These findings strengthen further the hypothesis of a prolonged turnover time of noradrenaline in the affected skin of patients with atopic dermatitis. All normal skin has sympathetic nerves contributing noradrenaline to a pool. In a steady state, there is an equivalent rate of production and of loss of this neurohormone. In atopic dermatitis, it is suggested that the skin is placed under stress so that there is an increase in the size of the noradrenaline pool.

SUMMARY

Since the turnover time of administered noradrenaline in the skin of patients with atopic dermatitis has been shown to be prolonged, it was of interest to demonstrate the site of uptake of noradrenaline-$^{14}$C in atopic dermatitis as compared with other eczematous and normal skin. Two patients with long-standing atopic dermatitis, a patient with contact dermatitis to nickel, and a patient with normal skin were intradermally injected with DL-noradrenaline-7-$^{14}$C acetate and 8 mm. punch biopsies of the injected site were performed 24 hours later. Radioautographs were developed. At 199 days, there was a reaction over arrectores pilorum muscles and the upper one-third of the epidermis, greater in atopic dermatitic skin than in control sections. Grains in the radioautographs were also visible in proximity to arterolar walls. These results confirm earlier studies suggesting that atopic dermatitic skin retains noradrenaline longer than other dermatoses, concentrating the hormone in arrectores pilorum muscles and upper epidermis.

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# Lung Changes in Woodworkers

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**Pathological changes were observed in the lungs of two workers who had been exposed to wood dust for many years. The cause of death in each case was unrelated to the lung condition. The histopathological changes in the lung were: (1) centrilobular fibrosis and emphysema, (2) the presence of intra-alveolar basophilic particles which had excited a histiocytic and foreign body reaction. Special studies of these bodies tended to confirm the suspicion that they were particles of wood dust. Studies have shown that woodworkers are in an environment heavily saturated with wood dust. The present study suggests that the wood dust is inhaled into the alveoli and may lead to changes in the lungs.**

**Des modifications pathologiques ont été observées dans le poumons de deux hommes qui, par leur travail, avaient respiré pendant des années de la poussière de bois. Dans aucun des deux cas, la cause le la mort n'a pu être attribué à la pathologie pulmonaire. Les modifications pulmonaires comprenaient: (1) de la fibrose et de l'emphysème du lobe central, (2) la présence de particules alvéolaires basophiles qui avaient déclenché une réaction d'histiocytose et de corps étranger. L'examen approfondi de ces corps étrangers ont confirmé le soupçon qu'il s'agissait de particules de poussières de bois. L'étude du milieu a permis d'indiquer que les travailleurs du bois vivent dans une atmosphère fortement saturée de poussière de bois. La présente étude permet de croire que la poussière de bois est inhalée dans les alvéoles et peut provoquer des lésions pulmonaires.**

THE industrial use of wood has greater economic importance in Canada than that of any other product. This industry, comprising work involving lumber, furniture, paper and wood itself, employs more than 200,000 people in this country. The sales value of the shipments of pulp and paper alone is higher than that of any other single product.[1] Any illness due to industrial association with wood products could, therefore, be of importance to Canada's economy and could affect the lives of a substantial proportion of the population.

Most of the industrial processes in which wood is handled involve the dissemination of considerable quantities of fine wood dust into the atmosphere. However, it is stated that pneumoconiosis does not exist among the workers in those industries.[2] I discovered microscopic intra-alveolar basophilic particles, thought to be wood, in the lungs of two men who had been working in the wood industry until shortly before their

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deaths; the lungs also showed inflammatory and degenerative changes. Although the two patients died from causes quite unrelated to the lung changes, these observations should be of interest to Canadian physicians faced with pulmonary problems in woodworkers. The purpose of this communication is to describe these changes and to discuss their significance.

### CASE 1

A 40-year-old man was crushed to death in an elevator accident in a large factory engaged in the production of paper from wood pulp. He had worked in most areas of the factory as an odd-job man for about 10 years. During his life he had not complained of any significant cough or dyspnea.

