb. of tissue respectively.

None of these patients enjoyed taking pronutrin; only one, (Case 16), was able to take it readily before operation. In order to allow of a liberal food consumption before operation, patients were chosen who could and did eat well and who did not suffer from pyloric stenosis. Only one patient (Case 15) refused to eat all the food provided, but this was because he was critical of the food and its service rather than physically incapable of eating it; this is a valid objection to such a diet and must be given due regard. The other three patients generally were able to take the whole of the food supplied and to enjoy it. To ensure success requires some persuasion and close supervision, but above all, the food must look good and taste good and be served as well and as hot as possible.

At operation, in all these four patients, it was noticed that /

that the gastric mucosa had a clean fresh appearance and that the gastric wall was thinner, firmer and less soggy and was more agreeable to work with than is often the case in patients with peptic ulcer. It is uncertain whether the appearance of the stomach is related to the high pre-operative intake of protein and calories or more particularly to the consumption of pronutrin, or to the longer period of pre-operative preparation.

The urinary nitrogen excretion was in the region of 12 to 15 g. per day on an intake of 120 g. protein (20 g. nitrogen) and 2600 calories per day. On the addition of 160 g. protein as pronutrin, the total nitrogen intake was between 38 and 41 g. per day and the urinary nitrogen excretion rose to between 21 and 26 g. nitrogen per day. There was usually also some increase in faecal nitrogen on the higher intakes of protein, but this was not excessive. Thus, in such patients as these during a short period on a basal diet of 120 g. protein and 2600 calories, doubling the protein intake resulted in a two- to three-fold increase in nitrogen retention. In the control subject, however, urinary nitrogen was rather higher (28 g. nitrogen per day) and nitrogen retention was poorer (about 7.0 g. per day) than in the patients with peptic ulcer. It should be recognised that such high protein consumption is wasteful of protein and that the waste increases as the daily protein consumption rises.

Comparison with the control case (No. 14) confirms the development of a catabolic phase, well marked in Cases 16, 18 and 19 but less severe in Case 17. When, however, one of these cases (for example, Case 16) is compared with Case 1 (Table 70), it /

it is seen that while in Case 16 there was a higher total nitrogen loss in the first 10 days after operation, there was also a greater intake of nitrogen during this period; in the first six days the disparity in nitrogen excretion was 6.0 g. nitrogen, in the next four days 16 g. nitrogen. The combined losses of nitrogen in faeces and suction fluid are equal in these two cases. The small total difference in the negative nitrogen balances (7.0 g. nitrogen) over the 10-day period after operation can thus be related to the greater loss of nitrogen in the urine being largely balanced by a greater intake of protein. There seems, therefore, to be little justification for the general use of such high protein and calorie diets before operation in most patients who are suffering from peptic ulceration. The total urinary nitrogen excretions during the six and ten-day periods after operation in Case 17 are appreciably less than those in Case 1 and Case 16, but are similar to those found in Case 5 whose food intake was severely restricted after operation. Case 17 was well fed after operation, and while there were large losses of nitrogen in stools and suction fluid, the total negative nitrogen balance over the ten-day period was only 31 g. This case demonstrates the need for caution in the interpretation of the data obtained from balance studies. It is tempting to suggest, but unjustifiable to conclude, that the unexpectedly low urinary nitrogen excretion after operation in Case 17 can be explained by a pre-existing protein deficiency, which was only partly corrected by the pre-operative high dietary intake.

After operation in this group the protein intake was increased more rapidly than in the control cases submitted to operation. /

operation. It is clear that the consumption of 70 g. protein accompanied by an intake of less than 1800 calories is not sufficient for nitrogen equilibrium. In Case 19, 80 g. protein per day failed to produce equilibrium until 1800 calories were provided. There is support, therefore, for the belief that the provision of adequate calories (e.g. 1800 per day) in addition to 70 g. protein or more per day are necessary for the restoration of nitrogen equilibrium after operation. It was also evident that after gastrectomy there was a limit to the physical capacity of these patients to ingest food, and that unduly large food intakes were undesirable.

Those patients who overcame their repugnance towards the hydrolysate said, when the hydrolysate was stopped, that they felt better; it was difficult to decide why they felt better. Of all the patients to whom hydrolysate has been given by the oral route, including a number not previously mentioned in this report, only about half were able to take it without nausea and fewer still acquired any taste for it. After a few days, in the majority, there was a reduction in food consumption because of nausea due to the pronutrin and a distaste for all food, a reaction which does not appear to be entirely a psychological one. Provided, however, that a patient is able to take a protein hydrolysate by mouth, without impairing his appetite for and consumption of ordinary food, the hydrolysate is a compact means of increasing the protein intake when this is desired. The preparation of a severely malnourished patient for a major surgical operation involves the consumption of an abundant diet over a period of several weeks, and cannot be assisted in every case /

case by casein hydrolysates in the preparations at present available.

Pronutrin after Operation.- Most patients who had consumed pronutrin before operation were loath to take it after operation because of its nauseous taste or odour. However, one patient (Case 17) who had taken large quantities readily before operation, agreed to take pronutrin again after operation provided he was allowed to take it when he felt he could tolerate it. Nitrogen equilibrium was regained on the seventh day after operation on 100 g. protein and 2400 calories. On the eighth day he signified his ability to take pronutrin and consumed 100 g. on this day and 85 g. on the ninth day, but was then nauseated and could not consume any more. The hydrolysate sharply increased the already slightly positive nitrogen balance, but by causing nausea, interfered with the consumption of ordinary food for three days. Other patients, with the exception of Case 15, were even less tolerant of pronutrin after operation. In Case 15, pronutrin was well tolerated for five days and resulted in marked positive balance.

In two cases (Nos. 18 and 19) of the present series, and in others not reported in detail, a mixture of pronutrin and glucose dissolved in water (100 g. pronutrin, 174 g. glucose, 800 ml. water) was injected into the gastric remnant through the indwelling Ryle's tube used for gastric aspiration. The gastric fluid removed by suction two hours after injection was analysed, ferric chloride being used as a marker to indicate dilution and loss. Both in normal subjects and in patients, about 60 per cent. of the pronutrin and most of the glucose had been absorbed. /

absorbed. This mixture has been introduced within as little as three or four hours after operation with no ill effects except nausea. The repeated or continued use of such a hypertonic mixture resulted in a profuse flow of gastric and upper intestinal secretions, and the subsequent aspiration of large volumes of fluid from the stomach. This loss of fluid is undesirable and may result in delayed recovery and resumption of normal feeding. There is no suggestion that the intractable hiccough in Case 17 was related to the use of pronutrin. It is possible, however, that the large volumes of fluid removed by gastric aspiration were due to the injection of pronutrin and glucose solution. The loss of these large quantities of gastric and intestinal secretion caused intense thirst, and the unlimited consumption of water which was then allowed also stimulated intestinal secretion. Thus gastric aspiration continued to remove large volumes of fluid from the body and this loss ceased only when, following reduction in water consumption, the volume of secretion fell, and the aspirations could be stopped.

Discussion

Even when protein and calorie consumption had been greatly increased, subsequent restriction of intake led to an immediate reduction in urinary nitrogen excretion which continued while the intake was restricted; there was no increase in urinary nitrogen in simple food restriction after abundant feeding. There was no significant difference in the behaviour of Case 14 and the other four controls (Cases 10, 11, 12, 13) who had not been /

been fed with a protein supplement, apart from the large loss of weight in Case 14 for which an explanation has not been found.

It would be wrong to assume that the retention of nitrogen during a period of high protein high calorie feeding is necessarily associated with the deposition of protein tissue or an increase in body weight. New tissue is not formed without good reason, for example in growth, in response to increased physical requirements as in athletic training, or in recovery from depletion. Nitrogen may be retained in the form of one of the various protein compounds. Such nitrogen retention is not associated with the combination with water which is responsible for four-fifths of the increase in weight when new protein tissue is laid down. It seems likely that well-nourished and depleted subjects will deal differently with similar protein supplements because of their different planes of nitrogen equilibrium. Another possibility is that while nitrogen is being retained, and even perhaps new protein tissue is being formed, there is a loss of body water which obscures or balances the weight gain due to nitrogen retention. To define these possibilities in man will be difficult, but further knowledge could undoubtedly be obtained by the use of compounds containing heavy nitrogen and deuterium.

A period of high protein high calorie feeding before operation resulted in the retention of nitrogen to a degree which varied widely in the subjects studied. Important amongst the factors concerned in this variation are those of the previous level of dietary intake and the state of protein nutrition. Weight changes are not directly related to nitrogen retention.

The /

The form in which the nitrogen is retained in the body is unknown. There was a strong impression that the general condition of these patients was improved by the very generous diets provided, but apart from the retention of nitrogen, little objective support has been obtained for this impression. After operation there was an increase in urinary nitrogen excretion in four subjects in this group, as compared with control subjects also submitted to operation. In one subject after operation the urinary nitrogen output was unexpectedly low.

When the food intake of an already adequately fed subject is increased, the additional food is stored or burned. Cuthbertson and Munro (1937) said that only if the total energy requirement of the body be exceeded, and the substance in excess of its normal content be protein, did storage of some of this protein take place. They believed that in the case of protein, as the metabolic plane rose because of the continued ingestion of an excess, storage gradually diminished. For carbohydrate, on the other hand, once the tissues had taken their fill of an excess of glycogen, there was the possibility of conversion of some of the remainder to fat.

The present experiments with dietary supplements were of too short duration to give more than limited information. Nevertheless, there was retention of nitrogen, both when abundant ordinary food was consumed and when pronutrin was added. When the nitrogen intake was raised, there was no clear indication of a reduction in the proportion of nitrogen which was retained; this may be because of the short period of study. Faecal nitrogen was raised in some cases when the diet was increased, but most of the /

the additional nitrogen was absorbed.

The optimum composition of the diet was stated by Cuthbertson et al. (1937) to be when 10 per cent. of the total calories were derived from protein (approximately 1.0 g. protein per kg. body weight); 25 to 35 per cent. of the calories came from fat and the remainder from carbohydrate. In the present supplemented diets, over 30 per cent. of the total calories were in the form of protein; the additional protein was, however, added to a diet which was already adequate in respect of calories. Provided there was caloric cover for the specific dynamic action of the additional protein, retention could reasonably be expected. Cuthbertson and his co-workers also stated that apart from elevation of the metabolic plane, retention of protein might be limited by failure of appetite. This caused a reduction in the consumption of the basal diet, though all of the supplement was taken. The position was rather less simple in the present investigation. In patients other than those submitted to balance studies, it was found that there was a limit to the period for which a diet containing 120 g. protein per day could be fed. This was attributed to the addition of dried skimmed milk powder to some of the dishes, in order to increase the protein content compactly and cheaply. After about 10 to 14 days, food supplemented in this way was refused, even though the patient had no idea why he was refusing the food and certainly did not know it contained dried milk. Until the food was actually tasted, appetite was usually good, but after a few mouthfuls the desire for food seemed to go, the plate was pushed away, often a cigarette was lit and the patient lay back and looked /

looked round with a disgusted expression. When asked why he was not eating his food, the reply usually was, "I'm not hungry," or, "I was looking forward to it, now I just don't want it." Such patients retained their distaste for anything containing dried milk even after an interval of several days and after operation. This has been observed also by Browne et al. (1946).

Some means of estimating the presence or absence of protein deficiency before operation would be of great clinical value. Amongst the possible methods which were consideredwas the measurement over a short period of the urinary nitrogen excretion on a diet of known nitrogen and calorie content. Examination of the data obtained in the present study suggests, however, that this would almost certainly be misleading. A variation of this which was also considered and has been suggested independently by Browne et al. (1946), was the addition of a large amount of protein to an adequate daily intake; if this was not followed by a large additional output, then a severe deficiency must exist. The supplemented diet would then be continued until the urinary nitrogen excretion began to increase. The objection to these tests is obvious from what has been already mentioned regarding protein supplements. An equally good idea can probably be obtained of the degree and duration of protein depletion from a detailed history regarding diet and weight loss. Gain in weight is obviously of no value as a criterion in short-term attempts at replenishment. When changes in blood chemistry occur, they are probably more misleading than helpful.

INTRAVENOUS ADMINISTRATION OF PROTEIN

I. Protein Hydrolysates

It is well known that both for man and animals a protein loses none of its nutritional value when fed in a hydrolysed state rather than as whole protein, provided that it is not rendered deficient in important amino acids by the hydrolysis. The utilisation of protein by the mammalian body is governed by factors of which there is still only incomplete knowledge.

It seems desirable at this point to mention the particular meanings which have been attached to the terms utilisation and metabolism in the present report. The term metabolism includes all the changes which protein undergoes in the body regardless of their object. Thus of protein administered by mouth that part (or its components) which is not absorbed through the intestinal mucous membrane does not enter the internal environment and should be considered as wasted, not metabolised. When protein derivatives are injected into the blood stream, some may be excreted unchanged in the urine because their concentration in the blood has risen excessively. This urinary loss of unchanged injected components of protein is also waste, not metabolism; it is, of course, at present impossible to be certain what proportion of the amino acids excreted in the urine is of this nature. Utilisation has been taken to imply the "useful" part of protein metabolism, that is for purposes such as the production of new material apart from those solely directed to the production of energy. It is impossible at present /

present to measure the proportion of protein which is utilised in this sense; it may not always be possible to approximate the quantity which is metabolised.

What is known, however, of the conditions necessary for optimum utilisation presumably applies regardless of the route by which the protein is presented to the body or the form in which it is provided. The most important of these governing factors appears to be, first, that a mixture of all the amino acids that the body cannot readily synthesise in adequate quantities should be presented in suitable proportions at the same time; and, secondly, that sufficient carbohydrate should be provided with the protein to prevent the protein from being used merely as a source of calories.

Theoretical Indications for Use

The chief use of protein hydrolysates given parenterally would appear to be in conditions in which there is impairment or loss of the ability to digest and absorb protein. Such conditions are intestinal obstruction, pyloric stenosis, "the malabsorption syndrome," and when after operation ordinary feeding is impossible or undesirable. It remains to be shown that there is any real indication for the use of mixtures of amino acids in specific conditions. The hydrolysate must be safe to administer and such disadvantages as it may possess must be outweighed by the advantages conferred by its use. For the oral use of protein hydrolysates to be of value, a state must exist in which absorption of amino acids is undisturbed but digestion is impaired; such a state is difficult to conceive in the adult human subject but may rarely exist in premature infants.

Diets /

Diets containing large quantities of protein have been recommended in the treatment of many conditions both before and after surgical operations. In certain diseases the consumption of even a normal diet may be beyond the capacity of the patient. The use of hydrolysates in such states has been commended as a means of supplying protein in a compact and readily utilised form.

Assessment of Value

In man the assessment of the value of protein hydrolysates is difficult and as yet can be made only in a limited way. When hydrolysates are given by mouth, absorption from the bowel should be complete and there should be no increase in faecal nitrogen excretion. Ideally, no increase in the urinary excretion of amino acid nitrogen should follow the administration of protein hydrolysates either by mouth or intravenously. Following the administration of protein hydrolysates there may be an increase in urinary urea output, and this may indicate the metabolism of the administered peptide and amino acid nitrogen. It is evident from the work of Schoenheimer (1942), however, that it would be unwise to conclude that any increase or change in nitrogenous excretion is necessarily directly or even indirectly related to the administered amino acid or peptide nitrogen, though such is often assumed to be the case. It is convenient, however, to consider as retained in the body that proportion of parenterally injected nitrogen which is not excreted in the urine during the period of the injection or shortly afterwards. This does not imply any knowledge of the immediate /

immediate or ultimate fate of such untraced nitrogen. In the absence of contrary evidence, it may be wise to assume that any concurrent increase in urinary urea production is due to the metabolism of the injected nitrogen, rather than to say that it has had any other and more particular fate.

The present assessment of the value and effects of protein hydrolysates administered by the intravenous route before or after operation has been based on the close observation of the intake and output of nitrogen by various routes and of caloric intake. Other changes, such as those in body weight, in appearance and clinical behaviour, have also provided information of value in forming a judgment as to the clinical value of these preparations.

Production

Commercial protein hydrolysates are usually derived from casein, though in the past some were prepared from meat. The casein may be hydrolysed either by incubation with preparations of proteolytic enzymes or by boiling with acid. Enzymic hydrolysis results in only slight loss of amino acids and the optimum pH is obtained by the addition of comparatively small quantities of alkali. Technical difficulties are introduced by the risk of bacterial contamination during incubation. Acid hydrolysis avoids the dangers of bacterial contamination but results in the destruction of tryptophane and methionine; these amino acids must therefore be added afterwards which, especially in the case of tryptophane, increases the cost of preparation. If hydrochloric acid is used, neutralisation with sodium hydroxide results in a high salt concentration, while when sulphuric /

sulphuric acid is used its removal as calcium sulphate is expensive. The avoidance of bacterial contamination by technical improvements has led to almost universal use of enzymic digestion.

The three hydrolysates used in the present trial, pronutrin (oral), casydrol and amigen (intravenous), are all prepared by the enzymic digestion of casein with pork pancreas. All the details of the methods of preparation are not known, but some information has been obtained. In the case of pronutrin, the digestion is continued until 60 per cent. of the total nitrogen is present as free amino nitrogen; that is, until analysis shows a total nitrogen content of 12 per cent. and amino acid nitrogen content of 7 per cent. The hydrolysate contains the ten essential amino acids including tryptophane, and about 5 per cent. of sodium chloride derived from the use of sodium carbonate in the digestion. Casydrol as supplied for parenteral use contains 5 per cent. amino acid nitrogen, 5 per cent. dextrose and 0.3 per cent. sodium chloride, and has a pH of 6.5. In the preparation of amigen, following digestion, the mixture is inactivated by heat, the pH adjusted and the solution decolourised and filtered. The resulting clear solution is concentrated under reduced pressure, pasteurised and dehydrated to a fine powder.

In all three preparations the powder is a light yellowish-brown in colour, sticky and hydroscopic; it is readily soluble in water to give a light brown clear solution. The odour of the dry powder and of the solution is strong and offensive; the taste is strong and meaty but is overwhelmed by the smell. Both taste /

taste and odour vary in strength, but not in kind, in different preparations. Amigen is the least offensive, pronutrin the most nauseating and casydrol occupies an intermediate position. The variation seems to be due to the success with which the material which causes the smell and taste has been removed during manufacture; there has been a great improvement in both casydrol and pronutrin during the course of the present study. The material causing the smell and taste is alleged to be a peptide, and it is said to be partly removed by adsorption on to charcoal. While the taste can be masked fairly successfully by adding large quantities of glucose or flavourings such as syrup of orange, the smell persists and results in an unpleasant after-taste. Only small quantities can be disguised by addition to soups, stews or gravies. The mixture of hydrolysate with food renders the diet unpalatable and reduces rather than raises the consumption of food. The method was therefore adopted of giving the hydrolysate in about eight doses a day as a medicine. The dry powder was dissolved in the smallest quantity of water necessary for complete solution and was swallowed in one or two gulps, and followed by any highly flavoured "bonne bouche" the patient desired and could obtain.

For parenteral use a hydrolysate solution must be free of any material liable to cause pyrogenic reactions or anaphylaxis and from depressor substances. Appropriate tests are therefore carried out on each batch of their product by the manufacturers. The pH must be adjusted so that disturbance of the acid-base regulating mechanisms of the body is minimised.

The /

The manufacturers of casydrol and amigen each state that these products contain all the so-called essential amino acids, that is to say arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophane and valine. The detailed structure of these hydrolysates in respect of the proportions in which each of these amino acids is present was considered to be outside the scope of the present study.

Intravenous Administration of Protein Hydrolysates

Method of Administration.- It has been stated already that a daily intake of at least 70 gm. protein (11.2 g. nitrogen) and more than 1800 calories is believed to be necessary for nitrogen equilibrium to be achieved when the catabolic phase has subsided. To show whether the catabolic phase could be affected by the intravenous administration of casein hydrolysate (casydrol), it was decided that at least 11 g. of nitrogen must be given per day as casydrol, from the day after operation until food could be eaten, that is to say, throughout the catabolic period. This meant in effect, that a constant intake of 11 g. nitrogen per day should be maintained throughout the post-operative period, either as food or as casydrol or as a combination of both. In addition, as much glucose solution as possible was to be infused as a source of calories.

The casydrol was administered by intravenous drip infusion at a rate of 500 ml. in three to five hours; between each bottle of 500 ml., saline was infused for up to half an hour as this appeared to reduce the incidence of phlebitis. The following method was employed. A cannula was tied into a suitable vein and a saline drip infusion was started. A

standard /

standard transfusion service delivery set was attached to the casydrol bottle, but an autoclaved hypodermic needle was substituted for the service needle. After filling the delivery tubing with casydrol, the hypodermic needle was thrust obliquely through the side wall of the rubber tubing of the saline infusion, this tubing having been previously cleaned by vigorous scrubbing with gauze soaked in ether. A sterile dressing was wrapped round the casydrol needle and saline drip tubing, and fixed with strapping. Two or three litres of casydrol were given each 24-hour period by this method for four or five days after operation, which provided 80 to 120 g. protein and 100 to 150 g. glucose, that is, up to 1080 calories per day, of which rather more than half were derived from carbohydrate.

The composition of the hydrolysate solutions used was as follows:-

	Casydrol	Amigen
Total nitrogen	0.68 g. per 100 ml.	0.65 g. per 100 ml.
Amino acid nitrogen	0.42 g. per 100 ml.	0.42 g. per 100 ml.
Sodium chloride	0.3 g. per 100 ml.	0.17 g. per 100 ml.
Carbohydrate	5.0 g. per 100 ml.	5.0 g. per 100 ml.
Calories	37 per 100 ml.	36.28 per 100 ml.
pH	6.25	5.26

Summary of Cases.- A solution of casein hydrolysate and glucose has been administered by the intravenous route to 22 patients, either before or after operation; in 20 casydrol was used, in 2 amigen. Of the 5 patients who received pre-operative infusions, 4 were suffering from severe obstructive jaundice and the other from carcinoma of the stomach. Nine of the 17 patients who were given post-operative infusions had been operated on for some form of peptic ulceration; 5 were severely jaundiced /

jaundiced, this being due in one case to hepatitis; 2 had advanced ulcerative colitis and one was suffering from the effects of prolonged self-inflicted starvation and simple prostatic hypertrophy.

Five of the patients with peptic ulceration who received casydrol and the two who were given amigen were studied in detail by nitrogen balance and blood and urinary chemical analyses. They will be compared with a patient submitted to partial gastrectomy and similarly investigated, but who did not receive any hydrolysate.

(1) Casydrol

A. Patients Submitted to Nitrogen Balance Studies

(a) Control, no casydrol infusion

Case 20 (Tables 22, 42).- W.P., aged 41 years. Ropewalker. Twelve years' history of frequent pain after meals; 20 months ago perforation of duodenal ulcer with satisfactory recovery, returned to work; four months ago relapsed and did not improve with diet and in-patient treatment in a medical ward. Radiological examination showed ulcer deformity of duodenum with an active ulcer; no obstruction. In last three months had lost 21 lb. in weight; appetite impaired. At laparotomy: posterior duodenal ulcer penetrating pancreas; partial gastrectomy; gastro-jejunostomy.

After operation, intravenous drip infusion for 72 hours; gastric aspiration 48 hours; superficial thrombosis of drip vein with later abscess formation following extension of thrombosis to mid-calf and knee; abscesses incised on 15th and 20th days. Cough and purulent sputum towards end of first week after operation. Pre-operative period too short to permit valid conclusions. Urine lost on 2nd day after operation but urinary nitrogen excretion rose on 4th and 5th days and again on 10th, 11th and 12th days, presumably because of vein thrombosis and subsequent abscesses. Urinary amino acid nitrogen not raised until 7th day after operation, but thereafter remained high to 14th day. Nitrogen equilibrium established on 12th day on 80 to 100 g. protein and 2400 calories per day.

It seems from this case that in the presence of complications such as purulent bronchitis and superficial thrombosis and abscesses, nitrogen equilibrium will not be achieved in spite of intake having reached an otherwise adequate quantity, that such complications increase the daily requirements for protein and calories, and that increasing protein intake alone will not result in nitrogen equilibrium. But for the formation of abscesses, nitrogen equilibrium would have been achieved on the seventh or eighth day. The elevation of urinary amino acid nitrogen excretion appeared to be related rather to the phlebitis and thrombosis than to the operation which did not cause any change in the daily quantities excreted. The persistence of an increased excretion in association with suppuration suggests that this perhaps more than extensive thrombosis may be the important factor.

(b) Casydrol infusion

Case 21 (Table 23).- T.B., aged 36 years. Shopkeeper. History of stomach trouble for 17 years; six years ago discharged from Navy for duodenal ulcer; two years ago perforated duodenal ulcer; symptoms continued after closure of perforation; had been losing weight and had much pain and worry before admission. At laparotomy: duodenal ulcer; partial gastrectomy; gastro-jejunostomy. After operation, intravenous drip and gastric suction for four days; no complications.

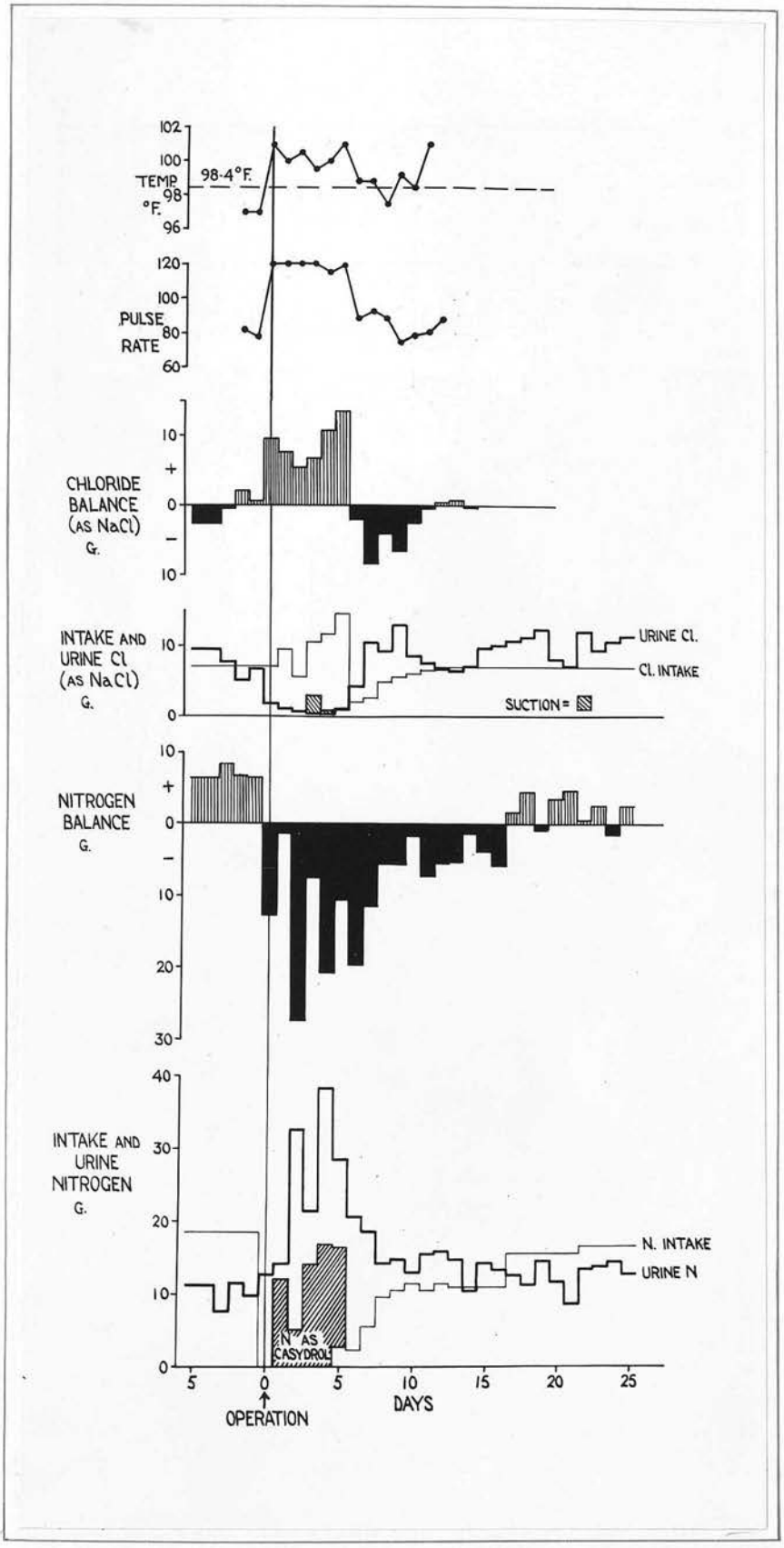
Before operation in positive nitrogen balance on 105 g. protein and 2570 calories. On day after operation 620 ml. casydrol given by intravenous injection. Casydrol started at 2.40 p.m.; by 3.40 p.m. less than 200 ml. had been given and by 4.40 p.m. about 270 ml. had been given. Infusion rate then increased and after about 50 ml. in three or four minutes, patient began to look flushed and wiped brow with his hand; there was no visible sweating. At 4.55 p.m., after about 200 ml. at fast rate, he complained of nausea. Drip rate slowed to 40 drops per minute, and within two minutes he admitted nausea was less severe, took a drink of water; two minutes later nausea had passed off, and /

and after a further five minutes (nine minutes after drip was slowed) flushing of face had subsided. By 5.5 p.m. 500 ml. had been injected; bottle changed. At 5.20 p.m. when 120 ml. had been run in from second bottle, he complained of a "peculiar ill feeling," the exact nature of which he could not describe or explain but which he said was "terrible". He was so upset that casydrol was stopped and saline was restarted. Rapid partial improvement followed, but an hour later he was still feeling "rotten." There was no flushing with this second reaction and the impression was formed that it was at least in part due to fear or worry about the effects of the casydrol; there was evident relief and improvement when the casydrol bottle was removed. The next morning he complained of a bad taste in his mouth, he felt generally ill but not as bad as during the reaction on the previous evening, and he had not slept well. General condition satisfactory, severe mental setback due to reaction. Two days after reaction he was still not feeling really well because, he said, of the reaction; he was hungry and wanted food in spite of being on intermittent gastric aspiration by which large volumes of greenish fluid were being withdrawn. On the third day after the casydrol he was very well, morale excellent. Feeding was started but was increased only slowly. Urinary nitrogen excretion increased from 2nd to 6th days, maximum on 3rd day. Nitrogen equilibrium was reached on the 10th day after operation on 66 g. protein and 1800 calories. Lost 10 lb. in weight in eight days after operation. He got up on the 14th and was discharged on the 18th day.

This was the first infusion of casydrol to be given, and after starting very slowly the rate was increased to see what could be tolerated. Blood was withdrawn during the reaction but the results of the analysis for amino acid concentration were doubtful. Hydrolysate of the same batch was later administered to other patients without reaction. After operation there was the usual increase in urinary nitrogen excretion which lasted until the sixth day when nitrogen equilibrium was re-established; the urinary nitrogen had stabilised well below the pre-operative level on an intake which also was proportionately lower than before operation.

Case /

CHART VII



Case 22.- To show the effect of intravenous infusion of casydrol on urinary nitrogen excretion. Estimated chloride intake is shown for comparison with measured urinary chloride excretion.

Case 22 (Tables 24, 43, 52, 66; Chart VII).- F.N., aged 38 years. Joiner. Twelve years' history of abdominal pain after meals, worst at night and relieved by food or alkaline powders; five years ago perforation of duodenal ulcer treated by excision, pyloroplasty and drainage; some relief after this operation; in last six months pain became worse. Strict diet for past three years; has not lost weight. On radiological examination there was gross deformity of duodenal cap. At laparotomy: duodenal ulcer; partial gastrectomy; gastro-jejunostomy. After operation, gastric aspiration for two days; intravenous drip infusion for five days. There were hiccough, nausea and vomiting before casydrol infusion was started but not during the infusion; hiccough recurred the day after the infusion was stopped; in addition, on this day (the 7th after operation), an extensive thrombosis of the left long saphenous vein developed from the calf to the groin. On the 11th day an abscess of the lower third of the thigh secondary to this thrombosis was incised and drained under pentothal anaesthesia; Staph. aureus was grown on culture of the pus. Another abscess was emptied by aspiration six days later.

The casydrol infusion was started 22 hours after operation, 10.26 litres being given during the next five days without reaction or complication other than venous thrombosis. Chemical phlebitis necessitated change of vein four times, three litres being the maximum run in without change of vein. Food was given from the second day onwards, though intake was impaired by lack of appetite during and for two days after the infusion. During the casydrol infusion calories were maintained at above 1000 per day except on the first day. In spite of this, much additional nitrogen was excreted in the urine. There was a marked drop in the calorie intake when the casydrol was stopped. By the 10th day, however, oral intake of food had reached 69 g. protein and 1900 calories, but, presumably because of the sepsis associated with the saphenous phlebitis, nitrogen equilibrium was not attained until the 16th day, when the intake of food reached 97 g. protein and 2500 calories per day.

Before operation was in strong positive balance on 114 g. protein and 2750 calories. Urine nitrogen excretion increased after operation and was above probable pre-operative level of 11 g. per day for 14 days. Negative balance for 16 days. On the 2nd, 4th and 5th days after operation, the urinary nitrogen excretion reached much larger daily quantities than is usual. At the same time there was marked increase in amino nitrogen, but while the peptide nitrogen excretion was large, no pre-operative figures were available for comparison. This increase in amino acid nitrogen excretion might be due to phlebitis, thrombosis and suppuration as in Case 20, but was ascribed rather to the infusion of casydrol. "Retention" of injected amino acid nitrogen was about 63 per cent. Loss of /

of weight did not begin until 8th day after operation and was then rapid, 7 lb. being lost in six days. Marked reduction in urinary chloride excretion for six days after operation.

Although the only complication was repeated superficial venous thrombosis, it was concluded that these thromboses and the painful phlebitis, the two superficial abscesses and the limitations which five days' continuous infusion imposed on the patient, were not worth any benefit which might have been derived. No objective evidence of benefit was obtained. The equivalent of the infused nitrogen was lost in the urine in addition to that to be expected normally after gastrectomy. There was the usual loss of body weight although this was much later than usual.

Case 23 (Tables 25, 44, 52).- T.R., aged 26 years. Sewing machine mechanic. For past five years pain two hours after meals relieved by food, treated by diet and medicines, relapsed when called up for Army and discharged four years ago because of duodenal ulcer. Two years ago further relapse; treated medically but not free of pain; vomited occasionally. Weight below average but no recent change. Radiological evidence of scarring of duodenum and small ulcer crater. At laparotomy: chronic duodenal ulcer; partial gastrectomy; gastro-jejunostomy. After operation, some vomiting during first 36 hours in spite of gastric aspiration; intravenous infusion for five days. Rigor on third evening; temperature and pulse rate raised on first to fourth days after operation. Up on 13th day, home on 16th day.

Casydrol infusion started within 24 hours of operation, 10.8 litres being given in 96 hours; vein changed twice only. Symptomless flush appeared half an hour after infusion started and persisted as long as casydrol was being run; was vomiting when casydrol started and vomiting continued for another 12 hours; no anorexia but no food eaten during first two days of casydrol infusion; thereafter intake progressively increased to 65 g. protein and 1650 calories by 7th day, but nitrogen equilibrium not achieved, except intermittently, even on 86 g. protein and 2160 calories; pre-operative period too short to give any indication of level of protein metabolism. Prolonged increase in urine nitrogen excretion after operation, rising to /

to 41.8 g. on 2nd post-operative day but falling by about 10th day. Marked increase in urinary amino nitrogen excretion during and after casydrol infusion. "Retention" of amino acid nitrogen was 60 per cent. Marked chloride retention. Weight gain of 1.25 lb. during casydrol infusion but following end of casydrol infusion on 4th day 8.6 lb. were lost between 5th and 15th days, mostly before the 11th day.

As a result of the casydrol infusion, there was nitrogen equilibrium on the day after operation but this was more than counter-balanced on the next day by the large quantity of nitrogen excreted in the urine. There was an increase in weight during the first four days after operation, and at the same time marked retention of water and reduction in urinary chloride excretion. No particular benefit resulted from the infusions.

Case 24 (Tables 26, 45, 52).- J.B., aged 35 years. Pig farm manager. Thirteen years ago peptic ulcer perforated, closed at operation and followed three months later by gastro-jejunostomy. Two years ago pain recurred in upper abdomen after meals; perforated stomal ulcer in jejunum closed at operation; since this operation had never felt really well; frequent pain sometimes relieved by food or powders; adhered strictly to diet; ten weeks before admission passed black stools and had severe pain. On admission, pale, thin but not wasted man. Radiological evidence of narrowing of stoma and efferent loop but no sign of ulcer. At laparotomy: stomal ulcer; gastro-enterostomy undone; partial gastrectomy; gastro-jejunostomy.

Before operation was in strong positive nitrogen balance on 123 g. protein and 3000 calories per day. After operation gastric suction for three days, drip infusion for four days. Marked increase in urinary nitrogen excretion for nine days after operation, maximum on 3rd day. Much wound pain at first; crepitations in chest but no dulness; coughed little because of pain; frothy sputum. As pain eased coughed more freely and much frothy sputum was brought up.

Casydrol infusion started 24 hours after operation, 6.5 litres being given during next three days. Within five minutes of start of casydrol severe pain complained of /

of in vein which was tender on palpation from ankle to mid-thigh; pain increased by running either 0.9 per cent. saline or casydrol; this chemical phlebitis was present before casydrol started. Pain ceased within half an hour of stopping infusion; redness subsided; vein then tender only on pressure. New vein used; cannula filled with clot, and drip stopped after 28 hours and 2500 ml. casydrol; no phlebitis. Infusion continued in new vein for further 26 hours when total of 5940 ml. given; rigor; temperature rose to 102°F. and skin became very flushed, dark brick-red colour and very hot. No nausea, retching or vomiting, but was belching as he had been doing for two days at intervals. No complaint of pain; casydrol stopped; saline infusion turned on; an hour and a half later sweat appeared on face; five hours after rigor temperature was 100.4°F. so casydrol was restarted. Three hours later, at 2.0 a.m., rigor had just begun when he was seen; he was sweating and shaking, the shaking being most marked in the lower jaw and teeth; respiratory rate rose to 32 per minute, pulse to 120 per minute, pain was complained of in back on both sides in the renal angles. Casydrol was stopped and saline was turned on until another rigor began 11.5 hours later at 1.30 p.m. when saline infusion was stopped and cannula removed.

It appeared that rigors were due to something other than casydrol as one occurred as saline was being given 11 hours after casydrol had been stopped; it was therefore decided to give more casydrol. Using same tubing but new bottle, casydrol was restarted 75 minutes after last rigor; no saline was given; after just over an hour another rigor started. At first he was cold and shivery, this lasted about five minutes and then he began to feel hotter and hotter, temperature rose to 102.8°F., and after about 20 minutes he said he was "all right but awfully tired;" no nausea, vomiting or retching. Drip was stopped. Four hours later drip was restarted with casydrol, but within 20 minutes a rigor began and temperature rose to 102°F., pulse 120 and respirations 26 per minute. Again the shaking was generalised but started and was worst in the lower jaw. In 10 minutes was sweating profusely all over the body, having been heated with an electric cradle; rigor stopped within 20 minutes of onset; casydrol infusion again started but after two and a half hours another rigor began and lasted half an hour, temperature rising to 103°F., pulse and respiration rates to 128 and 30 per minute respectively. The infusion was stopped and the cannula removed. Temperature was elevated from time of operation until 16 hours after casydrol infusion was stopped; at this time there were still audible crepitations in the chest but no sign of consolidation.

During casydrol infusions low calorie intake which did not reach 1000 per day until 6th day. Marked increase of urinary amino acid excretion during casydrol infusions but "retention" of amino acid nitrogen infused was estimated to /

to be 73 per cent.; it was very low on last two days of the infusion. Urinary chloride excretion not much altered. Weight fell before 5th day. Water retention was not marked.

It was concluded that the temperature was related rather to the casydrol infusion than to the pulmonary oedema. The cause of the rigors is uncertain, saline infusion caused one, though the others seemed closely related to casydrol infusion. The tubing and glassware were supplied by the Blood Transfusion Service and the rubber tubing appeared clean when split open, no sediment was noticed in the casydrol, and rigors followed casydrol from different batches. So-called "pyrogenic" rigors encountered with other fluids infused intravenously are usually heralded by a small increase in respiratory rate some minutes before the restlessness which immediately precedes the onset of shivering; no such rise in respiratory rate was noticed before the later rigors in this case. No apparent benefit was derived from the casydrol infusions.

Case 25 (Tables 27, 46, 52).- J.F., aged 42 years. Miner. For over 20 years pain in stomach after meals, not improved by diet. Two years ago perforation of duodenal ulcer, followed by five months' remission and then continuous pain and discomfort. Marked loss of appetite, some loss of weight. On admission, thin, pale man; gastric succussion four hours after meal. At laparotomy: chronic duodenal ulcer; partial gastrectomy; gastro-jejunostomy. Intercostal block T5 to T10 with procaine in beeswax, analgesic effect of which lasted less than 24 hours. After operation gastric suction for four days; intravenous infusion for five days, 10.7 litres of casydrol being given, starting 22 hours after operation; frothy sputum throughout this infusion with pulmonary crepitations and some basal dulness. Radiological evidence suggestive of consolidation in lower zone, right lung field, on 6th day. Temperature raised throuhout period of casydrol infusion. Weight increased by 3.25 lb. between operation and 4th day, and fell by 5.25 lb. between 6th and 12th days, most of this being lost between 6th and 9th days; net loss after operation was 2.75 lb.

Before operation in positive nitrogen balance of 4.0 g. per day on 114 g. protein and 2400 calories. After operation, urine nitrogen markedly increased, during casydrol infusion reaching maximum of 35.65 g. on 3rd day after operation. Urine nitrogen fell after casydrol stopped and nitrogen equilibrium regained about 10th day of intake, having reached 70 g. protein and 1760 calories on 7th day and 114 g. protein and 2500 calories on 9th day. Food intake during casydrol infusion was negligible and the casydrol was not well tolerated by this patient though no frank reactions or complications developed apart from a facial flush and the pulmonary oedema and basal pneumonia; the former cleared rapidly after the infusion was stopped but there was still some chest pain and poor tolerance of excretion on discharge on the 17th day after operation. The caloric intake during casydrol infusion was about 1000 per day for the first four days, but fell to 480 on the last day. Pre-operative urinary amino acid nitrogen excretion was higher than in any of the other patients at average of 1.4 g. per day; amino nitrogen excretion rose during casydrol infusion, "retention" of injected amino nitrogen was estimated to be 60 per cent and became less each successive day of the infusion. Marked but delayed reduction in urinary chloride excretion. Increase in body weight but only moderate water retention during casydrol infusion.

No particular benefit was observed as a result of the casydrol infusions. As in the other three patients, there was after operation a more prolonged increase in urinary nitrogen excretion and a quantity of nitrogen, roughly equivalent to that injected as casydrol, was lost in addition to what could reasonably be expected to be due to a normal post-operative catabolic output. There was in every case a systemic disturbance characterised by flushing of the skin, elevation of temperature and pulse rate, frothy sputum and some malaise. In two cases superficial venous thrombosis went on to suppuration and abscess formation which required incision and drainage. It was concluded that the intravenous administration of casydrol is of no value in the post-operative treatment of well-nourished patients who have been submitted to partial gastrectomy.

Comment /

Comment

After gastrectomy most patients drank readily anything they were given and often began to take milk and light food on the second day after operation. So far as drinking was concerned, the casydrol patients were no exception, but their appetites were poorer than usual and their intake of the ordinary post-operative diet was less than average. This persisted to some extent for up to two days after the casydrol infusion was stopped, and in two cases led to a delay in the intake of an adequate diet (70 g. protein and 1800 calories per day). As the result of taking milk and milky foods during the casydrol infusion, as many as 1500 calories were ingested on one day (Case 24), but this was exceptional. In Case 25 the calorie intake remained below 1000 per day throughout the intravenous infusion, but in the other three cases the calorie intake was maintained above 1000 per day except on single days. Immediately after the infusion was stopped, in all cases there was a drop in both protein and calorie intakes, and as urinary nitrogen excretion continued at the previous high rate, a serious nitrogen loss resulted. On the whole, once the oral intake of food was started, it was possible to increase the daily quantities rapidly, provided the capacity of the stomach remnant was not exceeded. This does not mean that any benefit was derived from the casydrol infusion in this respect, since, if anything, the casydrol patients were a day or so behind the controls in ascending the dietetic ladder, and several days behind in achieving nitrogen equilibrium. This ability to increase food intake more rapidly was due rather to the greater ability of the /

the stomach remnant to tolerate food, presumably because of a greater lapse of time since the operation.

Of the five patients studied by nitrogen balance estimations one case (No. 21) had received only 620 ml. when the infusion was stopped because of a reaction. The behaviour of this patient was otherwise similar to that of a control and will not be further discussed. The remaining four patients received after operation from 43 g. to 70 g. of nitrogen as casydrol infusions in addition to ordinary food. Table 70 shows some of the data of these patients. The period covered is the 10 days starting with that of operation. In addition the urine nitrogen excretion on the day of operation and the succeeding five days, that is of the catabolic phase, is shown separately in each case. In two cases the total nitrogen intake was about twice that of the controls, but the food intake, other than casydrol, was in all four cases rather less than in the control patients. All the patients to whom casydrol was given excreted more nitrogen in their urine than did the controls, both in the six-day and ten-day periods; this additional urinary nitrogen excretion was roughly equivalent to the quantity of nitrogen injected as casydrol. The negative nitrogen balance over the ten-day period was more marked in the patients given casydrol; in spite of the calories provided by the injected casydrol and glucose, this may be partly due to the reduced oral food intake already mentioned.

In Case 5, after vagotomy food was severely restricted and there was almost complete starvation for 10 days; the urine nitrogen was less than in the control (Case 1) who, after operation, was fed in the routine manner. The negative nitrogen balance /

balance for the ten-day period was greater in Case 5 than in Case 1 and about equal to that found in two of the casydrol patients. This shows the futility of blind summation of balance studies and suggests a cause for some of the confusion that exists regarding the value of casein hydrolysates.

The dark brown colour of the casydrol is believed to be due to caramelisation of the glucose during sterilisation of the solution. This is supported by the observation of a similar darkening of colour of the amigen solution when this was sterilised in an autoclave. In spite of much enquiry, no information has been obtained as to the fate of injected caramel in human subjects and it has been assumed therefore that the caramel is largely excreted unchanged and is also responsible for the dark brown colour of the urine during infusions of casydrol. This assumption is to be further examined. The strong odour of the urine was so like that of the casydrol as to justify the conclusion that the substance responsible was excreted unchanged. This indicated that some part of the casydrol solution was not metabolised in the body, and as it has been suggested that the odour is linked to peptide, it appeared that peptide was being excreted unchanged. It was important to measure the urinary excretion of amino acid and peptide nitrogen to discover how much of the material infused was being excreted unchanged.

In order to establish normal values, in three control subjects and nine patients the total daily amino acid nitrogen excreted in the urine was measured by the method already described; the results are shown in Table 71. In the three unoperated control subjects on the same diet, the excretion varied /

varied from 0.3 g. to 0.8 g. per day but was fairly steady in each individual. Following starvation of protein and calories for three days, in two subjects there was a slight reduction and in one a slight increase in the daily amino acid nitrogen excretion. In six of the seven patients submitted to operation, the pre-operative excretion varied between 0.2 g. and 0.6 g. per day, but in the remaining one patient, the average was 1.4 g. per day. After operation there was little change in the urinary excretion of amino acid nitrogen except in the patients to whom hydrolysates were administered in whom there was a marked increase above the pre-operative level.

It was therefore decided that in estimating the possible loss of injected amino acid and peptide nitrogen in the urine, it would be assumed that after operation the normal average daily excretion continued at the pre-operative rate. In each case this average quantity would be subtracted from the post-operative excretion, and the remainder would be assumed to be due to the urinary loss of unchanged injected material. This daily loss in the urine would then be subtracted from the total quantity injected in the same 24 hours and the remainder would be considered as retained in the body for metabolic processes and expressed as a percentage "retention" of the quantity injected. There are obvious objections to these assumptions. There may be a delay in excretion and nitrogen injected in one period of 24 hours may be excreted only during the next period and cause an unduly high "retention" during the earlier period. The additional amino nitrogen excreted may not be derived from the injected material but may in some way be due to the injection. There /

There seemed, however, to be no other readily available method for the measurement of the quantity of nitrogen available for metabolic purposes.

In the two patients (Case 24, Table 45, and Case 25, Table 46) in whom daily amino acid nitrogen excretion was measured before operation, average daily values were found of 0.5 g. (Case 24) and 1.4 g. (Case 25). In Case 24 amino acid nitrogen excretion rose during casydrol infusion and remained above the pre-operative level for several days after the infusion was stopped; total urinary nitrogen excretion also rose and remained high at the same time. Similar changes were observed in Case 26 but after the casydrol infusion was stopped the fall was more rapid and complete. In Case 24, assuming that the average daily urine amino acid nitrogen was 0.5 g., only an additional 6.0 g. of amino acid nitrogen were excreted during the period that 23 g. were injected as casydrol. In Case 25, the average daily excretion was assumed to be 1.4 g., and on this assumption 14 g. of additional amino acid nitrogen were excreted during the period in which 35 g. were injected. In each case, as the duration of the casydrol infusion lengthened, the daily amino acid nitrogen excretion increased. There was an interval of some hours between the start of the infusion and the appearance of an appreciable quantity of amino acid or peptide nitrogen in the urine.

The smallest increase in amino acid nitrogen excretion occurred, as might be expected, in the patient with the most severe protein depletion (Case 40); the so-called retention of amino acid nitrogen amounted to 80 per cent. during the three days /

days of the infusion and the succeeding day. The increase in urine amino nitrogen was, however, threefold and this is similar to that found in Cases 24 and 25. It is essential then to take into consideration the initial or pre-operative level of urinary amino acid excretion in judging the loss in the urine during casydrol infusion. In view of the appreciable variation of the total daily amino nitrogen excretion between patients, the assumption of an arbitrary figure seems of doubtful value for the purpose of estimating the relationship between amino nitrogen administration and retention. The figures obtained in Cases 22 and 23 are therefore of limited value, but they suggest that similar quantities of amino acid nitrogen were lost in the urine in these cases. It was concluded that amino acid nitrogen equivalent to 40 per cent. of that as casydrol was excreted in the urine during the course of the infusion in patients who were not grossly malnourished, in other words there was a "retention" of 60 per cent. for metabolic processes.

A considerably greater excretion of peptide nitrogen was found in several cases, but owing to difficulties in analysis, the figures for peptide nitrogen excretion are sparse. It appears that the peptide nitrogen present in casydrol may be more readily excreted unchanged than the amino acid nitrogen, and presumably is less readily metabolised by the human subject in the immediate post-operative period.

In all cases after gastrectomy there was a more marked rise in temperature and pulse rate during the period of casydrol infusion than was found in similar patients who did not receive these infusions. While it is difficult to exclude the effects of /

of venous thrombosis as factors in the production of these increases in temperature and pulse rate, the rapid subsidence of both elevations usually within 12 to 24 hours after the cessation of casydrol infusion, suggests strongly that the casydrol was the important factor. On starting the infusion, the flush usually appeared in about half an hour at an infusion rate of about 60 drops per minute; when the infusion was stopped, the flush passed off in about the same period of time. This facial flush was such a constant feature during casydrol infusion that its absence was a sure indication that the infusion had stopped, and had been very slow or stopped for half an hour or more. It was possibly due to the specific dynamic action of the injected protein or more probably to one of the constituents of the casydrol, since with highly purified amino acid solution flushing is said not to occur.

The four patients who received prolonged casydrol infusions all coughed up clear frothy sputum, and in each crepitations were heard in the lung bases during the period of the infusion and for a short time afterwards. In two patients there was some evidence of basal consolidation, either on physical or radiological examination. However, there were no serious pulmonary complications, though the increased coughing and expectoration caused unnecessary wound pain and discomfort. The most striking feature was the rapidity with which the sputum and crepitations cleared when the infusion was stopped.

