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Annual Report
of
The Saranac Laboratory.
for the
Study of Tuberculosis
OF THE
EDWARD L. TRUDEAU FOUNDATION

FOR THE YEAR
1941

SARANAC LAKE, N.Y.

F/a Reprint

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THE SARANAC LABORATORY

THE fact that the Saranac Laboratory has always been a separate institution from the Research and Clinical Laboratory of the Trudeau Sanatorium is not generally understood. Both laboratories are sponsored by the Trudeau Foundation, but the Saranac Laboratory is located at 7 Church Street in the village of Saranac Lake and not at the Sanatorium.

The properties of the Saranac Laboratory consist of the original building, given to Dr. E. L. Trudeau by Mr. George C. Cooper in 1894 as a private research laboratory, together with the John Black wing, donated by Mr. and Mrs. Frank B. Black in memory of their son. The addition contains the library and lecture room, erected in 1927 and 1928, and private research rooms constructed in 1933. There are also two animal houses.

To avoid confusion, the Trudeau Foundation publishes separate reports of the Trudeau Sanatorium and the Saranac Laboratory.

02 018 1915

THE SARANAC LABORATORY

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Assistant Director in charge of Field Work

THE SARANAC LABORATORY
FOR THE STUDY OF TUBERCULOSIS
OF THE
EDWARD L. TRUDEAU FOUNDATION

LABORATORY STAFF

Leroy U. Gardner, M.D.	Director
Arthur J. Vorwald, Ph.D., M.D.	Pathologist
Thomas M. Durkin, M.E.	Chemist and Engineer
Esper S. Larsen, 3rd, B.S., M.A., Ph.D.	Petrographer
Douglas S. McCrum, B.S., (E.E.)	Photographer and Assistant Engineer
Morris Dworski, B.S., C.P.H.	Clinical Bacteriologist and Assistant in Experimental Pathology
Hurston F. Heslington, M.D.	Fellow in Pathology
Catherine M. Cummings	Librarian and Secretary
Roy Dayton	Financial Secretary
James V. Luttrell	Purchasing Agent and Technician
George C. Hulpritt	Technician
Anthony B. Delahant	Technician
John G. Schmidt	Clinical Laboratorian
Andrew J. Redlin	Technician
Francis T. Creedon	Technician
Edward Gockler	Technician
Robert E. Liddy	Assistant Technician
Raymond LaRose	Assistant Technician
Stephen Phillips, B.A.	Voluntary Assistant
Robert Banker	Assistant
Henry C. Stout	Assistant

FIELD AND CONSULTING STAFF

Donald E. Cummings, B.S.	Assistant Director in charge of Field Work
Edward C. J. Urban, B.S., M.S.	Field Engineer
Homer L. Sampson, D.Sc.	Consulting Roentgenologist
Daniel M. Brunsfel, M.D.	Clinical Consultant
Robert N. Dawns	Roentgenological Supervisor
Richard Walters	Roentgenological Technician
Hugo Linquist	Roentgenological Technician
E. Clayton Quinn	Bacteriological Technician and Clerk
Helen R. Smith	Stenographer

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ANNUAL REPORT OF THE DIRECTOR
of the Saranac Laboratory
for 1941

LEROY U. GARDNER, M.D.*

A YEAR AGO the idea probably seemed academic to most people that healthy workmen in mines, factories and munitions plants are as essential as armies in the field. Today this statement is generally accepted as a basic objective and a concerted effort is being made to reduce time lost from sickness. In the interlude after the last war we learned how to protect workmen against chronic diseases like lead and benzol poisoning, silicosis, asbestosis and tuberculosis; what we need now is more trained physicians and industrial hygienists to put this knowledge into practice in every plant in the country. Their job will never be finished for the old hazards are inherent in industrial practice and new ones are constantly arising with technological advance. These chronic conditions often cause total permanent disability in skilled workmen whose replacement means months of training. But today we are coming to realize that the aggregate of time lost from acute illnesses is even more seriously hampering industrial output.

As the Saranac Laboratory played a part in discovering and disseminating knowledge for the control of chronic diseases of the lungs, so it is hoped that it may be useful in the case of the more acute conditions. Some of our old problems, to be discussed in this report, must be set aside until more propitious times even though they may be important in the control of disease; others we shall try to continue. Tuberculosis is a chronic disease but in times of stress, with restrictions upon diet and hygienic living, its frequency always increases. Already the rates are beginning to rise, even in this country, and abroad there are hints that tuberculosis is taking its usual war time toll. We must know more about the factors that are responsible for such increases; it is possible that research might reveal essential ingredients that could be supplied to deficient diets at a cost that would not prove insuperable. We should continue to inquire whether the promising leads with the newer chemotherapy offer any hope for tuberculosis. There is much to be done but, like every one else, we are trying to adjust ourselves to the needs of the hour and to make our facilities available for study of the health problems that are most urgent.