At autopsy there was a severe crushing injury of the lower chest and abdomen with extrusion of abdominal contents into the thoracic cavity through a ruptured diaphragm. There was no hypertrophy or dilatation of the right ventricle or any other abnormality.

### CASE 2

A 53-year-old man suddenly experienced severe pain in the mid-chest region. On examination he was found to be severely shocked and hypotensive and was admitted to hospital. Morphine, oxygen and heparin were administered, but he died two hours after the onset of his symptoms.

He had never complained of cough or dyspnea. He had worked as a carpenter for 12 years in a large wood construction company. During the week before his death he had been sawing wood in a confined space indoors.

At autopsy a thrombus completely occluded the descending branch of the left coronary artery near its origin. The major coronary arteries showed marked atherosclerotic narrowing. Patchy fibrosis was present in the myocardium in the apical region of the left ventricle. There was no enlargement of the right ventricle.

#### *Gross Description of Lungs*

In Case 1 the lungs were incised at autopsy before fixation. The cut surfaces of the lungs showed marked hemorrhage into the lower lobes on each side. No adhesions were present in the pleural cavities and bullous emphysema was not seen.

In Case 2 the left lung was examined in the fresh state and the right lung after inflation by the injection of 10% formalin solution into the main bronchus. No adhesions were present on either side. The visceral pleural surfaces of both lungs showed numerous small fibrous nodules, each surrounded by a zone of increased anthracosis. There was no bullous emphysema, but the cut surfaces of the lungs showed a moderate degree of centrilobular emphysema, which in the fixed inflated right lung was present mainly in the upper and middle lobes (Fig. 1).

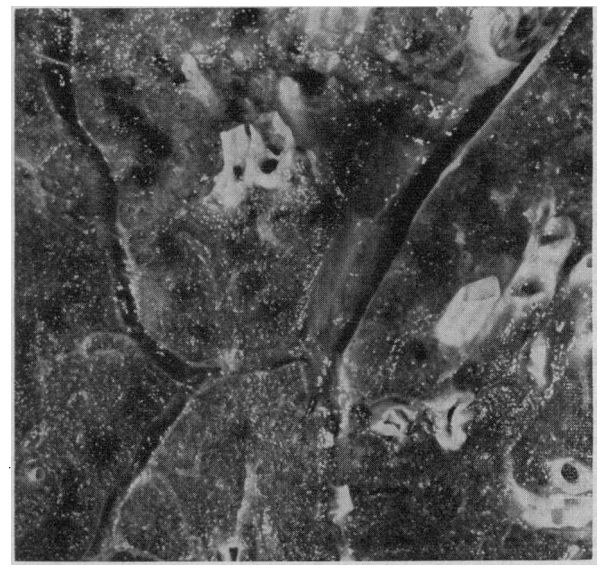

**Fig. 1.**—Close-up of cut surface of the upper lobe of the right lung of Case 2 fixed by injection of 10% formalin into the main bronchus. Areas of dilatation of air spaces associated with increased pigmentation are regularly distributed throughout the tissue. (Specimen was not photographed under water.)

#### *Microscopic Description of Lungs*

In both cases histological examination of the lungs showed areas of peribronchiolar fibrosis and anthracosis with surrounding emphysema of alveolar spaces (Fig. 2). Clusters of foreign-body giant cells and histiocytes were seen in some alveolar spaces. Within many of these there were one to six particles of a basophilic material. Each of these particles was engulfed by a thin rim of the cytoplasm of a

