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Original Articles

DISABILITY DUE TO INHALATION OF GRAIN DUST

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THE existence of occupational disease resulting from exposure to grain dust has been confirmed by the observations of many authors.^{1, 2, 3, 4} The causative mechanism of this disease, however, is still open to controversy. There remains unanswered the question as to whether this disease is due to an allergy to grain dust or whether it is a type of pneumoconiosis. In order to cast some light on this problem an analysis of the case histories of 19 workers who suffered disability as the result of exposure to grain dust was made. These cases were drawn from the files of our own practices and from those of 3 other Buffalo allergists.*

Workers in and around grain elevators are heavily exposed to dusts from crude grains as the grain carriers are loaded and unloaded or as the grain is transferred from elevators to mills. One of the authors has been in a passageway beneath grain elevators, where the suspended dust was so thick that near-by electric lights were seen dimly as in a heavy fog.

Workers in feed mills also are exposed to considerable densities of dust from raw grain either in connection with the handling of the grain, or in handling and mixing the different ingredients of the feeds.

Workers in flour mills proper are, as a rule, definitely less exposed to crude grain dust. To prevent contamination of the refined flour by such crude dusts and by other discarded portions of the grain kernels, these undesired materials are first removed by screening, agitation, and suction. Such preliminary processes are carried out in fairly well-enclosed systems. Also the grinding and packaging areas of the better flour mills have ventilating systems to carry away excess dust.

In feed mills, on the contrary, where a large proportion of the material handled consists of the discards from flour mills together with other substances, equal precautions are not usually taken to remove dust from their processing areas, probably because the end product is not intended for human consumption

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and therefore need not be kept so free of contaminants. Moreover, the qualities of the grains utilized in feed mills need not be so high as for flour mills, and therefore they contain larger amounts of smuts, molds, and other extraneous substances. Feed mill dust thus more closely resembles grain elevator dusts than flour mill dusts.

Elevator and feed mill dusts are complex mixtures consisting of the bristles and other particles from the outer coats of grain kernels, spores of smuts and molds, insect debris, pollens, field dust, and other organic and inorganic materials. Presumably it is intrinsically more irritating to the respiratory mucosa than refined flour dust.

FLOUR MILL WORKERS

Eight workers in flour mills who suffered from respiratory disability were originally included in our study. They have been excluded from the present report, primarily because of their small number and because their dust exposure, as outlined previously herein, differs both quantitatively and qualitatively from that of the elevator and feed mill workers. These eight flour mill workers also differed in several other respects: their average age when first studied for respiratory disability was thirteen years younger than the elevator and feed mill workers, 43.2 years as against 56.5 years; their total length of exposure was half that of the latter group, average 14.5 years against 27.2 years; and the length of exposure before the onset of symptoms was less than half, average 9.8 years against 21.4 years.

GRAIN ELEVATOR AND FEED MILL WORKERS

The group reported herewith consists of eleven workers from grain elevators and feed mills in the Buffalo area. Four of these died while under observation, and autopsies were done on three of these.

Each worker had been referred to an allergist because of symptoms suggestive of asthma. This consisted of progressive dyspnea both at rest and on exertion, cough and frequently "wheezing."

Medical and allergic histories and details of occupational exposure were obtained on each worker and all were physically examined on several occasions. The amount of laboratory work and the number of intracutaneous tests done on each patient varied somewhat with the needs of the case, as determined by the individual allergist. No evidence of active tuberculosis was found in any patient either by x-ray, by sputum smear, or by physical examination.

CLINICAL DATA

The plant where employed and the type of exposure are given in Table I. Statistical data as to age, length of exposure, etc., appear in Table II. In this table it will be noted that the age when first seen varied from 39 to 76, with a total average of 56.5 years, and an average of 54.6 years excluding the 76-year-old patient. The majority therefore fall in the age group considered characteristic of intrinsic asthma.

TABLE I. GRAIN ELEVATOR AND FEED MILL WORKERS—PLACE OF EMPLOYMENT AND EXPOSURE

CASE	NAME	TYPE OF PLANT	TYPE OF EXPOSURE
5	J. S.	Feed mill	Crude grain
7	F. M.	Grain elevator	Crude grain
8	T. R.	Grain elevator	Crude grain
9	C. C.	Grain elevator	Crude grain
10	J. H.	Feed mill	Crude grain
11	B. T.	Feed mill	Crude grain
12	A. M.	Grain bins	Crude grain
15	M. C.	Grain elevator	Crude grain
17	S. S.	Grain elevator	Crude grain
18	M. V.	Feed mill	Crude grain
19	G. K.	Grain elevator	Crude grain

The total length of exposure of the eleven workers to grain dusts averaged twenty-seven years, with a range of from fifteen years to fifty-two years. The length of exposure before well-marked symptoms appeared averaged twenty-one years, with a range of from ten to thirty-five years. The average duration of symptoms, by the time the workers were referred to a specialist, was six years, although minor respiratory symptoms probably had existed longer.

TABLE II. GRAIN ELEVATOR AND FEED MILL WORKERS—STATISTICAL DATA

CASE	AGE, YEARS	TOTAL YEARS OF EXPOSURE	LENGTH OF EXPOSURE BEFORE ONSET OF SYMPTOMS, YEARS	AGE AT ONSET, YEARS	DURATION OF SYMPTOMS, YEARS
5	39	15½	10	33½	5½
7	55	40	26	41	14
8	62	25	24	61	1
9	50	20	20	50	0
10	49	19	10	40	9
11	58	25	22	55	3
12	64	31	28	61	3
15	76	52	35	59	17
17	54	25	19	48	6
18	53	25	19	47	6
19	62	22	20	60	2
Average		Average	Average	Average	Average
56.5		27.2	21.1	50.5	6

Clinical data are presented in Tables III and IV. In ten of the eleven patients (see Table III) the onset of disability was gradual, slowly progressive dyspnea being the outstanding symptom. In one patient (No. 9, aged 50) the onset apparently was rather rapid and may have been related to an attack of pneumonia a year previously. By the time the patients were referred for study, the dyspnea was marked in nine patients and eight had to quit work. In nine patients, although not in all, cough preceded the onset of dyspnea. Excessive sputum was not often complained of.

