MANGANESE PNEUMONITIS

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I. CLINICAL AND ENVIRONMENTAL STUDIES

Manganese dioxide (MnO_2) or pyrolusite is mined in Norway, Germany, India, Russia, Brazil and the Gold Coast. Manganese dioxide is employed in the manufacture of manganese steel, in the dry battery industry, for the colouring and bleaching of glass, and in the chemical industry. Basic slag contains about 10 per cent. of manganese.

Literature

Though Brezina (1921) reported that 5 out of 10 men working in a pyrolusite mill had died of pneumonia after working 2, 6, 3, 1 and 2 months, Baader (1932) was the first to ascribe to manganese the high incidence of pneumonia amongst workers making dry battery cells. Elstad (1939) observed a great increase in pneumonia among the inhabitants of Sauda, a small town in Norway, after the opening of works where manganese alloys are smelted. The mortality for pneumonia in Sauda was ten times greater than for the rest of Norway, and in Elstad's opinion was due to the pall of smoke, containing manganese dust, overhanging the town.

Buttner (1939) observed that men working in a Rhenish pyrolusite mine suffered an average pneumonia rate, for the years 1934-37 inclusive, of 17 (range 8-25) per thousand (with an average death rate of 6.3 per thousand). As a control group he examined the experiences of the Leipzig Local Sick Fund whose male members had a pneumonia rate of 0.54 per thousand. In Buttner's opinion the death rate was due to a mild silicosis which by fibrosis paved the way for the pneumonic process. The Giessen pyrolusite ore contains 17 per cent. manganese, 20 per cent. iron and 20 per cent. silicic acid, which probably accounts for the silicotic process observed by Buttner.

The Present Inquiry

Manganese acts in two ways: (1) manganese poisoning, characterized by changes in the central nervous system, and (2) by causing pulmonary symptoms commonly termed manganese pneumonia.

The present inquiry was the result of the observation that men employed in the manufacture of potassium permanganate, exposed to the inhalation of dust of manganese dioxide and higher oxides of

manganese, suffered a high incidence of pulmonary symptoms, in particular illness diagnosed as pneumonia. Clinical and environmental studies were completed by the exposure of animals to the inhalation of manganese dioxide dust.

Description of Manufacturing Process

In the manufacture of potassium permanganate manganese dioxide is ground in a ball mill, 'reacted' with melted caustic potash (KOH) in the presence of lime (at a temperature of 400°C .) (fig. 1), roasted in rotary kilns (figs. 2 and 3) and subsequently in solution submitted to electrolysis (fig. 4) so that manganite, manganate and permanganate of potassium are formed in succession. Recovered manganese dioxide is dried in a roaster (fig. 5).

Of 34 batches of pyrolusite examined on delivery, 30 contained less than 2 per cent. of silica, and the remaining 4 batches less than 2.7 per cent. (with an average manganese dioxide content of 87-88 per cent.). Minor constituents are phosphorus pentoxide (0.2 per cent.), lead (0.002 per cent.), iron (3.5 per cent.), alumina (1.0 per cent.) and chromium (0.001 per cent.).

The work is heavy but the plant is not unduly hot (except during blackout) though the clothing needed to protect against caustic splashes adds to the heat and sweating (fig. 6). The cloakrooms are good and well supplied with hot water and fitted with shower baths, and from some parts of the plant can only be reached by going outside but no worker need walk more than 10 yards out of doors to reach the cloakroom. The majority need not leave the building. When 'reactions' are being done, a thick cloud of steam and dust, mostly manganese dioxide and lime, is given off, and at all times the plant is very dusty. Potassium manganate and permanganate spray is liberated in the electrolytic process (fig. 4). Except in special places no forced ventilation was provided though the plant was freely open to the outside air. Ventilation varies considerably with the direction of the wind, and by general consent is considered to be good when the wind is blowing from the west. This is partly because of the layout of the plant and partly because the most dusty jobs are on the east side.

Incidence of Illness diagnosed as Pneumonia

The incidence of illness diagnosed as pneumonia in a group of 40-124 men, exposed to the inhalation of manganese dust, varied from 15 to 63 (average 26) per thousand over the years 1938-45 inclusive, compared with an average rate of 0.73 per thousand for the years 1938-44 amongst the male members of Boots Health Insurance Society (Table 1).

In all cases the diagnosis of pneumonia in a manganese worker was made by the patient's medical attendant and confirmed by communication with the doctor. The first N.H.I. certificate of pneumonia received by Boots Health Insurance Society whose male members are, with few exceptions, equally divided between chemical and pharmaceutical manufacture and retail business, provided a control group.

The restriction of the inquiry to 'pneumonia' is artificial, and as became evident in the course of the animal experiments, does not take account of the mode of action of manganese. On the other hand, diagnoses such as 'bronchitis' are too vague for statistical purposes. For example, in 1944 no cases of 'pneumonia' in manganese workers were recorded but 2 cases of bronchitis, stated by their medical attendants to be 'very severe,' occurred.

Clinical Features

The commonest complaint amongst workers is 'bronchitis,' a term which covers changes varying from nasopharyngitis to bronchitis and broncho-pneumonia. People unused to exposure to manganese dust notice an irritation of the nose shortly after exposure: some hours later the nose feels

blocked and epistaxis may occur. During the development of the animal chamber and of the method of creating dust-laden air, inadequate precautions were taken to enclose the dust, and two persons (T. A. L. D. and E. W.) concerned in the investigation suffered repeated colds and epistaxis, culminating in attacks lasting two or three days, which were thought to be influenza. When the association was recognized the use of adequate dust filters immediately stopped the attacks. This observation is of interest as the men working on the plant have for many years been provided with 'influenza mixture' * which they imbibe liberally and with great faith when coming off work. The inhalation of potassium permanganate dust and permanganate spray is especially irritating to the nasopharynx, giving rise to coughing and retching. Men working on the plant become immune to the above symptoms.

Clinical examination of the respiratory system is unequivocal. A chronic granular pharyngitis is almost universal but cannot be said to occur more frequently than in other chemical workers. Foul teeth are very common and tracheitis is common. Except in men who have developed bronchitis, asthma or pneumonia, examination of the chest shows nothing abnormal.

'Pneumonia.'—So far as can be determined, all cases were diagnosed as lobar or broncho-pneumonia, and no special points were noticed by the sufferers' private medical adviser. No special features were noticed except that the temperature and general condition of the patient responded

* A mixture containing ammonium acetate, camphor, squill and ether.

TABLE 1
THE INCIDENCE OF ILLNESS DIAGNOSED AS PNEUMONIA

	Manganese plant				Boots Health Insurance Society. Males 21-65 years			England and Wales †		U.S. Public Health Report, Washington §
	Maximum number employees (at end of any quarter)	Average monthly output (units)	Number cases pneumonia	Pneu-monia rate per 1000	Number of male members	Number first certificate of pneu-monia	Pneu-monia rate per 1000	Number reported cases of pneu-monia	Pneu-monia rate per 1000 ‡	Pneumonia rate per 1000 males
1936	23		Records destroyed		5580	4	0.72			
1937	53	19.7			5763	1	0.19			
1938	47	31.11	3	63	5991	3	0.52			
1939	40	39.9	2	50	6342	3	0.47	42,312	1.0	
1940	67	53.9	1	15	6586	6	0.91	47,875	1.2	
1941	101	79.19	3	30	6678	4	0.59	50,942	1.2	
1942	124	97.7	3	24	6751	6	0.89			
1943	101	91.16	2	20	4899*	6	1.20*			
1944	70	86.1	—	—	5008*	5	1.00*			
1945	75	81.19	2	26	4645*	1	0.02*			

* Civilians only; the pneumonia rate for these years is probably artificially high owing to removal of young and healthy males.
† Summary Report by the Ministry of Health, 1942. Appendix II, H.M.S.O. (including women and children).
‡ Population (estimated mid-year 1939) 41,460,000.
§ Public Health Report, 1943. Washington, 58, 677.

FIG. 1.—Melted caustic potash ($400^{\circ}\text{C}.$) is poured into manganese and lime and stirred: a violent reaction ensues in which large volumes of steam and quantities of dust are emitted.

FIG. 2.—Filling rotary kilns.

FIG. 3.—Discharge end of rotary kilns. Note enclosure and dust extraction.

FIG. 4.—Electrolysis to form potassium permanganate in caustic solution.

FIG. 5.—Charging roaster to dry recovered manganese dioxide.

FIG. 6.—Protective clothing to guard against caustic splashes and the inhalation of dust.

more slowly than usual to sulphonamides. The possible causal relationship to manganese was not suspected until subsequent enquiry.

Case No. 1. A male, aged 48 years, employed in the manufacture of potassium permanganate for ten years (previous employment general labourer and shop assistant), was seen during an attack by the kindness of Dr. R. Davidson. Clinically he appeared to be suffering from a typical lobar pneumonia with a high temperature (105°) which responded to sulphonamides though more slowly than usual. The right lower lobe appeared to be consolidated and pneumococci were present in the sputum in large numbers. Two months later an x-ray of the chest showed slight generalized fibrosis but no consolidation or other evidence of an earlier pneumonia.

