



Aluminum Company of America

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Pittsburgh 19, Pa.

March 13, 1957

Mr. F. L. Seamans
Smith, Buchanan, Ingersoll, Rodewald
& Eckert
1301 Alcoa Building
Pittsburgh 19, Pa.

Dear Mr. Seamans:

The attached letter from Dr. Nicholas C. Leone is a personal communication in which he outlines those fluoride studies in which he is directly or indirectly involved.

These clinical investigations pertain to basic studies on individuals residing in areas where the fluoride content of the drinking water varies from 0.04 ppm F. to 8.0 ppm F. You will appreciate that this range of fluoride exposure brackets the range in which a number of us are interested. I have reason to believe the results of these investigations will show no evidence of deleterious effects due to fluoride absorption. The publication of these results will be a very worthwhile contribution.

Dr. Leone has given me his permission to supply copies of this letter to you for distribution to your group of "fluorine lawyers" on a confidential basis.

Sincerely yours,

A handwritten signature in cursive script that reads "Dudley A. Irwin".

Dudley A. Irwin, M.D.
Medical Director

DAI/db

Encl.



Department of HEALTH, EDUCATION, AND WELFARE • Public Health Service

National Institutes of Health • Bethesda 14, Md.

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THE CLINICAL CENTER
DIVISION OF RESEARCH GRANTS

March 5, 1957

Dr. Dudley A. Irwin
Medical Director
Alcoa Building
Room 1501
Pittsburgh, Pennsylvania

Dear Dr. Irwin:

It was a pleasure to see you again and discuss the current status of the fluoride problem.

I am very sorry that I failed to give you the promised copy of the "Pallid Giant" and, therefore, I am enclosing it with this letter.

In keeping with our conversation about our own fluoride studies interests, I would like to briefly enumerate the various research projects now in progress. The greatest part of this work is in the final stages and, therefore, I anticipate early publication in the form of 5-6 papers, several with two or three parts.

It is important to note that in addition to our own studies, I have been closely associated with a number of other projects, carefully integrated with our program, so as to constitute complementary information. Therefore, I will briefly comment on these studies also.

Our own immediate studies are as follows:

1. A Human Autopsy Study consisting of seventy-five cases, all of whom experienced sudden death. Cases with generalized or chronic ailments were ruled out. Each individual resided in the respective area for a minimum of ten years and the cases are derived from 8 ppm, 4 ppm, 2½ ppm and 1 ppm fluoride areas. The control cases are from non-fluoride areas. Histologic and chemical evaluation of the bones and soft tissues are being made. Identical tissues

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have been taken in each case and analyses have been made of the sixth rib on the right, the anterior portion of the lumbar vertebra 1 through 5 and the right iliac crest. Dr. McClure is doing the bone analyses. The soft tissues (heart, kidney, liver, lung spleen and aorta) have been sent to Dr. Smith in Rochester for analyses. The material is now in the final stages of preparation and evaluation and we plan the following publications:

- a. A paper in three parts entitled "The Histologic and Chemical Evaluation of Human Tissues with Prolonged Exposure to Fluoride at Various Levels". This paper will be presented in three parts: the first, (authors, Leone and Geever) discusses the background for study, procedure, methods, discussion of case histories and histologic evaluation of the tissues. Part II (authors, McClure and McCann) deals with the chemical analyses of the bones. Dr. Smith's work on the soft tissues will be published as Part III. We then plan a summary that will tie the histological and chemical findings together in terms of age, time and level of exposure, plus any other factors that may be pertinent.
- b. We plan a second paper on the bones alone, dealing specifically with the histological description of the bones. Dr. Geever, our pathologist, has been making careful measurements of ~~the~~ trabecular size and number. Dr. Geever has started this paper which is currently entitled "Microscopic Studies of Bones in Man Following Prolonged Ingestion of Fluoride Containing water", (authors, Geever, Leone and Lieberman).
- c. I am preparing a third paper entitled "A Comparative Histologic and Chemical Evaluation of Human Bones and Tissues of Persons Residing in Fluoride and Non-Fluoride Areas" (a report of two cases). This is not actually another study, but deals with one of the participants

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in our Bartlett-Cameron Study, a resident of Bartlett for fifty years who died suddenly from a cerebral vascular accident shortly after our second re-examination in 1953. We were fortunate to get a very complete autopsy. In view of the fact that this 78-year-old woman was in excellent health, except for hypertension, of long standing, I felt it might be desirable to compare the histologic and chemical findings of the tissues from a matching case from a non-fluoride area. After two-years I was fortunate in being able to use one of our own patients who resided in a non-fluoride area for twenty-four years prior to death and who expired suddenly with a rupture of the left ventricle. The matching case is almost exact as to age, sex, weight and nativity and, ideal for our purpose. This paper is in the final stages of preparation for publication. A more complete comparison of histology and chemistry of tissues will be made than in our larger autopsy series, as we were able to get complete autopsies in both instances. (Authors, Leone, Geever, Stinson and Sunbury).

