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Pernicious anemia

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PERNICIOUS ANEMIA

Ray B. Farnsworth

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PERNICIOUS ANEMIA -- TREATMENT

CLASSIFICATION. At the present time, there are *(1) two classifications of the anemias that are, perhaps, equally popular. These are: (1) Barker's, which outlines two groups, for example, (a) anemias caused by hemolytic or augmented blood destruction, and (b) anemias caused by impaired bone marrow activity or decreased blood formation; and (2) Vogel and Todd's which outlines four groups, for example, (a) anemias due to (1) increased fragility of erythrocytes or hemolysins (II), (b) anemias due to loss of blood from the body, (c) anemias due to failure in hemogenesis and (d) anemias due to increased hemolysins combined with decreased hemogenesis.

In Group (a) of Todd and Vogel's classification we find: Addisonian anemia, Dibothriocephalus anemia, some anemias due to cancer, syphilis and puerperal toxemia, hemolytic jaundice malarial anemia and anemias due to hemolytic poisons (venom, mushrooms, etc.). To Group (b) belong: anemias caused by hemorrhage (acute or chronic), with low urobilin content in the feces. In Group (c) are anemias due to faulty hemogenesis (chlorosis, aplastic anemia and anemia from benzol poisoning). To Group (d) belong most secondary anemias, anemias of leukemia and those of bone marrow neoplasms.

* See Bibliography.

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Today the following opinions are widely held:

1. That the blood destruction in pernicious anemia is caused by some hemolytic agent.
2. That specific treatment cannot be begun until this hemolytic agent is found.
3. That aplastic anemia is the result of an etiological factor totally different from the exciting cause of Addison's anemia.

BLOOD PICTURE IN PERNICIOUS ANEMIA

1. Low red cell count (usually below 2,000,000 and perhaps less than 500,000); anisocytosis, with marked eccentric achromia; abundance of macrocytes, microcytes and poikilocytes; considerable polychromatophilia, basophilic stippling and sometimes nucleated red cells of all kinds.
2. Considerable decrease in hemoglobin, yielding color index of plus and plus 1.5 - occasionally higher.
3. Leukopenia - with absolute decrease in polymorphonuclear neutrophiles and eosinophiles and relative increase in lymphocytes and mononuclears.

Because of the striking remissions in this disease, the blood picture varies considerably from time to time, and repeated examinations are necessary for a correct diagnosis.

TREATMENT. The generally accepted therapeutic methods are: (1) hygiene and diet, (2) iron, arsenic and kindred drugs and (3) transfusions.

PERNICIOUS ANEMIA -- LIVER EXTRACT THERAPY

Over 160 cases have been treated by means of liver ^{*(2)} extract in thirteen clinics that have collaborated with the committee on Pernicious Anemia in estimating its therapeutic value.

The amounts given daily have usually varied from the extract derived from 300 to 600 gm. of liver. A few cases have been given daily extract from 800 to 1200 gm. of liver. The amount of this extract given has, therefore, varied usually from about 10 to 20 gm. per day.

Sometimes cases with less than 2 million red blood cell corpuscles per cu. mm. of blood, fed daily extract from 500 to 600 gm. of liver, have had their cells increased by 3 million per cu. mm. in a month, but on the average either of these amounts of extract has caused an increase of about 2.6 million cells per cu. mm. in this period of time. Cases treated daily with liver extract obtained from 800 to 1200 gm. of liver for the first six to fourteen days and then daily an amount from 600 gm., yield no definite evidence that these large amounts cause the manufacture of cells at a faster rate. No definite distinction in the number of cells produced during the first thirty days of therapy has been observed when the standardized extract derived from 400 to 500 and 600 gm. of liver has been given daily to entirely comparable cases. There is perhaps a

slightly greater rate of increase of the corpuscles, especially in the first ten days, when the larger amounts are given, and a statistical study of the maximum productions of cells further suggests that extract derived from 500 to 600 gm. of liver is slightly more efficacious than 400.