Case No. 2. A male process worker, aged 43 years, entered the building trade on leaving school and became a builder's labourer until 38 years of age when he became a chemical worker. He was first employed on general chemical work, including the manufacture of halazone. He claims to have suffered from bronchitis at frequent intervals and to have had pneumonia as an infant, though when examined 16 months prior to the present illness no abnormality was discovered in his chest or elsewhere except for septic teeth. For the past five years (with the exception of two intervals of 3 months) he has been employed on the manufacture of potassium permanganate and latterly in recovering manganese dioxide which has to be 'dug' out of a vat, dried and sieved. His present illness started suddenly with pain in the left side of the chest, a cough and shortness of breath. Three days later he was admitted to Nottingham General Hospital under the care of Dr. J. W. Scott.

On admission, temperature was 103°, pulse 120, respiration 24. His teeth were septic, tongue clean. Air entry was diminished and coarse râles were present over the left chest. Blood pressure was 150/116. Other systems were normal. Sputum examined on two occasions did not show tubercle bacilli. A diagnosis of pneumonia was made.

He was treated with sulphathiazole and penicillin (120,000 units daily for three days) but his condition improved more slowly than would have been expected (see Temperature Chart).

An x-ray of his chest four days after admission (fig. 8) showed consolidation of the left upper lobe. The remainder of the lung field had an appearance of 'fluffiness' similar to that seen with early or slight pulmonary oedema. The bronchial shadows appeared swollen and indefinite in outline; some consolidation was present in the right lower lobe.

Fourteen days later the consolidation was resolving and the radiographic appearance of the rest of the lung field was normal except for increased bronchial markings

(fig. 9). Nine weeks after admission to hospital an x-ray of the chest showed increased lung markings within normal limits (fig. 10). At this time he was free from symptoms; slight oedema of his left leg was present, probably due to circulatory stasis. The cardiovascular system showed no abnormality; the urine was normal.

Of the 16 men who suffered from 'pneumonia' (see Table 1), 8 examined in August and September 1945 showed neither clinical nor radiographic changes in the lungs which might be definitely ascribed to the inhalation of manganese. One man examined 18 months after pneumonia showed radiographic evidence of pleural thickening at both apices. Otherwise, the x-ray films showed increased lung markings such as are commonly ascribed to chronic bronchitis.

Bronchitis.—Attacks of mild bronchitis are frequent; records prior to 1942 are defective owing to enemy action, but since then 3 cases of very severe bronchitis with a superimposed asthmatic element have resulted in prolonged disability.

*Case No. 3.** A man who had previously been a miner for 26 years, after working in the potassium permanganate plant for 4 years, suffered from three attacks of 'bronchitis' within a period of 2 months. Two months after the last attack he was in bed for 3 weeks with an illness diagnosed as 'pneumonia.' After getting up for 2 weeks he endeavoured to return to work but when examined prior to restarting work he was noticed to be very short of breath, with obvious asthma, even when at rest. Temperature 98°, pulse 80, and moist crepitations and wheezy expiratory ronchi were present all over the chest. A purulent gingivitis was present. An x-ray of his chest showed increased lung markings.

He was provided with a light outdoor job but he remained short of breath (with wheezy ronchi present all over his chest) for 2 months, when his symptoms and chest signs gradually improved. One year later, at his own request, he returned to work in the potassium permanganate plant, but after 2 months' exposure, suffered a recurrence of severe bronchitis and asthma.

*Case No. 4.** A man was employed in shovelling recovered manganese mud, consisting mostly of manganese dioxide, into a dryer. He developed a

* Details of previous occupational history and age are irrelevant but not reported to avoid identification.

FIG. 7.—Temperature Chart of Case No. 2.

FIG. 8.—X-ray showing consolidation of left upper zone: some consolidation right base and indefinite outline of lung markings.

FIG. 9.—X-ray taken fourteen days later. Consolidation resolving: increased lung markings.

FIG. 10.—X-ray taken nine weeks later: normal appearance.

cough, and one week after starting this work the cough was severe, with much purulent sputum, and he was very short of breath even when at rest. Breathing was of the asthmatic type. In order to sleep he had to prop himself up into a semi-sitting position with pillows. Wheezy expiratory ronchi were present all over his chest. On removal from work his symptoms improved but recurred suddenly 2 weeks later on again inhaling manganese dust. An x-ray of his chest showed increased markings at both bases with fluffy patches of consolidation. No tubercle bacilli were present in the sputum.

He continued to suffer from severe shortness of breath with attacks of asthma relieved by ephedrine for 3 months when he suffered a haematemesis due to a gastric ulcer. When he resumed work 8 months later, his chest symptoms were much improved, but 2 years after the original incident he is still liable to attacks of shortness of breath at night or on exertion. An x-ray of his chest showed increased bronchial shadows but no consolidation or fibrosis.

Seven other men besides those reported above, examined at various times because of absence due to chest symptoms, showed neither clinical nor radiographic abnormality on return to work.

Three men who were examined as they had been employed for 9 years on the plant were free from symptoms and showed no abnormality on clinical and x-ray investigation.

Environmental Studies

The environmental studies are summarized in Tables 2 and 3. All dust counts were made with a thermal precipitator (Green and Watson, 1935).

The opinion that the dustiness of the plant varied with the weather is confirmed, dust counts being less when the wind is in the east. The particle size of the dust is small, approximately 80 per cent. of particles being less than 0.2μ in size, and nearly all particles less than 1μ . The mass concentration determined by the electrostatic precipitator bore no relation to the number of particles per cubic centimetre of air determined by the thermal precipitator or to the calculated mass concentration (Bedford and Warner, 1942).

TABLE 2
ENVIRONMENTAL STUDIES

Date	Time	Site	Out- side temp. ° F.	Wind direc- tion	Speed m.p.h.	Climate	Plant temp. ° F.	Dust count: par- ticles per c.c.	Differential count (per cent.)										
									0-2μ	-4μ	-8μ	-12μ	-1.6μ	-2.0μ	-2.5μ	-3.0μ	-4.0μ	-5.0μ	Above 5μ
26.10.43	3.15 p.m.	1	56	S.W.	2-3	Fine	N.R.	8751	80.6	12.4	3.6	2.0	0.6	—	—	—	0.4	—	7μ, 0.2; 15μ, 0.2
21.12.43	11.30 a.m.	1	46	S.S.W.	17-20	—	N.R.	3654	75.25	9.75	6.0	3.25	1.5	1.5	1.0	0.5	0.5	0.25	—
1.11.44	2.55 a.m.	1	45	N.	4-7	Dull	N.R.	4740	84.4	10.1	2.1	1.4	0.3	0.3	0.1	0.3	0.1	0.5	7μ, 0.2; 10μ, 0.1; 15μ, 0.1
7.12.44	2.45 p.m.	1	36	S.W.	1-3	Frosty	45.0	2669	78.8	11.9	4.2	2.0	1.1	0.6	0.3	0.2	0.2	0.3	7μ, 0.1; 15μ, 0.1
7.12.44	3.7 p.m.	1	36	S.W.	1-3	Frosty	47.0	9019	86.5	9.3	2.2	0.7	0.2	0.1	0.3	0.1	0.4	0.1	7μ, 0.1
26.10.43	4.15 p.m.	2	56	S.W.	2-3	Fine	N.R.	9360	79.8	13.0	3.2	1.4	0.6	0.4	0.6	0.2	0.4	0.4	—
16.12.43	2.50 a.m.	2	39	E.	10-15	Misty	N.R.	4068	74.2	16.4	5.0	1.4	1.6	0.2	0.2	—	—	0.4	7μ, 0.2; 22μ, 0.2; 30μ, 0.2
2.11.43	10.15 a.m.	3	56	N.E.	3-6	Drizzle	N.R.	4811	83.9	12.3	2.7	0.5	0.3	0.3	—	—	—	0.4	15μ, 0.2
12.1.44	11.45 a.m.	3	54	S.	Slight breeze	Mist	N.R.	8136	87.2	9.2	2.2	0.4	—	—	0.2	—	0.4	0.2	—
18.1.44	—	3	52	S.W.	7-15	—	N.R.	19496	92.6	5.4	1.4	0.2	0.4	—	—	—	—	—	—
27.10.43	4 p.m.	5	59	S.W.	10-15	Sunny	67-68	1617	78.4	10.8	4.4	1.6	1.0	1.0	0.8	—	1.2	0.6	7μ, 0.2
15.12.43	2.35 a.m.	5	27	N.E.	5-10	Misty	51	7583	81.0	12.0	3.6	1.8	0.6	0.6	0.2	0.2	—	—	—
29.10.43	2.30 p.m.	6	56	S.E.	4-6	Fine	65.2	2653	87.6	10.2	1.4	0.6	—	—	0.2	—	—	—	—
14.12.43	4.5 a.m.	6	26	—	—	Fog	43.0	15143	80.0	13.6	4.8	1.4	0.2	—	—	—	—	—	—
2.11.43	11.45 a.m.	7	58	N.E.	3-6	Drizzle	65.0	6275	72.6	17.4	4.6	1.6	0.4	0.2	0.4	0.4	0.8	0.6	7μ, 0.4; 50μ, 0.4; 55μ, 0.2
15.12.43	7.13 a.m.	7	27	N.E.	5-10	Misty	53.0	8975	85.2	10.8	2.4	0.6	0.2	0.4	0.2	0.2	—	—	—
29.10.43	4.30 p.m.	8	55	E.	4-6	Fine	68.0	4060	92.5	5.6	0.9	0.5	0.2	0.1	0.1	—	—	0.1	—
14.12.43	4.40 a.m.	8	26	—	—	Fog	45.5	13503	81.6	12.4	4.2	1.4	0.4	—	—	—	—	—	—
18.1.44	—	8	—	S.W.	7-15	—	—	5169	82.4	12.0	3.4	0.8	0.6	0.4	—	—	0.2	0.2	—
29.10.43	10.40 a.m.	9	52	S.S.E.	2-6	Dull and misty	N.R.	11668	92.0	3.8	1.2	0.8	0.6	0.4	0.6	—	0.4	0.2	—
16.12.43	1.59 a.m.	9	39	E.	10-15	Misty	N.R.	8352	64.0	24.4	5.6	2.2	1.0	0.6	0.4	0.2	0.4	0.4	7μ, 0.2; 13μ, 0.2; 15μ, 0.2; 17μ, 0.2
1.11.43	3.30 p.m.	10	56	N.E.	3-6	Raining	N.R.	5438	81.6	13.4	3.0	1.4	0.2	—	0.4	—	—	—	—
15.12.43	5.03 a.m.	10	27	N.E.	5-10	Misty	N.R.	5268	79.0	13.4	4.2	2.0	0.8	—	—	0.4	0.2	—	—
4.11.43	11.45 a.m.	11	53	Still	—	Fog	N.R.	4119	72.0	18.8	5.2	3.2	0.6	—	—	—	—	—	7μ, 0.2
28.10.43	10.20 a.m.	12	52	S.W.	2-3	Fog	N.R.	8510	78.6	10.8	2.6	1.4	1.4	2.2	0.8	0.6	0.8	0.4	7μ, 0.2; 10μ, 0.2
16.12.43	3.05 a.m.	12	39	E	10-15	Misty	N.R.	2085	69.0	22.0	4.6	2.2	0.6	0.6	—	—	0.2	0.4	18μ, 0.2; 100μ, 0.2

