1933

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

REPORT OF DIRECTOR
AND
FINANCIAL REPORT

FOR THE YEAR ENDING SEPTEMBER 30, 1933

REPRINTS OF SCIENTIFIC PAPERS

The Saranac Lake Academy of Medicine

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

Leroy U. Gardner, M.D. ---------- *Director and Pathologist*
Thomas M. Durkan, M.E. ---------- *Assistant Chemist*
Winfield O. Kelley, B.A. ---------- *Clinical Pathologist*
Douglas S. McCrum, B.S. (E.E.) ---------- *Photographer*
Morris Dworski, C.P.H. ---------- *Assistant in Experimental Pathology*
Catherine M. Cummings ---------- *Librarian and Secretary*
Roy Dayton ---------- *Financial Secretary*
James V. Luttrell ---------- *Purchasing Agent and Technician*
George Hulpritt ---------- *Technician*
Anthony Delahant ---------- *Technician*
Andrew J. Redlin ---------- *Voluntary Assistant in Chemistry*
Everett L. More ---------- *Voluntary Technical Assistant*
William LaBounty ---------- *Assistant*
Henry C. Stout ---------- *Assistant*

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Donald E. Cummings, B.S. ---------- *Assistant Director in Charge of Field Work*
Homer L. Sampson ---------- *Consulting Roentgenologist*
Daniel M. Brumfiel, M.D. ---------- *Clinical Consultant*
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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 and controlled 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 Room, an addition which houses the medical library and lecture room, and special buildings for animals.

While the Saranac Laboratory co-operates with the Sanatorium in every possible way and serves as the headquarters for the Trudeau School of Tuberculosis, it provides diagnostic facilities to the physicians practicing in the village and carries on independent researches in the field of tuberculosis and associated conditions.

To avoid the existing confusion, the Trudeau Foundation is publishing an annual report of the Saranac Laboratory under separate cover from that of the Sanatorium.

REPORT OF THE DIRECTOR OF THE SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

1933

LEROY U. GARDNER, M.D.

It is a pleasure to announce the consummation of the plan suggested in the Director's report of last year whereby the Saranac Laboratory is enabled to undertake a comprehensive experimental, clinical, epidemiological, and engineering investigation of pneumonokoniosis as a causative factor in the production of tuberculosis. This most desirable approach to the problem should advance our knowledge more effectively than by attacking it along any single avenue of approach. Clinical study of disease as it develops under industrial conditions is obviously essential to point out the medical problems involved, but since many of these problems are concerned not only with the individual but with groups and families, epidemiological methods must also be employed. The engineering aspects of the subject are essential to comprehend and alleviate dust hazards which may be discovered and furthermore they are fundamental to define the etiology of a disease like pneumonokoniosis. With a knowledge of all these factors at our command, animal experiments can be planned to interpret the principles involved in a more intelligent manner.

Such a program of investigation has been made possible by the establishment of an intimate association between the Laboratory, the x-ray department of Trudeau Sanatorium, and the Saranac Lake specialists practicing in the field of chest diseases. Not only will this combination of resources permit a more comprehensive scientific investigation but it allows us to offer industry a consulting service for the detection of possible hazards from dust, for the proper examination of its employees, for recommendations to improve working conditions where these are necessary and for the treatment of any employees who may be found to suffer from occupational disease.

Mr. Cummings, the assistant director of the Laboratory, is supervising the work in the field. He will train engineers already employed by the industries in the technique of making atmospheric dust determinations; he will have supervision over ventilation, over clinical laboratory work in the field, and will co-ordinate the activities of all parts of a study. He is assisted by Mr. Robert N. Downs, a former associate of Mr. Sampson in the x-ray department, who is now in charge of all roentgenological examinations. Under their direction are technicians also trained by Mr. Sampson. At the present time Mr. Richard Libby is already at work and Mr. Richard Walters will begin in the near future. Their excellent training will insure satisfactory films which will be sent to Mr. Sampson for interpretation. Where plant physicians are available we propose to secure their co-operation in making physical examinations; if no suitable local physician can be found Dr. D. M. Brumfiel of Saranac Lake will make them.

Simultaneously with this investigation in the field, a laboratory study of the particular dusts and their effect upon the normal and tuberculous animals will be undertaken. The final co-ordination of data from all of these sources should enable us to obtain a clearly defined picture of any given dust hazard.

As reported last year, a contract was made with Oglebay Norton and Company to carry out such a study in an iron mine which they operate. This work is now in progress, together with animal experiments using ore and rock dusts from the mine in question.

In the Spring we were approached by the United States Gypsum Company to make a survey of their plant and employees in Oakfield, N.Y. Their operations comprise mining, pulverizing and calcining gypsum dust together with the manufacture of gypsum plaster, wall board and various other products. A series of dust counts was made in representative parts of this plant; one hundred men employed for maximum periods of time in various departments were given physical and x-ray examinations, and three different animal experiments with gypsum dust were begun. We were able to demonstrate that in spite of rather heavy dust concentrations developed in certain parts of the plant, there were no significent changes produced by the inhalation of this dust during periods as long as twenty years. The animals also have thus far failed to exhibit serious reaction and there has been no effect upon tuberculous infection. The evidence thus accumulated corroborates the prevalent opinion that the inhalation of gypsum, or calcium sulphate, does not cause changes in the lungs which are deleterious to health, nor does it predispose to tuberculosis.

During the Fall the entire group of companies operating iron mines in the northern part of Michigan decided to employ the Laboratory to make a survey of all their mines. They desired to know whether iron mining involves any risk from dust inhalation and if so they wished to take measures to minimize this hazard. On November first a contract for $30,000 annually, for a period of three years, was signed between the Laboratory and the following operators: The Cleveland Cliffs Iron Company, The Corrigan, McKinney Steel Company, Davidson Ore Mining Company, The M. A. Hanna Company, Agent, Inland Steel Company, Oglebay Norton and Company, Agents, Oliver Iron Mining Company, Pickands Mather and Company, Agents, and Republic Steel Corporation. The original contract with Oglebay Norton and Company is, of course, superseded by the new one to which they are party.

Under Mr. Cummings' direction this field investigation is already under way. Engineers are being trained to make dust determinations. Large numbers of roentgenograms made by the technical staff are being sent to Mr. Sampson for interpretation and a series of laboratory investigations of the action of mine dust has been started in Saranac Lake. It is as yet too early to venture an opinion as to the results of this study, but in time we will have all the necessary information to evaluate the effects of work in iron mines.

These contacts have permitted the Laboratory to proceed with its program of research which would otherwise have been seriously hampered by the lack of funds. Mr. Cummings will, of course, not be able to continue his work

in the Laboratory but arrangements have been made to continue certain portions of it.

Research

The new dust house built last year is now operating at full capacity with five dust inhalation experiments in progress, using pure silica, hematite, gypsum, and various combinations of these substances. Nearly 500 guinea pigs and a smaller number of rabbits and white rats are involved in these experiments.

The chief problems now being investigated are the determination of the maximum amount of silica which must be inhaled before progressive disease develops; the determination of the minimum amount of silicosis which predisposes to tuberculous infection; the effects of non-siliceous dusts inhaled simultaneously with silica; the continuation of previous studies upon the effect of particle size in the production of tissue reaction. A method for recovery and measurement of all the extremely fine inhaled dust particles in portions of the silicotic lung promises to yield valuable information.

The previously mentioned attempt to develop a rapid method for determining the dangerous characteristics of various kinds of dusts is still in progress. The immediate effects of different kinds of dust particles have been determined but to be of significance these changes must be correlated with the chronic effects produced after months or years have elapsed. Publication must therefore be delayed.

Much additional experimental data has been accumulated on the relationship between silicosis and tuberculous infection, but it has seemed advisable to defer reporting these findings until they can be correlated with the condition in human beings. In this connection the general problem of the relationship between immunity and silicosis is receiving careful attention.

Some of the chemical problems which Mr. Cummings had started are being continued, notably a study of the various forms of silica and alumina, and the reaction which they produce in animal tissues. Much time is being devoted to the determination of the type of dust found in the lungs of persons dying with different forms of pneumonokoniosis. During the year material from thirty-six such cases has come to the Laboratory for examination. Chemical analysis is not an altogether satisfactory method for the identification of inhaled dust. It is desirable to develop a petrographic technique that may be applied to the minute particles which gain access to the pulmonary air spaces. It is hoped that the co-operation of some specialist in this field may be secured for this purpose.

Aside from the major research, other problems are being studied by various local physicians. Dr. Baldwin is investigating the occurence of non-pathogenic acid fast bacilli in various habitats. Dr. Kinghorn and Mr. Dworski are continuing their work on vaccination against tuberculous infection. Mr. Cummings and Mr. Delahant have nearly completed their study of hypersensitiveness and immunity in tuberculosis. Dr. J. N. Hayes has been testing the reactions of the lungs to various oils and is also studying their relative effectiveness in the maintenance of oleothorax in the experimental animal. Recently he has obtained a grant of $200 from the E. R.

Squibb Company to investigate the effect of irradiated mineral oil on tuberculosis of the pleura. Mr. Winfield Kelley, in co-operation with the x-ray department of the Sanatorium, is attempting to produce pulmonary tuberculosis in cats and to follow the course of the infection roentgenographically. If this could be accomplished in a resistant animal like the cat it would prove a valuable tool in our studies, for silicosis has been reproduced in this animal which has very large lung fields that are easily visualized in roentgenograms. Dr. D. M. Brumfiel is assisting in the study of several of the laboratory silicosis problems. Dr. E. M. Jameson is continuing his investigation of genito-urinary tuberculosis.

Teaching

There has been no change in this part of our program during the past year. We have participated in the instruction in the Nurses' Training School at the Sanatorium and in the Trudeau School of Tuberculosis. For the latter the course in Pathology was altered to correlate it more intimately with the roentgenological aspects of tuberculosis.

In the coming session of 1934 we hope to have several physicians from the mining companies for whom we are making the field study. If this plan materializes considerable time will be devoted to the pathology and x-ray appearance of pneumonokoniosis.

Clinical Laboratory Work

The diagnostic department has been under the direction of Mr. Winfield O. Kelley since September when Dr. Schwartz left us to accept a position in the Sanatorium. He is assisted by Mr. Delahant. As will be seen in the appended summary, the total number of examinations fell below that for last year by 371. This is a reflection of the decrease in the number of the patients in the village rather than a lack of the use of the Laboratory facilities by the physicians. Much of this work has been done without cost, as many patients were unable to pay even a moderate fee. The contributions of $2,010 received from the Academy of Medicine have been devoted to the support of this department. Mr. Kelley, who receives no salary but is dependent upon fees, is the recipient of a fellowship and spends part of his time in the Sanatorium.

Summary of Diagnostic Examinations
November 1, 1932 to November 1, 1933

Cultures for diphtheria	16	Stomach contents	25
Smears for Vincent's angina	21	Sputum for tubercle bacillus	1451
Blood:		Milk, bacteriological counts	17
Agglutination for typhoid	10	Water, bacteriological examination	53
Differential counts	102	Water, chemical examination	365
Red and white counts	201	Smears for gonococcus	7
Hemaglobin determinations	89	Urine	920
Coagulation time	47	Autogenous vaccines	6
Grouping	78	Pathological specimens	129
Cultures	10	Autopsies, human	53
Chemistry	41	Animals inoculated for diagnosis	14
Spinal fluid, urine and other miscellaneous material for tubercle bacillus	81	Miscellaneous examinations	102
Grand total			3838

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Staff

Mr. Cummings' absence and the increased amount of work that will be undertaken will necessitate the employment of more full time members of the staff. An effort is being made to find a properly trained pathologist and bacteriologist to relieve the director of some of his responsibilities. Several prospective candidates are being considered. Mr. Thomas M. Durkan, a graduate of Cornell in mining engineering, has been serving as voluntary assistant in the chemistry department for eight months; he is now joining the regular staff as assistant chemist. We are fortunate to find a man with his training to devote to the laboratory phases of a problem such as ours. Mr. Winfield O. Kelley has taken over the direction of the diagnostic department and is also engaged in research here and at the Sanatorium.

The director takes this opportunity to express his appreciation to every member of the staff for their loyal co-operation during the year of reduced incomes and salaries To Dr. Spencer Schwartz, who retired in September, everyone is grateful for his faithful though inadequately compensated services in the diagnostic department. Gratitude is expressed to three voluntary assistants, Miss Laura Ladd, Mr. Everett L. More and Mr. Andrew J. Redlin. Miss Ladd and Mr. More will not be with us during the coming year, but Mr. Redlin will continue as assistant in chemistry.

Great credit is due to Mr. Cummings for developing and organizing the field research activities, for without the income from this source very little of the Laboratory work could continue. It is regrettable that his own researches must be interrupted, but his engineering training particularly qualifies him for the type of work in which he is now engaged.

Buildings

Even at the present time the accommodations of the Laboratory are inadequate to carry on the work in progress, and for the proposed increase in the staff additional space becomes imperative. The logical place for expansion is above the John Black Room which was erected with this possibility in mind. It gives us very great pleasure to announce that Mr. and Mrs. Frank B. Black have most generously offered to provide the needed addition to the building. This further manifestation of their faith in the Saranac Laboratory is inspiring and gratifying. Plans are now under consideration and it is hoped that construction may be commenced in the Spring. For furnishing and equipping this addition the support of other friends will undoubtedly be secured. Mr. Henry Upham Harris has already given $250 for this purpose.

Publications and Reports

In the field of pneumonokoniosis seven papers have been delivered before various scientific organizations. Reprints of five of them that deal with original work are bound with this report. Material for study is being gathered from every possible source, both human and experimental animal. Whenever possible personal inspection of field conditions is being made. For example, the paper on "So-Called 'Acute' Silicosis" was written after studying all available data at the place where this condition was developed.

The two remaining reprints in this volume are by Dr. Brumfiel and Dr. Jameson respectively. The former deals with cardiac displacements in chronic tuberculosis and the latter is a report of further observations on experimental genital tuberculosis.

Finances

The accompanying financial statement for the past fiscal year shows a balance in the treasury. This was made possible by various economies and by the receipt of income that was not anticipated when the budget was prepared and the work for the year was planned. The extra income was derived from contributions to the Academy of Medicine, from the contract with the U. S. Gypsum Company and from a contribution of $500 from "a group of friends". These friends are a number of industrialists in Milwaukee and the vicinity who, under the leadership of Mr. Benjamin E. Kuechle of the Employers Mutual Insurance Company, and Mr. Harold Falk, raised a fund to bring together a group of specialists to inform themselves about silicosis. This was the meeting mentioned in last year's report which Mr. Cummings and the director, among others, addressed in Chicago. After all expenses for this meeting had been paid an unexpended balance was turned over to the Laboratory for research purposes. We take this opportunity to thank them publicly for their help.

For the coming year an income of approximately $42,000 is anticipated from various sources. Salaries have been raised at least to the same level as they were before the enforced reduction of last year and in some instances there have been further increases commensurate with the services rendered. One additional man has already been placed upon the payroll of the research staff and another will be employed some time during the year. Six new names appear on the payroll of field personnel and Mr. Cummings has been transferred from laboratory to field work.

The field expenses and moneys allocated to the x-ray department will amount to approximately $16,500, leaving a balance to be expended in the Laboratory of about $25,500. With the increases in salary that have been made this sum will hardly be adequate to carry on the full program of research that has been outlined. However, we have fairly good assurance that certain new sources of income will become available and that some of the older pledges on which we had not counted may be renewed. All receipts from the Academy of Medicine will be devoted to carrying the diagnostic department. The only contribution that will be asked of the Trudeau Foundation, whose income is depleted, will be a fellowship for the maintenance of the clinical diagnostician.

It is a pleasure to acknowledge our debt and sincere appreciation to all the friends who have so loyally supported the Laboratory during a trying period. The assistance of the many lay contributors to the Academy of Medicine is extremely gratifying. The contributions of one large donor, the Metropolitan Life Insurance Company, have been the mainstay of the experimental work during the past five years. To this company we are deeply grateful.

The outlook for the coming year is brighter, but we have greatly widened the scope of our work and it behooves us to be diligent in seeking out new sources of support. It is hoped that our activities may justify the trust that has been placed in us.

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RECEIPTS AND EXPENDITURES

SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

OCTOBER 1, 1932 TO SEPTEMBER 30, 1933

Receipts:

Balance on hand Oct. 1, 1932			$2,853.70
From endowment held in trust by Trudeau Foundation:			
Interest on securities	$2,450.00		
Interest on cash balances	11.22		
		$2,461.22	
Gifts for maintenance of work:			
Adirondack Fund for the Tuberculous	1,000.00		
Anonymous (per Dr. Baldwin)	100.00		
Agnes Musser Eckert Fellowship	1,000.00		
"Group of Friends"	500.00		
Metropolitan Life Insurance Co.	5,000.00		
Milbank Memorial Fund	3,000.00		
*Miscellaneous donations	120.00		
Oglebay Norton & Co.	3,750.03		
*Saranac Lake Academy of Medicine	2,010.00		
U. S. Gypsum Company	2,375.00		
U. S. Public Health Service	1,099.98		
Total of gifts		19,955.01	
From Trudeau Foundation		3,000.00	
			25,416.23
Total Receipts (carried forward)			$28,269.93

*See following pages for list of donors

RECEIPTS AND EXPENDITURES

SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

OCTOBER 1, 1932 TO SEPTEMBER 30, 1933

Total Receipts (brought forward)			$28,269.93
Disbursements:			
Salaries	$17,452.48		
Animals and feed	1,147.10		
Supplies and equipment	1,232.40		
Fuel	506.56		
Gas	136.55		
Light and power	335.45		
Telephone	95.37		
Laundry	81.94		
Repairs	79.32		
Library	544.99		
Publications	258.55		
Traveling expenses	271.82		
Animal House:			
Building	92.22		
Equipment	830.59		
	922.81		
Miscellaneous expenses and supplies	185.22		
Contingent: extra supplies and equipment for new work	864.90		
Total cost of work carried on		$24,115.06	
Donation returned to donor		500.00	
Total disbursed			$24,615.06
Balance on Hand Sept. 30, 1933			3,654.87

1934

The Saranac Laboratory

for the

Study of Tuberculosis

THE TRUDEAU FOUNDATION

REPORTS OF THE DIRECTOR

FINANCIAL REPORT

FOR THE YEAR ENDING OCTOBER 31, 1917

REPRINTS OF SCIENTIFIC PAPERS

The Saranac Lake Academy of Medicine

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The Saranac Laboratory, showing at the left the new John Black Wing

The Saranac Laboratory, showing at the left the new John Black Wing

THE SARANAC LABORATORY

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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, of which a reproduction of a photograph appears in this report. The wing has been 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 which are now in the process of construction. There are also two animal houses.

While the Saranac Laboratory cooperates with the Sanatorium in every possible way and serves as the headquarters for the Trudeau School of Tuberculosis, it provides diagnostic facilities to the physicians practicing in the village and carries on independent researches in the field of tuberculosis and associated conditions.

To avoid the existing confusion, the Trudeau Foundation is publishing an annual report of the Saranac Laboratory under separate cover.