Research Program

One study of immediate significance has just been completed with equipment loaned by the General Electric Company. This involved daily exposure of normal and tuberculous animals to fumes produced by electric arc welding for a period of one year. Coated rods were burned to produce a fume consisting largely of iron and oxides of nitrogen. In establishing the concentration that would be tolerated by guinea pigs, white rats, and mice, 15 percent of the guinea pigs died from chemical pneumonia during the first three weeks and considerably more must have suffered non-fatal attacks judging by scars seen in animals killed at later dates. In spite of these severe inflammatory reactions in their lungs, animals already infected with attenuated tubercle bacilli failed to develop progressive tuberculosis, as they do with quartz dust. From this we could conclude that continued exposure to such fumes does not unfavorably influence developing tuberculosis. Animals with partially healed tuberculous infections of the lungs likewise showed no reactivation of their tubercles when subsequently exposed to the fumes for 1 to 10 months. Inhalation infection after 10 months daily exposure to welding fumes produced essentially the same type of tuberculosis as that in normal controls. These experiments led us to conclude that the fumes from this type of welding rod have no effect upon native susceptibility to tuberculosis. The results have practical significance in view of the widespread use of arc welding in industry of all kinds and they are of theoretical interest in indicating that pulmonary irritation *per se* is not necessarily unfavorable to the course of associated tuberculosis.

Another study by Dr. Vorwald and Dr. Benjamin Esten, anaesthetist at the Saranac Lake General Hospital, bears on the same general problem. They are investigating the effects of the anaesthetic gases, ethylene, cyclopropane, nitrous oxide and ether upon tuberculosis in animals. Completion of their work will give information of practical and theoretical significance.

The experiment on the inhalation of glass wool fibres, mentioned in last year's report, continued to show negative results after 19 months of daily exposure. To make doubly certain that fibres of glass have properties which prevent their being inhaled into the lungs, we have obtained from the manufacturers some exceedingly fine glass wool, not in commercial production, and are continuing the exposure of the animals for another six months. In spite of the fact that the new fibres are 3 microns or less in diameter, we are still finding practically none of it in the lungs. It seems highly improbable that the commercial glass fibres used for insulating purposes could ever be inhaled into the lungs for they are at least three times as thick. It is therefore concluded that glass wool, which is irritating to the skin of many individuals, can have no effect upon the lungs.

A report on the inhibitory action of aluminum hydroxide was deferred to include chemical confirmation of the anatomical studies and for the inclusion of comparative data on the action of metallic aluminum. We are now certain that some of the hydroxides of aluminum will absolutely prevent the development of silicosis when introduced in sufficient quantities into the same tissues where quartz is concentrated. Immature silicotic lesions can be abated and made to regress by starting aluminum therapy after the introduction of quartz, but mature fibrous silicotic nodules are not altered. Injected into the animal body, aluminum hydroxide is retained for at least a year. Attempts to substitute finely powdered metallic aluminum for the hydroxide have repeatedly failed to have any effect upon silicotic reactions. The reason is not that the metal is incapable of neutralizing the quartz, but that it flocculates so readily that it is not distributed to the cells containing quartz. Our experience is limited to various methods of injection and has not included the crucial one of inhalation. However, we feel that even by inhalation the hydroxide should be more effective and have therefore just started an inhalation test with one form of this substance. Extensive research is also in progress upon the effects of these compounds on tuberculous infection.

A number of collateral experiments are being done to learn whether aluminum in natural compounds, like the different clay minerals and certain silicates, can be freed by action of living tissues to protect against free silica.

Further study of ceramic materials is indicating that at the high temperatures to which they are subjected much of the quartz is converted to tridymite and cristobalite. These conversion forms of free silica we have previously shown to be as active or more active than quartz itself. However, the heat also forms layers of inert glass about the fine grains of free silica and relatively little of this is broken away in the process of grinding. As a consequence, injection of "grog" particles ground to 10 microns and under causes no silicotic reaction in spite of the fact that the material contains approximately 50 percent free silica. After treatment with acid, which dissolves the protective layer of glass, injected "grog" produces typical silicosis. Similar results are being produced with a settling clay from a pottery. This material contains about 18 percent free silica as cristobalite, tridymite and quartz, 30 percent glass and 50 percent mullite. At first it was thought that the aluminum in the latter compound might be the inhibitor, but as the glass and not the mullite is attacked by acid treatment it now seems probable that the protective mechanism is mechanical in nature.