TABLE 2—continued
ENVIRONMENTAL STUDIES—continued

Date	Time	Site	Out- side temp. ° F.	Wind direc- tion	Speed m.p.h.	Climate	Plant temp. ° F.	Dust count: par- ticles per c.c.	Differential count (per cent.)										
									0-2μ	-4μ	-8μ	-1.2μ	-1.6μ	-2.0μ	-2.5μ	-3.0μ	-4.0μ	-5.0μ	Above 5μ
28.10.43	2.45 p.m.	13	56	S.W.	2-3	Misty	66.0	7589	78.0	12.6	3.8	2.4	0.6	0.8	0.2	0.2	0.6	0.6	40μ, 0.2
14.12.43	3.12 a.m.	13	26	Still	—	Fog	53.5	15098	78.2	13.0	6.0	2.0	0.6	0.2	—	—	—	—	—
21.10.43	11.20 a.m.	14	62	S.	15-20	Showery	84.0	2015	—	—	—	—	—	—	—	—	—	—	—
21.10.43	3.0 p.m.	15	61	S.	15-20	Showery	66.4	953	—	—	—	—	—	—	—	—	—	—	—
15.12.43	3.50 a.m.	15	27	N.E.	5-10	Misty	62.0	9389	84.6	9.4	4.4	1.2	0.4	—	—	—	—	—	—
14.12.43	7.30 a.m.	16	26	Still	—	Fog	52.0	8346	73.6	11.6	7.4	2.4	1.2	0.8	0.2	0.2	—	0.8	7.5μ, 0.2; 10μ, 1.0; 15μ, 0.2; 22μ, 0.2; 34μ, 0.2
15.12.43	2.55 a.m.	16	27	N.E.	5-10	Misty	55.0	7392	70.4	19.0	5.2	2.0	1.6	0.6	0.2	—	—	0.4	50μ, 0.2; 67μ, 0.2; 75μ, 0.2
1.11.44	11.30 a.m.	16	45	N.	4-7	Dull	—	5008	77.4	13.1	4.4	2.1	0.5	0.6	0.4	0.4	0.3	0.3	7μ, 0.2; 10μ, 0.1; 20μ, 0.1
7.12.44	11.10 a.m.	18	36	S.W.	1-3	Frosty	58.0	4826	75.7	16.0	2.5	1.0	0.7	0.7	0.6	0.8	0.5	0.6	7μ, 0.5; 10μ, 0.3; 15μ, 0.1
7.12.44	11.30 a.m.	18	36	S.W.	1-3	Frosty	58.0	3361	66.0	12.7	5.0	3.8	1.6	1.1	0.8	1.7	2.1	1.9	10μ, 1.5; 15μ, 0.8; 20μ, 0.5; 25μ, 0.1; 40μ, 0.2; 70μ, 0.1; 300μ, 0.1
26.10.43	11.50 a.m.	19	48	S.W.	2-3	Fine	56.0	31830	86.0	10.8	2.0	0.2	0.4	—	0.2	—	—	—	25μ, 0.2; 50μ, 0.2
15.12.43	1.47 a.m.	19	27	N.E.	5-10	Misty	41.5	9064	79.6	11.4	6.0	1.4	1.0	0.2	—	0.2	0.2	—	—
25.10.43	12.20 p.m.	20	50	S.W.	2-3	Fine	60-62	14995	71.8	23.6	3.5	0.4	0.5	0.1	—	0.1	—	—	—
14.12.43	1.55 a.m.	20	26	—	—	Fog	45.5	22903	79.6	12.4	5.2	2.0	0.4	0.2	—	0.2	—	—	—
1.11.44	5 p.m.	20	45	N.	4-7	Dull	—	7908	87.8	9.5	1.4	0.5	0.2	0.1	0.1	—	0.1	0.1	10μ, 0.1; 15μ, 0.1
7.12.44	12.10 p.m.	20	36	S.W.	1-3	Frosty	58.0	5937	87.8	8.6	1.7	0.8	0.3	0.1	—	—	0.1	0.3	10μ, 0.3
26.10.43	11 a.m.	21	36	S.W.	2-3	Fine	52.0	37040	84.6	11.6	2.0	0.4	0.2	—	—	0.2	0.4	—	7μ, 0.4; 10μ, 0.2
14.12.43	2.30 a.m.	21	26	Still	—	Fog	45.0	21439	82.4	11.4	2.8	0.6	1.2	0.4	0.2	0.2	0.2	0.2	7.5μ, 0.2; 10μ, 0.2
22.10.43	9.50 a.m.	22	52	S.	10-15	Fine	84.2	1850	82.8	14.7	1.5	0.3	0.3	0.2	—	—	0.1	0.1	7μ, 0.2; 10μ, 0.2; 20μ, 0.2;
16.12.43	3.43 a.m.	22	39	E.	10-15	—	50-52	2843	76.4	13.8	4.0	1.2	1.0	0.4	0.2	0.4	0.2	1.0	22μ, 0.2; 50μ, 0.4; 100μ, 0.2
22.10.43	12.10 p.m.	23	59	S.	10-15	Fine	79-81	8652	88.4	9.0	0.8	0.6	0.4	0.2	0.2	—	0.2	—	10μ, 0.2
16.12.43	4.15 a.m.	23	39	E.	10-15	—	57-59	5965	83.0	11.0	3.8	1.2	0.6	0.2	0.2	—	—	—	—

TABLE 3
ANALYSIS OF DUST (COLLECTED BY ELECTROSTATIC PRECIPITATOR) AND COMPARISON WITH THERMAL PRECIPITATOR DUST COUNTS

Date	Site	Thermal precipitator											Calculated mass concentration: mg./cu. m. as MnO ₂ . Sp.gr. 3.0	Electrostatic precipitator. Mass concentration: mg./cu. m.	Analysis	
		Differential count (per cent.)														
		No. particles per c.c.	0-2μ	-4μ	-8μ	-1.2μ	-1.6μ	-2.0μ	-2.5μ	-3.0μ	-4.0μ	-5.0μ	Above 5μ	All particles		Particles 1-5μ
1.11.44	1	4740	84.4	10.1	2.1	1.4	0.3	0.3	0.1	0.3	0.5	7μ, 0.2; 10μ, 0.1; 15μ, 0.1	40.2	4.5	43	Other major constituents Ca and K. Ba and Na present to extent of 1 and 0.1 per cent. respectively. Smaller traces of Si, Fe, Li.
7.12.44	1	2669	78.8	11.9	4.2	2.0	1.1	0.6	0.3	0.4	0.3	7μ, 0.1; 15μ, 0.1	17.1	2.5	66	
7.12.44	1	9019	86.5	9.3	2.2	0.7	0.2	0.1	0.3	0.1	0.4	7μ, 0.1	9.6	4.5	58	
1.11.44	16	5008	77.4	13.1	4.4	2.1	0.5	0.6	0.4	0.4	0.3	7μ, 0.3; 10μ, 0.1; 20μ, 0.1	83.4	4.5	54	Ba and Na present to extent of 1 and 0.1 per cent. respectively. Smaller traces of Si, Fe, Li.
7.12.44	18	4825	75.7	16.0	2.5	1.0	0.7	0.7	0.6	0.8	0.5	7μ, 0.5; 10μ, 0.3; 15μ, 0.1	68.4	7.8	41	
7.12.44	18	3361	66.0	12.7	5.0	3.8	1.6	1.1	0.8	1.7	2.1	10μ, 1.5; 15μ, 0.8; 20μ, 0.5; 25μ, 0.1; 40μ, 0.2; 70μ, 0.1; 300μ, 0.1	—	16.8	65	
1.11.44	20	7908	87.8	9.5	1.4	0.5	0.2	0.1	0.1	—	0.1	10μ, 0.1; 15μ, 0.1	53.4	1.8	0.42	
7.12.44	20	5936	87.8	8.6	1.7	0.8	0.3	0.1	—	—	0.1	10μ, 0.3	29.7	3.0	9.2	

* Two thermal precipitator counts during one run of electrostatic precipitator.