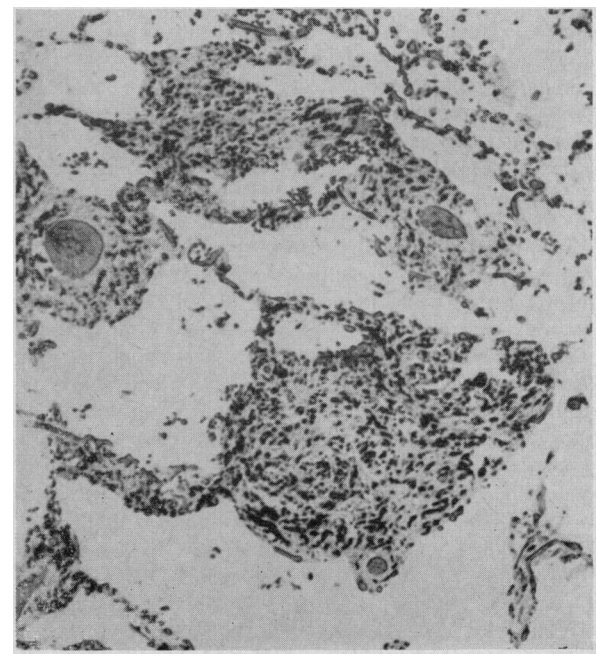

**Fig. 2.**—Microphotograph of Case 1 showing fibrosis, anthracosis and chronic inflammation around terminal bronchioles with emphysematous change in surrounding alveoli (centrilobular emphysema). (Hematoxylin and eosin, × 101.)

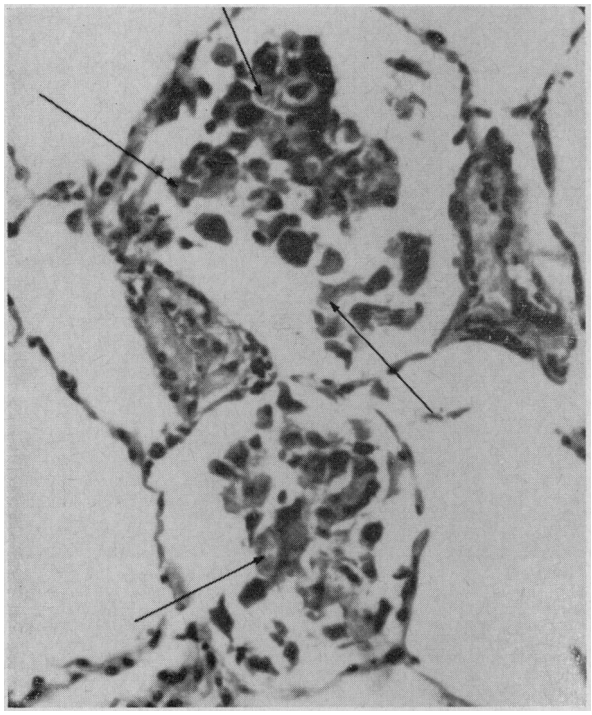

Fig. 3.—Low-power view of section of lung in Case 2 showing intra-alveolar foreign-body giant cell and histiocytic infiltrate and basophilic particles. Arrows indicate some of the basophilic particles. (Hematoxylin and eosin, × 300.)

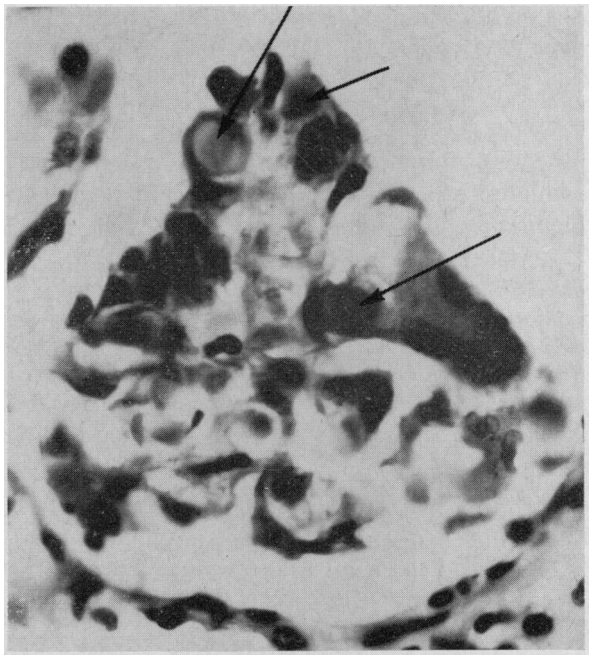

Fig. 4.—High-power photograph of basophilic particles, intra-alveolar histiocytes and giant cells in Case 2. Some of the phagocytosed basophilic particles are marked by arrows. (Hematoxylin and eosin, × 978.)