The accumulated evidence indicates that the red cells continue to rise in an orderly manner when the daily feeding of suitable amounts of potent fractions is continued beyond thirty days. The exact rate of their increase after a month as a result of taking fraction cannot be determined yet, since until recently there has been little potent material available. In many instances as soon as the patient had improved distinctly and his red blood cells had increased two million per cu. mm. he was placed on liver or kidney, reserving the supply of fraction for individuals who were in a more serious condition.

The necessity for prolonged continuation of liver therapy must be emphasized. Up to the present time the chief cause for patients with pernicious anemia to develop significant decreases in the level of their red blood cells, after they have once reached normal, following the eating of liver or kidney has been the omission of these foods from their diet, or the ingestion of an inadequate amount. It is possible that a suitable maintenance dose of liver extract will be found to vary for different patients. The further experience of many observers will unquestionably establish concrete information, concerning dosage, particularly when the concentration of red blood cells

is above 4.5 million per cu. mm.

Numerous cases with high counts have been placed daily either upon the standard extract from 200 to 100 gm. of liver, and it appears that more than this latter amount is often a desirable quantity. It is important not to allow the dose to become too small to maintain at normal the red blood cell level. It is also desirable not to put an unnecessary strain upon the bone marrow. Red blood cell counts in the vicinity of six million per cu. mm. have occurred as a result of liver therapy. Under these circumstances the amount of active principle administered should be curtailed.

Blood of patients should be examined from time to time, and the amount of active principle prescribed be dependent upon the state of blood, and upon symptoms or signs manifested by the patient. If neurological disorders appear to progress, more of the active principle should be given. An infectious process may cause the red blood cell count to fall, or prevent its rise, and under such circumstances maximal amounts of potent material should be fed.

Although the rate of increase in the concentration of red blood cells often has been more rapid in patients upon fraction than in those given whole liver, the rate of hemoglobin formation on the average has appeared to be somewhat slower.

The patients who have received liver extract have been given routinely no treatment other than an adequate well-

balanced diet containing no liver or kidney; and when their red corpuscles were low complete rest in bed. The diet for each patient is prescribed for that individual, taking into consideration his weight and all aspects of the case. The importance of partaking of sufficient food to supply liberally, but not excessively, all requirements of the body has been emphasized and patients have been advised that their diet should contain liberal amounts of green vegetables and fruit and that an excess of carbohydrate and free sugar be avoided. No unusual amount of protein is necessary but the patient must receive a sufficient supply of various sorts of protein to promote nutrition and stimulate digestive secretion. Fat in large amounts can hinder digestion and for various reasons may be undesirable in some cases, yet in others large amounts, or substances contained in fats--may be advantageous to help improve and maintain the patient's health.

Dilute hydrochloric acid, U.S.P. may aid in decreasing gastrointestinal symptoms and improving disordered gastric function. Transfusion of whole blood in desperately ill patients, exercise to retain muscles, and various symptomatic measures must be considered upon occasions.

No contraindication to the use of liver extract is known. Liver extract #343 gave uniform results during the five months period that it was being tested in the clinics collaborating with the Committee on Pernicious Anemia of the

Harvard Medical School.

PERNICIOUS ANEMIA -- HYDROCHLORIC ACID AND PEPSIN THERAPY

The importance of hydrochloric acid in gastric *(3)
digestion has long been known, though its value as a gastro-
intestinal antiseptid does not seem to have been sufficiently
realized.

In a normally secreting stomach, the gastric juice maintains the stomach contents and probably the upper part of the duodenum in a relatively sterile condition. On the other hand, impairment of acid secretion paves the way for infection via the channel. To counteract this weakening of the body's defense to infection through the upper alimentary tract, hydrochloric acid has been given therapeutically; its use in the treatment of pernicious anemia was based upon this idea, small doses of 10 to 20 minims of the official British preparation being given. It was shown by several investigators that these small doses are inadequate, and that, in order to maintain an acid condition in the stomach, at least 2 drams would be necessary, given by a continuous method.