THE SARANAC LAKE ACADEMY OF MEDICINE

In the early part of July, 1931, a group of physicians in Saranac Lake met in the John Black Room to discuss ways and means for supporting the diagnostic and research activities of the Saranac Laboratory during a period of diminishing income. They were of the unanimous opinion that this institution is essential to the continued existence of the village as a center for the scientific treatment and study of tuberculosis. As a concrete expression of this feeling they constituted themselves the nucleus of a body to be known as the Saranac Lake Academy of Medicine. Its object is "to foster interest in the pursuit of scientific medicine in Saranac Lake" through the agency of the Saranac Laboratory. Its members pledge themselves to support the activities of this institution in every possible way and to seek assistance from others for its operation. The active members are physicians practising in Saranac Lake, but associate, sustaining, and life memberships are also open to interested laymen. In the financial report for the current year will be found a list of the present members.

The formation of the Academy created nothing new; the Laboratory, the Library, the diagnostic service, the scientific lectures and research have always been an integral part of the medical life of the village, but by many they have been freely accepted as a natural heritage from the great founder of this health community. By membership in the Academy of Medicine, or by contributions through it, anyone can feel that he has a part in keeping alive the Trudeau ideals for the furtherance of medical science.

CADEMY

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Richard Walters ---------- *X-ray Technician*
Melvin Berg ---------- *Bacteriological Technician and Clerk*
Dorothy P. Rogers ---------- *X-ray Stenographer*

SPECIAL RESEARCH STUDENTS

A. O. Severance, M.D. ---------- Baltimore, Md.
A. Landau, M.R.C.P ---------- Cape Town, South Africa

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___ Director and Pathologist
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STUDENTS

_____ Baltimore, Md.
_____ Cape Town, South Africa

REPORT OF THE DIRECTOR OF THE SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

— 1934 —

LEROY U. GARDNER, M.D., *Director*

A well known authority in the field of public health once remarked that the research student only begins to produce results of real significance when he is taken out of his laboratory and sent into the field. While some might qualify this generalization, it cannot be gainsaid that effective investigation of disease can only progress in close contact with the patient. In times past the Saranac Laboratory was a successful pioneer institution in the study of tuberculosis. Dr. Trudeau and Dr. Baldwin, with their associates, had ample clinical material about them on which they could draw for their scientific studies of this disease. When the problem of the inhalation of dust as a factor in the production of tuberculosis was begun there was little thought that it might deserve years of study and that it would subsequently prove to be a subject of widespread popular interest. For years the attack was directed almost wholly along experimental lines. Few persons suffering from disease due to inhaled dust found their way to Saranac Lake. To study silicosis in the human subject it was necessary to visit the centers of industry and such visits at best could be infrequent and of short duration. There seemed no choice but to continue on a purely experimental basis unless the investigation were removed to a mining or other industrial community. Then came years of stringency when the outlook for financial support from private philanthropies was most gloomy. But this apparent misfortune proved to be a turning point in the program of the institution. Because other sources of income had failed we were forced to make new alliances and in doing so were brought into intimate contact with the much needed clinical material for a well balanced investigation. It is hoped that we may profit by our opportunities and justify the confidence that has been placed in us.

To take advantage of the situation it was necessary to expand. Important members of the research staff had to be sent into the field to study conditions of dust generation and its effects upon men who work in it. New members had to be secured to investigate the problems that developed. More space was essential that these men might work, for the old laboratory was not expected to accommodate more than five or six investigators. Last year's report cited the progress that had been made in this program of expansion. This year sees us ready to begin operations on the broader basis.

Two major field investigations are in progress under the supervision of Mr. Cummings, the assistant director. Several thousand x-ray films have been taken and interpreted by Dr. Sampson and his assistants. Three more members have joined the regular laboratory staff and two graduate students will work with us during the coming year. The John Black Wing, providing six new rooms for research purposes, is now nearing completion and almost enough funds are in sight to satisfy a $54,390.00 budget for the coming year.

FIELD PROGRAM

On November first a contract was renewed with members of the Lake Superior Iron Ore Producers Association to continue the program of investigation and prevention of disease due to dust among their miners. One company of the group decided not to participate in the program this year for reasons other than dissatisfaction with the services rendered. While their withdrawal materially reduces the income that we derive from this source, it is probable that responsibility for fewer men will enable us to make a more thorough study of those that remain. Last year's effort was devoted largely to a general survey of the industry and the inauguration of a program to prevent the formation of dust. This year the data already in hand will be analysed, the dust prevention measures will be applied to all parts of the various mines involved and examination of many of the miners will be repeated to determine whether they have developed changes that may be progressive. A considerable number of autopsies have been obtained upon men previously examined. A comparative study of the anatomical changes with the x-ray shadows in films made before death will add to the general knowledge of the action of mixtures of silica and other substances like iron. There is good reason to believe that the presence of the iron favorably influences the picture so that the silica is not as harmful as it might be when inhaled in the pure state. A bacteriological study of the sputum of miners with non-tuberculous infections of the lungs is in progress and autogenous vaccines are being used to treat some of these cases. A considerable number of infections with the Friedlander bacillus and associated organisms have been discovered.

Another study was begun in a small group of fluorspar mines and mills during the summer. The program involved the determination of a possible hazard from this substance and, if such exists, the recommendation of methods for its correction. A considerable group of employees has been examined by the mine physician and their x-ray films have been studied here. Tuberculosis is prevalent in the community as a whole but whether exposure to fluorspar dust is responsible has not yet been ascertained. No autopsies have yet been secured to determine the anatomical effects of inhaling this dust so that we shall be forced to rely upon animal experiments that are now in progress.

The field work in the gypsum plant reported last year is completed and it has been possible to give the industry a clean bill of health. Recently a survey was made of a porcelain plant and a plan of investigation was mapped out. It will proceed along the lines of other investigations.

All credit is due to Mr. Cummings for the successful prosecution of this work. The officials of the companies with whom he is working have repeatedly praised the work which he doing and, here in the laboratory, we are appreciative of the financial support made possible by his efforts, and of the x-ray and autopsy material that comes through him. Without the co-operation of Dr. Sampson, at the Sanatorium, such an investigation would be quite impossible and the director is glad of the opportunity to express his appreciation. The associated field workers, Mr. Downs, Mr. Libby and Mr. Walters have loyally done their part in making a success of the undertaking. They all deserve praise for their devotion to their work.

LABORATORY RESEARCH

The problems already under investigation have been continued during the year. The inhalations of pure quartz, pure gypsum, pure hematite, ferruginous chert and a mixture of gypsum and quartz are still in progress The hematite and gypsum dusts cause no appreciable damage in the lungs and have no serious effect upon coexistent tuberculous infection. The chert, which contains a considerable amount of quartz, causes more damage in the normal lung and results in some progression of a tuberculous infection. However, the changes that develop are not nearly as severe as those produced by pure silica. Tuberculosis in the chert animals progresses for a time and then becomes stationary or tends to heal with marked scarring, or fibrosis. Mixtures of equal parts of gypsum and quartz dust fail to produce significant changes in the lungs. On the other hand, groups of animals exposed on alternate weeks to pure quartz and pure gypsum dust are developing typical silicosis. This experience points to a protective action on the part of gypsum dust; probably because the gypsum particles tend to clump together in the atmosphere, they prevent the inhalation of significant quantities of quartz. The experiment is not yet complete but the implications are fascinating in their possible bearing upon silicosis prevention.

A study of the comparative reaction of different species of animals to silica dust is now completed. Guinea pigs, rabbits, cats, white rats, white mice, and domestic fowl have developed reaction to inhaled silica. The rats develop changes most nearly resembling those in human beings. The injection of silica suspensions into tadpoles and goldfish produces a marked tissue reaction which resembles that in the mammals. One may conclude that silica is a poison for the tissues of a large variety of animals.

Injection of silica and other forms of dust into the veins of rabbits is being used extensively to test their capacity to cause damage. Silica causes a specific cirrhosis of the liver which does not occur with other dusts thus far treated. The minimum dose necessary to produce reaction and the effect of different petrographic forms of silica are being investigated.

The progressive nature of silicosis in animals is being studied in animals exposed for varying periods of time and then removed to a normal atmosphere. X-ray films are taken from time to time to demonstrate progression.

The subject of tuberculosis susceptibility in the silicotic tissues is still under investigation. This year the possibility of alteration in the immune

state is being studied in silicotic animals infected with tubercle bacilli. Collateral experiments with pneumococcus and spirochaetal infections are planned to check the observations on tuberculosis. The marked similarity between the tissue reaction to the tubercle bacillus and silica particles suggests that the injury produced by these two substances may be fundamentally the same in spite of their obvious difference in composition.

Another set of experiments just started will test the tissue reaction to a representative group of silicates (silica in combination with bases) which have common industrial uses. Theoretically these silicates are not expected to produce serious damage in the body but the possibility that they may constitute an industrial hazard is often questioned. One of them, asbestos, is exceptional and is now a well recognized cause of pulmonary disease. Another known as sericite has been suggested as an important factor in aiding silica to produce the condition of silicosis.

Mr. McCrum has completed a series of wax models of silicotic nodules from the lungs of experimental animals and from those of human beings. These models demonstrate the similarity between the animal lesions and those in man. Both develop very largely in relation to branches of the pulmonary artery. Another group of models graphically illustrates how silicotic nodules compress and thus interfere with the function of the lymphatic vessels, the drainage system of the lung. Still another demonstrates how tuberculous infection penetrates into the interior of a preestablished silicotic nodule.

In addition to these studies, carried on by the regular laboratory staff, Dr. H. M. Kinghorn is continuing his study of a tuberculosis vaccine. Dr. J. N. Hayes is still working on the effect of inhaled oil and upon the problem of experimental oleothorax; Dr. E. M. Jameson is still studying genito-urinary tuberculosis. Dr. D. M. Brumfiel is collecting data on the number of silicotic patients under treatment in tuberculosis sanatoria throughout the country. He is especially interested in ascertaining the effect of treatment in patients with a complicating tuberculosis.

TEACHING

In addition to the usual program of teaching, five days of the 1934 session of the Trudeau School of Tuberculosis were devoted entirely to the subject of silicosis. A program was arranged covering all phases of the subject: etiology, pathology, diagnosis by clinical and roentgenological methods, prevention, and medico-legal aspects. It is a pleasure to acknowledge our gratitude to the eminent authorities in their various fields who volunteered their services to lead the discussions. Dr. R. R. Jones, of the U. S. Public Health Service, spoke on etiology; Mr. D. E. Cummings, assistant director of the laboratory, covered other phases of his subject with special reference to atmospheric dust determination. The pathology of the disease was discussed by the director of the laboratory. Prof. Philip Drinker, of the Harvard School of Public Health, discussed engineering methods of dust prevention and elimination. Dr. H. K. Pancoast, of the University of Pennsylvania, and Dr. Homer L. Sampson, of the Trudeau X-ray Laboratory, spoke on the roentgenological appearances in silicosis. Dr. Henry S. Kessler, N. J. Rehabilitation Clinic,

described the clinical aspects of the disease. Prof. Wm. S. McCann, of the University of Rochester, spoke on the physiology of the fibroid lung. Dr A. J. Lanza of the Metropolitan Life Insurance Company summarized the scientific aspects of the discussion and outlined the measures that are being adopted to handle the problem both from the medical and legislative viewpoints. Mr. Paul Folger, an attorney from Rochester, N.Y., discussed the medico-legal phases of the subject. Most of the speakers remained for the entire week and took part in the informal discussions that constituted a very important part of the session. The John Black Room was crowded to capacity. Fifty-two special students registered for the week; 14 men from the regular tuberculosis course elected to remain and the rest of an audience of 130 was made up of invited guests and local physicians. The group was composed of industrial physicians and executives, insurance officials, and state compensation commissioners.

An unofficial transcript of the proceedings was prepared by Mr. B. E Keuchle of the Employers Mutual Insurance Company of Wausau, Wisconsin, and his associates Drs. Belknap, Benton, Carhart, Enzer, Ford, Gray, Habbe, and Lotz. Copies were offered for sale at $5.00 and the entire proceeds were donated to the laboratory. It is with peculiar pleasure that we express our gratitude to Mr. Kuechle and those who assisted him in this work.

PUBLICATIONS AND REPORTS

Only four papers have been published this year owing to the fact that pending experiments have not yet been completed. These have been of a general nature, dealing with the etiology and pathology of silicosis and other pneumonokonioses. A reprint of one of them, delivered before the general session of the American Medical Association and representatives of the group is included in this volume. Others were presented before the American Institute of Mining and Metallurgical Engineers, the National Safety Congress, and the Radiological Society of America. A general article, "Pneumonokoniosis," written for International Clinics, will appear in June. Three papers by Dr. Gerald R. Dowd, formerly bacteriologist on the staff, are in press. Addresses were made before the physicians of the General Electric Company at Schenectady, and before a legislative committee of the State of Massachusetts. Considerable time has been devoted to the meetings of a committee of the Koniside Club appointed to formulate a classification of silicotic lesions and their appearances on the x-ray film. It is the hope of this committee to offer a standard nomenclature that can be generally adopted.

This volume also contains reprints of an address on Hypersensitiveness and Immunity in Tuberculosis by Mr. Cummings and Mr. Delahant, of a paper by Dr. Jameson on Tuberculosis of the Uterus and Fallopian Tubes, and a Summary on Tuberculin by Dr. Baldwin and the director.

STAFF

On October first Dr. Arthur J. Vorwald joined the staff as assistant

pathologist. Trained at the University of Chicago, and coming to us after a year of post-graduate work at Cambridge, he brings to our problems fresh points of view. His excellent training and his enthusiasm have already satisfied everyone that he is a most fortunate choice.

Mr. J. Cloyd Downs, a chemical engineer of distinction, is a voluntary assistant who has many times proved his worth by solving problems concerned with the preparation of dusts for animal injection. We consider ourselves most fortunate that he can be with us.

Mr. Frank Creedon worked so well and faithfully as a voluntary assistant last year that he was taken on to the regular staff as histological technician on October first.

Two special research students are already at work upon silicosis problems, and a third will arrive shortly. Dr. A. O. Severance, of Baltimore, has carried on experiments dealing with silicosis in fish and amphibia. Dr. A. Landau, M.R.C.P., of Cape Town, South Africa, recently came to us from Brompton Hospital on a Dorothy Temple Cross Research Fellowship. He is working on the comparative influence of various silicates on the susceptibility to tuberculous infection. Dr. F. Warden Brown, an Oxford graduate holding a Radcliff Travelling Fellowship, will shortly begin an intensive study of the action of one of the silicates known as sericite. It was recently claimed that this substance rather than quartz was the cause of silicosis.

In the field Mr. Richard Walters served faithfully as x-ray technician for six months until his health forced him to return for a period of rest. His work was appreciated not only here in his own organization, but by the physicians with whom he was associated at a mine hospital. We trust that the interruption is only temporary.

The other members of the staff remain as heretofore. The director takes this opportunity to thank all of them for the loyal service that they are rendering and expresses his appreciation of their cooperation.

BUILDINGS

A year ago it was announced that Mr. and Mrs. Frank B. Black had offered to provide funds for additional laboratory work rooms. The John Black Wing is now nearing completion. It consists of the John Black Room, the library and lecture room which these generous donors gave in 1927, and their recent gift of five new private laboratories located in a story above. In order to satisfactorily join the roof of the new wing with that of the old building it was necessary to extend the front gable of the latter. By so doing another large, well-lighted room was created in the attic of the old building. The photograph as reproduced in the front of this report shows the great improvement made in the front elevation by this change. The six additional work rooms and offices will fill a long-felt want by relieving the chronic state of congestion that has seriously hampered our work in the past several years. A necessary adjunct to the new addition was an increase in the heating plant. Rather than supplement an already overloaded system, it was found to be more economical to install new furnaces and to repipe the entire plant. Two new oil furnaces with a coordinated system of piping

are now in operation. It appears that the heating costs for the entire plant, including the new addition, may be less than that for the old building alone. Our gratitude to Mr. and Mrs. Black for this new gift is unbounded, and as we occupy and use the new plant we shall have a continual cause to be mindful of their generosity.

Toward furnishing and equipping the new work rooms, we have already received $1250. Of this sum $250.00, from Mr. Henry U. Harris, was acknowledged last year. Dr. Frederick Willson has recently donated $1000. which is deeply appreciated. This sum will suffice to put two or more rooms into commission, and as fast as further funds can be procured the others will be furnished and occupied.

CLINICAL LABORATORY WORK

The diagnostic department has operated most effectively under the direction of Mr. Kelley, assisted by Mr. Delahant and Mr. Hulpritt. While the fees collected are entirely inadequate to support the service, the receipt of $1229. from the Saranac Lake Academy of Medicine has made its continuation possible. Mr. Kelley's fellowship at the Sanatorium secures him his living expenses and his part-time associates receive part of their salaries from the Academy receipts. The following is a summary of the various diagnostic examinations made during the year ending December 31, 1934:

SUMMARY OF DIAGNOSTIC EXAMINATIONS

November 1, 1933 to December 31, 1934

Diphtheria cultures	9	for tubercle bacillus	109
Smears for Vincent's Angina	30	Stomach contents	4
Blood:		Milk, bacteriological counts	48
Agglutination for typhoid	36	Water, bacteriological examination	75
Differential counts	161	Water, chemical examination	426
Red and white counts	269	Smears for gonococcus	6
Hemoglobin determinations	111	Urine	1337
Coagulation time	43	Autogenous vaccines prepared	19
Grouping	101	Pathological specimens	130
Cultures	13	Autopsies, human	24
Chemistry	82	Animals inoculated for diagnosis	46
Sedimentation	54	Miscellaneous examinations	280
Sputum for tubercle bacillus	1577		
Spinal fluid, urine and other material		Total	4990

Of the autopsies performed, 7 were on cases of silicosis with tuberculosis sent to the laboratory from the field. One was a case of uncomplicated silicosis with death from generalized cardio-vascular renal disease. Of the "pathological specimens" 8 were lungs or portions of lungs from individuals who died after being exposed by occupation to dust of one kind or another. These were submitted for diagnosis by physicians in various parts of the country.

FINANCES

At the end of the fiscal year, September 30, 1933, the financial statement showed an apparent balance of $3,654.87. This was accounted for by advance payments of certain annual grants made during the fiscal year. The money was allocated to specific researches that were completed during the year. Likewise, at the end of the current year, there is an apparent balance of $10,390.81, which represents advance payments for work to be done during the coming year. In June a group of Mutual Insurance Companies through the American Mutual Alliance pledged their support to a three years' silicosis research program and paid their first annual installment of $5,000 in September. In October a similar group of stock insurance companies, through the National Bureau of Casualty and Surety Underwriters, made a similar three-year pledge and recently paid one semi-annual installment of $2,500. Each of these groups is financing certain specific problems of mutual interest to them and to the laboratory. The Metropolitan Life Insurance Company has renewed its annual pledge of $5,000. for the continued study of infection in association with silicosis.

The U. S. Gypsum Company made an additional grant of $1,000. for the continuation of experimental studies on the protective action of gypsum dust against the inhalation of silica. Experiments begun during the past year were not completed and they seemed of sufficient importance to warrant continuation.