2. Another of our research projects involves the determination of the fluoride content of renal and gall stones. I've obtained stones from a number of cases in Colorado Springs where the fluoride content of the water is about 2.5 ppm and this material is controlled by renal and gall stones from non-fluoride areas. This paper has been completed in rough draft, (authors, Zipkin, Lee and Leone).
3. Colorado Springs Necropsy Study.--This project involves evaluation of 750 autopsy cases done by Dr. Geever, in Colorado Springs during the period 1947 through 1953. At that time Dr. Geever was associated with the Glockner-Penrose and St. Francis Hospitals and had no interest or in fact, knowledge of his later participation in a fluoride program. His work is meticulous and the protocols, which he prepared, were excellent for review. We have gone to Colorado Springs with Dr. Geever, abstracted and tabulated this material, which is now about ready for first draft. It is our intention

to report the cause of death, primary, secondary and contributing accessory factors. The material will be analyzed and presented in a manner that will permit evaluation as to whether or not fluoride in the amount of 2.5 ppm produces any unusual conditions.

4. Framingham Roentgen Study.--This is part of a 30-year heart study in Framingham, Mass. (5,280 participants). X-rays identical to those made in Bartlett and Cameron are being done on every fourth patient and we hope to have between 750 and 1,000 cases for final evaluation. The fluoride content of the Framingham water is .04 ppm F. This study will make interesting comparison with the Bartlett-Cameron Study. To-date, nearly 700 cases have been completed and we are hopeful that by July we will have reached our goal of 1,000 cases. After we have evaluated the films we will then decide whether to go back in two, five or ten years and repeat the procedure on the same individuals. Identical views to those taken in Bartlett and Cameron were used and a method of standardization was developed through the assistance and interest of the Medical Research Division of the Eastman Kodak Company. (Published as an editorial in Public Health Reports, January 1957, page 76).

In addition to the above studies, I have been consultant to a study series in Provo, Utah which may have direct interest to you. The Utah group have been working on a research grant from the Public Health Service and from funds supplied by another Bureau for the purchase of X-ray film to facilitate identical studies to those which I have reported above. The interests of the Provo group under Drs. Call, pathologist, Greenwood, Biochemist and Hales, Meteorologist, relate directly to atmospheric pollution of fluorides and its effect on humans. As you know, it has been proven beyond a question of a doubt that similar conditions have an effect upon animals.

- a. A human autopsy study is in progress, using my protocol (copy attached). Similar chemical and histologic evaluations are being done on bone and soft tissues of persons experiencing sudden death and who have lived in the immediate vicinity for more than ten years. Inmates of a mental institution close by comprise the study material. Identical procedures and methods of analyses are being used. In addition, a radiological study, identical to the Framingham Study, using the same standards and procedures is in progress in the local state hospital. It is hoped that a good portion of the 1,400 inmates can be studied.

- b. In addition to the radiology study, 24-hour urinalyses are being made of these people to determine their intake and output of fluorides. Simultaneously, meteorological studies are being done by Dr. Hales to tie the concentration of atmospheric fluoride with the influence of air currents and of other meteorological conditions that have produced positive effects in cattle.

In reviewing the above studies, I feel a great deal of ground has been covered. Dr. Le Grande Shupe has some excellent material on cattle with reference to fertility, transplacental passage of fluorides, milk production and a number of other important facts.

In view of the vast amount of material soon to be available for publication, we are all very enthused about a group presentation at some carefully selected meeting in the near future. I believe we discussed this briefly while you were here and I hope that you have had opportunity to give further thought to the type of meeting that would best suit our purpose. A "one-shot" presentation and publication in a single issue or monograph should be of more value than publication in a number of publications.

Incidentally, you discussed the study of renal clearance of fluorides. Just after you left I recalled that Phillip Chen, Frank Smith, Dwight Gardner, James O'Brien and Harold Hodge of

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Rochester have done some excellent studies on renal clearance. They have also done some good work on clearance of fluorides in animals whose kidneys have been damaged by radioactive substances. I am enclosing one reprint on renal clearance which you may keep. I am sure Frank Smith would be happy to send you a copy of his studies of renal damage and the subsequent handling of fluorides. Just talked with Dr. Arnold and he informs me that there is a lot of renal clearance work being done in Dr. Armstrong's lab in Rochester. He is sending me a copy of the research grant and under separate cover, I will send you a list of what is being done and who is doing it.

Again, it was a pleasure seeing you and I hope that we will have opportunity for further discussions in the near future.

Best personal regards.

Sincerely



Nicholas C. Leone, M.D.
Chief, Medical Investigations
National Institute of Dental Research

Enclosures