In administering these larger doses of acid, well diluted, with each meal, it was found that many patients were unable to tolerate single doses of more than $1-1\frac{1}{2}$ drams; but doses of $\frac{1}{2}$ dram, or 1 dram at a time, well diluted were tolerated by nearly all patients.

In a study of 110 cases of pernicious anemia, on the liver diet it was noted that a relatively high percentage of

patients suffer from a flatulent dyspepsia frequently associated with diarrhoea. As a rule neither of these symptoms has been relieved by the liver diet, either with or without the addition of dilute hydrochloric acid; in some cases they have been increased. In these cases there was always found, in addition to the absence of hydrochloric acid, a marked diminution of peptic activity. The persistence of achylia, despite the striking improvements shown in the blood counts, and indeed in the patient's condition generally, has been observed by many workers.

In all cases of pernicious anemia, in addition to liver, a mixture of three parts official glycerinum pepsini and one part acid hydrochlor. dil., two drams, was prescribed, to be taken as a routine measure in six to eight ounces of water, flavored if necessary with lemon or orange juice--and sipped throughout each meal. This has never failed to relieve the symptoms of dyspepsia and diarrhoea. Patients take it four times daily at first, later three times daily. Three cases in the series reported call for comment.

1. A man developed urticaria when put on the liver diet; this was marked with fresh liver, less marked with liver extract. He was troubled also with flatulence and a persistent diarrhoea. All these symptoms cleared up at once when the prescribed pepsin and hydrochloric acid mixture was taken.

2. A woman was found to have achlorhydria and diminished peptic activity. She was not at the time suffering from

Pernicious Anemia, although several members of her family had the disease. The routine mixture was prescribed, but unfortunately developed urticaria, which was cured only when the medicine was discontinued.

3. A man was unable to tolerate hydrochloric acid in any way, not even in the form of betaine hydrochloride, which has been used occasionally as a source of hydrochloric acid.

The value of pepsin as an adjunct in the treatment of pernicious anemia has been recognized for some time. Hurst advocated the addition of a grain of pepsin to each dram of dilute acid in order to improve gastric digestion, although this suggestion does not appear to be widely known. It should, of course, be remembered that commercial pepsin and hydrochloric acid alone do not constitute an adequate treatment for pernicious anemia; liver treatment must be the standard, but the combination is efficacious in the relief of the frequently distressing gastrointestinal symptoms associated with the condition--the flatulent dyspepsia associated with diarrhea and the occasional cases of urticaria developed by the liver therapy.

The use of hydrochloric acid in the treatment of pernicious anemia has been advised and practiced for many years. The attempt to replace the acid which is absent from the stomach of these patients is certainly rational, but it is extremely doubtful whether the maximal dosage ordinarily employed accomplish-

es very much in this direction. However, one or two drams (4 or 8cc.) of the U.S.P. dilute acid in a glass of water before or during meals and again upon retiring is frequently followed by remissions of long duration.

The use of the acid, and the good results which sometime follow thereon, accord well with one of the theories of the etiology of the disease, namely, that one which holds the disease to be due to the fact that the absence of gastric acid permits the fecal flora to contaminate the small intestine and also allows pathogenic organisms to enter from above; these organisms, once established in the absorptive portion of the tract, give rise to hemolytic and neurotoxic substances which cause the characteristic symptoms of the disease.

PERNICIOUS ANEMIA -- USE OF DESSICATED STOMACH THERAPY

After the discovery by Minot and Murphy of the ^{*}(4) beneficial effects of liver therapy in pernicious anemia and the preparation of an active extract by Cohn and his associates, the way for further study was opened by the demonstration by Castle that the stomach of normal persons secreted a substance which could develop a blood-maturing principle from meat. After a consideration of these investigations, it seemed advisable to test the activity of gastric tissue itself. Work was started at the Simpson Memorial Institute on the nature of the material in stomach which could produce a hematopoietically active substance but the experiments were later carried on with the association

of Dr. Elwood A. Sharp. Dr. Sharp working on the basis of an original theory, concluded that the feeding of stomach should have the same effect on patients with pernicious anemia as liver. The work of both laboratories was then centralized and the experimental material tested under controlled conditions. The preparation used was made by desiccating fresh whole hog stomach so that 30 Gm., of the dried substance represented 190 Gm. of fresh tissue. In later material the fat from the preparation was removed by petroleum benzin, so that 30 Gm. of the final material represented 218 Gm. of the fresh tissue. The resultant product was a great improvement, as it had very little odor and practically no taste.