foreign-body giant cell or surrounded by histiocytes. The basophilic foreign particles are difficult to illustrate adequately in black-and-white photographs owing to their tinctorial similarity to cell nuclei. They were irregular in shape, often roughly spherical and measured 10 to 15 $\mu$. in maximum diameter. Smaller fragments were also present (Figs. 3 and 4). Some of the particles showed as many as four concentric laminations of darker blue staining material alternating with lighter zones (Fig. 5). In Case 1 only three or four particles with their surrounding cellular reaction were seen in any single section of lung tissue. In Case 2, in which the whole of the fixed inflated right lung was available for study, many such structures were found in some sections, particularly in those taken from the middle lobe or the posterior portion of the upper lobe, where numbers of basophilic bodies were present in most random low-power fields. Occasional groups of basophilic particles engulfed by histiocytes or giant cells were seen in the lumen of bronchioles. In Case 2 occasional basophilic particles were seen surrounded by histiocytes, lymphocytes, fibroblasts and collagen in the thickened walls of alveoli and alveolar ducts (Fig. 6). It may be presumed that these lesions would become areas of peribronchiolar fibrosis similar to those shown in Fig. 2.

## BASOPHILIC INTRA-ALVEOLAR PARTICLES COMPARED WITH WOOD DUST

Because of the occupational involvement with wood in each of these two cases it was suspected that the basophilic intra-alveolar particles were products of wood dust inhaled by the patients in the course of their work. The microscopical structure of wood dust is that of fragments composed of variable numbers of narrow hollow spindle-shaped fibres called tracheides. In section these tracheides appear as polygonal structures, forming a honeycomb of spaces lined by walls composed mainly of cellulose. A resinous substance, lignin, is present mainly between the cellulose walls. The tracheides are strongly birefringent (Fig. 7).

A comparison of the properties of the basophilic particles with tracheides from wood dust was undertaken. To obtain samples of the latter in histological section, portions of dust from the floor of the factory in which Case 1 worked were dehydrated, embedded in paraffin wax cut and mounted like tissue. The staining reactions carried out are shown in Table I. It will be seen

TABLE I.—COMPARISON OF STAINING PROPERTIES OF BASOPHILIC INTRA-ALVEOLAR PARTICLES WITH TRACHEIDES FROM WOOD DUST

| | *Lung particles* | *Wood dust (tracheides)* |
|---|---|---|
| Hematoxylin-eosin | Basophilic | Basophilic |
| Periodic-acid Schiff | Strongly-positive | Strongly positive |
| Alcian blue | Positive | Positive |
| Toluidine blue for metachromasy[3] | Slightly metachromatic<br>Alcohol eliminates metachromasy<br>Birefringence enhanced | Slightly metachromatic<br>Alcohol eliminates metachromasy<br>Birefringence enchanced |
| Hale's colloidal iron | Pcsitive | Positive |
| Prussian blue (control for Hale's colloidal iron) | Slightly positive | Slightly positive |
| Phlorglucinol for lignin[4] | Negative | Intercellular cement positive. "Cell wall" of tracheide negative |
| Congo red | Negative | Negative |