On physical examination (see Table IV) all patients showed wheezing or "sibilant and sonorous, expiratory and inspiratory râles" on one or more occasions. The presence of bronchial obstruction can therefore be said to have been

TABLE III. GRAIN ELEVATOR AND FEED MILL WORKERS—CLINICAL DATA

HISTORY OF FAMILY ALLERGY	ONSET OF SYMP.		SYMPT. WORSE ON EXP. TO GRAIN DUST	EVID. OF ALL. TO OTHER THAN GRAIN DUST	PROB. ALL. TO GRAIN DUST	PRESENTING SYMPTOMS			EXCESS. SPUTUM	VASOMOTOR RHINITIS
	SLOW	ABRUPT				DYSPNEA	COUGH	WHEEZE		
0	+		+	+	+	+	+	+		+
+	+		+	+	+	+	+			
0	+		?	0	0	+	+			
0		+	0	+	0	+				
0	+		+	+	+	+	+			
?	+		?	0	0	+				
?	+		?	0	0	+				
0	+		+	?	0	+	+		+	
0	+		?	+	+	+	+		+	
0	+		+	+	+	+	+			
0	+		+	+	+	+	+			
1	10	1	6	7	5	11	7	7	2	1
No record			No record							
2			4							

TABLE IV. GRAIN ELEVATOR AND FEED MILL WORKERS—OBJECTIVE FINDINGS

CASE	SIGNS			X-RAYS OF CHEST							SED. RATE MM.	BLOOD EOSIN.	OUTCOME	
	WHEEZE	RÂLES	EMPHY-SEMA	EMPHY-SEMA	INCREASED MARKINGS	BRONCHO-PNEUMONIA		NEG. CHEST						
						FIBROSIS								
5	+		+						+	90%	15.0	1	6%	Still working
7	+		+						+	46%	13.0	22		Quit working
8	+		+	+						44%	14.5	15		Quit working
9	+		+	+	+					40%	15.0	26		Quit working
10	+		+	+						48%	14.5	28		Died
11	+		+	+				+			15.5	6		Quit working
12	+		+						+					Died
15	+		+	+							12.0	5		Quit working
17	+			+	+			+						Still working
18	+		+	+					+		10.0	10		working
19	+		+	+						25%	16.5			Died
Total	11	7	8	4	3	1	1	1	4					Died

served in three cases and emphysema was diagnosed by x-ray in four. Fibrosis was diagnosed by the radiologist in only one patient, aged 76. A "negative chest" was reported in 4 patients. Radiography, therefore, showed no findings which could be interpreted as characteristic of this disabling disease.

Vital capacities were measured in six patients. In one it was within normal limits. In the other five it was greatly reduced, being from 25 per cent to 48 per cent of the predicted value. Hemoglobin determinations were made on 9 of the patients. It was normal or slightly elevated in six, and moderately reduced in three. The sedimentation rate was determined in eight of the patients. In three it was normal, and in five it was moderately increased. Blood eosinophilia was within normal limits in the five patients so tested. Too few sputum examinations for eosinophiles were done to yield any significant information.

Intracutaneous tests were done on all patients and the results are summarized in Table V. A plus mark in this table indicates that a significantly positive reaction was obtained to one or more of the extracts in the group of tests; it does *not* indicate the intensity of the reaction. All patients were tested with at least the common pollens, inhalants, and some foods. The extensiveness of the tests, however, varied with the indications.

Nine of the eleven patients were tested with extracts of crude grain dust. These extracts differed as to source and as to method of preparation, since the cases were not worked up as a group, but were drawn from the files of the different allergists. Some dusts were mixtures from several similar plants; some were dusts obtained from the plant in which the particular worker was employed. Some extracts were dialyzed, some were not. A positive reaction to grain dust reported in Table V is one which the attending allergist interpreted as significant. It must be kept in mind, however, that some of the positive reactions may have been due to an irritative quality in the extract used.

TABLE V. GRAIN ELEVATOR AND FEED MILL WORKERS—REACTIONS TO INTRADERMAL TESTS

CASE	CRUDE GRAIN DUST	REFINED FLOURS	GRAIN SMUTS	MOLDS	POLLENS	COMMON INHALANTS	FOODS	TOTAL TESTS	TYPE OF PATIENT
5	+	+	+	0	+	0	+	90	Atopic
7	+	+		+	+	+	+	64	Atopic
8	0	0		?	0	0	0	81	Nonatopic
9		0		0	0	+	9	34	Nonatopic
10	+	0		0	+	+	+	116	Atopic
11	+	0		0	0	0	0	168	Nonatopic
12	+	0		0	0	+	0	127	Nonatopic
15	0	0		0	?	0	?	?	Nonatopic
17		0		+	+	0	0	80	Atopic
18	+	+	+	0	+	+	+	100	Atopic
19	+	+		+	+	+	+	232	Atopic

*Judged to be "nonspecific" or irritative.

Blank space indicates that the patient was not tested with any of this group.

A plus mark in the table indicates that a significantly positive reaction was obtained to one or more substances in the group; it does not indicate the intensity of the reactions.

After careful consideration of all the evidence in each case, we have classified six of the eleven cases as being atopic and five as nonatopic.

Five of the six *atopic* patients were skin-sensitive to crude grain dust, and four of these five were also skin-sensitive to refined flours. Four, and probably five, of the atopic patients were, we believe, clinically sensitive to grain dust and

to flour. The sixth was not tested with grain dust and failed to react to flours; he was skin-sensitive, however, to molds and to pollens.

Two of the five *nonatopic* patients yielded positive skin reactions to crude grain dust, with negative reactions to flours. One of these two reacted to grain dust alone, out of 168 tests done; the other yielded a few additional nonspecific reactions to common inhalants out of 125 tests. It is conceivable that these two patients actually were sensitive to grain dust, but we have rated the reactions as nonspecific or "irritative." Two other nonatopic patients gave negative reactions to both grain dust and flours.

Five of the eleven patients, therefore, were considered sensitive to grain dust and four were not. Tests on the remaining two patients were insufficient to draw conclusions.

Four of the eleven grain workers died, and autopsies were obtained on three. These three cases are reported. Five of the seven living patients have quit work because of their respiratory disability. The remaining two are still employed in grain handling plants.

FATAL CASES

CASE 10.—J. H., 49-year-old man first seen March 7, 1950, was a sampler of crude grain in a feed mill where he was exposed to considerable grain dust as well as to dusts from cottonseed and soybean meals; he had worked in this mill nineteen years. No family history of allergy was elicited. The patient had had asthma as a child, and had had one attack of pleurisy.

About 1940, after ten years of exposure, he began to have cough with slight dyspnea on exertion. While in Army service from November, 1942, to March, 1943, he had dyspnea on hikes and was in the station hospital on one occasion for a week with a severe cold. After this episode he was placed on limited service and was finally discharged as over age. He returned immediately to his former job, where he averaged two absences a year because of bronchitis. He continued to have some asthmatic attacks. In the summer of 1949 these attacks became more frequent and were severe after October, 1949. In December, 1949, he developed marked shortness of breath and fatigue which caused him to stop working.

He was hospitalized for three weeks in January, 1950, because of extreme dyspnea. Physical examination showed cyanosis and distended neck veins. Wheezing and râles were present throughout both lungs, with dullness at the right base. The liver extended two fingers below the costal margin and there was slight pitting edema of the shins. The heart was slightly enlarged, with a systolic murmur at the apex. He had slight fever; the blood pressure was 140/100; the white blood count was 14,800. X-rays suggested bronchopneumonia at the right base. An electrocardiogram showed right ventricular predominance. With antibiotics, digitalis, and symptomatic treatment, he improved. Just before discharge his vital capacity was 2,300 c.c., the predicted being 4,500 c.c. An x-ray on discharge showed resolution of the pneumonitis and no evidence of excessive fibrosis or nodulation. He was discharged on Feb. 1, 1950.