Daily feedings of from 15 to 30 Gm. of this residue in suspension in water were given to three consecutive patients with typical pernicious anemia. In all three there was a prompt and very active response characterized by an increase in the percentage of reticulated red blood cells which was at least comparable with, if not greater than, the increase in the reticulocyte percentage induced by feeding an active commercial extract made from 300 to 600 Gm. of fresh liver.

The observation that the feeding of desiccated whole hog's stomach produces a complete remission in pernicious anemia supplements and substantiates the work of Castle, since it indicates that stomach tissue contains a red blood cell maturing substance. The question of the origin of the active principle in the desiccated stomach is now being tested experimentally. Several possibilities may be considered. One is the presence of an enzyme or similar

substance which may act on the protein present in the stomach tissue during the period that elapses after the organ is removed from the animal and before it is dried. This would be in accord with Castle's experiments. Another possibility is that there may be a supply of the active hematopoietic principle itself present in the stomach wall, as it apparently is in liver and kidney. Experiments are now in progress to determine whether the mucosa or the muscle layer of the stomach or both contain the red blood cell maturing substance which is active in patients with pernicious anemia. The observations so far are in accord with the idea that patients with pernicious anemia evidently have lost, or have never had, the ability to secrete a substance in their stomachs which has the power to produce a blood-maturing material from food.

From the limited amount of available data, it is suggested that stomach tissue, per gram of fresh material, is more active than liver, as a smaller amount of the former is required to induce a remission in a patient with pernicious anemia. It is interesting to note that stomach tissue and liver are both active as a red blood cell maturing agent in patients with pernicious anemia, in the absence of "free hydrochloric acid". Whole desiccated hog stomach and hog stomach defatted with petroleum benzine produce a satisfactory hematopoietic remission in pernicious anemia.

PERNICIOUS ANEMIA -- LIVER DIET

There was little significant advancement in the treatment of pernicious anemia from the time that Addison described the *(5)

disease in 1855 until Minot and Murphy, in 1926, announced that liver contained a principle which stimulated blood regeneration. These Harvard investigators, whose work was based directly upon the painstaking investigations of Whipple and his associates, who worked with dogs, found that a diet rich in liver was regularly followed by a remission of the disease, without the employment of the time-honored therapeutic agents, arsenic and transfusion. They first reported forty-five cases, but later brought the number up to 105 cases. Since that time, Cohn and others have isolated a liver "extract" which seems to be similarly effective. The number of patients that have been snatched from death and apparently returned to normal health by the use of either liver or the liver extract is now very large; so uniformly successful has been the treatment indeed, that the few failures reported are looked upon with suspicion--either, it is felt, the liver was not properly taken or else the diagnosis was faulty.

It is now well established that one-half pound (0.2kg.) of liver taken as part of the daily diet will cause an increase in the number of new red blood cells in the circulation. By the fourth day of such treatment the number of reticulocytes, which usually constitute about one percent of the total of red blood cells, begins to rise, continuing for from five to six days, and reaching a maximum of from five to fifty percent on the seventh day to the ninth day of treatment. By the twenty-first day the number of reticulocytes returns to normal. After this initial outpouring of reticulocytes the red blood cells are delivered from the bone marrow in a more mature stage and the total red blood cell count

begins to increase. The new corpuscles are more normal in size, shape and color, and the abnormally large cells and the distorted ones rapidly decrease in number.

When the liver or liver extract is taken by a patient with pernicious anemia whose blood count is two and one half million or less, the number of reticulocytes increases appreciably in the peripheral circulation during the first one or two weeks. When the liver or liver extract is taken by a patient with pernicious anemia whose count is higher (three million per cubic millimeter or above) or by a normal person, the increase in the number of reticulocytes in the blood stream is very slight or negligible. This appears to be related to the stage of red blood cells in the bone marrow. The active principle, when given in the form of liver extract, does not appear especially to influence hemoglobin formation, although other substances in whole liver may be effective in this respect.