TABLE 4
STANDARDIZATION OF APPARATUS
(All air flows 4 litres over dust and 6 litres through by-pass)

Experiment No.	Manganese dust: Dust count particles per c.c.	Interval after preceding count	Differential count (per cent.)										
			0-2μ	-4μ	-8μ	-1.2μ	-1.6μ	-2.0μ	-2.5μ	-3.0μ	-4.0μ	-5.0μ	Above 5μ
Control 1 2 3 4 Control 5 6 7 Control 8 9 10 11 Control 12 13	No strip	Consecutive 10 minutes 15 minutes	62.9	13.8	9.0	5.0	3.0	1.2	0.6	1.5	1.2	1.0	7μ, 0.6; 10μ, 0.1; 15μ, 0.1
	2552		65.8	16.8	8.0	3.4	1.2	1.0	0.6	0.6	0.8	0.7	7μ, 0.5; 10μ, 0.4; 15μ, 0.1; 50μ, 0.1
	2199		65.1	15.3	8.5	3.6	2.0	1.2	0.8	0.9	1.2	0.5	7μ, 0.4; 10μ, 0.3; 15μ, 0.1; 20μ, 0.1
	2125		70.8	14.3	8.6	2.7	0.9	0.7	0.4	0.6	0.5	0.2	10μ, 0.1; 15μ, 0.1; 50μ, 0.1
	No strip	5 minutes 5 minutes	58.8	17.6	9.6	4.4	3.4	1.0	0.7	1.3	1.1	1.2	7μ, 0.3; 10μ, 0.4; 15μ, 0.1; 20μ, 0.1
	1663		66.6	14.7	8.0	4.0	2.6	0.7	0.6	0.5	0.6	0.7	7μ, 0.6; 10μ, 0.2; 15μ, 0.2
	1401	60.3	15.6	9.4	6.0	2.0	1.6	0.7	1.4	0.8	1.3	7μ, 0.6; 10μ, 0.1; 15μ, 0.1; 22μ, 0.1	
	No strip	2½ hours Air off for 16 hours 5 hours	74.4	13.0	4.5	2.4	1.0	0.8	0.6	1.1	1.1	0.6	7μ, 0.3; 10μ, 0.2
	1629		72.3	17.4	5.0	1.9	0.8	0.9	0.6	0.5	0.4	0.1	7μ, 0.1
	1891		46.1	20.7	10.6	5.4	5.1	4.1	2.0	1.4	1.9	1.5	7μ, 0.8; 10μ, 0.4
	1948		51.9	23.1	9.6	5.8	2.6	1.5	1.2	0.8	1.6	1.1	7μ, 0.5; 10μ, 0.3
	No strip	3 hours	32.6	22.9	17.6	8.0	4.7	3.9	2.3	2.7	1.7	1.7	7μ, 0.9; 10μ, 0.6; 15μ, 0.3; 20μ, 0.1
	2689		39.7	24.5	14.0	6.5	4.6	2.9	1.0	2.0	2.0	1.6	7μ, 0.45; 10μ, 0.3; 15μ, 0.3; 50μ, 0.15
1370													
Control 14 15 16 Control 17 18 19 20 21 22 23 Control 24 25	Foundry sand												
	No strip	5 minutes	26.5	11.5	13.0	6.5	9.0	4.5	2.0	5.0	6.5	8.0	7μ, 3.5; 10μ, 1.0; 15μ, 2.0; 20μ, 1.0
	1150		51.2	10.2	7.4	4.7	3.5	3.7	2.2	4.1	4.2	4.7	7μ, 2.0; 11μ, 1.1; 15μ, 0.6; 20μ, 0.1; 22μ, 0.1; 25μ, 0.2
	1133	10 minutes	48.2	17.1	10.7	6.6	3.6	2.8	2.1	2.2	2.1	2.3	7μ, 1.3; 10μ, 0.5; 15μ, 0.3; 20μ, 0.1; 22μ, 0.1
	1709		33.2	11.6	10.8	9.5	7.3	4.7	4.0	5.8	4.7	4.1	7μ, 2.6; 10μ, 1.1; 15μ, 0.6
	No strip	2 hours 10 minutes	20.7	9.3	13.5	10.4	9.4	7.0	4.3	6.9	8.1	5.4	7μ, 3.2; 10μ, 1.2; 15μ, 0.3; 20μ, 0.1; 22μ, 0.1; 25μ, 0.1
	1825		47.7	11.8	11.5	6.8	4.7	3.6	2.2	3.3	3.2	2.3	7μ, 1.6; 10μ, 1.0; 15μ, 0.3
	1658	30 minutes	32.1	8.8	10.4	8.3	7.1	5.9	3.8	6.2	6.1	5.0	7μ, 3.6; 10μ, 1.3; 15μ, 1.0; 20μ, 0.1; 22μ, 0.2; 30μ, 0.1
	1914		49.2	15.0	8.0	4.8	3.7	3.7	2.6	3.6	3.7	3.3	7μ, 1.1; 10μ, 0.5; 15μ, 0.5; 22μ, 0.2; 25μ, 0.1
	2917	55 minutes 35 minutes 30 minutes	62.0	15.6	9.2	3.6	2.6	1.8	1.0	1.4	0.8	1.0	7μ, 0.4; 10μ, 0.6
	3213		59.6	17.4	7.4	3.2	3.6	1.6	2.2	1.6	1.6	1.0	7μ, 0.8
	3737	4 hours 15 minutes											
	No strip		33.8	15.2	8.6	7.8	5.4	5.2	5.4	6.4	4.6	5.0	7μ, 1.2; 10μ, 0.6; 15μ, 0.6; 22μ, 0.2
1988													
1561													

Samples of dust for analysis were obtained with an electrostatic precipitator. The constitution of the dust varies in different parts of the plant. In the mill room the dust consists of manganese dioxide, but elsewhere, though the major constituent is manganese dioxide, manganite, manganate and permanganate of potassium may also be present. These substances would be rapidly reduced by body fluids to manganese dioxide. The manganese content of the dust, collected by the electrostatic precipitator, expressed as manganese dioxide varied from 41 to 66 per cent.

Other major constituents were potassium and calcium, the latter originating from the lime used in the reactions. Alkalinity of the dust collected from walls and ledges, calculated as potassium carbonate, varied from 1.01 per cent. in the mill room to 11.8 per cent. in the main hall. For the purpose of animal experiments dust was collected from the ledges and walls. (The absolute density of mixed samples was found to be 3.0.)

Since this investigation began, many improvements have been effected in working conditions, for example, exhaust ventilation has been fitted to the charging and discharging ends of the kilns (fig. 3).

II. ANIMAL EXPERIMENTS

Literature

Jötten and Reploh (1938) exposed rabbits to pyrolusite dust and produced broncho-pneumonia. The degree and severity of the broncho-pneumonia was increased by inoculation with pneumococci type II, either alone or accompanied by daily vigorous twisting of the animal. These authors do not report control experiments where animals not exposed to manganese dust were similarly inoculated.

Jötten, Reploh and Hageman (1939), discussing further experiments by Jötten (1939), described the histological changes in rabbits' lungs after exposure to manganese dust as a severe bronchitis with bronchiolitic changes. No signs of croupous pneumonia were present and these authors described the cellular reaction as a leucocytic and partly lymphocytic infiltration. Illustrations accompanying their paper show the large, apparently empty, mononuclear cells, characteristic of the present experiment. They also stated that changes could not be produced in mice's lungs unless a concomitant inhalation of pneumococci (either dead or alive) was employed. They concluded that manganese has a specific local action on the tissues.

Reploh (1943) has reported a series of experiments in which mice were exposed to various dusts including manganese carbonate dust from a Siemen-Martin furnace (manganese content 7-9 per cent.) and basic slag. With the exception of Siemen-Martin furnace dust, the mice failed to develop lung infections unless they were either previously treated with inhalations of dead pneumococci or previously

treated in a similar way followed by injection with dead or living pneumococci after the exposure of dust.

Dust-feed Apparatus

Owing to the heavy nature of manganese dioxide and the clinging nature of dust collected from the walls and ledges of the plant, the method described by Argyll Campbell (1934) did not prove satisfactory for the reproduction of the plant atmosphere. The major disadvantage of other dust-feed apparatus is the large amount of air required and the need to keep the level of the dust constant in relation to the large volume of relatively slow-moving air. The mechanical arrangements to achieve this are bulky, not easily movable and complicated (Stead, Dernell and Nau, 1944). If a small volume of air at a relatively high velocity were employed, and a compressed air cylinder* used as the source, many of these objections would be overcome (figs. 12 and 13).

