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THE PREVENTION OF SILICOSIS BY METALLIC ALUMINUM*

I. A PRELIMINARY REPORT

BY J. J. DENNY, M.Sc., *Metallurgical Engineer,*
W. D. ROBSON, M.B., *Chief Surgeon, McIntyre Mine, Schumacher, Ont.,*
DUDLEY A. IRWIN, M.B., *Associate Professor, Department of Medical Research, University of Toronto*

IN November, 1932, an investigation of silicosis was undertaken at the McIntyre Porcupine Mine, Schumacher, Ont., after a discussion of the problem with Sir Frederick Banting and his staff. As a result it was decided to carry on dusting experiments with animals at the mine in a manner that would duplicate as far as possible actual industrial conditions. At that time 50 guinea pigs were placed in the crusher house tunnel of the mill where a considerable quantity of fine dust, containing approximately 35 per cent of free silica, was being constantly produced. These animals lived in this atmosphere for periods up to one year, and, while on autopsy large amounts of dust were found in the lungs, not a single case of silicosis had developed. These negative results suggested, among other things, that the mine gases might be a predisposing factor in the production of silicosis, and the results of this investigation[1] led us to undertake the study of the hydrogen-ion concentration of the condensate of the atmosphere, both in the mine and in various sections of the mill. The CO_2 combining power of blood serum on a series of 400 miners was also studied at this time. While these results were inconclusive, the variation in the hydrogen-ion concentration of the condensate between the surface and underground atmospheres encouraged us to investigate the effect of neutral, weak acid and alkaline solutions on the solubility of silicious materials.

Gye and Purdy[2] were the first to point out that the chemical reaction and not the physical presence of silicious material was responsible for the production of the fibrosis in silicosis. This work was investigated by Gardner and Cummings,[3] who showed that the tissue reaction to quartz was definitely proportional to the size of the particle. They found that 1-3 micron particles of quartz produced an acute proliferative fibrotic response, while the 10-12 micron particles produced only a foreign body reaction up to a period of three years. It is accepted that the dangerous silica particles retained by the lung are under 5 microns in diameter. We assumed that if the solubility of the silicious material retained in the lung could be reduced sufficiently by the addition of some non-toxic element or compound the usual fibrotic response would be modified. We found that the addition of certain compounds to silica would reduce its solubility in the beaker to a slight extent. But these compounds, when mixed with quartz, injected subcutaneously or inhaled, did not lessen or else actually increased the tissue response produced by quartz alone. Some of these compounds were found to be toxic.

Various elements and compounds were then investigated, and on March 4, 1936, two of us (D. and R.) discovered at the McIntyre Mine that the presence of small amounts of metallic aluminum almost completely prevented silicious material from passing into solution. This discovery was made after investigating Heffernan's[4] theory, which was based on the work of Bragg.[5]

* As presented before the Academy of Medicine, Toronto, June 15, 1937.

Heffernan suggests that silica is active when freshly fractured because of its molecular structure, which presents numerous unsatisfied oxygen atoms to interact with tissue elements. This suggested to us that if the unsatisfied oxygen atoms could be satisfied with nascent hydrogen it might diminish the toxicity of silica in tissue and change a fibrotic response into a simple foreign body reaction.

Animal experimentation was commenced on June 10, 1936, dusting a group of rabbits with mine quartz, to which small quantities of metallic aluminum had been added. In this experiment 13 rabbits were dusted in specially constructed chambers. Six control animals were dusted with quartz alone, while 7 were dusted with quartz plus less than 1 per cent of metallic aluminum. At various intervals up to six months, the lungs and other organs of the animals were sent to one of us (I.) for pathological examination. On sectioning it was found that all the controls showed a picture varying from early to well established silicosis, depending on the length of exposure. The animals subjected to silica dust containing metallic aluminum all showed either minimal or no fibrosis of the lungs. No damage was seen in the lungs or other organs that could be attributed to the presence of aluminum. These results showed that silicosis was inhibited in this small group of rabbits by the admixture of *less than 1 per cent* of metallic aluminum to the quartz dust.

Dusting experiments similar to the one described above are being carried on at the present time, using larger groups of animals. From this group, following 3½ months' dusting, the lungs of one quartz control and two quartz and aluminum dusted animals were sectioned. The lungs of the control animal showed beginning silicosis, while the two animals dusted with quartz and *1 per cent aluminum* showed *no evidence of any fibrosis.*

I. Experimental Work

(*a*) Chemical

*Silicious materials used for solubility tests**.*— Samples of quartz were obtained from Porcupine, Kirkland Lake and Sudbury mining districts in Ontario and from South Africa. Samples of chert and quartzite were obtained from British Columbia. Gray Vermont, Georgia and Ontario granites and a red Ontario granite were collected. Samples of flint and various silicates were obtained. Some samples were reduced to a fine powder by grinding dry in a steel mortar, others (quartz) in a quartz-lined tumble box, to avoid contamination as much as possible. The quartz, flint, chert and quartzite powders were all –325 mesh, microscopic examination showing that over half of the material was composed of particles under 5 microns in their greatest diameter. The silicates were –100 mesh, but contained many fine particles.

Metallic aluminum powder.—Various grades of aluminum powder were tested. It was found that the activity of the aluminum depended upon its state of division and purity, (Table I).

TABLE I.

EFFECT OF ALUMINUM FINENESS ON THE SOLUBILITY OF QUARTZ

	Dissolved SiO_2 p.p.m.	*Percentage Reduction*
100 c.c. H_2O + 1.0 gm. McIntyre Quartz –325 mesh	50.0	–
100 c.c. H_2O + 1.0 gm. McIntyre Quartz + 1 mg. coarse Al	9.2	82
100 c.c. H_2O + 1.0 gm. McIntyre Quartz + 1 mg. medium Al	2.2	95
100 c.c. H_2O + 1.0 gm. McIntyre Quartz + 1 mg. fine Al	1.9	96

Ether-washed metallic aluminum powder was separated into three fractions by air separation.

Solubilities were determined in Pyrex flasks with continuous agitation.

Time—17 hours.

Temperature—40 to 50° C.

The sample that proved to be most satisfactory contained 99 per cent metallic aluminum and was –20 microns. The usual coating used in the manufacture of metallic aluminum powder was removed by washing with ether. This procedure was found to be imperative.

The solubility tests were done routinely in rubber-stoppered Bakelite tubes, but platinum and pyrex glass containers were also used. The concentration of the silicate ion was determined colorimetrically by the method of King and Dolan.[6, 7] This method was used routinely after it was found to check with gravimetric determinations.