The decreased income from the iron ore study has been apportioned between field and research laboratory expenses in approximatly the same ratio as last year. After deducting the costs of carrying on the work in the field and the payments due Dr. Sampson's laboratory for x-ray consultation, there remains only about $6,110. to carry on animal experimentation. This will not cover the actual cost of the work here but it is of such importance that the balance is being provided from other sources. The fluorspar study, with a grant of $3000. is self-supporting as no long-term dust inhalation on animals is involved.

The receipts from Mr. Kuechle's sale of Silicosis Symposium proceedings have amounted to $655., but none of this money was received prior to the end of our fiscal year on October 31, 1934. A contract for diagnostic work at the Northwoods Sanatorium has been renewed with the Adirondack Fund for the Tuberculous. This yields $1,000. which is applied toward an assistant's salary. The Agnes Musser Eckert Fellowship provides for another worker. The loyal support from the Milbank Memorial Fund constitutes a back-log on which we have relied so long. Receipts through the Saranac Lake Academy of Medicine amounted to $1,229., all of which was applied to the operation of the diagnostic department.

E. R. Squibb & Sons made an appropriation of $200.00 to Dr. J. N. Hayes for his investigation of the action of various oils in the pleural cavity.

For the coming year anticipated operating expenses will amount to $54,390. in addition to a sum of $8,500. to equip and furnish the new work rooms in the John Black Wing. Income is in sight to cover all but $4,000. of the regular budget and we have faith that this and the special

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equipment fund will be secured during the year. To make our staff complete we should have a petroprapher to identify and analyse the rock specimens from which dust for experiments are now prepared. At the present time we are forced to rely upon the generosity of others for this service.

In conclusion the director wishes to express his gratitude to Dr. Baldwin, director of the Trudeau Foundation, for his hearty support, to all his associates for their loyal cooperation, and to those whose financial assistance has made possible the continuation of our work.

SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

RECEIPTS AND EXPENDITURES

OCTOBER 1, 1933 TO SEPTEMBER 30, 1934

Receipts:

Balance on hand October 1, 1933			$3,654.87
From endowment held in trust by Trudeau Foundation	$1,875.00		
Other interest and exchange	15.69		
		1,890.69	
Gifts for maintenance of work:			
Adirondack Fund for the Tuberculous	1,000.00		
Mr. Henry Upham Harris	250.00		
Hillside Fluor Spar Mines	250.00		
Dr. Leroy U. Gardner	375.00		
Dr. Hugh M. Kinghorn (on pledge)	1,000.00		
Mr. Lawrence Macfarlane	300.00		
Metropolitan Life Insurance Co.	3,749.94		
Michigan Ore Mines	27,500.00		
Milbank Memorial Fund	3,000.00		
Miscellaneous Gifts *	105.00		
National Association of Mutual Casualty Companies	5,000.00		
Oglebay Norton & Company	416.67		
Mr. Arthur B. Purvis	750.00		
Rosiclaire Lead & Fluorspar Mining Companies	375.00		
Saranac Lake Academy of Medicine*	1,229.00		
E. R. Squibb & Sons	200.00		
U. S. Gypsum Company	2,875.00		
Total of gifts		48,375.61	
			50,266.30
Total receipts (carried forward)			53,921.17

* *See following pages for list of donors*

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:BER 30, 1934

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SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

RECEIPTS AND EXPENDITURES

OCTOBER 1, 1933 TO SEPTEMBER 30, 1934

Total receipts (brought forward) ----------			53,921.17
Disbursements:			
For Laboratory work and maintenance:			
Salaries ----------	18,905.14		
Supplies and equipment ----------	2,211.46		
Animals and feed ----------	1,915.04		
Fuel ----------	704.55		
Gas ----------	162.57		
Electric light and power --------	500.63		
Library ----------	450.66		
Telephone ----------	103.01		
Laundry ----------	79.52		
Publications ----------	396.35		
Travel ----------	246.84		
Repairs ----------	69.46		
Miscellaneous ----------	96.70		
----------		25,841.93	
For work in the field:			
Salaries ----------	14,219.98		
Travel, including automobile, etc --	1,533.43		
Advances to workers for expenses	625.00		
Miscellaneous ----------	111.54		
----------		16,489.95	
Total cost of work ----------		42,331.88	
Transferred to Trudeau Foundation, *reimbursement for funds advanced for new animal house built in 1933* ----------		1,198.48	
Total disbursed ----------			43,530.36
Balance on hand September 30, 1934 ----------			10,390.81

CONTRIBUTIONS
TO THE
SARANAC LABORATORY
From October 1, 1933 to September 30, 1934

(NOTE: Items in second column received after October 1st to be credited in 1935 financial report)

Adirondack Fund for the Tuberculous	1,000.00	249.99
Mr. and Mrs. Frank B. Black, for building		5,500.00
Mrs. Bigelow Crocker, thru Dr. H. M. Kinghorn . . .	5.00	5.00
Mrs. Charles L. Crocker, thru Dr. H. M. Kinghorn . . .	25.00	50.00
Mr. Henry Upham Harris, toward new building	250.00	
Hillside Fluor Spar Mines	250.00	500.00
Dr. Leroy U. Gardner	375.00	25.00
General Refractories Company . .	50.00	
Dr. Hugh M. Kinghorn (fulfilling pledge toward animal house completed 1933)	1,000.00	
Mr. B. E. Keuchle and associates, sale of publication, "Silicosis Symposium"		655.00
Mr. Lawrence Macfarlane, thru Dr. H. M. Kinghorn . .	300.00	
Metropolitan Life Insurance Company	3,749.94	2,499.96
Michigan Ore Mines, thru Pickands, Mather & Company	27,500.00	6,358.54
Milbank Memorial Fund	3,000.00	
National Association of Mutual Casualty Companies . .	5,000.00	
National Bureau of Casualty and Surety Underwriters . . .		2,500.00
North American Refractories Company	25.00	
Oglebay, Norton & Company . .	416.67	
Mr. Arthur B. Purvis, thru Dr. H. M. Kinghorn . . .	750.00	
Rosiclaire Lead and Fluorspar Company	375.00	375.00
Carried forward	42,971.61	18,718.49

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	750.00	
any	375.00	375.00
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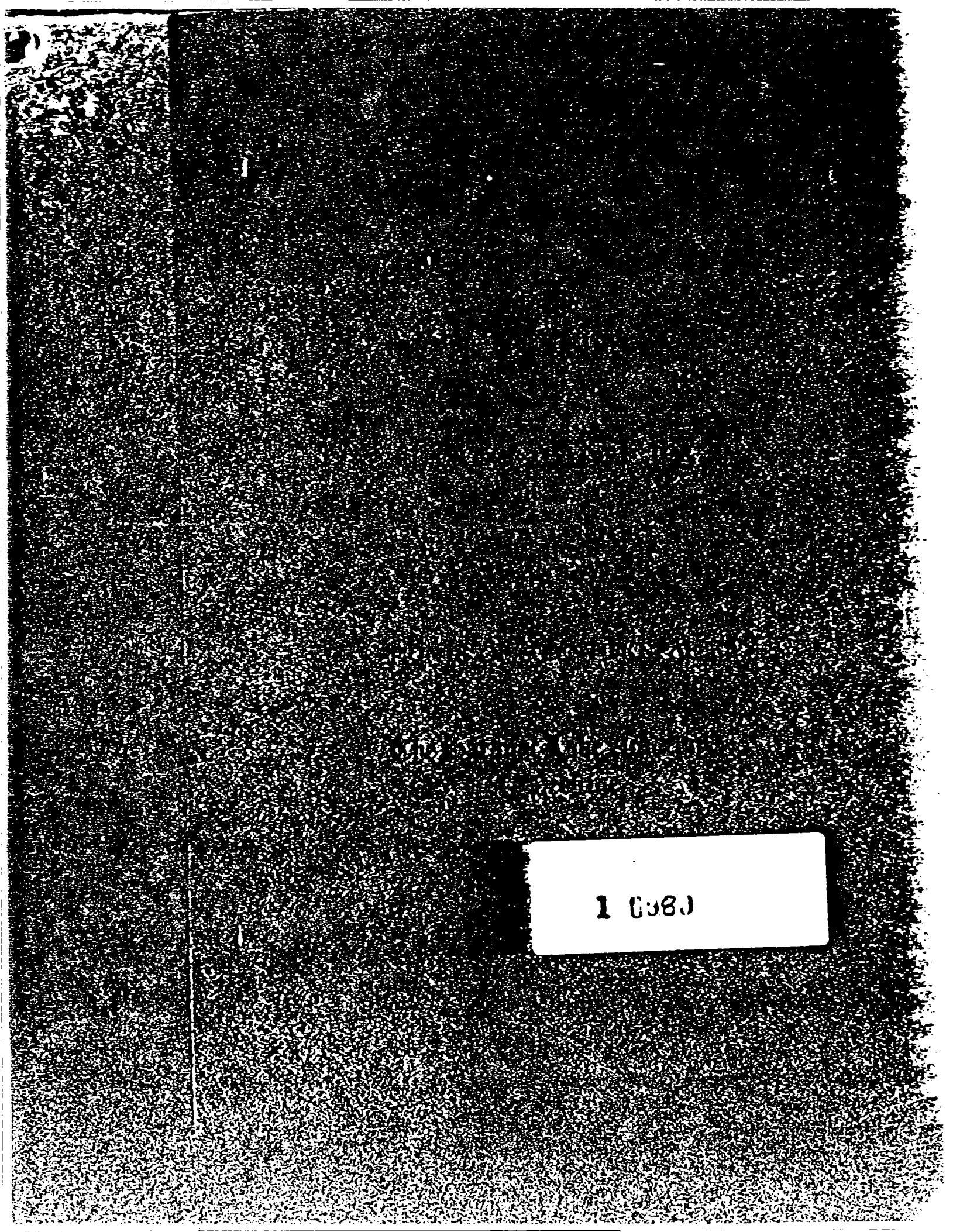
Brought forward	42,971.61	18,718.49
Saranac Lake Academy of Medicine		
Mrs. John F. Archbold	50.00	
Clinton J. Ayres, Inc.		25.00
Dr. Edward R. Baldwin	50.00	
Dr. Robert J. Beck	50.00	
Boyce & Roberson	15.00	
Dr. H. A. Bray		10.00
Dr. H. B. Brown	20.00	
Dr. Lawrason Brown	25.00	
Dr. David A. Cooper	10.00	
Mrs. F. C. Deemer	50.00	
Dr. Joseph T. Eagan	50.00	
Mrs. A. C. Erkander	50.00	
Mr. H. C. Eyer	25.00	
Miss Anna L. Gilbert	10.00	
Dr. Albert G. Hahn	10.00	
Dr. John N. Hayes	25.00	15.00
Dr. Fred H. Heise	10.00	
Mr. Fred A. Howland	50.00	
Dr. E. M. Jameson	25.00	
Dr. Hugh M. Kinghorn	50.00	
Mr. Herbert R. Leggett	25.00	
Mr. Wm. C. Leonard	5.00	
Dr. S. S. Lichtman	10.00	
Dr. Edgar Mayer	34.00	
Mr. H. S. Parker	50.00	
Mr. R. F. Plank	10.00	
Dr. Samuel Post	10.00	
Dr. J. Woods Price		25.00
Dr. Walter L. Rathbun	10.00	
Dr. John C. Russell	10.00	
Dr. Homer L. Sampson	50.00	
Sanatorium Gabriels	25.00	
Miss Ophelia Sawtell	10.00	
Dr. David T. Smith	10.00	
Miss Dorothy Smith		10.00
Mr. Robert B. Smith	100.00	
Carried forward	43,905.61	18,803.49

Brought forward	43,905.61	18,803.49
Dr. Willard B. Soper	50.00	
Dr. Earl R. Templeton	10.00	
Mr. Lewis S. Thompson	50.00	
Dr. Charles C. Trembley		25.00
Miss Jean Turnbull	20.00	
Dr. William A. Wardner	50.00	
Dr. George E. Wilson	65.00	
In Memory of Sydney Lunt Wood	50.00	
Dr. Warriner Woodruff		25.00
E. R. Squibb & Sons, thru Dr. J. N. Hayes	200.00	
U. S. Gypsum Company	2,875.00	250.00
Utica Mutual Insurance Company		100.00
Dr. Frederick and Mr. Thomas A. Willson, toward equipment of building		1,000.00
Mrs. S. L. and Mr. John P. Wood, in Memory of Sydney Lunt Wood	10.00	
	45,375.61	20,213.49

Mr. Frank Connable, thru Dr. Elliott P. Joslin, a Microchemical Sugar Apparatus

1936



— 1936 —

The Saranac Laboratory
for the
Study of Tuberculosis

OF THE EDWARD L. TRUDEAU FOUNDATION

REPORT OF THE DIRECTOR

AND

FINANCIAL REPORT

FOR THE YEAR ENDING SEPTEMBER 30, 1936

REPRINTS OF SCIENTIFIC PAPERS

The Saranac Lake Academy of Medicine

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 and controlled 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 1935. There are also two animal houses.

While the Saranac Laboratory co-operates with the Sanatorium in every possible way, and serves as the headquarters of the Trudeau School of Tuberculosis, it provides diagnostic facilities to the physicians practicing in the village and carries on independent researches in the field of tuberculosis and associated conditions.

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

THE SARANAC LAKE ACADEMY OF MEDICINE

IN the early part of July, 1931, a group of physicians in Saranac Lake met in the John Black Room to discuss ways and means for supporting the diagnostic and research activities of the Saranac Laboratory during a period of diminishing income. They were of the unanimous opinion that this institution is essential to the continued existence of the village as a center for the scientific treatment and study of tuberculosis. As a concrete expression of this feeling, they constituted themselves the nucleus of a body to be known as the Saranac Lake Academy of Medicine. Its object is "to foster interest in the pursuit of scientific medicine in Saranac Lake" through the agency of the Saranac Laboratory. Its members pledge themselves to support the activities of this institution in every possible way and to seek assistance from others for its operation. The active members are physicians practicing in Saranac Lake, but associate, sustaining, and life memberships are also open to interested laymen. In the financial report for the current year will be found a list of contributors.

The formation of the Academy created nothing new. The Laboratory, the Library, the diagnostic service, the scientific lectures and research have always been an integral part of the medical life of the village, but by many they have been freely accepted as a natural heritage from the great founder of this health community. By membership in the Academy of Medicine, or by contributions through it, anyone can feel that he has a part in keeping alive the Trudeau ideals for the furtherance of medical science.

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

LABORATORY STAFF

Leroy U. Gardner, M.D. ---------- *Director and Pathologist*
Arthur J. Vorwald, Ph.D., M.D. ---------- *Assistant Pathologist*
Thomas M. Durkan, M.E. ---------- *Chemist*
Richard V. Fletcher, M.D. ---------- *Clinical Pathologist*
Winfield O. Kelley, B.A. ---------- *Clinical Pathologist*
John R. Murphy, M.D. ---------- *Clinical Pathologist*
Douglas S. McCrum, B.S., (E.E.) ---- *Photographer and Assistant Chemist*
Morris Dworski, B.S., C.P.H. -------- *Assistant in Experimental 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*
Francis T. Creedon ---------- *Technician*
Edward L. Gockeler ---------- *Technician*
Andrew J. Redlin ---------- *Technician*
J. Cloyd Downs ---------- *Voluntary Assistant*
John G. Schmidt ---------- *Voluntary Assistant*
Leo A. Rabidou ---------- *Voluntary Assistant*
Stephen Worthen ---------- *Voluntary Assistant*
Roy A. Grinnell ---------- *Voluntary Assistant*
William E. Labounty ---------- *Assistant*
Henry C. Stout ---------- *Assistant*

FIELD AND CONSULTING STAFF

Donald E. Cummings, B.S. ---- *Assistant Director in Charge of Field Work*
Homer L. Sampson, D.Sc. ---------- *Consulting Roentgenologist*
John W. Karr, M.D. ---------- *Assistant Roentgenologist*
Daniel M. Brumfiel, M.D. ---------- *Clinical Consultant*
Robert N. Downs ---------- *Roentgenological Supervisor*
Richard Libby ---------- *Roentgenological Technician*
Richard Walters ---------- *Roentgenological Technician*
Melvin Berg ---------- *Bacteriological Technician and Clerk*
William Ficklin ---------- *Roentgenological Technician*
Hugo K. Loustari ---------- *Bacteriological Technician*
Helen R. Smith ---------- *Stenographer*

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REPORT OF THE DIRECTOR OF THE SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

— 1936 —

LEROY U. GARDNER, M.D., *Director*

THE policy and general nature of the work in progress at the Saranac Laboratory has remained unchanged during the past year. Problems discovered in field investigations of pneumoconiosis and associated tuberculosis are being studied and elucidated in the laboratory. A close co-ordination between field units, the roentgenological laboratory at Trudeau and the pathological division has insured a very practical trend to much of the research. But other problems of a more theoretical nature are also being attacked, their solutions may ultimately find application in the field of diagnosis and prevention of disease due to dust. Still other questions have been referred to the laboratory by industrial groups who have doubts as to hazards involved in the manufacture and use of their products.

The year has been a very busy one owing to the illness of the field director which has thrown additional responsibilities upon other members of the staff. Their willing co-operation has made it possible to fulfill our obligations, carry on an extensive program of investigation and secure the income necessary to maintain the laboratory.

LABORATORY RESEARCH

Important unsolved problems which are being investigated by experimental methods include: (1) An attempt to determine whether crystalline silica actually dissolves in the body. (2) A comparison of the biological activity of different forms of free silica. (3) A similar comparison of the effects of different forms of combined silica or silicates. (4) The modifying action of other substances inhaled or injected at the same time with silica. (5) The effect of particle size on the rate of tissue reaction. (6) A determination of the degree of retention of inhaled silica particles less than one micron in diameter in the lungs. (7) The effects of mouth breathing on the accumulation of dust in the lungs. (8) Assays of the biological activity of various industrial dusts. (9) A study of immunity in the silicotic host. These experiments, most of which were mentioned in last year's report, are not completed but some have progressed sufficiently to indicate their trend and probable outcome.

The effect of other dusts inhaled with silica. Gypsum, iron oxide, calcium fluoride, and perhaps some of the silicates appear to inhibit the action of silica and cause a delayed and often typical cellular response.

(1) *Gypsum and Silica.* A group of guinea pigs exposed to an atmosphere of nearly 172 million particles of pure calcined gypsum dust per cubic foot of air developed no significant changes in 2 years. At the present time, 16 months after concluding the exposure, the survivors still show no ill effects. So it has been concluded that the inhalation of gypsum dust in high concentrations is harmless. This conclusion is substantiated by negative results after the injection of an excessive dose into the peritoneal cavity of guinea pigs. It is also in accord with clinical observation.

Gypsum mixed with equal parts of pure quartz causes a clumping of the dust particles in the atmosphere. Many of the aggregates are too heavy to remain in suspension and too large to be inhaled. As a consequence relatively little of the quartz can enter the lungs and the development of fibrosis is very slow. Observations on animals exposed to such a mixture have now been extended over a period of 2 years and 7 months. They show less fibrosis than guinea pigs inhaling pure quartz for 12 to 15 months. The lesions that develop are modified in character as well as extent; very few of them exhibit the hyalinization that typifies mature silicotic fibrosis.