Even before the first morphologic blood changes can be noted, there is a very definite subjective improvement in the patient. On the third day, occasionally sooner, there is an increase in the appetite, a feeling of new strength, and a reawakening of interest in the surroundings. During the next week, before there is any demonstrable change in the red blood cell count, the pads of the fingers and palms, the chin, the cheeks and the tip of the nose may become flushed. This reaction appears to be a vasomotor phenomenon and is very striking, especially when the red blood cell count has been as low as one million per cubic millimeter.

The creases in the palms of the hands remain pale, however, and do not take on their red color until the blood count approaches about two and one-half to three million red blood cells per cubic millimeter. Nausea, if it has been present, rarely lasts after the fourth day, and diarrhea or constipation usually is relieved. Some patients, especially those taking whole liver, may complain of a mild diarrhea during the first week, but this soon disappears. The feeling of heaviness in the epigastrium is lost, although some patients continue to be bothered with abdominal distention for long periods. The stools, which often have a very offensive, putrefactive odor during the relapse, become more normal after a few weeks. The tongue, which is frequently sore when the treatment is first begun, usually becomes normal. Occasionally the condition of the tongue may be greatly improved by painting the lesion with one or two percent silver nitrate solution. However, the glossitis may recur in a mild way during the remission as the ingestion of liver does not seem to be entirely specific for this symptom.

The neurologic symptoms and evidences of degenerative changes in the nervous system seem to be benefited only secondarily when the blood count approaches normal, as there appears to be no direct action by the liver or liver extract on the diseased nerve tissue. Some patients develop neurologic changes after their red blood cell counts have increased to around five million per cubic millimeter. In some cases patients who were unable to walk and had incontinence of urine and feces have regained the power of

locomotion, control of urination and defecation, and severe decubitus ulcers have healed after the taking of liver extract, dilute hydrochloric acid and liberal diet, in conjunction with massage, regulated exercise and heat applied to the muscles of the legs, arms and back. Patients with marked neurologic changes and those with active infections do not respond as quickly to the liver therapy as those who have no complications. Infections which delay recovery include rhinitis, pharyngitis, pleurisy, bronchitis, gallbladder disease, cystitis and infected decubitus ulcers. While the dyspnea on exertion and other features of anemia disappear as the blood count rises, the feeling of weakness may remain with the patient until he is well into his period of convalescence. The patients perspire on slight exertion and require considerable rest. Eventually this weakness disappears and a hard day's work may be accomplished with ordinary effort. There is an actual increase in the muscular power. The tingling sensation in the hands and feet may persist for months after the blood has returned to normal, but it usually becomes less prominent as time goes on. The tingling appears to be due to involvement of the peripheral capillaries, as stasis and hyperemia, produced by a tourniquet, have no effect in relieving it. Edema of the ankles, which is frequently observed, usually disappears as the red blood count approaches normal, but in some patients the edema may persist long into convalescence. The latter patients are unable to hold their breath, without previous deep breathing, for fifteen seconds or longer as can the

former group. Although these patients show no definite cardiac changes it is possible that this factor may be of importance in this connection. The 'hemic' cardiac murmurs slowly decrease in intensity and finally are replaced by normal heart sounds. Sexual activities, which are usually lost during the first stages of the disease, are gradually brought back to normal when the blood count reaches normal.