During the following weeks he continued to be dyspneic on exertion, with some cough, and did not return to work. When seen by the allergist March 7, 1950 he was afebrile, with the pulse 96, blood pressure, 118/78. The nasal mucosa was red and dry; the lungs showed poor aeration but no râles or wheezes; the chest was emphysematous. The heart was somewhat enlarged to the left but no murmur was heard. The liver was not enlarged; there was no edema of the shins. The hemoglobin was 92 per cent; the sedimentation rate was 28 mm. in one hour; the urinalysis showed normal findings; the vital capacity was 2,040 c.c.

One hundred sixteen intracutaneous tests were done with pollens, molds, inhalants, foods, and grain dust. The significant reactions were: marked to house dust and soybean; moderate to cottonseed, grain dust, Pyrethrum, feathers, timothy, ragweed, plantain, and rice flour. Negative reactions were obtained to the refined flours of five other grains.

Injections of dust and feather extracts were started, but his wheezing and dyspnea gradually increased. His vital capacity on March 23 was 2,000 c.c.; on April 13, 1,900 c.c.; on April 24, 1,200 c.c.

On April 27, 1950, he became acutely dyspneic at home, and could not be relieved by palliative remedies. He was admitted to the hospital on April 29 in extremis and died shortly after admission.

An autopsy was performed under the direction of Dr. Kornel Terplan, Chief of Pathology at the Buffalo General Hospital. The autopsy report was as follows:

Name—JH Sex—Male Age—50

Time of Death—April 29, 1950, 9:33 A.M. Time of Autopsy—April 29, 1950

The body is that of a 50-year-old white male, well developed and well nourished; esthetic type of build; 170 cm. long. Lips and finger tips are cyanotic, and neck veins are distended. There are numerous needle punctures in the right cubital space. There are no abdominal scars. Hair is abundant and black. The pupils are dilated. The mouth is edentulous. On opening the thoracic cavity, the left lung is found to be adherent to the parietal pleura, diaphragm and mediastinal pleura in its entire extent by adhesions of a rubbery nature which are separated with some difficulty. The right lung is covered by a fibrinous exudate. After removal of the lungs, it is seen that the entire right upper lobe is entirely consolidated and the cut surface reveals a lobar pneumonia—partially red and partially gray hepatization. The left lower lobe is seen to be atelectatic, and all lobes are seen to be emphysematous and markedly congested and edematous. The heart presents the picture of cor pulmonale, with enlargement of the right ventricle and dilatation of the right auricle. The heart weighs 375 gms., and there is considerable fat around the heart infiltrating in the outer muscular layer. The right ventricle is thickened to 8 mm., and the left ventricle measures 14 mm. The valves measure: mitral 12.5 cm., pulmonic 8.5 cm., tricuspid 8.5 cm., and aortic 8.5 cm. The coronary arteries show no sclerotic changes.

On opening the abdominal cavity, the intestines are seen to be collapsed and feel rather dry. There is no excess fluid. The organs all appear pale but congested, and show some cloudy swelling. This is true of the liver, which weighs 1745 gm., the spleen, which weighs 130 gm., and the pancreas. Biliary system is not remarkable.

The left adrenal appears to have a considerable loss of lipid element, but the right adrenal appears to be not unusual. The left kidney measures $11.5 \times 6 \times 3$ cm., and the right kidney $12 \times 5 \times 3$ cm. There is considerable fat infiltration in each pelvis, and the cortex in each kidney measures about 7 mm. The cut surfaces of the kidneys are pale and show cloudy swelling with considerable capillary ectasia. Each capsule strips easily. The ureters and bladder are not remarkable. The aorta shows minimal sclerotic changes. There is a mass of calcified nodes at the base of the mesentery of the small intestine measuring $3 \times 2 \times 1$ cm.

The brain is found to be not unusual.

Chief diagnoses:

1. Lobar pneumonia, right upper lobe.
2. Chronic emphysema, bilateral.
3. Cor pulmonale

HISTOLOGIC REPORT

Heart.—Sections show congestion and interstitial edema. There is increased interstitial fibrous tissue, and in small scattered areas there is considerable replacement by fibrous tissue.

Lungs.—One section shows pneumonic consolidation with the alveoli filled with neutrophils and exudate. Other sections show severe congestion with many pigmented macrophages in the alveoli. There are other acute changes of atelectasis and interstitial pneumonitis. In all sections there is increased fibrous interstitial tissue and chronic emphysematous changes (Fig. 1).

Thyroid.—Moderately congested.

Liver.—Marked congestion with cloudy swelling and fatty degeneration in central cells.

Pancreas.—Congestion.

Kidneys.—Congestion is marked. There is cloudy swelling and fatty degeneration of the tubules.

Spleen.—Congestion, with marked increase of lymphocytes in the pulp.

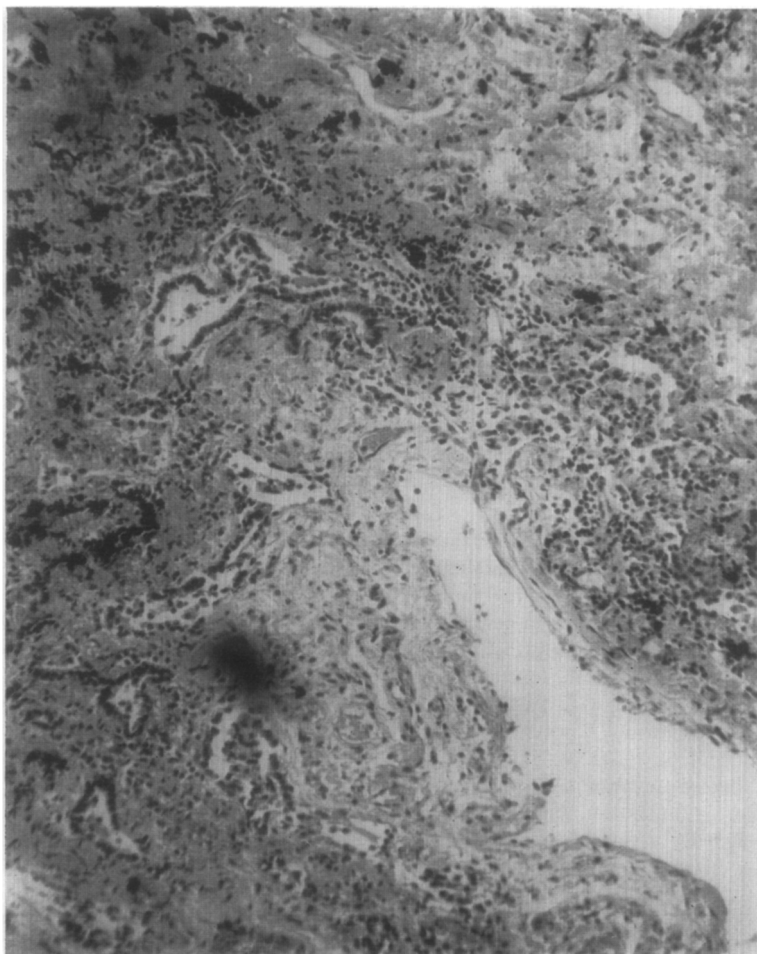


Fig. 1.—Section of lung of Case 10. This section shows chronic interstitial inflammation with infiltration mostly of round cells. There is considerable fibrosis in areas of chronically collapsed alveoli, the latter showing prominent lining epithelium. Eosinophiles are rare.