In the control group of patients body weight began to fall within four days after operation, and the weight loss had largely ceased by about the 7th or 8th day (Chart X). In two of the patients /

patients who received casydrol, weight increased during the infusions. In all four of the casydrol patients weight loss started only towards the end of the first week after operation, and continued until the tenth to thirteenth day (Chart XI). Comparison of the volumes of fluid injected and of urine excreted suggested that water was retained during the infusion and was later excreted during several days. Diuresis occurred, however, during the casydrol infusion in two patients. There was also retention of chloride indicated by the urinary chloride excretion; later this will be discussed more fully.

After major operations and in the course of certain severe illnesses, many patients exhibit a marked change in facial appearance; this is a common feature after gastrectomy and abdomino-perineal excision of rectum. For the first two or three days after operation in many patients there may be little change, or perhaps a slight increase in the fulness of the face, then, usually overnight, perhaps because this is the time of our longest absence from the patient, the flesh seems to shrink on the bones, the eyes deepen in their sockets and the skin becomes wrinkled, muddy and grey and drawn more tightly over the cheeks and forehead. These changes commonly appear on the third, fourth or fifth days and alter the patient's appearance entirely, to the great concern of his relatives and friends. There is a coincident loss of tissue in the rest of the body, and it seems remarkable that this change has not been more often associated with the catabolic phase described by Cuthbertson. Whether it is due to loss of water or destruction of tissue is, however, another matter, for it was noticed that in patients given intra-venous infusions /

infusions of casydrol, this change in appearance does not develop until after the end of the infusion, that is, on the fifth, sixth or seventh day. Since protein breakdown does not seem to be reduced by casydrol infusion, but as there is retention of water during the casydrol infusion, which is lost in a later diuresis, the facial change is perhaps related rather to loss of tissue water than of protein.

B. Patients not Submitted to Nitrogen Balance Studies

Case 26.- A.G., aged 67 years. Miner. Four weeks' history of dull, aching, upper abdominal pain, not related to food but had also had some distaste for fatty food; jaundice for three days; dark urine for three weeks. On admission, thin, unhealthy-looking man. Palpable, greatly enlarged but not tender gall-bladder; liver not enlarged. Diagnosis: neoplasm of pancreas.

Before operation, 7.0 litres casydrol given by intravenous infusion: facial flush; no nausea; no reaction; ate ordinary diet; urine had odour similar to that of casydrol and was sometimes darker in colour. No rise in temperature or pulse rate during casydrol infusion. Comparison of the following chemical tests done immediately before and after casydrol infusion showed no significant alteration: laevulose tolerance (diphenylamine), cephalin flocculation (Dick), alkaline phosphatase (King), carbon dioxide combining power (Van Slyke), blood chloride (Van Slyke), non-protein nitrogen (micro-Kjeldahl); the concentration of total plasma protein fell from 5.86 g. to 5.16 g. per 100 ml, that of albumin fell from 4.53 g. to 3.23 g. per 100 ml. (micro-Kjeldahl).

On clinical observation no particular benefit was observed to follow the casydrol infusions. At laparotomy: inoperable carcinoma of the head of the pancreas; cholecyst-jejunostomy. Died on 4th day after operation.

Case 27. J.W., aged 56 years. Paper mill worker. About 11 weeks before admission began to feel "off-colour" and to feel thirsty at work; drank more water and passed more urine than usual; after three or four days noticed urine to be darker in colour; a few days later stools were noticed to be pale. For six weeks skin had been yellow /

yellow in colour; this varied in intensity but never cleared; for a time had dragging sensation in abdomen; lost a great deal of weight in last month. On admission, small, thin man; liver enlarged to 3 in. below right costal margin, with large tense gall-bladder projecting below liver into right iliac fossa.

Before operation, 6.5 litres of casydrol given by intravenous infusion over four days; facial flush; temperature rose on three of the four days of the infusion to 99.6, 101, and 100°F.; slight increase in pulse rate; no nausea; no vomiting; ate ordinary diet. Similar chemical tests to those done in Case 26, showed no significant change; total plasma protein concentration fell from 5.61 g. to 5.56 g. per 100 ml.; albumin rose from 2.93 to 3.41 g. per 100 ml.; and globulin fell from 2.68 to 2.15 g. per 100 ml. At laparotomy: neoplasm of head of pancreas; cholecyst-jejunostomy. Subsequent partial pancreatectomy was performed. Patient died a week after discharge from hospital, from haemorrhage from gastro-jejunal anastomosis. No clinical improvement was noticed to result from casydrol infusion; no evidence of water retention.

Case 28.- T.L., aged 47 years. Railway coach examiner. Five months ago had jaundice for four weeks with diarrhoea, passing five pale stools a day. Then jaundice faded, he felt well, returned to work and normal diet but found that fried foods "just went right through him". Two months ago jaundice returned, with pale stools and dark urine. Jaundice became progressively deeper and there was severe itching and he scratched a great deal.

On examination, a thin, wizened but very cheerful little man with skin of a dark greenish-brown colour; liver enlarged 1 in. below costal margin; gall-bladder not palpable; many scratch marks. On radiological examination, no biliary calculi, barium enema showed constant filling defect in transverse colon. Liver function tests indicated obstructive lesion.

Before operation, 5.94 litres of casydrol were given by intravenous infusion over four days. Some darkening of facial colour; no nausea; ate ordinary diet. No significant change noted in same chemical tests as for previous two cases. At laparotomy: cholecyst-jejunostomy. Subsequently, at second laparotomy, hard masses in head and body of pancreas were diagnosed as chronic pancreatitis; later developed pneumo-peritoneum and died two months after admission. No clinical improvement was associated with casydrol infusion; no evidence of water retention.

Case /

Case 29.- Mrs B., aged 42 years. Pain in back for eight weeks; progressive jaundice for six weeks. On day before operation, was given 1890 ml. casydrol; facial flush seen; no nausea; no reaction; no improvement or change noticed. At laparotomy: inoperable carcinoma of head of pancreas; cholecyst-jejunostomy.

Case 30.- J.W., aged 49 years. Banker. Ten weeks' intermittent jaundice. One-stage duodeno-pancreatectomy for carcinoma of head of pancreas. Developed biliary and pancreatic fistula. Jejunostomy established but was unsatisfactory; good deal of leakage. Repeated infusions of casydrol in volumes of 540 to 2160 ml. at slow rate. Appetite impaired sometimes during and after infusions; urine dark in colour with strong odour of casydrol. Casydrol infusions appeared to help to maintain general condition in spite of profuse loss of secretions from fistula.

Case 31.- A.C., aged 58 years. Labourer. Epigastric pain for five years. Jaundice for 14 weeks. At operation: gastric and jejunal ulceration, with chronic cholecystitis and obstruction of common bile duct; cholecystectomy and choledochostomy. Twelve days after operation condition deteriorated, jaundice worsened, hiccough; low urinary output. Intravenous infusion of 2160 ml. casydrol given with glucose solution and saline. General condition was much improved by the infusion but there was no evidence that the improvement was due to casydrol rather than to saline and glucose solution.

Case 32.- Mrs S., aged 60 years. Cholecystectomy and choledochostomy for carcinoma of the extrahepatic bile ducts. Casydrol, 1720 ml., given day after operation; milk, glucose and pronutrin by mouth on second day; and milk, dried skimmed milk and lactose on third day after operation. No reactions. No benefit resulted and the patient died.

Case 33.- Mrs R., aged 65 years. Obstructive jaundice with cholelithiasis; cholecystectomy. On 4th post-operative day double incontinence developed, temperature rose and liver failure was suspected. Intravenous infusion of 1620 ml. casydrol was without effect. At autopsy there was thrombosis of the portal vein and centrilobular liver necrosis.

Case /

Case 34.- Miss J., aged 58 years. Housewife. For two months before admission, jaundice with dark urine, following bout of influenza; stools pale for two weeks after onset, then nearly normal in colour. History of contact with niece suffering from hepatitis two months before onset of illness. Chemical tests indicated hepatogenous basis for jaundice, but because of persistence of icterus laparotomy was carried out. Biopsy of liver showed evidence of regenerating acute hepatitis probably of virus origin; no evidence of biliary obstruction at laparotomy, choledochostomy. After operation, condition deteriorated and on fourth day casydrol infusion started and 6.5 litres given slowly during next five days; no flushing of skin; no elevation of temperature or of pulse rate during infusion; no adverse reaction. Died on ninth day after operation. Because of incontinence, regular specimens of urine could not be obtained; the urine was dark in colour before the infusion was begun and no increase was noticed; the characteristic odour was present but was not strong. No apparent benefit was derived from the casydrol.

Comment

In none of these nine jaundiced patientswas there any direct evidence of benefit resulting from casydrol infusions, although there was an impression that recovery from operation was helped by the post-operative infusions and that the urinary loss of the infusate, as judged by the smell of the urine, was less than after gastrectomy. In three cases of pancreatic neoplasm (Nos. 26, 27, 28), the effect of casydrol before operation was studied by repeated liver function tests but no evidence of improvement was obtained. It was, however, rather surprising to find, contrary to some reports that severe jaundice or liver disease was a contra-indication to the intravenous administration of casein hydrolysates, that, before operation, the hydrolysate was very well tolerated by these patients. No evidence of pre-operative water retention was obtained in these cases.

The condition of two patients (Cases 32, 33) was grave when the casydrol infusions were started. In Case 30 the repeated infusions /

infusions appeared to produce transitory improvement, but, as in Case 31, caution must be exercised in ascribing this to casydrol because in both these men there was dehydration and loss of chloride, and in Case 30 loss also of sodium. How much of the improvement, therefore, was due to the weak salinity of the casydrol it is impossible to estimate. Although there was evidence of regeneration in the piece of liver excised at laparotomy on Case 34, before casydrol was given, improvement did not result from casydrol and her condition steadily deteriorated until she died.

In contrast to the patients who were given casydrol after gastrectomy, the systemic disturbance in this group of jaundiced patients was slight and temperature and pulse rate rose for shorter periods and to a lesser degree; in some cases there was no systemic disturbance. This seems to be an observation of some importance in regard to post-operative protein metabolism, but its exact significance is not yet clear.

Case 35.- A.C., aged 40 years. Labourer.
Perforated duodenal ulcer with peritonitis and pelvic abscess. Casydrol, 540 ml., given over six hours. No reaction. No apparent benefit.

Case 36.- R.T., aged 69 years. Retired.
Perforated gastric ulcer with peritonitis, ileus, severe alkalosis; semi-comatose. Casydrol, 1450 ml., given without reaction or apparent benefit.

Case 37.- A.S., aged 58 years. Farm tractor driver.
Loss of weight and vomiting for three or four months; constipation and oliguria for two months. Severe disturbance of blood chemistry: carbon dioxide combining power 100 volumes per 100 ml. blood, blood chloride 250 mg. per 100 ml. blood, urea nitrogen 92 mg. per 100 ml. blood. Patient much improved by saline and glucose saline infusions; then 5400 ml. casydrol given over three days with glucose; further improvement in general condition and he felt and looked /

looked better. Little change in blood chemistry, blood chloride 240 mg. per 100 ml. blood, urea nitrogen 95 mg. per 100 ml. blood, albumin 2.8 g. and globulin 2.5 g. per 100 ml. plasma. At operation: inoperable carcinoma of stomach with widespread metastases; gastro-jejunostomy. Died on 4th post-operative day. No reaction to casydrol.

Comment

These three patients were treated early in the course of the investigation and the quantities of the hydrolysate given to Cases 35 and 36 were unlikely to produce any improvement, but their use without adverse effect was of value at that stage of the investigation. The patient A.S., Case 37, was very ill indeed from disturbances secondary to widespread malignant disease. The difficulty again arose of distinguishing between the effect due to the fluid and electrolyte and that due to the protein contained in the casydrol. It seems unwise to attribute any specific benefit to the protein when there was such a gross disturbance of blood chemistry which was unaffected by the casydrol infusions.

Case 38.- Mrs W., aged 34 years. Ulcerative colitis. Transfusion of packed cells, whole blood and saline was given in vain attempt to improve her general condition, and was followed by 2160 ml. of casydrol. No specific effect of the casydrol was noted; there was no reaction. The patient died.

Case 39.- Mrs L., aged 37 years. Ulcerative colitis; previous attacks seven and five years ago, present attack of eight months' duration. Terminal ileostomy, as first stage of proposed colectomy, was followed by slowly progressive deterioration. Casydrol, 5400 ml., given by slow intravenous drip infusion. Casydrol given intermittently at about 100 ml. per hour without reaction and with only slight venous irritation. Appetite was capricious and she ate surprisingly large meals of mince and other meats and vegetables; her desire for and consumption of ordinary food was unaffected by the casydrol infusion. There was little odour from the /

the urine which was usually of a dark colour; samples were not regularly obtained as she was incontinent so urine loss cannot be estimated. There was no apparent change in her general condition apart from an impression that the volumes of fluid which were infused were more than could be tolerated. She died during the infusion 37 days after operation, death having been anticipated on several occasions during the previous three weeks. At autopsy the colon was ulcerated throughout its length; the liver was larger than expected, soft and fatty.

Comment

In these patients there was again the difficulty of distinguishing the effect of casydrol from that of fluid and electrolyte replacement. It was generally believed that some benefit was derived from the casydrol, but no objective evidence was obtained; the slight odour from the urine suggests that most of the injected protein was metabolised.

Case 40 (Table 47).- P.H., aged 65 years. No occupation. A vegetarian suffering from prostatic enlargement, severe anaemia and malnutrition; there was little but skin, bone, tendons, blood vessels and nerves left in the limbs of this man who for many months had voluntarily restricted his food intake and had developed starvation anorexia. After transfusion with two pints of packed cells and one pint of whole blood, 2500 ml. of casydrol were infused; this was well tolerated without reaction, thrombosis or rise in temperature or pulse rate. There was some urinary wastage of peptide as judged by colour and smell of the urine. Appetite became poor during the casydrol infusion and for two days after the infusion there was anorexia followed by recovery of appetite.

After suprapubic cystostomy the patient became mentally depressed, ate less and less and his general condition became very poor. Fresh blood transfusion was again followed by casydrol infusion. Urine amino nitrogen, total nitrogen and chloride excretions were measured and are shown in Table 47. There was an increase in urine amino nitrogen excretion during and for one day after the casydrol infusion. Total urine nitrogen rose significantly on only one day. Urine chloride excretion (expressed as g. NaCl) fell at the start of the infusion and remained below the previous level for the two days after the infusion ceased. There was some reduction of the already low food intake during the infusion, but it seemed /

seemed doubtful whether this was enough to explain the whole reduction in chloride excretion. The casydrol contained about 0.3 g. per cent. sodium chloride so that some of the chloride from this source also was probably retained. Some isotonic saline, about one litre in all (9.0 g.) was administered in addition to the casydrol. Over the four days when urine amino acid nitrogen excretion was raised, nitrogen equivalent to about 80 per cent. of that administered as amino acid nitrogen was retained in the body. Flushing of the face was a prominent feature during the casydrol infusion; there was also some darkening of the colour of the urine which had the characteristic odour of casydrol.

The general impression was that the casydrol infusions produced a marked and sustained improvement in appetite and consumption of food after a short period of anorexia, and were of particular value in view of the peculiar attitude of the patient to diet and to life. The question arises as to whether, in this man who had starved himself for a long time, the intravenous injection of amino acids had any specific effect on the intestinal mucosa, and especially its villi, which promoted recovery of the ability of that mucosa once more to deal with ingested food. This will be discussed in more detail later.

(2) Amigen

The Medical Research Council supplied amigen in sealed tins each containing 50 g. of dried powder (Mead Johnson). The solution was prepared by dissolving 50 g. powdered amigen in a litre of 5 per cent. glucose solution. The resulting slightly cloudy fluid was cleared by being passed through a Seitz pad. This solution was of a pale straw colour and smelled much less strongly than did the casydrol solutions. The solution was sterilised by heat in an autoclave. This resulted in darkening of /

of its colour, presumably due to caramelisation of the glucose. As in the case of casydrol, the object was to provide at least 11.0 g. nitrogen per day as amigen, and as many calories as could be conveniently and safely infused in the form of 5 per cent. glucose solution. Thus the protein administered as amigen was accompanied by at least an equivalent quantity of carbohydrate as glucose.

The following two patients (Cases 41 and 42) were studied.

Case 41.- R.M., aged 33 years. Joiner. For 12 years had had intermittent upper abdominal pain an hour and a half after food, relieved by more food and by alkaline powders. Discharged from Army for duodenal ulcer. Recently had been having bouts of vomiting rather than pain, and had taken large quantities of alkaline powder and baking soda. Six days before admission pain came on in both calves and passed up to thighs and kept him awake. On night before admission he was noticed to be drowsy, talking nonsense and was very confused. Good appetite, no melaena, had recently lost weight. On admission to medical ward was confused, and there were some muscular spasms. Blood chloride 280 mg. per 100 ml. Intravenous infusion of eight litres of saline in less than 48 hours was followed by much improvement, but pain in legs and some patchy areas of numbness persisted. Transferred to surgical ward. Radiological examination showed gross deformity of duodenal cap with stenosis. Up to one litre of gastric residue in evenings. At laparotomy: chronic duodenal ulceration with dense and almost complete pyloric stenosis; partial gastrectomy; gastro-jejunostomy.

After operation, intravenous infusion 36 hours, gastric aspiration 50 hours. Intravenous infusion of amigen was started 22 hours after operation and ran well; mild skin flush, some drowsiness, frothy sputum and increase in temperature, pulse and respiration rates. About 12 hours after start of infusion when 900 ml. had been given, there was a marked increase in pulse rate from 100 to 130 per minute with respiration rate of 40 per minute and temperature 101 °F. There was also dulness and diminished air entry left lung base suggestive of basal pulmonary collapse. These elevations of pulse and respiration rate persisted for four hours and patient became anxious and restless. Infusion therefore stopped after 1150 ml. amigen had been given. Pulse rate subsided slowly during next three days, temperature elevated for a further four days, respiration rate for two days. There was /

was frothy sputum for three days after infusion was stopped. Patient up on 5th day, discharged on 11th day to convalescent house. Urine became a little darker in colour after amigen infusion and smelled slightly of the same odour as did the amigen solution. Total of 1150 ml. amigen injected containing 7.6 g. nitrogen.

The nitrogen balance study was stopped when the amigen infusion was discontinued; no urinary amino nitrogen estimations were done. Some consideration was given to the idea that the disturbance which occurred after 900 ml. of amigen had been given was due to acidosis because of the low pH of the amigen solution. Finally it was decided that the disturbance was largely due to anxiety on the part of both the patient and the observer.

Case 42 (Tables 28, 48, 55, 56).- R.K., aged 39 years. Miner. For 11 years had been troubled with heartburn; for a few years had had pain after meals relieved by food and alkaline powders, pain passed through to back; no vomiting; had lost weight recently. Perforation of duodenal ulcer three years ago closed at operation. On admission, spare type of man; upper abdomen tender on pressure. At laparotomy: chronic duodenal ulcer; trans-abdominal vagotomy; partial gastrectomy; gastro-jejunostomy. After operation, intravenous infusion for five days, gastric aspiration two days; temperature and pulse rate elevated for seven days, respiration rate for five days. Extensive phlebitis of the long saphenous vein began on 4th day, most severe on 7th and 8th days; no suppuration but intense local aseptic inflammation. Amigen infusion begun on day after operation and continued for four days, 6.4 litres being given. No rigors or nausea; mild anorexia. Some odour from urine which was darker than usual in colour. Respiration and pulse rates and temperature rose and remained elevated throughout infusion and for three days afterwards; first four days attributed to amigen, last three to phlebitis. Profuse watery sputum brought up during first three days, less profuse on last day. Mild flush of face throughout infusion. Appetite good at end of infusion and took all the food offered. Got up on 5th day, discharged home on 15th day. Seven and a half pounds of weight lost in 11 days after operation.

The intakes of sodium and of chloride were also controlled in this case, and as steady a level of ingestion as possible was maintained by the administration of saline intravenously and by mouth, flavoured with orange syrup.

Before operation was in positive nitrogen balance on daily intake of 90 g. protein (14.5 g. nitrogen) and 2600 calories. Only 350 ml. urine were secreted on day after operation, and as a result of this and the amigen infusions there was positive nitrogen balance of about 6.0 g. On the /

the 2nd day urinary nitrogen excretion was 30.5 g. with marked negative balance of 20 g. nitrogen; for four more days there was a raised urinary nitrogen excretion with another high excretion on the 8th day. On the first two days of amigen administration, only 700 and 634 calories respectively were provided; on the last two days over 1300 calories were provided each day, but at least 500 of these were derived from the ordinary food which was consumed on these days. There was a slight hangover of peptide excretion on the day after the infusion was stopped, but amino acid nitrogen excretion fell sharply when the amigen was stopped. There was an increase in amino acid excretion from the 6th to the 9th, and peptide excretions from the 8th to the 10th days. These increases were probably related to the extensive phlebitis which occurred after the amigen infusions. At the same time there was a gain in weight and apparent water retention. In spite of the low pH of the amigen solution, no evidence of acidosis was noticed; the carbon dioxide combining power was 66 volumes per 100 ml. about 20 hours after the amigen had been stopped. Detailed blood chemical studies and blood and plasma volume estimations had been planned but were abandoned when the patient expressed his unwillingness to be punctured so often.

During four days a total of 26.95 g. amino acid nitrogen and 9.0 g. peptide nitrogen were infused as amigen and there were excreted in the urine 3.35 g. amino nitrogen and 5.98 g. peptide nitrogen. If a deduction is made equivalent to four days' excretion at the average pre-operative daily rates of 0.2 g. amino acid nitrogen and 0.5 g. peptide nitrogen, then the total quantities excreted are 2.5 g. amino acid nitrogen and 3.98 g. peptide nitrogen. The quantities retained during the four days of the infusion are therefore equivalent to 93 and 56 per cent. respectively of the injected amino acid and peptide nitrogen. It should be noted that peptide nitrogen excretion was somewhat raised on the day after amigen was stopped.

Comment

There was less marked flushing of the skin and the odour and colour of the urine were less strong with amigen than with casydrol. The output of amino acid nitrogen in the urine fell sharply after the amigen was stopped; peptide nitrogen excretion was more than the pre-operative level on the day after amigen was stopped. Appetite was not so severely impaired by amigen as by casydrol. Less nitrogen was excreted during the period

of /

of the amigen infusion than was the case with casydrol. Table 70 shows, however, that there is no essential difference between the effects of casydrol and amigen on nitrogen excretion. The smaller total negative nitrogen balance (53.5 g.) in the case of amigen may as well be due to the larger intake of ordinary food (92 g. instead of 50 to 60 g. nitrogen) as to the amigen infusions. The total urinary excretion of 122 g. nitrogen in the first six days in Case 42 after 40 g. nitrogen as amigen, compares closely with 126 g. in Case 24 after 44 g. casydrol. During the seventh to tenth days, the four patients (Cases 22, 23, 24 and 25) who had received casydrol, excreted 3.0 to 5.0 g. nitrogen per day more than the man who had received amigen; this patient was given more ordinary food than the other four subjects.

Comparison of the results in Case 42 with those found in the four patients to whom casydrol was administered, shows that under the conditions of these trials there is no important difference between the effects of these two solutions on protein metabolism after partial gastrectomy. Because of its less offensive odour and lighter colour, amigen appears to be a more elegant preparation than casydrol. On the limited evidence available, less of it was wasted in that there was a smaller urinary excretion of both amino acid and peptide nitrogen during the infusions than was the case with casydrol. The systemic disturbances are similar in type and degree with both preparations, which appear to be equally undesirable in this respect.

II. Intravenous Administration of Human Plasma

Plasma protein as the sole source of protein has been claimed to be adequate for the maintenance of nitrogen equilibrium in dogs (Madden and Whipple, 1940). Plasma has been recommended as a good source of protein for the parenteral nourishment of patients suffering from protein lack or loss. Since it had proved to be impossible to reduce the post-operative urinary excretion of nitrogen, either by abundant pre-operative feeding or by post-operative infusions of casein hydrolysate solutions, it was important to try the effects of plasma infusions on a scale sufficient to provide comparable daily nitrogen intakes. The provision of 11 g. nitrogen per day requires the administration of 68.75 g. of plasma protein which will be contained in 1800 to 2000 ml. of fresh plasma. Sufficient plasma for one day therefore necessitates the bleeding of eight to ten donors, and for the whole experiment forty donors were required. All this plasma was prepared from blood freshly withdrawn for this purpose; the plasma was cleared by passage through Seitz pads. There were a number of reasons for believing that human albumin might be preferable to plasma, but it proved impossible to obtain salt-free human albumin in sufficient quantity to make a comparable trial of its value.

It was planned to start the plasma infusions on the day after operation and to continue them for five days, giving the equivalent of 11 g. nitrogen or more on each day. During this period, as much glucose solution was to be given in addition as was safe and convenient. It was recognised that while the provision /

provision of protein might be readily achieved, there was almost certain to be a lack of calories, as it would probably be unsafe to give a total of more than 2500 or 3000 ml. of fluid per day. The patients were not specially selected, but were placed on a nitrogen balance study regime several days before operation for chronic duodenal ulcer.

Case 43.- J.F., aged 45 years. Timekeeper. Eight years' history of gnawing epigastric pain or discomfort related to food, relieved by alkaline powders and to some extent by diet. Recently had pain in back and right shoulder. Always ate regular meals at home. On admission, thin, grey-haired man, not wasted. Pain and tenderness deep in upper abdomen. Radiological examination showed small ulcer crater in duodenum with persistent deformity. At laparotomy: chronic duodenal ulcer; partial gastrectomy; gastro-jejunostomy. After operation, intravenous infusion and gastric aspiration for two days. Blood transfusion after operation followed by saline; plasma started on day after operation.

After 100 ml. of plasma, rigor, with temperature of 102.8°F.; drip stopped during rigor. Fresh vein cannulated and drip restarted with fresh bottle of plasma. Cough produced much purulent sputum. Second vein thrombosed on second morning and thrombosis subsequently spread from ankle to groin along long saphenous vein. Third vein cannulated, thrombosed also, and fourth vein was used until third morning, by which time, as only 1700 ml. plasma had been given, as profuse purulent sputum was being coughed up and as there seemed to be some peculiar tendency to superficial phlebitis, the plasma infusion was stopped. No effect on protein metabolism was observed. Temperature and pulse rate were raised for four days and respiratory rate for three days. The purulent bronchitis subsided, recovery was complete, and he was discharged on 17th day.

Case 44 (Tables 29, 66).- A.H., aged 51 years. Railwayman. For past 24 years had had pain in stomach in repeated bouts lasting several days and occurring at varying intervals. Vomited frequently. Four years ago gastro-jejunostomy for duodenal ulcer. Pain recurred with vomiting. Radiological examination showed deformity of duodenal cap and some roughening of gastric mucosa in region of stoma but no definite ulcer. On admission, general condition good, no recent loss of weight. At laparotomy: stomal ulcer; gastro-jejunostomy undone; jejunum closed; partial gastrectomy; gastro-jejunostomy.

After /

After operation intravenous infusion and gastric aspiration. Plasma infusion started day after operation and continued for next five days interspersed with glucose saline. Gastric aspiration stopped on 2nd morning. Temperature elevated on evening of day of operation and on next day, pulse rose on 2nd evening after operation, but both pulse rate and temperature fell the next day. Sharp rise in temperature to 103°F. with some sweating on 3rd evening. Plasma was stopped for a time but restarted later. Temperature rose again on 4th evening but otherwise he was well. Temperature remained in region of 103°F. on 5th day, and pulse also began to rise; he felt rather weak but nothing abnormal found on clinical examination. Temperature rose to 105.8°F., pulse rate 140 per minute at 3 a.m. on 6th day after operation. Both fell by 9 a.m. when he looked drawn, greyish and ill with a muddy complexion; skin on face, ears, hands and feet felt cold; slight jaundice in sclerae and skin of trunk; respiration slightly stertorous; some consolidation basal regions of both lungs. As little urine had been passed for 24 hours, was catheterised, 60 ml. thick urine being withdrawn containing many granular, epithelial and hyaline casts. Desoxycorticosterone acetate, 20 mg. given four times by intramuscular injection from mid-day, at three to four hourly intervals; 4.285 per cent. sodium sulphate solution and 6 per cent. glucose solution infused intravenously. At 8.15 p.m. blood pressure 74/60 mm. mercury; at 8.25 p.m. aminophylline, 0.25 g., injected intravenously. Condition deteriorated steadily. Vomited some blood-stained fluid; comatose at 9 p.m., died at 9.20 p.m. about 152 hours after end of operation.

There were some striking changes in blood chemistry in this patient (Table 66). Total protein concentration fell from 6.94 before operation to 4.87 g. per 100 ml. on the day of death, the albumin falling from 4.52 to 1.93 g. per 100 ml., and globulin rising slightly from 2.41 to 2.93 g. per 100 ml.; over the same period the packed cell volume fell from 58 to 34 per cent. There was a marked terminal rise in creatinine and urea nitrogen concentration.

At autopsy, the skin and conjunctivae were of a faint yellowish hue and there was oedema of the sacrum and lower limbs. The region of the operation was satisfactory and there was a small quantity of clear brownish free fluid in the pelvis. There were small quantities of slightly blood-stained fluid in the pleural and pericardial cavities. The stomach contained some altered blood but no other abnormality was found in the alimentary tract. The liver weighed 2100 g., was soft and of a pale yellow mottled colour; the cut surface was pale yellowish, soft and with little lobular pattern to be seen. The spleen was large and soft. The kidneys were granular. The lungs were bulky, oedematous and congested, and there was some broncho-pneumonic consolidation in the left lower lobe. Microscopical /

Microscopical examination revealed a haemorrhagic broncho-pneumonia and marked capillary dilatation in the renal medulla, with relative cortical ischaemia. The liver exhibited post-mortem autolysis, round cell infiltration of the portal tracts and general congestion.

Until the evening of the fifth day no concern was felt regarding the progress of this man. The elevation of temperature for 48 hours after operation was not unusual in extent or duration. The rise of temperature on the third evening was ascribed to an effect of the plasma but the temperature subsided and by next morning, in spite of continuation of the plasma infusion, his pulse rate was down to 70 per minute. The sharp rise in temperature on the fourth evening was maintained throughout the fifth day and by that evening the pulse rate also had risen to 120 per minute. During this day urine secretion diminished. On the sixth day little urine was secreted and there was obvious jaundice. During the first three days after operation, body weight increased by 5.25 lb. from 152.5 to 157.75 lb. The records of fluid intake and output were incomplete, but from the morning of the day of operation until the time of death, about 18 litres of fluid were administered by oral and intravenous routes, including 6.4 litres of 0.9 per cent. saline and 6.2 litres of plasma. In the same period more than four litres of urine were excreted and 1.5 litres of fluid aspirated from the stomach. There was retention of about 12 litres of water in one form or another, without allowance being made for the insensible loss.

In Case 43 the quantity of plasma injected was inadequate and this case was not a fair trial of the method. The reason for failure was the repeated phlebitis and rigors and the onset of /

of bronchitis. In Case 44, during five days 6.2 litres of plasma were administered but the distribution of the infusions was irregular, on the second and third days only 400 ml. and 800 ml. were injected. Both in this respect and in the total volume used, the infusions were inadequate. In addition, few calories were provided by intravenous infusion of glucose and there was also inadequacy in this respect. During the first four days after operation, the urinary nitrogen excretion was increased as in other patients. Plasma from the blood of 17 donors was used in this case. This implies that a large proportion of the sodium citrate solution used as an anticoagulant was also injected. Since 50 ml. of 3.8 per cent. sodium citrate solution is employed for each lot of blood, up to 850 ml. of 3.8 per cent. sodium citrate might have been injected, containing over 30 g. of sodium citrate. Transfusions of up to eight litres of blood containing 30 to 35 g. citrate have been given and have not been followed by any manifestations of citrate poisoning. The symptoms and signs of sodium citrate poisoning are similar to those of calcium deficiency (White and Weinstein, 1947); no evidence of such a disturbance was seen in this case. The possibility of a transmitted virus infection or of other noxious agents carried in blood or plasma cannot be excluded.

The changes in blood chemistry, taken in conjunction with the low blood pressure, suppression of urine, jaundice and the general appearance of the patient, were suggestive of a profound disturbance of liver function. This was supported by the soft, pale, yellow liver found at autopsy, and by the water retention which /

which was present from an early point in the post-operative period. The most likely source of a cause for this liver disturbance appeared to be the plasma, although this opinion was not shared by others who observed this patient. It received some support, however, from the course of events previously observed in patients suffering from extensive burns and scalds, who were resuscitated by the infusion of large volumes of plasma. In these patients there was jaundice, elevation of temperature, oedema and alteration in blood chemistry; tannic acid and other agents suspected of causing liver injury were not employed in these cases. There was often marked oedema, especially in dependent parts of the body. Urine output was usually low, and even when allowance was made for loss of water in the exudations from the burn, there was a severe degree of water retention.

The unhappy outcome of Case 44 led to the abandonment of the extensive trial of plasma infusions which had been planned.

Discussion

A study of certain aspects of the intravenous administration of protein hydrolysates in surgical patients was the primary object of this investigation. Inevitably interest in the metabolic disturbances after operation overflowed this primary object in several directions, and this broadening of the scope of the enquiry led to new viewpoints and perhaps a different orientation of protein metabolism than might otherwise have been achieved.

On /

On the basis of results obtained in the present series of cases with the support of similar evidence derived from the analysis of many reported nitrogen balance studies, it was arbitrarily laid down that the minimum intake necessary for nitrogen equilibrium before operation in a healthy adult patient spending most of the day in bed was 70 g. protein (11.2 g. nitrogen) and 1800 calories. This daily intake of 11.2 g. nitrogen was achieved in the post-operative period by intravenous infusion of casydrol, but in no case was it possible safely to administer in addition 1800 calories by infusion of 5 per cent. glucose solution.

The inadequate provision of calories implies that at least part of the retained nitrogenous material would be wasted by use as a source of calories. The excretion, during and within a short period of time after the injection, of an additional quantity of nitrogen about equal to that contained in the injected material, suggested that all of the hydrolysate was used for fuel purposes. Such a judgment is probably too severe and could not be supported by the present knowledge of intermediary protein metabolism. Some use may be made of the hydrolysate during its apparently short stay in the body.

Browne and his group reported that after injury or operation in well-nourished patients the intravenous administration of amigen was followed within 24 hours by the excretion in the urine of additional urea containing nitrogen equivalent to that injected as amigen. In discussing nitrogen balance studies made by his group, Browne (1944) emphasised that patients could be divided into two groups according to their post-operative metabolic /

metabolic behaviour. In the first group was the previously healthy adult who was acutely injured, accidentally or surgically; after operation this patient exhibited a marked rise in urinary nitrogen excretion and negative nitrogen balance. The consumption of 100 to 150 g. protein and 2700 to 3000 calories in the post-operative period by this patient resulted in the excretion in the urine within 24 hours of a quantity of nitrogen equivalent to that ingested. This also applied to amigen injected intravenously but not to plasma transfusions. In the second group was the chronically ill subject in whom after similar acute injury there was no rise in urinary nitrogen output, and positive nitrogen balance was re-established soon after operation at a relatively low level of nitrogen intake. Similar observations were independently made in the present investigation.

These two groups tend to merge into one another and their clinical recognition may be difficult. The best means of doing this is probably by a detailed history of the illness and its effects on food consumption and body weight. In the debilitated patient there may be no increase in urinary nitrogen output in spite of large increases in protein and caloric intake. Browne, who pointed this out, suggested that it indicated retention and utilisation of the protein. This apparently contradicts Cuthbertson's idea that the protein-depleted patient has no labile stores left and so cannot break down protein after injury. The truth is probably that Browne and Cuthbertson are both right and are expressing different but concurrent aspects of the same phenomenon.

If /

If the indication for the intravenous administration of protein hydrolysates is regarded as an inability to ingest, digest or absorb protein, then impairment of appetite and consumption of food, nausea and vomiting as complications of the infusion of hydrolysate can hardly be considered valid objections to the use of hydrolysates. If, however, intravenous administration of protein hydrolysates is to be used as an adjuvant to the ordinary diet, then these disturbances may cause more trouble than the injections are worth.

With regard to the nausea and vomiting, Madden et al. (1945) found that, in dogs, when a mixture of pure amino acids was administered by the intravenous route, the addition of glutamic or aspartic acid caused vomiting; conversely mixtures of amino acids free of glutamic or aspartic acids have been injected into human subjects at very fast rates (Eckhardt and Davidson, 1948). Hoffman et al. (1946) stated that elevation of the amino acid nitrogen concentration of the blood to 10 mg. per 100 ml. or more, was associated with nausea and they believed this to be the important causal factor. Hecht (1946) suggested that it was the rapidity of elevation of amino acid nitrogen concentration rather than the concentration itself which was responsible. In the present series no significant rise in plasma amino acid nitrogen concentration was associated with uneventful infusions. The explanation of Madden et al. seems to be the most likely one; rapidity of injection and the temporary elevation of the blood level of glutamic or aspartic acid may underlie the explanations of Hoffman et al. and of Hecht.

It was found that superficial phlebitis was no more common with /

with casydrol and glucose solutions than with glucose alone, and this was also the experience of Gardner and Trent (1942). They, however, used a 3 per cent. solution of amigen in 5 per cent. dextrose and 0.9 per cent. saline, and gave one litre in an hour twice a day. There is a marked individual variation in the occurrence of phlebitis and thrombosis and, judging from remarks in many reports, there is no relationship to particular preparations. There was no doubt as to the safety of casydrol or of the freshly prepared amigen solutions used in the present series. The impression was formed that the method of administration employed by washing the vein with saline from time to time reduced the incidence of phlebitis but no statistically valid evidence on this point was obtained.

During casydrol infusions in four cases there was retention of 60 to 73 per cent. of the injected amino acid nitrogen. The retention of peptide nitrogen was much less than this, but detailed information was not obtained because of difficulties in the estimation of peptide nitrogen. After amigen infusion in one patient there was retention of 93 per cent. of amino nitrogen and 56 per cent. of peptide nitrogen. The difference between the amino acid and peptide loss in the urine after amigen and casydrol might be due to the properties of the preparations or to such factors as the rate of injection, quantity of hydrolysate injected and initial plane of protein metabolism in the patients employed. It was thought that in the present study the most important factor was the nature of the amigen solution.

Christensen et al. (1946) found that there was a greater accumulation and longer persistence in the blood and a higher proportionate /

proportionate loss in the urine (36 to 53 per cent. of that injected) of peptide nitrogen than of the amino acid nitrogen provided by the intravenous infusion of amigen. Christensen et al. (1947) found that loss of the peptides derived from the acid hydrolysis of fibrin was about half that found in the case of casein hydrolysates, but there was a higher rate of loss of amino acid nitrogen when the fibrin hydrolysate was employed. The source of the fibrin was not stated. The total urinary loss of free and bound amino nitrogen was equivalent to about 20 per cent. of the quantity injected of either preparation. They thought the differences in the peptide depended on the different structures of fibrin and casein. In the present trial there was a smaller loss of both amino and peptide nitrogen after amigen than after casydrol, and there seemed to be a difference between these two varieties of hydrolysate.

Eckhardt and Davidson (1945), using oral supplements of phenylalanine in conjunction with oral and intravenous administration of casein hydrolysates, showed that the minimum requirements for an amino acid may have to be increased when it is given in a hydrolysed preparation, and to a further degree when it is administered by the intravenous route. It is conceivable that the rapid injection of a mixture of highly purified amino acids once or twice a day may be more wasteful than the slow infusion of a less pure mixture throughout the day.

Into normal men whose calories were provided fully by a protein-free diet, Eckhardt and Davidson (1948) injected intravenously a purified amino acid mixture derived from the complete acid hydrolysis of casein, supplemented with dl-tryptophane, dl-methionine /

dl-methionine and glycine. This mixture contained no peptides, glutamic or aspartic acids and was injected at very rapid rates. They found that the loss of amino nitrogen in the urine was related more to the quantity of nitrogen given than to the rate of infusion. They also found that the daily requirements for phenylalanine increased from 1.97 g. to 2.78 g. if the mixture was given in one large intravenous infusion instead of in divided oral feeds. Further, compared with the oral consumption of the whole protein, the administration of the amino acid mixture by mouth resulted in eight times as great a urinary loss of nitrogen, and by intravenous infusion in twenty-four times as great a loss. In further examining the relationship of loss to quantity infused, they found that while at low rates of infusion there was a variation in the quantities of individual amino acids excreted in the urine, as the quantity given rose, the excretion pattern approached more and more that of the infusate. All the amino acids studied by Goettsch et al. (1944) were almost completely reabsorbed by the renal tubules at normal plasma concentrations and normally only small quantities are found in human urine. Eckhardt and Davidson (1948) found that although the ten "essential" amino acids constituted 64 per cent. of the injected amino acid nitrogen, they were responsible for less than one-third of the total amino acid nitrogen in the urine. At low rates of injection, there was a relatively higher rate of excretion of threonine, histidine, and to a lesser extent of lysine and tryptophane. In spite of the urinary losses, they stated that 85 per cent. of the administered protein was retained for metabolic processes. They believed that slow infusions /

infusions had no advantage over fast injection because the small saving of amino acids was counterbalanced by the inconvenience to patients and attendants of prolonged infusions.

Smyth et al. (1948) compared the results of the administration of solutions of amigen, a fortified acid hydrolysate, and a mixture of amino acids derived from the recombination and fortification of fractions of casein hydrolysates. These solutions were given at various rates to normal males. The major wastage was in the first few hours after the infusion, it was worst with amigen but there was a marked individual variation Increasing the rate of injection did not greatly increase the wastage of amino acids. It is probable that these conclusions apply only to isolated infusions for short periods; in continuous infusions they have a limited application due to variation in rate.

It seems reasonable to invoke the law of mass action once more. The rate and the accumulated total quantity of nitrogen injected were the important factors governing loss of nitrogen in the urine in the patients reported here. As the rate was increased, so was the nitrogen excretion (and the dark colour of the urine and the intensity of its odour). As the duration of the infusion increased, provided there was no great reduction in the rate of injection, so did the quantity of nitrogen in the urine, resulting in a falling daily "retention". Eckhardt and Davidson (1948) believed that the rapid injection of a large quantity of amino acids in a short period was preferable to a slower and more prolonged infusion. Rapid injection is not possible with preparations such as casydrol because of the nausea and /

and other disturbances which result. At the slow rates of infusion of casydrol reported here, reactions were uncommon, and 11 g. nitrogen or more could be provided in 24 hours, but the provision of calories as glucose solution was inadequate.

In comparing the present experiments with others, allowance must be made for variations in the rate of infusion of casydrol within the implications of the expression "continuous infusion"; rate varied widely in spite of all attempts to regulate it within safe limits. The total quantities of nitrogen injected, excreted and retained per 24 hour period are also liable to create a wrong impression if they are regarded as spread evenly over the whole period. It is difficult to imagine how a truer picture can be obtained except by the separation of injections and excretions in four-hourly periods; this, with the resulting increase in analytical and clinical work, might be undertaken only on a limited number of patients.

In maintaining nutrition wholly by intravenous infusions of amigen and glucose before and after operation, Bigham et al. (1947) calculated the basal daily requirements of nitrogen and calories on the assumption that 10 g. nitrogen and 1600 calories per 1.73 sq. m. body surface area was an adequate daily intake at bed rest. They then gave this calculated dose in the proportion of 6.25 g. nitrogen per 1000 calories. This is very similar to the arbitrary choice of 70 g. protein (11.2 g. nitrogen) and 1800 calories made in the present series on the basis of the examination of a number of the present and other observers' nitrogen balance figures. Bigham et al. (1947) mentioned that the average daily intake in their cases was 12 g. nitrogen /

nitrogen and 1900 calories in the form of 100 g. amigen and 375 g. glucose dissolved in 3500 to 4500 ml. water with 4.25 to 8.5 g. sodium chloride; less than 25 per cent. of the total calories were derived from protein. In the present series an average has not been struck, but an intake of over 11 g. nitrogen and 1000 calories was achieved in some cases, about half of the calories being derived from protein.

In normal subjects awaiting operation for hernia, Bigham et al. (1947) found that provided the injection rate did not exceed 7 to 10 ml. per minute, there was little urinary wastage of amino nitrogen and almost none of glucose. They gave their whole daily intake of protein and glucose in eight hours and found that the urinary amino acid excretion rose up to two and a half times the quantity excreted following oral administration of the same amount of food. They estimated, however, that not more than 3 to 6 per cent. amino nitrogen injected as amigen was wasted in the urine. This comparison would have been more useful if it had been made with the pre-injection excretion in the same subject rather than with the excretion rate after oral administration of hydrolysate. Their excretion rate for amino acid nitrogen during and after amigen is comparable to the values obtained after casydrol in the present series.

In patients suffering from oesophageal or pyloric obstruction, Kozoll et al. (1945) tried to achieve nitrogen equilibrium solely by intravenous infusion of glucose and of amino acids derived from acid hydrolysis of casein or fish protein. There is some doubt as to the adequacy of the preparations which they employed. They infused over a period of 12 to 14 hours, four litres /

litres of fluid containing 105 to 150 g. glucose, 90 to 135 g. amino acids and 9 g. sodium chloride; if the amino acids be excluded, the caloric value of this fluid was only 420 to 600. This small total provision of calories still required that three of the four litres infused should be hypertonic. They concluded that they could supply the full basic daily requirements of carbohydrate only if some of the carbohydrate were given by mouth. If nothing could be taken by mouth, the urinary nitrogen excretion rose above the true basal level. The ease with which nitrogen equilibrium was achieved was related to the quantity of nitrogen excreted per day in the control period; when this was low, equilibrium was easily reached by intravenous infusions of amino acids, when it was high the reverse was true. They found it more difficult to produce equilibrium after operation than before, even for such relatively minor procedures as gastrostomy, but here again the difficulty was closely related to the level of pre-operative nitrogen excretion and so to the plane of nitrogen metabolism and the mass of body protein.

Originally Elman (1939) tried to supply the full daily caloric requirements as glucose solution by intravenous infusion. To provide 1600 calories per day this required the injection of four litres of 10 per cent. glucose solution. On reducing this daily quantity of glucose solution, Elman et al. (1945) stated that nitrogen equilibrium could still be obtained in spite of what would be for a normal subject in good nutrition an inadequate intake of calories. They did not give details of these cases and this is unfortunate as from this observation they proceeded to the following animal experiments. Four dogs were fed /

fed by gavage with dextrimaltose and amigen only, but were allowed water freely. The proportions of protein and carbohydrate were varied isocalorically at two planes of intake, and they claimed that when the diet was restricted and the total calorie intake was at the lower level, positive nitrogen balance could be maintained if the proportion of protein to carbohydrate was 4 to 1 but not if it was 1 to 4. This startling conclusion does not seem to be the correct one to be drawn from their data. It is suggested that their findings result from the particular combination of several factors, and that their conclusion, stated above, is unjustified. In their Table 1, Dog L shows signs of stabilising in the third four-day period, having apparently adjusted its nitrogen metabolism from a higher to a lower plane in 12 days; the average negative balance figure of 0.49 g. per day is misleading. A similar process of adjustment of nitrogen metabolism is shown for Dog S. In both these dogs, when the intake of calories was halved, there was a reduction in urinary nitrogen excretion; that the total caloric intake was then inadequate is suggested by the negative nitrogen balance in each case. In Table 2, for two different dogs results are shown which suggest that the very large protein intake exceeded the ability of the animals to deal with it. In Table 3, Dog T, the reduction in urinary nitrogen excretion during the first four periods suggests that the experimental diet was lower than that fed before the experiment, and perhaps also was inadequate. The diet in the fifth period would be expected to cause retention of nitrogen for a short period at least, because of the sudden increase in protein intake.

Similarly, /

Similarly, in the other dog, negative balance would be expected after a change to a lower protein intake because of the continued excretion of nitrogen derived from the richer diet.

These experiments have been discussed in detail because of their importance in the field of hydrolysate therapy. If this suggestion of Elman et al. (1945) were to be substantiated, then the chief problem associated with the intravenous administration of protein hydrolysates, that of the simultaneous provision of adequate calories in the form of glucose, would be removed, and the present conception of the relationship of protein and carbohydrate in nutrition would be upset. The evidence on which Elman et al. base their conclusions is equivocal and their conclusions cannot be accepted.

Mok et al. (1948) also questioned the importance of carbohydrate intake in nitrogen metabolism. The experiments which they reported show rather wide variation in the results, and they did not quote the age, sex or diagnosis or estimate the state of nutrition of their patients. They suggested that the quantity of nitrogen injected intravenously was the important factor in improving nitrogen balance, and that the provision of calories as glucose solution was of lesser importance. They implied that the full provision of the basal caloric requirements in the form of glucose solution by the intravenous route was unnecessary. In their discussion they cited the findings of Block (1942) in support of their conclusions. His six patients suffered from obesity and it seems doubtful whether they can be closely compared with the 25 mixed patients of Mok et al. They also mention that Elman (1945) stated that if the amino acid intake

was /

was adequate, then the carbohydrate, which was the only other source of calories, could be reduced to 25 calories per kg. per day; in the case of a 60 kg. man being fed 70 g. protein per day, this would imply an intake of 1500 calories as carbohydrate and 1780 calories per day in all, which is similar to what has been suggested in the present study. This is probably a satisfactory basal dietary level, but it cannot be readily attained solely by the intravenous route.

The results of Spence et al. (1946), who claimed to have established nitrogen equilibrium after major operations, are difficult to evaluate since their studies were started at varying times after operation, the urines were pooled, and the results were expressed in terms of nitrogen balance from the third day onwards. They did, however, emphasise that oral rather than intravenous provision of food was the ideal method.

In some reports on the use of protein hydrolysates, the recommendations are surprising and even unsafe. For example, Werner (1947), in reporting the use of the VUJ mixture of amino acids, recommends infusions which provide each day 15 g. nitrogen, 900 calories, 4500 ml. water and 27 g. sodium chloride, although he mentioned that most of the sodium chloride might be omitted. He discussed the employment of this solution in a patient who died; apart from acidosis and pulmonary oedema the cause of death was unknown. There was, however, marked retention of water and oliguria, and the data provided suggested that water retention might well have been the cause of death.

Werner (1947) discounted the post-operative catabolic phase because it did not consistently appear in his patients. If his control /

control patients are any indication, this was probably because his patients were suffering from protein depletion at the time of operation. He claimed to have prevented negative nitrogen balance in a well-nourished man and woman, who suffered accidental fractures, by giving them high protein milk and casein hydrolysate by mouth. This, Cuthbertson (1935) had found impossible. Werner stated that nitrogen intake was essential for the development of the catabolic phase. This is not in agreement with the findings in the present series and in numerous other reported cases.

It has been pointed out by Magee (1945) that in the terminal stages of starvation in man copious diarrhoea and progressive dehydration are prominent. He suggested that these disturbances were due to irritation of the bowel by ingested food which was not absorbed. In starvation he regarded impairment of absorption as the fundamental lesion which ultimately led to an inability on the part of the bowel to absorb anything. He reached this conclusion from the observation made by Magee and Reid (1931) of a decrease after fasting in the motility of the intestinal villi, and from the earlier observation made by Sun (1927) that after fasting there was degeneration of the columnar epithelium lining the bowel, and after longer periods, almost complete disappearance of the villi. If degeneration had not progressed too far, rapid regeneration followed careful feeding. Diarrhoea is a well recognised if infrequent sequel to short periods of starvation of food, but is said to be more common after long periods of relative or complete starvation especially of high class protein. There seemed, therefore, to be /

be reasonable grounds for the intravenous administration of protein hydrolysates to patients suffering from ulcerative colitis; in the two cases in which this was tried there was no apparent improvement. It was perhaps better justified in the case of the self-starved man (Case 40) in whom it appeared to be followed by improvement in appetite and tolerance of food. In ulcerative colitis there is scope for a carefully controlled further trial of hydrolysates by the intravenous route, but assessment of their value will be extremely difficult. It is worth remembering that the suggestions of Magee (1945) were largely based on work on the small intestine of animals and therefore may not apply to the colon in man. After a period of inactivity as when, for example, a colostomy is closed or after fasting for a week or more, irritability of the human colon is frequent, and this may or may not be due to such changes as Magee has described.