We found that certain types of silica sand (*e.g.*, Montreal silica) were less soluble than naturally occurring quartz. This led to a complete analysis of mine quartz, which was found to contain 85 to 98 per cent silica with 2 to 15

* The term "solubility" is used to indicate the concentration of silica in solution obtained under the conditions as noted.

per cent impurities, the bulk of which were alkaline earth carbonates, (Table II). The addition of small amounts of these alkaline carbonates, or the hydroxides of Na, Ca, etc., added to the silica sand increased its solubility as shown in Tables III and IV. When the impurities of mine quartz were removed by leaching with hydrochloric acid, the solubility was comparable to that of the Montreal sand, (Chart 1). It is also shown in Chart 1 that the presence of metallic aluminum reduces the solubility of naturally occurring quartz to less than that of acid treated quartz.

TABLE II.

ANALYSIS OF MONTREAL SILICA AND MCINTYRE QUARTZ*

Percentage	*Montreal Silica Sand*	*McIntyre Quartz*
SiO_2	99.6	98.1
Fe_2O_3	0.02	0.20
Al_2O_3	0.19	0.42
CaO	None	0.34
MgO	Trace	0.12

PETROGRAPHIC ANALYSIS

Montreal Silica Sand.—"This sample is essentially composed of angular quartz grains. There is, however, some percentage of impurities present. Unlike the other sample these impurities are included in the quartz. They are mostly gas globules and minute hair-like crystals of rutile. There are other impurities but they are not prominent."

McIntyre Quartz.—"This sample is composed essentially of angular quartz grains. There is, however, at least 5 per cent of impurities present. These impurities are mostly ankerite and sericite. Chlorite and pyrite are not so prominent. These impurities are admixed and not present as inclusions in the quartz."

TABLE IIIa.

EFFECT OF INCREASING CONCENTRATIONS OF CALCIUM CARBONATE ON THE SOLUBILITY OF MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
100 c.c. H_2O + 1 gm. Montreal Silica Sand −325 mesh	3.8	6.8
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 5 mg. $CaCO_3$ (0.5%)	12.3	7.1
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 20 mg. $CaCO_3$ (2.0%)	12.1	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 53 mg. $CaCO_3$ (5.3%)	12.9	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 111 mg. $CaCO_3$ (11.1%)	12.2	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 250 mg. $CaCO_3$ (25.0%)	12.4	7.8
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. ankerite (1.0%)	6.9	
100 c.c. H_2O + 1 gm. $CaCO_3$ (blank)	Trace	

Time—24 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

* We are indebted for the above petrographic analysis to Dr. Eugene Poitevin, Chief, Section of Mineralogy, Department of Mines, Ottawa.

TABLE IIIb.

EFFECT OF CONSTANT METALLIC ALUMINUM AND VARYING CALCIUM CARBONATE CONCENTRATIONS ON MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
100 c.c. H_2O + 1 gm. Montreal Silica Sand −325 mesh + 10 mg. Al	0.5	6.9
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 5 mg. $CaCO_3$	0.5	7.1
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 53 mg. $CaCO_3$	0.5	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 250 mg. $CaCO_3$	0.5	7.8
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 10 mg. Al + 1.0 mg. $CaCO_3$	0.5	–

Time—12 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

TABLE IIIc.

EFFECT OF VARYING CONCENTRATIONS OF CALCIUM HYDROXIDE ON THE SOLUBILITY OF MCINTYRE QUARTZ AND MONTREAL SILICA SAND

	$Ca(OH)_2$ mg.	*Dissolved SiO_2 p.p.m.*	*pH*
1 gm. McIntyre Quartz −325 mesh + 100 c.c. H_2O	0	27.1	7.0
1 gm. McIntyre Quartz + 100 c.c. 0.006% $Ca(OH)_2$ solution	6	56.0	9.3
1 gm. McIntyre Quartz + 100 c.c. 0.064% $Ca(OH)_2$ solution	64	2.7	12.2
1 gm. McIntyre Quartz + 100 c.c. 0.127% $Ca(OH)_2$ solution	127	0.6	12.4
1 gm. Montreal Silica Sand −325 mesh + c.c. H_2O	0	3.0	6.8
1 gm. Montreal Silica Sand + 100 c.c. 0.006% $Ca(OH)_2$ solution	6	25.2	9.5
1 gm. Montreal Silica Sand + 100 c.c. 0.064% $Ca(OH)_2$ solution	64	2.5	12.2
1 gm. Montreal Silica Sand + 100 c.c. 0.127% $Ca(OH)_2$ solution	127	0.6	12.4
100 c.c. 0.127% $Ca(OH)_2$ solution (blank)	127	0.3	12.4

Time—20 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.
$Ca(OH)_2$ solution prepared by igniting Bakers C.P. Calcium Carbonate, dissolving in water and filtering. The strength was determined by titration with HCl.

TABLE IIId.

EFFECT OF PORTLAND CEMENT ON THE SOLUBILITY OF MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
100 c.c. H_2O + 1 gm. Montreal Silica Sand −325 mesh	2.0	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 20 mg. cement	41.2	–
100 c.c. H_2O + 20 mg. cement (blank)	23.4	–
100 c.c. H_2O + 1 gm. Montreal Silica Sand + 1.0 gm. cement	1.0	12.4

Time—20 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

The effect of varying amounts of metallic aluminum powder on the solubility of quartz was determined (Chart 2). The solubility of flint and quartz from other localities was found to be comparable to that of McIntyre quartz, and was reduced to the same extent on the addition of metallic aluminum. Various other samples of quartz, quartzite and chert were found to react in a similar manner (Table V).

A number of silicates were then tested with results as tabulated in Table VI.

TABLE IV.

EFFECT OF SODIUM CARBONATE AND SODIUM HYDROXIDE ON THE SOLUBILITY OF MONTREAL SILICA SAND

	Dissolved SiO_2 p.p.m.	*pH*
1.0 gm. Montreal Silica Sand –325 mesh + 100 c.c. H_2O	2.7	6.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.006% NaOH solution	12.9	11.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.06% NaOH solution	60.9	12.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.13% NaOH solution	64.2	12.4
100 c.c. NaOH solution 0.13% (blank)	0.6	12.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.006% Na_2CO_3 solution	8.7	8.8
1.0 gm. Montreal Silica Sand + 100 c.c. 0.06% Na_2CO_3 solution	21.7	11.4
1.0 gm. Montreal Silica Sand + 100 c.c. 0.13% Na_2CO_3 solution	21.0	11.8
100 c.c. Na_2CO_3 solution 0.13% (blank)	0.6	11.8

Time—20 hours.