Air was blown from a jet on to the surface of the dust 6 cm. away from the jet (fig. 12). The resultant lowering in the level of the dust during the experiment was negligible in relation to the air speed and distance from the jet. The dust was stirred with a paddle which revolved four times a minute. If desired, the dust-laden air could be diluted with clean air so that the dust concentration of the air entering the animal chamber might be controlled.

A rectangular animal chamber 600 × 550 × 500 cm., similar to that described by Argyll Campbell (1934) was used. The dust count in the chamber was kept constant by adjusting the flow of air through the jet between 1½-4 litres per minute and the clean air between 8½-6 litres per minute so that a total flow of 10 litres per minute was maintained. Before estimating the dust concentration the apparatus was run for at least half an hour to displace the air from the animal chamber. Standardization was effected by placing the thermal precipitator in the animal chamber: for any given dust and air flow it was always possible to reproduce within practical limits the same dust concentration for periods up to 5 hours (Table 5). The dust container was refilled as necessary but would, at the above air flows, last for 3 or more hours. In order to prevent the temperature rising in the animal chamber during an experiment, a coil of copper tube ½ inch in diameter, making three circuits of the chamber, through which cold water was passed, proved very effective. For experiments with mice the chamber temperature was kept at 65° F. The whole apparatus was installed in a thermostatically controlled room (temperature 65° F.) and in which the mice were kept when out of the chamber.

Animal Experiments

I. Manganese Dust (from Main Hall)

Seventy-two mice each weighing between 25-30 gm. were divided into two groups: (a) 60 mice

* A small compressor may be substituted but an after-cooling apparatus and filter are essential.

FIG. 11.—Plan of plant: figures refer to sites in which estimates of dust in atmosphere were performed.

1. Mill room near bags.	13. Dissolver.
2. Mill room near switch gear.	14. Cell room.
3. Sieve room near sieve.	15. Paxman filter room.
4. Caustic pots Nos. 1 and 2.	16. Reaction pots Nos. 1 and 2.
5. Main hall—general atmosphere centre.	17. Caustic pots Nos. 3, 4, 5 and 6.
6. Charge end kilns Nos. 1, 2 and 6.	18. Reaction pots Nos. 3 and 4.
7. Nos. 1, 2, 3 roasters near roaster.	19. General atmosphere.
8. Discharge and kilns Nos. 1, 2 and 6.	20. Charge end kilns Nos. 4 and 5.
9. Roast crusher.	21. Discharge end kilns Nos. 4 and 5.
10. Paxman mud discharge sump.	22. Charge end kiln No. 3.
11. Charging trays permanganate.	23. Discharge end kiln No. 3.
12. Discharging trays permanganate.	24. Unloading manganese ore on dock.

FIG. 12.—Diagram of dust-feed apparatus and animal chamber. Note cooling coil (see text) fitted inside chamber not shown in diagram.

FIG.13.—Photograph of the apparatus. Note cooling coil inside dust chamber and Mark IV respirator pad used as dust filter.

Day	Daily length of exposure (starting at 10 a.m. and 3 p.m.) minutes	Dust count: particles per c.c.	Remarks*	Day	Daily length of exposures (starting at 10 a.m. and 3 p.m.) minutes	Dust count: particles per c.c.	Remarks
1	2 × 120	2529	1 dead. ? reason.	21	2 × 70	—	1 ill—killed. <i>P.M.</i> Nares and stomach full of dust, ? broncho-pneumonia. <i>Lungs section</i> : slight infiltration; collection of large mononuclear cells around bronchi and arteries. Oedema of the lungs.
2	1 × 120	1747					
3	2 × 120	2364					
4	2 × 120	2786					
5	2 × 120	1441	1 dead. 1 blind—killed. <i>Lungs section</i> : intense infiltration with lymphocytes and large mononuclear cells especially around arteries and bronchi. 1 control dead.	22	No exposure.	—	1 dead.
6	2 × 120	940		23	2 × 70	—	1 ill—killed.
7	2 × 120	1658	3 dead.	24	2 × 70	1606	1 dead.
8	1 × 120 and 1 × 60	2472	1 blind and ill—killed. <i>Lungs section</i> : few small patches of mononuclear infiltration especially subpleural, and peribronchial. TOTAL died or killed 7 and 1 control.	25	2 × 70	763†	
9	No exposure.	—	1 dead. <i>Lungs section</i> : alveoli appear large; patches of consolidation and extensive generalized interstitial mononuclear infiltration; exudate in alveoli.	26	2 × 70	—	2 ill—killed. (1) <i>P.M.</i> Liver mottled, nil else apparent. <i>Lungs section</i> : interstitial mononuclear infiltration. (2) <i>P.M.</i> Large blood clot filling whole of pleural cavity; gross broncho-pneumonia. <i>Lungs section</i> : subpleural haemorrhage, generalized infiltration and patches of intense large mononuclear consolidation; some polymorphs seen; mediastinal glands showed heavy round cell infiltration. Bronchial epithelium swollen; exudate in bronchi and alveoli.
10	No exposure.	—					
11	No exposure.	—	1 dead. TOTAL died or killed 2.				
Mice made up to original number.							
12	1 × 30 and 1 × 120	1760		27	2 × 70	—	2 ill—killed. (1) <i>P.M.</i> Nothing abnormal. <i>Lungs section</i> : aggregates of dust cells in interstices of lungs. Mononuclear infiltration around bronchi and areas of consolidation and necrosis. (2) Paralysis of hind leg. <i>P.M.</i> Nothing abnormal. <i>Lungs section</i> : intense infiltration around arteries and bronchi with areas of consolidation. Brain ? round cell infiltration.
13	1 × 120	1749	1 dead. <i>P.M.</i> Nares obstructed with dust; stomach full of manganese dust. Lungs broncho-pneumonia. Spleen small with area of peritoneal thickening. <i>Section</i> : spleen nothing abnormal; lungs subpleural and peribronchial infiltration, patchy and intense. Stomach normal.				
14	2 × 120	—		28	No exposure.	—	3 dead. <i>P.M.</i> Nothing abnormal. <i>Lungs section</i> : intense peribronchial infiltration especially of large mononuclear phagocytic cells; few lymphocytes and some polymorphs. Swelling of bronchial and alveolar epithelial cells. (See Fig. 14, B.) Brain ? patches of round cell infiltration.
15	2 × 120	2387					
16	No exposure.	—	1 dead.				
17	2 × 120	2535	1 dead.				
18	1 × 120 and 1 × 70	923		29	No exposure.	—	1 dead. TOTAL dead or killed 16.
19	2 × 70	2392	1 dead. <i>Lungs section</i> : exudate in bronchi with dust-laden cells in bronchi, alveoli and interstitial spaces; intense peribronchial infiltration; small haemorrhagic areas.				
20	2 × 70	1925					

* Where no post-mortem examination has been made of dead mice this is because the time of death (for example, week-end) lead to autolysis, or because of cannibalism.

† One or more mice escaped from cage and interfered with thermal precipitator.

TABLE 5
NUMBER OF MICE ALIVE

Days after infection	Mice treated with manganese: 20 mice		Normal mice+ pneumococci		Manganese-treated mice+ pneumococci		Controls	
			Susp. A	Susp. B	Susp. A	Susp. B	Normal mice	Normal mice from manganese room
0	10	10	10	10	10	10	10	8
1	10	10	10	10	7	10	10	8
2	10	10	1	0	0	0	10	8
3	10	9	1	0	0	0	10	8
4	9	9	0	0	0	0	9	8
5	9	9	0	0	0	0	9	8
6	9	9	0	0	0	0	9	8

(in two cages of 30 each) which were exposed to dust, (b) 12 mice as controls, which except for exposure to dust were kept and treated in an identical manner. The dust contained 70 per cent. of MnO_2 and its alkalinity, mostly present in the form of potassium carbonate, calculated as KOH was 9.6 per cent., or calculated as K_2CO_3 was 11.8 per cent.

Exposures to dust for 2 hours twice daily were given 5 days a week for 14 exposures but the mice appeared ill and 7 exposed mice died or were killed. One control mouse died. After an interval of 8 days (during which 3 mice died) the mice were made up to the original number and exposed twice daily, but after 10 exposures the time of exposure was reduced to 70 minutes twice daily, 5 days a week, for 26 exposures (during which 16 mice died or were killed). Dust counts inside the chamber were performed every second or third exposure.

Bacteriological Results.—At the end of this time the exposed mice, though not obviously ill, were in poor condition and less well than the control mice. The exposed mice had lost weight, 11 mice weighing 23–24 gm. (As this was an unexpected effect, individual weights had not been kept.) Four days after the last exposure the exposed mice were tested for susceptibility to pneumococci.

The mice were divided by random selection in six groups as shown in Table 5, and given intraperitoneal injections of pneumococcus (type II): suspension A, each mouse received 0.5 ml. of a suspension containing 240,000 organisms per ml., suspension B, each mouse received 0.5 ml. of a suspension containing 12,000 organisms per ml.

The doses had been carefully standardized but the suspension proved about five times as toxic as expected. Post-mortem smears and cultures from the lung, spleen and heart showed large numbers of pneumococci.

Nine of the manganese-treated control mice were infected with 0.5 ml. of a suspension of pneumococci containing 800 organisms per ml., the remaining 9 being kept as controls.

