EDITORIAL

PERNICIOUS TYPES OF ANEMIA IN THE AMERICAN TROPICS

If there is one achievement of which internists should be proud it is the solution of the mystery enshrouding an ancient and heretofore hopeless affection, up to date universally known as pernicious anemia. It is totally unnecessary to rehearse at this late date what not only all physicians should thoroughly know, and many well-informed laymen in part do know, the comparatively simple basic facts regarding the mechanism of its production and means by which its progress can be stayed.

The truth is, there are so pitifully few ills that beset us under the name of disease from which we have so clear a scientific escape, that the sudden and dramatic termination of practically all argument as to what to do for a disease considered progressively fatal should make recent advances in the therapy of Addison's anemia an inspiration to those who labor to make the Science of Medicine simple and precise for the preservation of health and a higher level of physical efficiency.

The facts that so far seem clear are:

1. That pernicious anemia is not a disease but a condition liable to occur in the course of more than one disease.

2. That its mechanism is a failure on the part of the stomach to produce out of protein a substance later stored in high concentration in the liver, which causes the hemopoietic system to produce a normal output of red blood cells.

3. That whatsoever pathogenic organism, toxin, or condition may appear in the future as a cause or as a factor in the causation of the failure of the stomach to elaborate an enzyme by which this substance can be extracted from protein, its administration in adequate quantity will cause a remission in the anemia if the substance be absorbed and the hemopoietic organs themselves are sufficiently intact to respond.

But while the great work has been accomplished and stands out in the world of Science as a permanent landmark of our conquest of the wilderness which lies before us, there are still many details upon which scientific thought is being intensely employed. One of the most interesting to us here in the American tropics is the mechanism of our anemias of pernicious type.

Why do we see so many cases of a progressive macrocytic anemia which respond but feebly or not at all to the specific therapy, whole liver feeding, liver extract or ventriculin? This, of course, may be due to lack of absorption of the efficient substance. In its favor is the fact that the anatomical changes in the small intestine with marked thinning of the mucosa greatly diminishes absorption of food. This would also explain not only the emaciation for which sprue is famous, but indirectly still one more change whose effects are believed to be of extreme importance in closing the vicious circle, a faulty secretion of digestive fluids due to a reduction in normal output and quality of the glands secreting them through malnutrition.

But the reduction of efficiency of the glands of digestion is not merely a hypothesis. Practically all organs are at least reduced in size, and, through bits of evidence here and there, many of them are also found functionally deficient. Now, while many disease-conditions reaching a state of cachexia could theoretically produce this state of affairs, only a few seem to do so, perhaps because death is delivered by the cause of other diseases, such as cancer, nephritis and tuberculosis, long before the gastric function is sufficiently disturbed or because toxins generated by definite pathogens do not have a selective action on the mucous membrane of the stomach. One of the diseases which does produce these profound nutritional disturbances is tropical sprue, so prevalent in Porto Rico. Another, fortunately less fearsome, since its course has been interrupted by better sanitation and a removal of the cause in many infested, is uncinariasis. The anemia of uncinariasis at times used to reach such an extreme grade as to perfectly simulate, hematologically, pernicious anemia. Undoubtedly many such cases would have responded just as favorably to liver extract as does Addison's anemia. This actually has been proven to be the case in a pernicious type of anemia due to *Diphyllobothrium latum* by Isaacs, Sturgis and Smith (Arch. Int. Med., 42: 313, Sept. 1928), in which a complete remission was produced by liver extract without removing the worm.

But there is still another condition with which Medical Science must increasingly account—plain nutritional unbalance, protein starvation, avitaminosis or whatever more specific term we may employ to denote a definite failure of cellular vitality through deficiency of necessary food factors. And this is the other theory upon which some of these failures to produce reticulocytosis and a rise in blood values is based after adequate doses of a potent extract of liver. It rests, as does the first theory, on certain facts. Recognizing fully

the deficiency of the necessary substance for the stimulation of the hemopoietic organs, and the insufficiency of the stomach to produce it, admitting that at least half of the cases of sprue with a hematologic picture indistinguishable from the von Biermer type of Addison's disease respond in a normal manner to the administration of liver extract, there is still a moiety, or at least a large percentage, that respond to it feebly or not at all. In some of these cases which came to autopsy a great reduction or a complete lack of megaloblastic elements was found; in others, the same findings were reported from biopsies. On the other hand, perfect bone-marrow hyperplasia, as seen in pernicious anemia, was also frequently seen. The evidence is somewhat invalidated by the fact, that bone-marrow may be hyperplastic in spots and hypo—or aplastic in other places. The latter sites may have been placed alone in evidence and yet the sum total of hemopoietic tissue may have been in a state of hyperplasia.

It seems probable that either condition could exist in the pernicious types of anemia in sprue, an anemia at times due to lack of proper absorption from the bowel of the substance stimulating hemopoiesis, at other times from insufficiency of the bone-marrow, an organ which cannot be debarred from the general nutritional empoverishment of practically all other organs and consequent degeneration of cells of vital functional importance. Perhaps both of these conditions are more apt than not to coexist.

The second situation has been elaborated upon in this School since 1928 and the remedy has seemed to have been a high nitrogen diet of animal origin with fresh vegetables and fruits and an elimination of cereals and added fats and sugar with the double motive of replacing nitrogen loss by animal proteins, and preventing overgrowth of *Monilia psilosis* by carbohydrates. Before the advent of liver many hundreds of people with a pernicious type of anemia in the course of sprue were apparently cured by such a dietetic regimen and many have remained cured.

When the present investigations on the value of intramuscular injections of liver extract have been completed the relative importance of the two conditions in "stalling" a return to normal blood values will be clearer. For the present, we can say that both should be admitted, as non-absorption of the extract in some cases seems evident as a cause of lack of response of bone-marrow to liver extract.

The other outstanding question, a practical one, is, shall a maintaining dose of liver or its extract be exacted in sprue? For reasons above stated it would not seem so. There are many persons who have

been restored to normal blood values from a macrocytic anemia indistinguishable from pernicious anemia and who have remained apparently perfectly well for at least two years. Some have relapsed but generally because of the obsession of many of our people here that meat is indigestible, or on account of a popular distaste for it, or most frequently, on account of downright poverty.

The scientific factor is that while in Addison's disease there is usually a persistent achylia, in sprue, even in the midst of a picture of pernicious anemia, most patients do not have achylia. It is true that one may have free hydrochloric acid in the stomach contents and still lack the enzyme productive of the substance stimulating hematopoiesis, but how shall we explain the evident ability of our "cured" cases to manufacture enough of this substance to prevent a relapse?

This is a very vital question, for our people are poor and unable to buy the maintaining dose indefinitely, beef cattle is scarce and beef liver often invaded by *Fasciola hepatica,* apart from its high cost.

Whatever may be our particular reaction to these questions one thing seems certain: That "pernicious anemia" which Addison first described should be given a new and more scientific name in view of the monumental investigation of its hematology, apparently common to certain other diseases.—*B. K. Ashford.*