The reduction in plasma protein concentration which often occurs after operation has been studied by Casten et al. (1943) who found that it was most common after operations on the biliary and gastro-intestinal tracts, the spine and large joints, and for toxic thyroid disturbances. They ascribed the change to protein deprivation and to liver damage, and after operation found much improvement followed plasma or blood transfusions.

Elman and Lischer (1943) have emphasised that frequently this reduction may be missed because either a reduction in albumin is more than compensated for by an increase in globulin and only the total protein concentration is measured, or a low concentration is distorted by dehydration and appears to be

within /

within normal limits. There is some evidence from the present investigations that after operations such as gastrectomy, there is retention of water and electrolyte within the body and sometimes an expansion of plasma volume. In one case there was an increase in the total quantity of circulating plasma protein in spite of a small reduction in protein concentration in the plasma and an increase in plasma volume. Abbott and Mellors (1943) also have shown that there may be an increase in the total quantity of plasma protein in circulation, in spite of a reduction in concentration which they related to haemodilution. While insufficient data prevent confident discussion of these findings, they indicate a need for further examination of this aspect of the blood changes after operation. It is suggested that this could best be done by estimation of total circulating plasma protein and of the total quantities of extracellular ions of the plasma, blood and extracellular fluid volumes.

Alteration in plasma protein concentration has been used as a criterion of protein sufficiency or depletion by many investigators, notably G.H. Whipple and his collaborators. It is open to question whether in every case precautions have been taken to prevent or allow for changes in blood concentration. For example, Weech (1938) stated that on starting protein depletion experiments in dogs, there was an initial reduction in packed cell, plasma and whole blood volumes. The plasma volume reduction was most marked at first and therefore in the first ten days the red cell count and haemoglobin concentration appeared to rise; the packed cell volume rose if it changed at all. The haemoglobin and packed cell volume therefore gave completely /

completely misleading information.

It was found by Weech et al. (1937) that in a dog on a protein-free diet, 80 per cent. of the catabolised protein was derived from muscle, 18 per cent. from haemoglobin and only 3 per cent. from serum albumin. Sachar et al. (1942) in a series of experiments on dogs, found that there was an apparent relationship between the plasma albumin and the tissue protein. Each gram of plasma albumin appeared to be in equilibrium with 30 g. of tissue protein. In other words, for every gram of plasma protein lost or gained, there was a concurrent loss or gain of 30 g. of tissue protein. They emphasised that this relationship applied only to alteration induced by dietary changes. Spence et al. (1946) also have reported that on a high protein diet in the post-operative period anaemic or malnourished subjects formed protein in the proportions of 10 to 30 g. tissue protein and 2 to 4 g. haemoglobin for each gram of plasma protein. After severe blood loss in well-nourished subjects, a high proportion of the new protein was in the form of plasma protein and haemoglobin.

Some idea of the difficulty of the process of replenishment of the plasma protein concentration by dietary measures may be gained from the following example based on the work cited above and the relationship said to exist between plasma albumin and tissue protein; such direct application is, of course, most questionable. If a man weighing 60 kg. is assumed to have a plasma volume of 3 litres (5 per cent. body weight), a change in plasma albumin concentration of 1 g. per 100 ml. involves a total change of 30 g. albumin. By the relationship of Sachar et al., this /

this is in equilibrium with 900 g. tissue protein. So that to raise the plasma albumin concentration by 1 g. per 100 ml. would require the deposition of 900 g. protein containing 144 g. nitrogen. This might be expressed as a daily positive balance of 4 g. nitrogen for 36 days, or as the deposition of protein tissue weighing nearly 5 kg. In terms of protein administered by plasma transfusion, it is equivalent to the protein contained in about 20 litres of plasma, from the blood given by 80 to 90 donors.

Whipple and Madden (1944) based the use of plasma protein as an intravenous food on the assumption that the plasma proteins are a medium of exchange between the food and tissue proteins. When in nutritional deficiency, plasma protein is injected, it rapidly leaves the circulating plasma but there is no increase in urinary nitrogen excretion for some days. Elman and Davey (1943) found in the dog that after the cessation of plasma infusions, much of the retained nitrogen was excreted in the urine during the next two weeks as urea or ammonia. This has been confirmed in man (Albright, 1945; Moyer et al., 1947). Some of the retained nitrogen may be incorporated in tissue protein and some may remain in the circulation, but there is a delay in the metabolism of the protein or in its effect on urinary nitrogen excretion. There is no evidence as to the site of the metabolic changes. Both the fluid and the protein are rapidly removed from the blood stream when plasma is injected into well-nourished subjects (Sharpey-Schafer and Wallace, 1942). This is probably partly the reason why plasma has only a short-lived effect in maintaining the circulating blood /

blood volume in shock due to extensive burns and why it is less effective for this purpose than gum saline.

More recently, Eckhardt et al. (1948) compared the value of albumin and lactalbumin by mouth with amigen by vein in five normal male subjects, who received a basal protein-free diet containing 3000 to 3300 calories per day. They found that 50 g. albumin with full calories were adequate for maintenance of nitrogen equilibrium; in their experiments the nitrogen excretion was equal to or exceeded the nitrogen intake, and was much in excess of the minimal value to be expected on such a large caloric intake. On the other hand, when albumin was administered by the intravenous route, urinary nitrogen excretion was low, the plasma albumin concentration rose progressively, in one case to 6.1 g. per 100 ml. blood, and the plasma volume and total circulating plasma protein also rose. All these changes were reversed when the injections were stopped, but restoration to normal took about three weeks. When amigen was administered by intravenous infusion, nitrogen equilibrium was approached but 45 per cent. of the peptide nitrogen was excreted in the urine. These experiments indicate an important difference between intravenous and oral feeding. The albumin is metabolised soon after its oral administration, but there is a delay of at least several days when it is injected intravenously, presumably because there is no readily available means by which such large quantities, for example up to 75 g. albumin per day which Eckhardt et al. injected, can be dealt with. This does not imply that there is no means of dealing with injected albumin, but rather that the normal mechanism /

mechanism does not usually deal with such large quantities. The albumin administered by mouth was apparently well digested and absorbed. Their observations on the injection of amigen when the full caloric requirements are otherwise provided, are important. The loss of up to 45 per cent. of the administered peptide in the urine surely indicates that nitrogen equilibrium cannot be achieved when this method of administration is the sole source of nitrogen. They suggested that the albumin injected intravenously diffuses into the tissues and lymphatic vessels, and that this flow is reversed when the injections are stopped. Thus more of the protein is available for metabolism but less readily so than that provided by injections of hydrolysate.

In a valuable review, Weech (1938) has discussed many of the factors responsible for the production and maintenance of a normal concentration of plasma albumin. When the protein intake of dogs was greatly restricted, there followed a steady fall in albumin concentration, that of globulin remaining unchanged. This fall in albumin was most marked in the early days or weeks of dietary restriction and later flattened out; thus it took 11 weeks to double the reduction of the first three weeks. It was also noted that when protein was deficient, the reduction in albumin was almost independent of the caloric intake. When beef protein was fed to these dogs, there was a rapid restoration of plasma albumin to its original concentration, along a straight line, but no improvement beyond the initial level in health. This suggests that the stimulus to regeneration is of an all-or-none type and is not of itself related /

related to the degree of reduction in albumin level, and that on a given intake regeneration will be at a particular rate for that intake and type of protein.

When malnutrition is prolonged over a period of months and health and vitality are impaired, the mechanism for forming serum albumin may be disturbed; in refeeding dogs in this state, Weech found it was necessary at first to employ gavage to overcome anorexia. In an example he cited, there was an improvement from 1.4 to 2.3 g. per 100 ml. in the first week, 2.3 to 2.7 g. in the next two weeks, and to 2.9 g. per 100 ml. in the fourth week. Thereafter, there was a very slow gain to 4.0 g. per 100 ml. after six months, which was largely independent of the food administered. It was evident that after prolonged starvation the process was quite different to the rapid regeneration on meat protein in about ten days which followed rapid reduction over a period of about three weeks. This suggested to Weech that restoration of albumin concentration was delayed by the restoration of an organ responsible for albumin formation. He pointed out, however, that damage to this organ did not delay the rapid initial improvement to 2.7 g. per 100 ml. in the example cited, but rather fixed a subnormal level as the temporary upper limit of albumin concentration. In cirrhosis of the liver in man, the constant low concentration of albumin has been ascribed to liver damage, and it responds poorly, if at all, to high protein diet. There is albumin deficiency following starvation in man as in the dog. It does not seem unreasonable once more to suggest the application of the law of mass action to these long-term disturbances, even if there /

there is, in addition to prolonged protein depletion, some secondary disturbance of important organs such as the liver.

Both Whipple's group (1934, 1935, 1936), using plasmapheresed dogs in experiments of long duration, and Weech (1938) using dogs and refeeding them for a week after three weeks' depletion on a protein-free diet, have shown that different dietary proteins are of varying value in the formation of plasma protein. Both found that for the regeneration of serum albumin, beef serum was better than beef muscle, liver or casein which were of about equal value. These differences may also apply in the case of man, and hydrolysates or other preparations of beef serum protein may be of significantly greater value than those of casein. This is an aspect of which some study has been made but little information is as yet available. If the knowledge of protein and even amino acid requirements in such conditions as nephrosis and hepatic cirrhosis were more detailed, it might be possible to predict the most suitable source of protein for a nutritional assault on these chronic disturbances. This problem might well be approached through a study of the urinary amino acid excretion pattern. If it is accepted that the plasma albumin is in equilibrium with the main mass of body protein, then disturbances of water metabolism apart, total plasma albumin will rise only as the body protein is replenished. It seems reasonable to conclude that the protein which proves to be the best available for the regeneration of plasma albumin in a protein-depleted man is probably the best protein to feed to that man. But, "The futility of attempting to transfuse enough serum to replace deficits of disease impresses all who try it, the only practical way to meet the demands of the body for protein is in the diet" (Weech, 1938).

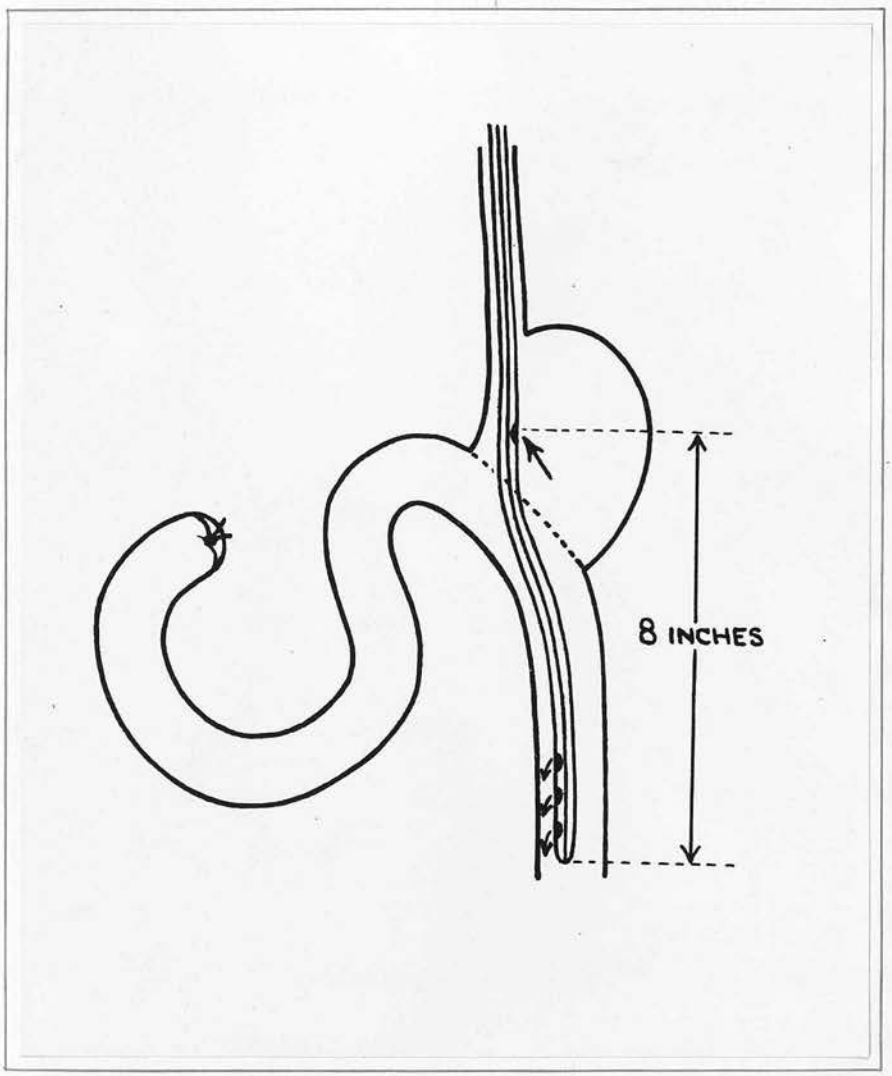
ADMINISTRATION OF MILK MIXTURE

A. Jejunal Feeding by Transgastric Tube

As it had proved impossible to reduce the post-operative increase in urinary nitrogen excretion by increasing the pre-operative diet or by post-operative infusions of casein hydrolysates, and since it had been suggested that this increased nitrogen excretion was due to starvation of calories and this had not been excluded by the previous experiments, the next step was to prevent the occurrence of starvation after operation. This involved the maintenance throughout the post-operative period of a constant intake of at least 70 g. whole protein and more than 1800 calories per day, including the day of operation and continuing until after the tenth day.

One of the disadvantages of using patients submitted to partial gastrectomy as the subjects for these studies of nitrogen metabolism is the interference with food intake which necessarily follows the operation. Because of the disturbance of gastric and jejunal motility which lasts up to three or four days after operation, the consumption of even fluids may be limited. The difficulty could be overcome by using patients who were submitted to operations of comparable severity to gastrectomy, but which did not interfere with the consumption of food. Such a solution is undesirable since it introduces a different kind of injury, and there are few operations which are both as severe and as common as partial gastrectomy for non-malignant disease in men. The alternative was to use the gastro-jejunostomy as a means of putting a tube sufficiently far into the jejunum to be away /

CHART VIII



Modified jejunal tube. To show the arrangement of the modified Miller-Abbott tube for gastric aspiration and jejunal feeding.

away from the local disturbances due to operation and so allow the injection of a fluid diet from within a few hours of the completion of the operation.

In 1921 Levin suggested that the gastric catheter which he had devised should be drawn across the stoma of a gastro-jejunostomy into the distal limb of the jejunal loop so that it might be employed for the introduction of fluids into the jejunum in the post-operative period. Although gastric aspiration was widely practised, Levin's suggestion of jejunal infusion or injection was apparently seldom adopted. In 1937 Abbott and Rawson described a more complicated tube by which the stomach could be emptied by aspiration and fluid could be injected into the jejunum. This was achieved by the use of two silver valves in a single lumen tube. They subsequently abandoned this complicated tube in favour of a double lumen tube with a bucket which also had certain disadvantages. As such a tube could not be obtained for the present investigation, a Miller-Abbott tube was modified according to a suggestion made by Professor R.A. Peters.

A piece of Miller-Abbott double-lumen tubing 40 in. in length was cut. The narrower lumen which was to be used for gastric aspiration was then cut open 8 in. from the lower end. It is unnecessary to cut more than one hole or in any way to close the distal end of the suction channel, since on aspiration fluid enters only by the highest hole. When solid matter blocks this hole, it also blocks the whole lumen of such a narrow tube. The usual double-nippled proximal metal endpiece of the Miller-Abbott tube was then tied into the proximal end of the rubber /

rubber tubing and the nipples labelled suitably "out" and "in". The distal end of the rubber tube was smoothed by burning it slightly in a bunsen flame.

The tube must be swallowed by the conscious patient before operation, since to permit its retention for several days it must be so soft as to make it impossible to pass it any other way. At operation care was necessary to ensure that the tube was not caught in the occlusion clamps, if these were used, or cut during the division of the stomach. When the posterior part of the anastomosis had been completed, the clamp was loosened and the tube caught and drawn down until the hole for gastric aspiration was well into the gastric stump. The distal end of the tube was inserted well down into the distal limb of the jejunal loop used in the anastomosis.

The milk mixture consisted of the following:-

1 pint whole milk		60 g.protein
120 g. dried skimmed milk powder	containing	23 g.fat
100 g. lactose		187 g. carbohydrate

Total calories: 1195

The dried milk powder and the lactose were added to the pint of whole milk and stirred. Water was then added until the whole passed into solution and sediment did not appear on standing. This usually required the addition of water to a final volume of 1200 ml. of mixture, and such a volume of mixture was, for convenience, referred to as "one unit of milk mixture". It is important to ensure that sediment is not thrown on standing, for the lumen of the tubing is so small that it /

it is readily blocked. The mixture must, therefore, be made in the cold but should be warmed before administration. Varying quantities of salt were added in different cases. Unless there is sodium or chloride depletion, this is probably unnecessary as one day's ration of the mixture contains the equivalent of over 4.0 g. of sodium chloride. The addition of more than 5.0 g. of sodium chloride per day may result in looseness of the stools and even diarrhoea. It was noticeable that patients fed with milk mixture produced more bulky stools more often than the patients in the other groups, and that they seldom needed enemas or laxatives after operation.

The rate of administration varied from one patient to another and was increased as they became accustomed to the use of this method of feeding. Apprehension is natural when such a procedure is started within a few hours of operation, and was another reason for cautious instillation in the early stages. Initially, therefore, 60 ml. were injected slowly with a syringe over about ten minutes, later the rate was gradually increased within the limits of individual tolerance. The use of continuous drip infusion was successful in several cases, but was more liable to blockage by sediment in the glass drip chamber or rubber tubing; intermittent instillation with a tube and funnel was better. Another disadvantage of a continuous infusion was the difficulty experienced in regulating the rate of flow, which was disturbed by changes in posture and by respiration. It was not uncommon for flow to cease for as long as an hour or more, and then for the fluid to run in so rapidly as to cause distention and pain.

Lactose /

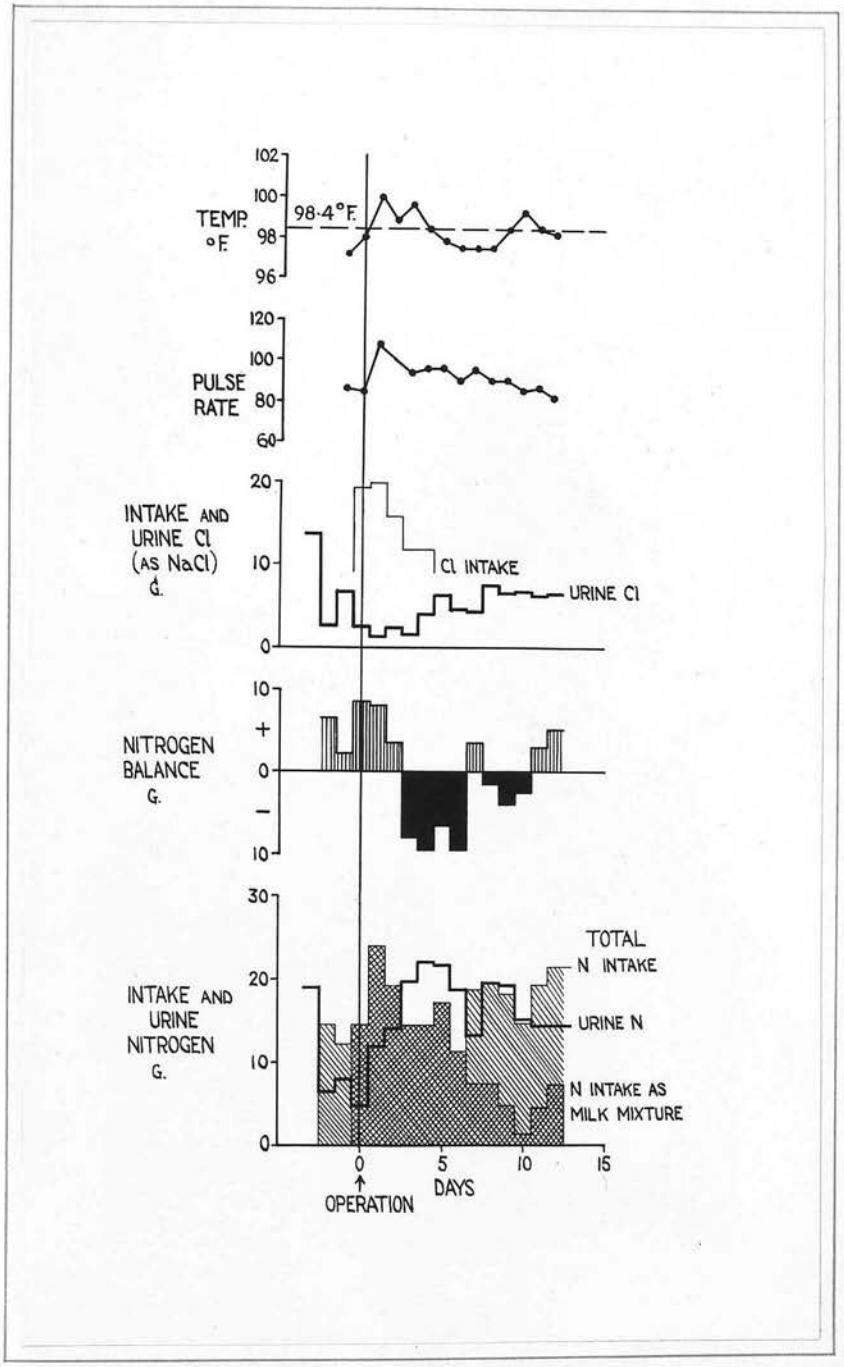
Lactose was chosen in preference to glucose because it is cheaper and less nauseating to most patients; being less popularly used than glucose, it is less likely to have diverting ideas associated with it; and finally it can be obtained in bulk without the many formalities and difficulties associated with the provision of equal quantities of glucose, at a cost of 1s. 2d. per lb. Dried skimmed milk powder was issued by the hospital steward; it costs 113s. per cwt. The total cost of the provision of 120 g. protein and 2200 calories per day in the form of milk mixture was about 1s. 9d. per day, assuming that the average cost of milk was 4d. per pint.

Case 45 (Table 30).- W.B., aged 52 years. Tourist guide. For 28 years had suffered from intermittent dyspepsia. Nine years ago perforation of duodenal ulcer closed at operation, followed two weeks later by severe melaena. Melaena again two and a half years ago followed by severe recurrent pain which passed through to the back and both shoulders; during past two weeks had been vomiting large volumes of fluid. On admission, tall, thin man of healthy and cheerful appearance; probably had not lost much weight. Epigastric tenderness and gastric succussion; nightly gastric lavage and up to 1800 ml. fluid aspirated. At laparotomy: cicatricial pyloric stenosis; partial gastrectomy; gastro-jejunostomy; jejunal intubation. Gastric aspiration for two days and intravenous infusion for three days after operation; total of 700 calories as glucose given by intravenous infusion. Injection of milk mixture was begun about six hours after operation, 40 ml. being run in slowly every hour; little fluid was obtained by gastric aspiration and there was no discomfort or nausea.

On the first morning the hourly feeds were increased to 60 ml. milk mixture and 20 ml. water; this caused some discomfort if run in too quickly. On the second day the feeds were increased to 90 ml. milk mixture and at 7p.m. the jejunal tube was removed and he was encouraged to drink the milk mixture which he did readily. The feeds were increased to 120 ml. hourly on the 3rd day and on the 4th day 240 ml. were given every two hours and he was allowed up. Daily urine volume below 1 litre for first seven days and above in all but one of 8th to 15th days. Slight diarrhoea on the 6th and 10th days otherwise no complications; diarrhoea controlled by tinct. opii. Discharged home on 16th day.

Before /

CHART IX



Case 46.- To show the effect of the provision of at least 70 g. protein (11 g. nitrogen) and 1800 calories per day as food, or as milk mixture, or as both, throughout the post-operative period, including the day of operation. The post-operative increase in urinary nitrogen excretion should be noted.

Before operation was in positive nitrogen balance on just over 60 g. protein (10 g. nitrogen) and 1900 calories per day. Caloric intake was low on day of operation and next three days, but thereafter intake was above 70 g. protein and 1700 calories. Urinary nitrogen excretion was low before operation and rose in the immediate post-operative period and remained elevated for eight days. There was a negative nitrogen balance for the first four days and again on the 7th and 8th days. There was marked nitrogen retention in the 2nd week after operation, on an intake of 90 g. protein and 2000 calories or more.

The low nitrogen excretion before operation and associated with adequate intake in the second week after operation suggests that this man may have been depleted of protein before operation; that he was in equilibrium on 10 g. nitrogen and 1900 calories indicates that he was accustomed to this level of intake. Because of the voluminous gastric aspiration before operation, sodium chloride was added to the milk mixture for the first two days.

Case 46 (Table 31, Chart IX).- J.S., aged 52 years. Miner. For about 20 years had had pain after meals at intervals; for last year had had epigastric pain about an hour after food, relieved by vomiting. Appetite remained good, but has lost about 28 lb. in weight. On admission, thin man who had obviously lost weight. Visible gastric peristalsis and loud succussion. Daily gastric lavage, residue about 450 ml. At laparotomy: chronic duodenal ulcer; severe pyloric stenosis; partial gastrectomy; gastro-jejunostomy; jejunal intubation. After operation, intravenous infusion for two days, gastric aspiration for three days. Milk mixture by drip infusion into jejunal tube started five hours after end of operation and continued for 48 hours; mixture was then given by mouth for two days; ordinary diet was then started in addition, because milk mixture was causing nausea. Slight diarrhoea occurred on 8th day. Daily urine volume below 1 litre in first week and above it in 2nd week. Got up within 24 hours of operation and was discharged home on 12th day.

After operation, the lowest intake was 70 g. protein and 1640 calories on the 6th day. Apart from this day, the food intake was adequate or abundant whether supplied as milk mixture, as ordinary food or as both. In spite of this there was an increase in urinary nitrogen excretion from /

from the 3rd to the 6th days which resulted in a negative balance of nitrogen of over 30 g.

This increase in nitrogen excretion might be ascribed, at least in part, to the high intake on the first and second days after operation, and the irregularity of the intake in this case is unfortunate. There were large losses of nitrogen in the faeces (over 7.0 g. nitrogen on the ninth day), but the intake of nitrogen remained above 11.0 g. per day even when allowance was made for these losses.

Case 47 (Tables 32, 53, 67).- R.H., aged 43 years. Post Office engineer. For 15 years had intermittent pain after meals, relieved by food and alkaline powders; much flatulence. Ten months ago, instead of pain had discomfort and nausea, and vomited foul liquid up to three hours after a meal; this lasted for three months and he lost weight. Then vomiting stopped and he was well until three weeks ago when pain, anorexia and nausea again became severe. On admission, a worrying type of man, thin, had evidently lost weight. Tender in epigastrium. At laparotomy: large chronic posterior duodenal ulcer adherent to pancreas; partial gastrectomy; gastro-jejunostomy; jejunal intubation. Gastric aspiration for two days.

Five hours after operation, milk mixture started as drip infusion through jejunal tube, continued until 2nd evening when tube was withdrawn and patient got up; thereafter fed orally. Some respiratory discomfort and distress on 3rd and 4th days with elevation of temperature and equivocal physical signs of basal pulmonary consolidation, probably due to localised atalectasis; some diarrhoea on 4th day. For six days milk mixture was sole source of food; on 7th day ordinary food added and milk mixture stopped.

Before operation, was in positive nitrogen balance on 91 g. protein and 2249 calories. After operation lowest intakes were on day of operation and on the 7th, 8th and 9th days. During the first six days after operation the intake was maintained at 90 g. protein (14.4 g. nitrogen) and 1700 calories each day. There was a large faecal nitrogen loss during the period of ingestion of milk mixture and for four days afterwards. When allowance is made for these losses in the stools, there is a deficient supply of protein and probably also of calories. It cannot be said, therefore, that an adequate intake was maintained in this case. Urinary nitrogen excretion rose on the 4th day and remained high until the 7th day.

In /

In this case there were the conflicting factors of raised temperature and pulse and respiratory rates on the first three days after operation, presumably related to the pulmonary atalectasis. After operation, temperature was raised for three days, pulse rate for ten days and respiratory rate for nine days, but during this disturbance he was distressed rather than ill.

Case 48 (Table 33).- J.L., aged 52 years. Railway linesman. For 16 years had had intermittent attacks of epigastric pain two or three hours after meals. Twelve years ago vomited intermittently for 14 days. On three occasions treated medically and improved. For three weeks before admission severe pain with occasional vomiting. On admission, a lean, placid man, had not obviously lost weight; tender in upper abdomen; gastric succussion. Radiological examination showed duodenal ulcer crater, gross deformity but no evidence of stenosis. At laparotomy: extensive duodenal ulcer penetrating pancreas; partial gastrectomy; gastro-jejunostomy; jejunal intubation. After operation, intravenous infusion for two days, gastric aspiration for four days; temperature not raised, pulse rate increased from 80 to 90 or more per minute for four days. Mild inflammation of drip wound on 4th day settled in two days. Six hours after operation, milk mixture infusion into jejunum begun, slight gastric reflux but no discomfort. Jejunal feeding continued without incident until tube withdrawn on 4th evening; thereafter, for two days, mixture was taken orally and ordinary food started on 6th day.

Before operation was in positive nitrogen balance of about 3.0 g. nitrogen per day on 90 g. protein (14.4 g. nitrogen) and 2500 calories. After operation, intake was maintained at over 11.0 g. nitrogen per day except for day of operation, but calories fell on day of operation and on 4th and 5th days. On the first three days after operation the urinary nitrogen excretion rose, in spite of the ingestion of adequate quantities of protein and calories as milk mixture.

Because of the loss of the urine on the fifth day, the exact duration of the catabolic phase is uncertain. Faecal nitrogen rose from the fifth day onwards but was not so great as to reduce intake to a significant amount. There was positive nitrogen balance from the eighth day onwards.

Case /

Case 49 (Tables 34, 53, 67).- W.S., aged 53 years. Colliery foreman. Five years ago was operated on for a perforated duodenal ulcer. Six months ago acute upper abdominal pain for a week, resulted in second admission to hospital and laparotomy; no perforation found but large ulcer in duodenum; appendicectomy. Four days before present admission vomited brown material and passed loose dark stool, felt very weak, went to bed; stool benzidine reaction present. At laparotomy: chronic duodenal ulcer; partial gastrectomy; gastro-jejunostomy; jejunal intubation. After operation, intravenous infusion and gastric aspiration for two days. Double lumen tube did not work well because milk mixture threw a sediment; the tube was removed and a Ryle's tube to stomach inserted instead; milk mixture was run through Ryle's tube for one day. Was unable to tolerate full ration of milk mixture (1800 ml.) in stomach remnant so early; milk mixture therefore stopped, and intake was reduced on 2nd day and on 3rd day ordinary food started. Temperature was not elevated at any time. Pulse rate slightly raised for four days. No complications. Up on 13th day; discharged on 15th day.

Before operation was in nitrogen equilibrium on 90 g. protein (14.4 g. nitrogen) and over 2000 calories. After operation intake fell on day of operation and on 3rd and 4th days but was otherwise adequate. Urinary nitrogen excretion rose on these days and was raised in all for six days during which there was negative balance. Average faecal nitrogen was less than 1.0 g. per day and absorption was probably normal.

Following the blockage of the jejunal tube, there was an inadequate intake of milk mixture.

Case 50 (Table 35).- D.T., aged 37 years. Chemical engineer. Six years ago, after short period of epigastric pain, duodenal ulcer perforated and was closed at operation. Recurrent attacks of pain followed remission for five months; one episode of melaena. Recently pain had been more severe with some vomiting of altered food. On admission, worrying, introspective, intelligent man, thin but not wasted; tender in upper abdomen. At laparotomy: chronic duodenal ulcer; partial gastrectomy; gastro-jejunostomy; jejunal intubation. After operation, intravenous infusion for 24 hours, jejunal feeding for two days, thereafter took milk mixture by mouth until 6th day, ordinary diet started on 3rd day and gradually increased. Temperature slightly raised on 2nd and 3rd days, pulse rate increased for two days. Up on 13th day, discharged on 16th day.

Before operation was in nitrogen equilibrium on 88 g. protein (14 g. nitrogen) and 2170 calories). After operation, intake fell on 3rd day to 65 g. protein

(10 g. nitrogen) and 1500 calories, but otherwise was adequate throughout. Urinary nitrogen excretion was increased on first five days after operation; urine lost on 6th day; average faecal nitrogen less than 1.0 g. per day; negative nitrogen balance lasted for seven days. No complications. There was a sharp fall in weight, in the first two days after operation 7.8 lb. were lost, and a total of 8.25 lb. were lost in all after some fluctuation about the end of the first week.

Comment

The chief object of this group of studies was to observe the effect of maintaining the intake of food above 70 g. protein (11.2 g. nitrogen) and 1800 calories per day throughout the post-operative period. This object was nearly achieved in three of the six cases (Nos. 46, 48, 50). Of the three failures, in one (Case 45), too little mixture was injected; in another (Case 47), the large quantities of faecal nitrogen loss must have seriously reduced that available for absorption; and in the last case (No. 49), intake was interfered with by blockage of the jejunal tube.

During the first week after operation, in all cases there was to a varying degree a reduction in the volume of urine compared with the volumes before and in the second week after operation. This reduction was rather surprising in relation to the comparatively large volumes of water ingested with the milk mixture, although in two patients the passage of bulky and fluid stools accounted for much of the additional fluid ingested. There was a notable absence of systemic disturbance evidenced by increases in temperature and pulse rate; indeed, the patients in this group had the most uneventful post-operative courses. After operation, in all cases, in spite of the reduction in urine volume and the large provision of protein and calories, there

was /

was an increase in urinary nitrogen excretion. This usually occurred a day or two later than in other groups. The highest daily urinary nitrogen excretion (32 g.) was observed in Case 47 on the fifth day after operation, with a nitrogen intake of 14 g. per day. In four other cases the maximum daily excretion was 20 to 22 g. on similar nitrogen intakes. Thus, although the starvation was largely prevented in these patients, certain features of the catabolic phase appeared as in other patients who were not fed immediately after operation. In three cases (Nos. 46, 48, 50), a constant intake of protein and calories was maintained except that in Case 50 only 65 g. protein and 1500 calories were taken on the third day; the large faecal nitrogen on the sixth day in Case 46, and on the fifth day in Case 48, should be distributed. The magnitude of the losses in the faeces of food injected as milk mixture and of water and electrolytes is not always recognised. Insufficient consideration, therefore, is given to this source of error in assessment of balances of several kinds; this point will be further considered in the next section. Its importance in studying patients after operations on the gastro-intestinal tract, such as vagotomy, requires emphasis. If unusually large quantities of nitrogenous substances are found on analysis of the faeces, it is almost certain that there has been interference with digestion and absorption of other constituents of the diet in addition to protein. In such cases it follows that the calculated caloric value of the ingested food may greatly exceed the caloric value of the products which are absorbed.

Although after operation in all the cases there was an increase /

increase in the urinary nitrogen excretion of comparable severity and duration to that found in the other groups of patients, there was a much less severe negative nitrogen balance during the ten days immediately succeeding the operation. Thus in Case 46 the negative balance was only 15 g. nitrogen; in Case 48 there was a positive balance of 16.6 g. nitrogen but one day's urine was lost and would probably have contained about this quantity; in Case 50 there was a negative balance of 28.8g. nitrogen (excluding one day's urine which was lost), but there was a loss of weight of 7 lb., most of which was lost in the first three days after operation.

In all the patients of this group there was the change in facial appearance and the obvious loss of body tissue which have already been described, although their severity was less marked than usual. On the other hand, in Case 47, following frequent bulky stools, the change was more severe than usual.

These cases show that during the immediate post-operative period, even the provision of over 70 g. of whole protein and 1800 calories per day will not prevent an increase in the excretion of nitrogen in the urine. However, unlike the hydrolysed protein administered by the intravenous route, such quantities of protein and calories do not seem to be entirely wasted, since in the present group of patients the accumulated negative nitrogen balances over the period of ten days after operation were smaller than in any of the other groups of patients who were studied. Unfortunately, there is inadequate information as to the loss of weight in these patients; in the only one in whom the figures are complete, a loss (7 lb.) was observed, /

observed, which is comparable to that found in other types of case. The chief differences between the milk mixture group and the casydrol group were the state of the protein, the quantity of calories provided per day and the method of administration. It should not cause surprise that whole protein accompanied by adequate calories in the form largely of carbohydrate should have proved a more efficient mode of protein nutrition than hydrolysed protein injected intravenously with an adequate accompaniment of calories as glucose.

B. Milk Mixture Given by Jejunostomy

It seems a waste of enjoyable food to use eggs and cream and other recommended constituents of jejunostomy feeds which cannot be tasted by the patient, since the protein of cow's milk is nutritionally adequate for the human subject and there is no objection to its use as the sole source of protein in the preparation of a simple and cheap mixture for jejunostomy feeding. The mixture of whole milk, dried skimmed milk powder and lactose described in the previous section has been used also in the feeding by jejunostomy of four patients, of whom two will be described in some detail. The first of these two was suffering from a benign stricture of the oesophagus and was fed entirely by jejunostomy for six weeks; the other patient was fed for ten days by jejunostomy after partial pancreatectomy.

Case /

Case 51 (Table 36).- A.B., aged 37 years. Clerk. Eleven years ago perforation of duodenal ulcer closed at operation, followed by repeated attacks of pain and several periods of hospital treatment. Admitted with perforation of large pyloric ulcer; closure of perforation. Much post-operative retention of gastric contents relieved by aspiration by Ryle's tube of up to two litres of fluid; twice transfused with blood. Slow progress; very depressed; frequent complaints. Readmitted from convalescent hospital 11 weeks after operation, complaining of difficulty in swallowing even fluids; unrelieved by atropine and belladonna. Ulceration and inflammation of lower end of oesophagus seen on oesophagoscopy.

Two weeks after admission started on supplement of 160 g. pronutrin per day, food intake having been small though weight not falling. Four months after perforation, laparotomy: high gastrectomy and jejunostomy; jejunostomy feeds begun three days after operation, but stopped 10 days later because he was taking fair quantities of liquid and soft food by mouth, though this caused some pain; jejunostomy allowed to close, no leakage from it. Six months after perforation readmitted unable to swallow any food; intravenous infusion for five days then jejunostomy reopened and feeding started next day and continued for six weeks. Nitrogen balance study begun two days before jejunostomy reopened. Initial discomfort during feeds if fluid run in too cold or too quickly, which caused colicky pain. First got up nine days after jejunostomy and within a few days was up and about for large part of day. After one month of jejunostomy feeding, drinks by mouth started; some pain in throat; gradually increased oral feeding until by two months after jejunostomy, was taking all food by mouth. Then transferred to thoracic surgical unit for resection of oesophagus and remainder of stomach. Lesion was a benign inflammatory stricture presumed to be due originally to ulceration by Ryle's tube inserted for gastric aspiration. Conservative treatment contra-indicated because of the doubtful nature of the tissue obtained by biopsy at oesophagoscopy.

Jejunostomy feeds consisted of a mixture of 240 g. dried skimmed milk powder, 200 g. lactose in two pints of milk per day. Sufficient water was added to ensure solution of all the milk and lactose, and this made the solution thin enough to run readily through tubing without throwing a sediment. In addition, a volume of water equal to the jejunostomy feed was run in after each feed. The feeds consisted of about eight to ten fluid ounces of the mixture run in every three or four hours from 8 a.m. until the day's supply of mixture was exhausted. Leakage did not occur, and difficulty was not encountered by the nursing staff or by the patient in the administration of feeds. "Complevite" tablets were /

were ground up, suspended in water and run through by tube.

Weight and health were improved and maintained by jejunostomy feeding alone for six weeks.

Varying quantities of salt were added and their effects noted. For the first 12 days 20 g. salt were added each day to the mixture; this resulted in 34 g. chloride (expressed as sodium chloride) being excreted in the urine on two days and was clearly excessive; it also appeared to cause frequent loose stools. For 32 days 10 g. salt per day were added, resulting in high urine chloride levels in the region of 10 g. per day.

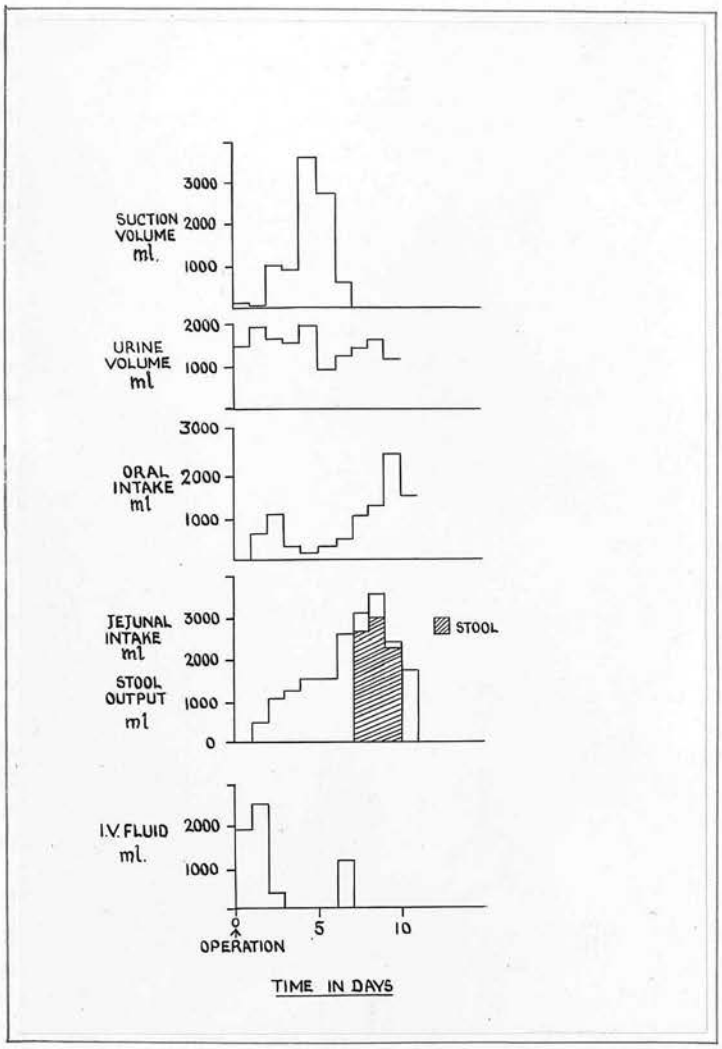
There was almost consistent nitrogen retention amounting to 116 g. in the first five weeks of the feeding period, equivalent to about 760 g. of protein. The daily retention of nitrogen varied, due partly to the frequent bulky stools in which on some days the equivalent of nearly a quarter of the nitrogen intake was lost. There were also variations in urine nitrogen.

Body weight rose slightly at first and then fell, and after a month 6 lb. had been lost in spite of substantial nitrogen retention; in the next two weeks 8 lb. were gained. This lack of relation between nitrogen retention and body weight change may be due to overwhelming changes in water content.

In another patient with complete oesophageal obstruction due to an encircling carcinoma, who was observed but who is not included in the present series, a jejunostomy was established and similar quantities of milk mixture were fed through the jejunostomy prior to operation. Full nitrogen balance studies were not made, but it was evident that in spite of successful jejunostomy feeding, there was a difference in the result obtained; weight was not regained though there was an improvement in general condition. The fluid lost by

expectoration /

CHART XVI



Case 52.- To show fluid intake and output during post-operative period following partial pancreatectomy.

expectoration of saliva accumulating in the oesophagus above the obstruction amounted to about 1500 ml. per day. The oesophageal neoplasm was subsequently proved to be inoperable.

Case 52 (Chart XVI).- T.C., aged 27 years. Gardener. Cystic disease of pancreas. Six months' history of passage of up to five soft bulky pale stools per day and five months' painless jaundice. Because of history of contact with probable case of infectious hepatitis, treated conservatively; some transient improvement in liver function; chemical tests suggested hepatic disease rather than biliary duct obstruction.

Laparotomy eventually done because of persistence of jaundice: mass found in head of pancreas believed to be neoplasm; one-stage excision of head of pancreas and duodenum with lateral anastomosis of common bile duct, stump of pancreas and stomach to jejunum lying in front of colon; jejunostomy. For details of fluid intake and output, see Chart XVI. Intravenous infusion stopped 48 hours after operation when fluid intake by mouth of 120 ml. every two hours seemed to be well tolerated. At about 53 hours after operation large volumes obtained on gastric aspiration; the quantity fell somewhat when drinking was restricted to 30 ml. per two hours, but at 86 hours volume increased again and in next 12 hours three litres were aspirated. The volumes fell in next 24 hours to two and a half litres and then the tube was withdrawn. Restriction of drinking was severe but not complete during this period, and appeared to have some bearing on the production of secretion.

Jejunostomy feeds of lactose solution begun tentatively within 24 hours of operation but established regularly from 42 hours after operation, two-hourly feeds of 120 ml. and later 150 ml. of milk mixture being given; feeds well tolerated; no discomfort; no evidence that fluid injected into jejunostomy was regurgitating across anastomosis into stomach. On 5th day after operation fluid aspirated from stomach was run into jejunostomy; glucose saline also given by jejunostomy and rapid intravenous infusion of 1200 ml. saline; two loose stools passed on this day. Volume of milk mixture and of other fluids by jejunostomy increased on 6th day; 540 ml. casydrol given into jejunostomy on 6th and 7th days without disturbance or apparent benefit. Seven stools passed on 6th and four on each of 7th and 8th days, resulting in loss of large volumes of fluid and presumably much of food which had been given by jejunostomy. Oral ingestion of fluid and of food increased from 5th day, and by 10th day light food being eaten; jejunostomy feeds stopped on 11th day; jejunostomy later healed without complications and with little leakage.

This case illustrates another advantage of a jejunostomy in addition to that of providing full caloric and protein intake from shortly after operation. Because of some disturbance of the stomach and upper jejunum, perhaps related to the premature oral ingestion of unduly large volumes of water, a high intestinal obstruction developed resulting in the loss of large volumes of bile, pancreatic and gastric secretions by aspiration. The aspirated fluid varied greatly in hue but was never thickly turbid or of foul odour; only at a late state was the opportunity taken of returning the aspirated fluid to the bowel below the obstruction by injecting it into the jejunostomy. The importance of being able to do this can hardly be stressed too much. In the present case, on the fifth day gastric aspiration was stopped and gastric distention fortunately did not persist. The treatment by intravenous infusion, of the disturbances of fluid and electrolyte balance which result from high intestinal obstruction of this kind is difficult and hazardous. By establishing a jejunostomy at the time of resection of the pancreas, the need for drinking is abolished and the likelihood of gastric retention due to delayed emptying is greatly diminished if not avoided entirely; if such a disturbance develops, the aspirated fluid should be injected forthwith into the jejunostomy.

In the present case there was no stool for five days after operation, but from the sixth day stools were large, fluid and frequent. This may have been due partly to the injection of saline into the jejunostomy in an effort to replace losses of electrolyte by aspiration; this effort failed. The jejunostomy provided /

provided a means of stabilising a severe disturbance of water and electrolyte equilibrium which threatened to progress.

In Case 30 (p. 97), following the development of biliary and pancreatic fistulae after duodeno-pancreatectomy, for two weeks there was a severe loss of water and electrolytes and complete starvation for fat and protein with inadequate carbohydrate intake as glucose by intravenous infusion. A jejunostomy was established as an emergency procedure in the hope of controlling and correcting the disturbances which had resulted. This jejunostomy functioned satisfactorily for only a short period, probably because of a technical fault in its construction; nevertheless it enabled the patient's condition to be stabilised though the improvement was not for long maintained.

Discussion

Before operation, none of the patients who were submitted to gastrectomy had suffered much reduction in diet, and in any comparison of the present results with those of other published investigations, this good average state of nutrition is an important factor. In most reports, the best evidence regarding the nutrition of the patients is the daily urinary nitrogen excretion considered in relation to the particular quantity and type of protein and calories consumed.

In a series of 55 patients submitted to severe gastric operations or to craniotomy, Riegel et al. (1947) investigated the effects of early post-operative feeding by means of an indwelling Abbott-Rawson tube. In addition to a mixture of skimmed /

skimmed milk, 500 ml., 50 g. each of skimmed milk powder, cheese and soy bean flour, and one egg, they gave amigen by mouth and amigen and glucose solution by intravenous injection. The urines were pooled in five-day specimens and this limits criticism of their data in regard to the occurrence of an increase in urinary nitrogen excretion after operation. They concluded that 0.3 g. nitrogen and 30 calories per kg. body weight per day was a minimum intake for the attainment of nitrogen equilibrium; they did not claim it was sufficient in all cases, and only 12 out of 18 of their patients in whom such an intake was achieved were in nitrogen equilibrium. This order of intake is equivalent in a 60-kg. man to 18g. nitrogen and 1800 calories per day. They believed that equilibrium could be achieved if the nitrogen intake was lower and that of calories was higher than this. They emphasised the higher loss of nitrogen in the faeces when gastric or jejunal tube feeding is employed, and recorded average quantities of 1.4 g. and 3.3 g. nitrogen respectively with these methods.

For jejunostomy, gastric tube and oral feeds, Varco (1947) recommended a milk mixture containing 120 g. protein, 37 g. fat, 400 g. carbohydrate, and 2500 calories in 1500 ml. This mixture includes six whole eggs, two egg whites but only 4 oz. skimmed milk powder. The small amount of milk powder would be an advantage in oral feeding because in some unknown way milk powder produces nausea or anorexia after about 10 to 14 days in all patients to whom it has been given. Distaste or lack of desire for food is experienced even when the patient does not know there is milk powder in the food, or when the flavour has been /

been successfully disguised. This does not happen with jejunal feeding, but insufficient evidence has been obtained in the present investigation in long-term experiments to say whether it occurs in gastrostomy feeding; it did not happen over short periods of up to eight days.

Varco (1947) considered intravenous infusion of casein hydrolysates an alternative to jejunostomy feeds since the latter are often accompanied by severe diarrhoea (he added salt as seemed indicated but does not relate the amount of salt to the diarrhoea). To provide adequate carbohydrate calories for the protein, he had to administer by intravenous infusion 6000ml. of solution over 15 to 20 hours. Even so, he found that urinary nitrogen excretion was often greater than with equivalent intakes of nitrogen as skimmed milk powder or bovine plasma protein. The high salt content (9.0 g. in 6 litres) was another disadvantage in patients with low plasma albumin concentrations in whom oedema developed.

Following operation, Mulholland et al. (1943) injected a mixture of a protein hydrolysate and dextrose through a modified Miller-Abbott tube into the jejunum of four patients submitted to partial gastrectomy. They claimed to have converted the usual post-operative negative nitrogen balance into a positive balance except perhaps in the first day or two after operation. The calorie intakes of their control patients were only about one-third of those of the patients who were fed with nutramigen and dextrose. After operation, the urinary nitrogen excretions of the controls averaged 10 to 18 g. per day, and in the only two cases in which the urines were not pooled, there was evidence of /

of a moderate post-operative increase in nitrogen excretion. In the patients who were abundantly fed, the urinary nitrogen excretions settled down to a low, but fairly stable, daily quantity often only half the amount of the nitrogen intake. Most of the urine specimens were pooled. In the absence of convincing evidence of an increase in urinary nitrogen after operation and in the presence of a caloric intake in the region of 3600 to over 4000 per day, these findings suggest that nearly half of the nitrogen ingested was retained, and that, before the operation, the patients had been severely deficient of protein. The production of positive nitrogen balance is to be expected in such patients receiving so much food. These experiments therefore indicate the benefit which may be derived by malnourished patients from early abundant feeding after operation; the results cannot be interpreted as indicating that the catabolic phase was abolished by abundant protein and calories.