Temperature—37° C.

All tests conducted in Bakelite tubes with continuous agitation.

TABLE V.

EFFECT OF METALLIC ALUMINUM POWDER ON THE SOLUBILITY OF QUARTZ DUST

Dust	*pH*	*Dissolved SiO_2 p.p.m.*	*Percentage Reduction*
Blank	7.0	0.3	–
P 2	7.0	17.7	
P 2 + Al	7.0	0.7	96
P 3	7.0	17.3	
P 3 + Al	7.1	1.0	94
P 4	7.0	24.0	
P 4 + Al	7.0	0.8	97
P 5	7.0	22.6	
P 5 + Al	7.0	0.6	97
P 6	7.0	13.7	
P 6 + Al	7.0	0.8	94
P 7	7.1	15.4	
P 7 + Al	7.1	0.9	94
P 8	7.0	14.0	
P 8 + Al	7.1	1.3	91
K 4	7.0	14.5	
K 4 + Al	7.1	0.9	94
K 5	7.1	16.8	
K 5 + Al	7.1	0.7	96
K 7	7.1	19.3	
K 7 + Al	7.0	1.5	92
S 1	6.9	21.5	
S 1 + Al	6.9	1.2	95
Kolar Quartz	7.1	28.2	
Kolar Quartz + Al	7.2	1.8	94
South African Banket	7.1	8.8	
South African Banket + Al	7.1	1.8	80
Chert	6.8	22.1	
Chert + Al	6.8	5.0	78
Quartzite	6.8	17.9	
Quartzite + Al	6.8	5.7	69
Flint	7.0	147.0	
Flint + Al	7.0	3.4	97.7

Dust used—1.0 gram.

Aluminum used—10 mg.

H_2O used—50 c.c.

Time—48 hours.

Temperature—37° C.

P—indicates Porcupine Quartz.

K—indicates Kirkland Lake Quartz.

S—indicates Sudbury Quartz.

All tests conducted in Bakelite tubes with continuous agitation at 20 r.p.m.

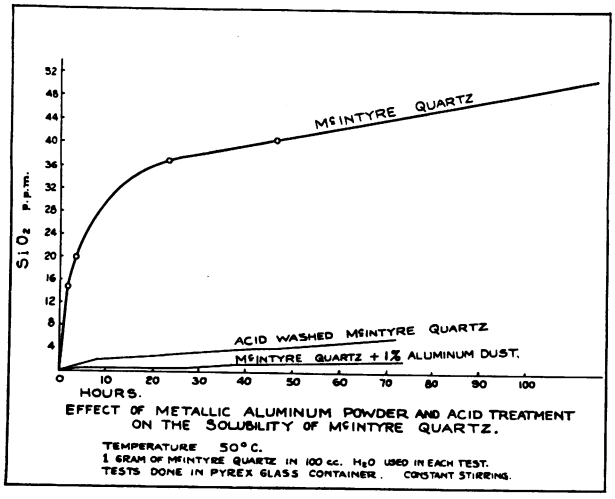

Chart 1

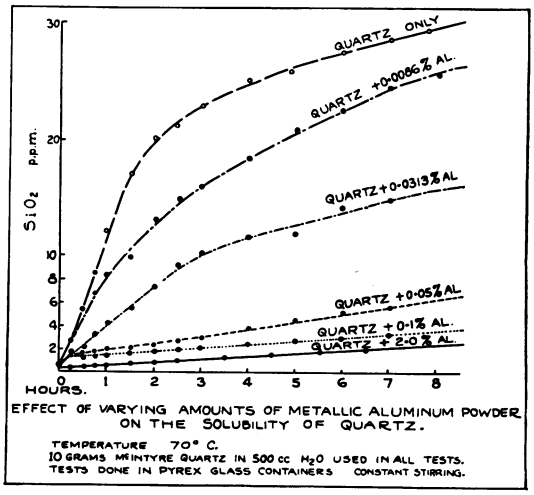

Chart 2

TABLE VI.

EFFECT OF METALLIC ALUMINUM ON THE SOLUBILITY OF SILICATES

	pH	*Dissolved SiO_2 p.p.m.*	*Percentage Reduction*
1.0 gm. dust P 14 + 50 c.c. H_2O	7.0	12.4	
" " dust P 14 + 50 c.c. H_2O + 10 mg. Al	7.0	0.7	94
1.0 gm. dust P 15 + 50 c.c. H_2O	7.2	6.1	
" " dust P 15 + 50 c.c. H_2O + 10 mg. Al	7.2	1.9	69
1.0 gm. asbestos + 50 c.c. H_2O	6.9	21.2	
" " asbestos + 50 c.c. H_2O + 10 mg. Al	7.0	0.8	96
1.0 gm. serpentine + 50 c.c. H_2O	7.1	10.0	
" " serpentine + 50 c.c. H_2O + 10 mg. Al	7.1	0.9	91
1.0 gm. talc + 50 c.c. H_2O	7.2	64.0	
" " talc + 50 c.c. H_2O + 10 mg. Al	7.1	1.0	98
1.0 gm. sericite + 50 c.c. H_2O	7.0	40.7	
" " sericite + 50 c.c. H_2O + 10 mg. Al	7.1	0.9	98
1.0 gm. oligoclase + 50 c.c. H_2O	7.0	7.6	
" " oligoclase + 50 c.c. H_2O + 10 mg. Al	7.0	0.4	95
1.0 gm. albite + 50 c.c. H_2O	7.0	7.6	
" " albite + 50 c.c. H_2O + 10 mg. Al	7.0	0.7	91
1.0 gm. orthoclase + 50 c.c. H_2O	6.9	7.1	
" " orthoclase + 50 c.c. H_2O + 10 mg. Al	7.0	0.5	93
1.0 gm. microcline + 50 c.c. H_2O	7.0	8.0	
" " microcline + 50 c.c. H_2O + 10 mg. Al	7.0	1.0	87
1.0 gm. wollastonite + 50 c.c. H_2O	7.4	27.2	
" " wollastonite + 50 c.c. H_2O + 10 mg. Al	7.2	0.8	97
1.0 gm. kaolin + 50 c.c. H_2O	6.8	6.2	
" " kaolin + 50 c.c. H_2O + 10 mg. Al	6.8	0.7	89
1.0 gm. labradorite + 50 c.c. H_2O	6.9	7.6	
" " labradorite + 50 c.c. H_2O + 10 mg. Al	6.9	0.5	93
1.0 gm. Canadian Grey Granite + 50 c.c. H_2O	6.9	6.4	
" " Canadian Grey Granite + 50 c.c. H_2O + 10 mg. Al	7.0	0.7	89
1.0 gm. Canadian Red Granite + 50 c.c. H_2O	7.0	6.7	
" " Canadian Red Granite + 50 c.c. H_2O + 10 mg. Al.	7.0	0.8	88
1.0 gm. Georgia Granite + 50 c.c. H_2O	7.0	7.7	
" " Georgia Granite + 50 c.c. H_2O + 10 mg. Al	7.0	0.8	90
1.0 gm. Vermont Granite + 50 c.c. H_2O	7.0	6.9	
" " Vermont Granite + 50 c.c. H_2O + 10 mg. Al	7.0	1.0	85

P 14—McIntyre Mine underground aerial dust.
P 15—McIntyre Mine surface crusher house aerial dust.
Time—48 hours.
Temperature—37.5° C.
All tests conducted in Bakelite tubes with continuous agitation.