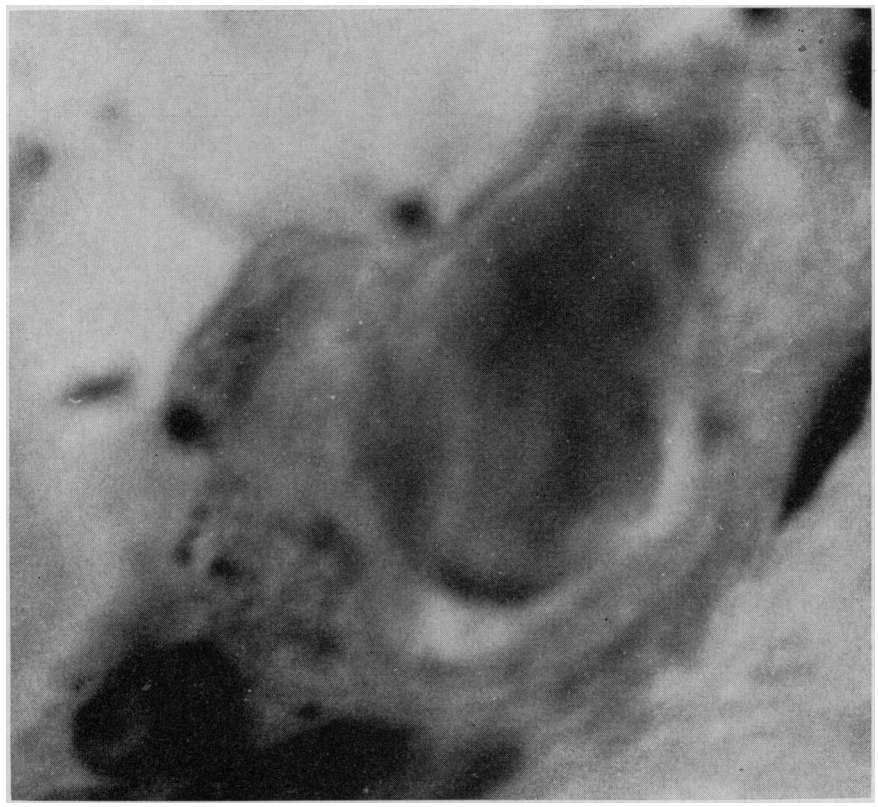

Fig. 5.—A single basophilic body showing (just below and to right of centre) concentric laminations in Case 2. Below and to the left of it the nuclei of the foreign body giant cell which has engulfed it are visible. (Hematoxylin and eosin, × 2875.)

that the particles resemble tracheides of wood dust in most of their reactions. The phlorglucinol test for lignin was negative, however. This test gave a positive reaction in the fine cement layers of the wood-dust tracheides although the

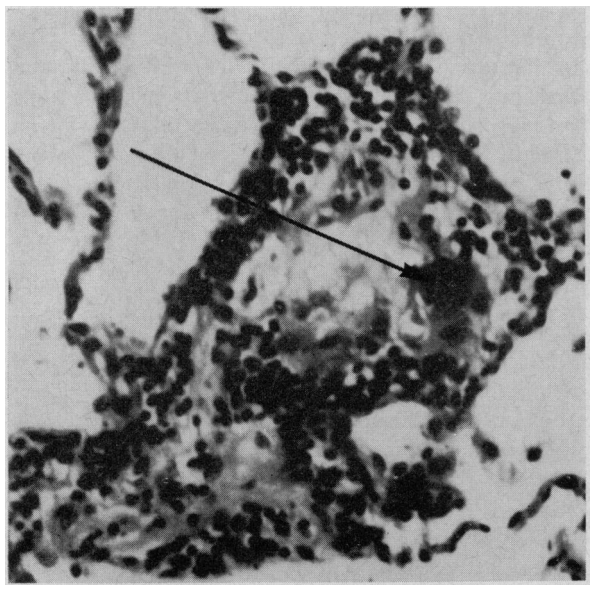

Fig. 6.—Giant cell and inflammatory infiltrate in alveolar wall around the basophilic particle are shown by the arrow. (Hematoxylin and eosin, × 443.)