That the protective action of gypsum dust takes place in the atmosphere rather than in the body is indicated by another experiment in which animals have been exposed on alternate weeks to atmospheres containing pure quartz and pure gypsum. In these guinea pigs silicotic fibrosis developed in typical form and at a rate comparable to amount of exposure to quartz.

A new experiment in which animals inhale a mixture of 1 part quartz and 3 parts gypsum is now in its 12th month; it is too soon to surmise the result as no specific reaction to silica has yet developed.

Tuberculous infection in association with inhaled gypsum manifests a temporary tendency to progress but this is followed by healing with fibrosis.

(2) *Iron and Silica.* For this study there have been three inhalation experiments and two in which the materials were injected into the veins of rabbits. We have worked with iron ore (hematite) containing 6 per cent free silica and with ferruginous chert, the rock in which the ore is found, which averages about 48 per cent of silica.

An 8 hour daily inhalation of approximately 500 million hematite particles per cubic foot of air produced no pulmonary fibrosis in 3½ years. Injection experiments are not yet complete. Guinea pigs infected with attenuated tubercle bacilli and kept in this atmosphere showed a temporary progression of the infection followed by healing with considerable fibrosis.

A similar exposure to inhaled chert with 48 per cent silica caused only slightly more reaction in 2½ years than the hematite with 6 per cent silica. In animals kept in a normal atmosphere for 13 months after stopping the exposure, the reaction already initiated has manifested little tendency to progress. Chemical examination of their lungs revealed that only 6 or 7 per cent of the ash was composed of silica. The figure is low; in human silicosis it generally exceeds 18 per cent. A check-up revealed that while most of the dust particles used for experiment were of inhalable dimensions those of the silica component were in the upper size limits while those in the iron were in the smaller range. This caused the silica particles to settle out of the air more rapidly than the iron. Accordingly a new lot of chert

was secured in which both the silica and the iron particles had been ground to the desired size. On suspending this dust in the atmosphere a dust cloud was produced that averaged over 800 million particles per cubic foot of air, 95 per cent of which were less than 3 microns in diameter. On analysing the atmospheric dust inside the animal cages only 33 per cent of the material was found to be silica. In other words, there was still some selective settling of the quartz particles in the air before it floated into the cages. But even so, the animals would be subjected to over 260 million particles of free silica in every cubic foot of air, which is far in excess of that necessary to produce silicotic reaction in a period of 12 months. The new experiment is now in the 15th month but no nodular fibrosis has yet developed. One is therefore compelled to seek some other explanation for the failure of the silica to produce its usual effect.

There is a definite tendency for particles of iron to adhere to the surface of silica particles suspended in the atmosphere. Theoretically the protective coating might interfere with the interaction between the silica and tissue; if the coating is applied chemically there is definite experimental proof that it does. If the suspension is made in water instead of air no evidence of protection is detected. The injection of an aqueous suspension of the same chert into the ear veins of rabbits causes silicotic fibrosis within a year. After the two dusts enter the body there is nothing to indicate that the iron is attracted to the silica and neutralizes its action although it does modify the character of the tissue response. Guinea pigs exposed on alternate weeks to pure quartz and to hematite dusts develop silicotic fibrosis of the lungs whose severity is directly proportional to the amount and duration of the silica exposure. The final solution of this problem will require time and extended observation involving animal experimentation and a study of the physical relationship of air suspensions of silica and non-siliceous particles.

Infection of guinea pigs exposed to ferruginous chert with attenuated tubercle bacilli produced a result like that in the hematite series but there was a tendency for the spread of the infection to occur more frequently and the scar tissue that followed healing involved larger areas of the lungs.

(3) *Granite dust* is recognized as one of the common causes of silicosis but its behavior is peculiar. The rock consists of a natural mixture containing about one-third quartz and two-thirds silicates in the form of feldspar and mica. Only the quartz component is thought to be harmful. Early inhalation experiments with granite dust in this laboratory failed to produce silicosis in guinea pigs although the same material causes numerous cases of the disease in the workmen at Barre, Vermont. At the time, the failure of the laboratory experiment was attributed to insufficient exposure. However the lungs of the animals contained quantities of dust which should have initiated at least the early stages of a silicotic response. Furthermore, guinea pigs exposed to granite inhalation and infected with attenuated tubercle bacilli developed a fibrosis which had some of the characteristics of silicosis although typical nodules did not form. In the human cases the reaction to granite dust has also been unusual. The roentgenograms of many of the Barre cutters show a linear type of reaction instead of the usual nodulation. Others have a nodulation but it is frequently associated with definite evidence

of infection. A few autopsies on granite cutters with histories of long exposures have revealed no nodules; the lungs of other men whose exposures were similar but in which there was evidence of tuberculosis showed typical silicotic nodulation. The number of such cases has been too small to warrant any conclusions but the findings cannot be disregarded.

The various observations have suggested the following hypothesis: The silicates in granite dust prevent the free silica component from exerting its usual effect in the normal tissues; in the presence of a complicating tuberculous infection the inhibition is released and the silica is free to act.

To test this hypothesis a number of experiments have been devised and some of them are already finished. First it is necessary to be certain that an excessive dose of granite dust will not produce silicosis in the body of a normal animal. Previous experience has adequately demonstrated the reliability of the intravenous method of injection to produce a characteristic tissue response in the case of pure silica. Such response is elicited within a year after the injection of 1 gram and even 0.1 gram of quartz particles all less than 3 microns in diameter. The results have been verified too many times to question the method. Granite dust was ground to the same degree of fineness and four series of rabbits were injected with the following doses: 3.33, 1.67, 1.0 and 0.5 grams. The largest dose contains approximately 1 gram of free silica in the form of quartz which theoretically is ten times the amount necessary to cause reaction. During the 14 months which have elapsed since completing the injections most of the animals have been killed. At autopsy none has shown even microscopic evidence of a silicotic type of reaction; the response is of the type produced by inactive silicates. This result has been encouraging but the animals that are still alive might possibly develop changes later so they will be kept as long as possible. To be absolutely certain that there has been no error the observation is being repeated with a duplicate series of injections using a dust that has been checked both chemically and petrographically before and after grinding. (In the first series only chemical checks were made on the composition of the dust.)

To test the action of the other components of granite individually, the same method is being employed. One gram of feldspar particles has caused no significant reaction in one year's time. The micas have not yet been investigated as there have been technical difficulties in grinding them to the required size.

There still remains the testing of granite and its individual components in tuberculous animals These experiments are now in progress. Granite is being injected into rabbits with systemic tuberculosis; into others with a localized infection in the liver and into a third group whose livers are sensitized by the injection of heat-killed tubercle bacilli. This should demonstrate whether the tubercle bacillus, its products or their interaction with the tissues will free the quartz in granite from the inhibitory action of the silicates.

(4) *Calcium fluoride and silica.* The inhalation of fluorspar dust which contained 10 per cent of quartz produced only a very early silicotic reaction in the lymph nodes but not the lungs of rats exposed for a period of 10

months. After 15 months there was still nothing in the lungs. Injection of 1 gram of this dust, ground so that all particles were less than 3 microns in diameter, caused an early silicotic cirrhosis of the liver after 15½ months although almost no change was seen at 12 months. It is probable that in this instance the spar was merely diluting the silica as the dose of the latter was relatively small. In the inhalation experiments it averaged only 68 million particles per cubic foot of air and in the injection experiments the gram of dust contained only 0.1 gram of silica. As this study was undertaken merely to test the activity of a particular type of rock the possibilities were not so thoroughly explored.

The data of this first group of experiments form the basis for our belief that other types of dust inhaled at the same time with silica modify its action. Thus far only retarding influences have been investigated. There may be substances, possibly the alkalies, which accelerate the action of silica. When opportunity permits they will be investigated although this problem presents many technical difficulties.

(5) *The different forms of free silica.* Free silica exists in crystalline and amorphous forms. As pointed out a year ago, there is evidence to indicate that one of the common types of crystalline silica known as chalcedony may be more active than normal quartz. In chalcedony the crystals are exceedingly minute and are cemented together with amorphous silica whereas normal quartz occurs in the familiar large crystal. The tests on these two substances have not progressed sufficiently to permit definite conclusions as to their relative irritating properties. There are also other forms of crystalline silica produced by heating normal quartz to different temperatures. These former are known as chrystobalite, tridymite and vitreous silica. For some unexplained reason tridymite seems to be more active in the tissues than the others, but all are capable of causing fibrosis.

Of the amorphous forms of silica it was stated last year that opal was active and this observation has been verified. It has now been demonstrated that another mineralogical form of opal known as diatomite or diatomaceous earth is also capable of producing silicosis in animals. (The mineral, diatomite, is composed of masses of microscopic plants known as diatomes which have "skeletons" of silica.

It is thus becoming apparent that silica in the free state, whether crystalline or amorphous, is capable of setting up progressive fibrosis in the body. Whether all forms are equally capable of penetrating the lungs from the air remains to be demonstrated. When this phase of the work is completed it may become possible to correlate the degree of biological activity with the physical properties which are somewhat different in the various forms of silica. This should be helpful in determining the mode of action of silica upon the tissues.

The silicates or combinations of silica with various bases. Clinically the only silicate which is generally accepted as a cause of disease in the lungs is asbestos. Technically asbestos is not a single species of mineral: the term includes a variety of more or less complicated hydrated silicates of magnesium which have the common property of a *fibrous structure*. Among

the other silicates that have been reported to cause nodular fibrosis are talc and slate. However, the possible part played by co-existant latent or active infection has not yet been given due consideration in these cases.

A systematic examination of representative silicates is now in progress, making use of the intravenous and intraperitoneal injection methods to determine whether excessive dosages are capable of producing reaction in living tissues. The behavior of most of them has been followed for at least a year and it seems quite obvious that they will prove to be practically inert in uninfected animals. The reaction in all cases is one of phagocytosis at the site where the injected particles happen to be carried by the blood stream. Most of the phagocytes are immobile and they do not tend to collect into localized masses as is the case with uncombined silica. It is of course possible that more reaction will develop later but since there has been no change in a year in the animals injected intravenously it is improbable that any will ever occur. The following silicates have already been studied: sericite (from two sources), feldspar, garnet, sillimanite, talc and zeolite (both synthetic and natural.) The injection of asbestos minerals has just been started, but they present technical difficulties which will have to be overcome before they can be injected into the blood vessels of animals. The final step will be the testing of the same substances upon animals with healed and active tuberculosis. It is quite conceivable that in such hosts some of the silicates may produce a different response.

Alterations of immunity in the silicotic subject. The explanation for the high frequency of infection, and particularly tuberculous infection, in the silicotic individual has not yet been discovered. This subject is still under investigation and is being attacked from several aspects.

It is known that tubercle bacilli grow very rapidly in a young silicotic focus produced artificially in experimental animals; in the old lesions of human silicosis the organisms are usually very few and hard to find. The question arises as to whether the tubercle bacillus is stimulated by the silica itself or by some of the products formed from the interaction between it and the tissues. (1) *Effects upon bacteria in vitro.* Previous experience in the laboratory had shown that the addition of silica particles to artificial culture media accelerated the rate of growth of tubercle bacilli but the amount of culture obtained after a given period of time was no greater than without the silica. Recently some exceedingly fine crystalline silica was sent to the laboratory that has had a very marked accelerating influence on cultured bacilli. The old experiment is being repeated on a quantitative basis. (2) *Effects upon bacteria in vivo.* An attempt is being made to determine on a quantitative basis the number of tubercle bacilli in silico-tuberculous lesions of various ages.

The effects of silicosis upon the host are manifested by the development of the obvious fibrous nodules in the lungs but there may also be more subtle changes in the body fluids that explain the peculiar susceptibility to tuberculosis. The immunity mechanisms of the body fluids are now the subject of intensive study.

Natural immunity. Among certain other species the white rat manifests a natural immunity to infection with the tubercle bacillus. If the organisms are injected into the animal's veins real tubercles do not develop; the bacteria merely circulate in the blood for an indefinite period of time. It has now been shown that tubercles will form in a silicotic rat. Whether this means an increase or a lowering of resistance in debatable, but at least it has been demonstrated that there is an alteration of natural immunity. A similar experience was demonstrated some years ago in rabbits, which are naturally resistant to human type tubercle bacilli. Thus it appears that it is possible to alter natural immunity with silica.

Acquired immunity. It is well recognized that a certain degree of artificial immunity can be induced in animals by vaccinating them with tubercle bacilli of low virulence. This procedure is very simple and the effects of the primary infection, which remains localized, can easily be differentiated from those of the reinfecting test inoculation with virulent tubercle bacilli. In the silicotic host this is not so simple as the silica causes the vaccinating infection to spread. It is possible, however, to induce immunity with heat-killed bacilli. This method is under investigation and although the results are not yet complete it seems probable that the usual protective action will not be destroyed. It may prove to be somewhat impaired. The sensitivity to tuberculin of animals in the acute and subacute stages of silico-tuberculosis is comparable to that in animals with simple tuberculosis. Unfortunately the extremely chronic forms of silico-tuberculosis found in man are not reproduced in animals.

As soon as silicosis has developed in a group of rabbits now being dusted their immune responses to pneumococcus infection will be tested. This experiment has a practical as well as theoretical bearing for it has never been proven whether the silicotic individual is actually more susceptible to pneumonia than the normal. There is considerable evidence for believing that he is not. The work on the possible alteration of immunity is not sufficiently advanced to draw inferences as to its outcome.

The effect of mouth breathing is being investigated by exposing animals whose nasal passages have been more or less completely stenosed with caustics to the inhalation of dusts in the same room with normal controls. The weight of inhaled dust will be the criterion of the effect of this procedure.

The solubility of silica in the body is being approached from the angle of excretion in the urine as suggested by King. The urinary output of silica in groups of normal, tuberculous, and silicotic subjects is being followed over a long period of time. While it is not possible to analyse all of their food for its silica content, an attempt is in progress to discover how much of the excreted silica may be derived from food and how much from inhalation.

Retention of extremely fine silica in the lungs. A request was received to test the biological activity of a silica powder composed of particles not greater than 20 Angstrom units in diameter. This material seemsd to offer the opportunity of proving whether, as some observers claim, the lung treats very fine particles like a gas and eliminates them with the expired air or

whether they are retained and cause disease. Unfortunately there is no way to prevent particles of this magnitude from clumping and it is impossible to determine the size of minute clumps by ordinary methods of measurements. Nevertheless an inhalation experiment with an imperceptible suspension of atmospheric dust is being started to learn whether any reaction will occur.

Testing of industrial dusts suspected of disease-producing capacities. A study has been completed on the action of glass wool and it has been demonstrated that this substance is incapable of causing fibrosis in the animal body. Injected intravenously it has no more effect than the inert silicates described above. Large quantities can be ingested either with food or by the fasting stomach without producing demonstrable reaction in any part of the alimentary tract.

Tests upon the action of dolomite, silica jell and several other substances have been started.

FIELD STUDIES

The third annual survey of the iron ore miners in the Lake Superior district has now been completed. The results of examinations made by the various company physicians and of the roentgenograms of the chest totalling well over 5000 have not yet been tabulated but new cases of sidero-silicosis or progression to more advanced stages of this condition have been rare. Likewise the production rate of new tuberculosis has not been as great as was anticipated. Particular interest attaches to the group of cases, rather rare in this industry, which exhibit massive conglomerate shadows in the roentgenogram. A few of them have apparently been observed in the process of evolution. Sometimes they develop rapidly in men still at work who have no symptoms of infection. Most of these shadows persist but a few have disappeared as rapidly as they come. Their ultimate outcome is still a matter of conjecture but with the opportunity to follow their course year after year it should be possible to establish their clinical significance. The dust concentrations in all the mines have been maintained at levels which can hardly produce new cases of silicosis. In all rock work involving exposures even to low concentrations of silica dust the wearing of respirators is enforced. Future observations on the men will therefore be largely concerned with the evolution of such disease as may have already started.

A medical clinic was established in a plant of the Inland Steel Company at the beginning of the year. Physical examinations are being made by a physician in their employ, stereoscopic films of every chest are taken by a member of Dr. Sampson's technical staff and a complete laboratory examination including blood count, Kahn test, urine examination and anything else indicated is made in the clinical laboratory. An engineering survey is being carried on in the plant to discover and correct any hazard that may exist

The program includes both pre-employment and periodic examinations of all employees. Out of more than 3000 examinations this year only 2 or 3 cases of tuberculosis have been discovered. These men were informed of their conditions and arrangements were made for their treatment. Other conditions were likewise brought to the attention of the men and after a

thorough explanation they were referred to their own physicians for treatment. The plan is working well as the employees have confidence in the clinic physician and they appreciate the company's interest in their health. From the scientific standpoint the opportunity to re-examine from time to time a very large industrial group that is exposed to no particular hazard is unique. The material accumulated will furnish a basis of comparison for mining and other groups constantly exposed to high concentrations of silica.

A third study is being made in the cement industry. Although there is no theoretical hazard from silica in the manufacture of this product, a good deal of dust is produced In spite of the negatiive chest findings in the survey made by the United States Public Health Service, the Cement Association, which has high ideals for the health and safety of men employed by its member companies, asked the Saranac Laboratory to survey more of its plants. Three of them, located in Pennsylvania, Alabama and Kansas, have now been studied. The men were examined either by local physicians or by the clinical consultant to the Laboratory. Stereoscopic roentgenograms of the chest were made and interpreted by the department at Trudeau. Laboratory engineers made surveys of the concentration and character of the dust in the plants. The data from the last plant have not yet been compiled; the positive findings at the others were surprisingly meager.

No pulmonary changes are visible after prolonged inhalation of finished cement dust. A few of the men show an increase in the linear markings of the lungs but the incidence of this change cannot be correlated with the intensity or duration of the exposure. With one exception, where a man had run a drill in sandstone, the same can be said of the inhalation of the raw materials, limestone and clay, of which cement is made. Tuberculosis is not influenced by the inhalation of cement dust; the frequence of healed lesions has been the same as that in the general population. Complaints referable to infection of the upper respiratory tract have been relatively uncommon in the men thus far examined. Final conclusions as to the influence of cement dust will only be drawn after analysing the findings from widely scattered plants; at the present time it hardly appears that evidence of serious injury will be discovered.

A similar study was made of the men and the possible industrial hazards in another gypsum plant. The findings confirmed the conclusions previously reached, that the long-continued inhalation of gypsum dust is not dangerous.

TEACHING, ADDRESSES, AND PUBLICATIONS

Various members of the staff gave their usual courses in the Trudeau School of Tuberculosis. The Silicosis Symposium, which had been held during the two preceding years, was omitted because it was felt that not enough new material was available for discussion. Dr. Vorwald, the assistant pathologist, has given a series of lectures on the anatomy, physiology and pathology of the lungs to the nurses at Trudeau. Clinical-pathological conferences were held from time to time as part of the program of the Saranac Lake Medical Society. Papers were presented by the director, the assistant pathologist, and the chemist, before the American College of Physicians, the American Society of Safety Engineers, the New York State Medical Society, the American Association of Pathologists and Bacteri-

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ologists, the Konicide Club, the National Tuberculosis Association, the Fourth District Branch of the New York State Medical Society, and the Franklin County Medical Society. Membership on federal, state, industrial and insurance committees dealing with silicosis has also required considerable time and thought. Five papers have been either published or are in press. Reprints of three are bound as part of this report.