Evidence is also accumulating to indicate that the presence of neither carbonates nor free alkalis accelerates the action of quartz in the body. This would controvert the theory that soluble silica is responsible for the production of silicosis.

Work on asbestos still progresses. The observations to date continue to indicate that the very short fibres produced by dry grinding have very little effect. Before reporting on this group of experiments we hope that collateral research will demonstrate the mechanism by which asbestos injures the tissues. Observations on the differences in the response of various species of animals to inhaled asbestos indicate that a chemical factor must be involved in addition to the one of mechanical irritation previously suggested. Extrapulmonary tissues of all species and the lungs of certain species have the power of dissolving these fibres quite rapidly. With the fibre gone there can be no mechanical irritation. Apparently the lungs of man and the guinea pig offer the optimum chemical environment for the preservation of the fibres in such state that it can continue to irritate the tissues. Probably the coating applied to the mineral fibres to form the asbestos body protects the cells against further irritation.

The work with asbestos has indicated that the chemical environment of the lung is unique and differs materially from that in other organs. This conclusion entirely escaped us in working with a universal irritant like quartz, which will cause reaction in any organ of any species of animal. If this is true, then the effects of minerals other than quartz and the various forms of free silica must be tested in the lungs to determine their essential capacities to produce fibrosis. Proceeding on this premise we are now checking the effects in the lungs of 16 of the 30 odd silicates that had been previously tested by intravenous and intraperitoneal injections. Time and limited facilities would not permit inhalation experiments with so many pure minerals so we have had to resort to injection by intratracheal tube. The guinea pig is the animal of choice as it is the one whose response to the asbestosiform silicates most closely approximates that of man. Dr. Vorwald and Mr. Delahant have solved the difficult problem of making repeated intratracheal injections into these small animals. Completion of a year's observation on each of these silicate dusts should provide much needed information on their capacity to cause significant degrees of pneumoconiosis.

A combined pathological and mineralogical study of eight pairs of lungs from miners of tremolite talc is in preparation for publication. Talc is one of the silicates whose clinical effect has long been questioned. Tremolite is a silicate that may exhibit fibrous structure like asbestos. The product of the mine where these men worked consists of about equal parts of these two minerals with small but variable amounts of quartz. All the lungs of the series show more or less pneumoconiosis but the reaction is apparently a response to the mixture of minerals. A siliceous element probably interferes with free lymphatic drainage and may cause nodular fibrosis within the lungs; the asbestosiform tremolite and probably accessory fibrous minerals produce asbestos bodies.

and also excite the formation of an unusually cellular type of connective tissue. The part played by the talc, the name under which the product is marketed, has not been established. The inference is clear that it would be unwise to assume that similar reactions would occur to everything known commercially as talc. The picture described is that which happened to result from inhaling an unusual combination of minerals in one location. An experimental study should be made in order to determine the relative importance of the different elements in this mixture. This is something we have long been anxious to undertake, but until funds are available the mechanism must remain a subject for speculation.

Enough determinations of the free silica content on the lungs of persons employed in dusty industries have been finished to indicate trends. Generally the range for free silica values is between one-half and one-fourth those for total silica although this is not invariably true. Often the advanced case of massive conglomerate silicosis seems to have less silica in the ash than the one with small scattered nodules. Comparisons based upon the usual factors of reference, such as weight of dry tissue, are not particularly informative because the weight of a given volume of diseased lung is much greater than that of a corresponding normal structure. In the latter, a cubic inch of lung tissue is made up of thin partitions between air spaces, whose size is determined by their degree of distention, and of the included vessels and bronchioles. The diseased organ may contain no empty spaces at all but be composed of dense scar tissue or of masses of exudate. In discrete nodular silicosis combinations of these two states are present. As the amount of solid tissue increases the ratio of its weight to that of a given weight of quartz decreases. This fact became obvious in analysing the lungs of groups of guinea pigs sacrificed at monthly intervals during an exposure to high concentrations of quartz. For the first 12 months the ratio of SiO_2 to dry lung tissue steadily increased; then it began to decrease in spite of the fact that the exposure continued. Until the twelfth month there was little proliferation of tissue; most of the reaction was limited to phagocytes within the air spaces. Then nodules began to form and the weight of the lungs materially increased. If one had the weight of the whole human lungs washed free of blood, as a point of reference, comparisons should be more valuable, but this is rarely determined and the organs are usually submitted to the laboratory immersed in fixing fluids. Of course the ideal analysis would be based upon the dry weight of a whole lung but such treatment would preclude other essential methods of study and would be most expensive. We have searched in vain for some chemical element which might remain sufficiently constant to serve as a basis of reference. Probably we shall have to be content with establishing the limits for free silica to be expected in different types of tissue. The study has convinced us of the futility of

attributing diagnostic significance to the quantities of total silica in the tissues.