Mulholland and his co-workers found also that although the control subjects lost weight, all those who after operation were fed abundantly, gained 4 to 5 kg. in weight in the first 12 days after operation. There was a remarkable correspondence between the quantities of nitrogen lost or gained and the theoretical and actual weight changes of these patients which has not been encountered before. It is difficult to explain the gain of weight after operation except as another sign of a very severe degree of pre-operative malnutrition; it seems unlikely that it could be due to water retention even though the patients were given up to 9.0 g. salt per day.

A later report from the same unit (Co Tui et al., 1944) described /

describes a further series of experiments in which an Abbott-Rawson tube, rather than the modified Miller-Abbott tube, was used because its larger lumen allowed the injection of a thicker feed. By using amigen and dextrose, they were able to supply 0.6 g. nitrogen per kg. body weight and at least 30 calories per kg. body weight (up to 230 g. protein and 1800 calories for a 60-kg. man). Until the third day after operation, intravenous infusion was maintained to allow of fluid replacement and adequate nitrogen and caloric intake without too much being given into the jejunum. This latter precaution seems hardly justified since one of the important advantages of a jejunal tube is that it makes intravenous infusion unnecessary. It is evident from the urinary nitrogen excretions of the controls that these patients were suffering from protein depletion before operation, and the authors stated that their patients were all mal-nourished. In only two of the eight controls was there a significant increase in urinary nitrogen after operation, and there was no large increase in the patients who were abundantly fed after operation, if allowance is made for the very large quantities of protein which were provided. Co Tui et al. attributed the difference between their results and those of Cuthbertson and Browne to the severely mal-nourished state of their own patients, and further suggested that this and the liberal diet might be the cause of the rising weight associated with nitrogen retention after operation which was again observed. They concluded that the principal cause of the nitrogen loss after gastrectomy was the unnecessary post-operative starvation, a point which, in a modified way, has also emerged from the present /

present study. They were surprised to find that, in spite of marked nitrogen retention, there was no rise in plasma protein concentration. Large quantities of nitrogen, up to 10 g. per day, were removed in the gastric aspirations, but by controlling any tendency to diarrhoea with amphogel, they reduced the nitrogen loss in the faeces to 0.5 to 2.0 g. per day.

In five of their eight controls there was from the sixth to ninth days a marked gastro-intestinal disturbance characterised by abdominal distention, vomiting and inability to take more than small amounts of fluid at frequent intervals. This they believed to be due to oedema of the stoma and reduced peristalsis, tone and absorption in the small intestine caused by malnutrition. It did not occur in any of the patients who were fed through a jejunal tube. A similar disturbance has been rarely and independently observed after gastro-jejunostomy and partial gastrectomy. It was ascribed at various times to calcium deficiency, oedema or altered gastric motility due to low plasma albumin concentration, and more recently to excessive saline administration.

The mixture recommended for jejunal feeding by Stewart et al. (1948) is similar to the one used in this series, consisting largely of sucrose and casein, but they added a mineral mixture containing 18 g. of sodium chloride. This is too much for a daily intake, as it will result in diarrhoea. It was found in the present study that in the absence of excessive loss of chloride by gastric aspiration and of base by diarrhoea, there was sufficient sodium and chloride in the ingredients of the milk mixture to satisfy ordinary requirements.

It /

It is clear, from the results in the present group of patients, that the post-operative increase in urinary nitrogen excretion is not solely dependent on starvation, and that it persists even when adequate calories and protein are supplied. It is equally certain, however, that much of the nitrogen loss from the body in the first two weeks after operation is related to starvation superimposed on the catabolic destruction of protein as originally described by Cuthbertson (1935), and that this might be prevented by more abundant feeding after operation. This conclusion does not imply the routine adoption of jejunal feeding as part of the post-operative treatment of patients submitted to partial gastrectomy. It may, however, play an important part in the post-operative treatment of ill-nourished patients submitted to emergency gastrectomy for haemorrhage. A comparison of the apparent fate of the ingested nitrogen as shown in Table 70, indicates the greater value of alimentary as opposed to intravenous feeding in the well-nourished subjects studied in this investigation. It seems reasonable to infer that this difference must become progressively less as the nutrition of the patient deteriorates and his ability to develop a catabolic response to injury declines.

It has been shown in Case 51 that, by feeding the milk mixture through a jejunostomy, weight and nitrogen equilibrium may be maintained for long periods. It seems reasonable to conclude from this that, in subjects who are severely mal-nourished as a result of prolonged and progressive interference with swallowing, improvements in their physical state could be achieved by jejunal feeding without the use of intravenous infusion. /

infusion. Starvation in the immediate post-operative period also could be minimised or avoided. The use of intravenous infusions of protein hydrolysates and glucose in severely malnourished subjects increases the risk of widespread oedema, especially in the post-operative period. Whether the common use of intravenous feeding increases or decreases morbidity is undecided, but there seem to be good reasons for preferring jejunal feeding. Many objections have been raised to the use of a jejunostomy in preparation for operation on oesophageal lesions. It should be possible so to arrange the site of the jejunostomy that it does not interfere with later operations; leakage seems to be dependent largely on the way in which the opening is made. A gastrostomy has the following disadvantages: it immobilises the stomach which may be required for anastomosis to the upper end of the oesophagus; vague sensations of fulness are more troublesome than with jejunal feeding; and regurgitation into the oesophagus is more likely and feeding can be continued only until operation is carried out.

OBSERVATIONS ON SODIUM AND CHLORIDE METABOLISM AFTER MAJOR OPERATIONS

It is commonly, but not universally, believed that after surgical operations the amount of chloride (expressed according to conventions as sodium chloride) excreted in the urine each day is a reliable indication of the daily requirements of the human organism for sodium and chloride. There is a less widely accepted belief that repeated gastric aspiration after operations on the stomach does not involve the removal from the body of significant quantities of chloride. To test the validity of these beliefs, it was decided to measure the total daily quantities of chloride excreted in the urine and removed in the gastric aspirations. It was conveniently possible to make these observations on patients who were already being subjected to nitrogen balance studies and for whom total daily collections of urine and gastric aspirations were being made.

It has been found that during the days immediately following partial gastrectomy and other major operations, there is a marked reduction in the excretion of chloride below that found before and later on after operation. During the period when urinary chloride excretion is reduced, measurements of sodium and chloride intake as well as of output have shown that there is a marked retention of sodium as well as of chloride. The combination of nitrogen balance studies with these measurements of urinary chloride excretion led to the observation of a coincidence in retention of chloride and sodium with that increased excretion of nitrogen that Cuthbertson (1932) has called the "catabolic phase".

Methods /

Methods of Study and Classification of Subjects

From the time of admission three to seven days before operation, until discharge from ten to twenty-three days after operation, measurements of the daily output and loss of chloride were made in 23 patients. Similar observations were made on four healthy young male volunteers. In the early stages of this investigation the daily intake of sodium and chloride was not measured or controlled. Later, however, attempts were made to measure and to control the intake of chloride and sodium. The chloride content of the stools was measured in a number of cases when stools were bulky or frequent.

For convenience of discussion, the subjects have been divided into five groups:-

(1) Four controls (Cases 10, 11, 12, 13) who submitted to various dietary restrictions but not to surgical interference or to anaesthesia.

(2) Eight patients, three of whom (Cases 2, 20, 21) received the routine post-gastrectomy treatment of this unit. The remaining five patients (Cases 5, 6, 7, 8, 9) were submitted in one case to vagotomy, in one to lumbar sympathectomy, in one to splanchnicectomy, in one to osteotomy of the femur, and in one to spinal fusion and bone grafting; gastric aspiration was not carried out in these cases.

(3) Five patients (Cases 22, 23, 24, 25, 42) who, in the immediate post-operative period, received intravenous infusions of an enzymic digest of casein (in four cases casydrol, and in one case amigen) in amounts which would yield as nearly as possible an intake of 11 g. of nitrogen per day. (Case 42 is included /

included also in Group 5).

(4) Six patients (Cases 45, 46, 47, 48, 49, 50) who, during the post-operative catabolic phase, received, initially by a jejunal tube and later orally, a mixture of whole milk, dried skimmed milk and lactose, the total amount of milk mixture or mixture plus ordinary food being calculated to yield at least 70 g. protein (11 g. nitrogen) and 1700 calories per day.

(5) Five patients (Cases 42, 55, 56, 57, 58) who were given, as nearly as possible, a constant intake of sodium and chloride throughout the pre- and post-operative periods, partly by intravenous salt solution and partly by the oral administration of known amounts of salt in the diet.

After operation, in all these groups, except the control group, the urinary excretion of chloride was depressed irrespective of the amount of salt administered. The time of onset of the depression of urinary chloride excretion varied. Although in some cases a fall in amount began two or three days before operation which might have been initially related to a reduction in appetite and in food consumption, and in a few the fall was delayed for one or two days after operation, in most cases the fall was abrupt on the day of operation. The depression lasted for five days after operation in five patients, for seven days in seven patients, for eight days in five patients, for nine days in two patients and for ten days in one patient; in three the exact duration was not determined. For two or more consecutive days the total urinary chloride excretion fell below 1.0 g. per day in eight patients, and below 2.0 g. per day in eight patients. There was no relationship between the time of onset, /

onset, duration or degree of depression of urinary chloride excretion and the type of post-operative treatment employed.

When, after partial gastrectomy, the intravenous intake of sodium chloride was compared with the excretion of chloride in the urine and the loss of chloride by gastric aspiration, it was found that there was retention or accumulation of chloride in the body although only modest quantities of saline (one litre per day) had been infused. The accumulation of chloride lasted for five to seven days and was later succeeded by a period when the loss of chloride exceeded the intake.

Group 1. Controls.- The two diets for the control subjects were designed to show the effects of maintenance of caloric intake on protein starvation, and this accounts for their particular form. In each of the diets the nitrogen intake was the same and was based on that of a typical patient after partial gastrectomy. In the one experiment (A), the calorie intake was maintained at or near 2500 calories per day throughout the experiment. In the other experiment (B), the calorie intake was restricted as it usually was after operation, falling to 500 calories per day for the day of operation and the succeeding two days, but thereafter rising as in a typical patient. While in Experiment B the salt intake was unrestricted, in Experiment A food was provided which had been cooked without salt and salt was added according to taste, from a weighed daily supply, the unused portion of which was later weighed. During the three days of starvation in Experiment B, salt intake was almost nil, whereas in Experiment A it was maintained at 6.0 to 8.0 g. per day. The daily excretion of chloride varied

according /

according to the salt intake; the characteristic patterns which resulted in the two experiments are shown in Tables 49, 50 and 51, and in Chart IV. Thus the urinary excretion of chloride in these varieties of food restriction was not related to the protein intake and could be largely controlled by the oral consumption of salt.

From the work of Benedict (1915) one would expect the urine chloride excretion to take several days to fall to 1.0 g. per day or less in fasting subjects who were well nourished before the experiment began. This is what might have happened in the controls starved of calories and protein if their intake had not been resumed after three days of starvation. Frequently in the patients after operation, however, the urine chloride excretion falls much more rapidly, suggesting that there is some factor causing this which is related to the operation and is additional to the starvation factor.

Group 2. Patients on Routine Ward Treatment.- Of eight patients in this group, three (Cases 2, 20, 21; Tables 2, 22, 23) underwent partial gastrectomy. After operation they were treated by continuous intravenous infusion of saline or glucose solution with two-hourly gastric aspiration for periods up to four days according to individual indications, only small quantities of water or milk and water being given by mouth during this time. Thereafter the oral intake of food was gradually increased to 70 g. protein and more than 1800 calories per day, this level being reached by the sixth to tenth day. One patient was submitted to splanchnicectomy (Case 7, Table 7, Chart III), one to lumbar sympathectomy (Case 6, Table 6), one to /

to vagotomy (Case 5, Table 5, Chart II), one to osteotomy of femur (Case 8, Table 8), and one to spinal fusion and bone grafting (Case 9, Table 9). In none of these cases was intravenous infusion or gastric aspiration employed.

In all cases there was a depression of urinary chloride excretion after operation. This depression occurred in spite of the intravenous administration of more than 10 g. salt per day in some cases. On the other hand, during the first three days after operation there might be a loss of chloride equivalent to 5 to 15 g. in the fluid aspirated from the stomach. It seemed curious that whether or not chloride was lost by suction, the urine chloride excretion was depressed to about the same degree.

In Case 7 (Table 7, Chart III), the total daily urine chloride fell to 1.07 g. on the day of operation, it was 2.72 g. on the next day and remained in the region of 1.0 g. per day for another five days. There was no intravenous infusion or gastric aspiration. The nitrogen intake and excretion are also shown. It will be seen that the period of increased nitrogen excretion coincides with that of depressed chloride excretion.

After operation in Case 5 (Table 5, Chart II), there was prolonged starvation for both protein and calories. On the day of operation the urinary chloride excretion was large, and this was probably related to the intravenous infusion of saline on this day. During the next five days there was a steady reduction in urinary chloride excretion which is reminiscent of the findings in the classical studies on starvation. From the sixth day after operation, however, there was a steady increase in chloride /

chloride excretion in the urine, although there had been little alteration in food intake and no such increase as, following five days' deprivation of food, could be expected to cause so large an excretion of chloride in the urine. These observations suggested that renal excretion of chloride was suppressed for a period of five days immediately following operation, and this was followed by the excretion of part of the retained chloride.

In both the patients submitted to operations on bones (Cases 8 and 9), the reduction in urinary chloride excretion was marked. Yet in neither of these patients was there much increase in urinary nitrogen excretion. In Case 8 this was assumed to be the result of insufficient injury at operation; in Case 9 it was ascribed to the absence of protein catabolism because of severe wasting and depletion of protein.

In all cases nitrogen balance studies were also made. The post-operative increase in urinary excretion (which is a more striking and constant phenomenon than the negative nitrogen balance) coincided roughly with the period of decreased urinary chloride excretion. Whether this is mere coincidence or whether the two phenomena are related as part of a general metabolic disturbance, these observations were insufficient to decide. Direct proof of this relationship is very difficult, but indirect support might be obtained if it were found that the two phenomena were inseparable under a variety of conditions.

Group 3. Intravenous Administration of Casein Hydrolysate.- In this group the nitrogen intake immediately after operation was kept at a moderate level throughout by the intravenous infusion of a casein hydrolysate (casydrol or amigen). The hydrolysate /

hydrolysate infusion was maintained until food intake was re-started, and because of this the intake of chloride was maintained, being, indeed, greater in the five or six days after operation than in both the pre-operative period and the subsequent post-operative period. In spite of this, the excretion of chloride fell to the low levels observed in the cases of Group 2, and returned to about the pre-operative level only after the usual period of five to eight days. Indeed it was particularly striking that the return of urinary chloride excretion to the pre-operative level occurred at a time when the chloride intake was lowest because of the transition from intravenous infusion to oral feeding. This may be due in part to the known delay in excretion of salt given by intravenous infusion. These features are illustrated in Cases 22 to 25 (Table 52, Chart VII). In Case 22 the salt intake, before operation and when ordinary feeding was resumed after operation, was estimated from tables to be about 7.0 g. per day. Only on the second post-operative day did the intake derived from intravenous saline or casydrol fall below 7.0 g.; on the other five days the intravenous salt intake was in the region of 10.0 g. per day. The urine chloride remained at less than 1.0 g. per day until the fifth day, when a rise began which was much more rapid than the rate of increase in the oral intake of food and of salt.

In these patients, after operation, the marked increase in nitrogen excretion again coincided with the period of decreased chloride excretion. During the casydrol infusion there was an abundant intake of protein, but the calorie intake (1000 to 1100 calories per day) was inadequate. In two cases (Nos. 23 and 25, Table /

Table 52) of this group, large amounts of chloride were removed in the gastric aspirations, but this made no significant difference to the extent or duration of the phase of lowered chloride excretion. Furthermore, the amounts lost in this way were less than the amount of salt supplied intravenously as hydrolysate and as saline, so that in all cases there was a marked retention of chloride in the first week after operation.

Group 4. Milk Mixture.- During the post-operative catabolic phase, six patients received, initially by a double-lumen tube inserted at operation into the distal limb of the jejunum and later orally, a mixture of whole milk, reconstituted dried skimmed milk and lactose. These feedings were designed to provide 70 g. protein and 1700 calories per day; on some days this intake was not achieved, on others it was exceeded. The salt intake was never less than 4.0 g. per day; while the intravenous infusion was being given it was in the region of 10.0 g. or more per day. In two of these patients the urine chloride excretion was less than 1.0 g. per day for two or more days, in three less than 2.0 g. and in one less than 3.0 g.

Case 46 (Table 31, Chart IX).- J.S., aged 52 years. Miner. Diagnosis: chronic duodenal ulcer; operation: partial gastrectomy. In this case salt was added to the milk mixture so that the daily intake was considerably greater than in the majority of the patients of this group, reaching nearly 20 g. on the day after operation. In spite of this large intake of salt, urine chloride excretion remained low for four days after operation. Some of the salt taken in the milk mixture was lost in stools passed on the 3rd, 4th and 6th days after operation.

The data of Cases 47 and 49 are shown in Table 53.

The pattern of chloride excretion was similar to that found after operation in the preceding groups. There is no essential difference /

difference in the urinary chloride excretion in the patients of Group 3 who received a large amount of salt and a high protein but low calorie intake immediately after operation, and those in Group 4 who received a smaller salt intake but adequate protein and calories. Whether the salt is given by the intravenous route or by mouth also appears to be immaterial.

Group 5. Constant Salt Intake.- There remain to be considered five patients who were studied in more detail. In addition to nitrogen, sodium and chloride balances, an attempt was made to maintain the salt intake at a constant level throughout the period of study before and after operation. A diet of known composition but low in salt was provided, the food being cooked without the addition of salt. The patient was supplied each day with a weighed quantity of salt which he sprinkled directly on to his food according to his taste. During the immediate post-operative period, before this diet was given and after intravenous saline had been discontinued, the requisite amount of salt was given orally in the form of saline flavoured with orange juice. An ample supply of distilled water was allowed and the amount consumed was measured daily. Tea and other beverages were made only with distilled water from this daily allowance. In addition, in some of the patients of this group the sodium and chloride content of the stools was measured.

In the tables the oral salt intake indicates the quantity of salt added to the food by the patient, together with the salt taken in the form of orange juice and saline in the period after operation, when the food intake was being restored; it does not include /

include the sodium and chloride content of the food.

The urinary chloride (expressed as g. NaCl) has been included for convenience in comparison. The sodium and chloride contained in transfused blood was assumed to be equivalent to the quantities estimated to have been lost at operation; therefore in computing the daily balances these have not been included.

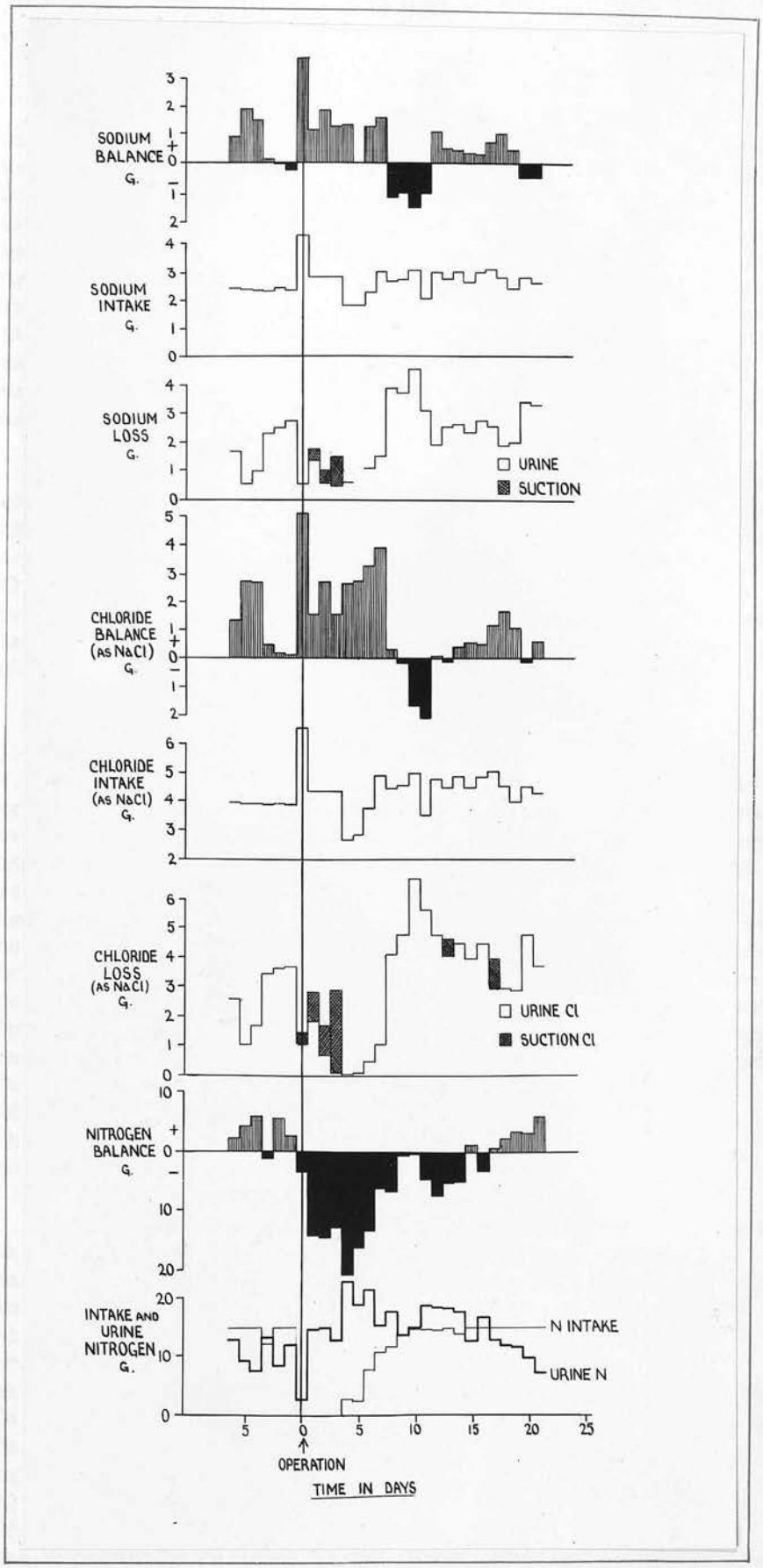
The composition of the orange juice and saline mixture and of the saline administered by intravenous infusion was checked and the saline was found to vary so widely that analysis of each flask of saline as well as measurement of the volume infused were necessary.

Case 55 (Tables 38, 54, 68).- J.I., aged 58 years. Blacksmith. For 10 years had had attacks of pain and vomiting at varying intervals, usually before food; pain sometimes shot up into neck. Pain relieved by taking food or alkaline powders. Appetite poor during attacks but patient kept to diet fairly well. Four years ago lost 14 lb. in weight which has never been regained; weight has been steady; work heavy, involving use of a 14 lb. hammer. On admission, small wiry man, thin but muscular; no abdominal tenderness. At laparotomy: small chronic duodenal ulcer; posterior gastro-jejunostomy. After operation, intravenous infusion for 24 hours; temperature elevated for seven days, pulse rate increased for six days. Cough, due to bronchitis, and good deal of sputum but no sign of pulmonary consolidation. Body weight increased during 2nd and 3rd days after operation but then fell, and 2.6 lb. lost in all over 10 days. Discharged on 16th day.

Before operation was in positive nitrogen balance on 90 g. protein (14 g. nitrogen) and 2200 calories per day. After operation food intake was slowly increased and nitrogen equilibrium regained on 8th day on 66 g. protein (10.6 g. nitrogen) and 1620 calories. Maximum urinary nitrogen excretion on first and second days after operation with reduction to below 10 g. per day after this time. This early return to a small daily urinary nitrogen excretion suggests that there was some protein depletion; the pre-operative positive nitrogen balance supports this conclusion, as does the small loss of weight.

The /

CHART XIII



Case 56.- To show nitrogen, chloride and sodium intake, output and balance before and after partial gastrectomy, with attempted regulation of sodium and chloride intake.

The operation did not involve a severe injury but some increase in nitrogen excretion occurred, indicating the tendency to produce a catabolic phase if this were possible. After operation there was retention of both sodium and chloride which became rather more marked about the 6th day; urinary sodium and chloride output were both high on the day after operation following a large intake of intravenous saline on the day of operation. Salt intake and output fell sharply in the last three days, and this reduced the value of the experiment, which shows retention but no marked reduction of urine output in the first six days after operation.

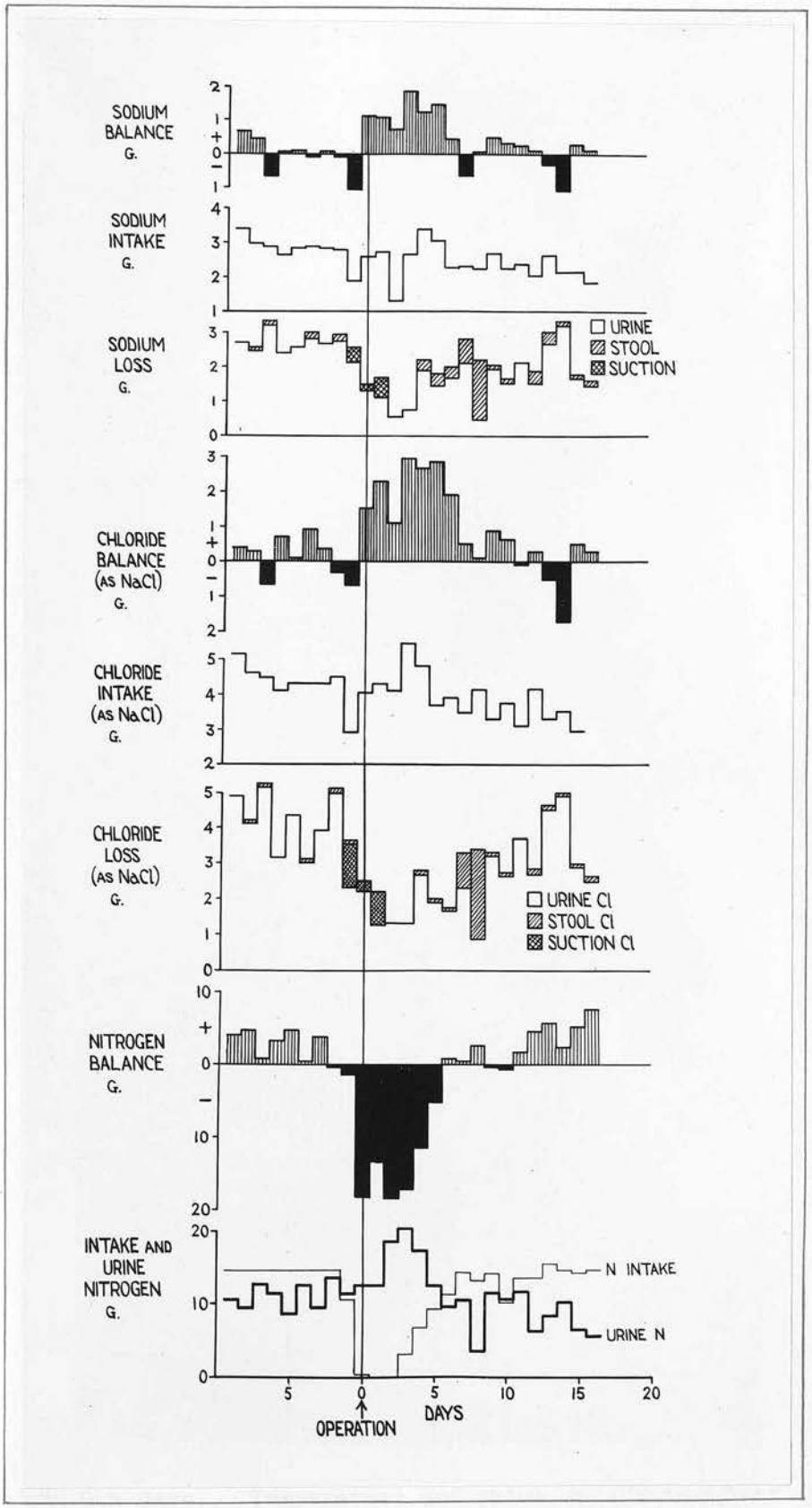
Following operation, packed cell volume fell markedly; there was a small reduction in plasma albumin but little change in plasma globulin concentration. Plasma chloride concentration changed little but that of chloride rose. When these changes were related by means of the packed cell volume in terms of plasma and cell chloride concentration per 100 ml. blood, there was a rise in plasma chloride and a fall in cell chloride concentration.

Case 56 (Tables 39, 57, 58, 68; Chart XIII).- W.S., aged 26 years. Miner. For five years had had epigastric pain an hour after meals relieved by more food or by alkaline powders. Had lost about 14 lb. in weight; had not been on a diet. On admission, large, very fat young man, who did not show any sign of loss of weight. Radiological examination showed deformity of duodenum but no ulcer crater. At laparotomy: chronic duodenal ulcer; transabdominal vagotomy; partial gastrectomy; gastro-jejunostomy. After operation, intravenous infusion and intermittent gastric aspiration for four days. Temperature and pulse rate elevated for 11 days. Abdominal distention for four days. Up on 11th day; stitches out on 15th day; wound broke down on 18th day and discharged pus; thereafter temperature settled. Discharged home one month after operation.

Before operation was in positive nitrogen balance on an intake of 92 g. protein (14.7 g. nitrogen) and 2500 calories per day. The intake of sodium was about 2.4 g. and of chloride about 3.8 g. per day which resulted in positive balance of both elements. After operation, prolonged increase in urinary nitrogen excretion, most marked on 4th day (22.9 g.). Urinary nitrogen excretion fell on 9th and 10th days but then rose again for four days. There was consequently negative nitrogen balance for 14 days after operation in spite of the daily ingestion of 90 g. protein (14.5 g. nitrogen) and over 2000 calories from the 10th day. This prolonged catabolic response was apparently related to the wound abscess to which also was attributed the elevation of body temperature which lasted for 18 days.

For /

CHART XIV



Case 57.- To show nitrogen, chloride and sodium intake, output and balance before and after partial gastrectomy, with attempted regulation of sodium and chloride intake.

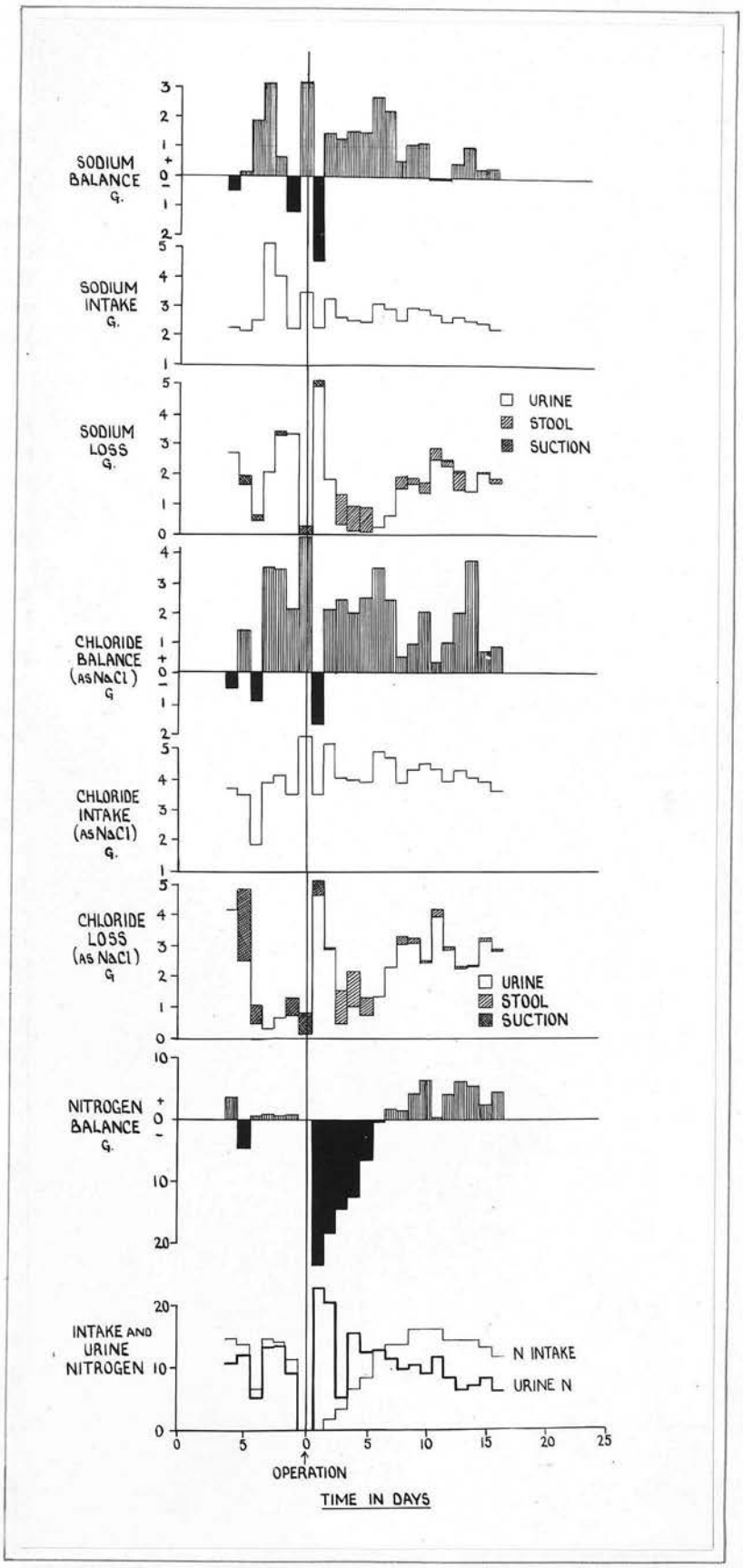
For seven days following operation, there was a marked reduction in urinary chloride excretion and retention of chloride in the body. There was then a considerable increase in chloride excretion for four days, after which equilibrium was regained. In the case of sodium there were similar changes but of a smaller magnitude. For the first three days after operation there was an increase in the intake of both sodium and chloride, followed by a reduction for three days to below the pre-operative level. There was marked retention of both during the first seven days after operation, and then a period of four days during which there was negative balance of both sodium and chloride.

There was a marked reduction in packed cell volume after operation which was most severe on the 5th to 7th days, this being the time at which the reduction in plasma albumin concentration was most marked, although the globulin concentration was increased and continued to rise after this time. A reduction in the serum concentration of sodium occurred soon after operation and persisted for a week. There was an elevation of the concentration of chloride in the plasma and a more marked increase in the whole blood chloride concentration. In Table 68 these changes of chloride concentration in serum and whole blood have been related by means of the packed cell volume, and the alterations in distribution of chloride between red blood corpuscles and serum are shown. Although there was no change in the plasma chloride concentration, there was an increase in the proportion of the chloride in a unit volume of blood which was derived from plasma chloride and a reduction in the proportion derived from the red corpuscles. This change is seen to be related to an increase in the proportions of plasma to cells.

Case 57 (Tables 40, 59, 60, 68; Chart XIV).- A.S., aged 43 years. Barman. Intermittent symptoms of duodenal ulcer for seven years with radiological evidence of crater. Perforation of ulcer closed at operation 18 months ago. Had lost 7 to 10 lb. in weight in past year or two. Appetite not good, found dieting difficult because of work; good deal of worry at work. On admission, thin wiry man not wasted. At laparotomy: chronic duodenal and more recent gastric ulcers; partial gastrectomy; gastro-jejunostomy. Post-operative gastric aspiration and intravenous infusion for 48 hours; up on 2nd day; hiccough on 3rd and 4th days. Chemical phlebitis in long saphenous veins and drip wounds inflamed in both legs between 7th and 12th days. Diarrhoea on 7th, 8th and 9th days. Temperature and pulse rate elevated for four days. Lost 5.7 lb. in weight in first 10 days after operation, but there was later some gain in weight.

Before /

CHART XV



Case 58.- To show nitrogen, chloride and sodium intake, output and balance before and after partial gastrectomy, with attempted regulation os sodium and chloride intake.

Before operation was in positive balance on 91 g. protein (14.5 g. nitrogen) and 2600 calories. For three days after operation very low intake of calories in form of intravenous glucose infusion. Food intake then rapidly increased and nitrogen equilibrium regained on 6th day on 70 g. protein (11.2 g. nitrogen) and 1600 calories. Marked increase in urinary nitrogen excretion, maximum (20 g.) being reached on 3rd day. From 11th day positive nitrogen balance on 80 to 90 g. protein and 2300 calories per day.

Sodium, chloride, potassium, sulphur and phosphorus intakes and outputs also were measured and an attempt was made to control the sodium and chloride intakes. After operation, the intakes of both sodium and chloride were erratic because of excessive saline administered after operation, and the provision of too little orange juice and saline on the 2nd day and of too much on the 4th day. There was, however, retention of both sodium and chloride on the day of operation and for five days afterwards, slightly more marked and prolonged in the case of chloride. The sodium and chloride content of the stools were included and during the first three days after operation there was an obvious reduction in urinary chloride excretion, but this was by no means as marked as in some other cases, nor could it be attributed entirely to oliguria. There was a rise in urinary sulphur excretion on the 3rd and 4th days; after operation the nitrogen-sulphur ratio varied a good deal within a small range, being raised except on the 4th and 6th days. There was a fall in total and urinary phosphorus excretion for the first eight days after operation. Urinary potassium was much increased on the day of operation but thereafter was decreased. There was negative potassium balance during the three days of starvation of food, but positive balance followed the resumption of ordinary food intake.

Packed cell volume fell but less markedly than in Cases 55 and 56. There was also a less marked alteration in the plasma and red blood cell content of chloride than in the other two cases but the pattern of change was similar.

Case 58 (Tables 41, 61, 62; Chart XV).- P.R., aged 54 years. Furnace-man in gasworks. Seven years ago began to have epigastric pain after meals; soon after this had haematemesis, treated in hospital; improved on diet and powders. Pain off and on ever since with bouts of vomiting large volumes of fluid and food. All symptoms much worse recently. On admission, thin nervous man, tender in upper abdomen under left ribs and in centre. Good deal of vomiting during gastric function tests. At laparotomy: chronic duodenal ulcer; transabdominal vagotomy; partial gastrectomy; gastro-jejunostomy. After operation, intravenous infusion and intermittent gastric aspiration for 24 hours. Temperature elevated for three days, pulse rate increased for five days. Some /

Some abdominal discomfort and distention on 2nd day followed on third day by diarrhoea, rigor and temperature elevated to 102°F. On 4th day five loose stools and on 5th day stools still loose but discomfort and frequency less severe. Tinct. opii produced marked improvement. On examination of stools, no ova, cysts or amoebae and no growth on culture. Subsequently patient settled down and made satisfactory progress, though stool remained soft. Got up on 13th day, discharged from ward on 17th day.

Before operation was in nitrogen equilibrium on an intake of 90 g. protein (14.5 g. nitrogen) and 2500 calories. The salt intake was fairly steady but sodium intake rose because of the use of alkaline powders to relieve severe epigastric pain. After operation there was a marked increase in urinary nitrogen excretion on the first two days after operation, but urine volume was low on the 3rd day and contained only 5.38 g. nitrogen; apart from this day the post-operative increase lasted for six days after operation. Nitrogen equilibrium was regained on the 7th day on an intake of 90 g. protein and 2150 calories. Sodium and chloride intake were maintained at a steady rate apart from some increase on the day of operation and the 2nd day after operation. Urinary excretion of both sodium and chloride was high on the first two days after operation but thereafter fell for five days, and there was marked retention of both sodium and chloride from the 2nd to the 7th days after operation. The reduction in urinary volume and nitrogen excretion on the 3rd day was no doubt related to the passage of bulky loose stools on this day. Over 12 g. nitrogen were lost in these stools of which only part was saved for analysis. On the 4th day also there were loose stools of which part only was saved for analysis. There was, therefore, incomplete measurement of sodium and chloride losses in the stools on these days, and the positive balance obtained is higher than it should be.

Case 42 (see also p. 104).- (Tables 55, 56). The clinical features and nitrogen metabolism of this patient have been discussed already in the section on Intravenous Administration of Hydrolysates. The sodium and chloride intake and output were controlled before and after operation and these aspects will be considered here.

Before operation, the regulation of intake of sodium and chloride was only partially effective. After operation, the quantities of saline and amigen solution and so of sodium and chloride injected with them fell below those intended, and the oral intake of saline was not started until the 3rd day and even then was insufficient. In spite of this, there was retention of sodium for eight days after operation. On the first and second days after operation, because of the high chloride content of the gastric aspiration, there was a negative chloride balance.

From /

From the 3rd to 6th days after operation the urinary chloride output was very low; during this period 12 g. chloride were retained. There was retention of about three litres of the fluid injected as saline and amigen. The chloride retention was again rather more marked than that of sodium towards the end of the period of retention, and was also slightly longer in duration.

Comment

The term "retention" has been employed to indicate that the intake of sodium or chloride exceeds the quantity excreted in the urine or lost by gastric aspiration or in the faeces. To this use of the term the same objections may be raised as in the case of its use for nitrogen retention or positive balance. The important disturbance is the reduction in excretion of chloride or sodium in the urine. The object of this part of the investigation was to find out whether this reduction persisted after operation in spite of variation or stabilisation of sodium and chloride intake. This is comparable to the experiments designed to show the relationship of the post-operative nitrogen excretion to operation injury and to the intake of protein and calories.

In each of these five cases there was retention of sodium and of chloride after operation, even when intake was stabilised. In two cases (Nos. 55 and 58) the reduction in urinary excretion of sodium and chloride was delayed for two days after operation; the explanation of this delay is not evident. In the remaining three cases, the reduction began on the day of operation, though in Case 42 it became marked only on the third day. The reduction lasted until the sixth day in two cases, the seventh day in two others and until the eighth day in the fifth case, although it was most severe from the third to sixth days. /

days. There was some indication that retention of chloride was more marked than that of sodium, whether the quantities were expressed as grams or as milliequivalents. In Case 56 there was some excess of excretion over intake of both sodium and chloride from the eighth to eleventh days after operation, and a similar but less marked disturbance has been observed in other patients. This may indicate either an excessive excretion just after the restoration of a normal intake of salt with the food, or it may be due to a process of restitution following the earlier retention.

In all these patients, there is the coincidence of increased nitrogen excretion in the urine with a reduced urinary excretion of sodium and chloride ions during the first six to eight days immediately after operations such as partial gastrectomy. These phenomena have not been disturbed by considerable variations in the amounts of the intake of salt, water, protein or calories, or in the routes by which these have been made available.

Discussion

The most obvious explanation for the reduction in urinary chloride excretion after operation would be that it is due to lack of intake of salt during the usual period of post-operative starvation or reduced food intake. The coincidence of the reduction in urinary chloride excretion with the post-operative increase in urinary nitrogen excretion associated with the catabolic phase, appears at first sight to support this explanation. However, the post-operative protein breakdown occurs /

occurs in spite of maintaining oral or jejunal protein and calorie intake at levels known to be adequate, and it is now recognised to be independent of the post-operative protein and calorie intake, though post-operative starvation does somewhat increase the severity of the catabolism. Similarly when salt intake was maintained by intravenous and oral routes, it was found that urinary excretion of chloride was still reduced after operation. Detailed studies of sodium and chloride intake and output have shown that there is a retention of both these ions during the week immediately following major surgical operations of different types.

The dangers of salt retention during intravenous infusions have long been emphasised, especially in the case of patients suffering from renal and cardiovascular disease. More recently emphasis has been laid also on the potential dangers in patients suffering from protein depletion with a low plasma albumin concentration, in whom oedema may result following haemodilution consequent on excessive saline infusion. In the patients of the present series there was seldom marked protein depletion or severe renal or cardiovascular disease, yet after operation sodium chloride and in some degree water retention were common features.

Experiments carried out in 1915 by Haldane and Priestley have some bearing on the present discussion. In studying the regulation of excretion of water by the kidneys, they showed that there was a marked ability on the part of the normal kidney to respond by diuresis to the oral ingestion of water. Of 5.5 litres of water drunk in just over eight hours, 5.46 litres were excreted /

excreted within a short time of the end of the period of drinking, the maximum rate of excretion being 1200 ml. per hour. They found, however, that the kidney was unable to maintain extreme diuresis for an unlimited period and that a rate of more than 750 ml. per hour could not be maintained. When two litres of 0.6 per cent. saline were drunk in 15 minutes, 800 ml. were vomited, but a big diuresis resulted and the specific gravity of the urine was less than that of the saline. These experiments were carried out on normal subjects with good renal function.

At low minute volumes of urine output, maximum concentrations of urea and chlorides do not occur simultaneously in human urine, presumably because of osmotic limitations in the kidney (McCance, 1946). Here is another possible explanation of the coincidence of chloride retention and increased nitrogen excretion after operation. After operation on two cases (Nos. 8 and 9), however, chloride excretion fell but nitrogen excretion did not markedly increase. On the other hand, it might well explain the delay of 48 hours or more in some cases before there was a reduction of chloride excretion associated with a similar delay in elevation of nitrogen excretion. This work of McCance was extended by Harvey et al. (1946) in experiments on themselves. They found that at any urine flow over 3 ml. per minute, the consumption of urea as well as of salt depressed the urine concentration of chloride, and had little or no effect in raising the osmotic pressure of the urine. They concluded that the reabsorption in the distal tubules is not limited by the concentration of chloride within them reaching

a /

a maximal value, but that there is a limiting osmotic pressure at all urine flows and that this falls as the minute volume rises.

The work of Haldane and Priestley has been taken a step further by two interesting experiments carried out by Moyer et al. (1947). After a 16-hour fast for water and food, fluid equivalent to 1 per cent. of his original body weight was injected intravenously each hour for five hours into each of two healthy normal men. The urine was collected in hourly samples. The rate of infusion in one man was 848 ml. per hour and in the other 743 ml. per hour. When 0.9 per cent. saline was infused, the urine flow increased in the first two or three hours to a maximum flow of 200 ml. per hour; in other words the injection rate was 1 per cent. body weight per hour and the urine flow was 0.26 per cent. body weight per hour. This resulted in retention of saline in the body which progressively increased since the urine flow remained relatively stationary. After the infusion was stopped, the rate of urine flow decreased, being constantly related to the amount of salty fluid still remaining; at the time of stopping the infusion there were 3000 ml. and 2500 ml. respectively in these two subjects.

When, under similar conditions, the same two men were given 5 per cent. glucose solution at the same rate as the saline, the urine volume exceeded the rate of infusion after three hours, and fluid, equivalent to all that had been injected, had been excreted by one hour after the infusion was stopped.

For 16 hours before either experiment, these men did not drink any water but insensible loss of water had continued.

Before /

Before the infusions were started, there was thus an appreciable water debt, but one which was comparable to that found before operation in many patients. When water was not taken by mouth and saline was infused, sodium was excreted in the urine in the same concentration as it was present in the infusate, that is, no water was freed by renal excretion of electrolyte.

When saline infusions and endogenous metabolism are the only sources of water, it is necessary for the kidney to excrete urine which contains sodium and chloride in higher concentrations than that of the infused fluid if water is to be provided for insensible loss. The ability to do this varies from one individual to another and with the concentration of the saline. Moyer et al. (1947) defined "load" as the total cumulative excess of a substance administered in a given time over the amount excreted in that time. They stated that when 0.9 per cent. saline was given by the oral or intravenous route, healthy men have excretion ratios of 0.03 to 0.1 per hour. For loads of saline between 2 and 5 per cent. of body weight, their ratios did not vary appreciably within a year in a healthy man. After a major operation, however, the ratios varied between 0.01 and 0.04 per hour.

In 1942 Stewart and Rourke reported their observations after gynaecological operations of moderate or mild severity under ether anaesthesia in 10 women, to whom infusions of 5 per cent. glucose and 0.9 per cent. saline were given. After saline infusions there was retention of water because of delay in excretion of the water of the saline. For over 80 hours after operation there was retention of sodium and chloride, more marked /

marked in the case of chloride because of poor initial renal conservation of sodium. Potassium balance was negative after operation and the loss exceeded that to be expected from the nitrogen excretion, suggesting intracellular dehydration. As a result of saline retention, there were increases in plasma and intracellular fluid volume, dilution of plasma protein and reduction of the red cell count. It was not until after several days that urine excretion equalled or exceeded the rate of infusion. After glucose infusions there was efficient renal conservation if the infusion was not too rapid. The weight-saving effect of glucose (in sparing protein catabolism for fuel) might, however, be offset by water loss, due to loss of extra-cellular fluid because of failure of renal conservation of sodium and chloride in the initial stages.

Cooper et al. (1949) observed that sodium, chloride and water retention were greatly increased after operation, and were not much affected by increasing the water intake in the form of 5 per cent. glucose solution. After abdomino-perineal excision of the rectum, none of their patients could concentrate 0.9 per cent. saline in urine formation. After severe injury, they found that neither dogs nor men can extract much water from massive saline infusions; this inability also occurs, though perhaps not for the same reason, in the aged, in arterial disease, malnutrition, malignant disease, obstructive jaundice and anaemias. They imply that after surgical operation there is an altered renal excretion of water, as well as and not because of changes in excretion of sodium and chloride. This retention of water seems to be independent of the rate of injection /

injection of glucose solution, of replacement of blood lost at operation and of the load of water.

Legueu et al. (1933) drew attention to a disturbance of chloride equilibrium following surgical operations. They observed a reduction in the ratio of the chloride concentration of red blood cells to that of plasma, and at the same time a lowering of the concentration of chloride in the urine to as low as 0.5 g. per litre, often accompanied by oliguria. They subjected rabbits to injuries simulating surgical operations on their liver, kidney or muscle, and after death found by direct examination of the injured tissues that these tissues contained a higher concentration of chloride than uninjured similar tissue. They suggested that the accumulation of chloride in damaged tissue after operations caused a disturbance of the "milieu interieur" and thus of the renal function. Since they believed alterations in chloride distribution to be one of the chief factors in the production of surgical shock, they recommended the administration of massive doses of saline by intravenous injection.

Robineau (1933) suggested that the change in the relative concentrations of chloride in cells and plasma might be due to a transfer of chloride from the cells to the plasma with or without loss of chloride from the whole blood. He stated that the injection of saline (of unstated concentration) assisted the return of a normal ratio; the urine chloride concentration which he too found to be lowered, was not raised even after the injection of large quantities of saline, and it appeared to him that after operation there was an enhanced demand for salt on the part /

part of the tissues.

Lambret (1933), in a study of the same phenomena, recommended the intravenous infusion of hypertonic saline after operation, but observed that little extra chloride appeared in the urine and that the rise in blood chloride concentration was of short duration. Theron and Wilson (1949) have recorded the reduction in urinary chloride excretion in peritonitis and paralytic ileus, and Barlow (personal communication) found a similar change after severe accidental injuries of various kinds.

Jones et al. (1934) produced oedema in the subcutaneous tissues and viscera of cats by manoeuvres simulating those of surgical operations. Rosenthal and Tabor (1945) reported their results in experiments on over 10,000 mice and rats, in which shock was produced by scalding, application of a tourniquet or bleeding. These were short-term experiments lasting up to 48 hours. Relatively large quantities of sodium were found by direct analysis in the injured areas of the animals. Oral administration of 0.9 per cent. saline to injured animals resulted in almost complete retention of sodium on the first day after injury, and up to 72 per cent. retention on the second day compared with normal controls. That this retention was not due to oliguria was emphasised by the finding of an increased urinary excretion of potassium compared with that of normal animals. In the belief that these findings indicated extra-cellular dehydration because of withdrawal of fluid into the cells affected by the injury, they employed 0.9 per cent. saline in the treatment of these animals and if this treatment was begun sufficiently early, obtained a high proportion of survivors. /

survivors. It is important to recognise that these experiments were of short duration - 48 hours, and that the period of survival after successful treatment with saline was no longer. It seems unjustifiable, therefore, to draw any wide conclusions regarding the treatment of burns and limb injuries in man from the results of these experiments. The unfavourable response to treatment with potassium salts, and the high excretion rate of potassium soon after injury were emphasised.