CLINICAL LABORATORY WORK

The diagnostic service to the clinicians and hospitals of the community has been maintained with a physician and three part-time technicians available to perform any tests that may be required. The work is financed by fees from patients, contributions to the Saranac Lake Academy of Medicine, an appropriation from the Trudeau Foundation and the proceeds of contracts with the General Hospital and Northwoods Sanatorium. The maintenance of this department is always difficult because many of the physicians elect to have only the more elaborate tests performed by the laboratory. Routine examinations, which constitute the bulk of the work and which would bring in more income are done elsewhere. Nevertheless it has been felt that the institution has an obligation to the community and every effort is being made to maintain the service. The remuneration is not sufficiently attractive to hold a qualified diagnostician very long and hence the personnel is constantly changing. However it has been possible to find competent physicians to perform this service during the period while they are finishing their cures. Dr. Vorwald, the assistant pathologist, has assumed the responsibility for this department and has not only improved the general quality of the service rendered but has personally given pathological diagnoses on over 200 surgical specimens without charge to the patients. During the year a total of 5038 examinations have been made in this department.

The unfortunate illness of Mr. Cummings, the field director, has kept him away since February, but the other members of the staff have loyally assumed extra responsibilities. Dr. Vorwald, assistant pathologist, has carried most of the load of supervising the experimental work in the laboratory, thereby relieving the director. Mr. Downs, field supervisor of roentgenology, has taken over the administrative details for the study in the iron ore industry and the supervision of the clinic in the Inland Steel Company. Mr. Durkan, the chief chemist, and Mr. MrCrum have made the engineering surveys in the cement and gypsum studies. Miss Cummings, the secretary, has spent many extra hours with the extra correspondence and voluminous reports that would ordinarily have emanated from the field director's office. The director takes this opportunity to express to them and to all the other members of the staff his appreciation for their support.

At the roentgen laboratory at Trudeau the laboratory budget provides the salary for an assistant to Dr. Sampson. Dr. John W. Karr, a graduate of the University of Rochester, joined the staff in this capacity in August. It is hoped that he will be able to relieve Dr. Sampson, who is now hard pushed to review the many thousands of films from our own and other industrial surveys.

Mr. J. Cloyd Downs, voluntary assistant chemical engineer, has not been able to spend much time in the laboratory but he still serves us as a valuable consultant. Mr. Edward Goeckler, who was a volunteer histological technician last year, has made his services so valuable that he is being taken on to the regular staff. Four more volunteers have served more or less time in the laboratory this year. Mr. L. A. Rabidou, Mr. John Schmidt and Mr. R. A. Grinnell have been assisting in the preparation of dust suspensions for animal injections and in various other ways. Mr. Stephen Worthen spent the summer in the chemical department, analyzing lung tissues. Our appreciation of their services is gratefully acknowledged.

In the diagnostic department the change in personnel has been unusually rapid. Dr. Robert Major left for his home in February and Dr. Richard V. Fletcher relieved him for three or four months until Mr. W. O. Kelley, who was formerly in charge of this work, returned for the summer. On October first Dr. John R. Murphy took over the responsibilities. All of them deserve the gratitude of the institution and the community for their able services.

FINANCES

The statement which follows indicates a balance of $15,031.06 at the end of the fiscal year. This sum is not surplus earnings but is made up of advance appropriations for research already in progress. Receipts during the year amounted to $62,608.43, which with the balance of $11,385.82 carried over from last year makes a total of $73,994.25. Of the current receipts $42,037.28 was in payment for consulting field and laboratory services and $10,000 was an appropriation by two associations of stock and mutual insurance companies for basic research. The balance consisted of earnings from income and miscellaneous gifts. The anonymous gift of $1,000 for equipping the new John Black Wing was acknowledged in last year's report, but was not credited to income as it was received after the expiration of the fiscal year. The sum of $1,278.15 was received from the sale of copies of the "Silicosis Symposium" published by the Employers Mutuals Insurance Company under the direction of Mr. B. E. Keuchle.

The director expresses his grateful appreciation for the support received from all who have contributed to the work in the laboratory. Special mention is made of the large contributions from the National Bureau of Casualty and Surety Underwriters, the American Mutual Alliance, the Employers Mutuals, and Mr. Samuel Eckert. The director acknowledges his debt to all the members of the staff who have rendered such faithful service and to Dr. Baldwin, the director of the Trudeau Foundation, for his unfailing sympathy and advice.

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SUMMARY OF DIAGNOSTIC EXAMINATIONS

January 1, 1936 — December 31, 1936

Diphtheria cultures	12	Stomach contents	4
Smears for Vincent's Angina	19	Milk, bacteriological counts	31
Blood		Water, bacterial examination	40
Agglutination for typhoid	14	Water, chemical examination	365
Differential counts	221	Smears for gonococcus	9
Red and white counts	393	Urine	1155
Hemoglobin determinations	178	Autogenous vaccines and filtrates prepared	31
Coagulation time	4	Pathological specimens	207
Matching and typing	205	Referred autopsy specimens	34
Cultures	15	Autopsies, human	45
Chemistry	124	Animals inoculated for diagnosis	55
Sedimentation	101	Miscellaneous examinations	725
Spinal fluid, urine and other material for tubercle bacilli	142		
Sputum for tubercle bacilli	909	Total	5038

SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

RECEIPTS AND EXPENDITURES

Year ending September 30, 1936

Balance on hand October 1, 1935			$11,385.82
Receipts:			
From endowment:			
Interest	1,875.00		
Dividends	1,000.00		
		2,875.00	
*Gifts and other receipts for maintenance of plant and work		55,633.43	
*Gifts for building and equipment		1,000.00	
Transferred from Elizabeth Milbank Fund		2,500.00	
Sale of old equipment		350.00	
Repayment of advance to worker		250.00	
Total receipts for year			62,608.43
Total of balance and receipts			73,994.25
Expenditures:			
Salaries, for research and field surveys		47,704.95	
Travel and other expenses of workers		2,421.90	
Fuel, light, supplies, animals, feed and other running expenses		7,964.54	
Permanent improvements of plant		871.80	
Total expenditures for year			58,963.19
Balance on hand September 30, 1936			15,031.06
Cash on hand:			
Bankers Trust Company (Saranac Laboratory Fund)		14,535.42	
Saranac Lake National Bank (Trudeau Foundation account)		495.64	
		15,031.06	

*See following pages for list of contributors

STUDY OF TUBERCULOSIS

ENDITURES

r 30, 1936

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CONTRIBUTIONS

TO THE

SARANAC LABORATORY

From October 1, 1935, to September 30, 1936

(Note: Items received after October 1, 1936, in second column, to be credited in 1937 report)

Adirondack Fund for the Tuberculous	999.96	249.99
American Mutual Alliance (Casualty Companies)	5,000.00	
Mrs. Bigelow Crocker	5.00	5.00
Mrs. Charles L. Crocker	50.00	50.00
Mrs. Francke G. Darte	50.00	
Agnes Musser Eckert Fellowship	1,000.00	1,000.00
Dr. Leroy U. Gardner	407.00	50.00
Dr. Albert H. Garvin.		7.00
Gulf Rock Oil Corporation	50.00	
Hillside Fluorspar Mining Company	1,250.00	
Inland Steel Company	12,899.98	4,299.99
Johns-Manville Corporation		1,250.00
Lake Superior Iron Ore Association	20,262.34	3,607.48
Mr. Lawrence MacFarlane	100.00	
National Bureau of Casualty and Surety Underwriters	5,000.00	
New Jersey Manufacturers Casualty Insurance Company	200.00	
Owens-Illinois Glass Company	600.00	
Pennsylvania Glass Sand Corporation		5.00
Portland Cement Association	2,400.00	2,400.00
Mr. Arthur B. Purvis	250.00	
Rosiclaire Lead & Fluorspar Mining Company	1,250.00	
Sales of Book "Silicosis Symposium" (thru Mr. B. E. Kuechle and Associates)	1,278.15	163.00
Carried forward	53,052.43	13,087.46

Brought forward	53,052.43	13,087.46
Saranac Lake Academy of Medicine:		
Mrs. John F. Archbold		50.00
Dr. Edward R. Baldwin	50.00	
Boyce & Roberson	25.00	
Mr. A. W. Currier	10.00	
Dr. Joseph T. Eagan	50.00	
Mrs. A. C. Erkander	50.00	
General Hospital of Saranac Lake	51.00	
Miss Anna L. Gilbert		10.00
Mrs. Henry Hudson	25.00	
Dr. David T. Smith	10.00	
Mr. R. B. Smith	100.00	
Dr. George E. Wilson	15.00	
Mr. Frank J. Tone		100.00
United States Gypsum Company	2,125.00	625.00
In Memory of Sydney Lunt Wood:		
Miss Sarah C. Armistead	5.00	
Mrs. S. L. Wood and Mr. John Wood	15.00	15.00
Miss Susan Wood	50.00	
	55,633.43	13,887.46

For New Building and Equipment

Anonymous, thru Dr. Henry B. Doust	1,000.00

For Endowment

(Held in trust by Trudeau Foundation)

Milbank Memorial Fund, completing pledge	50,000.00	
Mr. Frank J. Tone		5,000.00

1937

1937

The Saranac Laboratory

for the

Study of Tuberculosis

OF THE EDWARD L. TRUDEAU FOUNDATION

REPORT OF THE DIRECTOR

AND

FINANCIAL REPORT

FOR THE YEAR ENDING SEPTEMBER 30, 1937

REPRINTS OF SCIENTIFIC PAPERS

The Saranac Lake Academy of Medicine

— 1937 —

The Saranac Laboratory
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THE SARANAC LABORATORY

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

LABORATORY STAFF

Leroy U. Gardner, M.D. ---------- *Director and Pathologist*
Arthur J. Vorwald, Ph.D., M.D. ---------- *Assistant Pathologist*
Thomas M. Durkan, M.E. ---------- *Chemist*
Douglas S. McCrum, B.S. (E.E.) ---- *Photographer and Assistant Chemist*
Morris Dworski, B.S. C.P.H. ---------- *Assistant in Experimental 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*
Andrew J. Redlin ---------- *Technician*
Francis T. Creedon ---------- *Technician*
Edward Gockler ---------- *Technician*
John G. Schmidt ---------- *Clinical Laboratorian*
Roy A. Grinnell ---------- *Technician*
Leo A. Rabidou ---------- *Voluntary Assistant*
Steven Worthen, B.S. ---------- *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*
Homer L. Sampson, D.Sc. ---------- *Consulting Roentgenologist*
John W. Karr, M.D. ---------- *Assistant Roentgenologist*
Daniel M. Brumfiel, M.D. ---------- *Clinical Consultant*
Robert N. Downs ---------- *Roentgenological Supervisor*
Richard Libby ---------- *Roentgenological Technician*
Richard Walters ---------- *Roentgenological Technician*
Joseph Goldstein ---------- *Roentgenological Technician*
Melvin Berg ---------- *Bacteriological Technician and Clerk*
Hugo K. Loustari ---------- *Bacteriological Technician*
Helen R. Smith ---------- *Stenographer*

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_____ Stenographer

CONTENTS

REPORT OF THE DIRECTOR
of the Saranac Laboratory for the Study of Tuberculosis
1937

LEROY U. GARDNER, M.D.

RESEARCH in the laboratory is still intimately co-ordinated with clinical, roentgenologic and engineering field studies in industries where dust and tuberculosis constitute an occupational hazard. Animal experimentation is being used to test hypotheses formulated from field data to explain peculiar manifestations of disease and their causation. The income from the field studies has augmented appropriations from other sources so that it has been possible to continue various investigations. At times it has seemed than an undue proportion of the time of the research staff has been devoted to purely industrial problems but without the income thus produced it would have been quite impossible to carry on an expensive laboratory program. While the latter is intensely interesting, the data from the field are also valuable and often of more immediate and practical significance.

Laboratory Investigations

The main activities will be discussed in different groups, with no attempt to consider details. The problems being studied fall naturally into two groups, one which concerns the effects of dust alone and a second in which alterations in susceptibility to tuberculosis are of primary interest. Progress and tentative conclusions will be outlined briefly.

Protective Action of Various Substances Against Silica — A series of injection and inhalation experiments has demonstrated conclusively that different minerals, of various chemical composition, modify the deleterious influence of pure silica upon the tissues. This deduction is based upon an extensive experience with the natural mixtures of silica and other minerals, hematite (6% silica), anthracite coal (10.13% silica), crude fluorite (10.39% silica), granite (35% silica), ferruginous chert (50% silica), and South African Reef dust (70% silica), and with two artificial mixtures of quartz

and calcined gypsum (50 and 25% silica, respectively). All of these modifying substances seem to manifest two distinct modes of action, one taking place in atmospheric suspension of dust particles and the other within the body.

In atmospheric suspensions of quartz and other minerals the two kinds of particles tend to clump together and form aggregates which fall out of suspension because of their weight and which are not inhaled because they are too large to pass through the nose and other parts of the upper respiratory tract. The external physical phenomena are responsible for a retarded inhalation of the dust particles both silicious and non-silicious in character.

Internal effects taking place within the body are demonstrated by injection experiments. The introduction of various other minerals in the same suspension with quartz reduces the irritating properties of the latter and at least delays the appearance of tissue reactions characteristic of silicosis. There is apparently a wide variety of inhibitors of different chemical and physical composition. Some are more effective than others; some have afforded almost complete protection for periods of one or two years. To be effective they must apparently be injected at the same time as the silica. Little more is known about their mode of action; the explanation of their effect probably hinges upon more accurate information as to the cause of the injury from silica itself.

However this group of studies justifies the conclusion that the industrial hazard from a mixed dust containing silica is not defined solely by the number of particles of silica in that mixture; it is modified by the other components of the dust. Therefore an equitable industrial code should not be based merely upon the proportion of free silica particles in an atmospheric dust and even less should it depend upon analysis of the rock to be worked. For the present the hazard from each mixture must be evaluated empirically by studying the effects of particular combinations of silica and other substances upon the lungs of persons exposed for sufficient periods of time. It is unfair to impose penalties upon industries generating dust of low silica content without proof of injury from the specific mixture involved.

It remains to demonstrate whether any of these "inhibitors" are applicable to the field of prevention. The evidence now available would indicate that some of these substances merely retard the action of silica; that in course of time enough silica in the mixture will produce reaction but that the character of such reaction may be different from that provoked by pure silica. When the quantitative relationships between silica and inhibitors have been thoroughly investigated and when animals injected with the optimum combinations have been under observation for periods of three to five years it might be

possible to recommend some inhibitor for industrial use. As a matter of principle, however, it is undesirable to increase the total quantity of atmospheric dust in industry. The ideal objective is to decrease the concentrations of dust by preventing its formation. There are certain operations where the ideal may not be attainable and in such cases an inhibitor might be added. However, any general reliance upon the use of inhibitors should be decried.

Action of Silicates Upon Connective Tissue — Prevailing views of the action of silica upon the body are largely based upon the hypothesis that the mineral is slowly dissolved and liberates a toxic colloid. Since many of the combined forms of silica or silicates are more soluble than the very irritating quartz some observers have assumed that the silicates must also be highly injurious.

To determine whether the silicates as a class actually are irritating substances, a group of 24 of these minerals, which are used more or less commonly in industry, are now being studied. Since available space and funds would not permit inhalation tests of many dusts at one time their action is being tested first by injection techniques. These methods have proved entirely satisfactory to determine whether various forms of free silica are capable of causing fibrosis, even though the effects have been elicited in the connective tissues of organs other than the lungs. There is every reason to believe that similarly reliable results can be attained with silicates except those of a *fibrous* nature whose injurious action is apparently restricted to the lungs.

The negative character of the early responses to a few of the silicate minerals was mentiond in last year's report. As the study has progressed it is becoming more obvious that, as a class, the silicates are not necessarily irritating and that the mere presence of silica in the compounds does not constitute reason for assuming biologic activity. The action of 7 of these minerals in the animal body has now been followed for two years, 3 for one year, 6 for six months and the rest for shorter periods. In general none of the silicates has produced fibrosis in any way comparable to that provoked by free silica. The micas, observed for only six months, seem to be moderately irritating but whether these relatively early effects will ultimately cause a fibrosis awaits a demonstration. A few of the silicates, like talc, excite a moderate degree of chronic inflammation in the immediate vicinity of heavy deposit of particles, but this reaction has not progressed over a period of two years. There has been little tendency for delayed reactions to occur; tissue changes, which have not already made their appearance during the first six months of observation, have not usually developed at at later period. However, it is not gratuitously assumed that such an outcome is

impossible and five-year tests of silicates causing even slight degrees of inflammation have now been started.

The only outstanding exception to the general rule among the silicates has been the artificial compound sodium silicate, which is very soluble. Injected in high concentrations this substance causes immediate death. In more dilute solutions minute repeated doses have provoked chronic inflammation but there has been little tendency for fibrosis to develop. Probably toxic colloidal silica is liberated in the solution of sodium silicate and it is this product which has produced the fatal results. These results do not necessarily imply that human beings working in atmospheres polluted with sodium silicate dust are endangered. In fact it is very doubtful whether they suffer any ill-effects because the amount which could enter the body by inhalation would be too small to have appreciable effect. There would be no cumulative effect because of the rapid solution of the particles in the lungs.

The observations on silicates thus far made indicate that as a class these minerals are no more irritating than ones having no silica in their composition. If they are irritating it is because of some other property than their content of combined silica. This study casts considerable doubt upon the validity of the solubility hypothesis of the action of silica upon the body. It tends to minimize the possibility of industrial hazard from the inhalation of the majority of silicate dusts.

Asbestosis — Because the inhalation of asbestos dust in industry is a well-recognized cause of pulmonary fibrosis, the silicates known collectively as asbestos have been the subject of special study. Five different minerals in this category have been injected into rabbits and guinea pigs in the same manner as the other silicates and the action of one of them, Canadian chrysotile, is being tested by the inhalation method. For all of these studies the minerals were finely ground in steel mills; for inhalation tests most of the fibres did not exceed 7 microns, for the injections none were longer than 3 microns. The observations have not yet been completed but they have progressed to a stage where it is possible to surmise the probable outcome. Some of the injected animals have been sacrificed one year after introducing the particles; the minimum period for any species is three months. The inhalation tests are now in the ninth month. In none of these experiments has either the inhaled or the injected finely ground asbestos produced any fibrosis.

The negative findings thus far encountered are of unusual interest for they may have considerable bearing upon the nature of the injury from inhaled asbestos. The experiments were planned on the basis of certain premises, tentatively accepted as reliable. It was assumed that the pro-

ponents of the solubility hypothesis were correct and that asbestos was dissolved in the body to liberate irritating soluble silica. To permit solution to take place as rapidly as possible the fibres of the different minerals were ground to extreme fineness, for experience with quartz and other forms of free silica had demonstrated that under such conditions tissue reactions would develop with unusual rapidity. But the results would indicate that asbestos does not act like quartz. It will not produce fibrosis outside the lungs and it even seems that in grinding the fibres their capacity to injure the tissues has been minimized.