Dr. Vorwald is obtaining interesting therapeutic results in tuberculous animals given a sulphone drug analogous to promin. He is also experimenting upon the effects of continuous intravenous therapy with other compounds. This work, financed by a grant from Merck and Company, is not sufficiently advanced to justify discussion.

In collaboration with Dr. Oscar Richards of the Research Department of the Spencer Lens Company, Dr. Vorwald is also studying the specificity of auramine fluorescence of the tubercle bacillus. They are attempting to be certain that no other substance likely to be inhaled into the lungs will behave in a similar manner. They are also studying cases of tuberculo-silicosis in which acid fast bacilli are rarely demonstrable by ordinary staining techniques.

In June the Laboratory held its fifth symposium. The subject this year was "Tuberculosis in Industry" and silicosis was considered only incidentally among the many other environmental factors of the working place that have been alleged as causes of tuberculosis. Twenty-eight speakers presented data on the nature, causes, frequency, and control of the disease. The evidence presented indicated that no industrial factor is in any way comparable to free silica as a specific alterant of native resistance to tuberculosis. The effects of other pulmonary irritants and poisons that have been thought to lower resistance are not apparent on critical analysis of industrial experience. Most tuberculosis would appear to be precipitated by more subtle factors operating in the home rather than in the place of work. Infection can of course take place anywhere but the probabilities of contact infection while at work are no greater than those outside except in the case of the nurse, physician and hospital attendant. About 75 physicians and others interested in industrial hygiene attended the meeting. The proceedings have been published and are available at the National Tuberculosis Association in New York City. This organization has also helped us to dispose of the remaining copies of the Fourth Symposium on Silicosis, the supply of which is now completely exhausted.

We take this occasion to express our gratitude to the Employers Mutual Liability Insurance Company of Wisconsin who published the proceedings of the four Symposia on Silicosis at their own expense. Their contribution to the Laboratory from the sale of these books now totals \$6,519.57.

A most interesting study in the physiology of silicotic and normal persons exposed to dust is being carried on at a mine owned by the Republic Steel Corporation, preliminary to an investigation of the therapeutic value of aluminum in silicosis. The company has erected an addition to its hospital in which to house the physiological laboratory and is permitting us to study a large group of its employees on company time, a not inconsiderable contribution when it

is realized that each subject must be kept in the laboratory for a half a day for each period of study. The operating expenses are being carried by the Department of Physiology of the Trudeau Sanatorium supplemented by a grant from the American Mutual Alliance of Compensation Insurance Companies. The work is under the direction of our physiologist, Dr. George W. Wright, with the collaboration and advice of Professor William S. McCann and Dr. N. L. Kalreider of the School of Medicine of Rochester University. This study of pulmonary function in a group of active, working miners, on whom we have already seen four or five annual chest roentgenograms, should yield extremely valuable information upon the general subject of pulmonary disability. The correlation of pulmonary function with roentgenographic appearances, physical findings and subjective complaints is essential for evaluating the effects of subsequent aluminum therapy.

In February our Petrographer, Mr. Louis Berkelhamer, accepted a position with the U. S. Bureau of Mines. We are most fortunate to have in his place Dr. Esper S. Larsen, Jr., formerly of the Department of Mineralogy and Petrography at Harvard University. In June Dr. Hurston F. Heslington of Vanderbilt University Medical School joined the Laboratory staff as Fellow in pathology. He has been able to relieve Dr. Vorwald of much of the routine pathological work. Mr. Roy Grinnell left our staff to join the Department of Physiology as technician. Mr. Robert E. Liddy and Mr. Raymond LaRose graduated from the voluntary to the regular staff as assistant technicians.

The usefulness of the John Black Room has been greatly increased by an indirect fluorescent lighting system. We are indebted to the Saranac Lake Medical Society for a contribution of \$185.00 toward the cost of this improvement. The entire staff of the Laboratory has benefited by the installation of fluorescent lights throughout all the work rooms and offices, where the need for better illumination has long been felt. This has been made possible by contributions of \$250.00 from Mr. and Mrs. Woodward Clark and \$250.00 from Mr. Stephen Phillips. We are happy to acknowledge our gratitude to them.