TABLE VII.

COMPARISON OF VARIOUS FORMS OF ALUMINUM COMPOUNDS WHEN USED TO REDUCE THE SOLUBILITY OF SILICA

	Dissolved SiO_2 p.p.m.	*Percentage Reduction*
1 gm. McIntyre Quartz −325 mesh + 100 c.c. H_2O	35	–
1 gm. McIntyre Quartz + 100 c.c. H_2O + 10 mg. Al dust	0.3	99
1 gm. McIntyre Quartz + 100 c.c. H_2O + 29 mg. $Al(OH)_3$ (freshly pp't'd.)	2.8	92
1 gm. McIntyre Quartz + 100 c.c. H_2O + 29 mg. $Al(OH)_3$ (commercial product C.P.)	20.7	41
1 gm. McIntyre Quartz + 100 c.c. H_2O + 19 mg. Al_2O_3	1.8	95
1 gm. McIntyre Quartz + 100 c.c. H_2O + 29 mg. Bauxite	17.3	51
1 gm. McIntyre Quartz + 100 c.c. H_2O + 100 mg. Bauxite	4.3	88

Time—48 hours.
Temperature—37° C.
All tests conducted in Bakelite tubes with continuous agitation.

(*b*) DUSTING EXPERIMENTS

These experiments were planned with two fundamental principles in mind (*a*) to duplicate as far as possible the dust produced underground by blasting, (*i.e.*, freshly fractured, finely particulate dust particles, relatively dry); (*b*) to avoid as much as possible any contamination in the dust produced.

Method of experimental dusting.—Galvanized iron drums (Fig. 1), 31″ long and 22″ in diameter were used as dusting chambers. In the upper portion of each drum a tumbling box was installed. These boxes were constructed of ½″ oak and measured 7″ x 7″ x 26″ outside diameter. The boxes were lined with quartz slabs, ½″ to 1″ in thickness, which were keyed in position, leaving an inside space about 4″ x 4″ x 23″. This space was half filled with lump quartz, varying in size from ½″ to 1″ in

diameter. These boxes were driven by a 1/6 h.p. motor, and revolved at a speed of 60 r.p.m. The dust produced escaped through twenty-four 3/16" holes drilled through each face of the box. The drums were ventilated by a positive pressure at a rate of 2.5 cu. ft. per minute, which was sufficient to maintain the CO_2 content of the drum below 0.3 per cent during the dusting of the animals. One end of the drum was fitted with a removable cover, 16" in diameter, containing a glass window and a rubber port for air sampling. This cover provided access to the interior of the drum.

Four drums were constructed as described above. Each tumbling box contained about 10 lbs. of loose quartz as a grinding medium. Box No. 1 produced quartz dust alone. To each of boxes 2, 3 and 4 was added 100 gm. of aluminum pellets approximately ¼" in diameter, to produce a mixed quartz and aluminum dust. The dust produced by these boxes was found by chemical analysis to contain less than 1 per cent metallic aluminum by weight. Solubility tests were made on the dust collected from a shelf in each drum at intervals.

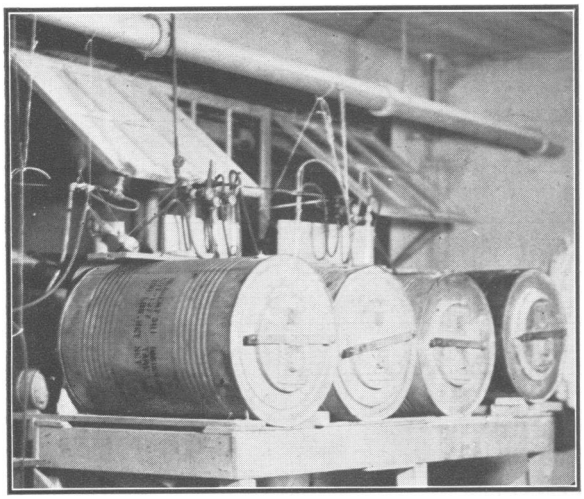

Fig. 1.—Photograph of drums used in dusting experiments.

Sample.—Continuous agitation in Bakelite tubes for 20 hours at 40° C.

	Dissolved SiO_2 p.p.m.	*Percentage Reduction*
Drum 1—Quartz only	76.3	..
Drum 2—Quartz plus Al ..	2.5	97
Drum 3—Quartz plus Al ..	2.4	97
Drum 4—Quartz plus Al ..	3.1	96

Four rabbits were placed in each drum for dust exposure from 12 to 16 hours daily.

During the period of dusting, konimeter counts were taken daily. The dust counts varied from 4,000 to 8,000 particles per c.c. Microscopic examination of the dust showed it to be very finely particulate, about 90 per cent of the particles being under 5 microns in diameter. When the konimeter counts fell below 4,000 particles per c.c., the tumbling box was replaced by one freshly loaded.

PATHOLOGICAL FINDINGS

The duration of the experimental dust exposure and the amount of silica found on chemical analysis in the lung tissue is given in Table VIII, for 6 rabbits dusted with quartz alone and 7 rabbits dusted with quartz and aluminum ground together.