In view of the poor condition of the manganese-exposed mice the results were not considered significant and do not suggest that the inhalation

TABLE 6
NUMBER OF MICE ALIVE

Time after infection	Manganese treated mice + pneumococci	Normal mice + pneumococci	Controls	
			Normal mice	Manganese treated mice
0 hours	9	9	9	9
24 "	9	9	9	9
48 "	4	8	9	9
54 "	1	3	9	9
72 "	1	0	9	9
4 days	1	0	9	9

of manganese increases the susceptibility to pneumococci.

Absorption of Manganese.—Four days after the end of exposure, 3 exposed mice and 3 control mice were killed. The lungs and brains were removed and grouped and 1 mouse of each group skinned. After wet oxidation, the total manganese content was estimated spectrographically, using the cathode layer D.C. method.

		Exposed mice		Control mice	
		Total of 3 mice	Average per mouse	Total of 3 mice	Average per mouse
Brains	..	μgm. 1.5	μgm. 0.5	μgm. 1.3	μgm. 0.4
Lungs	..	1.5	0.5	0.5	0.17

II. Calcium Carbonate Dust (Control Experiment)

Heavy calcium carbonate (s.g. 2.9) was used as a non-toxic dust of similar specific gravity and particle size.

Seventy-two mice each weighing between 25–30 gm. were divided as in Experiment I.

Exposures to dust for 70 minutes twice daily were given 5 days a week for 30 exposures. Dust counts inside the chamber were performed every second or third exposure. No control mice died.

Day	Daily length of exposure (starting at 9.30 a.m. and 2.30 p.m. minutes)	Dust count: particles per c.c.	Remarks
1	2 × 70	991	
2	2 × 70	—	
3	2 × 70	—	
4	2 × 70	1629	
5	2 × 70	—	
6	2 × 70	—	
7	2 × 70	1259	
8	2 × 70	1903	1 dead.
9	2 × 70	—	
10	2 × 70	1675	
11	2 × 70*	1025	1 dead. Lost 6 gm. in weight. <i>Lungs section</i> : slight round cell infiltration and some subpleural haemorrhage.
12	2 × 70	—	1 dead. <i>Lungs section</i> : some subpleural mononuclear and lymphocytic infiltration.
13	—	—	
14	2 × 70	2045	2 dead.
15	2 × 70	1640	1 dead.
16	—	—	2 dead. 1 killed. (1) No P.M. (2) P.M. <i>Lungs</i> normal, section few dust cells and phagocytic cells. (3) Eye injury—killed. <i>Lungs section</i> : normal.
17	2 × 70	—	1 dead. <i>Lungs section</i> : small collection of polymorphs and lymphocytes; few dust cells.
18	—	—	Exposures discontinued.
19	—	—	1 dead.
20	—	—	1 dead. <i>Lungs section</i> : normal. (See Fig. 14, A.)
			1 dead. No P.M.

* The mice were stained for identification purposes and 19 stained with brilliant green developed bald patches where they had been stained. These 19 mice were isolated on the 11th day together with 6 unstained mice and were not subjected to further exposures of dust. The remaining 33 mice were submitted to a further 8 exposures, making 30 exposures in all. Two unstained mice and one stained mouse died after cessation of exposure.

Weight.—Before exposure, 25–30 gm.
At end of experiment:
33 mice after 30 exposures average 29 gm. (range 21–32 gm.).
58 mice after 32 exposures average 27 gm. (range 21–31 gm.).
12 control mice average 32 gm. (range 28–35 gm.).

TABLE 7
NUMBER OF MICE ALIVE

Days after infection	Mice treated with calcium carbonate	Calcium carbonate-treated mice + pneumococci	Normal mice + pneumococci	Normal mice	Normal from CaCO ₃ room
		Susp. A	Susp. B	Susp. A	Susp. B
0	12	12	12	12	12
1	12	12	12	12	12
2	12	12	6	5	1
3	12	12	1	0	0
4	12	11	1	0	0
5	12	11	1		
6	11	10	1		
7	11	10	1		

Bacteriological Results.—(I) *Pneumococcus*. The mice were divided as shown in Table 7 and injected intraperitoneally with pneumococcus (type II). Suspension A, 0.5 ml. of suspension of 110 organisms per ml., and suspension B, 0.5 ml. of suspension of 20 organisms per ml.
(II) *Streptococci*. A similar test was performed using *Streptococcus Haem.* (Richards) 0.5 ml. of a suspension of 245 organisms per ml. being given intraperitoneally (Table 8).

TABLE 8
NUMBER OF MICE ALIVE

Days after infection	Mice treated with CaCO ₃	Mice treated with CaCO ₃ + Streptococci	Normal mice + Streptococci	Normal mice Controls
0	11	10	10	8
1	11	10	9	8
2	11	2	2	8
3	11	2	2	8
4	11	2	1	8
5	11	2	1	8
6	11	2	1	8

The results show no significant difference in the rate of death of mice exposed to calcium carbonate dust and normal mice.
It was very noticeable that the mice exposed to manganese in Experiment I were in a worse condition than those exposed to calcium carbonate. The latter group, apart from some loss of weight, appeared to be of normal vigour but the manganese exposed mice, though not obviously ill, were undoubtedly made less well by exposure to manganese.

III. Manganese Dust (from Mill Room)
Seventy-two mice, each weighing between 25–30 gm., were divided into two groups: (a) 60 mice (in two cages of 30 each) which were exposed to dust for 34 exposures of 70 minutes (twice daily for 5 days a week), (b) 12 mice as controls. The dust contained 74 per cent. MnO₂ and its alkalinity calculated as KOH was 0.8 per cent. or calculated as K₂CO₃ was 1.01 per cent.

FIG. 14.

- A. Section $\times 700$: lungs of mouse exposed to inhalation of calcium carbonate twice daily for 15 days. Normal lung structure.

- B. Section $\times 700$: lungs of mouse exposed to manganese dust (MnO_2 content 70 per cent. alkalinity as K_2CO_3 11.8 per cent.) twice daily for 25 days. Structure almost unrecognizable due to intense infiltration of large mononuclear cells, many of which contain cellular debris and a few contain dust particles.

- C. Section $\times 700$: lungs of mouse exposed to manganese dust (MnO_2 content 70 per cent. alkalinity as K_2CO_3 1.01 per cent.) twice daily for 19 days. Appearance is similar to B; intense infiltration with large mononuclear cells; swelling of alveolar cells can be seen. Note absence of polymorphonuclear cells.

Day	Daily length of exposure (starting at 9.30 a.m. and 2.30 p.m.) minutes	Dust count: particles per c.c.	Remarks
1	2×70	1077	
2	2×70	1838	
			Range gm. Average gm.
			Manganese-exposed mice weighed 25-29 26
			Control mice weighed 25-30 27
3	2×70	1242	
4	2×70	5412	
5	2×70	4136	
6	2×70	1559	
7	2×70	2261	
8	2×70	2643	
			Range gm. Average gm.
			Manganese-exposed mice weighed 18-28 23
			Control mice weighed 21-28 24
9	—	—	1 dead.
10	2×70	2506	
11	1×70	1189	
12	1×70	2185	
13	2×70	1242	1 ill—killed. <i>P.M.</i> Subpleural haemorrhages. <i>Lungs section</i> : occasional dust cells, mononuclear infiltration; some lymphocytes and a few polymorphs.
14	2×70	2455	
15	2×70	—	
			Range gm. Average gm.
			Manganese-exposed mice weighed 18-27 23
			Control mice weighed 18-30 25
16	—	—	1 dead.
17	2×70	1755	
18	2×70	—	1 dead. <i>P.M. Lungs</i> : few subpleural haemorrhages. <i>Section</i> : intense peri-bronchial mononuclear phagocytic infiltration, several dust cells, few lymphocytes and polymorphs. <i>Liver</i> engorged with numerous areas varying from pin-head to small pea, of yellow coloration all over surface and throughout section, probably necrosis or fatty infiltration. <i>Section</i> : areas of necrosis and early fibrosis, some interstitial haemorrhage.
19	2×70	—	1 dead.
			1 dead. No <i>P.M.</i> Both lungs were collapsed. No haemorrhages, liver 'opaque.' <i>Lungs section</i> : mononuclear infiltration and haemorrhage. <i>Liver</i> : interstitial haemorrhage and early general necrosis.
20	2×70	—	
			Range gm. Average gm.
			Manganese-exposed mice weighed 18-29 24
			Control mice weighed 18-31 25
	Exposure stopped.		
	3 days after exposure.		1 dead. <i>P.M. Lungs section</i> : large phagocytes loaded with dust in bronchi, alveoli and interstitial spaces. Numerous interstitial haemorrhages, no dust cells seen in lymphatic glands. <i>Liver</i> normal.
	4 days after exposure.		1 dead.
			1 dead. <i>P.M.</i> Haemorrhage in pleural cavity. <i>Lungs section</i> : intense phagocytic cell infiltration, few dust cells. Only occasional polymorphs or lymphocytes. (See fig. 10, C.) <i>Liver</i> , section normal.
	No control mice died.		

Bacteriological Results.—The mice were divided into groups as shown, and injected intraperitoneally:

(1) *Pneumococcus* (type II). Each mouse received 0.5 ml. of a suspension containing 70 organisms/ml.