The Field Division

The field division of the Laboratory functions efficiently under the direction of Mr. Cummings. We still maintain supervision of the industrial operations and mines mentioned in previous reports. Most important are the iron mines of the Lake Superior district, one iron mine in northern New York, and certain subsidiary operations like lime stone quarries and a coal mine in West Virginia. The repeated annual examinations of the employees in these industries have provided much of the data upon which our concepts of dust

diseases are founded. This has been supplemented by material from incidental surveys in other industries and by a considerable number of autopsies.

Diagnostic Work

Under Dr. Vorwald's able direction, Mr. Schmidt, Mr. Dworski, Mr. Delahant and Mr. Hulpritt, all members of the research staff, have provided the local hospitals and the patients in the village with adequate diagnostic laboratory service. The total number of specimens submitted was 5,758 with 1,796 supplementary examinations. These included all of the usual tests in clinical bacteriology, chemistry and histology. There were 55 post mortem examinations and 165 surgical specimens were received from the Saranac Lake General Hospital. Outside physicians have submitted lung tissue on 17 cases involving the diagnosis of silicosis and related conditions. Through Mr. Luttrell the Laboratory maintains daily supervision of chlorination of the village water supply with frequent bacteriological examinations. Mr. Dworski, by special arrangement, has charge of the Board of Health Laboratory of the village and he does the bacteriology there for the control of milk and food.

The three papers bound with this report do not constitute an index of the activities of the laboratory during the past year. The Director, and the Pathologist, Dr. Vorwald, have made numerous unpublished addresses before medical and other groups. On two occasions this involved a full day's discussion of the subject of disease due to dust in a post graduate course organized by Columbia University for Naval personnel. In addition to arranging and participating in the Laboratory Symposium on Tuberculosis in Industry, the Director spent considerable time in editing the proceedings of the meeting.

It has been decided that in the interests of economy future annual reports will not include reprints of published papers. There will be a brief abstract of each paper to indicate its content and anyone wishing a reprint may obtain it, without cost, on request.

Again the Director acknowledges his indebtedness to all whose support has made it possible to carry out this program, a loyal staff who have been working in their efforts, a sympathetic board of trustees, and the many financial supporters without whose confidence none of us could have accomplished anything.

SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

RECEIPTS AND EXPENDITURES

Year ending September 30, 1941

Balance on hand October 1, 1940 \$5,680.26

Receipts:

*Gifts and other receipts for maintenance of
plant and work \$52,547.32
Refunds of insurance premiums 22.90
From Trudeau Foundation 13,256.65
Total receipts for year 65,826.47

Total of previous balance and receipts 71,506.73

Expenditures:

Salaries for research and field surveys 14,384.11
Travel and other expenses of workers 2,907.55
Permanent equipment 667.25
Repairs and improvements 1,674.62
Fuel, light, insurance, animals, feed, supplies
and other running expenses 8,873.20

Total expenditures for the year 68,506.73

Balance on hand September 30, 1941 3,000.00

*See following page for list of contributors

CONTRIBUTIONS
TO THE
SARANAC LABORATORY

From October 1, 1940 to September 30, 1941

NOTE: — Items in second column received after October 1st,
1941, to be credited to 1942 report.

Adirondack Fund for the Tuberculous	\$1,000.00	\$249.99
Anonymous (for special apparatus)	3,000.00	
Mr. and Mrs. Woodward D. Clark		250.00
Mrs. Bigelow Crocker	10.00	10.00
Mrs. Charles L. Crocker	50.00	50.00
Dr. Leroy U. Gardner	335.00	90.00
General Hospital of Saranac Lake	1,000.08	250.02
Industrial Hygiene Foundation of America	3,500.00	750.00
Inland Steel Company	1,874.99	437.49
Johns-Manville Corporation	5,000.00	1,250.00
Mr. W. G. Laidlaw	1,000.00	
Merck & Company	2,500.00	
Miscellaneous contributions	373.50	337.50
Owens-Corning Fiberglas Corporation	2,955.00	449.00
Mr. Stephen Phillips		250.00
Pickands, Mather & Company, for		
Lake Superior Iron Ore Association	22,500.00	5,625.00
Portland Cement Association	251.00	
Republic Steel Corporation	3,000.00	750.00
Employers Mutuals Ins. Co. (Sale of		
Symposia Reports)	545.25	21.00
Saranac Lake Medical Society		185.00
St. Joseph Lead Company	1,375.00	
State Insurance Fund	750.00	125.00
Stebbins Engineering Company	350.00	
United States Gypsum Company	642.50	125.00
In memory of Sydney Lunt Wood:		
Miss Sarah C. Armistead	5.00	
Miss Susan Wood	50.00	
	52,547.32	11,205.00