McCarthey and Parkins (1947) submitted rats to standardised scalding of the back and judged the efficiency of their treatment by survival for ten days. The highest survival rate followed the administration of 5 per cent. albumin in 1.06 per cent. saline, but 1.06 per cent. saline alone was almost as effective. They attributed the success of the saline to the presence of sodium which they believed diffused into the cells of the damaged area, where there was a deficiency of extracellular sodium. It is surprising that saline was so effective in promoting survival though it had little effect on haemo-concentration.

Ricca et al. (1945) made direct observations on the tissues of dogs, one of whose hind limbs they crushed in a Blalock press. The crushed limb swelled after removal of the clamp. They found that the amount of fluid which collected on the limb was more than could be accounted for as plasma lost from the circulating blood. The damaged muscles gained water but most of the other tissues of the body lost water. There was more protein in the injured limb than could be accounted for by plasma loss alone, and most of the additional protein was in the form of albumin. /

albumin. There was an increase of sodium content amounting to 120 per cent. in damaged muscle and 20 per cent. in damaged skin. On the other hand, the sodium content fell by 25 per cent. in the liver, 20 per cent. in the kidney and 20 per cent. in the spleen.

Similar evidence has been put forward by Fox and Baer (1947). They applied a tourniquet to a dog's hind limb for two hours and found, by direct analysis of the affected and normal limbs, that in the injured limb there was a marked increase in water content, the sodium content was almost doubled and that of potassium was reduced by two-thirds. The uninjured limb showed a loss of sodium but an increase in potassium content. They confirmed these direct analyses by other studies employing radio-active isotopes. They further showed that, after injury, the normally low sodium content of injured muscle was much increased and the normally high sodium content of the injured skin was slightly increased. These changes may be summarised as oedema in the injured limb and extracellular dehydration in the uninjured limb.

Another possibility to be considered is that the retention of sodium is to compensate for the loss of potassium in the urine which follows injury. This loss of potassium from the body is now believed to be due partly to continued excretion of potassium in the presence of starvation, and partly to an increased excretion consequent on the catabolic breakdown of protein after injury. According to Gamble (1945), however, potassium may be lost in excess of nitrogen and phosphorus, and it has been shown in animals that half the muscle potassium can be replaced by sodium; /

sodium; there is some evidence that this also occurs in man.

It has been reported by Howard et al. (1946) that, contrary to Cuthbertson's observation, the relationship between the quantities of nitrogen on the one hand, and of potassium, sulphur and phosphorus on the other, is not exactly that to be expected if all the excess of these substances came from the same tissue source, for example, catabolised muscle. They further found that the relationship did not hold in time, the excessive output of potassium in particular did not coincide with that of nitrogen. Recently, Moller (1949) has reported that the loss of potassium is most marked in the first 24 hours after injury, and has attributed to cellular dehydration the chief responsibility for this maximal excretion.

The most likely explanation of these apparently conflicting pieces of evidence regarding potassium changes seems to be that they have been obtained under somewhat variable conditions, often by balance studies, and they represent the urinary end-points of several processes, some of which may have little to do with protein metabolism. Before any conclusions can be reached regarding disturbances of potassium in the immediate post-operative period, much more evidence, obtained under carefully controlled conditions, is required.

Disturbances of water balance in acute hepatic disease have been recognised for many years and diuresis has long been recognised as a good omen in the jaundiced patient. Many reports have appeared describing impairment of liver function after surgical operations and general anaesthesia. Labby and Hoagland (1947) combined observations on liver function, blood, plasma /

plasma and extracellular fluid volumes and the water tolerance test in patients suffering from acute liver disease. They found retention of sodium and chloride and of water in the early stages, with depression of plasma and urine chloride concentration and delayed water diuresis. At the same time there was expansion of the thiocyanate space which they believed prevented these changes being explained as due to dehydration. The apparent connection between the liver and kidney is difficult to explain. Labby and Hoagland suggested that it might be related to a factor having an antidiuretic effect on rats which is present in the urine of patients with cirrhosis and ascites, but is inactivated in the undamaged liver of normal subjects. This antidiuretic effect diminishes when the ascites is controlled (Ralli et al., 1945). On the other hand, Labby and Hoagland found that changes in plasma protein concentration might be little related to alterations in the ascites or plasma volume.

In the present investigations it has been shown that after partial gastrectomy there might be an expansion of thiocyanate space and plasma volume, an alteration in distribution of chloride in the blood, though concentration changes appear to be of minor degree, and retention of sodium and chloride and of water. These changes coincided with alterations in nitrogen metabolism. They may all stem from a disturbance of liver function related to operative injury or less probably to anaesthesia. In the present series of cases attempts to demonstrate alterations in liver function have proved disappointing. In an earlier investigation (Thomson and Wilkinson, 1940), impairment of liver function for conversion of /

of laevulose was obtained in children after herniotomy and similar operations under general anaesthesia with nitrous oxide-oxygen and minimal ether, cyanosis being avoided. Howard (1946) found that hepatic bromsulphthalein function was impaired by fasting without operation, while Browne (1944) found impairment of hepatic function by the same test which lasted as long as the period of negative nitrogen balance but nitrogen excretion was not altered.

It is clear that the decrease in chloride excretion during the post-operative period is an expression, not of a mere failure of intake, but of some active process leading to a retention of chloride and sodium. The coincidence in time between the retention of inorganic ions and the loss of nitrogen shown in the catabolic phase suggests that the two phenomena may be related.

It seems likely that the retention of sodium with chloride after injury or operation is related to the inflammatory reaction to injury, especially as there is now evidence not only of accumulation of increased quantities of sodium and chloride in damaged tissues after injury, but also of mobilisation of sodium and chloride from other, undamaged tissues.

In other words, the evidence, incomplete though it is, suggests that the sodium and chloride retention after injury form a part of a complex response associated with the inflammatory reaction, and that the increased protein breakdown is another part of this response, the two parts both being effects of a common cause rather than one being the cause of the other.

There /

There is obviously a field here for direct study of the effect of surgical operations on the ability of the human body to deal with solutions of various kinds and strengths presented orally, rectally or by intravenous injection. Apart from the valuable information to be obtained by the relatively simple procedures of measurement of urine volume, specific gravity and pH, the detailed study on a time basis of excretion patterns of sodium, chloride and potassium should provide further knowledge of the important changes in electrolyte and water balance which are caused by severe injury.

During the immediate post-operative period, the dangers inherent in intravenous infusions cannot be entirely avoided by oral or rectal intake of fluids, because, as Starling (1909) pointed out, "Absorption by the alimentary surface is a question of the local conditions rather than of the needs of the organism as a whole"; only in extreme cases of hydraemic plethora could the process of intestinal absorption be affected, never in the normal animal. The provision of the most suitable fluid, the choice of the safest route of administration and the decision as to the quantity to be employed are matters of great importance if, after major operations, uneventful convalescence is to be achieved.

ADMINISTRATION OF TESTOSTERONE PROPIONATE

In view of a report that testosterone propionate, oestradiol benzoate and methyl testosterone were each capable of promoting nitrogen retention (Schenker and Browne, 1942), a trial of one of these substances was undertaken. Testosterone propionate was administered in a dose of 25 mg. per day by intramuscular injection to two patients. In one of these operation was decided against after investigation of the patient and the experiment was abandoned after five days. The other is reported below.

Case 59 (Table 37).- A.B., aged 32. Process worker. For over 12 years had indigestion and abdominal pain after meals; for past seven years had taken powders and lived on a special diet with little improvement. Pain became worse and recently spread to back. On admission, tender in upper abdomen. Radiological examination showed deformity of duodenal cap. At laparotomy: small anterior duodenal ulcer, large deep posterior duodenal ulcer eroding pancreas; partial gastrectomy; gastro-jejunostomy. After operation, intravenous infusion and gastric aspiration for four days. Temperature and pulse rate raised on 2nd and 3rd days. Discharged on 15th day.

Before operation was in positive nitrogen balance of 6 g. per day on an intake of 116 g. protein (18.58 g. nitrogen) and 2800 calories. After operation urinary nitrogen excretion rose to 16.72 g. on day after operation and remained high until 6th day when it fell to region of 12 g. per day and later to about 10 g. per day. No food for three days after operation and then intake raised rapidly to 65 g. protein (10.4 g. nitrogen) and 1600 calories by 6th day. Nitrogen equilibrium regained by about 10th day on the same intake. From the day before operation for 12 days 25 mg. testosterone propionate as perandren was given by intramuscular injection.

This /

This patient exhibited a moderate catabolic response and there is no evidence that the testosterone had any effect.

Further trials have not been made as it appears that even in depleted subjects on an adequate diet, the quantity of nitrogen retained by the influence of these androgens is small. They have no effect on the catabolic phase and their effect is probably most marked during the later period of anabolism which was beyond the scope of the present enquiry.

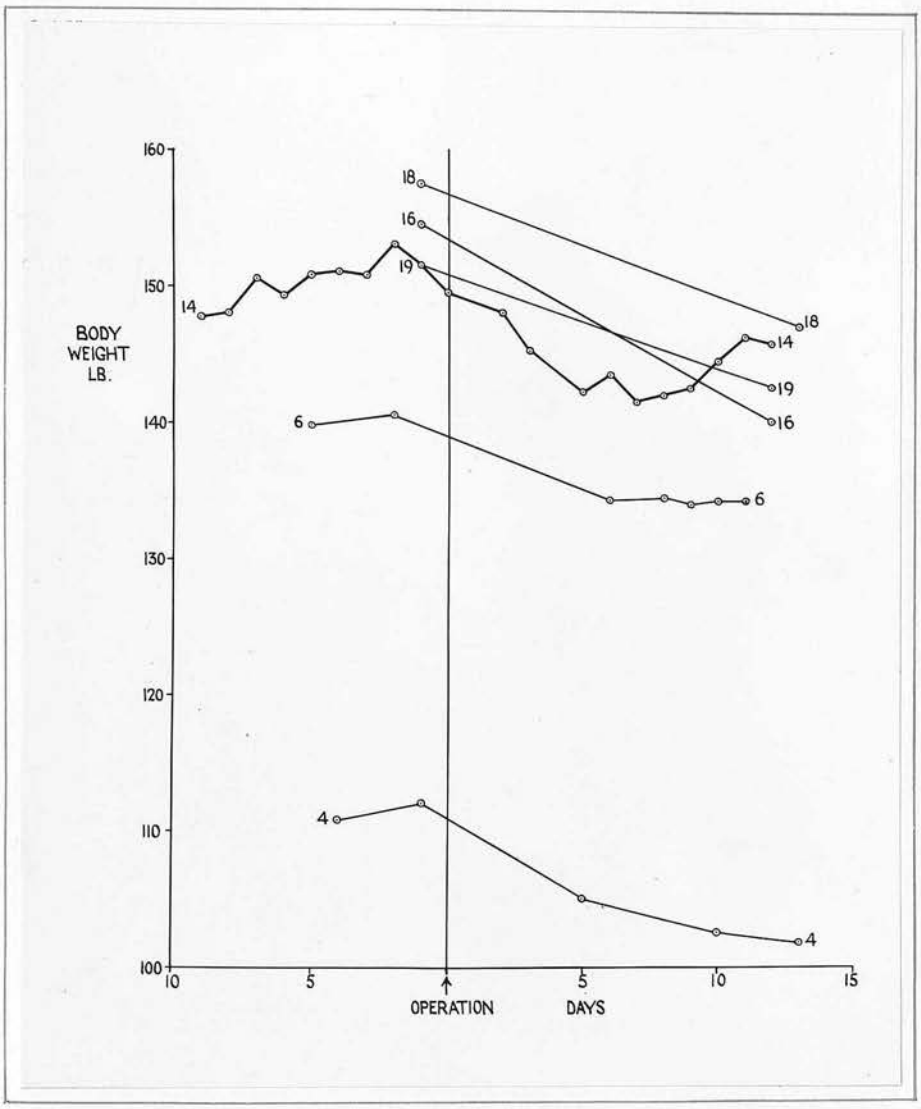
MEASUREMENTS OF LIMBS

Measurements of the circumference of all four limbs at the mid-point of the thigh, calf, arm and forearm were made on two patients (Cases 24 and 25, Table 72). The point of measurement was marked with ink and the mark was freshened from time to time. After partial gastrectomy these patients were given casydrol by intravenous infusion. There was a marked loss of substance from all the limbs of each subject. In the case of the thigh there was a reduction in circumference of up to 7 cm., while in the forearm it was only 2 cm. The reductions were roughly proportioned to the initial measurements and were at all points larger in Case 24. Whereas in Case 24 the fall was a steady one with only minor and unconnected exceptions, in Case 25 there was on the fourth day after operation an increase in size of both forearms and arms, and on the sixth day an increase in the right thigh and calf. The weight of this patient increased during the course of the casydrol infusions by nearly 3 lb.; this weight rise might be partly accounted for by the increase in the size of the limbs.

These reductions in limb size are in marked contrast to the results of similar daily measurements carried out on the limbs of the control subjects, in whom no change was observed during or after the period of starvation, although there was some reduction in weight in all but one case (No. 14). After operation the reduction in limb size thus appears to be related to some change connected with the operation or with the casydrol infusion. The most important difference between patients who received /

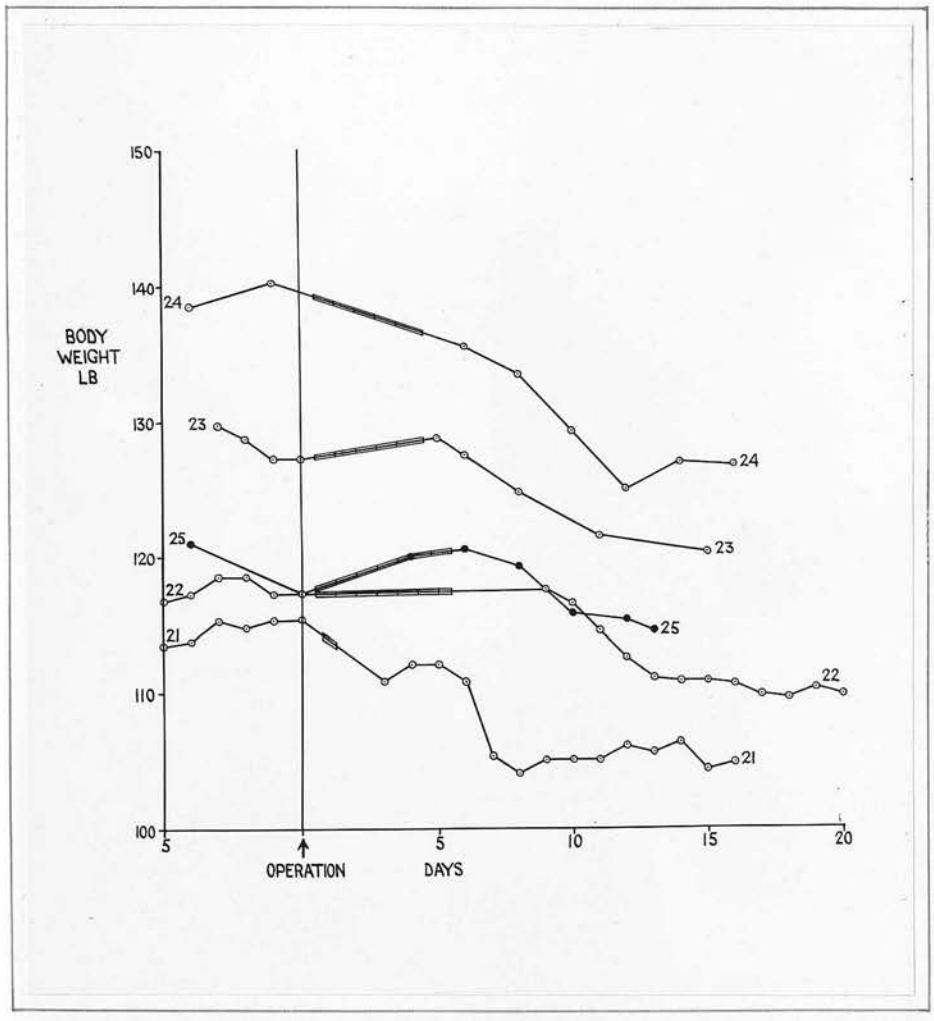
received casydrol and those who did not appears to be the delay in weight loss noted in the former group. The ultimate weight loss following operation was probably of the same order in both groups. The steady reduction in limb size, if due to muscle catabolism, indicates the removal of a large amount of muscle and provides some objective support for the clinical observations of loss of body tissue previously mentioned. The proportional loss occurring in all four limbs already mentioned, indicates a general process affecting the body as a whole, but whether it is largely due to protein catabolism or to water loss is uncertain. In the light of other evidence obtained from the present cases, the steadiness of the reduction in limb size suggests that some combination of these two processes may be the true explanation. The emphasis changes from protein catabolism and water retention in the first week to water loss in the second week.

CHART X



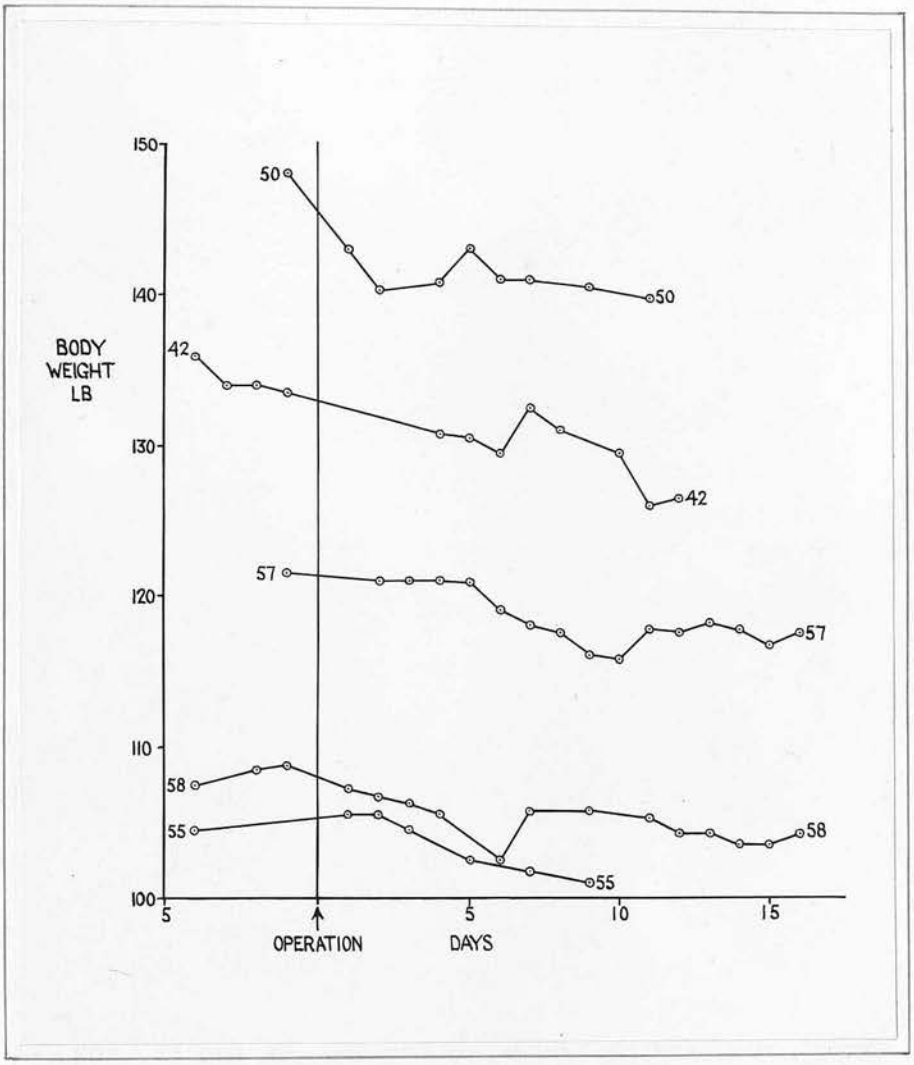
To show the weight lost after operation in two controls (Cases 4 and 6), in one control who was given high protein high calorie diet before starvation (Case 14), and on three patients who before operation were given high protein high calorie diet.

CHART XI



To show the effects of casydrol infusions (indicated by a treble line) on the weights of five patients after partial gastrectomy.

CHART XII



To show the effect on body weight of amigen infusion (Case 42), milk mixture (Case 50), and regulation of sodium and chloride intake (Cases 55, 57, 58) after partial gastrectomy.

CHANGES IN BODY WEIGHT

After operation all the patients lost weight. No relationship could be established in any period between the amount of weight lost and the quantity of nitrogen excretion in the urine or the negative balance of nitrogen. There was a little if any loss of weight in the controls except in Case 14 (Chart X), who gained a little weight before starvation, and, having lost nearly 10 lb. in just over a week, began to regain weight and at the end of the experiment had gained 4 lb. Although in several cases there was a reduction in urinary nitrogen excretion and positive nitrogen balance suggesting anabolism, there was no marked gain in weight. Unfortunately few patients were weighed in the early post-operative period; in Cases 50, 55 and 58 (Chart XII) there was an early fall in weight, while in Case 57 there was no reduction until the sixth day. In the patients to whom casydrol was administered, weight loss appeared to occur at a later period than in other patients who did not receive intravenous infusions over such a prolonged period. In two cases (Nos. 23 and 25, Chart XI), there was evidence of an increase in weight during casydrol infusion, and in Case 44 to whom plasma was given, weight also rose in the first week. There is a similar delay in Case 42 after amigen infusions (Table XII). These increases in weight lend support to the suggestion made elsewhere in this report that there was retention of water after operation; this would tend to be greater after infusions of casydrol or plasma.

It /

It seems possible that the failure to relate nitrogen losses or gains to weight changes may be due to simultaneous changes in the water content of the body, in the first week retention of water, in the second week loss of water. The ultimate severity of the weight loss was not affected by infusions of amigen or casydrol, by a pre-operative high protein high calorie diet or by the intrajejunal administration of milk mixture. The only consistent modification of weight loss occurred when the intake of sodium and chloride was maintained at about the same daily quantity as in Cases 55, 57 and 58. In these three cases, however, an equally good alternative explanation would be that protein catabolism was smaller than usual.

PHYSICAL AND CHEMICAL CHANGES IN THE BLOOD

More or less extensive studies were carried out twice a week on many of the patients submitted to nitrogen balance measurements and also on the patients with jaundice or liver disease. In order to cover as wide a range of estimations as possible, changes were made from time to time in selected groups and any suggestive lead was followed in more detail. In some cases (Nos. 55 and 56), daily estimations were done for a week after operation. In view of the absence of significant variations in most of the analyses carried out, specimen studies only from each group of patients will be presented.

The most consistent changes which were noticed in 15 out of 17 cases were a fall in packed cell volume accompanied in 12 out of 14 cases by reduction in haemoglobin concentration and red blood corpuscle count, which followed sharply on the operation. There was usually also a reduction in plasma albumin and total protein concentrations. A small increase in the plasma globulin concentration offset the reduction in albumin to a varying degree; in some cases it was sufficiently marked to result in an increase in total protein concentration (Case 1). A tendency to reversal of all these changes was evident about the end of the second week after operation.

The three starved controls (Table 64) all showed a slight increase in plasma protein concentration following starvation of both protein and calories.

No significant variation occurred in uric acid or creatinine concentrations. Plasma amino acid nitrogen estimations /

estimations were done both before and after operation in certain of the patients to whom casydrol was administered and in others. Slight increases were noted inconsistently after operation. The non-protein nitrogen and blood urea concentration also sometimes were increased, but no indication was obtained at any time of delay in removal of injected nitrogenous material from the blood. There were occasional changes in other constituents, notably chloride concentration and carbon dioxide combining power, but these were related to disturbance in a particular subject. No general pattern was detected until, applying the method of Legueu et al. (1933), simultaneous whole blood and plasma chloride estimations were done. From these analyses and the packed cell volume, the cell and plasma chloride concentration per 100 ml. blood, and hence the cell plasma chloride ratio, were calculated (Cases 55, 56, 57). There was a marked increase in plasma chloride and reduction in cell chloride following operation, with a drop in the cell plasma ratio. There being no alteration in serum chloride concentration and only a slight change in whole blood chloride concentration, these changes were due to haemodilution with a saline-like fluid.

It was therefore decided to make serial plasma, blood and extracellular fluid volume measurements in conjunction with blood chemical analyses in the hope of following the changes in total circulating albumin and globulin and of pursuing further the changes in chloride and plasma volume. Owing to the difficulties encountered in learning and applying the methods of measurement of plasma and extracellular fluid volume, little progress has been made up to the present with this aspect of the investigation. /

investigation. By withdrawing 15 to 20 ml. of blood at each puncture, no difficulty was encountered in obtaining enough blood for chemical analysis. In order to reduce the amount of interference any patient has to stand, it was thought undesirable in some cases to combine plasma and extracellular fluid volume estimations with nitrogen balance studies. The results of these estimations before and after gastrectomy in three patients (Cases 41, 53, 54) are shown in Table 69.

Case 41 (Table 69).- For case report, see p. 103.

Case 53 (Table 69).- D.W., aged 50 years. Policeman. For some years had had pain in upper abdomen after meals, but had not bothered much about it. During week before admission some increase in pain, then sudden onset of very severe pain 12 hours before admission. Perforation of large duodenal ulcer closed at operation. After operation, transfusion of two pints of whole blood. Stenosis of duodenum with accumulation of gastric contents which required nightly gastric aspiration and lavage. Thirty-five days after closure of perforation, gastro-jejunostomy done to relieve pyloric stenosis. Blood volume estimations four days before and one day after second operation.

Case 54 (Table 69).- N.O'D., aged 26 years. Docker. Four years ago began to have abdominal pain about two hours after meals. Two years ago discharged from Army for psychoneurosis and gastritis. Since then had had many attacks of pain and 11 months ago was treated in another hospital for haematemesis. Three weeks ago for five days he vomited repeatedly, but was eventually relieved by large dose of belladonna. On admission, very fit, thin, muscular young man, tender in upper abdomen. Radiological examination showed large ulcer at middle of lesser curvature of stomach. At laparotomy: partial gastrectomy; gastro-jejunostomy. Intravenous infusion and gastric suction for two days after operation. Superficial phlebitis. Up on 4th day; discharged home on 12th day. Blood volume estimations on day before operation, two days after operation when intravenous infusion was stopped, and on 10th day after operation.

In /

In Case 53 on the day after operation there was reduction in both blood and plasma volume, but an expansion of extracellular fluid volume (or thiocyanate space). Although after operation there was an increase in serum globulin concentration because of the reduction in plasma volume, there was a reduction in the total quantity of globulin in circulation. The increase in thiocyanate space of 2000 ml. is probably significant. In Case 41 after gastrectomy there was a small reduction in blood and plasma volumes, no significant change in thiocyanate space but a reduction in the total quantities in circulation of both albumin and globulin. In Case 54 on the second day after gastrectomy there was a reduction in packed cell volume, plasma volume rose and there was an expansion of thiocyanate space which was probably significant. After operation, in spite of a reduction in the concentration of albumin and globulin, there appeared to be an increase in the total quantities of both in the circulation.

The absence of detectable changes in the concentration of most of the blood constituents is not unexpected and emphasises the possible significance of the alteration in the distribution of chloride and of the dilution of the plasma. There is insufficient evidence regarding the alterations in blood and plasma volume and thiocyanate space and total circulating quantities to justify any conclusions. There is an indication that further study along these lines may be of value.

GENERAL DISCUSSION

Man may indeed be the proper study of mankind, but it must be remembered that man occupies a relatively insignificant place in the universe. It is of the utmost importance that such fundamental disturbances as those which follow injury to the mammalian body, should be viewed in their proper biological and evolutionary perspectives. Many aspects of contemporary human physiology and their essential delicacy and beauty can be understood only in relation to their evolution, and by comparison with similar functions in other animals.

The catabolic destruction of protein, of which Cuthbertson has given so detailed a description, had been observed in both man and animals from very early times. It is essential for survival in a hostile environment. An animal in the natural wild state lives under conditions of a fine biological balance. If such an animal be injured, in addition to its natural enemies it becomes at once vulnerable to other animals from whom it normally would have little to fear. The injured animal is forced to lie up either to die of its injuries or, if these are not mortal and the original physical condition of the animal was sufficiently good, to live on its own resources of carbohydrate, protein and fat until able once more to obtain water and food and to defend itself against enemies. Unless the animal has both the tissues to use and the means of using them, there cannot be a process of wasting for survival. It is natural to expect that man, perhaps the most highly organised form of life, should /

should possess to a marked degree this ability to live endogenously after injury. Since this ability is so necessary for survival in the natural state and has persisted into the present mode of human existence, it is hardly to be expected that such a response to injury will be readily disturbed. It is well known that it is the large, fit, heavily-muscled and well-nourished subjects who suffer the most obvious physical disturbance and loss of weight after even comparatively minor surgical operations and whether they are seriously injured or not. The wasted, ill-fed patients usually show little change, apart, perhaps, from delayed wound healing or other complications, and there is little alteration in their daily metabolic pattern. Objective data derived from the present nitrogen balance studies support these general observations. When, after injury, there is no increase in the urinary nitrogen excretion, this is more likely to be due to a lack of suitable tissue for catabolism than to any impairment of the ability to catabolise protein tissue. The increase in urinary nitrogen excretion shortly before death, the "premortal rise", which is found even in the severely depleted individual, is probably of a different nature to that found after injury in well-nourished subjects.

The undistorted normal response to injury is not often seen in animals because of an artificial and domestic environment, and in man because of various forms of treatment; yet in the initially well-nourished animal during and after illness or injury, regardless of individuality, there is a marked loss of flesh.

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A clear conception of the normal response in the well-nourished subject is essential before correct interpretation of the features observed in starved and depleted subjects is possible. That after injury protein tissue is catabolised seems fairly certain, and it seems probable that the additional nitrogen excreted in the urine during the first six to eight days after injury, is derived from the catabolised protein tissue. The purpose and the means by which this catabolism is brought about are unknown, but it is permissible to speculate in both respects. It is likely that the protein catabolism is closely related to recovery from the injury by which it is initiated, and this seems to be supported by its association with the retention of chloride, sodium and water which has been described.

It is usual to consider the response to injury under the various heads of shock and allied disturbances, inflammation, healing and repair, but this subdivision for the convenience of description tends to be perpetuated in the mind and to condition a sectarian attitude towards the inseparably merged parts of a continuous process. This process is an intricate and dynamic four-dimensional complex of physical, chemical and psychological equilibria of which perhaps only a small portion can be comprehended at any period.

Cuthbertson suggested that the catabolic phase was related to the provision of an endogenous supply of amino acids and protein components required for the process of healing and repair; and has emphasised the relation of protein catabolism to the other aspects of the response to injury. These suggestions receive some support from the results of the tissue culture experiments /

experiments of Fischer (1942, 1947). From a medium of blood plasma and embryonic tissue extract, Fischer dialysed all the amino acids, leaving only inorganic salts and sugar. He then added various combinations of amino acids to the dialysed medium and observed their effects on the growth of various tissue cells. From his results with various mixtures, Fischer suggested that individual tissue cells need other amino acids than does the intact organism which contains the means of synthesising any particular amino acid from an adequate supply of the ten "essential" amino acids; individual cells lack the means of synthesis.

The growth of tissue cells was shown to be affected by the source and nature of certain tissue digests which were added to the dialysed medium. By digestion with pepsin and erepsin, heterologous and homologous digests containing large and small protein components were obtained. In general it was found that with homologous protein, pepsin digests containing large molecular products were best. This, Fischer suggests, was because in the case of homologous protein the large polypeptide chains could be directly used in tissue growth, since it was similar in structure to the cytoplasm being formed, whereas with heterologous protein the smaller molecules are more readily used than the peptide chains which required further breakdown before being incorporated in the new cytoplasm.

In searching for some simple mechanism responsible for maintaining total and relative individual amino acid concentrations in the blood, Fischer was led to the conception of a dynamic equilibrium between plasma and tissue protein and their components. /

components. He suggested that there might be a breakdown of protein in the blood and in the pericellular space, the protein being fixed on the surface of the cell by a process of partial coagulation; in this state the protein was particularly susceptible to the action of proteolytic enzymes. Fischer has shown that fibrinogen may be broken down as far as the amino acid stage by plasma trypsin, and this might be a source of the amino acids which he stated were important for cellular proteolysis in vivo. In this way Fischer believed the plasma proteins themselves might be the regulating mechanism for the blood amino acid concentrations.

It does not seem to be carrying speculation unduly far to suggest that in this work of Fischer may be made the basis for an explanation of the superiority of beef serum in the regeneration of serum albumin, reported by both Whipple et al. (1936) and Weech et al. (1937), and for the differences in the value of various other proteins. It suggests also a possible explanation for the greater urinary wastage of injected peptide than of amino acid nitrogen during and after casein hydrolysate infusion. Differences in wastage between various hydrolysate preparations such as casydrol and amigen may be due to qualitative variations in the products of hydrolysis. The oral ingestion of serum albumin with an adequate caloric intake has been cited already as a highly efficient mode of protein nutrition. On the other hand, the intravenous infusion of plasma protein is followed by three to five days' inertia before urinary nitrogen excretion rises, hence, if the plasma protein is the sole source of protein, there is, because of this inertia, a period of protein starvation. /

starvation. This is presumably because the normal method of dealing with increases of circulating plasma protein is overwhelmed.

Albumin is regarded as the most important plasma protein fraction in the maintenance of a normal fluid equilibrium between the intravascular and extravascular compartments. If the implications of the work of Weech, Whipple and Fischer are accepted, it seems that albumin may also be the key protein fraction in the dynamic equilibrium of protein and its components, whether the equilibrium be that rather static one of "labile", "dispensable" or "fixed tissue" protein described by Whipple, or the rapid interchange on a lower molecular plane which the work of Schoenheimer has made acceptable. Certainly in size and structure the albumin molecule exhibits that suitability for this purpose which is the mark of sound biological design.

Judged in their proper surroundings of the complicated processes of inflammation and repair, the catabolic destruction of protein and the retention of chloride, sodium and of water seem to be provision for the molecular constituents of the four cardinal signs, calor, rubor, tumor and dolor. In the formation of the inflammatory exudate in response to local chemical irritants, a fluid rich in protein, especially albumin, and containing both sodium and chloride, collects in the region affected by the reaction. In this process lies another possible explanation of the changes in albumin and globulin concentrations, that of different rates of loss into the exudate. There may thus be some relationship between the formation of an albuminous /

albuminous exudate and the loss of body protein. The amount of nitrogen lost in the post-operative period is not wholly converted into useful amino acids or plasma protein, and speculation as to its intermediary metabolism is of slight value. The time at which the catabolic destruction of protein is at a maximum is so constant as to appear to be important; its coincidence in time with the onset of growth in the new fibroblasts laid down in the healing tissues during the second day after injury, is remarkable, if these two phenomena are unconnected.

Fibroplasia occurs in healing wounds in rats despite protein depletion (Rhoads et al., 1942; Kobak et al., 1947; Localio, 1948). Kobak et al. showed, however, that the tensile strength of the wounds of normal rats was three times that of the wounds of animals who had been fed on a low protein diet for three months. Subsequently, the tensile strength of the wounds increased in parallel, that of the low protein group lagging behind by two days. This weakness appeared to be due to reduction in the number of fibroblasts, decrease in the rate of their maturation, failure to organise with adequate density along the lines of stress and delay in the development of the reticulum into mature collagen. While it has been said that in man oedema due to low plasma protein concentration may be an important factor in causing weakness or disruption of wounds, it was not apparently present in the protein-depleted rats of Kobak et al. While the adjustment of plasma oncotic pressure by means of gum acacia did not affect the tensile strength of the wounds in these rats, Rhoads et al. have claimed by this means to have prevented the frequent disruption of wounds in plasmapheresed animals. /

animals.

The period when normal growth and development of the fibroblasts are most active, the third to fifth day, is also when nitrogen catabolism is most marked. The work of Fischer, already cited, suggests that normal fibroplasia may depend on an ample supply of particular amino acids and that in protein depletion delay may be due to an inadequate supply of some or all of these amino acids. Fischer's work also showed that while large molecules of homologous origin were well used, in the case of heterologous protein only small molecules were readily utilised. It may be that here is the crux of the problem of protein metabolism during the catabolic phase. The heterologous protein of intravenously administered casein hydrolysates is less readily used in tissue synthesis than is homologous protein, and therefore may remain for a longer period in circulation and reach a higher concentration in the blood stream and so be more liable to excretion in an unchanged state by the kidney; moreover within the limits of molecular size in casein hydrolysates the larger the molecule the more likely is it to be excreted in the urine. Casein, albumin or any other protein administered by mouth is probably broken down to a greater degree than the hydrolysate given by infusion and so may be more useful to the body, certainly less of it is wasted. It would be reasonable to expect then that the provision of an adequate oral intake of calories and protein to a well-nourished subject throughout the post-operative period would prevent the catabolic destruction. That this does not happen suggests that in the early stages the process of repair requires endogenous as well as /

as homologous protein components. This explanation is not entirely satisfactory and is not improved by the assumption that the portions of the protein molecules not utilised in tissue synthesis may be deaminated and may thereafter be used in part to aid the utilisation of fat for energy production.

By a biological method, Browne et al. (1942) demonstrated the presence of "cortin"-like substances in the urine of normal male subjects. They found there was an increased excretion of this substance after accidental injuries and surgical operations, in acute osteomyelitis, Cushing's syndrome and lobar pneumonia. There was some relation between the time and quantity excreted of this cortin-like substance and of nitrogen after operations: there was a rise in the first 24 hours, a maximum was reached on the fourth to sixth day, following which there was a decline. They suggested this cortin-like material was of a corticosterone type and possibly had some action on carbohydrate metabolism. The ketosteroid substances excreted in the urine bore no constant relationship to nitrogen excretion, although they might be present in the urine in increased quantities for up to 48 hours after injury.

That the increase in urinary corticosteroids was not the cause of the increased nitrogen excretion was suggested by Schenker and Stevenson (1943) who, by injecting pituitary corticotrophic hormone into normal subjects, produced an increase in urinary corticosteroid excretion without any increase in nitrogen excretion. The retention of chloride and of sodium after injury may be related to the increased output of corticosteroid and the retention of water is perhaps secondary

to /

to the retention of these electrolytes. The retention of chloride observed in certain cases of the present series in the absence of an increase in nitrogen excretion would not then agree, however, with the observation of Schenker and Stevenson that corticosteroid output also is reduced after injury in debilitated subjects.

In a number of the cases of the present series a reduction in urinary chloride excretion was observed one or two days before operation. This might be explained by reduction of food consumption and thus of salt intake, and this possibility cannot be excluded on the present data. The effects of anxiety and apprehension on the patients during the day or so immediately before an operation, such as gastrectomy, have not so far been investigated. It was considered to be unjustifiable to submit an already worried patient to the additional ordeal of postponement of the appointed operation, followed by an unexpected operation, in order to test the hypothesis that the reduction in urinary chloride excretion might be related to apprehension. An unplanned opportunity has been awaited in vain.

An attempt to apply directly Cuthbertson's hypothesis that there may be specific amino acid requirements after injury, was made by Croft and Peters (1945). They believed that after burns there might be a special need for methionine and that the provision of abundant methionine might reduce protein catabolism. That this was not the case does not invalidate Cuthbertson's hypothesis, and while direct support for it is lacking, there is perhaps some indirect support from the results of tissue culture experiments.

There /

There is no evidence that the post-operative protein catabolism is harmful, but its apparent wastefulness is puzzling. The failure to abolish or even to affect significantly the true catabolic increase in urinary nitrogen excretion should not occasion dismay butshould rather be regarded as a reassuring sign of the persistence of a fundamental and apparently beneficial process. This is not to excuse the inadequate feeding of the patient after operation or to condone arbitrary restriction of intake in the face of appetite and inclination.

Lusk's (1921) review of the physiological effects of undernutrition tempts one to speculate on how much effect the relative starvation, especially of protein, in the post-operative period has on the ability, as well as on the desire, of the patient to get well. The loss of "drive" and enthusiasm in the chronically starved man is an outstanding feature in the personal accounts of physiologists who have submitted themselves to long periods of deprivation of food and especially of protein, and in the history of the German industries during the Great War. The depressing effect of dietetic limitation after gastrectomy was repeatedly observed in the patients studied in the present investigation. This is all the more important in that in their new freedom from pain resulting from gastrectomy, they were eager to eat and to get well. Conversely, when the type of food consumed is conditioned by peptic ulcer pain, inability to afford sufficient calories and protein to do a full day's work is an indication, on economic grounds, for some form of gastrectomy.

"The /

"The nitrogen excreted in the urine may be regarded as part of the metabolic pool originating from the interaction of dietary nitrogen with the relatively large quantities of reactive body nitrogen" (Schoenheimer and Rittenburg, 1940). Unfortunately in man this metabolic sample is unlabelled and of unknown origin. The urinary nitrogen, none the less, has also been regarded as a quantitative index of the plane of protein metabolism and as such has been used in the present report as the basis of criticism of previously reported studies in protein metabolism, before and after surgical operations. It may be thought that criticism has been unduly adverse, but it is evident that most of the American groups of investigators have made their observations on patients suffering from the effects of severe and prolonged mal-nutrition. In the present investigation average patients were studied largely because only rarely was an ill-nourished man encountered. There is no justification for such enthusiastic administration of casein hydrolysate solution, in the attempt to achieve positive nitrogen balance, that the urea-ammonia mechanism is overwhelmed; nor does it seem reasonable to employ these protein derivatives in circumstances where, for lack of a contemporary supply of calories, much of the nitrogenous material will be deaminated and used to provide energy.

The supply of an adequate daily quota of calories in the form of 5 per cent. glucose solution seems to be the main limiting factor in the employment of protein hydrolysates in a temperate climate. The provision of a daily basal requirement of 1600 calories as 5 per cent. glucose solution requires the administration of 400 g. glucose contained in 8 litres of solution. /

solution. The generally accepted safe maximum volume for repeated daily intravenous administration is 2.5 litres or about 5 pints; this quantity of 5 per cent. glucose solution contains 125 g. glucose, equivalent to 500 calories. Because of chemical phlebitis and thrombosis of superficial veins, there is a limit to the duration of even isotonic glucose infusions which is more rapidly reached in some individuals than others and with hypertonic solutions. The clinical use of fat emulsions as a source of calories is not yet feasible.

Evidence has been cited which suggests that the human body deals differently with glucose solution and with saline when these are infused intravenously into the normal subject. There is other evidence which suggests that the treatment of these solutions is again different when they are infused after operations, and that there is marked retention of water and of sodium and chloride which is related in degree to the severity of the operation injury.

The present observations suggest that some re-examination of currently accepted methods of judging the body requirements for sodium chloride is desirable. For example, Marriott (1947) advised that in salt depletion treatment should aim at restoring a urinary chloride concentration of 3 to 5 g. per litre (expressed as g. sodium chloride), and an output of 570 ml. urine in each eight-hourly period. This may be satisfactory in patients who have not been recently subjected to a surgical operation, but in such subjects attempts to achieve a concentration of 3 to 5 g. per litre of urine is complicated by alterations in renal function and is unsafe. That such methods have /

have been widely employed with apparent success seems to be due to the admirable powers of adjustment of the healthy human kidney rather than to the soundness of the premises. There seems to be little doubt that large quantities of water may be retained in the body after unduly large infusions of plasma, 0.9 per cent. saline or even 5 per cent. glucose solution, especially after injury. Appreciation of this is important since, after major operations, there appears to be some profound alteration in renal function. The kidney is the primary regulating mechanism of the body content of water and electrolytes. Recent studies of the minute anatomy of the human kidney, and especially of the vascular arrangements, suggest that there are two distinct types of glomerulo-tubular units with widely differing functions and perhaps different times of activity. Further advances in understanding of the metabolic disturbances immediately after injury to man must to some extent wait for more knowledge of the secretions and mode of action of the two types of nephric unit. Since there are probably important species differences, this knowledge must in some way eventually be obtained from the human kidney.

SUMMARY AND CONCLUSIONS

(1) An investigation has been undertaken of certain post-operative metabolic disturbances in 59 surgical patients, and in 41 of these cases nitrogen balance studies were carried out. Control observations were also made on four healthy volunteers submitted to two types of food restriction, and on one patient who was not subjected to operation.

(2) It was found that after gastrectomy in well-nourished subjects there was an increase in urinary nitrogen excretion which lasted for from five to eight days, the maximum loss of nitrogen being on the second to fifth days. During the same period the reduction in food intake combined with this increased excretion of nitrogen resulted in a period of negative nitrogen balance. Extension of the duration of this period of negative nitrogen balance beyond the minimum was related to protein and caloric intake or to complications, such as wound infection, broncho-pneumonia or superficial phlebitis.

(3) In mal-nourished subjects there may be no post-operative increase in urinary nitrogen excretion, or this may be much less severe than in well-nourished subjects.

(4) The consumption of a high protein high calorie diet before operation has a variable effect on body weight: it is not related in any consistent manner to nitrogen retention, and does not alter the response to operation in any significant way in well-nourished /

well-nourished subjects. The catabolic phase is in no way diminished. An increase in the intake of calories after operation may accelerate the restoration of nitrogen equilibrium or positive balance. An increase in the protein intake without a proportionate increase in calories may lead to wastage of the protein. There is a physical limit to the quantity of food which may be eaten after gastrectomy, but this is much in excess of the diet which is usually provided.

(5) The oral consumption of protein hydrolysate (such as pronutrin) was employed to increase the quantity of protein ingested. In the form at present available, such hydrolysates offer a compact means of administering protein if the patient can tolerate the smell and taste of the preparation.

(6) Protein hydrolysates in the form of casydrol or amigen were administered by the intravenous route to 22 patients. In five of these detailed studies of the quantities of total nitrogen and the amino acid nitrogen excreted in the urine were made. The urinary amino acid nitrogen excretions during and after casydrol infusions were compared with those found in a control series of patients submitted to gastrectomy, and in a series of volunteers. About 60 per cent. of the amino acid nitrogen administered by the intravenous route as casydrol, and about 90 per cent. in the case of amigen, was apparently retained in the body for metabolism. After gastrectomy, well-nourished subjects to whom casydrol or amigen was given by the intravenous route, excreted in addition to the increased quantity of nitrogen normally expected from protein catabolism, an amount of nitrogen about /

about equal to that administered as hydrolysate. In the remaining patients, no apparent benefit was obtained by the infusion of casydrol, except in one who was suffering from the effects of prolonged restriction of food consumption. Provided that a rate of 100 to 150 ml. per hour is not exceeded, casydrol does not cause nausea or other disturbances when administered by the intravenous route, and thrombosis and phlebitis are not more frequent than with 5 per cent. glucose solution alone. The few indications for the use of casydrol by the intravenous route which still appear to be justifiable on theoretical grounds, such as prolonged starvation or ulcerative colitis, require further examination by clinical trial.

(7) Human plasma was administered to two patients as the sole source of protein. This method of supplying protein is condemned as unsound in conception and unsafe in practice.

(8) After partial gastrectomy, the prevention of starvation throughout the post-operative period was achieved in three out of six patients in whom it was attempted by the administration of adequate quantities of protein and calories as milk mixture by jejunal tube or by mouth. There was still an increase in urinary nitrogen excretion, that is to say, the catabolic phase was not abolished. The negative nitrogen balance over the period of ten days after operation was, however, greatly reduced, being smaller than after any other procedure.

(9) After partial gastrectomy there is usually some degree of haemodilution and increase in plasma volume indicated directly by measurement, and indirectly by reduction in haematocrit /

haematocrit red blood corpuscles and haemoglobin concentration. There is often a reduction in plasma albumin concentration and a rise in plasma globulin concentration which may equal or exceed the change of albumin concentration. There are other and probably more important changes in the total quantities of these proteins in active circulation in the plasma. There is a contemporary shift of chloride from red blood corpuscles to plasma. There was no consistent change in plasma amino acid nitrogen, non-protein nitrogen or blood urea nitrogen concentrations even during or after hydrolysate infusions.

(10) The observation of a reduction in urinary chloride excretion during the first six to eight days after major surgical operations led to further investigation and to a demonstration of a coincidence of reduction in urinary chloride excretion with the increased nitrogen excretion of the catabolic phase. Further investigation has revealed that following operation there is a retention in the body of chloride, sodium and water which is largely independent of the source or quantity of sodium and chloride, or the route by which they are made available.

(11) There is no relationship between weight loss and nitrogen balance; this is probably due to changes in water and electrolyte balance masking the effects of nitrogen retention on loss of weight. After operation there appears to be a steady loss of body tissue which also for several days may be masked to some extent by water retention.

(12) The possible clinical applications of these observations have been discussed and further hopeful lines of extension have been suggested.

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TABLE 1 (CASE 1)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance		Body weight
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Dec. 2	104	115	284	2587	16.64	940	14.06	1.98		16.04	0.6		157.5
3	104	115	284	2587	16.64	980	14.03	0.79		14.82	1.82		
4	107	115	295	1643	17.12	1650	13.8	0.3	lost	14.1	3.02		158.75
5*						660	5.48		3.92	9.40		9.40	
6						1100	18.26	nil	2.37	20.63		20.63	
7	18	17	48	417	2.88	500	11.18	nil	1.52	12.7		9.82	
8	19	18	49	434	3.04	890	23.7	nil		23.7		20.66	
9	33	38	86	818	5.28	1230	30.46	nil		30.46		25.18	
10	43	44	82	896	6.87	1090	17.96	nil		17.96		11.09	
11	65	70	165	1550	10.48	970	15.66	4.4		20.06		9.58	
12	87	93	209	2021	12.15	670	9.36	nil		9.36	2.79		
13	87	93	209	2021	12.56	885	10.5	2.22		12.72		0.16	
14	77	86	228	1994	12.32	320	4.94	2.16					
15	77	108	260	1994	10.0	1190	10.41	1.4		11.81		1.81	
16	102	108	260	2420	16.32	845	4.9	1.92		6.82	9.5		
17	102	108	260	2420	16.32	650	7.78	0.68		8.46	7.76		151.4
18	102	108	260	2420	16.32	lost							
19	102	108	260	2420	16.32	1130	11.82	0.94		12.76	3.56		153.0

*Operation. N content of 930 ml. transfused blood, 17.78 g.; lost blood, 16.6 g.; resected stomach, 1.98 g.

TABLE 2 (CASE 2)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance		Body weight lb.	Urine chloride as g.NaCl
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.		
Mar. 27	92	97	201	2045	14.72	1030	9.54	0.95		10.5	4.22		113.0	7.91
28	75	83	226	1951	12.0	910	10.42	2.93		13.35		1.35	112.6	5.79
29	75	83	226	1951	12.0	1090	12.17	nil		12.17		0.17	113.0	5.12
30	65	72	186	1652	10.4	790	11.98	2.35		14.33		3.93	113.6	4.06
31	62	70	158	1510	9.92	940	8.62	1.12		9.74	0.18		113.3	5.51
Apr. 1	65	72	181	1632	10.4	1510	7.65	nil		7.65	2.75		112.8	6.49
2	75	83	226	1951	12.0	1940	8.54	lost	1.08	9.62	3.38		113.25	6.68
3*						220	2.25	nil	0.11	2.36		2.36		4.57
4			72	288		1780	17.02	nil	0.835	17.86		17.86		5.41
5			24	96		550	8.03	nil	0.108	8.14		8.14		1.53
6	2	2.4	23	112	0.32	900	12.64	nil		12.64		12.32		1.296
7	27	32	41	520	4.32	810	12.01	nil		12.01		7.69		2.72
8	11	13	19	247	1.76	950	12.77	nil		12.77		10.51	112.0	6.13
9	67	80	200	1788	10.72	1200	11.31	nil		11.31		0.59	112.0	8.16
10	67	80	208	1820	10.72	1470	9.35	nil		9.35	1.37		111.9	7.79
11	67	82	208	1820	10.72	1480	8.62	6.36		14.98		4.26	111.8	
12	67	82	200	1806	10.72	1610	5.44	nil		5.44	5.28		111.25	
13	67	82	200	1806	10.72	840	6.47	3.78		10.25	0.47		110.75	
14	67	82	208	1806	10.72	1540	10.32	nil		10.32	0.40		110.0	

*Operation. N content of 1000 ml. blood transfused, 26.0 g.; blood lost, 25.04 g.; resected stomach, 5.41 g.