TABLE VIII.
TYPE AND DURATION OF DUST EXPOSURE AND SILICA ASSAY OF LUNGS OF RABBITS

Rabbit No.	*Type of dust*	*Dusting history Hours daily*	*Duration weeks*	*Lung SiO_2 mg. per 100 grams dry weight*
105	Quartz	12	20	2350
99	"	16	24	8140
104	"	14	24	4280
102	"	16	24	6260
91	"	16	37	1850
62	"	16	36	3610
100	" + Al ...	16	20	6780
98	" " ...	16	20	8230
97	" " ...	16	20	5700
95	" " ...	16	21	8730
94	" " ...	16	21	2700
96	" " ...	16	24	7780
93	" " ...	16	24	9200

The lungs of these animals were removed intact and gently distended by the intra-tracheal injection of 10 per cent formo-saline prior to immersion in the same fixative. As a routine, tissue blocks cut from the two upper and lower lobes of each lung and from the mediastinal lymphatic glands were dehydrated in alcohols of ascending concentration, cleared in xylol, and imbedded and cut in paraffin. The sections were mounted serially in sets of three; the first was incinerated, the second was stained with hæmatoxylin and eosin, the third was incinerated and treated with hydrochloric acid. Tissue blocks from the liver, spleen and kidneys were fixed, sectioned and stained in a similar manner.

Gross appearance of the lungs.—The lungs of all the quartz-dusted animals presented an appearance that was fairly uniform. Subpleural collections of dust were scattered over the surface of the lung. These areas were light in colour and varied in size from 1 to 5 mm. The cut surface of the lungs showed

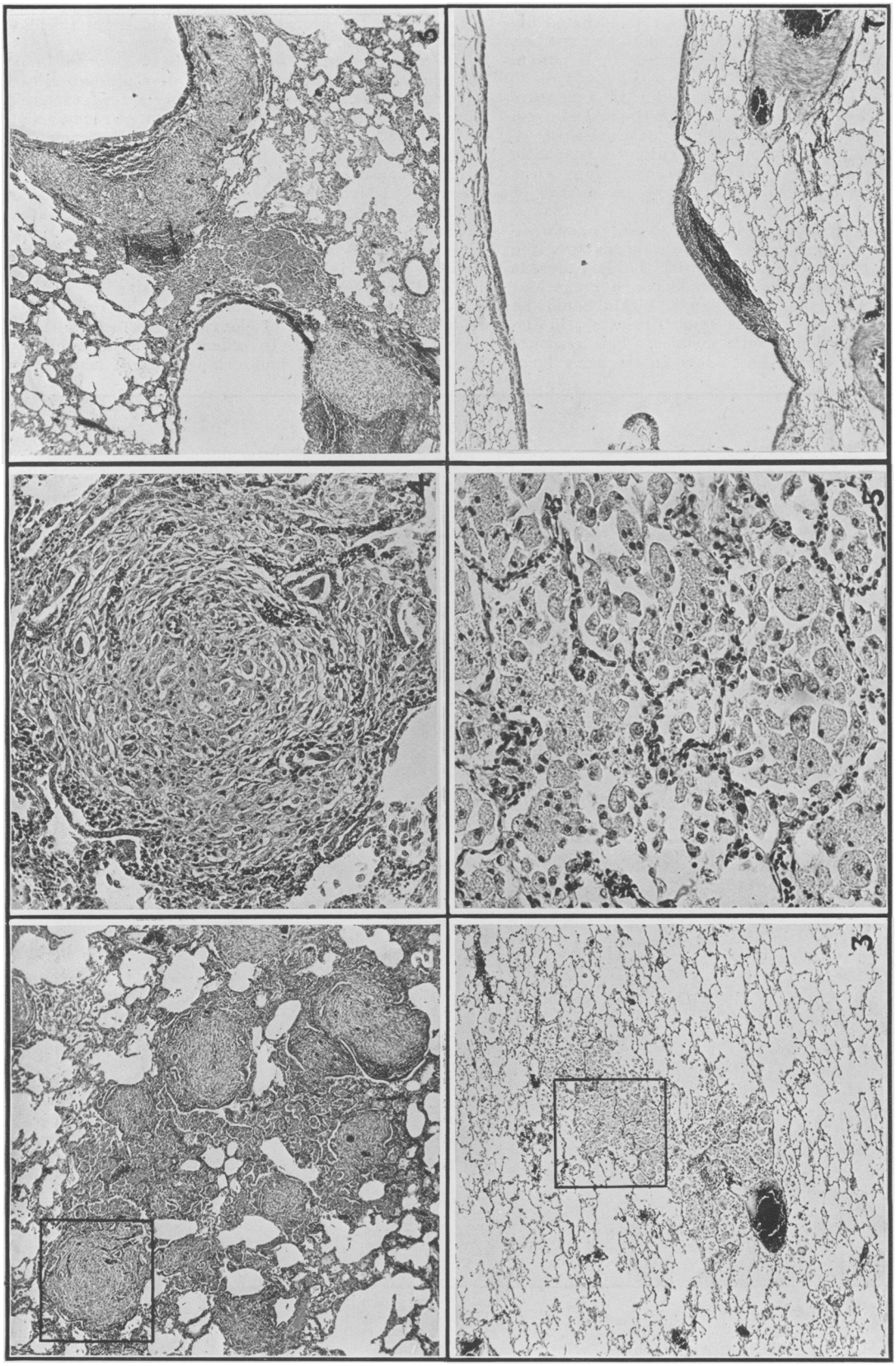

Fig. 2.—Proliferative response with fibrotic nodule formation produced in the lung of a rabbit dusted 16 hours daily for 6 months with quartz.
Fig. 3.—Foreign body response produced in the lung of a rabbit dusted 16 hours daily for 6 months with quartz and aluminum. **Fig. 4.**—Higher magnification of marked area in Fig. 2. **Fig. 5.**—Higher magnification of marked area in Fig. 3. **Fig. 6.**—Fibrotic areas in peribronchial lymphatic aggregations of a rabbit dusted with quartz 16 hours daily for 6 months. **Fig. 7.**—Peribronchial lymphatic aggregations of a rabbit dusted with quartz and aluminum 16 hours daily for 6 months, for comparison with Fig. 6.

numerous small grayish firm nodules scattered throughout. Some of these nodules were discrete, while others were surrounded by halos of condensation. The mediastinal lymphatic glands, usually 2 or 3 in number, were firm and enlarged to several times their normal size.

The lungs of the rabbits dusted with a mixture of quartz and aluminum could be distinguished from those dusted with quartz alone by the absence of nodules on the cut surface and of enlarged lymphatic glands. There were many dust-containing areas scattered under the pleura and on the cut surface of the lung.

Microscopic findings in quartz-dusted animals.—The striking feature seen in these lungs was the proliferative response associated with the dust present in the alveoli, peribronchial lymphatic aggregations and mediastinal lymphatic glands. This could be followed through the various stages, resulting in the formation of whorled fibrotic nodules. This response varied but little from lobe to lobe in the same lung, and from lung to lung. The bronchial epithelium showed scattered areas of flattening and loss of cilia. The walls of the bronchial tree showed slight lymphocytic infiltration.