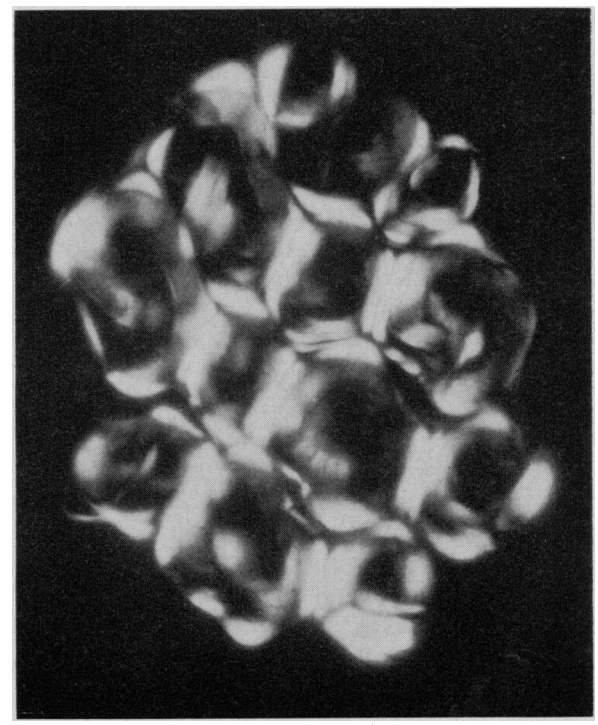

Fig. 7.—Section of wood dust from shop floor of factory where Case 1 worked, showing fragments of birefringent tracheides. (Unstained section photographed between crossed polaroids, × 300.)

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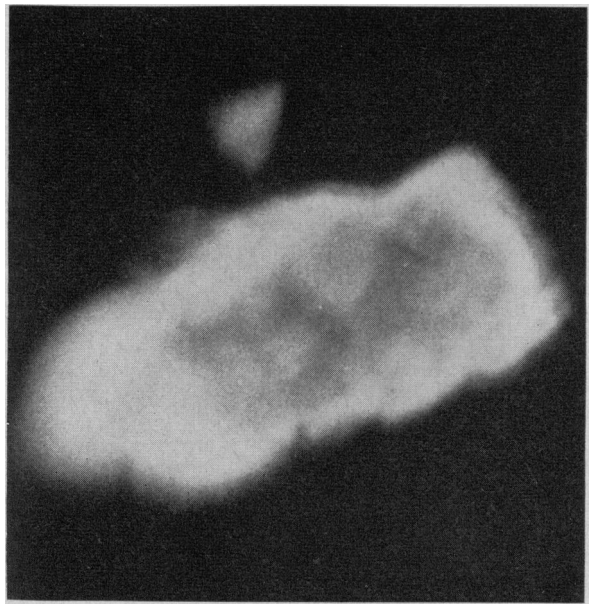

Fig. 8.—Section of lung of Case 2 showing intra-alveolar particle with non-birefringent centre surrounded by strongly birefringent wall. (Unstained section photographed between crossed polaroids, × 1150.)

tracheide structures themselves were negative. The structure of the intra-alveolar particles was seen most clearly when unstained sections were viewed between crossed polaroids. Many of the particles showed a dark, non-birefringent centre surrounded by a brightly birefringent wall (Fig. 8). The birefringence of the lung particles, although not of the tracheides from wood dust, was masked by hematoxylin but, like the wood dust, was enhanced by toluidine blue staining, which gave an alcohol-sensitive metachromasia to both. The lung bodies were easily detected by observation of unstained sections between crossed polaroids using the scanning lens of the microscope. Particularly large numbers were observed in this way after making scrapings of the cut surface of fixed (formalin) lung tissue, smearing them on to a microscope slide, drying them in air and then covering them with a layer of immersion oil.

### INVESTIGATION OF PULMONARY CHANGES IN PATIENTS EMPLOYED IN WOOD INDUSTRY

Paraffin blocks of the autopsied lungs of a further 21 patients who had worked in the timber industry in various parts of Northern Ontario were obtained through the files of the Sudbury General Hospital. In none of these subjects was a detailed history obtainable regarding the length and type of exposure to wood dust.

Sections were cut, mounted unstained on microscope slides and examined between crossed polaroids for birefringent bodies typical of the structures described here. In none of these sections were such structures observed.

A review of the autopsy reports and the routinely stained histological material from the 21 patients showed severe emphysema in three, squamous carcinoma of a lung in one and numerous pulmonary corpora amylacea in one.