CASE 18.—M. V., a 61-year-old man, first seen Sept. 1, 1950, was a grain scooper in a feed mill since 1925. On this job he was exposed to dusts from six different grains and from meals of linseed, cottonseed, soybean, alfalfa, meat, fish, and copra. He had quit work in November, 1949, on account of dyspnea.

Family and past history were noncontributory.

Beginning six years previously, the patient noted gradual onset of shortness of breath with very little cough. This dyspnea grew steadily worse until he had trouble both day and night, with no relief away from work. Finally he was very dysneic on mild exertion, with some wheeziness at night, expiratory in type, and with pain in the lower left side of the chest.

Physical examination showed a boggy nasal mucosa. The heart was normal; pulse, 80, blood pressure, 120/80. The chest was emphysematous. Scattered expiratory and inspiratory wheezes were audible. The blood showed a hemoglobin of 70 per cent, red cells, 4.25 million; white count, 8,500; differential count normal with 4 per cent eosinophiles. The sputum showed a rare eosinophile and no tubercle bacilli.

One hundred intracutaneous tests were done, to the following of which significant reactions were obtained: house dust, feathers, cotton linters, ragweed, orchard grass, wheat grain dusts, grain mill dust, barley smut, wheat smut, and a few foods. Scratch tests were done with the individual dusts from the plant where he was employed. These yielded significant reactions to the meals of cottonseed, corn, alfalfa, fish, and meat. X-ray in the fall of 1950 showed a relatively normal chest.

The allergist's diagnosis was asthmatic bronchitis with emphysema and allergic sensitivity to inhalants. He was started on treatment with injections of the inhalants on Sept. 15, 1950.

On Sept. 5, 1951, this patient was admitted to the Buffalo Veterans Hospital because of increasing shortness of breath and severity of his cough, pain in his chest on coughing, and chilly sensations. On physical examination, his temperature was 99° F., the pulse was 88, respirations, 20, blood pressure, 120/75. He appeared chronically ill, dyspneic, and slightly cyanotic. On examination of his chest there was noticed an increased anteroposterior diameter. On percussion his lungs were hyperresonant with dullness over the right lower lobe laterally. Râles were scattered throughout both lungs. On examination of the extremities there was clubbing of the fingers and toes and slight cyanosis. The initial impression of this patient's illness was of pulmonary fibrosis secondary to dust from grain, with the possibility of bronchogenic carcinoma.

Laboratory Studies.—The urine showed 8 to 15 white blood cells and 1 to 2 red blood cells per field in the microscopic examination. His white blood count was 10,000, with bands, 14 per cent, segmented cells, 77, lymphocytes, 9. Hemoglobin was 10 Gm. per 100 ml. Sedimentation rate was 53 mm. in one hour, the hematocrit, 37; platelets were 810,000 per cubic millimeter. Fasting blood nonprotein nitrogen was 39, glucose, 117, CO₂, 63 volumes per cent. Routine complement fixation test was negative. Electrocardiogram, done Sept. 27, 1951, showed a normal record with sinus rhythm. On Oct. 9, 1951, the electrocardiogram showed auricular fibrillation and T-wave changes suggesting myocardial damage. An x-ray of the chest, taken Sept. 5, 1951, was reported: Moderately extensive interstitial and parabronchial infiltration involving lower two-thirds of right lung, probably within lower lobe. No other abnormalities. Infiltration probably due to pneumonitis although neoplasm cannot be entirely excluded.

Microscopic examination, Sept. 21, 1951, of a twenty-four-hour sputum specimen showed no tumor cells. A biopsy specimen taken on Sept. 20, 1951, of a subcutaneous nodule on the right thorax showed undifferentiated carcinoma metastatic to the wall of the right thorax, primary site undetermined.

Course in Hospital.—At the time of admission, the patient was having gross hemoptysis which at first was mild but after a week increased in severity, until the patient was raising about three cupfuls of bright bloody sputum per day. On admission he was running a low-grade fever up to about a 100° F. daily; this increased until his temperature range was 103° to 104° F. daily. On several occasions it reached 106° F. rectally. He was given penicillin, terramycin, and Aureomycin with no effect on the fever. On Sept. 13, 1951, the patient complained of a lump in his right anterior chest and also of pain in his right lower ribs. Examination revealed a bean-sized firm nodule, superior and lateral to the right nipple which was attached to the skin, and somewhat tender. Several days later another nodule was noted somewhat posterior to this and at later dates other nodules were noted on the chest wall, lower extremities, and portions of the upper extremities and neck. These nodules all had a somewhat inflammatory appearance over them and were exquisitely tender. They were attached to the skin and to the subcutaneous tissues and gradually increased in size. As stated in the tissue examination one of these nodules was removed for biopsy and found to be due to carcinoma. The patient continued to complain of pleuritic pain in his right

lower chest and developed dullness and definite friction rubs over this area. After four weeks in the hospital his hemoptysis subsided considerably but he continued to run a fever of 103° F. daily. His condition became weaker. The pain increased and required codeine, Demerol, and morphine for relief. On Sept. 27, 1951, a grossly irregular cardiac rhythm was discovered which persisted up to the time of death. This irregular rhythm was partially controlled by Digoxin and quinidine. He became mentally confused seven days before the date of his death. Finally he developed Cheyne-Stokes respiration and expired Oct. 19, 1951.

An autopsy was done by Dr. Alfred Golden, Chief Pathologist, Veterans Administration Hospital, Buffalo, N. Y., on Oct. 19, 1951.

GROSS PATHOLOGIC FINDINGS

The body was that of a 62-year-old white man who appeared to be of the stated age. There were numerous nodules palpable within the skin, the largest lying in the third interspace on the right, in the anterior axillary line and covered by tense light pink and purplish skin. Another obvious nodule was found on the anterior and medial aspect of the left thigh and measured less than a centimeter in diameter. They were firm, almost rubbery in consistency. Incision into the largest nodule revealed typical, firm, nonencapsulated, poorly circumscribed cancer tissue.

The right lung was voluminous and diffusely nodular particularly to palpation; it lay in a thorax whose parietal pleura was studded with whitish nodules and covered with fibrous and fibrinous sheds, particularly at the base and posteriorly. The pleural cavity contained about 200 ml. of bloody turbid fluid. On resection of the diaphragm a single whitish tumor nodule could be seen under the capsule of the liver substance in its anterior aspect. The left lung weighed 500 grams and was moderately anthracotic and its tracheobronchial tree was filled with thick, tenacious, frankly mucopurulent secretion. The right lung weighed 1,500 grams. Within 1 cm. of the bifurcation of the trachea there was a plaque of white tumor tissue extending distally for a distance of 5 cm., practically obliterating the lumen of the right posterior basilar branch. The left lung itself was the site of diffuse palpable noncancerous nodularity present to a moderate degree in all lobes, resulting in no obvious confluent fibrosis but in nodular fibrotic areas, some of which were pigmented black.