Great numbers of dust cells, distended with finely particulate bi-refringent material, were present in the alveolar spaces. In some alveoli only a few scattered single dust cells were seen that presented regular cell outlines and nuclei that stained well. The enclosing alveolar walls showed little or no change. Other alveolar spaces were tightly packed with dust cells, many of which showed giant cell formation and evidence of degeneration. In such areas the associated alveolar walls showed marked thickening. Many alveolar nodules were seen (Figs. 2 and 4). These nodules varied in appearance and occurred singly or in fused groups of two or three. Single nodules varied from 0.1 to 0.8 mm. in diameter. The pre-fibrotic nodules were composed of elongated dust cells without definite arrangement. In others the peripheral cells were more elongated and arranged in a manner to

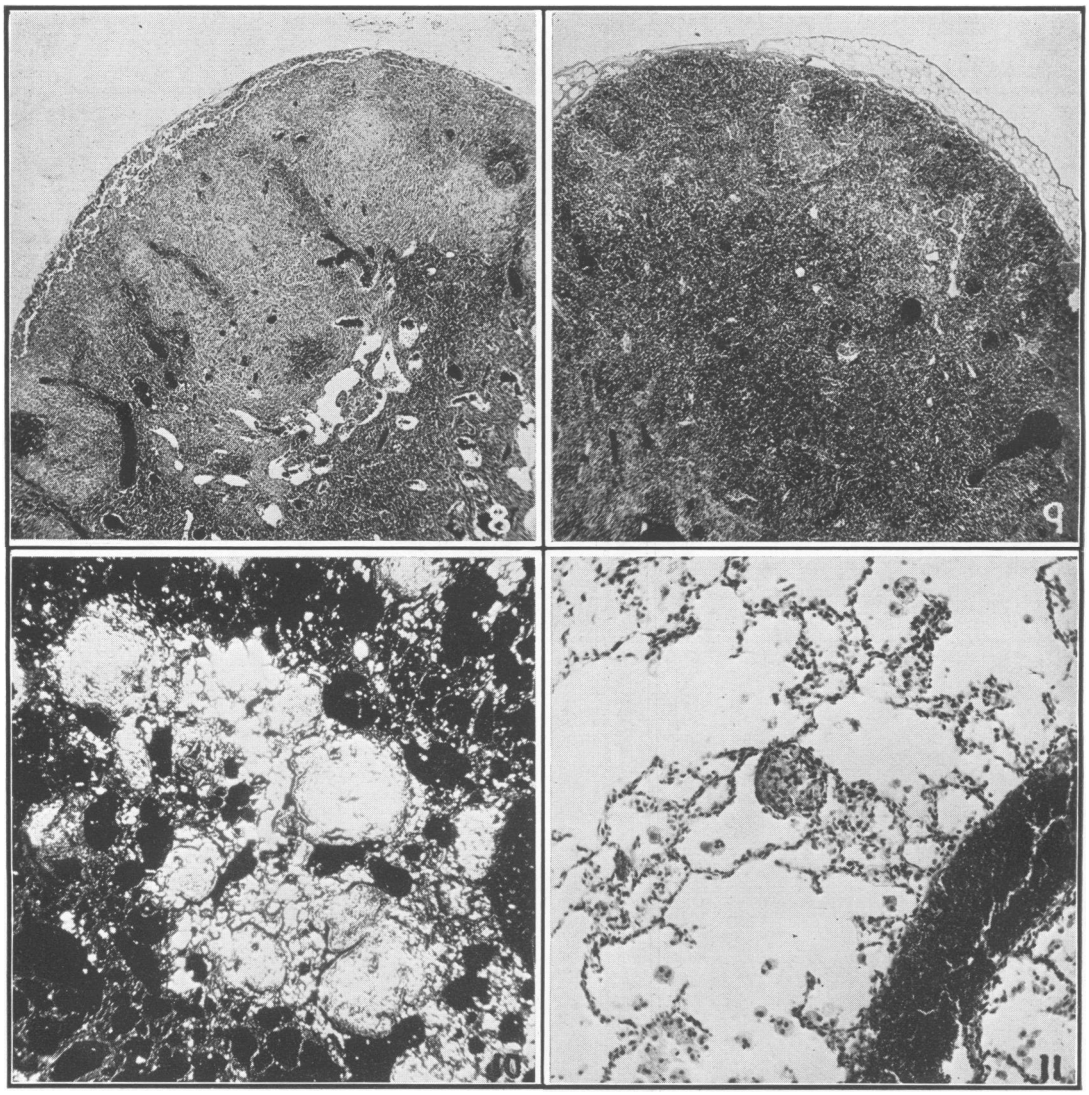

Fig. 8.—Fibrotic areas in a mediastinal lymphatic gland of a rabbit dusted with quartz 16 hours daily for 6 months. **Fig. 9.**—Mediastinal lymphatic gland of a rabbit dusted with quartz and aluminum 16 hours daily for 6 months. Note absence of fibrotic areas, and small number of dust cells present. **Fig. 10.**—Incinerated section of Fig. 2 showing large amount of silicious ash (dark field). **Fig. 11.**—Lung of rabbit dusted with quartz and aluminum 16 hours daily for 6 months, showing slight pre-fibrotic lesion in an alveolus.

enclose a degenerating centre. The fibrous nodules were composed of spindle-shaped cells and reticular fibres arranged in a whorl formation. The peribronchial lymphatic aggregations practically all showed fibrotic areas (Fig. 6) usually arranged in fused whorls, smaller than those seen in the alveoli. In some of the lymphatic aggregations the fibrous reaction occupied about one-half of the total area; others were completely obliterated and enlarged to several times their usual size. All the mediastinal lymphatic glands (Fig. 8) showed varying degrees of reaction, from mere collections of dust cells to well-developed fibrotic areas, formed by the fusion of adjacent nodules. These areas were usually present in the periphery of the gland.

The incinerated sections (Fig. 10) revealed a large amount of silicious ash composed of translucent bi-refringent particles. Practically all these particles were under two microns in their greatest diameter, though occasional ones measuring 5 microns were present. The distribution of the silicious ash corresponded to the distribution of the dust cells and fibrous tissue seen in the stained sections.

Microscopic findings in quartz and aluminum-dusted animals.—The tissue reaction associated with the dust in the lungs of these rabbits was essentially a foreign body response, contrasting in a striking manner with the proliferative fibrotic response seen in the lungs of the quartz-dusted animals.

