CHANGES IN CERTAIN ORGANS AFTER EXPERIMENTAL INTRAPERITONEAL INJECTION OF ASBESTOS-CONTAINING DUST

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UDC 616-003.667.6-032:611.389]-091

The formation of cell nodules penetrated at the periphery by collagen fibers was observed in the peritoneal cavity of albino rats receiving an intraperitoneal injection of dust of chrysotile asbestos, brucite, and two types of amphibolitic asbestos (actinolite and tremolite). Particles were found in the lungs. Dusts of brucite and chrysotile-asbestos were found to have the strongest fibrogenic action.

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In connection with the ever increasing use of asbestos materials in modern industry, it has become necessary to study the pathogenic properties of dusts of different forms of asbestos. Tissue reactions to intraperitoneal injection of asbestos dusts have still received inadequate study [4, 5, 7]. The information available on this problem is scanty and conflicting.

Policard and Collet [8] claim that the reaction of the lungs to dusts is in some respects less demonstrative than the reaction of the peritoneum, changes in the latter developing more rapidly and almost independently of the species of animal.

Inert dusts have been found not to produce changes in connective tissue, whereas under the influence of harmful fibrogenic dusts, solid and frequently confluent nodules are formed.

Miller and Sayers [6] were the first investigators to inject chrysotile and crocidolite asbestos into rats, but they concluded that these dusts are not fibrogenic. Vorwald and co-workers [9] injected large particles of a mixture of asbestos and serptentine and obtained fibrotic changes, although short fibers ($<3\mu$) did not cause fibrosis. Behrens [3] found that after injection of asbestos dust into mice, histiocytic nodules surrounded by collagen fibers are formed in the mesentery. However, these workers did no more than describe the changes in the peritoneal cavity.

The object of the present investigation was to study changes arising under the influence of migrating dust in other parenchymatous organs.

EXPERIMENTAL METHOD

Dusts of chrysotile-asbestos ($H_4Mg_3Si_2O_4$), of two other types of amphibolitic asbestos – tremolite ($Ca_2Mg_5Si_4O_{11}$) and actinolite [$Ca(Mg, Fe^{++}_5 Si_4O_{11}(OH)_2$], and also of brucite ($MgO \cdot H_2O$) – a fibrous mineral although not, like asbestos, a silicate, were used.

Experiments were carried out on 35 albino rats weighing 180-200 g, receiving an intraperitoneal injection of a suspension of 50 mg dust in 100 ml physiological saline. The size of the dust particles did not exceed 5μ. The animals were killed by decapitation 15 days and 4 and 6 months later. Histological examination was made of the mesentery, the mesenteric lymph gland, lungs, liver, kidney, and spleen. Material was fixed in 10% neutral formalin. Sections were stained with hematoxylin-eosin, by Van Gieson's method, and for iron compounds by Perles' method.

EXPERIMENTAL RESULTS

By the 15th day after injection of these dusts, round , dense, gray structures 3 mm in diameter were found in the peritoneal cavity of the rats, distributed on the mesentery, parietal peritoneum, and on the

Sverdlovsk Medical Institute; Sverdlovsk Institute of Work Hygiene and Occupational Diseases (Presented by Academician of the AMN SSSR A. P. Avtsyn). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 5, pp. 117-120, May, 1969. Original article submitted June 11, 1968.

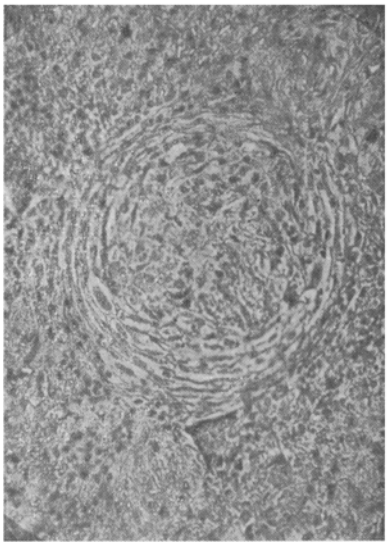

Fig. 1. Cell nodule in omentum with concentrically arranged collagen fibers around it. Actinolite, 15 days. Van Gieson, 160 ×.

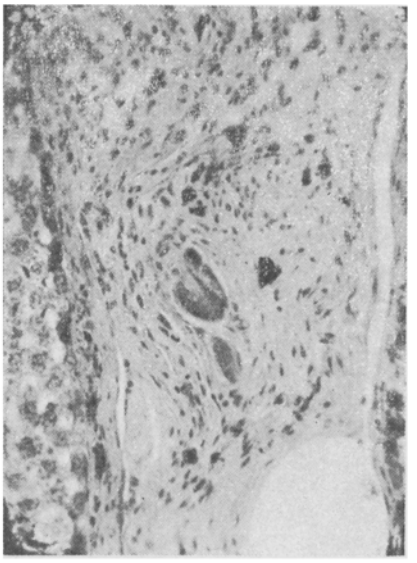

Fig. 2. Proliferation of collagen fibers with decrease in number of giant cells in cell nodule; dust particles surrounded by cells. Chrysotile-asbestos, 4 months. Van Gieson, 320 ×.

