

## LIVER THERAPY IN PERNICIOUS ANEMIA

By RANDOLPH WEST, M. D.

From the Department of Internal Medicine, College of Physicians and Surgeons,  
Columbia University, New York

The effective treatment of pernicious anemia with a liver diet was originated three years ago by Dr. George Minot of Boston. The method consisted in giving a well balanced nourishing diet which included a half pound of liver or kidney daily, preferably cooked rare. All cases of pernicious anemia who have followed this diet, excepting those with severe infections, have done well. About a week after starting the diet many reticuloocytes (young red blood cells) appear in the circulation; the patient begins to feel better, and the blood count begins to rise. Cases with as few as one million red cells may have a normal count of five million cells or more in one or two months. The liver must be continued indefinitely, its withdrawal from the diet being accompanied by a return of the anemia. The spinal cord symptoms so common in pernicious anemia are arrested by the liver therapy, and tend gradually to disappear. Withdrawal of liver from a patient who has been taking it may be followed by a marked increase in the cord symptoms. The anaecidity is improved.

The diet has been tried in many types of secondary anemia and while some cases appear to be moderately benefited the majority are not helped at all. None give the characteristic reticuloocyte shower regularly seen in pernicious anemia. It is not yet possible to predict what types of secondary anemia will be aided by liver therapy.

As Dr. Ashford has pointed out, many cases of tropical sprue are greatly benefited by liver feeding, so far as their anemia is concerned, showing reticuloocyte showers as do cases of pernicious anemia. Other cases, particularly those which are very emaciated or have 3 million or more red cells, show a much less marked response or do not respond at all. Since most of the cases treated have been also on a sprue diet it is difficult to say how much their improvement has been due to liver and how much to the sprue diet. It seems clear, however, that in many sprue patients the anemia which is generally of the primary or pernicious type, improves more rapidly with liver than without it.



Following the early success of the liver diet in pernicious anemia several investigators have made extracts of liver which appear to be as potent as the whole liver itself. The potent substance may be extracted from the liver with acidulated water at 80° C or with 60 per cent alcohol, and can be precipitated from this solution by evaporating the latter to a small volume and pouring it into a large volume of absolute alcohol. The active material is precipitated by phosphotungstic acid and appears to be either an organic base, a basic amino acid, or a peptide. It contains no iron. The only way that it can be identified is by feeding it to a person suffering from pernicious anemia or sprue and noting the rise of reticulocytes and red blood cells that follows. It has not yet been isolated in a state of chemical purity.

There are already several commercial extracts of liver on the market. That furnished by one firm, is controlled by the Committee on Pernicious Anemia of the Harvard Medical School. This extract is distributed in the form of a powder which dissolves readily in water. Three tubes daily is the proper dose. It is most conveniently taken in some cold beverage and should not be heated. This amount of extract produces results comparable to half a pound of liver.

The tendency to the miscellaneous use of these extracts by the laity for all sorts of chronic ailments, while perhaps inevitable, is to be condemned both for scientific as well as for economic reasons. As far as our present knowledge goes the extracts are of value only in certain types of anemia, and as in the case of every potent drug, should be used only on the order of a physician. The physician, on the other hand, should recognize the fact that he has a responsibility to the public in checking up the effects of the extract to the end that our knowledge of the value of the new agent may be more exactly defined. In this instance the human being is our only serviceable test animal.

Dr. Castle of Boston has shown that if lean meat, which does not help pernicious anemia, be digested in a normal human stomach, then removed by a stomach tube and fed to pernicious anemia patients, a rise in reticulocytes and red cells follows, similar to that produced by feeding liver. This experiment shows that the potent substance can be produced from meat (beef) by the action of gastric juice. Since pernicious anemia patients have an achylia they are unable to extract the blood-building substance from meat. Sprue patients, on the other hand, usually have abnormal or only slightly reduced gastric acidity and it is well known that they are markedly benefited by high meat diets. The obvious explanation is that with



their more abundant gastric juice they can extract from meat the blood building substance which pernicious anemias with achylia can get only from liver or kidney.

It has not been definitely settled yet as to just how liver extract acts. But it is known from autopsy studies that the bone marrow of a patient suffering from pernicious anemia is crowded with immature red blood cells, even the fatty marrow being replaced by great numbers of immature cells, while after feeding liver a few weeks biopsies have disclosed the fact that these immature cells are no longer present; the marrow of the long bones has returned to its normal fatty state, blood formation taking place at the epiphyses only, as it normally does in adults. It is concluded therefore that the whole liver or a potent extract of the organ supplies some missing substance which enables an immature red blood cell to mature rapidly to a normal adult erythrocyte.

In the following papers will be found details of the more important studies carried out thus far on this new therapeutic agent.

MINOT, G. R., Murphy, W. P., and Stetson, R. P.

The Response of the Reticuloocytes to Liver Therapy,  
Particularly in Pernicious Anemia.

Am. Jour. Med. Sci., 175 p. 581, 1928.

MINOT, G. R., Cobus, E. J., Murphy, W. P. and Lawson, H. A.

Treatment of Pernicious Anemia with Liver Extract.

Effects upon the Production of Immature and Mature Red Blood Cells.

Am. Jour. Med. Sci., 175 p. 559, 1928.

MINOT, G. R., and Murphy, W. P.

A Diet Rich in Liver in the Treatment of Pernicious Anemia.

J. A. M. A., 89, p. 759, 1927.