Great numbers of dust cells were present in the alveolar spaces. Areas comprised of a number of adjacent alveolar spaces, practically filled with dust cells (Fig. 3), were distributed uniformly throughout the lung. Most of the dust cells were contained in such areas, but a few were present in the adjoining alveoli. These cells were engorged with finely particulate bi-refringent particles. They were regular in outline, not elongated, and their nuclei stained well. The dust cells showed little evidence of degeneration (Fig. 5), and much less tendency to giant-cell formation than the dust cells in the lungs of the animals exposed to quartz alone. The walls of the alveoli containing only occasional dust cells were not thickened, and even in those alveoli filled with dust cells only slight thickening of the walls was present.

Few dust cells were present in the peribronchial lymphatic aggregations (Fig. 7) or mediastinal lymphatic glands (Fig. 9). Those present were in small clusters, and were not elongated or associated with a proliferative reaction.

The above description obtains for all the animals dusted with quartz and aluminum, except rabbits No. 93 and No. 96. Besides the above findings the lungs of these animals contained occasional small areas of proliferation in the alveoli and peribronchial lymphatic aggregations. The alveolar lesions were limited to a single alveolus (Fig. 11), and were composed of elongated dust cells without definite arrangement. The areas in the peribronchial lymphatic aggregations were not so large, but had much the same appearance as those seen in the alveoli.

The ash present in the acid-treated incinerated sections of the quartz and aluminum dusted animals was bi-refringent, and the individual particles were of the same size and appearance as those seen in the lungs of the animals dusted with quartz alone. The arrangement of this silicious ash had the distribution of the dust cells seen in the corresponding stained sections.

The liver, spleen and kidneys of the animals of both groups were normal.

DISCUSSION

Chemical.—From the findings as shown in Tables II, III and IV it would seem that other investigators have apparently overlooked the importance of the impurities contained in quartz or other silicious material as being a causative factor in the production of silicosis. It has been found that the alkaline earth carbonates, or carbonates in chemical combination with metals that may be easily decomposed, are responsible for the increased solubility of silicious material. It is also known that the solubility of silica is increased by the presence of small amounts of the carbonates and hydroxides of Mg, Na, K and Ca. Calcium hydroxide and cement, when used in large proportions, as shown in Tables IIIc and IIId, reduce the solubility of silica, but this reaction depends entirely upon the pH of the solution, as shown by Cummings and Miller.[8]

Many compounds of aluminum were investigated and found to be less satisfactory than the metal, since, being unstable, they gave erratic results (Table VII). It took larger quantities to produce the same effect and in some cases, as shown in the literature, certain compounds proved toxic to animals.

Haynes[9] (1931) demonstrated that aluminum hydroxide when inhaled alone caused damaging effects to the lungs of animals, but when mixed with precipitated silica in proportions to produce an artificial shale (80 per cent precipitated silica and 20 per cent aluminum hydroxide) it had a modifying effect on the reaction.

Metallic aluminum (specific gravity 2.68), having a specific gravity about the same as quartz (specific gravity 2.66), will naturally remain in suspension in a dusty atmosphere as long as the silicious particles. We are of the opinion that the aluminum reacts as in the beaker when taken into the lung with the dangerous dusts. That is, that the rapid initial rise and concentration of the solution of the silicious material is inhibited, thereby preventing degeneration of the dust cells and the production of fibrous tissue.

Due to the remarkable results obtained in the quartz and aluminum treated rabbits in conjunction with the beaker results, it seems reasonable to assume that metallic aluminum in small quantities administered in a similar manner will prevent other forms of pneumoconiosis, such as asbestosis, etc.

Comparative solubility tests, run under uniform conditions on silicious materials may indicate the relative fibrosis-producing properties of such materials. The literature does not report any record of damage to the body when small amounts of metallic aluminum are inhaled or ingested. This may be explained by its slow rate of dissolution in body tissues. At the present time we are not in a position to state the manner in which metallic aluminum reduces the solubility of silicious material. There are several ways in which this reaction may be accounted for and work is now in progress along these lines.

Dusting.—We believe that the rapid production of silicosis in the control animals (5 to 6 months) is due to our method of producing an extremely fine freshly fractured dust, uncontaminated with foreign material. The dust counts were kept at a concentration comparable to that produced under blasting conditions in the mine. It is imperative that the use of aluminum for the prevention of silicosis should in no way interfere with the standard practice of ventilation, as large quantities of even inert dust will damage the lung structure.*

Pathological.—The outstanding pathological finding seen in the lungs of the two groups of experimental animals was the marked difference in tissue reaction produced by the dust. The group dusted with quartz alone showed a proliferative fibrotic response, resulting in acute silicosis. Those dusted with quartz and aluminum showed a foreign body response. The slight lesions seen in the lungs of two of the latter group are insignificant when compared with the lesions of the control group. This difference in tissue response cannot be explained by the duration of dust exposure or the amount or the particle-size of the dust present, as the lungs of the aluminum-treated animals contained more quartz of the same degree of fineness, by chemical and microscopic investigation, than those of the control group. It is of interest to compare the appearance of the pulmonary dust cells in the two groups. The dust cells in the control group showed the degeneration, giant cell formation, and elongation to become fixed tissue cells, as well as the migration into the pulmonary lymphatics, which are so typical of the reaction produced by quartz dust in the lung. The dust cells in the lungs of the aluminum-treated rabbits showed little degeneration, much less tendency to giant cell formation and lymphatic migration, and practically no elongation. This is the type of reaction seen when relatively innocuous dusts are present in the lung. In our opinion this difference in tissue reaction is due to the presence of aluminum in the quartz dust inhibiting the formation of a toxic concentration of hydrated or dissolved quartz.

From this group of experimental animals it is impossible to say whether the aluminum is acting locally or systemically, or for what period after the cessation of dusting it will continue to act. These and many other questions will doubtless become clearer when the experiments being conducted at the present time are completed.

CONCLUSIONS

1. It has been shown that the addition of small quantities of metallic aluminum dust almost completely inhibits the solubility of silicious material in the beaker.

2. Seven rabbits dusted with quartz to which less than 1 per cent of metallic aluminum dust had been added showed practically no fibrosis, while 6 control rabbits, dusted with quartz only, showed well developed silicosis.

3. There is a great difference in the solubility of various types of silicious materials.

4. The solubility of quartz is increased by the presence of small amounts of the carbonates and hydroxides of magnesium, sodium, potassium and calcium.

5. The solubility of quartz is reduced by large amounts of calcium hydroxide, but is entirely dependent on the strongly alkaline reaction.