Cardiovascular System.—Along the course of the right main coronary artery there was an oval tumor nodule in the fat of the epicardium measuring 1 cm. at its greatest diameter. On the left side along the course of left circumflex branch was a discrete tumor nodule in the epicardial fat measuring 3 mm. in diameter. Other nodules were seen in the base of the heart, overlaying the papillary muscles of the mitral valve, under the endocardium and extending into the heart muscle, in the mid portion of the interventricular septum directly beneath the left coronary cusp, at the base of papillary muscles and within the substance of the myocardium. The heart musculature had a very definitely brownish tinge and was flabby.

Gross Diagnosis.—1. Bronchogenic carcinoma, right posterior basilar branch, with extension and metastasis to the lower lobe of the lung on the right, the tracheobronchial lymph nodes, the liver, the myocardium, and the skin.

2. Nodular pneumoconiosis, etiology undetermined.
3. Brown atrophy of the myocardium.
4. Cor pulmonale, slight.
5. Arteriosclerosis, coronary artery.

Comment.—This man with a twenty-year history of having worked as a wheat scooper had a nodular form of pneumoconiosis, more obvious to palpation than to inspection, mostly in the form of minute nodules not accompanied by appreciable fibrosis, except in the very immediate vicinity of these nodules.

MICROSCOPIC PATHOLOGY

The following description refers to the areas of the lungs not involved in the carcinomatous process, the description of which has been omitted (Figs. 2, 3, 4, 5, and 6). Sections of the lungs in many instances showed patchily distributed fibrosis, which was not circumscribed, was essentially nonnodular, and was frequently accompanied by isolation of

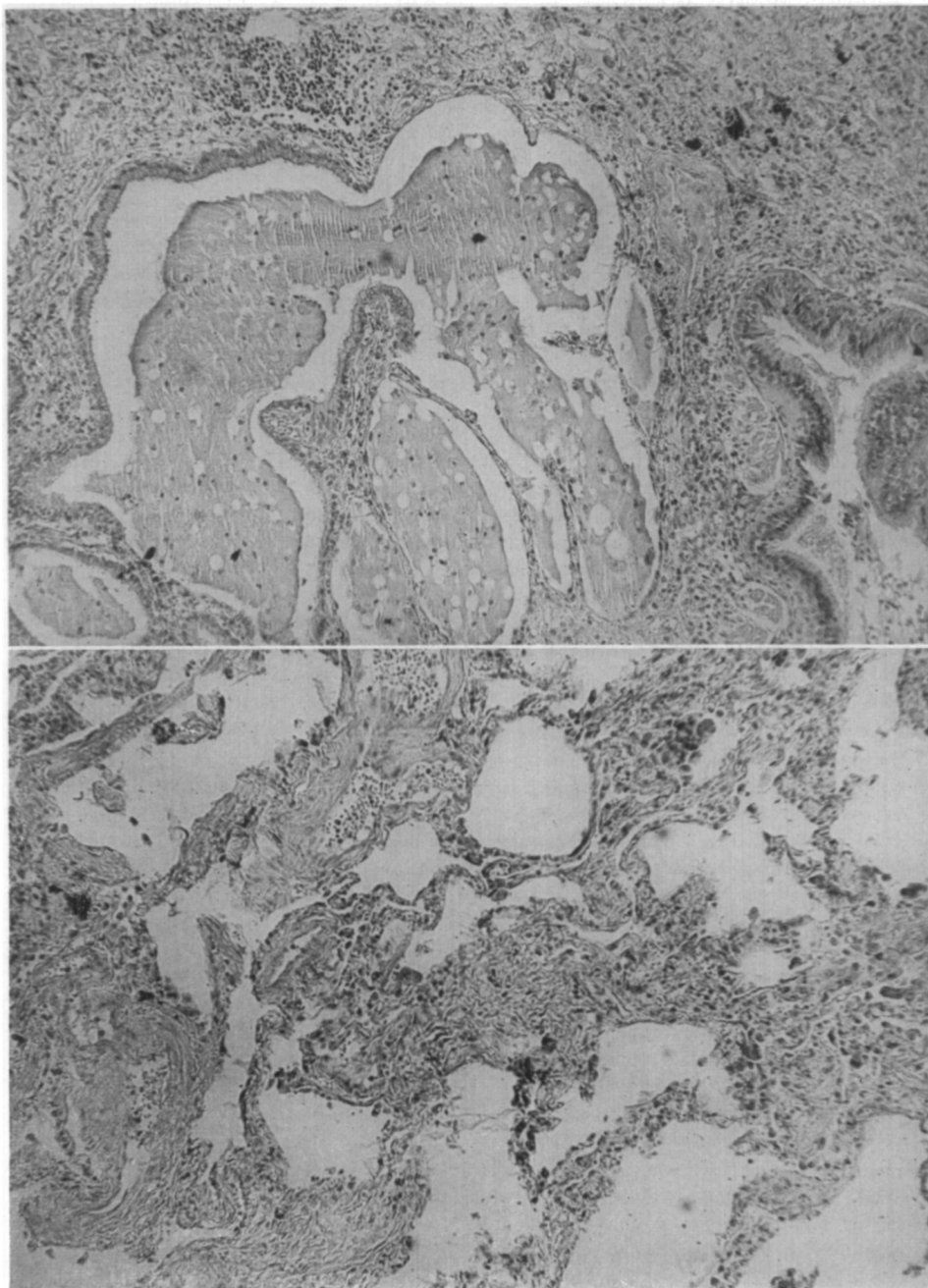


Fig. 2.

Fig. 2.—Section of lung of Case 18 showing patchy fibrosis between alveoli.

Fig. 3.

Fig. 3.—Section of lung of Case 18, showing great dilatation of a bronchiole whose lumen contains sheets of mucus, and scattered eosinophiles.