TABLE 3 (CASE 3)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance		Body weight lb.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Jan. 7	79	84	259	2108	12.64	1850	12.5			12.5	0.14		112.25
8	79	84	259	2108	12.37	960	8.68	2.7	2.32	13.71		1.33	
9*						660	6.89		3.02	9.91		9.91	
10	16	19	24	331	2.56	900	13.00	nil	4.36	17.36		14.8	
11	22	21	70	557	3.52	700	12.63	nil		12.63		9.11	
12	23	23	66	563	3.68	530	11.82	lost		11.82		8.14	
13	36	42	93	594	5.75	680	16.19	nil		16.19		10.44	
14	44	41	86	885	7.04	675	14.97	1.65		16.62		9.58	
15	60	74	195	1685	9.6	530	12.45	3.42		15.87		6.27	
16	60	74	195	1685	9.6	640	12.37	1.06		13.43		3.83	
17	60	74	195	1685	9.6	856	13.42	0.48		13.9		4.3	
18	60	74	195	1685	9.6	1040	13.23	0.99		14.22		4.62	
19	60	74	195	1685	9.6	900	11.4	2.74		14.14		4.54	
20	79	79	238	1979	12.64	1270	10.89	1.57		12.46	0.18		
21	86	84	266	2164	13.78	1710	13.9	2.8		16.7		2.92	
22	85	84	250	2096	13.6	1515	14.73	1.37		16.1		2.5	103.25
23	86	84	266	2164	12.43	830	8.12	2.2		10.32	2.11		
24	86	84	266	2164	13.78	880	10.71	0.7		11.41	2.37		

*Operation. N content of 785 ml transfused blood, 20.15 g.; lost blood, 9.66 g.; resected stomach, 4.25 g.

TABLE 4 (CASE 4)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance		Body weight lb.	Body temp. °F.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.		
Jan. 13						940	11.6			11.6			110.75	
14	81	97	292	2385	12.95	1140	11.12	1.09		12.21	0.74			
15	81	97	292	2385	12.95	880	9.13	0.62		9.75	3.2			
16	81	97	292	2385	12.95	1510	8.49	1.24	0.35	10.8	2.15		112.0	
17*					nil	1170	5.05		1.07	6.12		6.12		99.4
18	10	11	194	891	1.6	880	10.17	nil	2.36	12.53		10.9		100.0
19	12	13	90	525	4.92	790	8.97	nil	1.24	10.21		8.29		100.0
20	30	35	67	703	4.8	1270	12.36	nil		12.36		7.56		101.4
21	40				6.4	610	11.35	4.87		16.22		10.0		100.2
22	46	55	137	1317	7.41	870	9.5	2.58		12.08		4.67	105.0	99.4
23	67	61	135	1357	10.8	710	7.3	0.68		7.98	2.83			
24	67	69	178	1581	10.8	780	9.61	0.76		10.37	0.43			
25	62	64	171	1508	9.93	730	10.19	1.66		11.85		1.92		
26	62	64	178	1536	9.93	1470	12.25	nil		12.25		2.32		
27	64	65	194	1617	10.25	1290	10.0	1.04		11.04		0.79	102.6	
28	75	83	238	2000	12.0	1450	11.13	3.3		14.43		2.43		
29	75	83	238	2000	12.0	1310	10.3	nil		10.3	1.7			
30	75	83	238	2000	12.0	1060	8.51	nil		8.51	3.49		101.75	

*Operation. N content of 730 ml. transfused blood, 24.31 g.; lost blood, 6.94 g.; resected stomach, 2.14 g.

TABLE 5 (CASE 5)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl
Nov. 27	90	100	310	2500	14.4	1030	10.72	1.40	12.12	2.28		10.16
28	90	100	310	2500	14.4	1440	15.02	2.16	17.18		2.78	13.91
29	90	100	310	2500	14.4	1340	12.06	0.79	12.85	1.55		10.72
30	90	100	310	2500	14.4	1420	13.4	0.42	13.84	0.64		11.84
Dec. 1	90	100	310	2500	14.4	800	10.28	1.64	11.92	2.48		7.16
2	90	100	310	2500	14.4	750	11.8	nil	11.8	2.60		6.82
3	90	100	310	2500	14.4	1025	15.35	0.86	16.21		1.81	8.35
4	90	100	310	2500	14.4	630	9.12	3.60	12.72	1.68		7.1
5*						1320	12.36	nil	16.44		16.44	13.65
6						530	13.8	nil	13.8		13.8	5.25
7						690	8.25	nil	8.25		8.25	2.34
8	15	18	24	318	2.4	860	18.50	nil	18.50		16.1	1.41
9	7.5	10	15	180	1.2	610	14.68	nil	14.68		13.48	1.0
10	16	18.5	26.5	335	2.56	660	15.58	nil	15.58		13.02	0.71
11	15	18	22.5	312	2.4	670	10.7	1.06	11.76		9.36	1.3
12	12	14	19	250	1.92	600	13.85	0.66	14.51		12.59	1.51
13	8	10	12	170	1.28	520	9.84	0.68	10.52		9.34	2.46
14	20	24.5	31	424	3.2	790	12.90	1.10	14.0		10.8	6.33
15	20	20	21	344	3.2	660	9.42	0.64	10.06		6.86	3.23
16	27.5	23.5	49	517	4.4	525	6.97	1.30	8.27		3.87	5.0

*Operation. N content of blood lost, 4.08 g.

TABLE 6 (CASE 6)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance				
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	Body weight lb.	Urine chloride as g.NaCl	Plasma amino acid N as mg. %
Apr. 17	91	114	288	2542	14.56	1100	11.31	0.91	12.22	2.34		140.75	10.38	5.3
18	91	114	288	2542	14.56	740	8.4	0.33	8.73	5.83		140.12	6.42	
19	91	109	288	2497	14.56	2320	20.26	1.5	10.37	4.19		139.8	16.0	
20	91	114	288	2542	14.56				10.37	4.19				
21	91	114	288	2542	14.56	785	13.53	nil	13.53	1.03		140.0	8.41	4.9
22	91	114	288	2542	14.56	790	13.48	nil	13.48	1.08		140.25	7.54	
23	91	114	288	2542	14.56	1350	12.07	1.05	13.12	2.44		140.0	10.4	4.7
24	91	114	288	2542	14.56	880	10.46	lost	10.46	4.10			7.94	
25	91	114	288	2542	14.56	405	6.55	nil	6.55	8.0		140.0	2.77	
26*	3	2	89	386	0.48	790	19.9	nil	9.95		9.47		1.14	
27	6	2	91	406	0.96				9.95		8.99			4.1
28	11	7	89	463	1.76	400	9.496	nil	9.50		7.74		0.352	
29	35	33	158	1069	5.6	390	8.15	1.78	9.83		4.23		0.344	
30	52	64	220	1662	8.22	615	8.12	0.48	8.60		0.38		4.67	
May 1	59	66	233	1762	9.44	680	7.94	nil	7.94	1.5			6.46	4.5
2	61	60	221	1668	9.76	1070	11.2	0.84	12.04		2.28	134.25	9.18	
3	72	73	209	1781	11.52	1160	7.2	nil	7.2	5.32			9.28	
4	77	74	206	1798	12.32	1350	11.12	1.92	13.54		1.22	134.25	10.5	
5	89	111	275	2455	14.22	1230	12.73	lost	12.73	1.49		134.0	9.18	5.2
6	91	114	288	2542	14.56	925	11.64	0.46	12.1	2.46		134.12	6.36	
7	91	119	288	2641	14.56	660	7.06	0.52	7.58	6.98		134.25	4.29	4.9

*Operation

TABLE 7 (CASE 7)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance			
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl	Urine amino acid N as mg. %
Sept. 22	90	106	303	2500	14.4	1670	12.84	0.54	13.34	1.06			
23	90	106	303	2500	14.4	1460	12.90	1.07	13.97	0.43		10.66	0.42
24	90	106	303	2500	14.4	1560	11.91	0.6	12.51	1.89		10.59	0.26
25	90	106	303	2500	14.4	1300	13.4	1.66	15.06		0.66		0.47
26	90	106	303	2500	14.4	1630	14.85	0.16	15.01		0.61	10.26	0.41
27	90	106	303	2500	14.4	1400	14.28	0.96	15.24		0.84	8.96	0.36
28	90	106	303	2500	14.4	1700	14.43	nil	14.33	0.1		10.20	0.39
29	90	106	303	2500	14.4	1600	10.69	1.04	11.73	2.67		11.29	0.25
30*						400	1.32	nil	1.32		1.32	1.07	
Oct. 1	9	6	120	570	1.44	1130	16.32	nil	16.32		14.88	2.73	0.28
2	9	6	120	570	1.44	800	15.3	lost	15.3		13.86	1.22	0.26
3	9	6	120	570	1.44	700	13.5	nil	13.5		12.06	0.91	0.38
4	19	6	87	478	3.04	790	12.94	nil	12.94		9.9	1.14	0.21
5	30	19	132	819	4.8	720	11.38	0.49	11.87		6.93	0.93	0.18
6	40	24	131	900	6.4	900	11.94	nil	11.94		5.54	1.08	0.20
7	60	50	263	1502	9.6	1095	13.68	3.77	17.45		7.85	2.60	0.21
8	90	106	303	2500	14.4	1790	17.4	nil	17.4		3.0	9.42	0.35
9	90	106	303	2500	14.4	1320	13.28	2.58	15.86		1.46	9.75	0.32
10	85	106	303	2480	13.6	1860	16.72	1.09	17.81		4.21	12.7	0.32
11	90	106	303	2500	14.4	1000	9.56	nil	9.56	4.84		7.44	0.20
12	89	101	296	2433	14.24	1400	13.25	4.58	17.83		3.59	8.54	0.28
13	90	106	303	2500	14.4	1240	11.8	1.06	12.86	1.94		6.9	0.24
14*	Died												

*Operation

TABLE 8 (CASE 8)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl
May 5	87	86	213	1974	13.92	1670	16.31	nil	16.31		2.39	11.56
6	90	88	218	2024	14.4	910	12.08	0.74	12.82	1.58		4.53
7	83	84	218	1960	13.28	760	10.88	nil	10.88	2.4		4.44
8	83	84	218	1960	13.28	1120	8.15	2.54	10.69	2.59		6.79
9	83	84	218	1960	13.28	920	8.25	nil	8.25	5.03		6.77
10	83	84	218	1960	13.28	930	10.8	2.08	12.88	0.4		7.05
11*	21	22	81	606	3.46	640	3.1		3.3	0.16		2.64
12	9	11	48	326	1.44	1060	18.85	nil	9.43		7.99	1.59
13	9	11	48	326	1.44				9.43		7.99	
14	10	14	69	442	1.6	440	11.02	nil	11.02		9.42	0.07
15	26	32	93	764	2.56	370	8.9	2.84	11.74		9.18	0.067
16	51	58	167	1397	8.16	880	19.92	nil	19.92		11.76	0.903
17	68	62	175	1530	10.88	570	11.5	nil	11.5		0.62	1.39
18	81	78	205	1846	12.96	810	13.86	2.04	15.92		2.96	4.08
19	78	80	206	1856	12.48	1110	16.26	nil	16.28		3.80	6.48
20	71	65	196	1653	11.36	920	13.34	nil	13.34		1.98	4.69
21	82	84	213	1936	13.12	950	14.87	1.9	16.77		3.65	4.9
22	83	84	218	1960	13.28	970	15.9	nil	15.9		2.62	4.31
23	81	80	205	1864	12.96	1030	13.1	1.65	14.75		1.79	6.36
24	83	72	206	1804	13.28	1130	12.78	nil	12.78	0.5		6.44
25	81	80	208	1876	12.96	1330	14.5	nil	14.5		1.54	7.82
26	81	80	208	1876	12.96	1240	11.58	2.46	14.04		1.08	6.86
27	81	75	207	1827	12.96	980	12.35	nil	12.35	0.61		7.63
28	81	75	207	1827	12.96	2740	24.85	nil	12.42	0.54		15.38
29	83	84	209	1929	13.28			nil	12.43	0.85		
30	82	82	216	1930	13.12	910	12.82	0.6	13.42		0.3	6.25
31	82	84	218	1960	13.12	880	10.79	0.8	11.59	1.53		6.04

*Operation.

TABLE 9 (CASE 9)

Control: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl
May 9	91	107	174	2019	14.4	510	6.88	2.0	8.88	5.52		4.79
10	34	51	87	955	4.22	615	10.23	nil	10.23		6.01	5.0
11	24	40	56	680	3.84	450	8.08	nil	8.08		5.24	1.48
12	82	86	135	1642	13.12	440	10.2	1.18	11.38	1.74		1.34
13	62	76	154	1548	9.92	780	11.32	0.1	11.42		1.5	5.32
14	89	111	191	2119	14.24	700	9.83	0.82	10.65	3.59		5.95
15	76	99	162	1843	12.16	670	9.62	nil	9.62	2.54		5.39
16	69	97	154	1765	11.04	290	4.34	2.02	6.36	4.68		2.03
17	64	93	156	1717	10.24	710	8.4	nil	8.4	1.84		6.04
18	56	82	152	1570	8.96	740	7.13	2.87	10.0		1.04	6.31
19*	13	19	96	607	2.58	700	4.9	nil	4.9		1.32	2.86
20	8	15	35	307	1.28	420	6.53	nil	6.53		5.25	2.41
21	24	20	84	612	3.84	385	6.56	nil	6.56		2.72	0.82
22	38	51	97	1000	6.14	230	4.22	nil	4.22	1.88		0.24
23	55	66	152	1422	8.8	810	lost	0.82				0.07
24	70	71	166	1584	11.2	980	11.6	nil	11.6		0.4	3.0
25	70	86	185	1794	11.2	750	10.1	nil	10.1	1.1		3.02
26	89	94	185	1942	14.22	470	5.74	nil	5.74	8.48		2.59
27	66	80	151	1588	11.56	1220	18.1	nil	18.1		6.54	7.72
28	49	78	194	1674	7.84	610	9.15	1.54	10.69		2.85	3.6
29	64	83	198	1715	10.24	810	11.82	nil	11.82		1.58	4.8
30	52	75	198	1675	8.42	1600	9.50	1.9	11.4		2.98	4.36
31	64	83	198	1795	10.24	)1490	)15.42	nil	7.71	2.53		)11.71
June 1	64	83	186	1747	10.24	)	)	3.76	11.48		1.24	}
2	63	82	198	1782	10.08	650	6.79	nil	6.79	3.29		4.92
3	63	82	198	1782	10.08	740	7.55	nil	7.55	2.53		5.71
4	63	82	188	1742	10.08	720	8.2	nil	8.2	1.88		
5	61	85	203	1821	9.7	590	6.2	nil	6.2	3.5		

*Operation. N content of 950 ml. blood transfused, 26.56 g.; blood lost, 15.32 g.

TABLE 10 (CASE 10)

Control Starvation: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		Body weight lb.	Urine chloride as g.NaCl	Urine amino acid N as mg. %
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.			
Aug. 29	91	90	332	2502	14.56	1230	18.61	nil	18.61		4.05		12.7	0.90
30	91	90	332	2502	14.56	2920	27.3	nil	13.65	0.91			12.5	0.46
31	91	90	332	2502	14.56			2.02	15.67		1.11		12.5	0.46
Sept. 1	91	90	332	2502	14.56	1200	14.3	nil	14.3	0.26			10.92	lost
2	91	90	332	2502	14.56	980	16.7	2.19	18.89		4.36		15.5	0.31
3	91	90	332	2502	14.56	2295	15.08	nil	15.08		0.52		14.52	0.30
4*	10	4	126	580	1.6	1070	8.12	nil	8.12		6.52	158.0	4.1	0.14
5	10	4	126	580	1.6	650	9.4	nil	9.4		7.8	154.75	3.44	0.45
6	10	4	126	580	1.6	1110	12.4	nil	12.4		10.8	153.5	4.06	0.65
7	20	4	116	580	2.4	1350	10.0	2.58	12.58		9.38	155.5	5.8	0.58
8	30	13	142	805	4.8	1960	12.83	3.08	15.91		11.11	156.3	8.9	0.75
9	40	25	130	905	6.4	1270	11.42	nil	11.42		5.02	156.6	5.53	0.34
10	60	49	206	1505	9.6	1565	12.3	nil	12.3		2.7	156.4	8.55	0.47
11	91	90	332	2502	14.56	1390	13.18	nil	13.18	1.38		156.6	9.58	0.69
12	91	90	332	2502	14.56	1330	?16.38	nil	10.38	3.12		157.0	6.76	0.47
13	91	90	332	2502	14.56	2180	17.0	3.78	20.78		6.22	156.0	17.4	0.93
14	73	76	332	2304	11.66	1300	13.26	nil	13.26		1.6		10.0	
15	91	90	332	2502	14.56	880	9.68	2.18	11.86	2.7			7.35	0.26
16	91	90	332	2502	14.56	1620	14.45	nil	14.45	0.11		154.5	11.6	0.54
17	91	90	332	2502	14.56	1350	10.96	2.69	13.65	1.09		155.2	10.78	0.3
18	91	90	332	2502	14.56	1620	18.04	nil	18.04		3.43		8.80	0.82

*Day of imaginary operation

TABLE 11 (CASE 10)

Control Starvation, Calories Maintained: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		Body weight lb.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	
Mar. 14	90	91	331	2503	14.4	2460	21.23	nil	21.23		6.83	
15	90	91	331	2503	14.4	2090	17.83	nil	17.83		3.43	
16	90	91	331	2503	14.4	2625	18.8	nil	18.8		4.4	169.3
17	90	91	331	2503	14.4	1370	10.34	3.78	14.12	0.28		167.8
18	90	99	320	2531	14.4	1460	16.47	nil	16.47		2.07	167.75
19	10	29	550	2501	1.6	2340	11.55	nil	11.55		9.95	165.1
20	10	29	550	2501	1.6	2520	8.39	nil	8.39		6.79	165.3
21	10	29	550	2501	1.6	1120	5.07	nil	5.07		3.47	165.4
22	20	45	504	2501	3.2	1120	5.39	4.56	9.95		6.75	165.7
23	30	56	469	2500	4.8	1590	5.92	0.86	6.78		1.98	165.75
24	40	93	376	2501	6.4	1050	7.68	nil	7.68		1.28	164.2
25	60	92	358	2500	9.6	1160	9.28	0.8	10.08		0.48	163.6
26	90	93	326	2501	14.4	1740	10.85	nil	10.85	3.55		163.8
27	90	93	326	2501	14.4	1460	11.25	nil	11.25	3.15		164.12
28	90	93	326	2501	14.4	1130	14.4	2.2	16.4		2.0	164.3
29	90	93	326	2501	14.4	1960		nil				164.25
30	90	93	326	2501	14.4	2060	12.61	2.02	14.63		0.23	164.3
31	90	93	326	2501	14.4	1730	16.88	nil	16.88		2.48	163.8
Apr. 1	90	93	326	2501	14.4	2415	13.52	2.08	15.6		1.2	163.2

TABLE 12 (CASE 11)

Control Starvation: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance				
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	Body weight lb.	Urine chloride as g.NaCl	Urine amino acid N as mg. %
Aug. 29	91	90	332	2502	14.56	740	12.1	nil	12.1	2.46			9.26	0.53
30	91	90	332	2502	14.56	2740	29.4	nil	14.7		0.14		8.72	0.75
31	91	90	332	2502	14.56			1.58	16.28		1.72		8.72	0.75
Sept. 1	91	90	332	2502	14.56	1630	14.48	nil	14.48	0.08			9.9	lost
2	91	90	332	2502	14.56	1040	15.32	2.31	17.63		3.07		10.5	0.78
3	91	90	332	2502	14.56	1230	15.08	nil	15.08		0.52		9.8	0.82
4*	10	4	126	580	1.6	2230	12.9	nil	12.9		11.3	149.2	12.2	0.36
5	10	4	126	580	1.6	635	9.45	nil	9.45		7.85	148.2	4.48	0.66
6	10	4	126	580	1.6	960	10.72	nil	10.72		9.12	147.8	4.26	0.53
7	20	4	116	580	3.2	1360	9.75	4.74	14.49		11.29	147.6	6.16	0.44
8	30	13	142	805	4.8	650	10.51	nil	10.51		5.71	147.3	4.22	0.49
9	40	25	130	905	6.4	1510	12.01	nil	12.01		5.61	147.3	7.60	0.59
10	60	49	206	1505	9.6	1350	14.1	nil	14.1		4.5	147.5	13.1	0.57
11	91	90	332	2502	14.56	1350	12.2	nil	12.2	2.36		147.8	11.7	0.84
12	91	90	332	2502	14.56	2020	14.93	3.52	18.45		3.89	148.1	12.72	0.76
13	78	85	332	2401	12.5	1550	17.42	nil	17.42		4.92	148.5	13.96	1.12
14	91	90	332	2502	14.56	685	6.32	2.06	8.38	6.18			6.95	0.23
15	91	90	332	2502	14.56	1930	14.59	nil	14.59		0.3		14.7	1.16
16	91	90	332	2502	14.56	1400	13.25	1.73	13.25		0.32	149.12	10.94	0.5
17	91	90	332	2502	14.56	1710	11.49	nil	11.49	3.07		150.1	11.12	0.61
18	91	90	332	2502	14.56	1810	16.22	1.48	16.22		3.14		13.22	1.07

*Day of imaginary operation

TABLE 13 (CASE 11)

Control Starvation, Calories Maintained: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		Body Weight lb.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	
Mar. 14	90	91	331	2503	14.4	940	9.4	nil	9.4	5.0		
15	90	91	331	2503	14.4	1190	12.86	nil	12.86	1.54		
16	90	91	331	2503	14.4	980	14.03	1.34	15.37		0.97	147.75
17	90	91	331	2503	14.4	1935	14.78	nil	14.78		0.38	148.6
18	90	99	320	2531	14.4	2020	14.72	nil	14.72		0.32	147.9
19	10	29	550	2501	1.6	980	9.86	nil	9.86		8.26	148.6
20	10	29	550	2501	1.6	1590	8.41	1.0	9.41		8.81	148.0
21	10	29	550	2501	1.6	1300	7.65	nil	7.65		6.05	149.6
22	20	45	504	2501	3.2	970	6.27	2.16	8.43		5.23	147.8
23	30	56	430	2344	4.8	1200	5.8	nil	5.8		1.0	147.6
24	40	93	376	2501	6.4	900	7.14	nil	7.14		0.74	147.4
25	60	92	358	2500	9.6	840	7.50	1.16	8.66	0.94		147.3
26	90	93	326	2501	14.4	1365	11.1	nil	11.1	3.3		147.0
27	90	93	326	2501	14.4	1260	12.1	2.36	14.46		0.07	146.7
28	90	93	326	2501	14.4	890	13.29	nil	13.29		1.11	145.75
29	90	93	326	2501	14.4	905	14.8	nil	14.8		0.4	145.6
30	90	93	326	2501	14.4	1245	14.0	nil	14.0	0.4		145.3
31	90	93	326	2501	14.4	790	10.49	1.78	12.27	2.13		146.2
Apr. 1	90	93	326	2501	14.4	1900	10.11	nil	10.11	4.29		145.6

TABLE 14 (CASE 12)

Control Starvation: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		Body weight lb.	Urine chloride as g.NaCl	Urine amino acid N as mg. %
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.			
Aug. 30	90	91	332	2502	14.56	1050	20.84	nil	10.42	4.14			7.95	0.61
31	90	91	332	2502	14.56			2.18	12.60	1.96			7.95	0.61
Sept. 1	90	91	332	2502	14.56	1050	12.98	2.22	15.2		0.64		9.32	0.62
2	90	91	332	2502	14.56	1375	15.88	1.2	17.08		2.52		12.35	0.97
3	90	91	332	2502	14.56	2140	13.0	1.04	14.04	0.52			12.20	0.67
4*	10	4	126	580	1.6	2100	10.26	nil	10.26		8.66	120.2	9.8	0.11
5	10	4	126	580	1.6	685	8.38	nil	8.38		6.78	119.4	3.24	0.42
6	10	4	126	580	1.6	980	6.92	nil	6.92		5.32	118.2	2.84	0.43
7	20	4	116	580	3.2	1200	11.75	nil	11.75		8.55	116.6	3.38	0.54
8	30	13	142	805	4.8	1320	10.7	nil	10.7		5.9	115.8	3.09	0.67
9	40	25	130	905	6.4	1320	10.55	nil	10.55		4.15	116.0	3.32	0.59
10	60	49	206	1505	9.6	1430	13.85	3.02	16.87		7.27	117.25	5.0	0.4
11	90	91	332	2502	14.56	1890	12.9	0.78	13.68	0.88		117.9	9.97	0.42
12	90	91	332	2502	14.56	2050	14.53	nil	14.53	0.03		118.3	13.3	0.65
13	90	91	332	2502	14.56	2490	15.66	1.54	17.20		2.64	118.5	14.22	0.68
14	90	91	332	2502	14.56	1870	15.35	0.66	16.01		1.45	118.8	14.04	0.43
15	90	91	332	2502	14.56	1240	10.07	0.56	10.63	3.93		118.9	8.04	0.56
16	90	91	332	2502	14.56	1850	14.87	1.06	15.93		1.37	119.0	13.13	0.37
17	90	91	332	2502	14.56	2910	17.69	0.74	18.33		3.77	118.5	16.0	0.67
18	90	91	332	2502	14.56	1210	13.79	1.34	15.13		0.57		9.36	0.53

*Day of imaginary operation

TABLE 15 (CASE 13)

Control Starvation, Calories Maintained: Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		Body weight lb.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	
Mar. 14	90	91	331	2503	14.4	2110	18.74	nil	18.74		4.34	
15	90	91	331	2503	14.4	1035	13.21	2.42	15.63		1.23	
16	90	91	331	2503	14.4	1395	16.1	nil	16.1		1.7	150.6
17	90	91	331	2503	14.4	2080	14.56	1.86	16.42		2.02	151.2
18	90	99	320	2531	14.4	2210	14.73	nil	14.73		0.33	150.7
19	10	29	550	2501	1.6	1660	9.15	nil	9.15		7.45	150.2
20	10	29	550	2501	1.6	2360	9.34	1.2	10.54		8.94	
21	10	29	550	2501	1.6	1390	8.02	nil	8.02		6.42	151.1
22	20	45	504	2501	3.2	1000	6.76	1.32	8.08		4.88	152.6
23	30	56	409	2500	4.8	1925	8.16	nil	8.16		3.36	151.6
24	40	93	376	2501	6.4	1015	6.70	1.18	7.88		1.48	150.2
25	60	90	358	2500	9.6	920	7.95	0.72	8.67	0.93		149.6
26	90	93	326	2501	14.4	1520	12.5	nil	12.5	1.9		152.5
27	90	93	326	2501	14.4	2510	12.55	0.7	13.25	1.15		151.5
28	90	93	326	2501	14.4	1350	11.35	nil	11.35	3.05		150.8
29	90	93	326	2501	14.4	1490	13.96	1.61	15.57		1.17	151.12
30	90	93	326	2501	14.4	1490	15.40	0.82	16.22		1.82	148.9
31	90	93	326	2501	14.4	2805	15.15	1.18	16.33		1.93	149.6
Apr. 1	90	93	326	2501	14.4	1280	13.12	nil	13.12	1.28		148.9

TABLE 16 (CASE 14)

Control: High Protein High Calorie Diet before Imaginary Operation (with Pronutrin): Nitrogen Intake, Output and Balance

Date	Intake						Output				Balance		Body weight lb.	Urine chloride as g.NaCl
	Pro-nutrin g.	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.		
Feb. 22		97	120	300	2668	15.5	1990	12.64	1.9	14.54	0.96		151.5	
23		96	105	300	2529	15.4	2110	14.77	nil	14.77	0.63		151.6	
24		96	105	310	2569	15.4	1660	7.3	nil	7.3	8.1		147.75	
25		96	105	300	2529	15.4	1245	12.55	3.69	16.24		0.84	147.18	
26	160	96	105	300	3169	34.6	2540	22.95	0.44	23.39	11.2		147.75	
27	160	96	105	300	3169	34.6	2130	21.75	0.75	22.50	12.1		148.12	
28	160	118	114	322	3426	38.1	2900	28.3	3.47	31.77	6.33		150.5	
Mar. 1	160	118	114	322	3426	38.1	2690	31.9	nil	31.9	6.2		148.87	
2	160	118	114	322	3426	38.1	2790	30.6	nil	30.6	7.5		150.75	
3	160	118	114	322	3426	38.1	2500	28.0	1.62	29.62	8.48		151.0	
4	160	118	114	322	3426	38.1	3100	29.55	nil	29.55	8.55		150.75	
5	130	118	114	322	3305	34.5	3180	29.7	3.48	33.18	1.32		153.12	15.5
6	160	118	114	322	3426	38.1	2910	28.95	nil	28.95	9.15		151.5	12.4
7*		165	14	55	1006	26.4	1810	24.05	lost	24.05	2.35		149.5	9.3
8		3		124	508	0.48	2130	17.7	nil	17.7		17.22		5.65
9		3		124	508	0.48	910	9.72	1.56	11.28		10.8	148.0	2.22
10		8	10	16	186	1.28	920	11.08	nil	11.08		9.8	145.12	2.87
11		22	21	76	581	3.52	700	10.58	0.74	11.32		7.8		1.18
12		70	67	158	1635	11.02	1150	13.42	1.13	14.55		3.53	142.25	2.76
13		80	81	231	1973	12.8	1740	8.47	nil	8.47	5.33		143.37	7.8
14		81	86	236	2042	12.95	1246	10.17	3.56	13.73		0.78	141.6	
15		80	84	236	2020	12.8	1410	10.5	nil	10.5	2.3		142.0	
16		80	84	236	2020	12.8	1420	9.66	1.32	10.98	1.82		142.5	
17		96	105	300	2529	15.36	1450	9.22	nil	9.22	6.14		144.5	15.9
18		96	105	300	2529	15.36	1790	11.34	1.96	13.30	2.06		146.25	17.25
19		94	105	287	2469	15.04	1600	12.45	2.29	14.74	0.30		145.25	
20		96	105	300	2529	15.36	1880	11.23	nil	11.23	4.03			

*Day of imaginary operation. Intake to represent equivalent of blood transfusion.

TABLE 17 (CASE 15)

High Protein High Calorie Diet before Operation (Pronutrin after Operation): Nitrogen Intake, Output and Balance

Date	Intake								Output					Balance		Body weight lb.
	Pro-nutrin g.	Pro-tein g.	Fat g.	Carbo-hydrate g.	Calories	N in food g.	N in re-turned food, g.	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Oct. 5		119	160	258	2948			19.04	2100	16.3	2.42		18.72	0.32		138.1
6		119	160	258	2948			19.04	1400	13.6	1.02		14.62	4.42		
7		119	160	258	2948			19.04	1830	16.4	2.26		18.66	0.38		
8		113	160	258	2924			18.08	1980	14.8	1.0		15.8	2.28		
9		119	160	258	2948			19.04	1580	12.32	0.73		13.05	5.99		
10		119	160	258	2948			19.04	1560	15.7	0.73		16.43	2.61		
11		93	138	243	2584			14.9	1020	10.80	2.06		12.86	2.04		
12		84	119	251	2411			13.44	1610	10.7	1.53		12.23	1.21		
13		112	166	273	3034			17.92	1680	17.55	1.22		18.77		0.85	
14		109	157	261	2893			17.44	1910	12.15	1.03		13.18	4.26		
15		119	160	273	3008			19.04	890	9.4	1.05		10.45	8.59		139.0
16		119	154	273	2954			19.04	1500	14.28	1.5		15.78	3.26		
17		102	147	273	2823			16.32	2100	8.4	3.64		12.04	4.28		
18		119	154	273	2954			19.04	1220	10.03	1.04		11.07	7.97		140.5
19		119	154	273	2954			19.04	2120	14.06	2.12		16.18	2.86		
20		119	154	273	2954			19.04	2110	14.50	1.38		15.88	3.16		
21		80	125	229	2381			12.8	2400	8.65	lost		lost			
22*				36	144				130	0.6	nil	3.28	3.88		3.88	
23				96	384				950	9.34		3.08	12.42		12.42	
24		14	17	73	501			2.3	820	13.9		3.15	17.05		14.75	
25		20	19	74	547	3.2		3.2	1010	22.46	nil		22.46		19.26	
26		24	24	75	611	3.84		3.84	740	16.04	2.54		18.58		14.74	
27		44	44	119	1048	7.05	0.82	6.23	1220	12.7	nil		12.7		6.47	
28		45	60	104	1136	7.2	1.38	5.82	1490	10.43	nil		10.43		4.61	

*Operation. N content of 1000 ml. transfused and 400 ml. plasma not estimated, of lost blood, 11.79 g., of resected stomach, 4.3 g.

(Over)

TABLE 17 (Contd.)

Date	Intake								Output					Balance		Body weight lb.
	Pro-nutrin g.	Pro-tein g.	Fat g.	Carbo-hydrate g.	Calories	N in food g.	N in returned food, g.	N intake g.	Urine volume ml.	Urine N b.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Oct. 29		93	80	183	1849	14.9	1.52	13.38	1480	10.3	nil		10.3	3.08		
30		83	80	198	1865	13.3	3.14	10.16	1500	10.59	1.74		12.33		2.17	
31	160	82	83	198	2407	32.4	1.36	31.08	1860	18.69	1.56		20.25	11.83		
Nov. 1	160	82	83	198	2407	32.4	2.24	30.16	2470	23.15	1.38		24.53	5.63		131.6
2	160	99	113	259	3089	35.04	0.66	34.38	2660	24.98	1.25		26.23	8.15		
3	160	99	113	288	3205	35.04	3.0	32.04	2150	25.65	1.15		26.8	5.24		
4	140	99	113	288	3125	32.64	1.24	31.4	1810	18.95	0.96		19.91	11.5		131.6
5		99	113	288	2565	15.65	0.2	15.65	2310	16.91	1.08		17.98		2.33	
6		99	113	288	2565	14.71	1.14	14.71	1700	11.05	lost		11.05			
7		63	109	288	2385	9.6	0.49	9.6	1330	11.3	1.72		13.02		3.42	
8		99	113	288	2565	15.13	0.65	15.13	1990	14.6	1.72		16.32		1.19	
9		99	113	288	2565	15.85	4.36	11.49	1380	9.05	)2.03		10.06	1.43		
10		99	113	288	2565	15.85	2.6	13.25	1710	11.26	)		12.27	0.98		130.6
11		99	113	288	2565	15.85	0.5	15.35	1640	9.68	0.9		10.58	4.77		

TABLE 18 (CASE 16)

High Protein High Calorie Diet before Operation (Pronutrin before Operation): Nitrogen Intake, Output and Balance

Date	Intake								Output					Balance		
	Pro-nutrin g.	Pro-tein g.	Fat g.	Carbo-hydrate g.	Calories	N in food g.	N in returned food, g.	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Body weight lb.
Nov. 1		119	109	322	2745	19.04		19.04	1065	12.9	2.71		15.61	3.43		151.6
2		129	104	309	2684	20.48	0.3	20.18	1540	16.58	nil		16.58	3.6		
3		128	103	292	2604	20.32	2.70	17.62	1650	16.0	0.45	2.52	18.97		1.35	
4		126	103	285	2571	20.16	1.30	18.86	1150	12.22	1.26	3.42	16.90	1.86		153.9
5	160	126	103	275	3180	39.36	1.3	38.06	1450	20.58	0.76	2.78	24.12	13.94		
6	160	129	104	309	3328	39.8	0.84	38.96	2300	25.7	nil	2.19	27.89	11.07		
7	160	129	104	309	3328	39.8	1.08	38.72	1620	18.65	1.0	1.98	21.63	17.09		
8	160	129	104	309	3328	39.8	2.66	37.14	2800	21.76	nil	1.51	22.27	14.87		
9	160	129	104	309	3328	39.8	7.0	72.6	1590	22.9	nil	lost	22.9	13.4		
10	160	129	104	309	3328	39.8			2060	27.2	3.2	lost	30.4	5.9		154.3
11	160	101	78	279	2862	39.8	4.44	35.36	1340	18.09	2.9	2.9	23.04	12.28		
12*									1270	15.18	nil	0.61	15.79		15.79	
13		21	13	31.5	327	3.36		3.36	1770	27.5	nil	1.21	28.71		25.51	
14		21	13	31.5	327	3.36		3.36	660	12.48	nil	0.28	12.76		9.40	
15		19	12	29	301	3.1		3.1	1080	25.06	4.3		29.36		26.26	
16		41	7	81	551	6.55		6.55	1020	25.04	nil		25.04		18.49	
17		47	34	108	926	7.52		7.52	350	8.28	5.52		13.8		6.28	
18		97	37	213	1573	15.2		15.2	785	16.02	nil		16.02		0.82	
19		93	58	187	1642	14.8	3.24	11.56	640	11.95	0.5		12.45		0.89	
20		102	95	237	2211	16.32	1.39	14.93	770	12.35	3.36		15.71		0.78	
21		106	94	278	2382	16.96	4.0	12.96	1060	14.52	nil		14.52		1.56	
22		101	101	282	2441	16.16	5.2	10.96	990	14.61	0.96		15.57		4.59	
23		109	101	282	2473	17.45	4.28	13.17	620	10.47	1.48		11.95	1.22		
24		109	101	282	2473	17.45	3.64	13.81	1010	13.72	nil		13.72	0.09		140.0
25		109	101	282	2473	17.45	3.79	13.66	620	9.45	2.7		12.15	1.51		

*Operation. N content of 1974 ml. transfused blood, 41.78 g.; lost blood, 32.4 g.; resected stomach, 3.31 g.

TABLE 19 (CASE 17)

High Protein High Calorie Diet before Operation (Pronutrin before and after Operation): Nitrogen Intake, Output and Balance

Date	Intake								Output					Balance		Body weight lb.
	Pro-nutrin g.	Pro-tein g.	Fat g.	Carbo-hydrate g.	Calories	N in food g.	N in returned food, g.	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Nov. 1		126	110	305	2713	20.16		20.16	680	8.8	2.25		11.05	9.11		103.2
2		126	102	296	2605	20.16		20.16	1220	15.12	nil		15.12	5.04		
3		126	102	296	2605	20.16	0.26	19.9	1300	15.01	0.62		15.63	4.27		
4		126	102	317	2690	20.16		20.16	1050	15.58	3.66		19.24	0.82		
5	160	126	102	317	3330	39.36		39.36	1720	23.2	1.4		24.6	14.76		105.4
6	160	126	102	317	3330	39.36	1.84	37.52	2130	23.85	0.7		24.55	12.97		
7	160	126	102	317	3330	39.36	0.17	39.19	1900	22.12	2.7		24.82	14.37		
8	160	126	102	317	3330	39.36	0.10	39.26	1930	24.0	2.1		26.1	13.16		
9	160	126	102	317	3330	39.36		39.36	2050	29.9	nil		29.9	9.46		
10	160	126	102	317	3330	39.36		39.36	1800	25.2	2.69		27.89	11.47		105.2
11	160	126	102	317	3330	39.36		39.36	2260	26.58	nil		26.58	12.78		
12	160	126	102	317	3330	39.36		39.36	2010	23.2	2.92		26.12	13.24		
13	160	126	102	317	3330	39.36		39.36	2580	24.55	2.18	0.57	27.2	12.12		
14*									1230	10.38		1.56	11.94		11.94	
15		19	12	29	301	3.1		3.1	570	9.68		4.06	13.74		10.64	
16		42	26	63	654	6.72		6.72	180	3.22	1.0	3.81	8.03		1.31	
17		42	26	110	842	6.72		6.72	1030	24.25	0.5	0.37	25.12		18.4	
18		56	7	110	731	8.96		8.96	640	16.83	nil		16.83		7.87	
19		74	54	151	1386	11.82		11.82	730	15.95	nil		15.95		4.13	
20		82	54	152	1426	13.1		13.1	735	12.18	3.1		15.28		2.18	
21		99	97	294	2450	15.85	0.81	15.04	915	12.88	2.02		14.9	0.14		
22	120	97	97	284	2877	29.9	2.51	27.39	1290	15.88	1.38		17.26	10.13		
23	85	97	97	284	2737	25.7	1.8	23.9	1160	18.15	1.64		19.79	4.11		
24		97	97	284	2397	15.52	0.43	15.09	1240	15.04	1.78		16.82		1.73	101.0
25		97	97	284	2397	15.52	0.72	14.80	1115	13.42	2.02		15.44		0.64	

*Operation. N content of 1480 ml. transfused blood, 40.06 g.; lost blood, 24.0 g.; resected stomach, 4.12 g.

TABLE 20 (CASE 18)

High Protein High Calorie Diet before Operation (Pronutrin before and after Operation): Nitrogen Intake, Output and Balance

Date	Intake								Output					Balance		Body weight lb.
	Pronutrin g.	Protein g.	Fat g.	Carbohydrate g.	Calories	N in food g.	N in returned food, g.	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Nov. 27	160	137	98	328	3382	41.16		41.16	1840	26.03	2.2		28.23	12.93		159.0
28	160	137	98	328	3382	41.16		41.16	1845	28.1	2.55		30.65	10.51		
29	160	137	98	328	3382	41.16		41.16	2570	35.58	0.64		36.22	4.94		
30	160	137	98	328	3382	41.16		41.16	1780	31.65	2.5		34.15	7.01		
Dec. 1	160	137	98	328	3382	41.16		41.16	2090	29.16	nil		29.16	12.0		
2	160	137	98	328	3382	41.16		41.16	1130	15.68	2.68	0.64	19.0	22.16		157.7
3*	63			150	852			7.5	800	11.14		5.12	16.26		8.76	
4		47	34	149	1092			7.52	750	17.78		1.76	19.54		12.02	
5		40	24	127	994			6.4	890	21.05	lost	4.98	26.03		19.63	
6		28	33	49	812			3.52	1220	16.75		0.56	17.31		13.79	
7		28	33	49	605	4.48		4.48	1300	18.0	1.44		19.44		14.96	
8		17	20	32	376	2.72		2.72	1760	18.08	1.08		19.16		16.44	
9		78	67	202	1723	12.5		12.5	1250	15.5	1.04		16.54		4.04	
10		90	75	209	1871	14.4		14.4	2020	16.64	lost		16.64		2.24	
11		94	75	209	1887	15.0		15.0	1780	14.23	nil		14.23	0.77		
12		116	95	276	2425	18.55	0.2	18.35	1110	15.2	2.1		17.3	1.05		
13		128	68	305	2344	20.44	0.6	19.84	1300	16.7			16.7	3.14		
14		128	108	305	2705	20.44		20.44	2220	18.94	1.89		20.83		0.39	
15		127	105	313	2705	20.32		20.32	1420	13.01	nil		13.01	7.31		
16		127	105	313	2705	20.32		20.32	1470	15.7	nil		15.7	4.62		147.0
17		127	105	313	2705	20.32		20.32	1360	15.2	2.53		17.73	2.59		
18		127	105	313	2705	20.32	0.3	20.02	1500	14.55	1.94		16.49	3.53		
19		127	105	313	2705	20.32		20.32	990	9.52	nil		9.53	10.79		153.0

*Operation. N content of 990 ml. transfused blood, 21.31 g.; lost blood, 18.6 g.; resected stomach, 4.0 g.

TABLE 21 (CASE 19)

High Protein High Calorie Diet before Operation (Pronutrin before and after Operation): Nitrogen Intake, Output and Balance

Date	Intake								Output					Balance		Body weight lb.
	Pro-nutrin g.	Pro-tein g.	Fat g.	Carbo hydrate g.	Calories	N in food g.	N in returned food, g.	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Nov. 29	160	137	98	328	3382	41.16		41.16	1650	27.8	2.06		29.86	11.3		151.7
30	160	137	98	328	3382	41.16		41.16	1820	32.85	3.6		36.45	4.71		
Dec. 1	160	137	98	328	3382	41.16		41.16	1630	27.05	1.0		28.05	13.11		
2	160	137	98	328	3382	41.16		41.16	910	16.16	1.48		17.64	23.52		150.5
3	160	137	98	328	3382	41.16		41.16	1560	26.05	1.93		27.98	13.18		
4	160	137	98	328	3382	41.16		41.16	1820	24.43	1.43	0.83	26.69	14.47		151.5
5*	100			305	1620			12.0	630	8.68		8.23	16.91		4.91	
6	100			246	1384			12.0	1270	19.88		7.8	27.68		15.68	
7		26	14	61	474			4.16	930	24.0		4.76	28.76		24.6	
8		32	18	218	1162			5.12	1130	24.25	0.82	4.6	29.67		24.55	
9				126	504				795	14.98	3.1	0.64	18.72		18.72	
10				120	480				1490	22.12	1.6		23.72		23.72	
11									1430	18.9	lost		18.9		18.9	
12		32	40	64	742	5.12		5.12	1660	17.0	1.3		18.3		13.18	
13		80	70	189	1706	12.8		12.8	1680	17.92	1.39		19.31		6.51	
14		80	70	189	1706	12.8		12.8	2300	18.23	2.6		20.83		8.03	
15		80	70	189	1706	12.8		12.8	2280	15.19	4.95		20.14		7.34	
16		87	74	226	1918	13.92		13.92	2340	14.12	3.02		17.14		3.22	
17		87	74	226	1918	13.92		13.92	1880	13.68	1.68		15.36		1.44	142.25
18		87	74	226	1918	13.92	0.42	13.50	1680	8.7	1.56		10.26	3.24		
19		87	74	226	1918	13.92		13.92	1420	13.4	3.12		16.52		2.6	142.0

*Operation. N content of 930 ml. transfused blood, 24.33 g.; lost blood, 14.2 g.; resected stomach, 3.35 g.

TABLE 22 (CASE 20)

Casydrol Infusions: Control Nitrogen Intake, Output and Balance. No Casydrol Administered

Date	Intake					Output					Balance			
	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Body temp. °F.	Urine chloride as g.NaCl
July 7	74	46	182	1438	11.84	820	12.18	0.85		13.03		1.19		1.05
8	85	102	257	2286	13.6	1650	14.14	2.6		16.74		3.14		4.29
9	109	108	270	2460	17.4	1400	12.22	1.2		13.42	3.98			5.44
10*			48	192		158	2.04	nil	2.38	4.42		4.42		0.25
11	1.9	2.4	75	328	0.3	1420	21.2	nil	1.24	22.44		22.14		2.53
12	2.4	3.6	100.5	444	0.4	lost		nil					99.1	
13	9.9	12	63	400	1.5	790	13.1	nil		13.1		11.6	99.0	0.83
14	18.8	21.6	19.5	347	3.0	890	16.14	nil		16.14		13.14	100.4	2.65
15	87	79	213	1911	13.9	760	15.9	2.12		18.02		4.12		1.69
16	65	81	179	1705	10.4	640	9.6	1.27		10.87		0.47		3.83
17	70	78	222	1870	11.2	1000	14.7	nil		14.7		3.5		9.4
18	74	75	230	1891	11.82	1650	11.76	nil		11.76	0.06			10.32
19	66	72	169	1588	10.56	1110	13.3	nil		13.3		2.74	100.6	6.22
20	86	91	196	1947	13.26	1240	22.65	1.41		24.06		10.7	99.8	9.65
21	88	87	242	2103	14.08	1240	17.22	nil		17.22		3.14		4.45
22	60	82	232	1906	9.6	1510	15.5	1.27		16.77		7.11	99.1	9.64
23	101	107	268	2439	16.16	1190	13.04	nil		13.04	3.12		101.4	5.4
24	101	108	264	2432	16.16	2150	16.5	nil		16.5		0.34	99.4	4.64
25	87	102	270	2346	13.92	1610	12.88	0.18		13.06	0.86			3.77
26	102	108	270	2460	16.32	2670	26.65	nil		13.32	3.0			14.16
27	100	108	251	2376	16.00			1.22		14.54	1.46			
28	92	105	238	2265	14.72	1120	14.51	nil		14.51	0.21			3.42
29	98	112	245	2380	15.68	1720	14.28	0.95		15.23	0.45			5.63
30	89	102	204	2090	14.26	1050	10.36	nil		10.36	3.9			5.38

*Operation. N content of 950 ml. transfused blood, 21.95 g.; lost blood, 27.98 g.; resected stomach, 4.09 g.

TABLE 23 (CASE 21)

Casydrol Infusions: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance		Body weight lb.	Body temp. °F.	Urine chloride as g.NaCl
	Casydrol volume ml.	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.			
Feb. 14		105	106	299	2570	16.8	1080	13.87	2.5		16.37	0.57		114.6		
15		105	106	299	2570	16.8	1600	12.7	nil		12.7	4.1		113.5		
16		105	106	299	2570	16.8	1810	12.67	3.04		15.71	1.09		113.5		
17		105	106	299	2570	16.8	1180	14.1	nil		14.1	2.7		113.9		11.8
18		105	106	299	2570	16.8	2240	16.4	nil		16.4	0.4		115.5		9.75
19		105	106	299	2570	16.8	2880	15.0	1.46	0.14	16.6	0.2		114.8		6.8
20		105	106	299	2570	14.24	3230	13.83	2.76	0.42	17.01		2.77	115.25		6.9
21*							920	4.86	nil	1.71	6.57		6.57	115.25		3.5
22	620	24		31	220	3.8	1290	16.61	nil	0.17	17.78		13.98		102.0	3.42
23				96	384		720	16.55	nil	1.85	18.4		18.4		99.0	0.6
24				72	288		740	19.45	nil	0.08	19.53		19.53	110.75		0.74
25		2	2	16	80	0.32	630	16.57			16.57		16.25	112.0		0.69
26		15	18	23	314	2.4	760	16.3			16.3		13.9	112.0		0.87
27		17	11	84	503	2.72	940	10.9	2.0		12.9		10.18	110.75		0.98
28		43	48	141	1168	7.04	1150	12.1			12.1		5.06	105.25		1.55
Mar. 1		46	44	114	1034	7.65	870	9.72	3.88		13.6		5.95	104.0		1.24
2		60	75	190	1675	9.45	970	10.9			10.9		1.45	105.0		1.82
3		65	88	184	1788	10.4	1400	12.38	1.48		13.86		3.46	105.0		3.55
4		66	88	203	1868	10.56	1080	9.92	0.9		10.82		0.26	105.0		5.03
5		66	88	203	1868	10.56	1380	9.55	0.26		9.81	0.75		106.0		9.95
6		66	88	203	1868	10.56	1620	10.04	0.54		10.58		0.02	105.5		6.8
7		62	84	206	1828	9.92	850	7.31	1.66		8.96	0.96		106.25		4.17
8		74	81	208	1857	11.85	1360	8.84	1.68		10.52	1.33		104.25		5.37
9		73	81	206	1845	11.68	830	7.14	0.68		7.82	3.86		104.75		5.65

*Operation. N content of 980 ml. transfused blood, 22.95g.; lost blood, 27.1 g.; resected stomach, 3.44 g.

