December 5, 1947

Mrs. John Moran Mendon Road Cumberland, Rhode Island

Dear Rita:

Saba Hatan Hart Rita (Mrs.)

Enclosed is a copy of the reply which I have received from Doctor Watt regarding the clipping in which you were interested. This will probably answer some of the questions you may have had.

> With warm personal regards, Iam, Sincerely yours,

> > John E. Fogarty, M. C.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE



PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

November 29, 1957

Dear Mr. Fogarty:

I am glad to comment on the research findings mentioned in the clipping enclosed with your letter of November 21.

Chlorothiazide is a non-mercurial compound which has marked ability to increase the excretion of sodium and chloride. Clinical studies at a number of institutions, including the National Heart Institute, have shown it to be a good diuretic and a useful addition to the drugs available for the treatment of edema since to date it appears to have no serious side effects. The studies reported by Drs. John H. Laragh and Felix E. Demartini of Columbia University show that it is useful in treating many patients who have in the past required use of injected mercurials or other measures.

The known fact that depletion of salt in the body increases the blood-pressure-lowering effect of antihypertensive drugs prompted investigations by Drs. William Hollander and Robert W. Wilkins of Boston University and by Dr. Edward D. Freis and co-workers of Georgetown University to study the effects of diuretics on hypertension. Of the various oral diuretics tried by both groups, only chlorothiazide was found to have consistent pressure-lowering action. Both groups have found that, when given in combination with commonly used antihypertensive drugs, it enhances pressure-lowering effects. Since chlorothiazide has only recently become available, these reports are preliminary and long-term effects of the drug are not presently known.

It will be of interest to you that Drs. Laragh, Wilkins, and Freis are all research grantees of the National Heart Institute and that Dr. Hollander has a Heart Institute Research Fellowship.

The research by Dr. William Likoff of the Albert Einstein Medical Center, and his associates, on radioactive fat absorption patterns is of much interest since it contributes additional evidence indicating that the process underlying atherosclerosis may be due to abnormalities of fat metabolism.

National Cancer Institute National Institute of Dental Research Division of Biologics Standards

National Heart Institute National Institute of Mental Health Division of Business Operations

National Institute of Allergy and Infectious Diseases National Institute of Neurological Diseases and Blindness Division of Research Grants

National Institute of Arthritis and Metabolic Diseases The Clinical Center Division of Research Services

Mr. John E. Fogarty--

It is in the area of fat metabolism that the Heart Institute has made substantial contributions to knowledge. A large part of the Institute's research program is concerned with the study of mechanisms involved in the absorption, distribution, and utilization of fat and fatty substances in the body. The aim is to determine how these processes operate normally, at what points they may become disturbed, and to determine the departures from the normal in patients with atherosclerosis and disorders associated with the development of atherosclerosis.

Fats absorbed from the intestine are transported to the tissues in the form of large molecular aggregates of fat and protein. Heart Institute studies have discovered that there is in the tissues a lipoprotein lipase, or "clearing factor" system, which is responsible for removal of the fat and its deposition in the tissues, and for the later breakdown of tissue fats to supply the needs of the body for fuel. The various components of this lipoprotein lipase system have been identified and their significance is under continuing study. It has also been shown that unesterified fatty acids released from the body's fat depots by specific enzyme action are a major resource in meeting the caloric requirements of tissues. The regulation of their release and uptake is under intensive study since when there is interference with this process, large fatty aggregates of the type associated with atherosclerosis appear in the blood. We are convinced that a basic understanding of normal and abnormal fat metabolism is an essential part of the solution of the problem of atherosclerosis.

Kind personal regards,

Sincerely,

James Watt, M. D. Director National Heart Institute

Hon. John E. Fogarty House of Representatives

Enclosure