This belief is substantiated by the results in two inhalation experiments, one reported several years ago, and another now in progress. In the former attempt to reproduce the lesions of human asbestosis, the dust, of moderate concentration, contained many long fibres; fibrosis developed but it was not as advanced or as widespread as has been anticipated. In the hope of producing a more severe reaction in a short period of time the new experiment was planned using three or four times the concentration of a much finer dust. As the results are compared, it is becoming obvious that there is less reaction to the fine than to the long-fibre asbestos.

To test this hypothesis further, long-fibre asbestos has already been injected into the subcutaneous tissues, whose local movement is very limited, and in seven months no fibrosis has developed. The crucial test of injecting suspensions of long- and short-fibre asbestos minerals directly into the lung is now in progress. An inhalation experiment with higher concentrations of long-fibre chrysotile will be started as soon as space permits. It is hoped that these various tests will definitely settle the moot question as to the nature of the injury from this material.

The evidence now available suggests that the injury from asbestos dust may be mechanical rather than chemical in nature. A stiff fibrous foreign body might well be injurious to the cells of an actively mobile organ like the lung and have little effect upon those of the spleen and liver whose motions are relatively sluggish. Mechanical irritation would be more likely if the fibre were so long that it could not be completely surrounded by the body of a phagocyte. If the fibre were short enough to be completely engulfed by such a cell it could not come in contact with the fixed connective tissues. The tests now in progress should determine whether these preliminary deductions are correct and establish the nature of the injury by this unusual fibrous type of dust. They may explain the puzzling absence of asbestosis among those employed in certain extremely dusty processes of the asbestos industry. They may indicate the points at which special precautions must be taken in attempting to prevent the development of asbestosis.

Free Silica and the Nature of its Action on the Tissues — No definite conclusions have been reached upon this subject but the work of the past year has produced more evidence which is not in accord with the generally accepted solubility hypothesis. Tests of the solubility of various forms of free and combined silica in water indicate no parallel between the amount of solution and the capacity to provoke reaction in the tissue. The very irritating quartz yields only about 7 parts per million of soluble silica, while silica gel which is inert gives the figure 126 parts per million. The silicates, which have caused so little reaction in animals, now are being tested and they have shown a wide variation in solubility. The returns to date range from 4.5 to 52.3 parts per million. The present results are open to the criticism that the solvent has been water rather than a buffered fluid of slightly alkaline reaction. The recent purchase of a more accurate potentiometer will permit rechecks of solubility under more ideal conditions.

Observations on the biologic activity of different forms of amorphous silica have indicated that the physical state of the soluble matter may be of more importance than the amount of silica which is dissolved. Soluble silica in dispersed colloidal state is extremely toxic. In sublethal doses it produces reactions in the tissues which simulate those caused by fine quartz although they do not persist as long because much of the fluid colloid is eliminated from the body. If the same specimen of dispersed colloidal silica that has proved so irritating is allowed to stand for a few days it spontaneously gels. Injections of suspensions of the finely ground gel are absolutely inert and have produced neither inflammatory reaction nor fibrosis within the period of one year. The mere aggregation of the colloidal particles in the original suspension has completely altered the properties of the silica and rendered it harmless. Tests of natural minerals composed of amorphous colloidal silica have demonstrated variable degrees of irritating capacity. Opal is moderately irritating and causes a self-limited reaction which subsides after a year in contact with the tissues but leaves an appreciable amount of diffuse fibrosis. Another form, diatomaceous earth, as already reported causes a reaction indistinguishable from that to quartz. Studies of the possible influence of hydration in amorphous silica are now in progress in the hope of shedding more light upon this perplexing question.

Action of Submicroscopic Silica Particles — Last year's report mentioned tests upon an extremely fine free silica whose maximum particle size did not exceed 20 Angstrom units (0.02 micron). Previous experience had indicated that this substance should be exceedingly toxic when injected into animals. To our great surprise rabbits tolerated intravenous injections of the usual quantity (1 gm.) without apparent effect. All of them survived and were sacrificed

at intervals over a period of one year but guinea pigs injected intraperitoneally with 200 mg. died at once. Examination of the rabbit's tissues revealed little evidence of the acute inflammatory response that had been anticipated; the last member of the series killed after one year showed small foci of silicotic fibrosis in the spleen and liver. Apparently the material injected into the veins was so very fine that most of it was excreted through the kidneys without retention of enough to injure the tissues. Examination of the urine from time to time revealed high concentrations of soluble silica. The fine particles injected into the closed peritoneal cavity of guinea pigs could not escape and hence destroyed so many cells that death ensued.

An inhalation experiment was tried with this dust to determine whether such small particles would be retained in the lungs or whether they would be exhaled. The ordinary inhalation room could not be used as so little of the dust was available. A special box was built to accommodate 32 guinea pigs. Pneumonia developed and spread quite rapidly through the group. After five months of exposure the 9 survivors were killed. The lungs in every case showed rather large numbers of Langhan's giant cells, which customarily form in early silicosis, and there was lymphocytic infiltration in the adjacent walls. In the lymph nodes draining the lungs there was an early proliferative reaction.

Although the experiment was terminated prematurely by epidemic pneumonia, not due to the dust, there was enough reaction to conclude that appreciable quantities of this fine silica had been retained in the lungs. The proportion of the amount inhaled could not be ascertained as no means of measuring the atmospheric concentration of such small particles was available.

Effect of Mouth Breathing — Animals with nasal stenosis produced by the local application of caustics were made to inhale iron ore for approximately one year. Upon autopsy their lungs contained less dust than those of normal controls exposed at the same time. Whether one is justified to conclude that mouth breathing permits less dust to enter the lungs than the physiological nasal respiration is doubtful.

In the field of *tuberculosis* associated with pneumoconiosis there have been no unusual advances although this phase of the work is still the subject of active investigation.

Repeated attempts to demonstrate whether the addition of silica to artificial culture media stimulates ths growth of tubercle bacilli have produced inconsistent results.

Injection of living tubercle bacilli into areas of silicotic necrosis results in a rapid multiplication of the organisms. Simultaneous injection of silica and the lipoids extracted from tubercle bacilli produces more tubercle-like reaction

than either irritant alone will cause. This is hardly surprising in view of the fact that both of these substances cause a proliferation of the same type of cell and produce similar alterations in the morphology of these cells. The proteins of the tubercle bacillus have no such influence upon a silicotic reaction.

Injection of various silicates into tuberculous rabbits has failed to influence the course of the infection. During the eight to nine months period of observation the background of infection has not appreciably altered the response of the tissues to the mineral particles. Possibly the silicate, talc, will prove to be an exception for it seems to evoke more proliferation in tuberculous than in normal rabbits. No definite conclusions are possible at the present time.

Field Studies

Iron Ore Mining — From the time when the study in northern Michigan and Wisconsin was begun in 1933 until November 1, 1936 approximately 11,000 complete medical examinations were made by the different mine physicians upon 6,805 men. Over half of this group (4,043) have been re-examined; those with conditions considered of any significance were re-examined at least once a year and those with evidence of infection at more frequent intervals. Each of these examinations involved the taking of a pair of stereoroentgenograms which have been interpreted by Dr. Sampson. In each case there have been routine clinical laboratory studies of the blood (counts, sedimentation and Kahn tests) urine and sputum and special tests where indicated. Most of these tests have been performed in the local laboratories set up in each mining district. Special tests, such as guinea pig inoculations and extraordinary bacteriological studies have been done at the Saranac Laboratory. On the basis of these reports the personnel department in each mine makes all necessary changes in employment, shifting men who may show evidence of silicosis to positions where there is no exposure to dust and providing treatment for those with evidence of active infection.

At the end of each contract year the summaries of all these conditions have been rendered to the mining companies which serve as a guide to the effectiveness of their program of dust prevention. This information is of course confidential but it may be stated that the incidence of silicosis is no greater than that generally found in other hard rock mining; that the average miner has not developed silicosis until he has been employed in this industry for at least 20 years, when he is 45 years of age or older. The sidero-silicosis which these iron miners have acquired progresses very slowly; the rate of progression from one stage of pulmonary fibrosis to the next higher one has

been only 0.6 cases per year per 1000 men employed. The incidence of all pulmonary infections, active and inactive, increases with the amount of dust reaction in the lungs. In men with no evidence of such change 5 per cent have roentgenologic evidence of infection, in those with silicotic nodulation almost a third have such complications. It is interesting to note that of the infections interpreted as inactive at the time of their discovery only 11 per cent have reactivated and that of those originally considered active at the time of their discovery, less than one-fourth have become worse. Of the active cases 37 per cent have improved. These figures, which are rather favorable for a silicotic group, are in accord with experimental experience. Tuberculosis in animals exposed to mixtures of iron and silica tends to heal with the formation of scar tissue; in guinea pigs exposed to pure silica the infection almost invariably progresses to a fatal outcome. Of the miners who died, tuberculosis was the leading cause of death with a rate twice that for normal individuals. The mortality from diseases of the cardio-vascular-renal system has been lower than that in the general population. The incidence of syphilis has been remarkably low; only 1.5 per cent of the group have shown a confirmed positive Kahn test. The statistics fail to show any correlation between the incidence of syphilis and the development of pulmonary fibrosis from dust.

The clinic at the Inland Steel Plant, mentioned in previous reports, has examined 7,000 men during the past year. In the early part of this period so many new men were employed that relatively few old employees could be examined. From our own point of view this was valuable experience as it permitted the accumulation of more basic data upon the physical condition of the average industrial male population. Among the older employees of the plant very little evidence of industrial disease has been discovered; the incidence of healed tuberculosis has not exceeded the average and there have been only a few cases of active tuberculosis. The latter have been offered sanatorium treatment as soon as it was diagnosed. Engineers from the laboratory have made many visits to the plant, calling attention to operations which involved possible dust hazards and collaborating with plant engineers in devising means of correction. The management has been extremely cooperative and has made every effort to safeguard the health of its employees.

Further studies of *cement plants* have been carried on during the past year. Three of them located in Indiana, Texas and New York have involved complete physical examinations with roentgenograms of the chests of all employees as well as engineering surveys of the dust in different parts of the plants. Fourteen other studies in plants located in Ohio, Illinois, Missouri, Michigan, Iowa, Texas, California and Washington have been confined to an analysis of the raw materials and determinations of the composition and concentration

of atmospheric dusts. Although some of the mills have shown more dust than is compatible with the standards of good housekeeping, analysis of the findings in over 1,300 employees has failed to demonstrate that the inhalation of cement dust has a significant influence upon the respiratory tract. Among the entire group two or perhaps three men showed roentgenologic evidence of non-clinical dust reactions in their lungs. They usually had worked in quarries, where they were subject to high concentrations of raw materials. Neither could one conclude that men who had spent their industrial lives in such atmospheres were unusually susceptible to infections. The incidence of influenza, disabling colds, and pneumonia has not been high. No cases of clinical tuberculosis have been discovered and the incidence of the scars of healed or latent foci as revealed in roentgenograms is the same as that found in the general adult male population (4.5 to 5 per cent). The boils and dermatitis of which one hears so much in cement workers seem to occur locally in plants where wash house facilities might be improved.

In the *gypsum industry* one more plant has been surveyed. Miscellaneous examinations of employees have only served to strengthen our belief in the harmlessness of gypsum dust.

Teaching, Addresses and Publications

The usual courses in etiology, bacteriology and pathology were given in the Trudeau School of Tuberculosis. A third symposium on silicosis, held in June, was attended by a group of 100 physicians, engineers and administrators. Approximately half of the registrants had been present at previous sessions and almost every one had had practical experience in some phase of the dust problem. The week's discussions were led by Prof. Philip Drinker of Harvard University, Dr. R. R. Sayers of the U. S. Public Health Service, Dr. A. R. Riddell of the Ontario Department of Health, Mr. Theodore C. Waters of the Maryland Occupational Disease Commission, Dr. E. P. Pendergrass of the University of Pennsylvania, Prof. W. S. McCann of the University of Rochester and members of the laboratory staff, Dr. H. L. Sampson, Mr. D. E. Cummings, Mr. T. M. Durkan and the director. Illness prevented Dr. A. J. Lanza of the Metropolitan Life Insurance Company from attending. The mutual exchange of ideas was considered generally profitable. A full report of the proceedings of this meeting has been prepared and published by the Employers Mutuals Insurance Company of Wausau, Wisconsin. As in previous years the company is bearing all of the expense in this matter and donating the proceeds to the Laboratory for research purposes.

Numerous addresses have been made by different members of the staff. The director has spoken on thirteen occasions to different medical and industrial groups. The assistant director, Mr. Cummings, since his return to work in the summer has made an address before the Western Branch of the American Mining Congress and has lectured to the students of the University of Colorado. The assistant pathologist, Dr. Vorwald, has spoken before three medical societies. Since many of these talks have dealt with the same subject not all of them have been published. Reprints of five papers are bound with this report. The director has contributed a chapter on experimental pneumoconiosis to a monograph on diseases due to dust to be published by the Oxford University Press. Dr. Vorwald conducts classes in anatomy and pathology for the nurses of the Trudeau Sanatorium and he has also given a most excellent series of clinico-pathological conferences before the Saranac Lake Medical Society.

Clinical Laboratory Work

As heretofore the Laboratory has made serious effort to provide diagnostic facilities to the physicians of the community. Contributions from the Trudeau Foundation, the Saranac Lake Academy of Medicine and contracts for services with the Saranac Lake General Hospital and Northwoods Sanatorium supplemented by fees from individuals have made it possible to keep one or two men available for this work. During the major part of the year the clinical laboratory was successively in charge of Dr. John R. Murphy, Mr. David H. Cohen and Mr. B. Schultz, both the latter being medical students who were completing their cures. While it has been the policy to attempt to provide employment with remuneration for any physician or student who is finishing his cure, it has often proved difficult to find men with enough training who would carry on this work very long. As no one was available in the fall, it was decided to put the work in charge of regular members of the laboratory staff. Dr. Vorwald agreed to accept the responsibility of supervision, Mr. Morris Dworski was made part time clinical bacteriologist and Mr. John Schmidt was assigned the bulk of the remaining work. Mr. Anthony Delahant is available for pneumococcus typing day and night and he is also responsible for bacteriological examinations of milk and water. By this arrangement the laboratory sacrifices the time of valuable assistants but it is able to offer the community a more dependable consultation service.

In the table which follows are summarized the 6809 examinations made in this department, an increase of 1778 above that for the previous year.

Summary of Diagnostic Examinations

January 1, 1937 to December 31, 1937

Diphtheria Cultures	21	Stomach Contents	21
Smears, Vincent's Angina	8	Milk, bacterial counts	27
Blood:		Water, bacteriology	91
Typhoid Agglutination	6	Water, orthotolidine	415
Differential Counts	211	Smears, gonococcus	9
Red and White Counts	375	Urine, routine and special tests	2224
Hemoglobin	167	Autogenous Vaccines	32
Matching and Typing	220	Surgical Pathologic Specimens	208
Cultures	23	Autopsies, human	45
Chemistry	151	Referred Autopsy Tissue	14
Sedimentation	129	Animals Inoculated for Diagnosis	67
Spinal Fluid, Urine and Other Material for Tubercle Bacilli	121	Ascheim Zondeck Test for Pregnancy	30
Sputum for Tubercle Bacilli	1515	Miscellaneous Examinations	679

Among the autopsies were six cases with a history of industrial exposure to dust, four of whom had silicosis. The "referred autopsy tissues" were all of a similar nature and were submitted to confirm a questionable diagnosis. In many instances roentgenograms of these persons had been taken before death so that correlation with the post mortem findings was possible.

Staff

It is a pleasure to report that Mr. Cummings, the assistant director in charge of field work, has recovered his health and that since July has been able to assume responsibility for supervising his department. Aside from the changes in the personnel of the diagnostic department already mentioned, the only others are the resignations of Mr. William Ficklin, x-ray technician and of Mr. Leo Rabidou, voluntary assistant, both of whom have accepted positions elsewhere. Their past services are gratefully acknowledged. Mr. Roy Grinnell proved to be so valuable a voluntary assistant that he has been appointed a regular staff technician. Mr. Steven Worthen, an instructor in chemistry at Dartmouth College, assisted in the chemical department during the summer. His help was appreciated by all with whom he came in contact.

The director takes this occasion to express his gratitude to all the loyal

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even Worthen, an instructor
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is gratitude to all the loyal

members of the staff who are collaborating with him. Their co-operation and interest are largely responsible for such results as have been acheived. If his own functions were as successfully fulfilled as theirs he would have cause for satisfaction. He also acknowledges his debt to Dr. Baldwin, the director of the Trudeau Foundation, to whom he can always turn with perplexing questions of administrative policy.

The newly appointed board of trustees of the Laboratory consisting of Dr. Baldwin, Mr. Oliver James, Dr. Wm. P. Thompson, Mr. Roy Dayton and the director has had one meeting since its organization last summer. The opportunity to discuss new proposals and to share the responsibilities of financing the research program with such a group has been a source of encouragement and gratification.

Finances

The statement of our financial condition on the succeding pages indicates a balance of $10,989.88 at the end of the fiscal year but this does not constitute a surplus. It merely represents funds appropriated in the previous year but not yet expended. The receipts from various sources have amounted to $59,518.64, which with the balance of $15,031.06 carried over from last year make a total income of $74,549.70. Of this sum $39,849.29 was received for consulting field and laboratory services and $9,973.00 from various donors. The Employers Mutuals Liability Insurance Company, which has published the proceedings of the silicosis symposia under the editorship of its vice-president, Mr. B. E. Keuchle, turned over the sum of $289.25 from the sale of previous reports.

It is the director's privilege to publicly express his appreciation to all who have contributed to the support of the laboratory and its work. The insurance groups, The National Bureau of Casualty and Surety Underwriters, The American Mutual Alliance and the Employers Mutuals Insurance Company, Mr. Samuel Eckert and The Montreal Mining Company have each made substantial contributions to research. Through the Saranac Lake Academy of Medicine ten loyal friends of the institution contributed the sum of $302.00 during the fiscal year toward the support of the diagnostic service. Additions to the endowment fund include a bequest of $5,000.00 from the late Isadore S. Lazard and a gift of $5,000.00 from Mr. Frank J. Tone, president of the Carborundum Company. To them and to every other contributor mentioned in the financial report that follows we are deeply grateful.

SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

RECEIPTS AND EXPENDITURES

Year ending September 30, 1937

Balance on hand October 1, 1936		$15,031.06
Receipts		
From endowment:		
Interest and dividends	$9,288.60	
*Gifts and other receipts for maintenance of plant and work	50,230.04	
Total receipts for year		59,518.64
Total of balance and receipts		74,549.70
Expenditures:		
For research and field surveys	53,401.79	
Travel and other expenses of workers	1,789.24	
Fuel, light, animals, feed, supplies and other running expenses	8,368.79	
Total expenditures for the year		63,559.82
Balance on hand September 30, 1937		
In Saranac Laboratory Fund	9,989.88	
In Trudeau Foundation Fund	1,000.00	
		10,989.88

Note: In addition to the above receipts the following were received for endowment:

Gift, Mr. Frank J. Tone	5,000.00
Bequest, Estate of Isadore Sidney Lazard	5,000.00

*See following pages for list of contributors

\$15,031.06

\$9,288.60

50,230.04

59,518.64

74,549.70

53,401.79

1,789.24

8,368.79

63,559.82

9,989.88

1,000.00

10,989.88

5,000.00

5,000.00

CONTRIBUTIONS

TO THE

SARANAC LABORATORY

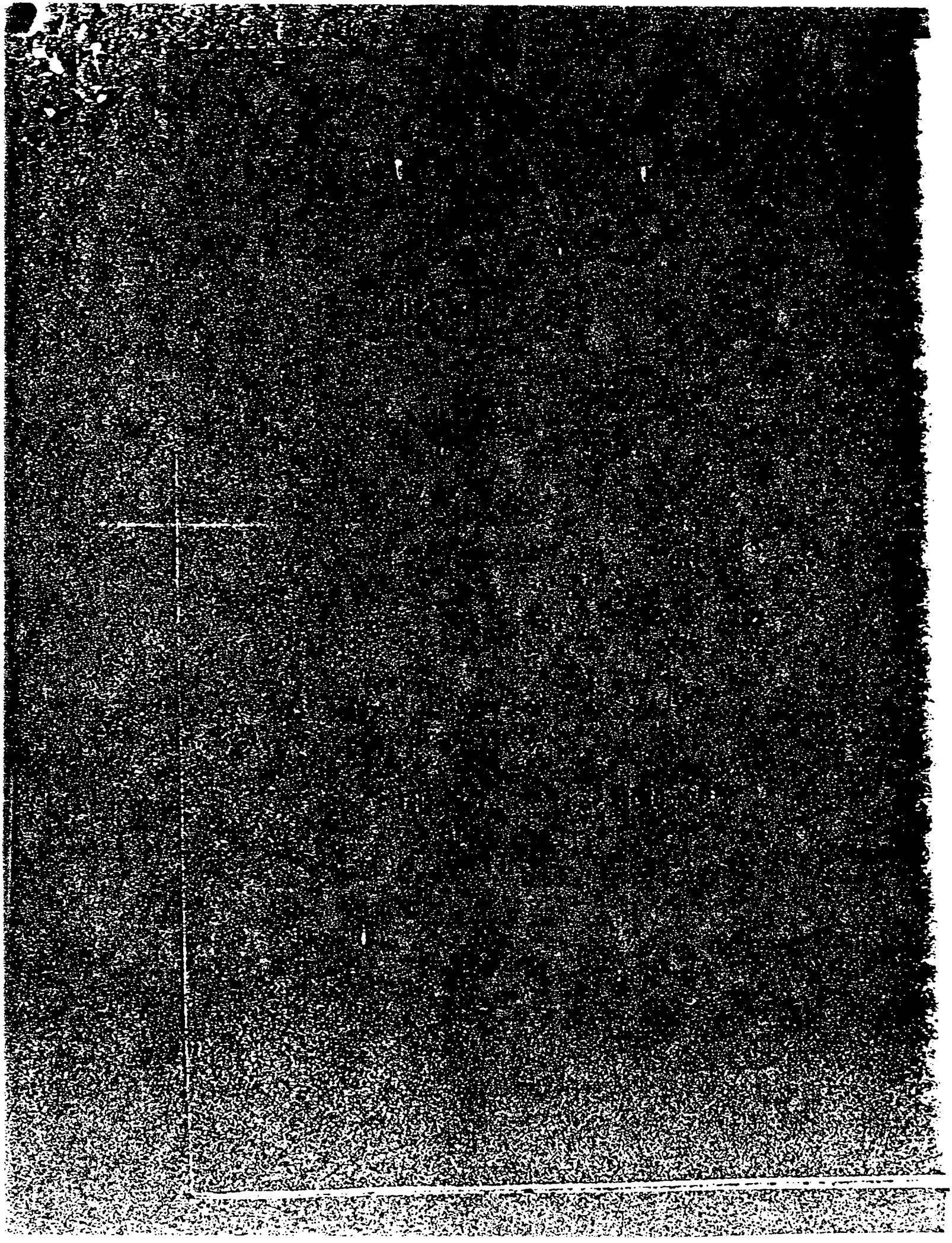
From October 1, 1936, to September 30, 1937

(Note: Items received after October 1, 1937, in second column, to be credited in 1938 report)

Adirondack Fund for the Tuberculous	\$1,000.00	\$249.99
Air Hygiene Foundation of America		750.00
Agnes Musser Eckert Fellowship	1,000.00	
Agnes Musser Eckert Fellowship (securities valued at)	1,052.50	
Mrs. Bigelow Crocker	5.00	10.00
Mrs. Charles L. Crocker	50.00	50.00
Dr. Leroy U Gardner	310.00	350.00
Dr. Albert H. Garvin	32.00	
Inland Steel Company	17,633.37	5,000.01
Johns-Manville Corporation	3,750.00	1,250.00
Lake Superior Iron Ore Association	11,294.92	6,568.99
Mr. Lawrence Macfarlane	100.00	
Montreal Mining Company	500.00	
National Association of Mutual Casualty Companies		5,000.00
National Bureau of Casualty and Surety Underwriters	5,000.00	
Portland Cement Association	4,716.00	
Mr. Arthur B. Purvis	250.00	
Sales of Book "Silicosis Symposium" (through Mr. B. E. Kuechle)	289.25	9.00
Saranac Lake Academy of Medicine:		
Mrs. John F. Archbold	100.00	
Dr. Edward R. Baldwin	50.00	
Carried forward	47.133.04	19,237.99

Brought forward	47,133.04	19,237.99
Dr. Helen Evarts	10.00	
General Hospital of Saranac Lake	16.00	
Miss A. Louise Gilbert	10.00	10.00
Mrs. Henry Hudson		25.00
Mrs. McCaffery	1.00	
Dr. David T. Smith	10.00	
Miss Dorothy Smith	5.00	
Mr. Robert B. Smith	100.00	
Mr. Frank J. Tone	100.00	
United States Gypsum Company	2,500.00	625.00
In Memory of Sidney Lunt Wood:		
Miss Sarah C. Armistead	5.00	
Miss Susan Wood	50.00	
Mrs. S. L. Wood and Mr. John Wood	15.00	20.00
	49,955.04	19,917.99

1939



— 1939 —

The Saranac Laboratory for the Study of Tuberculosis

OF THE EDWARD L. TRUDEAU FOUNDATION

REPORT OF THE DIRECTOR

AND

FINANCIAL REPORT

FOR THE YEAR ENDING SEPTEMBER 30, 1939

REPRINTS OF SCIENTIFIC PAPERS

The Saranac Lake Academy of Medicine

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 1935. There are also two animal houses.

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

THE SARANAC LAKE ACADEMY OF MEDICINE

IN July, 1931, a group of physicians in Saranac Lake met in the John Black Room to discuss ways and means for supporting the diagnostic and research activities in the Saranac Laboratory during a period of diminishing income. They were of the unanimous opinion that this institution is essential to the continued existence of the village as a center for the scientific treatment and study of tuberculosis. As a concrete expression of this feeling, they constituted themselves the nucleus of a body to be known as the Saranac Lake Academy of Medicine. Its object is "to foster interest in the pursuit of scientific medicine in Saranac Lake" through the agency of the Saranac Laboratory. Its members pledge themselves to support the activities of this institution in every possible way and to seek assistance from others for its operation. The active members are physicians practicing in Saranac Lake, but associate, sustaining, and life memberships are also open to interested laymen.

The formation of the Academy created nothing new. The Laboratory, the Library, the diagnostic service, the scientific lectures and research have always been an integral part of the medical life of Saranac Lake, but by many they have been freely accepted as a natural heritage from the great founder of this health community. By membership in the Academy of Medicine, or by contributions through it, anyone can feel that he has a part in keeping alive the Trudeau ideals for the furtherance of medical science.

THE SARANAC LABORATORY

TRUSTEES

LEROY U. GARDNER, M.D., *Director*

EDWARD R. BALDWIN, M.D. — WILLIAM P. THOMPSON, M.D.

OLIVER B. JAMES, *Treasurer* — ROY DAYTON, *Secretary*

DONALD E. CUMMINGS, B.S.

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. Durkan, M.E. ----------*Chemist and Engineer*
Louis Berkelhamer, B.S., M.S. ---------- *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*
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*
Roy A. Grinnell ---------- *Technician*
Robert E. Liddy ---------- *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*
Homer L. Sampson, D.Sc. ---------- *Consulting Roentgenologist*
Daniel M. Brumfiel, M.D. ---------- *Clinical Consultant*
Robert N. Downs ---------- *Roentgenological Supervisor*
Richard Libby ---------- *Roentgenological Technician*
Richard Walters ---------- *Roentgenological Technician*
Joseph Goldstein ---------- *Roentgenological Technician*
Melvin Berg ---------- *Bacteriological Technician and Clerk*
Helen R. Smith ---------- *Stenographer*

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Chemist and Engineer
------- Petrographer
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cal Technician and Clerk
--------- Stenographer

CONTENTS

REPORT OF THE DIRECTOR

of the Saranac Laboratory for the Study of Tuberculosis

1939

LEROY U. GARDNER, M.D.

ACTIVITIES in the Laboratory the past year have followed their usual trend. No startling discoveries have been made but these rare occurrences in the study of chronic diseases are the good fortune of few investigators. Most of us must be satisfied to observe the successive manifestations of such diseases as they evolve in human beings and experimental animals. Our attempts to simplify nature's processes by creating highly artificial conditions sometimes lead us astray but at others they provide the means of forging a link in a chain of evidence.

The reprints of published papers bound with this report in no sense reflect the extent of experimental work in progress. Possibly our policy of publication is unsound. "Point papers," based upon individual tests, are rarely issued because we ourselves are not always certain of their significance and reports on industrial diseases are often misinterpreted or given unwarranted importance by non-medical readers. It has, therefore, been customary to defer publication until the completion of collateral experiments bearing on the same topic. This method permits evidence to be weighed and evaluated in the light of experience, but it may defeat itself by necessitating papers so long that few but specialists are interested in reading them.

The annual report of the Director is his vehicle to indicate the nature of the work of the Laboratory and to speculate upon its significance. The purpose is not to draw final conclusions, but to inform the sponsors of the work and others of its trends and of any apparent progress.

Experience with the action of asbestos dust still confirms the impression reported a year ago that grinding the fibres of this mineral to an extremely fine state of subdivision destroys or at least minimizes their capacity to irritate the lungs. Nothing has been discovered that is incompatible with the theory that the irritating properties of the longer fibres is of a mechanical nature. A crucial test on which we had relied to prove the point has failed for reasons

beyond our control. On the premise of a report by another observer to the effect that dogs would develop asbestosis, we experimented upon this species of animal but found that no reaction had developed after a year's contact with asbestos fibre. The test for which such high hopes were entertained consisted in the introduction of large doses of asbestos fibre into both lungs by means of a bronchoscope, followed by collapse of one of them induced by stenosing the stem bronchus with silver nitrate. According to our theory of mechanical irritation the collapsed lung should move very little with respiration and hence the fibres within it would exert little influence. The reasons for the failure of the dog to respond to this dust are unknown, but the same is true of all other species tested with the exception of man and guinea pigs. The probable significance of the results has made it seem profitable to repeat the experiment on guinea pigs. If the technical difficulty of bronchoscopy in this small animal can be overcome we should be able to substantiate our belief in this theory.

A series of experiments by Messrs. Dworski and Delahant upon the nature of the injury produced by silica particles has yielded most interesting, though in some respects perplexing results. It will be recalled that the majority of obeservers believe that slow solution of silica particles in the tissues results in chemical injury of the tissues. This solubility hypothesis, at least in the simple form thus stated, is not consistent with all the experimental observations. Chief among the latter are, first, the lack of reactions suggestive of silicosis to repeated injections of soluble silica of any known form and, second, the fact that the tissues respond to injections of fine silica so rapidly that it is hard to conceive of solution having occurred.

The experiments to be cited deal with the second objection to the solubility hypothesis. In the living animal a specific response to very fine quartz particles, under 3 microns in diameter, occurs within a few minutes, the rate depending upon the site and manner of injection. Similar introduction of other minerals of the same particle size produces no such effects. On injecting enough quartz of this size into the blood stream, the animal almost immediately suffers profound shock and dies within a few minutes to one hour. Intraperitoneal injections of too much silica cause acute illness for several hours and even subcutaneous injections produce inflammatory reactions of characteristic appearance within as short a period as 15 minutes.

Such responses appear too rapidly for any solution to have occurred after contact with the tissues. In the test tube traces of soluble silica can only be discovered after 24 hours of contact between fine quartz particles and blood serum at the temperature of the body. Tests that have been performed seem

to rule out the possibility that the reaction is due to soluble silica already present in the saline solution used to suspend the particles. If they are completely removed by centrifugation, delicate colorimetric tests reveal the presence of soluble silica, but injection of this fluid has no effect upon animals. In other words, the particles of quartz themselves induce the symptoms.

The only explanation now tenable is suggested by the observation that similar reactions are produced by injecting *small* doses (larger ones have different effects) of colloidal silicic acid. It is possible that during the prolonged immersion in water necessary to separate the quartz particles of the proper size there has been chemical reaction and that a thin film of colloidal silica covers the surface of each grain. Certainly it is hard to conceive that formation of such a film during the few minutes preceding the onset of symptoms that follow injection.

Further evidence that the injurious principle resides on the surface of the particle and not in the suspending fluid is indicated by the lack of toxicity of the blood of a guinea pig dying in silica shock. Transfusion of such blood into another animal causes no symptoms. And finally it has been shown that the injection of quartz grains whose surface has been coated with other substances like the hydroxides of aluminum or iron is likewise followed by no symptoms.

The nature of the injury resulting from the introduction of large numbers of fine quartz particles directly into the blood stream is unknown but it presumably affects some part of the circulatory system or its nervous control. The symptoms and pathological changes simulate those of surgical shock, practically all of the blood in the body being rapidly concentrated in the dilated vessels of the abdominal cavity and spleen. The blood no longer clots on removal from the vessels. In contradistinction to surgical shock this condition does not respond favorably to injections of adrenalin. A feature that is most difficult to understand is the development of tolerance in animals that survive sublethal injections. After several such treatments they may be given three to four times the original dose with impunity.

The mechanisms responsible for these acute reactions to fine quartz and their possible significance in the chronic phases of silicosis are still a mystery. They may be merely indicative of a capacity to react to silica, for these acute effects are only observed in the species that readily develop fibrosis. The dog, for example, is an animal with an apparently high tolerance to silica although prolonged contacts with excessive quantities of fine quartz will ultimately produce nodulation. Very large amounts of the same suspensions that promptly killed rabbits and guinea pigs may be injected into a dog's veins without apparent effect

It has been indicated that the toxic action of quartz is limited to particles 3 microns or less in diameter. The same is apparently true in the production of the more chronic tissue reactions. While particles more than three times this size may be breathed into the lungs, it would appear that only those less than the critical size are biologically significant. This effect has always been attributed to the greater amount of surface presented by a given number of small than large bodies.

To learn more of the influence of this factor of surface area Mr. Dworski and Mr. Delahant prepared a series of suspensions of graded sized quartz particles. In making suspensions they varied the concentrations so that unit quantities of each would present equivalent amounts of quartz surface. When groups of animals were injected with each of these suspensions, it was found that no silicosis developed if the necessary surface area of quartz was supplied by particles greater than 3 microns in diameter.

Microscopic examination of the tissues disclosed that in the case of particles exceeding the 3 micron limit not more than 3 or 4 fragments had been ingested by any phagocyte and more often there would be only 1 per cell Below the critical size the number increased inversely with particle size. This evidence indicates quite clearly that surface area of the irritant only becomes important in relation to the interior of the cells. The quartz surface in contact with extra-cellular fluids apparently has little to do with the development of silicotic nodulation. This observation suggests that the immediate reactions to intravenous injections of quartz may be a non-revelant index of toxicity exerted upon tissues not concerned with the disease, silicosis.

The intracellular injury, however, becomes important when it is recalled that these changes are essentially the same as those produced by tubercle bacilli resulting in the pathological forms commonly designated as "epithelioid cells." Among other characteristics such cells exhibit droplets of visible fat. The presence of this product of degeneration in the phagocytic cells of both tuberculosis and silicosis led Fallon to hypothesize that it was these non-specific fatty or lipoid substances, liberated in large amounts, that led to the formation of the nodules characteristic of each disease. For years it has been known that lipoids from the tubercle bacillus would produce nodules, but no one had thought of testing the action of lipoids from injured cells. Fallon injected the fatty substances extracted from silicotic tissue and produced nodules, but he had difficulty in freeing his material of all particulate silica. We are repeating his work, hoping to surmount this obstacle and demonstrate the validity of his hypothesis.

A word of caution should be added; no one should infer from these ex-

periments that silica dissolves in the cells and is liberated in the blood stream where it may poison other tissues. Apparently its effect is exerted only upon tissues in immediate contact with the quartz particles. Phagocytes are injured or die and connective tissues undergo a peculiar hyaline transformation that Mr. Baisden, working in this laboratory, showed to be analagous to that in tanned leather. In these processes practically all of the dissolved silica is absorbed. Analysis of the blood of all human beings reveals minute quantities of soluble silica, but in silicotics there is no excess. Likewise in the urine there are even larger amounts but it is probable that most of it is derived from vegetable foods and water.

Other experiments by Mr. Steenken, in which fine quartz was injected into the brains of guinea pigs to study its effect upon local susceptibility to tubercle bacilli, suggest an interesting contribution to cytology. The silica first produced small abscesses whose walls were composed of large phagocytic cells. After five months the nodules located in the meninges had been partially replaced by hyaline fibrous tissue but deep in the substance of the brain itself the lesions remained unchanged. In the latter location the ordinary connective tissue cell or fibroblast is lacking; in the meninges and in the walls of blood vessels such cells occur as in all other parts of the body. Since the silicotic reaction only became fibrous in parts of the brain normally containing fibroblasts it would appear that this cell is essential to fibrosis. This conclusion would not be acceptable to cytologists of the Maximow school, who hold that the phagocytes are themselves transformed into fibroblasts.

New impetus to the study of the protective effects of calcined gypsum against quartz has been given by an observation that on intraperitoneal injection of a mixture of these two minerals, no silicosis developed in eight month's time. Control animals given the same quantity of quartz alone showed silicotic nodules on all the peritoneal tissues. We are now attacking the problem in other ways to verify the original observation and to discover whether the mechanism is the same as that in the case of aluminum hydroxide. In all previous experiments, limited to the inhalation method, it had been inferred that the protection from gypsum was due to atmospheric flocculation with the quartz and reduction in the amount of dust inhaled.