TABLE 24 (CASE 22)

Casydrol Infusions: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance				
	Casydrol volume ml.	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Body weight lb.	Body temp. °F.	Urine chloride as g.NaCl
Apr. 26		114	114	319	2758	18.24	1700	22.5			12.22	6.02		116.8		19.25
27		114	114	319	2758	18.24			1.72		13.94	4.30		117.25		
28		114	114	319	2758	18.24	620	7.69	1.17		8.86	9.38		118.75		7.63
29		114	114	311	2726	18.24	690	11.58	nil		11.58	6.66		118.75		4.93
30		114	114	311	2726	18.24	710	9.8	1.84		11.64	6.6		117.4		6.54
May 1*				48	192		660	12.86	nil		12.86		12.86		101.0	1.74
2	1970	78		98.5	800	12.96	650	14.11	0.46	0.08	14.65		1.69		100.0	0.96
3	730	60	35	125	1050	9.6	1210	32.6	nil		32.6		22.0		100.4	0.73
4	2430	106	9.6	173	1200	16.6	720	21.2	0.12	1.56	22.88		6.28		99.6	0.32
5	2700	127	22	170	1386	20.75	1440	38.2	0.24	0.2	38.64		17.89		100.0	0.37
6	2430	117	24	147	1272	18.54	1260	28.4	0.72		29.12		10.58		101.0	0.78
7		13	19	40	383	2.08	1270	20.57	1.44		22.01		19.93		99.6	4.19
8		39	39	118	979	6.25	1330	18.52	0.21		18.73		12.48			10.44
9		62	75	170	1603	9.9	1400	14.21	2.1		16.31		6.41	117.75		9.06
10		65	81	162	1637	10.4	2090	14.92	2.32		17.24		6.84	116.5	99.2	13.00
11		69	79	232	1913	11.04	1290	13.00	nil		13.00		1.96	114.5		8.55
12[x]		66	76	234	1880	10.56	1380	15.51	2.08		17.59		7.03	112.6	101.0	7.13
13		70	86	233	1986	11.2	1290	15.8	0.84		16.64		5.44	111.0		6.71
14		68	83	244	1995	10.88	1020	14.74	1.5		16.24		5.36	110.75		6.52
15		68	83	244	1995	10.88	1280	10.62	1.28		12.9		2.02	110.75		7.07
16		68	83	244	1995	10.88	1730	14.26	0.528		14.79		3.91	110.5		9.95
17		68	83	244	1995	10.88	1700	13.4	3.0		16.4		5.52	109.8		10.03
18		97	94	317	2502	15.52	1910	12.8	0.78		13.58	1.94		109.75		10.9
19		97	94	317	2502	15.52	2180	11.25	nil		11.25	4.27		110.5		11.25
20		97	94	317	2502	15.52	1840	14.5	1.94		16.44		0.92	109.6		12.3
21		97	94	317	2502	15.52	1770	11.86	nil		11.86	3.66		110.75		8.04
22		97	94	317	2502	15.52	810	8.55	2.45		11.0	4.52		110.7		7.2
23		103	102	352	2738	16.48	1670	13.58	2.62		16.20	0.28		109.9		12.28
24		103	102	352	2738	16.48	1300	13.9	nil		13.9	2.58				9.25

*Operation (1): Gastrectomy. N content of 970 ml. transfused blood, 27.79 g.; lost blood, 18.51 g.; resected stomach, 2.7 g.

[x]Operation (2): Incision and drainage of abscess of leg.

TABLE 25 (CASE 23)

Casydrol Infusions: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance		Body weight lb.	Body temp. °F.	Urine chloride as g.NaCl
	Casydrol volume ml.	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.			
May 12		109	120	288	2666	17.44	2280	18.53	0.26		18.79		1.35	129.75		13.4
13		107	120	278	2620	17.12	2040	9.3	2.18		11.48	5.64		128.75		8.53
14		81	105	240	2229	12.96	740	12.1	2.36		14.46		1.5	127.25		2.88
15*				28	112		660	11.1	nil	0.35	11.45		11.45	127.25	100.0	2.11
16	2700	135		135	1080	16.6	840	14.7	nil	1.4	16.1	0.5			98.8	0.94
17	3750	187.5		187.5	1500	23.2	2250	41.8	nil	2.66	44.46		21.26		99.9	0.34
18	2160	112	5	118	965	13.3	1570	28.8	nil	0.13	28.93		15.63		101.0	0.06
19	2580	146	20	169	1440	19.1	1600	26.6	2.74		29.34		10.24		103.0	0.56
20		42	48	124	1096	6.72	1340	20.03	1.69		21.72		15.0	128.8	99.0	1.93
21		46	50	130	1131	7.35	1850	23.55	nil		23.55		16.2	127.5	98.9	7.33
22		65	74	182	1654	10.4	1220	16.0	1.78		17.78		7.38			6.22
23		65	74	182	1654	10.4	2050	17.55	nil		17.55		7.15	124.8		9.4
24		65	74	182	1654	10.4	2380	15.62	nil		15.62		5.22			8.24
25		65	75	170	1615	10.4	2240	17.3	2.2		19.5		9.1			8.87
26		84	90	218	2020	13.4	1770	11.8	nil		11.8	1.6		121.5		5.27
27		86	96	240	2168	13.76	1750	16.44	3.72		20.16		6.4			8.82
28		86	96	240	2168	13.76	1860	13.2	nil		13.2	0.56				9.25
29		86	96	240	2168	13.76	2150	13.33	2.24		15.57		1.81			
30		86	96	240	2168	13.76	2080	14.56	1.42		15.98		2.22	120.12		

*Operation. N content of 495 ml. transfused blood, 19.18 g.; lost blood, 10.7 g.; resected stomach, 3.68 g.

TABLE 26 (CASE 24)

Casydrol Infusions: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance		Body weight lb.	Body temp. °F.	Urine chloride as g.NaCl
	Casydrol volume ml.	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.			
July 10		123	146	316	3070	19.7	1040	14.52	0.77		15.29	4.41				8.2
11		123	137	316	2989	19.7	1030	13.76	0.98		14.74	4.96		138.5		8.96
12		123	146	316	3070	19.7	1450	18.34	nil		18.34	1.36				10.97
13		123	146	316	3070	19.7	910	12.6	nil		12.6	7.1				7.57
14		123	146	316	3070	19.7	1660	5.94	1.97	0.73	8.64	10.06		140.25		0.996
15*		1.9	2.4	3	40		740	9.78	nil		9.78		9.78		100.8	5.62
16	2700	108		135	970	16.74	1360	23.2	nil		23.2		6.46		100.0	5.94
17	2160	87.5	4	117	854	14.2	1420	24.2	nil		24.2		10.0		101.0	2.13
18	1620	74	8	97	848	11.82	2430	26.78	0.89		27.67		15.85		102.0	6.45
19	540	49	31	32	703	7.8	1430	16.19	1.89		18.08		10.28		103.6	2.12
20		16	20	45	424	2.56	1820	26.6	nil		26.6		24.04		101.0	0.49
21		70	53	209	1593	11.2	1750	25.15	nil		25.15		13.95	135.4	99.2	2.62
22		57	64	213	1656	9.22	1610	18.2	1.7		19.9		10.68		99.4	5.02
23		72	61	215	1697	11.52	1820	18.74	nil		18.74		7.22	133.5	99.2	11.04
24		74	74	226	1866	11.84	2150	16.5	nil		16.5		4.66			12.4
25		81	84	250	2080	12.96	1180	10.74	1.50		12.24	0.72		129.3		6.64
26		109	112	267	2512	17.44	1680	20.0	nil		20.0		2.56			11.02
27		109	112	267	2512	17.44	1360	19.26	2.03		21.29		3.85	126.0		7.4
28		109	112	257	2472	17.44	1190	16.66	nil		16.66	0.78				5.66
29		110	118	267	2619	17.44	1260	16.07	3.8		19.87		2.43	128.0		6.4
30		107	113	266	2509	17.12	1150	14.43	nil		14.43	2.69		127.8		6.48

*Operation. N content of 490 ml. transfused blood, 15.28 g.; lost blood, 8.68 g.; resected stomach, 4.38 g.

TABLE 27 (CASE 25)

Casydrol Infusions: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance				
	Casydrol volume ml.	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Body weight lb.	Body temp. °F.	Urine chloride as g.NaCl
July 10		114	98	299	2466	18.2	1870	15.78	nil		15.78	2.42				7.96
11		114	89	299	2389	18.2	840	12.18	1.05		13.23	4.97		120.25		5.75
12		114	98	299	2466	18.2	910	10.62	3.0		13.62	4.58				5.11
13		114	98	299	2466	18.2	1100	15.85	nil		15.85	2.35		121.0		6.91
14		114	98	299	2466	18.2	910	12.93	0.65		13.58	4.62				6.59
15		114	98	299	2466	18.2	1450	14.08	nil		14.08	4.12				8.32
16		114	98	299	2466	18.2	1900	8.55	1.23	0.09	9.87	8.33				4.82
17*							240	2.19	nil	0.96	3.15		3.15	117.25		0.81
18	2620	108		131	1048	17.22	1920	25.0	nil		25.0		7.78		100.2	6.14
19	2700	113		135	1080	18.15	1580	22.49	nil	1.39	23.88		5.73		101.2	2.46
20	2160	99	12	138	1056	15.80	2160	35.65	nil	0.53	36.18		20.38		100.8	0.82
21	2700	130	28	170	1352	20.79	2270	34.0	0.69		34.69		13.9	120.0	101.6	1.13
22	540	36	17	46	481	5.69	1860	25.2	0.4		25.6		19.91		99.0	1.34
23		46	47	145	1187	7.36	2150	21.55	0.22		21.77		14.41	120.5		1.93
24		74	75	198	1763	11.82	2350	19.8	1.65		21.45		9.63			4.37
25		71	75	235	1900	11.36	2120	17.7	0.69		18.39		7.03	119.25		10.34
26		114	116	264	2556	18.34	2440	19.7	nil		19.7		1.36			12.4
27		114	116	264	2556	18.34	2440	18.8	3.15		21.95		3.61	115.8		10.0
28		114	116	264	2556	18.34	1940	19.3	nil		19.3		0.96	115.25		7.64
29		110	118	267	2610	17.6	1920	17.8	0.76		18.56		0.96			6.37
30		110	118	267	2610	17.6	1640	17.33	0.57		17.9		0.3	114.5		6.4

*Operation. N content of 460 ml. transfused blood, 11.0 g.; lost blood, 3.03 g.; resected stomach, 15.0 g.

TABLE 28 (CASE 42)

Amigen Infusions: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance		Body weight lb.	Body temp. °F.
	Amigen volume ml.	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.		
Feb. 21		91	101	330	2593	14.56	1280	11.12	0.88	1.33	13.23	1.23		136.0	
22		75	92	295	2308	12.0	1780	9.98			9.98	2.02		134.0	
23		91	101	330	2593	14.56	720	10.62		0.32	10.94	3.62		134.0	
24		92	104	343	2676	14.72	760	9.98	2.12	3.19	15.29		0.57	133.5	
25*							500	5.66		3.24	8.9		8.9		100.0
26	1830	74		103	708	11.92	350	5.38		0.61	5.99	5.93			101.4
27	1780	72		89	634	11.56	1210	30.54		1.34	31.88		20.32		101.8
28	1940	101	25	169	1305	15.84	920	23.5		0.32	23.82		7.98		100.8
Mar. 1	869	79	53	144	1349	12.64	930	21.56			21.56		8.92	130.75	99.6
2		57	65	121	1297	9.12	720	16.92	lost		16.92		7.8	130.5	101.0
3		79	87	160	1739	12.64	980	19.05			19.05		6.41	129.4	100.5
4		90	96	222	2112	14.4	650	10.72	2.04		12.76	1.64		132.4	99.2
5		94	106	268	2402	15.04	1220	20.3	1.06		21.36		6.32	131.0	
6		94	106	268	2402	15.04	1430	13.62			13.62	1.42			
7		93	105	258	2349	14.88	1030	10.8	0.94		11.74	3.14		129.5	
8		79	104	237	2200	12.64	600	10.0	1.42		11.42	1.22		125.9	
9		83	114	267	2426	13.28	920	9.26			9.26	4.02		126.5	

*Operation. N content of 480 ml. transfused blood, 16.7 g.; lost blood, 13.8 g.; resected stomach, 2.48 g.

TABLE 29 (CASE 44)

Plasma Infusions: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance		Body weight lb.	Body temp. °F.	Urine chloride as g.NaCl
	Plasma volume ml.	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.			
Oct. 12							1590	15.32	0.42		15.73					8.58
13							1320	15.85	nil		15.85					9.86
14							905	7.24	nil		7.24					5.05
15		90	97	256	2257	14.4	830	6.30	nil		6.30					2.57
16		90	97	256	2257	14.4	1540	11.91	lost		11.91	2.51		152.5		9.15
17		87	94	256	2218	13.92	1280	13.08	0.18		13.26	0.66		152.5		7.09
18		90	95	255	2235	14.4	1640	11.81	nil		11.81	2.59				6.2
19		90	97	256	2257	14.4	1530	9.46	0.71		10.17	4.23		152.5		7.45
20		90	97	256	2257	14.4	1570	12.71	nil		12.71	1.69				8.04
21		90	97	256	2257	14.4	1340	14.5	nil		14.5	0.1		152.6		
22		90	97	256	2257	14.4	1410	9.9	0.79	1.42	12.31	2.09		152.6		6.55
23*				80	320		970	8.73		2.73	11.46		11.46	152.5	100.4	5.52
24	1555	44.4		60	417	7.1	1340	15.08		0.92	16.0		8.9		100.4	6.6
25	400	10.3		60	281	1.66	1150	20.3			20.3		18.64		100.8	4.46
26	800	14.2		60	297	2.27	1320	23.5		0.08	23.5		21.23	157.75	103.0	5.8
27	1774	56.25		20	305	9.01	lost								103.2	lost
28	1670	62.6			250	10.26	77	0.55			0.55				103.4	0.49
29	DIED 9.20 p.m.			40	160		nil								105.8	

*Operation. N content of 420 ml. transfused blood, 10.84 g., lost blood, 9.9 g., resected stomach, 2.49 g.

TABLE 30 (CASE 45)

Milk Mixture: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance			
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl
Oct. 14	70	87	290	2223	11.2	880	8.43	nil	1.39	9.82	1.38		0.91	
15	66	67	267	1935	10.56	615	5.92	0.19	1.8	7.91	2.65		1.85	11.42
16	63	62	270	1890	10.08	500	4.88	nil	4.23	9.01	1.07		0.79	21.9
17*	9	4	29	188	1.44	510	5.96			5.96		4.52	0.76	
18	71	28	218	1408	11.36	1560	28.0	1.19	nil	14.6		3.24	0.31	
19	40	15	125	795	6.4					14.6		8.2	0.31	
20	60	23	187	1195	9.6	600	11.42	nil		11.42		1.82	0.67	
21	119	46	374	2386	19.04	980	17.5	nil		17.5	1.54		1.61	
22	119	46	374	2386	19.04	975	15.85	2.73		18.58	0.46		6.16	
23	84	69	182	1685	13.46	650	10.73	2.03		12.76	0.7		5.93	
24	96	86	275	2258	15.36	990	15.88	1.38		17.26		1.9	9.5	
25	89	81	259	2121	14.24	1280	18.59	nil		18.59		4.35	9.84	
26	93	90	290	2332	14.88	520	6.63	1.66		8.29			5.1	
27	94	81	258	2137	15.04	1120	9.4	0.94		10.34	4.7		6.8	
28	103	87	278	2308	16.48	1660	11.95	0.84		12.79	3.69		9.96	
29	100	100	329	2616	16.00	1295	9.74	1.29		11.03	4.97		8.65	
30	93	92	282	2328	14.88	1620	8.74	0.88		9.62	5.26		8.3	
31	92	84	248	2131	14.88	1460	9.41	lost		9.41			8.6	
Nov. 1	93	85	255	2172	14.88	1455	10.14	nil		10.14	4.74			

*Operation. N content of 450 ml. transfused blood, 11.65 g.; lost blood, 6.02 g.; resected stomach, 4.42 g.

TABLE 31 (CASE 46)

Milk Mixture: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance				
	Type of food intake	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Body temp. °F.	Urine chloride as g.NaCl	Suction chloride as g.NaCl
Nov. 8							1535	18.91	2.90		21.81				13.75	
9	F	90	97	256	2257	14.4	750	6.34	0.44	0.39	7.17				2.63	
10	F	75	96	265	2224	12.0	1570	7.96	nil	lost	7.96				6.65	
11*	MM	90	35	280	1715	14.4	390	3.91			3.91	10.49			2.51	
12	MM	150	58	468	2860	24.0	605	12.08		1.85	13.93	10.07		100.0	1.18	1.03
13	MM	119	46	280	2386	19.04	960	14.15	0.95	0.52	15.62	3.42			2.23	1.41
14	MM	90	35	280	1715	14.4	960	19.91	0.58	0.46	20.95		6.55	99.6	1.56	1.69
15	MM	90	35	280	1715	14.4	1000	22.08	2.42		24.5		10.1		4.1	
16	MM	45	17	140	896	17.2	995	21.98	0.2		22.18		4.98		6.2	
	F	62	50	186	1452											
17	MM	12	5	37	239	11.2	1090	18.81	1.98		20.79		9.59		4.57	
	F	58	51	179	1407											
18	MM	45	17	140	896	18.88	1200	13.21	4.04		17.25	1.53			4.25	
	F	74	68	224	1776											
19	MM	45	17	140	896	19.85	1090	19.56	2.56		22.12		2.27		7.36	
	F	84	76	224	1896											
20	MM	30	11	93	591	18.24	1200	19.05	7.48		26.53		8.29		6.71	
	F	84	75	230	1971											
21	MM	7.5	3	23	149	14.8	1230	15.15	3.31		18.46		3.66	99.4	6.93	
	F	85	80	218	1932											
22	MM	30	11	93	591	19.2	?680	10.34	3.09		13.43				3.62	
	F	90	97	250	2257											
23	MM	45	17	140	896	21.42	2100	20.22	3.09		23.31		1.89		9.32	
	F	89	96	255	2240											

*Operation. N content of lost blood, 4.88 g., resected stomach, 6.16 g.

MM = milk mixture

F = ordinary food

TABLE 32 (CASE 47)

Milk Mixture: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance			
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl
Nov. 21	91	101	256	2297	14.56	1025	11.77	nil	0.17	12.94	1.62		3.36	0.81
22	91	101	256	2297	14.56	1036	10.36	1.52	0.32	12.2	2.36		2.24	0.59
23	91	101	256	2297	14.56	2000	12.88	nil	0.35	13.23	1.33		1.8	0.44
24						lost								
25*	60	23	187	1195	9.6	360	5.03	nil	1.42	6.45	3.15		1.44	0.88
26	90	35	280	1795	14.4	505	7.68	3.06	0.71	11.45	2.95		1.74	3.39
27	90	35	280	1795	14.4	330	3.56	8.04	0.12	11.72	2.68		0.16	5.18
28	90	35	280	1795	14.4	820	12.42	1.56		13.98	0.42		0.38	
29	90	35	280	1795	14.4	1340	28.05	3.25		31.3		16.9	0.35	
30	90	35	280	1795	14.4	1420	32.2	4.24		36.44		22.04	0.86	
Dec. 1	128	73	389	2725	20.48	800	17.38	9.8		27.18		6.7	0.77	
2	52	54	130	1114	8.32	1190	24.98	5.22		30.2		21.88	2.02	
3	48	51	162	1299	7.68	665	12.22	1.28		13.5		5.82	1.95	
4	62	64	189	1580	10.22	660	4.96	3.04		8.0	2.22		0.77	
5	90	82	231	2022	14.4	lost	lost	3.27					lost	
6	89	101	280	2385	14.26	1470	9.82	0.7		10.52	3.74		5.4	
7	86	104	255	2300	13.78	1650	11.92	1.42		13.34	0.44		9.36	
8	86	94	229	2106	13.78	1720	11.17	1.06		12.23	1.45		8.8	
9	90	92	264	2244	14.4	1470	9.95	nil		9.95	4.45		6.82	
10	90	92	266	2252	14.4	1800	10.74	1.02		11.76	2.64		6.87	
11	90	92	264	2244	14.4	1920	13.98	0.4		14.38	0.02		8.2	

*Operation

TABLE 33 (CASE 48)

Milk Mixture: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance		
	Type of food intake	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl
Nov. 26	F	90	100	310	2500	14.4	760	8.16	nil		8.16	6.24		7.05
27	F	90	100	310	2500	14.4	640	9.76	0.84		10.6	3.8		4.88
28	F	90	100	310	2500	14.4	645	10.28	nil		10.28	4.12		5.36
29	F	90	100	310	2500	14.4	870	11.22	1.30		12.52	1.88		7.25
30	F	90	100	310	2500	14.4	875	10.07	2.46		12.53	1.87		7.55
Dec. 1	F	90	100	310	2500	14.4	820	9.39	nil		9.39	5.01		7.27
2	F	90	100	310	2500	14.4	665	9.12	nil		9.12	5.28		5.76
3	F	90	100	310	2500	14.4	1250	11.71	nil		11.71	2.69		6.2
4	F	90	100	310	2500	14.4	1005	9.61	lost		9.61	4.79		5.40
5*	MM	60	23	187	1195	9.6	110	0.48	nil		0.48	9.12		0.57
6	MM	90	35	280	1795	14.4	1310	17.70	nil		17.7		3.3	3.97
7	MM	90	35	280	1795	14.4	990	21.0	nil	2.74	23.74		9.34	2.73
8	MM	90	35	280	1795	14.4	840	17.9	nil		17.9		3.5	2.67
9	MM	77	31	237	1535	12.3	540	10.86	nil		10.86	1.44		2.03
10	MM	70	27	218	1395	11.2	lost	lost	3.90					
11	MM	30	11.5	93	593	14.4	690	13.90	1.80		15.7		1.3	2.91
	F	60	58	161	1406									
12	F	90	71	238	1951	14.4	680	13.08	1.96		15.04		0.64	4.42
13	F	90	92	264	2244	14.4	540	9.38	0.54		9.92	4.48		4.92
14	F	90	92	264	2244	14.4	780	13.7	0.52		14.22	0.18		7.82
15	F	90	92	264	2244	14.4	780	12.62	0.58		13.2	1.2		8.03
16	F	90	92	264	2244	14.4	965	13.89	2.08		15.97		1.57	8.59
17	F	90	92	264	2244	14.4	840	11.52	1.02		12.54	1.86		7.7

*Operation. N content of 750 ml. transfused blood, 19.27 g.; lost blood, 19.5 g.; resected stomach, 2.3 g.

MM = milk mixture

F = ordinary food

TABLE 34 (CASE 49)

Milk Mixture: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance			
	Type of food intake	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl
Jan. 12	F	90	92	246	2172	14.4	2005	13.3	2.48		15.78		1.38	13.15	
13	F	91	92	246	2176	14.56	1700	12.3	nil		12.3	2.26		10.95	
14	F	91	96	246	2212	14.56	1240	12.74	1.46		14.2	0.36		8.18	
15	F	76	91	245	2103	12.16	1430	11.44	0.27		11.71	0.45		8.44	
16*	MM	53	24	200	1228	8.48	265	2.66		2.56	5.22	3.26		1.38	2.9
17	MM	80	36	300	1844	12.8	965	13.06		5.29	18.35		5.55	5.70	5.62
18	MM	37	17	148	893	5.93	1210	17.09		0.56	17.65		11.72	5.18	0.85
19	F	59	52	233	1636	9.44	920	20.53			20.53		11.09	2.26	
20	F	72	61	269	1913	11.52	700	14.08	3.20		17.28		5.76	1.32	
21	F	82	96	280	2312	13.12	700	16.27	nil		16.27		3.15	1.33	
22	F	90	78	268	2134	14.4	790	16.28	3.16		19.44		5.04	1.47	
23	F	94	84	229	2048	15.04	740	14.19	nil		14.19	0.85		2.06	
24	F	88	88	239	2100	14.09	1540	12.80	nil		12.80	1.29		6.16	
25	F	85	86	224	2010	13.76	1060	13.08	2.12		15.20		1.44	4.21	
26	F	91	92	246	2176	14.56	1020	13.12	1.76		14.88		0.32	7.98	

*Operation
MM = milk mixture
F = ordinary food

TABLE 35 (CASE 50)

Milk Mixture: Nitrogen Intake, Output and Balance

Date	Intake						Output					Balance		Body weight lb.	Urine chloride as g.NaCl.	Suction chloride as g.NaCl.
	Type of food intake	Protein g.	Fat g.	Carbohydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.			
Jan. 27	F	88	93	246	2173	14.12	1280	10.42	0.41		10.83	3.29			10.87	
28	F	88	93	246	2173	14.12	1400	14.38	1.2		15.58		1.46		9.65	
29	F	88	93	246	2173	14.12	1340	8.42	0.67	1.62	10.71	3.41		147.9	4.21	0.37
30*	MM	54	24	190	1192	8.74	825	10.79	nil	1.22	12.01		3.27		2.43	1.68
31	MM	89	36	285	1820	14.28	760	17.55	nil	nil	17.55		3.27	143.25	1.87	
Feb. 1	MM	89	36	285	1820	14.28	785	21.65	nil	2.79	24.44		10.16	140.1	1.68	1.30
2	MM & F	68	48	206	1516	10.4	570	16.65	1.9		18.55		8.15		0.94	
3	MM & F	87	53	282	1953	13.96	790	18.65			18.65		4.69	141.6	3.49	
4	MM & F	86	72	238	1944	13.80	980	18.8	2.76		21.56		7.76	143.2	7.13	
5	F	73	73	206	1773	11.68	lost							141.0	lost	
6	F	88	55	225	1747	14.12	940	13.56	0.96		14.52		0.40	141.0	5.30	
7	F	90	75	249	2031	14.40	780	12.08	nil		12.08	1.32				
8	F	88	74	242	1986	14.12	1000	15.04	1.96		17.0		2.88	140.6	5.66	
9	F	76	76	217	1856	12.16	930	10.24	2.2		12.44		0.28		6.12	
10	F	90	88	259	2188	14.40	lost		0.58					139.75		

*Operation. N content of 430 ml. transfused blood, 11.1 g.; lost blood, 4.44 g., resected stomach, 2.98 g.
MM = milk mixture
F = ordinary food

TABLE 36 (CASE 51)

Milk Mixture (Jejunostomy Feeding): Nitrogen Intake, Output and Balance

Date	Intake					Output				Balance		Body weight lb.	Urine chloride as g.NaCl
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.		
Oct. 12			40	160		1890	8.48	nil	8.48		8.48		12.08
13			80	320		1915	5.83	1.29	7.12		7.12		5.11
14*			40	160		375	1.87	nil	1.87		1.87		3.29
15	87	37	260	1721	13.92	965	9.34	nil	9.34	4.58			6.86
16	119	46	374	2386	19.04	1680	17.9	2.49	20.39		1.35		21.6
17	119	46	374	2386	19.04	1730	15.6	0.53	16.13	2.91			24.6
18	119	46	374	2386	19.04	4360	25.00	3.14	14.07	4.97		116.5	53.4
19	119	46	374	2386	19.04				14.07	4.97			
20	119	46	374	2386	19.04	2050	13.58	nil	13.58	5.46			34.7
21	119	46	374	2386	19.04	1950	18.12	3.09	21.21		2.17		34.8
22	119	46	374	2386	19.04	1335	14.13	0.93	15.06	3.98			22.4
23	119	46	374	2386	19.04	1500	16.92	1.57	18.49	0.55			22.5
24	119	46	374	2386	19.04	1750	17.55	nil	17.55	1.49		117.5	18.32
25	119	46	374	2386	19.04	2400	15.94	1.60	16.74	2.3			16.32
26	119	46	374	2386	19.04	1705	14.75		15.55	3.49			13.3
27	119	46	374	2386	19.04	1300	13.88	1.23	15.11	3.93			9.0
28	119	46	374	2386	19.04	3100	19.95	2.48	22.43		3.39		18.74
29	119	46	374	2386	19.04	1435	14.3	2.22	16.52	2.42			14.15
30	119	46	374	2386	19.04	2020	15.15	1.63	16.78	2.26			10.5
31	119	46	374	2386	19.04	1420	15.27	nil	15.27	3.77			6.65
Nov. 1	119	46	374	2386	19.04	2940	25.2	7.68	16.44	2.6		116.75	21.38
2	119	46	374	2386	19.04				16.44	2.6			
3	93	36	292	1864	14.88	510	7.65	nil	7.65				4.91
4	119	46	374	2386	19.04	770	11.4	4.0	15.4	3.64			7.15
5	119	46	374	2386	19.04	1090	11.55	3.08	14.63	4.41			10.38
6	103	43	354	2215	16.48	1350	9.5	2.8	12.3	4.18			11.25
7	119	46	374	2386	19.04	1565	10.45	nil	10.45	8.59			10.48
8	119	46	374	2386	19.04	1610	15.15	7.45	18.87	0.17			11.65
9	119	46	374	2386	19.04	1060	7.90		11.62	7.42			8.01

*Operation

(Over)

TABLE 36 (Contd.)

Date	Intake					Output				Balance			
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	N output g.	+ g.	- g.	Body weight lb.	Urine chloride as g.NaCl
Nov. 10	119	46	374	2386	19.04	1400	8.4	1.18	9.58	9.46		114.4	10.6
11	119	46	374	2386	19.04	lost	lost	1.98					lost
12	119	46	374	2386	19.04	2040	11.5	1.58	13.08	5.96			12.85
13	119	46	374	2386	19.04	1200	13.4	0.98	14.38	4.66			7.53
14	119	46	374	2386	19.04	2700	19.2	1.22	20.42		1.38		12.04
15	53	20	166	1056	8.46	1100	14.47	nil	14.47		6.01		5.43
16	119	46	374	2386	19.04	920	10.45	nil	10.45	8.59		110.5	7.90
17	119	46	374	2386	19.04	2080	11.32	2.88	14.2	4.84			7.37
18	128	57	389	2581	20.48	2210	12.63	0.72	13.35	7.13			6.28
19	128	57	389	2581	20.48	2100	15.71	2.60	18.31	2.17			13.80
20	128	57	389	2581	20.48	1925	15.91	nil	15.91	4.57			11.42
21	128	57	389	2581	20.48	2210	17.55	2.14	19.69	0.79			12.06
22	128	57	389	2581	20.48	2130	17.71	2.02	19.73	0.75		114.25	15.15
23	128	57	389	2581	20.48	2760	13.38	1.88	15.26	4.22			12.59
24	128	57	389	2581	20.48	2980	16.35	3.32	19.67	0.81			12.05
25	128	57	389	2581	20.48	3810	16.45	2.70	19.15	1.33			17.09
26	147	78	429	3006	23.58	2960	18.60	1.24	19.84	3.64			18.39
27	129	68	394	2704	20.62	3335	16.95	3.92	20.87		0.25		19.7
28	153	85	438	3129	24.52	2610	19.4	2.48	21.88	2.64			16.7
29	147	79	442	2987	23.6	2645	17.38	1.50	18.88	4.72		118.25	19.4
30	140	79	417	2939	22.4	1790	15.83	2.36	18.19	4.21			10.42
Dec. 1	123	64	357	2496	19.68	2350	19.4	2.04	21.44		1.76		14.62
2	142	74	410	2874	22.72	2360	17.95	2.32	20.27	2.45			18.9
3	144	78	414	2934	23.24	2380	18.4	0.88	19.28	3.96			21.25
4	132	67	398	2723	21.12	2360	18.4	0.86	19.26	1.86			20.0
5	149	84	428	3064	23.84	1880	18.06	1.06	19.12	4.72			12.4
6	133	75	377	2715	21.28	2376	19.84	1.60	20.44	0.84			17.5
7	150	82	427	3046	24.0	2300	19.62	2.50	20.12	3.88			14.7
8	140	71	407	2827	22.4	1760	20.38	4.1	24.48		2.08		11.25
9	146	83	417	2999	23.36	2470	17.3	3.20	20.5	2.86			18.45

TABLE 37 (CASE 59)

Administration of Testosterone Propionate

Date	Intake					Output					Balance		Body weight lb.	Urine chloride as g.NaCl
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.		
Mar. 3	109	117	258	2521	17.04	960	10.33	0.65		10.98	6.06		138.0	7.7
4	116	120	322	2832	18.58	980	12.5	nil		12.5	6.08		140.25	7.67
5	116	120	322	2832	18.58	920	10.99	0.76		11.75	6.83		139.25	9.2
6 TP	116	120	322	2832	18.58	1150	11.07	1.36	0.71	13.14	5.44		140.25	8.25
7*TP			80	320		400	4.84		0.89	5.73		5.73		2.04
8 TP			60	240		1050	16.02	nil	0.7	16.72		16.72		4.37
9 TP			60	240		950	15.23	nil	0.19	15.42		15.42		3.42
10 TP	7	8	10	140	1.12	770	15.56	lost	0.09	15.65		14.53		0.8
11 TP	10	12	15	184	1.6	630	14.53	2.88		17.41		15.81		1.23
12 TP	29	49	165	977	4.63	680	14.08	nil		14.08		9.45	130.75	1.86
13 TP	65	71	175	1600	10.4	710	12.2	nil		12.2		1.8	131.12	2.8
14 TP	65	71	176	1603	10.4	870	13.17	1.1		14.27		3.87	130.75	
15 TP	65	71	176	1603	10.4	760	11.33	nil		11.33		0.93	129.5	
16 TP	65	71	176	1603	10.4	870	12.35	nil		12.35		1.95	130.0	
17 TP	65	71	176	1603	10.4	760	10.32	nil		10.32	0.08		129.25	6.25
18	65	71	176	1603	10.4	700	10.22	1.47		11.69		1.29	129.25	5.5
19	65	71	176	1603	10.4	810	9.9	nil		9.9	0.5		130.5	6.03
20	87	90	206	1982	13.92	880	9.9	0.66		10.56	3.36			6.75

TP = Testosterone propionate, 25 mg. as Perandren I.M.I.

*Operation. N content of 500 ml. transfused blood, 13.32 g.; lost blood, 12.6 g.; resected stomach, 2.52 g.

TABLE 38 (CASE 55)

Controlled Intake of Sodium and Chloride: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance		Body weight lb.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.	
Feb. 24	87	87	277	2239	13.92	1660	10.22	nil		10.22	3.7		
25	84	92	267	2232	13.44	2350	10.34	0.86		11.2	2.24		
26	90	93	267	2265	14.4	2490	12.5	2.42		14.92		0.52	104.7
27	87	91	265	2227	13.92	2010	10.77	1.5		12.27	1.65		
28	90	93	267	2265	14.4	1900	9.80	0.88		10.68	3.72		
29	89	84	262	2160	14.24	1630	8.18	1.54		9.72	4.52		
Mar. 1	90	93	267	2265	14.4	1515	6.08	0.16	0.45	6.69	7.71		
2*								nil	0.25	0.25		0.25	
3						1410	18.25	nil	0.18	18.43		18.43	105.5
4	14	15	35	341	2.24	1060	17.0	nil		17.0		14.76	105.5
5	42	46	144	1158	6.72	800	9.15	nil		9.15		2.43	104.5
6	48	46	117	1074	7.68	950	8.38	7.28		15.66		7.98	
7	48	46	117	1074	7.68	1580	8.9	3.6		12.5		4.82	102.4
8	56	46	141	1234	8.98	1520	9.12	0.84		9.96		0.98	
9	64	67	147	1447	10.25	1690	11.6	1.46		13.06		2.81	101.75
10	66	66	192	1626	10.58	1020	7.95	nil		7.95	2.63		
11	68	59	209	1639	10.90	1220	7.75	1.62		9.37	0.53		101.0
12	82	80	195	1828	13.14	720	5.62	1.56		7.18	5.96		

*Operation. N content of lost blood, 1.44 g.

TABLE 39 (CASE 56)

Controlled Intake of Sodium and Chloride: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance	
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.
Apr. 24	92	96	297	2420	14.72	700	12.05	0.66		12.71	2.01	
25	92	105	297	2501	14.72	650	9.42	0.98		10.4	4.32	
26	92	105	299	2509	14.72	440	7.88	0.9		8.78	5.94	
27	76	95	251	2160	11.98	750	13.0	0.36		13.36		1.38
28	92	105	299	2509	14.72	585	8.32	0.82		9.14	5.58	
29	92	105	299	2509	14.72	840	11.09	0.98		12.07	2.65	
30*						250	2.67		0.4	3.07		3.07
May 1			40	160		750	14.14	nil	0.51	14.65		14.65
2			40	160		770	14.52	nil	0.47	14.99		14.99
3			40	160		760	12.2	nil	0.92	13.12		13.12
4	18	12	36	312	2.88	1010	22.9	1.24		24.14		21.26
5	16	16	36	352	2.56	745	18.65	nil		18.65		16.09
6	48	41	127	1060	7.66	960	21.1	0.39		21.49		13.83
7	64	75	168	1603	10.24	780	15.0	1.28		16.28		6.04
8	70	77	191	1737	11.2	1310	17.35	0.94		17.82		6.62
9	83	74	207	1826	13.26	1020	13.25			13.72		0.46
10	91	87	227	2051	14.56	1240	14.95	nil		14.95		0.39
11	90	96	225	2130	14.4	1120	18.75	0.6		19.35		4.95
12	89	96	220	2100	14.24	1040	18.30	3.63		21.93		7.69
13	91	104	270	2380	14.56	1210	18.21	1.62		19.83		5.27
14	85	93	258	2209	13.61	1155	17.6	1.02		18.62		5.01
15	92	101	297	2465	14.72	1025	12.25	1.42		13.67	1.05	
16	92	101	297	2465	14.72	1600	16.89	1.33		18.22		3.50
17	92	101	297	2465	14.72	1300	12.57	1.4		13.97	0.75	
18	92	101	297	2465	14.72	1110	11.65	1.04		12.69	2.03	
19	92	101	297	2465	14.72	950	11.25	nil		11.25	3.47	
20	92	101	297	2465	14.72	940	9.88	1.6		11.48	3.24	
21	92	101	297	2465	14.72	610	7.04	1.9		8.94	5.78	

*Operation. N content of 1000 ml. transfused blood, 23.0 g.; lost blood, 29.7 g.; resected stomach, 0.72 g.

TABLE 40 (CASE 57)

Controlled Intake of Sodium and Chloride: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance		Body weight lb.	Body temp. °F.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.		
Oct. 3	91	101	330	2593	14.56	1500	10.56	nil		10.56	4.0			
4	91	101	330	2593	14.56	1760	9.1	1.36		10.46	4.1			
5	91	101	330	2593	14.56	1900	12.76	1.0		13.76	0.80			
6	91	101	330	2593	14.56	1200	11.38	nil		11.38	3.18			
7	91	101	330	2593	14.56	710	8.7	nil		8.7				
8	91	101	330	2593	14.56	1740	12.65	1.86		14.51	0.05			
9	91	101	330	2593	14.56	1480	9.64	nil		9.64	4.92			
10	91	101	330	2593	14.56	1880	13.60	1.34		14.94		0.38		
11	66	72	247	1900	10.56	1870	11.08	0.42	0.53	12.03		1.47	121.4	
12*			20	80		1200	12.43	nil	1.56	13.99		13.99		
13			40	160		710	12.38	nil	1.08	13.46		13.46		
14			18	72		910	18.68	nil		18.68		18.68	121.0	101.0
15	19	20	68	528	3.04	900	20.2	nil		20.2		17.16	121.1	100.0
16	43	53	99	1045	6.88	1380	17.08	1.5		18.58		11.7	121.0	100.1
17	57	65	126	1317	9.12	930	12.58	1.56		14.14		5.02	120.9	100.2
18	70	80	153	1612	11.2	890	9.94	0.84		10.78	0.42		119.1	
19	88	91	213	2013	14.08	1030	10.44	3.52		13.96	0.12		117.9	
20	82	79	220	1919	13.12	670	3.48	7.1		10.58	2.54		117.45	
21	88	95	301	2401	14.08	1410	11.71	2.63		14.34		0.26	116.1	
22	65	96	282	2172	10.4	900	10.8	1.18		11.98		0.58	115.9	
23	87	104	253	2296	13.92	1510	11.95	nil		11.95	1.97		117.7	
24	86	101	263	2365	13.78	1110	6.19	3.16		9.35	4.43		117.4	
25	97	108	274	2456	15.52	1500	8.36	1.4		9.76	5.76		118.1	
26	91	105	267	2377	14.56	2200	10.29	1.96		12.25	2.31		117.9	
27	89	104	262	2340	14.24	1430	6.85	2.2		9.05	5.19		116.75	
28	91	106	268	2390	14.56	1270	5.72	1.04		6.76	7.8		117.45	

*Operation. N content of lost blood, 18.7 g.; resected stomach, 2.88 g.
N content of 850 ml. transfused blood not estimated.

TABLE 41 (CASE 58)

Controlled Intake of Sodium and Chloride: Nitrogen Intake, Output and Balance

Date	Intake					Output					Balance		Body weight lb.	Body temp. °F.
	Protein g.	Fat g.	Carbo-hydrate g.	Calories	N intake g.	Urine volume ml.	Urine N g.	Stool N g.	Suction N g.	N output g.	+ g.	- g.		
Aug. 14	91	101	314	2529	14.55	1160	10.47	0.32		10.79	3.76			
15	86	87	289	2283	13.78	1030	11.99	3.26	2.81	18.06		4.28	107.5	
16	43	58	122	1182	6.88	490	5.16	0.54	0.53	6.23	0.65			
17	91	101	314	2529	14.55	1230	13.26	0.31		13.57	0.98			
18	88	98	330	2554	14.08	1360	13.28	0.11		13.39	0.69		108.4	
19	70	92	291	2272	11.2	1340	9.16	1.19	0.077	10.43	0.77		108.75	
20*			54	216				nil	0.6	0.6				
21			45	180		2100	23.0	nil	0.27	23.27		23.27	107.25	99.4
22	11	10	19	210	1.75	1440	20.9	nil		20.9		18.15	106.75	99.3
23	22	24	73	596	3.52	380	5.38	12.44[x]		17.82		14.3	106.2	101.6
24	43	53	99	1045	6.89	1260	15.76	3.41[x]		19.17		12.38	105.4	
25	54	66	126	1314	8.65	870	12.62	2.22		14.84		6.19		
26	79	86	172	1778	12.66	1100	12.96	nil		12.96		0.3	102.4	
27	87	93	242	2153	13.92	1190	11.24	lost		11.24	1.68		105.8	
28	87	99	282	2367	13.92	1350	9.94	2.34		12.28	1.64			
29	101	106	310	2598	16.16	1170	10.34	1.68		12.02	4.14		105.8	
30	101	100	310	2544	16.16	990	9.1	0.64		9.74	6.42			
31	101	100	310	2544	16.16	1470	11.73	3.32		15.05	1.11		105.25	
Sept. 1	89	101	310	2505	14.24	1360	8.56	1.68		10.24	4.0		104.25	
2	89	101	310	2505	14.24	990	6.5	1.56		8.06	6.18		104.25	
3	89	101	310	2505	14.24	1110	7.08	1.66		8.74	5.50		103.5	
4	82	101	300	2437	13.12	1340	8.6	2.08		10.68	2.44		103.5	
5	72	78	292	2158	11.68	1000	6.12	1.02		7.14	4.54		104.1	

*Operation. N content of 390 ml. transfused blood, 8.76 g.; lost blood, 1.85 g.; resected stomach, 1.12 g.

[x]Part of large fluid stools lost.

TABLE 42 (CASE 20)

Control for Casydrol Infusions: Details of Urinary Nitrogen Excretion

Date	Urine output				Plasma amino acid nitrogen mg./%
	Total nitrogen g.	Urea nitrogen g.	Amino acid nitrogen g.	Peptide nitrogen g.	
July 7	12.18		0.47		
8	14.14	12.5	0.67		
9	12.22	10.4	0.55		
10*	2.04	1.64	0.09		
11	21.2		0.99		4.8
12	lost				
13	13.1	8.73	0.62	1.66	
14	16.14	11.9	0.69	1.06	4.98
15	15.9	9.47	0.43	1.65	
16	9.6	7.38	0.58	1.01	
17	14.7	11.12	1.24	0.85	
18	11.76	8.62	1.3	1.7	4.78
19	13.3	11.14	lost		
20	22.65	17.48	1.78	1.15	
21	17.22	15.18	1.24		5.1
22	15.5	10.1	2.18	1.87	
23	13.04	8.55	1.24	0.76	
24	16.5	13.36	2.42	0.84	

*Operation

TABLE 43 (CASE 22)

Casydrol Infusions: Details of Nitrogen Intake and Excretion

Date	Casydrol intake			Urine output				Amino acid nitrogen		Plasma amino acid N mg./%
	Volume ml.	Amino acid N g.	Peptide N g.	Total N g.	Urea N g.	Amino acid N g.	Peptide N g.	Balance g.	Retention %	
May 1*				12.86		0.33				4.4
2	1970	6.5	3.15	14.11		1.46	1.82	5.04	77	5.6
3	730	2.61	0.97	32.6		3.47	4.21			5.8
4	2430	8.03	3.87	21.2		1.69	2.34	6.34	79	
5	2700	9.93	3.28	38.2		3.36	3.2	5.57	56	4.8
6	2430	8.03	3.87	28.4		3.15	4.29	4.88	60	
7				20.57		1.67	2.55			
8				18.52		3.4				4.5
9				14.21		1.96				
10				14.92		4.08				5.3
11				13.0		2.09				
12				15.51		2.48				5.6

*Operation.
No allowance made for pre-operative amino acid N excretion.
In 5 days 35.1 g. amino acid N injected
13.13 g. amino acid N excreted = 63 per cent. "retention"

TABLE 44 (CASE 23)

Casydrol Infusions: Details of Nitrogen Intake and Excretion

Date	Casydrol intake			Urine output				Amino acid nitrogen		Plasma amino acid N mg./%
	Volume ml.	Amino acid N g.	Peptide N g.	Total N g.	Urea N g.	Amino acid N g.	Peptide N g.	Balance g.	Retention %	
May 14				12.1		1.48	0.89			6.0
15*				11.1		0.66	1.32			6.1
16	2700	8.9	4.42	14.7		1.66	1.89	7.24	81	4.8
17	3780	12.48	6.02	41.8		6.75	7.65	5.73	46	
18	2160	7.13	3.45	28.8		3.14	5.66	3.99	55	4.9
19	2580	8.53	4.11	26.6		3.4	1.8	5.13	60	
20				20.3		1.13	1.09			
21				23.55		2.5				4.6

*Operation.

No allowance made for pre-operative amino acid N excretion.

In 4 days 37.0 g. amino acid N injected

15.0 g. amino acid N excreted ≡ 60 per cent. "retention"

TABLE 45 (CASE 24)

Casydrol Infusions: Details of Nitrogen Intake and Excretion

Date	Casydrol intake			Urine output				Amino acid nitrogen		Plasma amino acid N mg./%
	Volume ml.	Amino acid N g.	Peptide N g.	Total N g.	Urea N g.	Amino acid N g.	Peptide N g.	Balance g.	Retention %	
July 10				14.53		0.54	0.62			
11				13.76		0.4	1.86			
12				18.34	15.65					
13				12.6	9.54	0.52	1.82			
14				5.94	5.38	1.53				
15*				9.78	7.75	0.41	0.09			
16	2700	8.93	4.2	23.2	16.5	1.62	2.47	7.81	87	4.98
17	2160	7.15	3.46	24.2	17.4	1.69	3.8	5.96	83	4.78
18	1620	5.35	2.59	26.78	18.3	3.5	4.1	2.35	44	4.78
19	540	1.78	0.87	16.19	11.72	1.4	2.15	0.88	47	4.78
20				26.6	22.36	0.84				
21				25.15	21.8	1.15	1.58			4.57
22				18.2	15.28	1.32	0.52			
23				18.74	15.3	1.44				
24				16.5	14.0	0.93	1.0			
25				10.74	9.15	0.66				4.8
26				20.0	16.62	0.94	0.61			
27				19.26	14.66	0.62	1.66			
28				16.66	13.32	1.09				

*Operation.

Average daily urinary amino acid N excretion before operation, 0.5 g.

In 4 days 23.0 g. amino acid N injected

6.0 g. amino acid N excreted ≡ 73 per cent. "retention"

TABLE 46 (CASE 25)

Casydrol Infusions: Details of Nitrogen Intake and Excretion

Date	Casydrol intake			Urine output				Amino acid nitrogen		Plasma amino acid N mg./%
	Volume ml.	Amino Acid N g.	Peptide N g.	Total N g.	Urea N g.	Amino acid N g.	Peptide N g.	Balance g.	Retention %	
July 10				15.78		1.4	0.81			
11				12.18		1.18	0.23			
12				10.62		1.3	1.4			
13				15.85		1.52	0.87			
14				12.93	9.15	1.67	0.22			5.3
15				14.08	11.5	0.86	0.47			
16				8.55						4.6
17*				2.19	1.8	0.36	0.12			
18	2620	8.67	4.2	25.0	15.08	3.02	1.51	7.06	82	
19	2700	8.93	4.33	22.49	13.74	3.3		7.04	79	5.1
20	2160	7.15	3.46	33.65	22.35	4.23		4.33	60	
21	2700	8.93	4.33	34.0	23.72	5.95		4.39	49	4.94
22	540	0.87	1.62	25.2	18.1	4.62				5.1
23				21.55	18.58	1.68	1.16			
24				19.8	15.17	2.75	1.53			
25				17.7	13.06	1.62				
26				19.7	15.03	2.07				
27				18.8	16.99	1.76	0.46			
28				19.3	15.77	1.23				

*Operation.

Average daily urinary amino acid N excretion before operation, 1.4 g.

In 5 days 35.0 g. amino acid N injected

14.0 g. amino acid N excreted ≡ 60 per cent. "retention"

TABLE 47 (CASE 40)

Casydrol Infusions: Details of Nitrogen Intake and Excretion

Date	Casydrol intake		Urine output			Amino acid nitrogen		Urine Chloride as g.NaCl
	Volume ml.	Amino acid N g.	Volume ml.	Total N g.	Amino acid N g.	Balance g.	Retention %	
July 3			1145	6.64	0.33			3.37
4			1050	7.66	0.43			3.78
5			850	8.67	0.38			3.94
6			740	8.62	0.34			2.78
7			)147	)1.97				)0.188
	1620	5.35	)480	)5.52	0.53	5.19	97.0	)0.404
8	540	1.78	965	12.4	0.54	1.61	90.4	0.656
9	540	1.78	965	8.94	1.01	1.14	63.0	0.81
10			1160	8.98	1.02			0.186
11			1290	5.26	0.39			0.214

Average daily urinary amino acid N excretion before casydrol, 0.37 g.
In 3 days 8.91 g. amino acid N injected
1.7 g. amino acid N excreted ≡ 80 per cent. "retention"

TABLE 48 (CASE 42)

Amigen Infusions: Details of Nitrogen Intake and Excretion

Date	Amigen intake			Urine output				Amino acid nitrogen		Peptide nitrogen	
	Volume ml.	Amino acid N g.	Peptide N g.	Total N g.	Urea N g.	Amino acid N g.	Peptide N g.	Balance g.	Retention %	Balance g.	Retention %
Feb. 21				11.12	9.18	0.22	0.54				
22				9.98	8.52	0.22	0.57				
23				10.62	8.11	0.13	0.55				
24				9.98	8.28	0.2	0.44				
25*				5.66	4.47	0.14	0.28				
26	1830	7.69	2.56	5.38	4.66	0.18	0.36	7.61	100	2.0	80
27	1780	7.47	2.5	30.54	25.38	1.36	2.03	6.3	80	1.0	70
28	1940	8.14	2.72	23.5	21.25	0.96	1.72	7.4	90	1.5	55
Mar. 1	869	3.65	1.22	21.56	18.88	0.85	1.87	3.0	80		
2				16.92	13.98	0.24	1.16				
3				19.05	16.95	0.34	0.87				
4				10.72	7.77	0.31	0.49				
5				20.3	15.98	0.5	1.02				
6				13.62	11.08	0.47	0.73				
7				10.8	8.05	0.27	0.74				
8				10.0	7.48	0.24	0.57				
9				9.26	7.62	0.2	0.38				

*Operation.

Average daily urinary amino acid N excretion before operation, 0.2 g.

" " " peptide " " " " 0.5 g.