### DISCUSSION

Basophilic intra-alveolar particles of the type described here are unlike any normal structures found in the lungs. Pulmonary corpora amylacea might be considered to have some resemblance to these structures in their intra-alveolar position, their concentric lamination and their close association with histiocytes and giant cells. But corpora amylacea are always larger, uniformly rounded and usually eosinophilic.[5] There is little doubt that the structures described here originated outside the body.

These foreign particles, identical in appearance in both cases, were found in persons whose occupations brought them into an atmosphere contaminated with wood dust. The particles show the staining reactions of a polysaccharide material, for the most part similar to the reaction of tracheides from wood dust. Physical and chemical differences due to electric charge phenomena between minute and larger particles of wood dust probably exist,[6] and these may explain the slight differences in staining reactions between the intra-alveolar particles and factory wood dust described in this work. It seems reasonable to assume that the intra-alveolar particles originated from inhaled wood dust.

Very few studies of the public health aspects of the wood industry are available in the English language. Hanslian and Kadlec[7] of Czechoslovakia have devoted much attention to this subject, mainly from the point of view of dermatological lesions in woodworkers. They contend that respiratory as well as skin disturbances may result in this industry from the very high concentrations of wood dust to which woodworkers are exposed.[8] They have shown that during the manufacture of furniture a concentration of wood dust as high as 200 mg./cu.m of air may develop; the average level of 40 mg./cu.m. of wood dust in the air found in this work was far above the maximum level which they state should be allowed—10 mg./cu.m. of air. These authors found that at high concentrations of wood dust 90% of the wood particles were smaller than 5 $\mu$. In the lungs of the two patients described in this communication the particles were mostly about 10 $\mu$. in diameter, although smaller particles were also observed.

Hanslian and Kadlec[8] have, moreover, carried out chemical and biological studies on different types of wood and have divided wood into three groups depending on the degree of toxicity of their component substances: (a) woods with low biological activity (relatively non-toxic), e.g. oak, beech, maple and ash; (b) woods with high biological activity (relatively toxic), e.g. pine, larch and mahogany, and (c) strongly allergenic woods, e.g. yew, mansonia. Case 1 in the present study worked in a paper mill where softwood mainly of the active, second group was used. Case 2 was employed in a general wood construction plant and was involved in working with all three types of wood. Thus both men inhaled large amounts of a type of wood dust which, according to Hanslian and Kadlec, could have harmful effects on human tissues.

A brisk foreign-body giant cell and histiocytic reaction had taken place around all of the intra-alveolar basophilic particles in each case. This could indicate a simple reaction to a foreign substance, similar to the cellular exudate seen around a splinter of wood embedded in the skin, and does not necessarily have the pathological implication of toxicity. It seems possible, however, that large numbers of particles, even if non-toxic, inhaled into the alveoli could over the years lead to a degree of fibrosis of the lungs, and stages possibly intermediate to parenchymal fibrosis were seen in Case 2 (Fig. 6).

Centrilobular fibrosis and emphysema were present in both cases and may have been the result of this repeated insult to the lungs over the years. However, neither patient reported any respiratory symptoms and it must be admitted that centrilobular emphysema is sometimes seen in the lungs of urban residents in the absence of any relevant industrial history. Whether the emphysematous lesions described in these two patients are the direct result of the repeated previous aspiration of wood dust cannot be determined in the light of our present knowledge.

I suggest that because of the observations presented here more attention should be directed to possible respiratory changes in woodworkers and to investigation of their clinical, physiological and immunological conditions. From the large concentration of basophilic bodies in the lungs of Case 2, basophilic bodies might well be excreted in the sputum of affected patients and the strongly birefringent properties of these particles could be of value in screening unstained slides of smeared sputum. The environmental conditions of woodworkers at work merit further attention, and additional pathological studies of these people would be of interest.

## SUMMARY

Two woodworkers in whom basophilic intra-alveolar particles were seen at autopsy are described. Both died from non-respiratory causes. The particles excited a foreign-body and histiocytic reaction, and centrilobular fibrosis, anthracosis and emphysema were present in both cases. A comparison of the microscopical features of these bodies with those of wood dust is presented. Recommendations for further study of the possibility of a woodworkers' pneumoconiosis are put forward.

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