For the average patient, without complications, one-half pound (0.2kg.) of beef, calf's or other liver should be prescribed daily. They may be taken raw and finely ground, or it may be cooked in any way that makes it palatable and easily digested. As the active principle is soluble in water, any liquid used in boiling should be added to the liver when it is eaten. The liver is more easily digested if it is finely ground. When liver extract is used the contents of from three to six vials, or the equivalent of one half-pound (0.2kg.) of raw liver, may be dissolved in water or a suitable liquid, and taken once a day. Each vial contains the extract made from 100 gm. of liver. For very sick patients, the larger dose should be used. There is some evidence that a very large dose taken at one time is as effective as the same amount taken at intervals. There are several liver extracts available commercially, but evidence has not been produced which proves that they are all potent. An effective liver extract should cause an appreciable rise in the number of reticulated red blood cells in from the fourth to the sixth day, in patients whose initial

red blood cell count, is below two and one-half million per cubic millimeter. The higher the initial red blood cell count, the less marked is the immaturity of the newly delivered red blood cells, and those showing a reticulum are but few in number in the peripheral circulation. Some prescribe dilute hydrochloric acid (2 to 4 or more cc.) in a glass of water or lemonade with meals. The liver diet is effective without this, but many feel that it has a therapeutic action. The rest of the diet should be liberal and well balanced, and should include meat, eggs, greens, vegetables fresh fruits, especially peaches, apricots and strawberries. Fat does not appear to hinder the development of the remission but heavily fried foods, especially liver, are not desirable.

Comatose or semicomatose patients may be revived with a blood transfusion, and the liver may then be given in the form of the extract. In these very sick patients it may be necessary to resort to the use of the stomach tube.

Patients should be watched carefully to note whether there is retention of urine, as the bladder sensations may be lost with the neurologic changes in the spinal cord. If retention is noted, it may be necessary to use the catheter. The patient should be urged to try to void every three hours. In this way the sensory part of the process is not an important factor, and control of the bladder may be regained. Control of the bowels is a more difficult matter, but several patients who had been incontinent at times regained control of defecation by careful attention to regularity

of movements. Abdominal distention may be a troublesome feature and every effort should be expended to control it.

Patients with pernicious anemia, especially those with changes in the spinal cord, must be given careful attention to prevent bed-sores. These may form over any of the bony prominences, especially the sacrum and the hips. Ulcerations may appear in the intergluteal folds. Besides the systemic treatment, reddened skin areas may be painted daily with collodion solution. The ulcers tend to heal more rapidly and with less discharge if they are exposed to light. Deep ulcers may be treated with hot packs of gauze wet with a saturated solution of boric acid until the infection clears, and the parts then exposed to air without dressings. When the blood count is below two million per cubic millimeter, especially if the patient is weak, bed rest should be prescribed; but the patient should be allowed to get up as soon as his strength will allow it, in order to avoid the skin irritation.

When the patient is unable to control his legs, he should be given passive and active exercises and should be encouraged to try to walk with aid. The muscles may be massaged, coincident with the application of dry heat. Some patients are able to walk better if they separate their legs and use a wide base. Many apparently hopeless patients have regained the use of their legs under this regimen, although they remain somewhat spastic. In patients with mild loss of joint sensation, every effort should be made to teach them to take advantage of other sensations to guide their movements. Bandages may be tied about the legs, or

adhesive tape may be strapped from areas of no sensation to areas where the sensation is normal. Occasionally enough sensation may be obtained when the shoe-strings are tied very tightly to aid the patient in walking more normally. The vibration sense of the tibias may be regained as the patient improves.

The blood count usually reaches normal in from two to four months. During this time the liver diet or the taking of liver extract must be carefully followed. When the red blood cell count is normal, the amount of liver may be reduced to one-half pound (0.2kg.) five times a week, and later, with periodic blood examinations, to three times a week. The maintenance dose of liver extract has not been determined, but the minimum probably is around the equivalent of 300 gm. of liver three times a week. Some patients will require more. In reducing the amount of liver or liver extract, it must be remembered that a spontaneous remission lasts for varying lengths of time and the blood count may be maintained not because of the small amount of ingested liver, but because of the natural duration of the induced remission. When this terminates there will be a relapse if the liver intake is too low. Several patients have shown a tendency to a form of relapse even while on an adequate liver intake. This manifests itself by a loss of appetite, sore tongue, and aversion for liver, and when it is discontinued, the development of anemia. It is during this period that liver extract will be found valuable to tide over the days when the patient cannot take liver. There appears to be less tendency

to develop an aversion to liver extract than to liver.