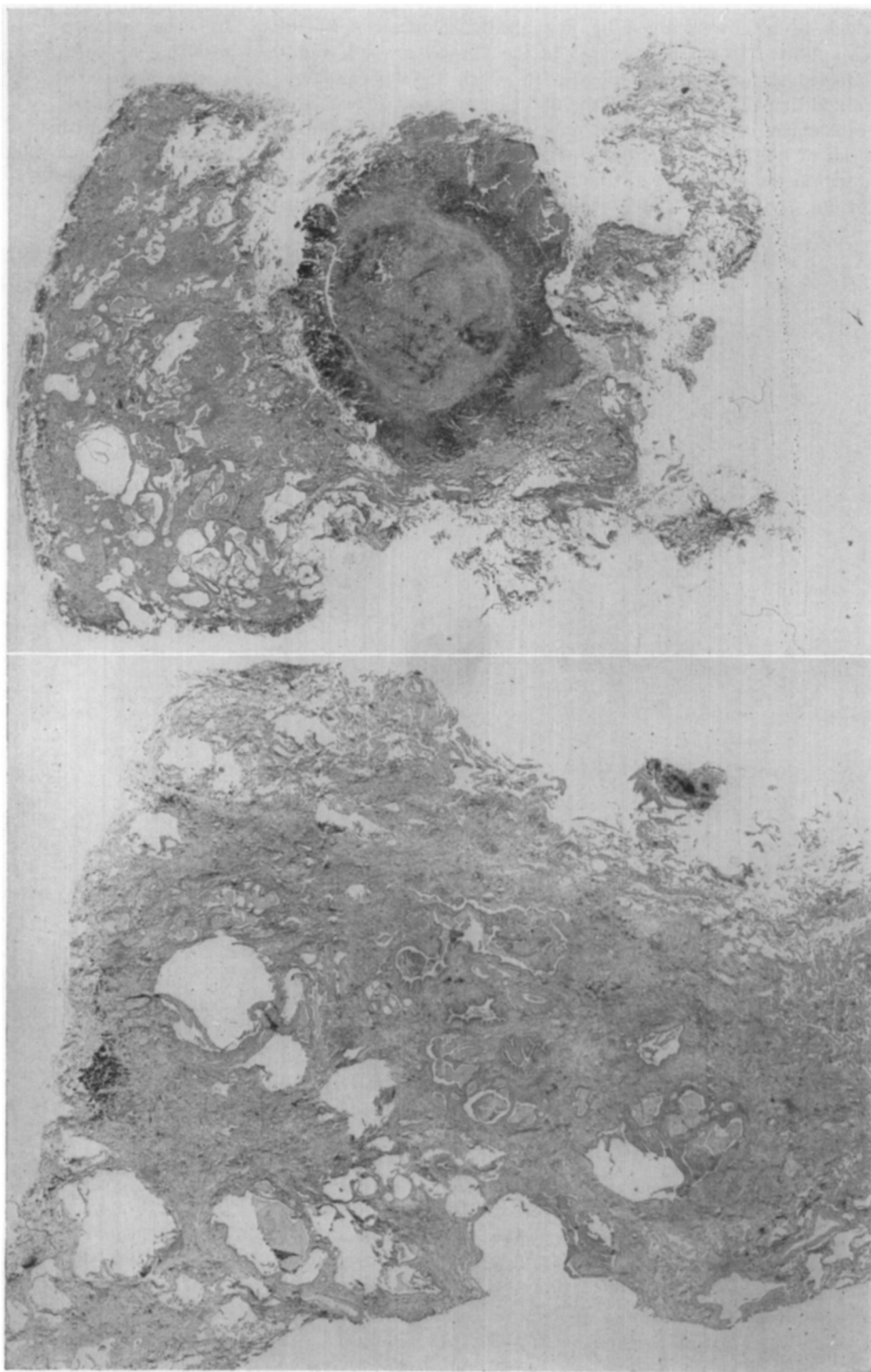


Fig. 4.

Fig. 4.—Low-power view of lung section (Case 18), showing great patches of fibrosis isolating groups of alveoli, and dilated bronchioles. For the details of one of the latter see Fig 3.

Fig. 5.—Low-power view of lung section (Case 18), showing one of several nodular fibrous lesions containing crystals consistent with silica particles.

alveoli, which in turn were lined by metaplastic columnar epithelium. In some instances bronchioles appeared to be incorporated in the fibrotic process, and their resulting apparent isolation yielded an adenomatous picture in which the lumens were filled with inspissated mucus. In addition to the preceding the fibrotic areas not infrequently showed isolated poorly defined granulomas, usually composed only of a small cluster of giant cells, sometimes with a slender rim of epithelioid cells, but rarely of a well-defined granuloma. In such areas, and sometimes within the cytoplasm of giant cells, minute colorless crystals were identified, rarely the size of an erythrocyte, more frequently only a very small fraction of that diameter.

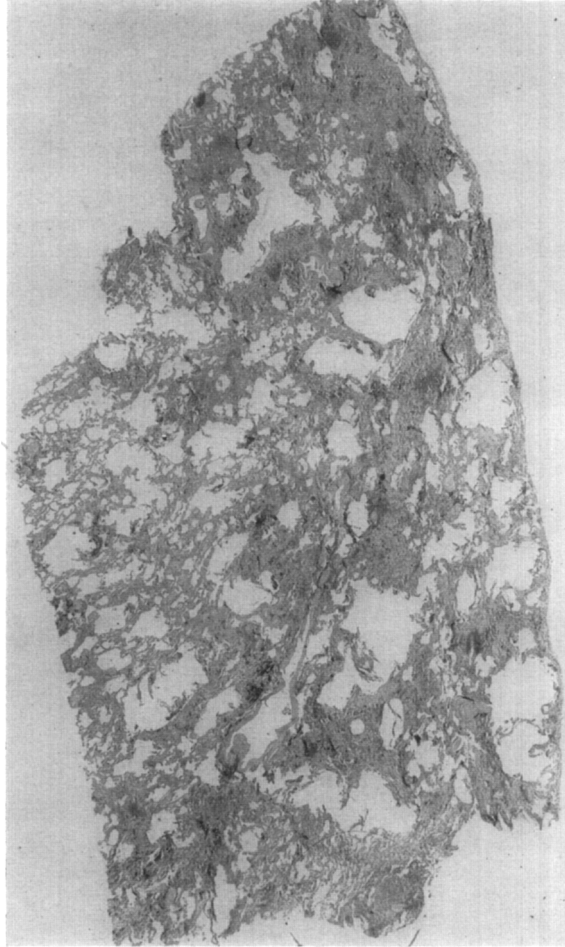


Fig. 6.—Another low-power view of a lung section showing diffuse patchily distributed fibrosis indicative of old organization (Case 18).

Under the polarizing microscope, these crystals were doubly refractile. They appeared to be limited either to the fibrotic or to the frankly granulomatous zones. A search of the tissue sections for bacteria and fungi failed to reveal such organisms.

Skin.—Sections of skin showed great replacement of the dermis and subcutaneous tissue by tumor elements identical to those described in the lungs.

Heart.—Section of the muscle wall and of the epicardial fat showed tumor metastases identical in their histologic structure to those described previously herein. Frequently they

were accompanied by moderate fibrosis. Most were surrounded by cardiac musculature which showed no significant abnormalities and were covered by intact endothelium, except in a few instances where the tumor cells appeared to have broken through on the surface where on either side of the neoplastic ulcer an organizing thrombus could be identified. The tumor nodule in the epicardial fat was essentially similar to that described above. It showed no invasion into underlying muscle. A section of coronary artery showed extensive atherosclerosis with sloughing of the atheromatous elements into the lumen. The cardiac muscle fibers proper showed no significant abnormalities both from the left and right sides of the heart. The over-all thickness of the right ventricular wall was greater than normal but the muscle fibers proper were not appreciably enlarged.

Lymph Nodes.—Those of the tracheobronchial group showed extensive replacement of lymphoid substance by frankly infiltrating, poorly differentiated adenocarcinoma.

Microscopic Diagnoses.—

1. Pneumoconiosis, nodular, widespread.
2. Poorly differentiated adenocarcinoma, bronchogenic, with extensive infiltration and metastases to both lungs.
3. Metastatic carcinoma in tracheobronchial lymph nodes, skin, and myocardium.
4. Right ventricular hypertrophy, moderate.
5. Coronary artery sclerosis.