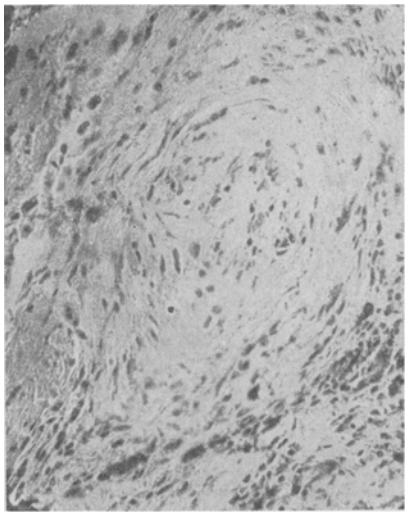

Fig. 3. Concentric and whorled arrangement of collagen fibers in cell nodule. Brucite, 6 months. Van Gieson, 160 ×.

serous membranes of the intestine. Collections of cells (nodules), consisting of macrophages and lymphocytes, were seen on a film specimen of the mesentery after injection of chrysotileasbestos dust, penetrated at the periphery by collagen fibers. Giant cells with nuclei situated peripherally were also observed. After injection of tremolite and actinolite dust cell nodules consisting of numerous dust macrophages surrounded by concentrically arranged collagen and argyrophilic fibers (Fig. 1), were found in the mesentery. After injection of brucite dust, cell nodules with numerous syncytia of 25 nuclei or more were formed.

Four months after injection of chrysotile-asbestos dust, thickening of the collagen fibers was observed in the nodules and a decrease in the amount of dust in the surrounding tissue. The larger dust particles were surrounded by fibers and cells resembling a capsule. The number of giant cells was reduced (Fig. 2). The greatest increase in collagen fibers in the nodules was caused by brucite dust; the cells meanwhile became fewer in number and developed necrosis. Similar, although less marked, changes were found after injection of tremolite and actinolite dust.

Six months after injection of all the types of dust studied, changes in the mesentery were almost identical with those described above. However, especially after injection of brucite dust, the number of cells was reduced and, on the other hand, the collagen fibers proliferated, often assuming a whorled appearance (Fig. 3).

In the lungs 15 days after intraperitoneal injection of dust, the number of free-lying alveolar epithelial cells containing a few dust particles in their cytoplasm was appreciably increased. Four months after injection of chrysotile-asbestos dust, small clusters of cells consisting of macrophages with a high content of dust particles were found in the interalveolar septa and along the course of the blood vessels. Occasionally small foci of lymphoid infiltration were observed near them. Changes in the bronchi produced by

actinolite dust were distinguished by the development of numerous foci of lymphoid infiltration, on account of which the continuity of the muscular layer of the bronchi was frequently disturbed.

After 6 months cell nodules were found only in animals receiving brucite dust.

In the lymph glands after 15 days, an almost identical morphological picture was observed in all groups of animals: hyperplasia of the reticular syncytium and a decrease in the amount of lymphoid tissue. The nuclei of many cells were in a stage of karyorrhexis, and some were degenerating. Among the lymphocytes were some with 2-3 nuclei and pale cytoplasm.

Hyperplasia of the reticular syncytium and intensive eosinophilic infiltration of lymphatic sinuses persisted four months after injection of dust.

In the liver, 15 days after intraperitoneal injection of chrysotile-asbestos dust, small perivascular foci of lymphoid infiltration and hypertrophy of nuclei of hepatic cells were observed.

Four months after injection of brucite dust, nodules appeared in Glisson's capsule at the site of collections of dust, surrounded at the periphery by thickened collagen fibers. The cells in the center of the nodules were in a state of necrobiosis. These nodules were similar in structure to the omental nodules.

Small foci of lymphoid tissue and slight development of collagen fibers around the tubules and glomeruli were found in the kidneys after injection of chrysotile-asbestos. In the spleen, 4 months after injection of dust, the outlines of the Malpighian corpuscles had become indistinct.

Hence, when injected intraperitoneally, the dusts produce a uniform response: nodules, consisting mainly of dust macrophages, surrounded by collagen fibers with a tendency toward development, appeared in the mesentery. After injection of chrysotile-asbestos and brucite, giant multinuclear cells appeared in the nodules. The observations made showed that they developed by fusion of single reticular cells. Degeneration of the cytoplasm was observed in the mast cells, evidently a sign of the toxic action of the injected dust.

These investigations showed that brucite and chrysotile-asbestos dusts possessed the strongest fibrotic action.

Dust injected intraperitoneally migrated and was found in the peribronchial and perivascular tissues of the lung and also in the alveolar epithelial cells, without, however, producing any significant changes in the septa; the septa were only slightly thickened through an increase in the number of lymphocytes, unaccompanied by any increase in the collagen fibers, as occurred after intratracheal administration of brucite and chrysotile-asbestos dust [2].

The observations showed that the fibrotic action of dust is manifested principally at the site of primary injection (mesentery). This is in aggrement with the results obtained by Belobragina [1], who performed similar experiments with quartz dust and observed the formation of typical silicotic nodules only at the site of injection.

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