While the liver extract appears to be specific for pernicious anemia it has little or no effect on most secondary anemias. Whole liver has an additional element, not possessed by this extract, which may be valuable in other types of blood regeneration. The diagnosis should be based on an adequate history, the characteristic physical observations, mild or severe neurologic symptoms, achlorhydria, anemia with macrocytosis, a wide dispersion of the size of the red blood cells, a high color index, leukopenia, a mild thrombopenia, and a high icterus index and bilirubin content in the blood serum. The stools should be studied for parasite ova and for blood. The therapeutic test--feeding liver to see whether the anemia will disappear--may cause loss of valuable time in anemias due to chronic hemorrhage or those associated with cancer.

Treatment is not complete unless details of ordinary hygiene are carefully followed. Sunlight may have more than incidental value and there is some work that suggests that ultraviolet rays may induce a remission. Fecal infection should be eliminated whenever possible, particularly if the patient does not show a favorable response to liver therapy. Teeth should not be removed unless one is fairly certain that the remaining ones are adequate for the proper chewing of food or that a suitable false set can be provided. The occasional occurrence of a nutritional anemia in adults from defective ability to take solid food makes this point one of importance.

A thorough and widespread use of the liver diet and of effective liver extracts has placed the treatment among the standard methods of treating disease. Problems for the future are isolation of the active principle of liver, determination of the maintenance of dose, accessory factors in cell and hemoglobin formation, and the adequate treatment of neurologic symptoms.

PERNICIOUS ANEMIA -- TRANSFUSION

Prior to the institution of liver treatment, undoubtedly blood transfusion produced better and more permanent results than any other therapeutic measure. It is by no means a cure but it has certainly brought many a moribund patient back to life, and in some cases it has been responsible for the occurrence of a remission. Such cases as do respond with a remission may require anywhere from five to fifteen transfusions before a normal blood count is approached. The utmost extension of active life attainable by the use of this measure probably follows upon the restoration of the blood volume to normal by several large transfusions and the maintenance of a relatively normal blood volume by repeated small transfusions to offset the hematopoiesis. The usual procedure is to transfuse every two weeks, but there are objections to this.

In pernicious anemia the hemoglobin and red blood cells are increased following a transfusion, but in from three to seven days, in most instances, a drop of these elements occurs. This reduction is often greater than the previous increase, bringing

the blood count to a lower level than before the transfusion. Because of this, when the interval between the transfusions is too long, the good accomplished by a single transfusion is lost. The result is similar when a second transfusion is given. Recently, a patient was seen who had received six transfusions of from 500 to 800 cc. every two weeks, whose red blood cells and hemoglobin were lower after the series of transfusions than before. Permitting too long an interval to elapse between transfusions is responsible for more of the poor results in pernicious anemia than any other single factor. To overcome this, the transfusions are given every three to five days, thereby adding blood elements before there is a decided decrease. With the use of these smaller amounts of whole blood, from 350 to 450 cc., depending on the weight of the patient, from every three to five days, it has been possible to bring the red blood cells and hemoglobin to a normal point in nearly every instance. In addition when smaller amounts are given, a donor can be used more frequently.

ARSENIC IN THE TREATMENT OF PERNICIOUS ANEMIA

It has long been felt that arsenic has some value in the treatment of pernicious anemia. Usually it is employed as in the treatment of secondary anemia, but recently the arsenical shock treatment, the administration by mouth of subcutaneous injection of a few large doses of arsenic, has apparently, been followed by

strikingly good results in a few instances. One has always to be wary in a condition so prone to wax and wane as in this disease. Most practitioners use the drug in the belief that it is a stimulant to blood building tissues, but Barker has very well asked, "is this tissue not overstimulated at all times in Pernicious Anemia?" He suggests that arsenic because of its toxicity may produce its good effects by inhibition of phagocytic activity within the reticulo endothelial system.

IRON IN THE TREATMENT OF PERNICIOUS ANEMIA

It has not been shown that Iron has any value whatever in the treatment of Pernicious Anemia.

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