The only point to be mentioned on the experiments with aluminum as a protector substance is the apparent discovery of the cause of our previous failures with this mineral that proved so successful in the hands of the Canadian investigators. They used it in dry state and completely neutralized the action of inhaled quartz. We used it in saline suspension with quartz to perform injection tests and observed no evidence of protection. It has recently

been noted that if the suspensions are not heated for sterilization, as we had been doing, the associated aluminum completely protects animals against acute silica shock. We have now started to repeat our previously unsuccessful experiments, using unheated aluminum to see whether we can prevent the development of chronic tissue changes. Numerous other tests with the hydroxide of aluminum continue to demonstrate the value of this substance as an inhibitor of silica.

Aside from problems dealing with mineral dusts, a study is in progress upon the therapeutic value of a special compound of sulphanilamide. This powerful bacteriostatic agent had been combined with an oil on the theory that it would then be capable of solution in the wax-coated tubercle bacillus and destroy the organism. Mr. Stephen Phillips, Jr. generously offered funds to study the effects of the new compound (dodecanoyl-sulphanilamide) upon acute tuberculosis in silicotic guinea pigs and also upon very chronic infections of the same nature in guinea pigs previously immunized with Calmette's low virulent strain, BCG. We regret to state that the results thus far obtained offer little cause for encouragement; although some of the animals are still alive it now seems improbable that the drug has had any beneficial effect. Our experience confirms that of most other investigators who have used it to treat primary tuberculous infection in animals.

Diagnostic Work

The table which follows indicates the number and variety of diagnostic examinations made upon patients in Saranac Lake and its vicinity. In spite of a decrease in the total number of patients there were 945 more tests this year than last, indicating a greater tendency to use this service of the Laboratory. The fact that 76 sputa were submitted for pneumococcus typing, 47 more than in 1938, calls attention to the effectiveness of the publicity given this subject. The 24 referred autopsy specimens represent cases of suspected pneumoconiosis, submitted for confirmation of diagnosis. On most of them there was not only a histological but chemical and petrographic examination of the minerals recovered from the lungs.

Summary of Diagnostic Examinations

January 1, 1939 to December 31, 1939

Diphtheria Cultures	32	Feces: Smear, Culture and Parasites	40
Vincent's Angina	20	Milk, Bacterial Counts	27
Pneumonia Typing	76	Water; Bacteriology	61
Undulant Fever	19	Water, Ortho-tolidine	365
Enteric Diseases	11	Urine, routine and special tests	1144
Gonorrhea, smears	11	Autogenous Vaccines	26
Blood		Surgical Pathological Specimens	200
White and Differential	640	Autopsies, Human	46
Red and Hemoglobin	514	Referred Autopsy Tissue	24
Matching and Typing	309	Animals Inoculated for diagnosis	62
Cultures	32	Ascheim-Zondek Pregnancy Test	20
Chemistry	307	Miscellaneous Examinations	276
Sedimentation	149	Supplementary Tests	777
Spinal Fluid, Urine and other material for tubercle bacilli	101		
Sputum for tubercle bacilli	1136	Total Examinations	6425

The only radical administrative change to be reported has occurred in the Field Division. Mr. Cummings, who has so successfully directed this activity for the past seven years, accepted an appointment as Associate Professor of Medicine in the University of Colorado in September. However, we consider ourselves fortunate that this new arrangement will still permit him to spend one-third of his time in the Laboratory Field Division. While we cannot but regret the change, preventive medicine will be the gainer for he now has the facilities of a university hospital located near large mining communities in which to expand his activities.

It will be necessary to employ an assistant engineer to help Mr. Cummings maintain his contacts in the field. A man with considerable experience has already been approached and it is anticipated that he may join the staff in the near future.

In June the Fourth Symposium on Silicosis was attended by about one hundred enthusiastic participants. This year the character of the program was varied by presentations of the experience in a wide variety of dusty

industries with and without silica hazards. The interchange of ideas served to emphasize the fact that while the essentials of the dust problem are the same everywhere there are minor variations that are real and that may be the cause of misunderstandings. It is a pleasure to express publicly our appreciation to the twenty-one guest speakers who presented the topics for discussion and whose presence made this five-day meeting such a success.

Mr. Kuechle, Vice-President and Claims Manager of the Employers Mutuals, has again undertaken the editing and publication of the report of the Symposium. His company has defrayed all expenses and has turned over the proceeds to the Laboratory as their contribution to research in industrial disease. In view of the fact that the past donations from the sale of previous symposia have amounted to $4,395, we have reason to be doubly grateful to both Mr. Kuechle and the Employers Mutuals.

Without the financial support of those whose names appear on other pages of this report none of these activities would have been possible. For their contributions, which amounted to $54,575 during the past year, the Director and his co-workers are deeply indebted. Of this total approximately $12,000 represents unrestricted donations which could be used for any research purpose. Industry contributed approximately $35,000 for the solution of its special problems. Income on endowment in trust of the Trudeau Foundation of $5,951 and unexpended appropriations of $17,134 received during the previous year brought the total amount available to $77,661.51. The apparent balance of $7,234 shown on September 30, 1939, the end of the fiscal year, represents overlapping contributions.

This report would be incomplete without an expression of the director's appreciation of the sympathetic support of his board of trustees and the loyal co-operation of his fellow workers. All have worked together harmoniously in the various activities of the institution.

It may not be amiss to review the development of the Laboratory's program of industrial research and to explore the possibilities for future usefulness. Twenty-two years have passed since Dr. Baldwin asked why the granite cutters in Barre were dying of tuberculosis when the marble cutters, working with the same tools, under similar conditions in Proctor, only a few miles away, had less tuberculosis than the general male population of the state of Vermont. To answer this question and others developing out of it has been our major objective since 1918. Physical facilities have been developed for this special kind of research and to the original staff of pathologists and bacteriologists we have added engineers, chemists and a physicist-petrographer. The scope of the work has gradually expanded from an academic interest in a

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possible cause of altered susceptibility to tuberculosis to include the direct application of knowledge in preventive medicine. A consultation service has been offered industry to solve its problems of dust prevention and in collaboration with the Roentgen Laboratory at Trudeau, medical control of employee health has been fostered. The Field Division of the Laboratory has even organized and participated in a community campaign for the eradication of tuberculosis. Through its individual efforts and through contacts with other agencies, the Laboratory has attempted to disseminate information on these subjects to medical and lay groups that could apply this knowledge. The cost of these efforts has been supported by industry, insurance, and private philanthropy, whose contributions have amounted to thousands of dollars. It is not my purpose to attempt an evaluation of these activities but to explore the future possibilities of this organization, built with such a considerable expenditure of effort and money. I am naturally concerned to discover whether this private institution can continue to carry on activities that in so many places are functions of universities and governmental agencies.

The first and most practical question is whether such a program will continue to be valuable enough to attract the necessary financial support. Are there still enough unsolved problems in the field of industrial diseases of the chest to justify the cost of this expensive plant and staff? Is there now enough information about the diseases due to inhaled dust and their effect upon tuberculosis so that further research is unnecessary? If so, are there other irritants used in industry that increase susceptibility to tuberculosis and thus constitute a proper subject for our investigation? If work in this field is to continue would it be more profitable to narrow the range of our activities and devote more time to the solution of the fascinating research problems that have already been uncovered?

Before trying to answer these questions, let us look at the industrial situation. As far as the two known major dust diseases, silicosis and asbestosis, are concerned there probably is enough information today so that they could be either eradicated or at least reduced to negligible frequency. But to put this knowledge into practice requires constant expert supervision and considerable expenditure of money. This is now being done with eminent success in a number of our large industries because they can afford the trained personnel and the necessary protective equipment. The small manufacturer with limited capital, on the other hand, still needs help. If he thinks of medical advice at all, he must discover some physician who either knows or is willing to become acquainted with the hazards in the local plant and who will deal fairly with both employee and employer. For his engineering advice

the dust-conscious small manufacturer often turns to the makers of protective equipment, or, if he can offord it, he may engage an outside engineer to design apparatus to meet his special requirements.

But the essence of the control of a dust hazard is constant supervision; the reason it works in the large plant is the presence of physicians and engineers whose main duties are to keep both men and machines functioning properly. For success in the small plants, there must be other experts who, either as private practitioners or employees of the state, will spend their time in going from shop to shop, checking the health of the employees and the operation of the machinery. Today there are not enough experts to meet this demand. Those who are qualified are either employed by the large industries that can pay attractive salaries, or they are in the service of state or federal governments where, as inspectors, they guard agains infractions of industrial codes and, as investigators, they discover new dust hazards. In some states the departments of industrial hygiene are doing much to minimize these hazards but with limited personnel they cannot supervise routine activities in individual plants. The conclusion is inevitable that more experts must be trained.

Most modern dust control codes seek to prevent the formation of dust of all kinds with especially stringent restrictions for those that contain dangerous proportions of free silica or asbestos. This philosophy indicates that we shall always need expensive ventilation, exhaust systems and engineers to insure their proper operation. Antidotes against the action of the toxic quartz dust, whose effects are being studied in the Banting Institute and the Saranac Laboratory, must necessarily play a minor role in prevention. Perfection of practical methods for their use may somewhat reduce the cost of dust elimination because it may be possible to permit somewhat higher atmospheric concentrations. However, regardless of health hazards, industry is coming to realize that men do not work as effectively in atmospheres polluted with visible dust.

Fully as profitable as discovering agents to neutralize the action of silica would be the discovery of the factors that govern individual susceptibility. In the case of benign dusts, like those in the cement plants, there are certain men who seem to suffer no inconveniences and have spent their whole lives in an industry which in the past was notoriously dusty. Others apparently found it so disagreeable that they sought employment elsewhere after a few months. Where there is a silica hazard the fact that only about one-fourth of any exposed group develops silicosis leads to the suspicion that some individuals are immune or at least highly resistant. If only such individuals were selected

for employment in the silica industries the advantage would be obvious. An experimental study of this difficult problem is now in progress and if the results are at all encouraging it is hoped to extend the investigation to human subjects.

Much more needs to be known of the subtle relationships between dust diseases and the superimposed tuberculosis that is responsible for most of the disability in silicotic subjects. Some new method of treatment is indicated for the very chronic forms of tuberculosis that commonly complicate silicosis because they do not respond favorably to ordinary sanatorium regimen.

While uncompleted studies are helping to define the conditions under which asbestosis develops, there is need for more information on the influence of this diesase upon susceptibility to tuberculosis. Although such infection seems to be less frequent in employed workmen with asbestosis than in those with silicosis, tuberculosis is a common complication in those who die. There is still some question whether the association is a specific result of the dust reaction, as in the case of silicosis, or whether other factors are dominant

New forms of dust disease are constantly being reported now that x-ray examinations of the chest have become routine procedure in industry. Investigation of some of these has disclosed a silicosis masquerading under the name of another causative agent. In other cases the peculiar shadows in the films are apparently due to harmless collections of inhaled particles in the lungs that have no significant effects upon the function of these organs. In order to combat unjustified compensation claims based upon mere shadows in a film with no actual disability, every industry is forced to become familiar with the effects of its materials upon the lungs.

The widespread use of chest roentgenograms in industry has led to other abuses that can only be corrected by education. Many employers, faced with the possibility of future claims for compensation, refuse to hire individuals whose films show evidence of disease interpreted as tuberculosis. They need to be taught that this infection may heal completely and that in mature adults the scars of old disease in the top of the lungs are not likely to be the source of new disease. To refuse employment to such persons, who constitute about 5 percent of the population, will create a serious social problem. On the other hand, employees have learned to use x-ray films as the basis for compensation claims that often have no justification. They may feign disability after learning that their lungs show evidence of old scars, or when they actually suffer from active pulmonary tuberculosis they claim that inhaled dusts or fumes were responsible. While it has been quite well established that of the dusts, only free silica and possibly asbestos have any influence

upon associated tuberculosis, there is a real need for authoritative information on the effects of other industrial by-products. In spite of the experience with war gases and other irritating substances some physicians hold to their opinions that there must be pulmonary inflammation which in turn must influence co-existent tuberculous foci.

There also is a wide scope for research upon the effects of various fumes and gases upon the normal lungs. Many of them produce unpleasant reactions in the eyes, nose and throat but whether they cause chronic changes in the lungs and are responsible for all of the symptoms that have been alleged is questionable. If they actually do, every effort should be made to control them, but, on the other hand, industry should not be penalized for injuries that do not exist.

The subject of non-tuberculous pneumonia in industry is another that needs clarification. Opinion is changing on the role of dust in altering susceptibility to this disease; it is now believed that other factors are responsible for the high incidence of pneumonia in at least some of the dusty trades. An appended paper by Vorwald, Delahant and Dworski, reports the first of a series of experiments on this subject. Here it is shown that silicosis has had no influence upon susceptibility to one of the most virulent types of pneumococcus nor upon the character of the resultant disease.

From this summary of the situation in industry it would appear that there are still important problems to be solved. In scope they vary from those of general education and administration to detailed investigations of particular hazards and disease. Since these must be studied in plants or mines, in hospital wards and in experimental laboratories it would appear that there is still need for the specialized facilities of the Saranac Laboratory and associated departments at the Sanatorium.

The study of silicosis has now reached the stage where certain observations must be made on human subjects. The important problems of therapy for associated tuberculosis, of individual susceptibility and objective measurement of disability cannot be investigated on experimental animals alone. A program of clinical research is now receiving detailed consideration. Trudeau Sanatorium has already provided funds to establish a department of pulmonary physiology with the understanding that in subsequent years one half of the cost will be born by the University of Rochester as an active partner in this endeavor. Dr. Wright, the physiologist, started his work in September. A group of clinicians specializing in pulmonary and cardiac diseases has been interested in the program and the necessary laboratory facilities will of course be available.

The primary objective would be the discovery of some satisfactory method of treating tuberculo-silicosis. This extremely chronic combination of occult tuberculosis and silicosis, which is being discovered all too frequently in industrial surveys, does not respond favorably to the ordinary sanatorium methods of treatment — at least the results have been unfavorable in cases treated after symptoms of the infection have appeared. We would hope to experiment upon a carefully selected group whose disease was discovered in its incipiency.

While these men were under observation it should be possible to obtain useful data bearing on the evaluation of disability and perhaps something could be learned about susceptibility by intensive study with all the available means. For the latter objective there would also have to be supplementary work on men with silicosis and no tuberculosis, and on others who had had long exposures to dust without contracting silicosis.

Since it has been estimated that there are several thousand cases of tuberculo-silicosis in the United States whose treatment is either inadequate or delayed until too late to expect favorable results, it behooves someone to attack this problem of therapy. Saranac Lake has adequate facilities for such an investigation, the background of experience in tuberculosis and silicosis and many contacts with industries where this disease is prevalent. With funds to provide full maintenance for a group of ten or twelve silicotic subjects for a period of perhaps two years, much could be learned. It is earnestly hoped that the money can be found to subsidize this project.

In the educational field a proposal has been made to establish a "registry" for cases of pulmonary disease due to dust, similar to those now functioning for the review of diagnoses of tumors. Under this plan pathological material together with the occupational history and, where possible, x-ray films of the deceased person's lungs would be sent to a committee for review. The Saranac Laboratory, which already renders such service on a limited scale, might hope to participate in return for the information that would be gained Such a registry should be helpful to pathologists whose experience in this field is limited to an occasional case.

For financial support the institution now looks largely to industry, but its only guarantee of income from this source is the successful solution of problems that are troublesome and expensive in particular trades.

To realize its fullest possibilities the Laboratory should have a backlog of unrestricted income. It could then explore new fields by attacking abstract problems that might appear to have no immediate application. It could experiment with therapy for diseases already contracted. It could play a much larger

part in the training of the personnel needed to supervise preventive programs in the smaller plants. With the university affiliation, which may some day materialize, it could assist in undergraduate teaching. Industry can hardly be expected to supply all the funds for such general purposes; other groups who might also benefit could share the cost. In the past the insurance companies have been liberal contributors, in fact the annual grant of the Metropolitan Life Insurance Company and that of the Milbank Memorial Fund largely maintained the Laboratory for years before industrial contacts were established. More recently the respective associations of both the stock and the mutual companies have been substantial contributors. An intimation that their support cannot continue is cause for concern and we must seek new sources of unrestricted income.

There is work to be done and industrial development is constantly creating new problems. The Saranac Laboratory may reasonably hope to take part in their solution. Like most educational institutions it needs greater financial security.

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SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS

RECEIPTS AND EXPENDITURES

Year ending September 30, 1939

Balance on hand October 1, 1938		$17,134.0
Receipts:		
From Trudeau Foundation	$5,951.88	
*Gifts and other receipts for maintenance of plant and work	54,575.67	
Total receipts for the year		60,527.5
Total of balance and receipts		77,661.5
Expenditures:		
For research and field surveys	58,464.74	
Travel and other expenses of workers	1,460.90	
Permanent equipment	1,651.53	
Fuel, light, insurance, animals, feed, supplies and other running expenses	8,840.85	
Total disbursed		70,418.02
Balance on hand September 30, 1939		7,243.55

*See following pages for list of contributors.

CONTRIBUTIONS

TO THE

SARANAC LABORATORY

From October 1, 1938 to September 30, 1939

NOTE: — Items in second column received after October 1st, 1939, to be credited in the 1940 financial report.

Adirondack Fund for the Tuberculous	1,000.00	249.99
Air Hygiene Foundation of America	6,275.00	500.00
Ass'n of Casualty & Surety Executives	2,500.00	
Dr. Edward R. Baldwin	50.00	
Colorado Fuel & Iron Company	2,000.00	1,000.00
Mrs. Bigelow Crocker	10.00	
Mrs. Charles L. Crocker	50.00	
Mr. Thomas M. Durkan	50.00	
Employers Mutuals Insurance Co., thru Mr. B. E. Kuechle, Proceeds from Sale of "Silicosis Symposium"	198.52	57.00
Dr. Leroy U. Gardner	155.00	375.00
General Hospital of Saranac Lake	916.74	250.02
Miss A. Louise Gilbert	10.00	
Inland Steel Company	3,854.16	875.03
Johns-Manville Corporation	5,000.00	1,250.00
Edna Perrin Labarrere: Bequest in Memory of Dr. Jacques Louis Labarrere	1,000.00	
Mr. Lawrence Macfarlane	100.00	
Miscellaneous Contributions	339.00	90.00
National Carbon Company	1,375.00	1,375.00
Owens-Corning Fiberglas Corporation	625.00	36.00
Penn-Dixie Cement Corporation	750.00	
Pickands, Mather & Company, for Lake Superior Iron Ore Association	15,000.00	2,916.00
Carried forward	41,258.42	8,974.04

Brought forward	41,258.42	8,974.04
Mr. Stephen Phillips	6,500.00	
Portland Cement Association . . .	2,747.00	
Mr. Arthur B. Purvis	250.00	
Republic Steel Corporation . . .	3,250.00	750.00
St. Joseph Lead Company	250.00	125.00
United States Gypsum Company . .	247.50	32.50
In Memory of Sydney Lunt Wood:		
Miss Sarah C. Armistead . . .	5.00	
Miss Susan Wood	50.00	
Mrs. S. L. Wood & Mr. John Wood	20.00	20.00
	54,577.92	
Less exchange on two Canadian cheques	2.25	
	54,575.67	9,901.54