Comment.—The pneumoconiotic picture just described appears to be active in the sense that old fibrotic areas are found side by side with intact granulomas. The process appears to have been an indolent one without severe necrosis on the one hand and without the degree of nodular, concentric, and hyalinized sclerosis so often associated with those pneumoconioses in which silica particles can be demonstrated. Chemical analysis of the lung tissue fails to reveal significantly high figures for silica (1.1 mg. SiO_2 per gram of dry lung tissue; normal is 1.13 mg.). There are, therefore two types of fibrosis present: the nodular form and an irregular parenchymal form, present to a moderate degree but with no distinguishing features.

The microscopic examination of the tissues confirms the gross observation that at least some of the metastatic foci of the carcinoma in the heart were subendocardial in distribution and are in areas where they could conceivably have interrupted conduction fibers in their course. Death is ascribed to a poorly differentiated bronchogenic adenocarcinoma with significant metastases to the heart musculature.

CASE 19.—G. K., a 62-year-old male grain handler in a malt company since 1926, was first seen Nov. 9, 1948. His family history and past history were noncontributory.

Beginning about 1945 the patient had noted cough and shortness of breath with wheezing. There was very little sputum, which was foamy and dusty, but had shown no blood. The dysnea and wheezing grew progressively worse and there was a loss of 20 pounds in weight. Periods of up to a week away from work had given no relief. His wheezing was worse when exposed to dust at work and also when lying down at home. There had been some nasal occlusion but no sneezing.

Physical examination showed marked dyspnea and considerable cough, productive of small amounts of sputum. The lips were cyanotic. The nasal mucosa was hyperemic with some occlusion high up. The bases of the lungs were hyperresonant with distant breath sounds. Wheezes, both expiratory and inspiratory, were heard throughout both lungs. The heart was not enlarged; no murmurs were heard.

The hemoglobin was 16.5 mg., red cells, 4.68 million, leukocytes, 12,600; the differential count was normal with no eosinophiles seen. The electrocardiogram showed right axis deviation.

Two hundred thirty-two intracutaneous tests were done with pollens, molds, inhalants, and a large number of foods and also with extracts of barley and malt dusts. He gave marked skin reactions to the barley and malt extracts, also to house dust, feathers, cotton, and kapok lint, horse dander, and to several foods including barley, oat, and corn flour.

Diagnosis: Allergic sensitivity to inhalants and probably to his occupational dusts; emphysema; early cor pulmonale.

He was given palliative treatment and was started on hyposensitizing injections of the grain dusts and inhalants. He was changed to an easier job away from dust and his symptoms improved for a time. During the course of the next year he continued to be dyspneic until he was admitted to the hospital on Dec. 2, 1950, for extreme asthma and congestive heart failure.

Blood counts showed the following variations:

Dec. 4, 1950 Hgb. 19.2 mg. Red cells, 7.0 million

Dec. 14, 1950 Hgb. 17.5 mg. Red cells, 6.5 million

Dec. 18, 1950 Hgb. 17.0 mg. Red cells, 5.9 million

The leukocyte count varied from 14,000 to 7,500 the differential count showed 1 per cent to 2 per cent eosinophiles. The venous pressure was 25 mm. of water; the circulation time, arm to tongue, was 17 seconds, and the vital capacity was 1,000 c.c.

An x-ray of the lungs showed diffuse emphysema with secondary vascular changes and dilatation of the pulmonary artery. The lung markings and heart were otherwise not remarkable.

With digitalization, intermittent oxygen inhalation, and palliative remedies he improved and was discharged Dec. 19, 1950. He did not return to work.

He was seen at long intervals during the next nine months. He continued to have dyspnea and was usually somewhat cyanotic. On Sept. 17, 1951, he developed extreme dyspnea at home, was rushed to the Buffalo General Hospital where he died within a few hours.

An autopsy was done at the hospital under Dr. Terplan's direction.

PATHOLOGIC DIAGNOSIS

The body was that of a well-built, poorly nourished white man, 56 years of age; body length, 156 cm. There was moderate rigor mortis and dependent cyanosis. Face, neck, and fingernails were cyanotic. The neck veins were markedly distended. The chest was barrel-shaped. Genitalia were normal. The right ring finger was missing. No lymph gland enlargement was palpable.

Permission for examination of the head was not granted.

On opening the thoracic cage, both lungs were found to bulge slightly out into the gap in the chest wall. Thin, fine, easily separable pleural adhesions were found on both sides. No fluid was found in either pleural sac. The larynx was normal. The trachea and bronchi showed slight mucosal congestion. Both main bronchi and their branches were filled with thick, viscid, greenish, mucopurulent material. There was no bronchial obstruction. The pleurae showed blue-red discoloration near the bases and along the vertebral gutters. There were whitish indurated patches in the pleura on both sides, in the apical regions; they probably represented scar tissue. The interlobar fissures were obliterated by fine adhesions. Multiple large emphysematous bullae were found in both apices and in the right base. Both lungs did not deflate when left on the dissecting table, and freely crepitated on pressure. Section revealed definite emphysema. The parenchyma had a dark red-blue color, due to severe congestion. There was evidence of early consolidation in the upper portion of the left lower lobe, probably inflammatory in nature. Very fine pinpoint nodules could be felt on palpation, diffusely distributed through both lung fields and in the pleurae.

The pericardial sac contained a very small amount of clear thin yellow fluid. The pericardium was smooth and shiny. The visceral epicardium over the anterior surface of the right ventricle contained an area of fibrosis measuring roughly 5 by 5 cm. There was a small amount of epicardial fat. The heart was enlarged, weighing 480 grams. The right ventricle was markedly dilated and its wall measured 7 mm. in thickness. The left ventricle was of normal size, its wall measuring 17 mm. in thickness. There were no visible myocardial scars or infarcts. The tricuspid valves showed slight sclerosis. The ring of the latter measured 15 cm. in circumference, the pulmonic, 8 cm., the mitral, 11 cm., and the aortic, 8.5 cm. Both coronaries were of good caliber and patent; there was, however, slight degenerative change.

The abdominal subcutaneous fat was scanty. The liver weighed 1,180 grams; its surface had a pale brown color and was smooth and shiny. On section the capsule was thin and the parenchyma revealed marked congestion. The gall bladder contained a moderate amount of dark green-black bile. The wall was thin and showed cholesterosis. The extrahepatic biliary system was not remarkable. The spleen was small in size. The capsule was smooth and blue-gray in color. Section revealed pale red pulp with visible follicles.