(2) *Pneumococcus* (type IV). Each mouse received 0.5 ml. of a suspension containing 8400 organisms/ml.

(3) *Streptococcus Haem. Richards*. Each mouse received 0.5 ml. of a suspension containing 200 organisms/ml.

TABLE 9

PNEUMOCOCCAL AND STREPTOCOCCAL INFECTIONS IN MANGANESE-TREATED MICE

Organisms	Pneumococcus, type II		Pneumococcus type IV		Strep. haem. (Richards)		Controls		
Number organisms injected	35		4200		100		—		
Days after infection	Normal mice	Man- gane- se- treated mice	Surviving mice						
			Normal mice	Man- gane- se- treated mice	Normal mice	Man- gane- se- treated mice	Normal mice	Normal mice from manganese room	Man- gane- se- treated mice
0	10	10	10	10	10	10	10	12	15
1	10	9	10	10	10	8	10	12	15
2	6	5	10	10	5	1	10	12	15
3	5	4	10	9	3	1	10	12	15
4	5	4	10	8	2	1	10	12	14
5	5	4	10	8	2	1	10	12	14
6	5	4	10	8	2	1	10	12	13
7	5	4	10	8	2	1	10	12	13
8	5	4	10	8	2	1	10	12	13

The results prove that the mice showed no difference in susceptibility to pneumococcus type II and IV after exposure to manganese, and the small difference in the mice injected with *Streptococcus Haem.* (Richards) may be due to the poorer condition of the mice exposed to manganese.

Absorption of Manganese.—Three mice exposed to manganese dust and 3 control mice were killed on the last day of exposure. All mice were carefully brushed, skinned and dissected.

Manganese content organisms for 3 mice	Manganese exposed		Control	
	3 mice	Average per mouse	3 mice	Average per mouse
Skins (including fur)	μgm. 74	μgm. 24.7	μgm. 30.6	μgm. 10.2
Brains ..	1	.3	1	.3
Livers ..	1	.3	1	.3
Lungs ..	1.2	.4	0.6	.2
Remainder of body excluding guts	lost in analysis			

IV. Manganese Dust (from Mill Room)

One hundred and twenty-four mice were divided into two groups: 63 placed in two cages for exposure to manganese dust, and 61 retained as controls. The dust was the same as used in Experiment III.

Weight of mice	Range gm.	Average gm.
Manganese exposed mice weighed	25-30	27
Control mice weighed	25-30	28

Thirty-three exposures to manganese dust were given: 17* exposed mice and 7 control mice died.

Bacteriological Results.—An attempt was made to set up pneumococcal infection of the lungs of the mice by spraying the air in enclosed chamber in which the mice were placed with a broth culture of pneumococci. No extensive experiments were, however, undertaken.

Culture.—A 24-hour serum broth culture of pneumococcus (type IV) was used. This culture was found to be virulent to mice only when given intraperitoneally in large doses.

Technique.†—The groups of mice were placed in small metal cages with open tops in the chamber, and broth containing pneumococci sprayed in through a hole at one side of the chamber, using a De Vilbiss atomizer for this purpose. The spraying continued for 1 minute, then the mice were left exposed in the chamber for a further 15 minutes. At the end of this time they were removed and transferred to fresh cages.

Blood agar plates were exposed for 1 minute each, at intervals of 1, 5, 10 and 15 minutes after the spraying had ceased.

The results obtained are indicated below:

COUNTS OF ORGANISMS ON BLOOD AGAR PLATES IN CHAMBER AFTER SPRAYING WITH PNEUMOCOCCUS TYPE IV

1 minute after Plate absolutely covered with colonies. spraying.

* Shortly after this experiment began, intensely hot weather and room temperatures over 80° F. were experienced. This probably accounts for the high mortality in the exposed and control mice, but does not invalidate the purpose of this experiment to determine susceptibility to pneumococci.

† A similar technique had previously been used successfully for the investigation of aerosols.

Day	Daily length of exposure (starting at 9.30 a.m. and 2.30 p.m.) minutes	Dust count: particles per c.c.	Remarks
1	2×70	2216	
2	2×70	1555	
3	2×70	—	1 dead. No P.M.
4	1×70	2381	1 dead. No P.M.
5	2×70	—	1 dead.
6	2×70	—	1 dead. P.M. Lungs normal. <i>Lungs section</i> : small subpleural peribronchia and periarterial areas of monocytic infiltration.
			<div> <div>Range</div> <div>gm.</div> </div> <div> <div>Average</div> <div>gm.</div> </div>
			Manganese-exposed mice weighed 18-31 25
			Control mice weighed 23-32 28
7	2×70	2404	
8	2×70	—	
9	—	—	3 dead.
and 10	—	—	
11	2×70	2637	
12	2×70	—	
13	2×70	1339	2 controls dead. P.M. Lungs normal. <i>Lungs section</i> : some polymorph and lymphocytic interstitial infiltration, few mononuclear cells; lung structure preserved.
14	2×70	—	1 dead.
			1 control mouse dead. <i>Lungs section</i> : slight lymphocytic infiltration around bronchi. Remainder of lung normal.
15	2×70	—	2 dead.
16	—	—	1 dead.
and 17	—	—	
18	2×70	2051	1 control mouse dead. <i>Lungs section</i> : areas of consolidation mostly due to lymphocytes and polymorphs; few mononuclear cells, ? pneumonia process due to temperature. Some dust cells.
19	2×70	1828	3 dead. (1) Eaten. (2) P.M. Nothing abnormal. <i>Lungs section</i> : subpleural areas of mononuclear infiltration; few dust cells. (3) P.M. Lungs: haemorrhagic areas. <i>Lungs section</i> : intense mononuclear proliferation especially around arteries, extending throughout lung.
20	2×70	—	1 dead. P.M. White patches on lung and liver. <i>Lungs section</i> : widespread and intense mononuclear infiltration with haemorrhage.
			<div> <div>Range</div> <div>gm.</div> </div> <div> <div>Average</div> <div>gm.</div> </div>
			Manganese-exposed mice weighed 17-32 26
			Control mice weighed 17-35 25
21	2×70	2509	2 control mice dead. (1) Eaten. (2) P.M. Nothing abnormal. <i>Lungs section</i> : some polymorph infiltration; few dust cells.
Exposures ended. Total exposures 33×70 minutes.			
5 manganese mice (1 mouse showed numerous areas of consolidation in lungs) and 3 control mice killed for chemical analysis.			
22	—	—	1 ill—killed. P.M. Lungs apparently normal. <i>Lungs section</i> : peribronchial mononuclear infiltration; few polymorphs.

5 minutes after spraying. Very large number of colonies.

10 minutes after spraying. Large number of colonies.

15 minutes after spraying. About 2000 colonies.

At the end of 15 minutes there were still pneumococci present in the air.

Control mice were treated in exactly the same way but were sprayed with sterile serum broth instead of pneumococci. They were exposed in the same chamber, being done before the pneumococcal mice. A blood-agar plate exposed for the full 15 minutes the mice were in the chamber gave a count of 50 organisms, all of which appeared to be of the usual air contamination type.

Experiment.—(1) Ten manganese-treated mice were exposed to pneumococcal infection for a period of 15 minutes.

(2) Ten normal mice were similarly treated.

(3) Ten manganese-treated mice were exposed to pneumococcal infection for 15 minutes on three different days, with an interval of a day in between each exposure.

(4) Ten normal mice were similarly treated.

Controls.—(5) Ten manganese-treated mice were sprayed with serum broth only and exposed for 15 minutes.

(6) Ten normal mice were similarly treated.

(7) Ten manganese mice were untreated.

(8) Ten normal mice were untreated.

TABLE 11
SURVIVING MICE—AFTER EXPOSURE TO PNEUMOCOCCAL INHALATION

Time after exposure	Pneumococci + broth		Pneumococci + broth		Broth only		Unexposed	
	1 exposure		3 exposures		1 exposure			
	Manganese mice	Normal mice	Manganese mice	Normal mice	Manganese mice	Normal mice	Manganese mice	Normal mice
0 day	10	10	10	10	10	10	10	10
1 "	10	10	10	10	9	10	10	10
2 days	10	10	10	10	9	10	10	10
3 "	10	10	10	10	9	10	10	10
4 "	10	9	10	10	9	10	10	9
7 "	10	9	10	10	9	10	10	9
2 weeks	10	9	10	10	9	9	10	9
3 "	9	9	9	10	9	9	see Table 12	

The normal mice had been kept in the same room as the manganese chamber. The results are summarized in Table 11.

As it appeared after 7 days that under these relatively simple experimental conditions the manganese-exposed mice were not going to prove more susceptible to the pneumococcus infection, the two groups of unexposed control mice were removed and injected intraperitoneally with pneumococcus (type IV). Each mouse received 0.5 c.c. of suspension of organisms containing 220,000 organisms per ml. (Table 12).

TABLE 12
SURVIVING MICE INFECTED WITH PNEUMOCOCCUS (TYPE IV)

Time after infection	Manganese mice	Normal mice
0 day	10	9
1 "	10	9
2 days	9	8
3 "	9	8
4 "	8	6
6 "	7	6
7 "	6	6
2 weeks	6	6

These results also show no increase in susceptibility to pneumococcal infection in manganese-treated mice.