In conclusion, it affords us pleasure to record that the experimental work above described was made possible by the enthusiasm of Mr. R. J. Ennis, General Manager of McIntyre Porcupine Mines, Limited, and by the financial support of the same company, supplied on the recommendation of its President, Mr. J. P. Bickell.

We would particularily express our appreciation of the assistance so generously proferred and supplied by and through the good offices of Sir Frederick Banting and Dr. W. R. Franks, of the Banting Institute, and finally we would record that same appreciation of the splendid work and dependable results provided through the efforts of Mr. F. Bremner, Chief Chemist of the McIntyre Porcupine Mines, Limited, and Mr. H. L. Collins, of the Department of Medical Research.

* Further animal experimentation has been under way for some months, both at the McIntyre Mine and the Department of Medical Research, Banting Institute, the latter using large groups of rabbits, guinea pigs, cats and dogs. Our next paper will be published within the course of the next twelve months.

REFERENCES

1. ROBSON, W. D., IRWIN, D. A., AND KING, E. J.: Experimental silicosis: quartz, sericite and irritating gases, *Canad. M. Ass. J.*, 1934, **31**: 237.
2. GYE, W. E. AND PURDY, W. J.: Poisonous properties of colloidal silica, *Brit. J. Exp. Path.*, 1924, **5**: 238.
3. GARDNER, L. U. AND CUMMINGS, D. E.: The reaction to fine and medium-sized quartz and aluminum oxide particles, *Am. J. Path. (Supp.)*, 1933, **9**: 751.
4. HEFFERNAN, P.: Acute silicosis, *Tubercle*, 1932, **14**: 109.
5. BRAGG, W.: The structure of silicates, *Zeitschr. f. Krystallographie*, 1930, 74, no. 3-4.
6. KING, E. J. AND DOLAN, M.: Silicosis and the metabolism of silica, *Canad. M. Ass. J.*, 1934, **31**: 21.
7. BELT, T. H., IRWIN, D. AND KING, E. J.: Silicon and dust deposits in the tissues of persons without occupational exposure to silicious dusts, *Canad. M. Ass. J.*, 1936, **34**: 125.
8. CUMMINGS, A. B. AND MILLER, A. B.: Effect of lime on silica, *J. Ind. & Eng. Chem.*, 1934, **26**: 688.
9. HAYNES, F.: Experimental dust inhalation in guinea pigs, *J. Hygiene*, 1931, **31**: 96.

TWO CASES OF HYPERPARATHYROIDISM

BY GORDON S. FAHRNI

Winnipeg

PARATHYROID adenoma causing osteitis fibrosa cystica is still sufficiently rare to justify a report of each case. Although many cases have been reported since Mandl's classical case of 1925 it would appear that there is still much to be learned about this condition.

The increased interest in calcium metabolism that has been aroused during the past few years is due chiefly, no doubt, to the great enthusiasm with which the profession took up the subject of hyperparathyroidism. Interest has also been renewed in the pathology of bone, inasmuch as the skeleton in this disease is the seat of great pathological changes.

The following report is about two young women whom I first saw in the well-advanced stage of the disease, and in each case a diagnosis of hyperparathyroidism with extensive bone decalcification was made. Following the removal of a parathyroid adenoma in each patient, the deposition of calcium is followed radiographically in the one case for eighteen months, and in the other for three years. Both these young women were bedridden, profoundly emaciated, with marked osseous deformities, while today they are quite well and carrying on a normal life.

CASE 1

E.D., a female, aged 22, referred by Dr. A. C. Scott. She had the following complaints: completely bedridden for six months; profound loss of strength (her weight down from 122 to 85 pounds); severe soreness in the limbs, pelvis and chest (any movement caused severe pain); periodic attacks of gastric upsets, with vomiting and dizziness; polyuria and polydipsia.

This patient first consulted a physician on July 10, 1929, complaining of physical weakness, soreness in the limbs and pelvis. This condition persisted, and in December, 1930, she developed a swelling in the right mandible. She consulted a dentist who said it came from a tooth and opened into it through her mouth, but said blood alone escaped. January, 1931, another dentist took a radiograph, and said she had osteomyelitis and curetted the cavity. In September, 1931, a tooth close to the swelling was extracted and the cavity again curetted. She gradually became weaker and in November, 1932, became bedridden. After five months' complete confinement to bed the "sides of her chest fell in" (patient's statement). Her physician was called and a radiograph taken of her chest showed almost complete destruction of her ribs. At this time I was consulted by telephone and suggested a complete radiographic study of the skeleton and estimation of the blood serum calcium. The latter was 18 mg. per 100 c.c. of blood, and radiographs showed extensive decalcification of many bones. I went to see this patient in a cottage hospital in a town in a neighbouring province.

Examination revealed a frail, emaciated young woman, unable to move her legs or feet because of pain. There was a marked deformity of the chest, the sides of which expanded and retracted with respiration. There appeared to be separation of the costochondral junction of the second to sixth ribs on the right side and of the third to sixth ribs on the left side, the costal cartilages sticking out like fingers, their ends covered only by skin, the anterior ends of the ribs having fallen backwards. This made respiration rather difficult. Pulse 100, blood pressure 100/66.

After viewing the radiograph and the serum calcium having been checked by a reliable laboratory (18 mg. per 100 c.c.), a diagnosis of hyperparathyroidism was made. The emaciated condition of the patient made examination of the neck easy. There was a suggestion of a palpable irregularity low on the right side against the vertebral column, but this was rather indefinite.

General inhalation anæsthesia seemed inadvisable because of the poor general condition of the patient and the partially collapsed bony cage of the thorax, so the neck was explored under local anæsthesia (novocaine) on May 1, 1933. What appeared to be three normal parathyroid bodies were demonstrated, the two lower and the right upper. The left upper was not seen and there was no sign of a tumour. The mediastinum was then explored, and I felt a globular irregularity against the vertebral column just below the level of the right sterno-clavicular joint. This small mass was exposed and found to have a smooth glistening capsule. It was elevated, two arteries were clamped, and the small tumour, which was spherical and about 2.5 cm. in diameter, was easily delivered. Photographs and photomicrographs of this adenomatous tumour, are shown below, with the radiographs and the blood serum calcium record.

An attempt has been made to show the rate at which calcium is redeposited so that each bony part is featured with its consecutive radiographs before another bony part is shown. The date of each radiograph is stamped on the picture. The negative shadows in the frontal area in Figs. 1 and 2 have been replaced by positive shadows in Figs. 3 and 4, showing that a greater amount of calcium than normal has been laid