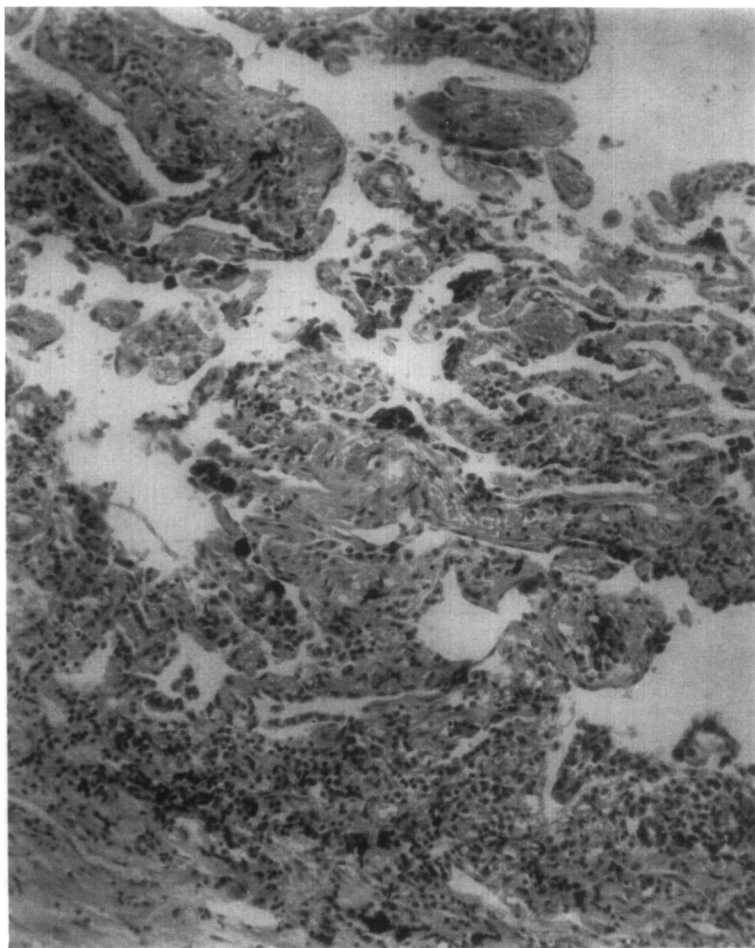


Fig. 7.—Case 19. The right upper portion of this section shows congestion of the capillaries and atelectasis, with compensatory emphysema in the upper two-thirds of the field. The lower portion shows chronic interstitial fibrosis and infiltration with round cells.

The esophagus was not remarkable. The mucosa of the stomach revealed capillary congestion. The intestinal tract revealed no abnormalities except for slight mucosal congestion of the upper small intestine.

Both kidneys were of approximately equal size, measuring 12.5 by 5.5 by 4 cm., weighing 370 grams together. The capsules stripped fairly easily, revealing dark red, grossly lobulated cortical surfaces. Section revealed marked parenchymal congestion. The corticomedullary junction was distinct and the cortex measured 10 mm. in thickness. The calices, pelves, ureters, and bladder were grossly not remarkable.

The thyroid was small and had a red fleshy appearance on section. The adrenal glands were of normal size and revealed a good amount of cortical lipid. The pancreas was not remarkable; the pancreatic duct was patent.

Chief diagnoses.—

1. Severe emphysema of lungs.
2. Cor pulmonale with right heart failure.
3. Pulmonary congestion.
4. Pneumonia.
5. Bilateral adhesive pleuritis.
6. Possible old healed pericarditis.

HISTOLOGIC REPORT

Lungs.—There was marked emphysema, congestion, and a small area of lobular pneumonia. One of the sections showed extensive fibrosis of the alveolar walls. The bronchi in this section were filled with mucopurulent material. Most of the lung tissue in this section was autolyzed, and there was chronic passive congestion. An old subpleural, partly calcified, rounded tuberculous lesion was seen in one section. There was an area of organization of the intra-alveolar inflammatory exudate (carnification) (Fig. 7).

Hilar Lymph Nodes.—There were congestion and anthracosis.

Liver.—There was marked congestion. Lipochrome pigment was seen in the liver cells.

Spleen.—There was an increase in fibrous tissue. The follicles and trabeculae were crowded together. This was a small atrophic spleen. The red pulp was congested.

Myocardium.—Some of the fibers showed atrophy, and brown pigment was found in the muscle cells near the nuclei. In the endocardium, there was slight leukocytic infiltration. There was also similar infiltration in the adjacent areas of the myocardium.

Kidney.—Sections revealed congestion and cloudy swelling of the tubular epithelium.

Pancreas.—There was slight fat infiltration. Some autolytic changes were seen. The islets were adequate in number and appearance.

Adrenal Glands.—No abnormalities were seen except for congestion. The lipid content was adequate.

DISCUSSION

The three autopsied cases happen to fall in the group which we have classified as atopic. The significant autopsy findings were emphysema, marked interstitial and peribronchiolar and peribronchial fibrosis without bronchiectasis. Two of these cases showed cor pulmonale. Evidence was present of neither silicosis nor fungus disease. The pathologic changes were a competent cause of the respiratory disability from which these three patients had suffered for years, although they showed no pathognomonic features.

While atopic sensitivity to crude grain dust plays a role in the production of respiratory disability in some cases of grain handler's disease, there are other cases in which there is no allergic sensitivity to these dusts. In the latter the pathologic changes in the lungs, productive of the symptoms and of the disability, are due, we believe, to the long-continued action of the inhaled dust acting as an irritant to the bronchial mucosa.

The mechanisms by which this dust induces the changes are obscure. Insufficient silica was found in the lungs of the autopsied cases to explain it. It would be of value, in proof of our opinion, if it could be shown that respiratory symptoms and pulmonary tissue changes can be produced experimentally in lower animals by exposure for a number of hours each day over long periods to

an atmosphere laden with dust from grain elevators and from other plants where raw grain is handled in volume. Certain of the animals should be studied for evidence of acquired sensitivity to the dust and to its various components. In our survey of recent literature, we have discovered no reports of such experiments.

SUMMARY

From consideration of these eleven grain workers with respiratory disability, certain features stand out. First, each of them had worked in the environment of crude grain dust for ten years or more before well-marked symptoms appeared. Second, all attributed their symptoms to the inhaled dust. Third, the onset of symptoms was gradual. Fourth, the symptoms, especially the dyspnea, showed a progressive increase until they became disabling. Fifth, study and examination of all eleven patients showed evidence of chronic bronchitis and recurrent bronchial obstruction. In eight patients, this led to clinically apparent emphysema. Finally, the three autopsied cases showed marked pulmonary fibrosis and emphysema, with cor pulmonale present in two.

CONCLUSIONS

We believe that workers handling crude grain may become allergically sensitive to crude grain dust or to some of its allergenic components, and that this sensitivity can result in disabling respiratory disease when the exposure is continued over a long period of time. The minimum exposure in our series of cases was ten years.

We believe, however, that allergic sensitivity to crude grain dust is not the only causative factor in the production of this grain handler's disease.

We believe that crude grain dust, inhaled over a long period of time, is capable of inducing disabling respiratory symptoms and pulmonary changes in the absence of allergic sensitivity to crude grain dust.

We feel that experimental work on lower animals should be carried out, by exposing them over long periods of time to an atmosphere laden with grain dust, to determine whether or not such exposure is capable of inducing chronic pulmonary changes or allergic sensitivity or both.

We wish to acknowledge with thanks our indebtedness to Dr. Kornel Terplan, Pathologist, and to Dr. John Sheffer of the pathology staff of the Buffalo General Hospital, and to Dr. Alfred Golden, Chief Pathologist at the Veterans Administration Hospital, Buffalo, for their generous advice on the autopsy findings. We also wish to express our thanks to Mr. Leland Bowerman, of the Buffalo General Hospital, for preparing the photomicrographs.

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