In 4 days 26.95 g. amino acid N injected

2.5 g. amino acid N excreted ≡ 93 per cent. "retention"

9.0 g. peptide N injected

3.98 g. peptide N excreted ≡ 56 per cent. "retention"

TABLE 49 (CASE 10)

Control: Intake, Output and Balance of Sodium and Chloride

Date	NaCl in addition to food g.	Urine chloride as g.NaCl	Sodium						Chloride					
			Intake			Output	Balance		Intake			Output	Balance	
			Food g.	Salt g.	Total intake g.	Urine g.	+ g.	- g.	Food g.	Salt g.	Total intake g.	Urine g.	+ g.	- g.
Mar. 14	5.81	11.58	1.65	2.28	3.93	4.98		1.05	2.57	3.54	6.11	7.04		0.93
15	5.78	12.05	1.57	2.27	3.84	5.42		1.58	2.5	3.52	6.02	7.34		1.32
16	5.81	13.75	1.61	2.28	3.89	5.3		1.41	2.62	3.54	6.16	8.36		2.20
17	5.80	9.24	1.53	2.28	3.81	3.16	0.65		2.42	3.53	5.95	5.62	0.37	
18	5.78	11.36	1.75	2.27	4.02	4.07		0.05	2.9	3.52	6.42	6.9		0.48
19	7.81	11.68	0.94	3.07	4.01	4.28		0.27	1.33	4.75	6.08	7.1		1.02
20	5.82	8.15	0.94	2.28	3.22	3.06	0.16		1.36	3.54	4.9	4.96		0.06
21	7.81	6.31	0.94	3.07	4.01	2.1	1.91		1.33	4.75	6.08	3.84	2.24	
22	5.45	6.22	1.3	2.14	3.44	1.89	1.54		1.96	3.32	5.28	3.78	1.5	
23	6.36	8.08	1.48	2.5	3.98	2.82	1.16		2.20	3.87	6.07	4.92	1.15	
24	3.44	10.79	2.57	1.35	3.92	4.48		0.56	3.98	2.09	6.07	6.56		0.48
25	0.90	9.04	1.45	0.35	1.8	3.78		1.98	1.92	0.55	2.47	5.5		3.03
26	5.47	9.33	1.7	2.14	3.84	3.88		0.04	2.74	3.33	6.07	5.68	0.39	
27	5.48	10.01	1.6	2.15	3.75	3.92		0.17	2.74	3.33	6.07	6.08		0.01
28	5.48	10.5	1.77	2.15	3.92	4.26		0.34	2.88	3.33	6.21	6.39		0.18
29	6.08	13.29	1.86	2.39	4.25	5.15		0.9	3.0	3.69	6.69	8.05		1.36
30	6.77	11.11	1.62	2.66	4.28	4.47		0.19	2.57	4.12	6.69	6.74		0.05
31	5.94	10.18	1.69	2.33	4.02	3.81	0.21		2.79	3.61	6.4	6.18	0.22	
Apr. 1	5.60	11.19	1.52	2.2	3.72	4.05		0.33	2.67	3.41	6.08	6.77		0.69

TABLE 50 (CASE 11)

Control: Intake, Output and Balance of Sodium and Chloride

Date	NaCl in addition to food g.	Urine chloride as g.NaCl	Sodium						Chloride					
			Intake			Output	Balance		Intake			Output	Balance	
			Food g.	Salt g.	Total intake g.	Urine g.	+ g.	- g.	Food g.	Salt g.	Total intake g.	Urine g.	+ g.	- g.
Mar. 14	5.34	6.02	1.65	2.1	3.75	2.48	1.27		2.57	3.24	5.81	3.66	2.15	
15	4.74	9.43	1.57	1.86	3.43	3.52		0.09	2.5	2.88	5.38	5.72		0.34
16	5.3	6.79	1.61	2.08	3.69	2.63	1.06		2.62	3.22	5.84	4.12	1.72	
17	5.01	11.62	1.53	1.97	3.5	4.82		1.32	2.42	3.04	5.46	7.05		1.59
18	5.37	11.4	1.75	2.11	3.86	4.32		0.46	2.90	3.26	6.16	6.92		0.76
19	5.63	6.64	0.94	2.22	3.16	2.37	0.79		1.33	3.42	4.75	4.03	0.72	
20	3.01	4.83	0.94	1.18	2.12	1.64	0.48		1.36	1.83	3.19	2.93	0.26	
21	3.97	6.7	0.94	1.56	2.5	2.1	0.4		1.33	2.41	3.74	4.06		0.32
22	2.19	5.48	1.3	0.86	2.16	1.81	0.35		1.96	1.33	3.29	3.33		0.04
23	0.99	5.06	1.43	0.39	1.82	2.08		0.26	2.18	0.6	2.78	3.07		0.29
24	1.24	8.64	2.57	0.48	3.05	3.79		0.74	3.98	0.75	4.73	5.23		0.5
25	2.06	7.13	1.45	0.81	2.26	2.98		0.72	1.92	1.25	3.17	4.32		1.15
26	5.48	12.4	1.7	2.16	3.86	5.33		1.47	2.74	3.33	6.07	7.53		1.46
27	5.48	12.01	1.6	2.16	3.76	4.4		0.64	2.74	3.33	6.07	7.28		1.21
28	4.80	9.07	1.77	1.89	3.66	4.17		0.51	2.88	2.92	5.8	5.5	0.3	
29	?4.0	9.12	1.86			3.81			3.0			5.53		
30	5.65	11.95	1.62	2.22	3.84	4.24		0.4	2.57	3.43	6.0	7.25		1.25
31	5.60	8.4	1.69	2.2	3.89	3.88	0.01		2.79	3,4	6.19	5.11	1.08	
Apr. 1	5.60	8.26	1.52	2.2	3.72	2.76	0.96		2.67	3.4	6.07	5.02	1.05	

TABLE 51 (CASE 14)

Control: Intake, Output and Balance of Sodium and Chloride

Date	NaCl in addition to food g.	Urine chloride as g.NaCl	Sodium						Chloride					
			Intake			Output	Balance		Intake			Output	Balance	
			Food g.	Salt g.	Total intake g.	Urine g.	+ g.	- g.	Food g.	Salt g.	Total intake g.	Urine g.	+ g.	- g.
Mar. 14	5.03	11.45	1.65	1.96	3.61	5.21		1.6	2.57	3.06	5.63	6.94		1.31
15	5.76	10.1	1.57	2.23	3.8	4.11		0.31	2.5	3.5	6.0	6.13		0.13
16	5.81	8.25	1.61	2.28	3.89	3.49	0.4		2.62	3.53	6.15	5.0	1.15	
17	5.8	9.56	1.53	2.28	3.81	3.25	0.56		2.42	3.52	5.94	5.8	0.14	
18	5.8	10.35	1.75	2.28	4.03	3.88	0.15		2.9	3.51	6.41	6.27	0.14	
19	7.83	8.06	0.94	3.08	4.02	3.01	1.01		1.33	4.75	6.08	4.89	1.19	
20	7.79	8.25	0.94	3.06	4.0	3.3	0.7		1.36	4.72	6.08	5.09	0.99	
21	5.16	8.37	0.94	2.03	2.97	3.01		0.04	1.33	3.13	4.46	5.11		0.65
22	6.71	7.2	1.3	2.64	3.94	2.53	1.41		1.96	4.02	5.98	4.37	1.61	
23	3.32	9.44	1.48	1.31	2.79	3.67		0.88	2.2	2.01	4.21	5.72		1.51
24	1.88	9.54	2.57	0.74	3.31	4.02		0.71	3.98	1.14	5.12	5.78		0.66
25	5.79	7.84	1.45	2.28	3.73	2.99	0.74		1.92	3.51	5.43	4.75	0.68	
26	5.47	11.04	1.7	2.15	3.85	4.19		0.34	2.74	3.32	6.06	6.7		0.64
27	5.17	14.75	1.6	2.03	3.63	5.83		2.2	2.74	3.13	5.87	8.94		3.07
28	5.48	9.64	1.77	2.16	3.93	3.72	0.21		2.88	3.32	6.2	5.84	0.36	
29	5.10	13.85	1.86	2.01	3.87	5.5		1.63	3.0	3.1	6.1	8.4		2.3
30	6.72	11.17	1.62	2.64	4.26	4.25	0.01		2.57	4.07	6.64	6.76	0.12	
31	6.43	15.15	1.69	2.53	4.22	6.08		1.86	2.79	3.9	6.69	9.19		2.5
Apr. 1	5.60	8.42	1.52	2.21	3.73	3.38	0.35		2.67	3.39	6.06	5.11	0.95	

TABLE 52

CHLORIDE BALANCE (as g. NaCl)

Case No.	Date	Intake				Output		Balance	
		Food	Casydrol	Saline	Total	Urine	Suction	+	-
22	Apr. 28	7.0			7.0	7.63			0.63
	29	7.0			7.0	4.93		2.07	
	30	7.0			7.0	6.54		0.46	
	May 1*			7.2	7.2	1.74		5.46	
	2		5.92	3.6	9.52	0.96	0.06	8.5	
	3		2.19	3.6	5.79	0.72		5.07	
	4		7.29	3.24	10.53	0.32	3.02	7.51	
	5		8.1	3.78	11.88	0.38	0.52	10.96	
	6		7.29	7.2	14.49	0.78		13.71	
	7	2.0			2.0	4.09			2.09
	8	2.5			2.5	10.4			7.9
	9	5.0			5.0	9.06			4.06
	10	5.5			5.5	13.0			7.5
	11	6.0			6.0	8.55			2.5
	12	6.5			6.5	7.13			0.6
23	May 15*			10.8	10.8	2.11	0.65	8.05	
	16		8.1	1.7	9.8	0.94	5.0	3.86	
	17		11.25	3.2	14.45	0.34	8.95	5.2	
	18		6.48	3.2	9.68	0.06	0.75	8.93	
	19		7.64		7.64	0.56		7.08	
24	July 15*			10.8	10.8	5.62		5.18	
	16		8.25	7.2	15.45	5.94		9.51	
	17		6.5	3.6	10.1	2.13		7.97	
	18		4.9	7.2	12.1	6.45		5.65	
	19		1.6		1.6	2.12			0.52
25	July 17*			10.8	10.8	0.81	0.68	9.31	
	18		7.86	7.2	15.06	6.12	lost	?	
	19		8.1	3.6	11.7	2.46	7.44	1.8	
	20		6.48		6.48	0.82	4.74	0.92	
	21		8.1		8.1	1.14		6.96	
	22		1.62		1.62	1.34		0.28	

*Operation

Chloride content of food is an estimate

TABLE 53

CHLORIDE BALANCE (as g. NaCl)

Case No.	Date	Intake			Output			Balance	
		Milk mixt.	Saline	Total	Urine	Suction	Total	+	-
	Nov. 25*	2.96	7.2	10.16	1.44	0.88	2.32	7.84	
	26	4.44		4.44	1.74	3.39	5.13		0.69
	27	4.44		4.44	0.16	5.18	5.34		0.9
47	28	4.44		4.44	0.38		0.38	4.06	
	29	4.44		4.44	0.35		0.35	4.09	
	30	4.44		4.44	0.86		0.86	3.58	
	Dec. 1	4.9		4.9	0.77		0.77	4.13	
	Jan. 12				13.5		13.5		
	13				10.95		10.95		
	14				8.18		8.18		
	15				8.44		8.44		
	16*	2.96	7.2	10.16	4.28		4.28	5.88	
	17	4.64		4.64	11.32		11.32		6.68
49	18	1.97		1.97	6.03		6.03		4.06
	19	2.36		2.36	2.26		2.26	0.1	
	20	3.41		3.41	1.32		1.32	2.09	
	21	3.89		3.89	1.33		1.33	2.56	
	22	4.15		4.15	1.47		1.47	2.68	
	23				2.06		2.06		
	24				6.16		6.16		

*Operation.
Salt content of milk mixture estimated from tables (McCance and Widdowson, 1946).

TABLE 54 (CASE 55)

Intake, Output and Balance of Sodium and Chloride

Date	NaCl in addition to food g.	Urine chloride as g.NaCl	Sodium							Chloride						
			Intake			Output		Balance		Intake			Output		Balance	
			Food g.	Salt g.	Total intake g.	Urine g.	Suction g.	+ g.	- g.	Food g.	Salt g.	Total intake g.	Urine g.	Suction g.	+ g.	- g.
Feb. 24	5.26	7.96		2.06							3.20		4.84			
25	5.42	6.7	1.74	2.12	3.86	2.66		1.20		2.85	3.29	6.14	4.16		1.98	
26	4.71	4.58	1.72	1.85	3.57	1.69		1.88		2.87	2.86	6.13	2.78		3.35	
27	3.13	3.86	1.83	1.37	3.2	1.79		1.41		2.97	1.9	4.87	2.34		2.53	
28	3.09	4.06	1.72	1.35	3.07	1.46		1.61		2.87	1.88	4.75	2.46		1.29	
29	2.82	2.51	1.73	1.11	2.84	0.97		1.87		2.79	1.71	4.50	1.52		2.98	
Mar. 1	0.79	2.09	1.81	0.35	2.16	1.24		0.92		2.89	0.48	3.37	1.27		2.10	
2*	12.39	0.27		4.86	4.86		0.12	4.74			7.52	7.52		0.16	7.36	
3	9.6	10.07		3.87	3.87	3.47	0.07	0.33			5.95	5.95	6.12	0.37		0.17
4	9.39	7.3	0.19	3.69	3.88	2.54		1.34		0.37	5.70	6.07	4.43		1.64	
5	8.21	6.85	0.59	3.22	3.81	2.37		1.44		1.09	5.0	6.09	4.16		1.93	
6	6.58	4.72	0.65	2.54	3.19	1.55		1.64		1.06	3.99	5.05	2.86		2.19	
7	6.88	5.18	0.65	2.7	3.35	1.48		1.87		1.06	4.18	5.24	3.12		2.12	
8	6.44	3.26	0.86	3.06	3.92	1.09		2.83		1.54	3.9	5.45	1.96		3.49	
9	5.28	1.83	0.98	2.07	3.05	1.21		1.84		1.73	3.15	4.88	1.11		3.77	
10	1.04	1.56	1.2	0.41	1.61	1.04		0.57		1.94	0.63	2.57	0.95		1.62	
11	1.80	3.64	1.2	0.71	1.91	1.67		0.24		1.8	1.09	2.89	2.15		0.74	
12	1.44	3.24	1.11	0.57	1.68	1.54		0.14		1.9	0.87	2.77	1.97		0.8	

*Operation

TABLE 55 (CASE 42)

Sodium Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl	Sodium intake				Sodium output				Balance	
				Salt g.	Food g.	Amigen & saline I.V. g.	Total intake g.	Urine g.	Stool g.	Suction g.	Total loss g.	+ g.	- g.
Feb. 21	1.15	6.77		0.45	2.17		2.62	2.34		0.35	2.69		0.07
22	1.12	4.14		0.44	1.97		2.41	2.29			2.29	0.12	
23	2.7	2.84		1.06	2.14		3.2	1.93		0.12	2.05	1.15	
24	0.71	2.71		0.28	2.27		2.55	2.2	0.71	0.65	3.56		1.01
25*		1.61	3.12			2.49	2.49	0.7		1.27	1.97	0.52	
26		1.74	2.87			2.01	2.01	0.66		0.86	1.52	0.49	
27		1.86	6.45			2.42	2.42	0.66		1.73	2.39	0.03	
28		0.18		0.15		2.03	2.18	0.59		0.37	0.96	1.22	
Mar. 1		0.35		0.29		1.46	1.75	0.98			0.98	0.77	
2	4.79	0.78		1.88	0.91		2.79	0.25	lost		0.25	2.54	
3	4.56	0.98		1.79	1.41		3.2	1.03			1.03	2.17	
4	4.83	2.21		1.9	1.78		3.68	1.57	0.37		1.94	1.74	
5	2.1	6.58		0.83	1.75		2.58	3.32	0.1		3.42		0.84
6	0.57	8.72		0.22	1.75		1.97	3.92			3.92		1.95
7	0.94	6.67		0.37	1.66		2.03	2.74	0.21		2.95		0.92
8	0.47	3.9		0.18	1.57		1.75	1.41	0.08		1.49	0.26	
9	0.72	4.71		0.28	1.67		1.95	1.7			1.7	0.25	

*Operation

TABLE 56 (CASE 42)

Chloride Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl	Chloride intake				Chloride output				Balance	
				Salt g.	Food g.	Amigen & saline I.V. g.	Total intake g.	Urine g.	Stool g.	Suction g.	Total loss g.	+ g.	- g.
Feb. 21	1.15	6.77		0.69	3.37		4.07	4.1	0.06	3.08	7.24		3.17
22	1.12	4.14		0.68	3.02		3.7	2.51			2.51	1.19	
23	2.7	2.84		1.64	3.37		5.01	1.72		1.23	2.95	2.06	
24	0.71	2.71		0.43	3.43		3.86	1.64	0.07	2.75	4.46		0.6
25*		1.61	3.12			3.85	3.85	0.98		1.9	2.88	0.97	
26		1.74	2.87			2.23	2.23	1.06		1.74	2.8		0.57
27		1.86	6.45			2.88	2.88	1.13		3.92	5.05		2.17
28		0.18		0.22		2.3	2.52	0.01		1.12	1.13	1.39	
Mar. 1		0.35		0.46		1.99	2.45	0.21			0.21	2.24	
2	4.79	0.78		2.91	1.51		4.42	0.48	lost		0.48	3.94	
3	4.56	0.98		2.77	2.34		5.11	0.6			0.6	4.51	
4	4.83	2.21		2.93	2.95		5.88	1.34	0.09		1.44	4.44	
5	2.1	6.58		1.27	2.97		4.24	3.99	0.12		4.11	0.13	
6	0.57	8.72		0.35	2.97		3.32	5.29			5.29		1.87
7	0.94	6.67		0.57	2.89		3.46	4.04	0.06		4.1		0.64
8	0.47	3.9		0.29	2.48		2.77	2.36	0.08		2.44	0.33	
9	0.72	4.71		0.44	2.68		3.12	2.86			2.86	0.26	

*Operation

TABLE 57 (CASE 56)

Sodium Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl	Sodium intake				Sodium output			Balance	
				Salt g.	Food g.	Saline I.V. g.	Total intake g.	Urine g.	Suction g.	Total loss g.	+ g.	- g.
Apr. 24	0.99	4.3		0.39	2.06		2.45	1.61		1.61	0.84	
25	1.0	1.69		0.39	2.02		2.4	0.49		0.49	1.92	
26	1.0	2.7		0.39	2.0		2.39	0.93		0.93	1.46	
27	0.98	5.62		0.38	1.99		2.37	2.27		2.27	0.1	
28	0.99	6.24		0.39	2.05		2.44	2.45		2.45		0.01
29	1.0	6.11		0.39	1.99		2.38	2.7		2.7		0.31
30*		1.73	0.69			4.26	4.26	0.49		0.49	3.77	
May 1		3.04	1.39			2.84	2.84	1.3	0.4	1.7	1.14	
2		1.11	1.66			2.84	2.84	0.52	0.46	0.98	1.86	
3		0.18	4.52			2.84	2.84	0.42	1.19	1.61	1.23	
4	3.6	0.6		1.42	0.4		1.82	0.52		0.52	1.3	
5	4.0	0.19		1.58	0.24		1.82	lost				
6	4.0	0.79		1.58	0.74		2.32	1.01		1.01	1.21	
7	5.12	1.69		2.01	1.03		3.04	1.45		1.45	1.59	
8	3.98	6.81		1.57	1.16		2.73	3.87		3.87		1.14
9	3.91	7.84		1.54	1.23		2.77	3.72		3.72		0.95
10	3.99	11.12		1.57	1.54		3.11	4.57		4.57		1.46
11	1.12	9.24		0.44	1.66		2.10	3.09		3.09		0.99
12	3.47	5.97		1.37	1.64		3.01	1.87		1.87	1.14	
13	2.71	7.57		1.07	1.73		2.80	2.46		2.46	0.46	
14	2.79	7.35		1.09	1.95		3.05	2.58		2.58	0.43	
15	2.0	6.53		0.79	1.98		2.67	2.3		2.3	0.37	
16	2.63	7.28		1.03	2.03		3.06	2.7		2.7	0.36	
17	2.98	6.43		1.17	2.0		3.17	2.51		2.51	0.66	
18	2.07	4.82		0.81	2.02		2.83	1.83		1.83	1.0	
19	1.13	4.75		0.45	1.98		2.43	1.97		1.97	0.46	
20	2.15	7.88		0.85	1.97		2.82	3.4		3.4		0.58
21	1.58	6.07		0.62	2.06		2.68	3.26		3.26	0.32	

*Operation

TABLE 58 (CASE 56)

Chloride Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl	Chloride intake				Chloride output			Balance	
				Salt g.	Food g.	Saline I.V. g.	Total intake g.	Urine g.	Suction g.	Total loss g.	+ g.	- g.
Apr. 24	0.99	4.3		0.61	3.32		3.93	2.61		2.61	1.32	
25	1.0	1.69		0.61	3.25		3.86	1.03		1.03	2.73	
26	1.0	2.7		0.61	3.25		3.86	1.64		1.64	2.72	
27	0.98	5.62		0.60	3.24		3.84	3.41		3.41	0.43	
28	0.99	6.24		0.61	3.25		3.86	3.7		3.7	0.16	
29	1.0	6.11		0.61	3.24		3.85	3.71		3.71	0.14	
30*		1.73	0.69			6.55	6.55	1.04	0.4	1.44	5.11	
May 1		3.04	1.39			4.37	4.37	1.84	0.96	2.8	1.57	
2		1.11	1.66			4.37	4.37	0.67	1.01	1.68	2.69	
3		0.18	4.52			4.37	4.37	0.11	2.74	2.85	1.52	
4	3.6	0.6		2.18	0.5		2.68	0.04		0.04	2.64	
5	4.0	0.19		2.43	0.42		2.85	0.11		0.11	2.74	
6	4.0	0.79		2.43	1.33		3.76	0.48		0.48	3.28	
7	5.12	1.69		3.11	1.82		4.93	1.03		1.03	3.8	
8	3.98	6.81		2.42	2.0		4.42	4.14		4.14	0.28	
9	3.91	7.84		2.48	2.09		4.57	4.75		4.75		0.18
10	3.99	11.12		2.42	2.58		5.0	6.76		6.76		1.76
11	1.12	9.24		0.68	2.77		3.45	5.61		5.61		2.16
12	3.47	5.97		2.10	2.69		4.79	4.74		4.74	0.05	
13	2.71	7.57		1.65	2.81		4.46	4.6		4.6		0.14
14	2.79	7.35		1.69	3.17		4.86	4.47		4.47	0.39	
15	2.0	6.53		1.21	3.24		4.45	3.98		3.98	0.47	
16	2.63	7.28		1.6	3.25		4.85	4.42		4.42	0.43	
17	2.98	6.43		1.81	3.25		5.06	3.9		3.9	1.16	
18	2.07	4.82		1.26	3.28		4.54	2.92		2.92	1.62	
19	1.13	4.75		0.69	3.23		3.92	2.88		2.88	1.04	
20	2.15	7.88		1.3	3.21		4.51	4.78		4.78		0.17
21	1.58	6.07		0.96	3.31		4.27	3.68		3.68	0.59	

*Operation

TABLE 59 (CASE 57)

Sodium Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Sodium intake				Sodium output				Balance	
			Salt g.	Food g.	Saline I.V. g.	Total intake g.	Urine g.	Stool g.	Suction g.	Total loss g.	+ g.	- g.
Oct. 3	3.04	7.81	1.2	2.18		3.38	2.73			2.73	0.65	
4	2.11	6.86	0.83	2.15		2.98	2.47	0.1		2.57	0.41	
5	1.89	8.2	0.75	2.13		2.88	3.32	0.2		3.52		0.64
6	1.37	5.57	0.54	2.12		2.66	2.4			2.4	0.18	
7	1.64	1.75	0.65	2.16		2.81	1.04			1.04	1.77	
8	1.69	5.57	0.67	2.14		2.81	2.8	0.1		2.9		0.09
9	1.66	6.5	0.65	2.16		2.81	2.71			2.71	0.1	
10	1.72	8.27	0.68	2.12		2.8	2.77	0.12		2.89		0.09
11	0.82	3.78	0.32	1.52		1.84	2.13	0.2	0.54	2.87		1.03
12*		3.65			2.6	2.6	1.3		0.22	1.52	1.08	
13		1.85			2.76	2.76	1.13		0.61	1.74	1.02	
14	0.13	1.9	0.13		1.3	1.43	0.58			0.58	0.85	
15	5.92	1.9	2.32	0.31		2.63	0.77			0.77	1.86	
16	6.84	4.42	2.69	0.71		3.4	1.91	0.28		2.19	1.21	
17	5.54	3.12	2.18	0.9		3.08	1.27	0.35		1.62	1.46	
18	2.58	2.83	1.0	1.28		2.28	1.56	0.31		1.87	0.41	
19	1.77	3.85	0.7	1.63		2.33	2.17	0.77		2.94		0.61
20	1.8	1.39	0.71	1.54		2.25	0.45	1.72		2.17	0.08	
21	1.75	5.32	0.69	1.97		2.66	1.96	0.17		2.13	0.53	
22	1.24	4.46	0.49	1.64		2.13	1.58	0.18		1.76	0.37	
23	1.57	6.24	0.62	1.78		2.4	2.12			2.12	0.28	
24	1.12	4.48	0.44	1.57		2.01	1.52	0.35		1.87	0.14	
25	1.82	7.5	0.71	1.92		2.63	2.64	0.36		3.0		0.37
26	1.33	8.2	0.52	1.67		2.19	3.2	0.17		3.37		1.18
27	1.2	4.86	0.47	1.7		2.17	1.74	0.1		1.84	0.33	
28	1.0	4.07	0.39	1.51		1.9	1.57	0.15		1.72	0.18	

*Operation

TABLE 60 (CASE 57)

Chloride Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Chloride intake				Chloride output				Balance	
			Salt g.	Food g.	Saline I.V. g.	Total intake g.	Urine g.	Stool g.	Suction g.	Total loss g.	+ g.	- g.
Oct. 3	3.04	7.81	1.84	3.32		5.16	4.76			4.76	0.4	
4	2.11	6.86	1.28	3.31		4.59	4.17	0.05		4.22	0.37	
5	1.89	8.2	1.15	3.26		4.41	4.98	0.07		5.05		0.64
6	1.37	5.57	0.83	3.27		4.1	3.38			3.38	0.72	
7	1.64	1.75	1.0	3.32		4.32	1.06			1.06	3.26	
8	1.69	5.57	1.03	3.28		4.31	3.38	0.02		3.4	0.91	
9	1.66	6.5	1.01	3.3		4.31	3.92			3.92	0.39	
10	1.72	8.27	1.05	3.4		4.45	4.8	0.02		4.82		0.37
11	0.82	3.78	0.5	2.4		2.94	2.3	0.04	1.25	3.59		0.65
12*		3.65			4.03	4.03	2.22		0.31	2.53	1.5	
13		1.85			4.27	4.27	1.12		0.9	2.02	2.25	
14	0.13	1.9	0.13		2.03	2.16	1.15			1.15	1.01	
15	5.92	1.9	3.6	0.54		4.14	1.15			1.15	2.99	
16	6.84	4.42	4.2	1.22		5.42	2.68	0.07		2.75	2.67	
17	5.54	3.12	3.36	1.46		4.82	1.92	0.05		1.97	2.85	
18	2.58	2.83	1.58	2.13		3.71	1.72	0.05		1.77	1.94	
19	1.77	3.85	1.07	2.75		3.82	2.34	0.97		3.33	0.49	
20	1.8	1.39	1.1	2.35		3.45	0.84	2.6		3.44	0.01	
21	1.75	5.32	1.06	3.09		4.15	3.23	0.05		3.28	0.87	
22	1.24	4.46	0.75	2.58		3.33	2.7	0.02		2.72	0.61	
23	1.57	6.24	0.95	2.79		3.74	3.75			3.75		0.01
24	1.12	4.48	0.69	2.36		3.05	2.72	0.1		2.82	0.23	
25	1.82	7.5	1.11	3.08		4.19	4.57	0.12		4.69		0.5
26	1.33	8.2	0.81	2.48		3.29	4.98	0.04		5.02		1.73
27	1.2	4.86	0.73	2.8		3.53	2.96	0.04		3.0	0.53	
28	1.0	4.07	0.61	2.36		2.97	2.49	0.11		2.6	0.37	

*Operation

TABLE 61 (CASE 58)

Sodium Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl	Sodium intake				Sodium output				Balance	
				Salt g.	Food g.	Saline I.V. g.	Total intake g.	Urine g.	Stool g.	Suction g.	Total loss g.	+ g.	- g.
Aug. 14	0.7	6.9		0.27	1.94		2.22	2.73			2.73		0.51
15	0.89	4.1	3.94	0.35	1.8		2.16	1.66		0.32	1.98	0.18	
16	0.33	0.76	0.9	1.49[x]	1.02		2.51	0.43		0.21	0.64	1.87	
17	1.0	0.54		3.11[x]	2.05		5.16	2.05			2.05	3.11	
18	1.35	1.09		1.89[x]	2.16		4.05	3.3		0.13	3.43	0.62	
19	1.07	1.21	0.96	0.42	1.74		2.16	3.36			3.36		1.2
20*			1.95			3.49	3.49			0.31	0.31	3.18	
21	2.27	7.64				2.27	2.27	4.98		0.15	5.13		2.86
22	8.4	4.84		3.12	0.15		3.27	1.82			1.82	1.45	
23	5.71	0.76		2.25	0.36		2.61	0.37	1.02		1.39	1.22	
24	4.54	1.66		1.79	0.71		2.5	0.18	0.79		0.97	1.53	
25	4.01	1.27		1.59	0.89		2.47	0.16	0.79		0.95	1.52	
26	4.4	2.42		1.73	1.39		3.12	0.34			0.34	2.78	
27	4.41	3.82		1.28	1.62		2.9	0.65			0.65	2.25	
28	1.15	5.07		0.45	2.08		2.53	1.59	0.35		1.94	0.59	
29	2.0	5.08		0.78	2.2		2.98	1.71	0.2		1.91	1.07	
30	1.99	4.17		0.78	2.13		2.91	1.41	0.34		1.75	1.16	
31	1.66	6.37		0.65	2.07		2.72	2.51	0.25		2.76		0.04
Sept. 1	1.02	4.74		0.4	2.02		2.42	2.33	0.14		2.47		0.05
2	1.77	3.7		0.7	1.95		2.65	1.51	0.62		2.13	0.52	
3	1.32	3.86		0.52	2.01		2.53	1.47	0.04		1.51	1.02	
4	1.36	5.23		0.53	1.91		2.44	2.05	0.05		2.1	0.34	
5	1.85	4.48		0.73	1.5		2.23	1.74	0.1		1.84	0.39	

[x]Includes sodium in alkaline powders

*Operation. Sodium and chloride of transfused blood not included

TABLE 62 (CASE 58)

Chloride Intake, Output and Balance

Date	Oral salt intake g.	Urine chloride as g.NaCl	Suction chloride as g.NaCl	Chloride intake				Chloride output				Balance	
				Salt g.	Food g.	Saline I.V. g.	Total intake g.	Urine g.	Stool g.	Suction g.	Total loss g.	+ g.	- g.
Aug. 14	0.7	6.9		0.42	3.28		3.7	4.18			4.18		0.48
15	0.89	4.1	3.94	0.54	2.93		3.47	2.49		2.39	4.88	1.41	
16	0.33	0.76	0.9	0.2	1.64		1.84	0.46		0.55	1.01		0.83
17	1.0	0.54		0.6	3.29		3.89	0.33			0.33	3.56	
18	1.35	1.09		0.82	3.33		4.15	0.66			0.66	3.49	
19	1.07	1.21	0.96	0.65	2.85		3.5	0.73		0.58	1.31	2.19	
20*			1.95			5.37	5.37	0.12		0.7	0.82	4.55	
21	2.27	7.64				3.51	3.51	4.63		0.52	5.15		1.64
22	8.4	4.84		4.82	0.29		5.11	2.94			2.94	2.17	
23	5.71	0.76		3.46	0.63		4.09	0.46	1.09		1.55	2.54	
24	4.54	1.66		2.78	1.22		4.0	1.01	0.97		1.98	2.02	
25	4.01	1.27		2.43	1.45		3.88	0.77	0.54		1.31	2.57	
26	4.4	2.42		2.67	2.25		4.92	1.37			1.37	3.55	
27	4.41	3.82		2.05	2.7		4.75	2.32			2.32	2.43	
28	1.15	5.07		0.7	3.17		3.87	3.08	0.22		3.3	0.57	
29	2.0	5.08		1.22	3.13		4.35	3.09	0.17		3.26	0.99	
30	1.99	4.17		1.21	3.37		4.58	2.43	0.07		2.5	2.08	
31	1.66	6.37		1.01	3.37		4.38	3.87	0.12		3.99	0.39	
Sept. 1	1.02	4.74		0.62	3.33		3.95	2.88	0.06		2.94	1.01	
2	1.77	3.7		1.07	3.25		4.32	2.25	0.05		2.3	2.02	
3	1.32	3.86		0.8	3.29		4.09	2.32	0.04		2.36	3.73	
4	1.36	5.23		0.83	3.11		3.94	3.18	0.05		3.23	0.71	
5	1.85	4.48		1.12	2.5		3.62	2.72	0.05		2.77	0.85	

*Operation

TABLE 63

BLOOD CHEMISTRY

Date	Case No.	Haemoglobin % Haldane	Red blood corpuscles millions per cu.mm.	Packed cell volume %	Albumin g. per 100 ml.	Globulin g. per 100 ml.	Total protein g. per 100 ml.	Whole blood chloride mg. per 100 ml.	CO_2 combining power volumes per 100 ml.	Creatinine mg. per 100 ml.
Dec. 2		116	5.62	47	4.2	1.55	5.75			
5*		114	5.7	50	4.19	1.58	5.77			
9		96	4.64	41	4.03	2.0	6.03	440	56	1.0
12	1	98	4.8	40	3.9	2.63	6.53	450	65	1.0
16		98	4.89	41	3.68	2.98	6.66	464	65	1.0
19		92	4.62	42	3.6	2.95	6.55	464	60	1.0
Jan. 16		114	5.08	47	3.53	3.08	6.61	412	61	1.1
17*										
20		104	4.73	45	3.75	2.6	6.35	396	75	1.2
23	4	100	5.07	43	3.69	2.6	6.29	460	56	1.0
27		100	5.11	44	4.14	2.45	6.59		65	1.3
30		108	5.29	46	3.99	3.0	6.99	428	63	1.7
Apr. 17		114	5.57	50	4.29	2.05	6.34	432	62	
21		116	5.74	51	3.6	3.35	6.95	420	56	
26*	6									
28					3.99	2.43	6.42	436	62	1.0
Mar. 1		110	5.38	47	4.06	1.95	6.01	470	58	1.0

*Operation

TABLE 64

BLOOD CHEMISTRY

Date	Case No.	Albumin g. per 100 ml.	Globulin g. per 100 ml.	Total protein g. per 100 ml.	Whole blood chloride mg. per 100 ml.	CO_2 combining power volumes per 100 ml.	Urea nitrogen mg. per 100 ml.
Sept. 1	10	3.8	2.5	6.3	408	62	18
4*		4.0	2.5	6.5	414	67	17
8		4.6	2.5	7.1	420	68	15
10		4.9	2.4	7.3	440		15
15		4.7	2.1	6.8	440	70	14
18		4.8	2.0	6.8	456	61	15
Sept. 1	11	4.0	2.1	6.1	448	66	15
4*		3.8	2.7	6.5	414	66	12
8		4.8	2.0	6.8	430	64	12
15		4.4	2.1	6.5	408	62	12
18		4.4	1.9	6.3	450	63	12
Sept. 1	12	4.0	2.0	6.0	420	59	19
4*		4.4	1.9	6.3	380	60	13
8		4.5	2.3	6.8	380	60	16
11		4.6	2.2	6.8	434	61	19
15		4.6	2.4	7.0	402		20
18		4.6	1.7	6.3	438	74	17

*First day of three-day period of starvation

TABLE 65

BLOOD CHEMISTRY

Date	Case No.	Haemoglobin % Haldane	Red blood corpuscles millions per cu.mm.	Packed cell volume %	Albumin g. per 100 ml.	Globulin g. per 100 ml.	Total protein g. per 100 ml.	Non-protein nitrogen mg. per 100 ml.	Plasma chloride mg. per 100 ml.	Whole blood chloride mg. per 100 ml.	Serum sodium mg. per 100 ml.	Serum potassium mg. per 100 ml.
Oct. 1					3.35	1.68	5.03	32				
4		116	5.7	48	3.81	2.1	5.91		600		322	
9		114	5.59	51	4.03	1.75	5.78		600		308	
15		112	5.42	46	4.43	2.4	6.83	28	588		326	
22*		110	5.48	47							315	
24	15				3.88	2.3	6.18			452	317	
29		100	4.92	44	3.63	2.14	5.77			460	312	
31		96	5.22	41	3.75	2.6	6.35			448		18.3
Nov. 5		94	5.14	41	3.18	2.85	6.03	36		476	309	
7		94	5.17	40	3.79	2.6	6.39			496	338	19.8
11		92	4.98	41	3.92	2.2	6.12	37		488	315	20.6
Nov. 1		114	5.43	50	4.15	2.53	6.68				306	
5					3.75	2.53	6.28	34		452	315	
7		110	5.1	50	4.29	2.13	6.42				308	
11	16	114	5.58	51	4.56	2.83	7.39	34		450	304	
12*												
14		94	4.61	41	3.74	2.63	6.37	34		442	304	
18		96	4.68	40	3.75	2.63	6.38	32		450		
21		98	4.81	43	3.58	2.6	6.18	32		466		

*Operation

TABLE 66

BLOOD CHEMISTRY

Date	Case No.	Haemoglobin % Haldane	Red blood corpuscles millions per cu.mm.	Packed cell volume %	Albumin g. per 100 ml.	Globulin g. per 100 ml.	Total protein g. per 100 ml.	Whole blood chloride mg. per 100 ml.	CO_2 combining power volumes per 100 ml.	Urea nitrogen mg. per 100 ml.	Creatinine mg. per 100 ml.	Plasma amino acid N mg. per 100 ml.
Apr. 28		120	5.51	51	4.49	2.15	6.64	456	62	21	1.2	4.76
May 1*							6.56	428	60	15	1.7	4.4
2								420	62		1.2	5.56
3									70			5.84
5		110	5.33	47	3.19	1.98	5.17	440	67	39	1.1	4.76
8	22	88	4.54	40	3.15	2.08	5.23	480	54	20	1.0	4.5
10								472		14		5.3
12		100	4.89	42	3.45	2.08	5.53	480	55	18	1.5	5.6
15		96	4.91	42	3.88	2.65	6.23	460	55	22	1.2	5.5
19												4.8
Oct. 11					4.06	1.70	5.76		67	17		
13				60	3.9	1.65	5.55	410		18	1.8	5.2
21				58	4.54	2.41	6.94	400	61	12	1.9	5.2
23*	44	96	5.27	59	3.75	2.33	6.18	404	70	11	1.6	5.7
27		98	5.18	40	3.63	2.25	5.88	404	64	18	1.9	5.8
29				34	1.93	2.94	4.87		54	50	3.3	5.7

*Operation

TABLE 67

BLOOD CHEMISTRY

Date	Case No.	Haemoglobin % Haldane	Red blood corpuscles millions per cu.mm.	Packed cell volume %	Albumin g. per 100 ml.	Globulin g. per 100 ml.	Total protein g. per 100 ml.	Whole blood chloride mg. per 100 ml.	CO_2 combining power volumes per 100 ml.	Urea nitrogen mg. per 100 ml.	Non-protein nitrogen mg. per 100 ml.	Creatinine mg. per 100 ml.	Plasma amino acid N mg. per 100 ml.	Uric acid mg. per 100 ml.
Nov. 20		112	5.37	51	4.33	2.5	6.83	400	64	13	24	1.8		
24		110	5.35	54	4.19	2.25	6.44	430	64	12	47	1.8		
25*														
27		110	5.31	52	4.1	2.25	6.35	364	64	37	68	1.8		
Dec. 1	47	92	4.95	44	3.8	2.08	5.88	370	59	33	68	2.0		
4		92	4.57	40			5.06	410	52	17	38	2.1		
8		94	4.48	42	3.13	2.18	5.31	400	57	17	38	1.7		
11					3.24	2.2	5.44	440	61	21	37	2.2		
Jan. 15				41				444		26	42		11.05	
16*				44						18	37	1.4	10.4	4.46
17				38				474		18	39	1.4	9.75	3.32
18				40				456		19	37	1.4	9.75	3.16
19				39				448		24	39	1.3		3.0
20	49			39				496		25	44	1.4	10.56	3.15
21				38				458		23	42	1.4	11.42	3.05
22				38				474		23	42	1.4	10.4	3.14
23				38				456		21	40	1.4	10.4	3.68

*Operation

TABLE 68

BLOOD CHEMISTRY

Date	Case No.	Packed cell volume %	Albumin g. per 100 ml.	Globulin g. per 100 ml.	Non-protein nitrogen mg. per 100 ml.	CO_2 combining power volumes per 100 ml.	Serum sodium mg. per 100 ml.	Plasma chloride mg. per 100 ml.	Whole blood chloride mg. per 100 ml.	Plasma chloride, mg. per 100 ml. of blood	Cell chloride, mg. per 100 ml. of blood	Cell/plasma ratio
Feb. 25		50	5.13	1.10	42.4		305	552	408	276	132	0.49
28		49	5.05	1.15	55.2	64	317	564	434	298	136	0.46
Mar. 2*		48	4.84	1.35	38.4	66		554	418	288	130	0.45
3		45	4.81	1.11	44.8	68	H	572	452	315	137	0.43
4		42	4.24	1.14	32.8	64	321	570	450	331	119	0.36
5		40	4.3	1.19	32.4	70	326	562	432	337	95	0.28
6	55	38	4.23	1.14	44.8	73	314	542	456	336	120	0.36
7		38	4.37	1.2	23.2		323	542	444	336	108	0.32
8		38	4.45	1.21	25.6	61	324	536	420	332	88	0.26
9		38	4.25	1.25	27.2		327	554	468	344	124	0.36
10		36	4.43	1.29	32.8	70	328	560	476	358	118	0.33
11			4.33	1.08	34.4		327	556	474			
12		36	4.83	0.78	28.0		326	548	474	350	124	0.36
Apr. 28		48	4.76	1.08	34.4			568	436	296	140	0.47
29		48	4.71	1.15	33.6		310	568	440	296	144	0.49
30*		49	4.76	1.35	33.6	65	302	566	436	289	147	0.51
May 1			4.0	1.17		68	299	552				
2		36	H	H	H	H	293	564	440	361	79	0.22
3		32			27.6	61	306	556				
5	56	30	3.93	1.7	30.4	67	304	552				
6		30	3.83	1.7	31.2	68	300	552				
7		30	3.79	1.6	30.4		310	546	462	396	66	0.17
8		31	4.06	1.87	19.2	62	311	566				
10		32	4.19	1.79	28.4		310	568	450	400	50	0.12
12		35	4.23	1.9	32.0		308	570	478	370	108	0.29
14		34	4.13	1.8	29.2	65	303	566	468	362	106	0.29
Oct. 5		48				58		550	440	286	154	0.54
8		48				70	326	530	434	276	158	0.57
11		46				65	324	562	440	304	136	0.45
14*		42				63		552	424	320	104	0.33
16	57	37				65	310	550	424	347	77	0.22
18		42				63	lost	566	442	328	114	0.35
21		41				55	326	568	464	335	129	0.39
25		40				63		560	454	336	118	0.35
28		42					326	546	440	317	123	0.39

*Operation

H = blood haemolysed

TABLE 69

Blood Volume Estimations

Case No.	Day	Packed cell volume per 100 ml. blood	Plasma volume, ml.	Blood volume, ml.	Extracellular fluid, volume ml.	Total protein g. per 100 ml.	Albumin, g. per 100 ml.	Globulin, g. per 100 ml.	Total circulating albumin, g.	Total circulating globulin, g.	Non-protein nitrogen, mg. per 100 ml.	Serum sodium, mg. per 100 ml.	Serum potassium, mg. per 100 ml.	Whole blood chloride (as NcCl) mg. per 100 ml.
53	0*- 4	31.0	2500	3620	15,550	6.19	2.56	3.63	64.0	90.8	69.6	300		442
	0 + 1	38.0	2100	3380	17.580	6.35	2.42	3.93	48.8	82.6	36.0	300		488
41	0 - 16	37.5	2820	4520	13,300	6.87	3.51	3.36	99.0	95.0	77.6	317	19.1	484
	0	40.0	2880	4800	12,700	6.67	3.72	2.95	107.0	85.0	35.2	324	18.6	522
	0 + 2	40.0	2510	4200	12,000	6.11	3.29	2.82	82.5	71.0	51.2	320	16.0	494
	0 + 12	33.0	2960	4420		5.6	2.95	2.65	87.4	78.6	20.0	321		574
54	0 - 1	48.0	2770	5320	14,400	6.07	3.82	2.25	106.0	62.0	22.4	308	17.4	572
	0 + 2	43.0	3430	6020	15,900	5.45	3.42	2.03	117.0	69.6	21.6	302	18.4	522
	0 + 10	42.0	3380	5830	14,800	5.84	3.39	2.45	115.0	83.0	17.6	304	16.9	556

*0 = day of operation

TABLE 70

Comparison of Nitrogen Intake, Output and Balance

Case No.	Operation	Dietetic Treatment	Intake nitrogen (0-10 days)			Output nitrogen					
			Food N g.	Casydrol N g.	Total N g.	Urine N g. (0-6 days)	Urine N g. (0-10 days)	Stool N g. (0-10 days)	Suction N g. (0-10 days)	Total output N g. (0-10 days)	Total -ve N balance g (0-10 days)
1	Gastrectomy	Routine	65.54		65.54	107.04	147.5	8.78	7.81	164.09	98.55
5	Vagotomy	Very low intake	14.96		14.96	83.17	121.46	3.5	nil	124.96	110.0
16)	Gastrectomy	High protein caloric intake before operation	78.54		78.54	113.54	168.23	13.68	2.1	184.01	105.47
17)			116.76		116.76	80.31	139.4	9.64	9.8	158.84	42.08
46)	Gastrectomy	Milk mixture after operation	171.61		171.61	94.11	164.74	20.21	2.83	187.78	16.17
50)			129.78		129.78	104.09	144.77*	9.78	4.01	158.56*	16.62*
22)	Gastrectomy	Casydrol infusion	31.19	66.83	98.02	147.37	215.59	7.61	1.84	225.04	127.02
23)			48.47	69.0	117.47	143.03	215.75	6.21	4.54	226.5	109.03
24)			53.01	43.89	96.9	126.75	205.34	4.5	nil	209.84	112.94
25)			56.06	70.47	126.53	144.53	223.28	3.63	2.88	229.79	103.26
42	Gastrectomy	Amigen infusion	77.26	40.96	118.22	103.56	167.25	3.1	5.51	175.86	57.64

*One specimen of urine lost, probably containing about 15 g. nitrogen.
Post-operative periods, 0-6 days and 0-10 days, are, respectively, day of operation and succeeding 5 and 9 days.

TABLE 71

Total Urinary Amino Acid Nitrogen Excretion (g. per day)

Case No.	Operation and Treatment	Days before Operation						Operation	Days after Operation														
		6	5	4	3	2	1		1	2	3	4	5	6	7	8	9	10	11	12	13	14
10)	Controls:	0.9	0.46	0.46	lost	0.31	0.3	0.14	0.45	0.65	0.58	0.76	0.34	0.47	0.69	0.47	0.93	lost	0.26	0.54	0.3	0.82
)	Starvation of																					
11)	protein and	0.53	0.75	0.75	lost	0.78	0.82	0.36	0.66	0.53	0.44	0.49	0.59	0.57	0.84	0.76	1.12	0.23	1.16	0.5	0.61	1.07
)	calories.																					
12)	No operation.		0.61	0.61	0.62	0.97	0.67	0.11	0.42	0.43	0.54	0.67	0.59	0.4	0.42	0.65	0.65	0.43	0.56	0.37	0.67	0.53
7	Splanchnicectomy	0.26	0.47	0.41	0.36	0.39	0.25		0.28	0.26	0.38	0.21	0.18	0.2	0.21	0.35	0.32	0.32	0.2	0.28	0.24	D
20	Gastrectomy					0.67	0.55	0.09	0.99	lost	0.62	0.69	0.43	0.58	1.24	1.3	lost	1.78	1.24	2.18	1.24	2.42
24)	Gastrectomy:		0.54	0.4		0.52	1.53	0.41	1.62*	1.69*	3.5*	1.4*	0.84	1.15	1.32	1.44	0.93	0.66	0.94	0.62	1.09	
25)	Casydrol	1.18	1.3	1.52	1.67	0.86	1.98	0.36	3.02*	3.3*	4.23*	5.95*	4.62*	1.68	2.75	1.62	2.07	1.76	1.23			
40	No operation: Starvation, Casydrol				0.33	0.43	0.38	0.34	0.53*	0.54*	1.01*	1.02	0.39									
42	Gastrectomy: Amigen			0.22	0.22	0.13	0.2	0.14	0.18*	1.36*	0.96*	0.85*	0.24	0.34	0.31	0.5	0.47	0.27	0.24	0.2		
43)	Gastrectomy:	0.45	0.46	0.45	0.57	0.16	0.26	0.11	0.23	0.22	0.14	0.3	0.64	0.31	0.35	0.31	0.19	0.47	0.17	0.15	0.31	0.3
44)	Plasma	0.36	0.25	0.19	0.28	0.23	0.18	0.21	0.33	0.3	0.35	lost	0.2	D								
45	Gastrectomy: Milk mixture							0.11	0.44	0.44	0.2	0.25	0.32	0.22	0.32	0.36	0.18	0.22	0.23	0.34	0.34	0.16

D = died. * = casydrol, amigen or plasma infusion

TABLE 72

LIMB MEASUREMENTS (in cm.)

Case No.	Date	Mid thigh		Mid calf		Mid arm		Mid forearm		Body weight in lb.
		R	L	R	L	R	L	R	L	
	July 14	48.0	48.0	32.5	32.5	27.5	27.5	27.0	27.0	140.25
	15*									
	16	46.5	46.5	32.5	32.5			27.0	26.5	
	17	45.5	44.5	D	32.5	26.0	26.0	26.0	26.0	
	18	46.5	46.0	D	32.5	26.5	26.5	26.0	26.0	
24	20	43.5	44.5	D	32.0	25.0	25.0	25.3	25.0	
	21	43.5	44.5	D	30.5	25.0	25.0	25.5	25.0	135.4
	23	43.5	43.5	32.0	30.0	25.0	24.5	25.0	25.0	133.5
	27	42.0	43.0	T	28.5	24.5	24.0	25.0	25.0	126.0
	28	42.0	41.5	T	29.0	24.0	24.0	24.5	25.0	
	29	41.0	42.0	T	28.8	24.0	24.0	25.0	26.0	
	31	42.0	39.0	T	29.0	24.5	23.5	25.5	24.5	

D = drip infusion. T = venous thrombosis.

Case No.	Date	Mid thigh		Mid calf		Mid arm		Mid forearm		Body weight in lb.
		R	L	R	L	R	L	R	L	
	July 14	44.0	42.0	29.6	29.6	24.3	24.6	24.3	24.0	120.25
	16	42.0	42.5	29.5	29.0	25.0	25.0	24.5	25.0	117.25
	17*									
	18	41.5	40.0	D	28.5	23.5	23.0	24.0	24.5	
	20	41.0	39.0	D	28.0	22.0	23.0	23.0	23.0	
25	21	40.0	39.0	29.5	D	22.5	23.2	23.5	24.0	120.0
	23	42.0	39.0	30.0	28.0	22.5	23.0	23.0	23.5	120.5
	27	38.5	37.0	27.5	26.5	22.2	22.5	23.0	23.0	115.8
	28	39.5	37.2	27.0	26.0	22.2	22.5	24.0	23.2	
	29	38.0	37.8	27.0	27.0	22.5	22.5	23.8	23.5	
	31	37.5	37.0	27.0	26.5	22.5	23.0	23.8	23.5	114.5
	Aug. 2	38.0	37.0	26.5	26.5	22.5	23.0	24.0	23.8	

D = drip infusion.