Absorption of Manganese.—Five exposed and 3 control mice were washed, skinned and dissected, and submitted for analysis.

	Manganese-exposed		Control	
	Average	Range	Average	Range
	μgms.	μgms.	μgms.	μgms.
Body ..	46	28–84	24	21–28
Skin ..	9.7	6.1–13.8	3.2	1.7–2.8
Brain ..	0.21	0.17–0.25	0.12	0.10–0.14
Lungs ..	0.2	0.15–0.28	0.03	0.01–0.05

Discussion

The incidence of pneumonia, observed in the present investigation, of 26 (range 15–63) per thousand in men exposed to the inhalation of manganese dioxide corresponds closely to that given by Buttner (1939) except that no fatal cases have been experienced. It seems very probable that the conditions in the factory described in this report were much better than in German mines or pyrolusite mills. No overt case of manganese poisoning has been observed (even after careful clinical examination of men exposed for 9 years), whereas reports of manganese intoxication are constantly appearing in the German literature.

No definite evidence of fibrotic or other specific changes have been found in the present investigation, and Schwartz (1942) agrees that manganese does not cause fibrosis. The fibrotic changes observed by Buttner (1939) are almost certainly due to 20 per cent. silica present in the Giessen pyrolusite.

Basic slag contains about 10 per cent. of manganese dioxide, and there have been many Continental reports of Thomasslachen pneumonia. Gundel and Fischer (1938) state that 2 per cent. of basic slag workers die of pneumonia, and a sudden death in an agricultural worker (Koch, 1942) who had been employed in spreading basic slag has been ascribed to broncho-pneumonia caused by slag. As Jötten and Reploh (1938) remark, the factors in basic slag giving rise to pneumonia have to be elucidated. It would be wrong, at the present time, to necessarily incriminate manganese. Respiratory disease, including Thomasslachen pneumonia, in workers grinding basic slag and manufacturing artificial fertilizers (but not agricultural workers) has been a scheduled disease, for which compensation is payable, in Germany since 1936.

The dust present in the atmosphere studied in the present report, collected by an electrostatic precipitator, had a manganese dioxide content varying from 41 to 66 per cent. (The dust used for animal experiments was analogous, having a manganese dioxide content of 70 per cent.) The environmental studies, the first of their type to be reported,

are significant in showing the degree of exposure, and though the dust counts vary considerably and exposure is discontinuous high counts are not infrequent. Practically all particles were below 1μ in size, and roughly 80 per cent. below 0.2μ .

In the first animal experiment of the present report the dust had a high alkalinity and though this may have further increased the damage to the lung (or even laid open the way for the action of manganese), similar changes were induced on subsequent experiments with dust of low alkalinity. In practice, however, the alkalinity of the dust on the human lung cannot be discounted without further investigation (especially in view of the effect of basic slag).

The animal experiments were complicated by the very obvious toxic effect of the manganese; all animals exposed to manganese dust were, at the end of the experiment, in a less well condition than the control animals, and some exposed animals were in a frankly poor condition. Loss of weight occurred and the maximum exposure, which it appeared mice were able to tolerate, was 70 minutes twice daily for about 30 exposures at a dust count of about 2000 particles per c.c. of air. Even in their poor condition the exposed animals, under the conditions of the experiment, did not show any increased susceptibility to a pneumococcus type II or type IV administered by intraperitoneal injection and pneumococcus type IV by inhalation. No great increase in susceptibility to haemolytic streptococci was apparent.

The present experiments were undertaken with the object of determining whether manganese causes an increase in susceptibility to the pneumococcus. For the investigation of the effect of manganese on the lungs a larger animal would have been chosen, but the histological effects were so uniform and so striking that a detailed description is warranted.

The changes in the lungs were dependent on the length of exposure, and varied from slight mononuclear infiltration (an exaggeration of the normal) to intense mononuclear interstitial infiltration with many dust-laden cells, and finally to consolidation (with haemorrhagic areas), leading to complete disorganization of the lung structure. The changes appeared to occur especially around the bronchi.

The alveolar cells and the cells lining the bronchi were swollen and had undergone a hydropic change. The alveoli and interstitial spaces were packed with large mononuclear cells which were either desquamated alveolar cells or histocytes which had undergone intense proliferation. In many areas this monocytic reaction was so intense that only a faint outline of the normal lung structure could be seen. The mononuclear cells in some cases contained particles of dust and cell debris and appeared to be dead. Areas of necrosis were not uncommonly present in the lung. Lymphocytes were few in number and granular cells were conspicuous by their rarity (see fig. 10).

The oedema of the bronchial and alveolar epithelium suggests that manganese has a direct

action on these cells. The presence of dust cells, though few in number, suggests that some particles of dust were phagocytosed in the normal manner but after absorption killed the phagocytic cells. Though dust-laden cells were observed in the bronchi, alveoli and interstitial tissues, none were observed in the lymphatic glands; this may be explained by the absorption or solution of manganese by cellular fluids.* (This agrees with Jötten's (1939) opinion that the action was local and that deep-seated interstitial changes do not occur.) Either before or after absorption manganese would appear to have a specific chemical action, causing intense mononuclear proliferation and infiltration, sufficient in many areas to cause consolidation of the lung and, as the action of manganese proceeds, cellular death, necrosis and haemorrhage.

From these facts it seems that following the inhalation of particles of manganese dust, phagocytosis proceeds in the usual way, but is overshadowed by the chemical action of manganese, and that this action results in a characteristic mononuclear celled proliferation.

No permanent pulmonary changes were observed in the men working in the factory, either on clinical or radiographic examination. Though naso-pharyngeal catarrh was common, attacks of bronchitis were frequent and in some men a spasmodic element gave rise to attacks similar to asthma, all changes eventually subsided after removal from exposure. It seems probable that in man the primary change is an oedematous reaction affecting the epithelium of any part of the respiratory tract. Further investigation is required to establish whether illnesses in the human subject diagnosed as pneumonia are due entirely to the chemical action of manganese or whether the irritative action of manganese allows

* To test this theory the solubility of manganese in serum was determined by Mr. N. H. Law, M.Sc., F.R.I.C.

Method. Manganese dust was sterilized by heating ($T = 160^\circ \text{C.}$) for two hours. 0.4 gm. of dust was added, under sterile conditions, to 20 ml. of serum and mechanically shaken.

The suspended dust was separated by high-speed centrifuging and the supernatant liquid syphoned through a No. 32 Whatman filter paper. A 10 ml. aliquot was subjected to a pre-treatment of evaporation to dryness, ashing at a temperature not exceeding 600°C. sulphation and nitration, to ensure complete freedom from chloride, prior to the development of the permanganate colour using the method of High (1944). The colour was estimated photo-metrically by a Spekker absorptiometer using Ilford Spectrum Green Filters 604, a heat-absorbing Filter H. 503 and 4 cm. cells.

	Main Hall Dust	Mill Dust
Alkalinity (as K_2CO_3)	per cent. 12.4	per cent. 0.03
Particle Size (less than 1μ diameter) ..	70	87
Solubility (mgm. per 100 ml.)—		
24 hours	0.34	1.18
48 hours	0.39	1.42
96 hours	0.27	1.37
144 hours	0.43	2.30

Control. Modified Ringer solution (King 1945) under exactly comparable conditions for the same times did not dissolve any manganese.

Accuracy. Results are accurate to ± 0.04 mgm. per 100 ml.

Conclusion. Manganese dioxide dust examined under the above conditions appears to dissolve in the serum but the dissolution is hindered by the presence of alkali. The fall in the amount dissolved at 96 hours followed by a steep rise at 144 hours suggests some change taking place in the serum.

secondary infection by the flora of the nose and mouth. Clinical experience suggests, and the histological appearance in mice confirms the suggestion that manganese has a specific action on the whole respiratory tract from the nose to the alveoli—the symptomatology depends on the part most affected and this in the present state of knowledge seems largely fortuitous. The term ‘manganese pneumonia’ would seem to attach too much importance to anatomical considerations. Manganese pneumonitis is a better term.

The chemical observations were complicated by the small amount of manganese to be estimated, and the tediousness of the wet oxidation of the samples. No conclusion can be drawn other than that the mice exposed to manganese dust were absorbing manganese.

Summary

(1) Men exposed to the inhalation of manganese dust suffer a high pneumonia rate (averaging over the years 1938–45 inclusive 26 per thousand compared with 0.73 per thousand in a control group).

(2) For the purpose of exposing mice to the inhalation of manganese dust, a new dust-feed apparatus is described. After the inhalation of manganese dust, mice do not show an increased susceptibility to pneumococci or streptococci.

(3) After the inhalation of manganese dioxide dust, some particles may be phagocytosed in the normal manner, but all particles, whether phagocytosed or not, pass into solution in tissue fluids. Manganese is toxic to the respiratory epithelium and exerts a specific chemical action, which in mice results in an intense mononuclear proliferation and infiltration of the lung tissues and, as the action of manganese proceeds, in cellular death and necrosis.

(4) Manganese dust may affect any part of the respiratory tract, from the nose to the alveoli. Further investigations are needed to confirm the theory, suggested by these experiments, that manganese dust has a specific action on the human lung. Manganese pneumonitis appears a more appropriate term than manganese pneumonia.

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