

Intraperitoneal Reactions caused by Dusts G20, G21 and G22.
Preliminary Report.

As a means of orientation as to the ultimate tissue reactions of two given dusts, G20, "raw" enamel and G21, "atmospheric dust", a short preliminary experiment was carried out, using as controls lamp-black, a known inert substance and "silica smoke" G22, a known active one.

Technique.

Aqueous suspensions of each of these four dusts were prepared so that one cubic centimeter contained 50 mg. of dust.

Only two guinea pigs were used in the preliminary experiment. After rendering the fields as sterile as possible by shaving the fur, washing with soap and water, and disinfecting with alcohol, fifty mg. of each substance to be tested were injected subcutaneously in each abdominal quarter of the animal. Sections of the ensuing lesions (q.v.) were made at the end of forty-eight and of ninety-six hours.

One of the animals, whose peritoneal cavity was inadvertently penetrated when the carbon inoculations were made, was allowed to live and served as a control in the longer experiment.

Intraperitoneal injections were used in the second, larger series of pigs, following exactly the technique described by Miller et al.¹. The only planned control in this group was the "silica smoke". Its known irritating properties were used as a basis of comparison with the unknowns G20 and G21.

On September 23, 1936, three pigs were injected intraperitoneally with 2 cc. of a 10% suspension of G20; three more were injected with a similar quantity of G21, while the last three received G22. Considerable difficulty was encountered in making these injections, because

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some of the dust particles caused clogging of the piston in the syringe barrel. If the injections were made quickly, however, approximately all of the .2 gms. could be introduced.

The original plan of killing the animals so as to observe tissue reactions at monthly intervals could not be carried out because some of them died prematurely. One pig, which was injected with G20, died shortly before the end of the second month, but was not replaced. Two others, inoculated with G21 and G22 respectively, died after five weeks. Two freshly inoculated animals were substituted, but they, too, died exactly at the end of two months. Thus, the progression of lesions at one, two, and three months intervals could be observed only in the animals injected with enamel. Fortunately, the animal with the accidental peritoneal injection of carbon, lived for over four months and offered an opportunity for studying intraperitoneal carbon nodules and subcutaneous silica nodules of four months duration.

The Subcutaneous Lesions.

As was to be expected, the most intense reaction was produced by the silica. At the end of 48 hours there was considerable hemorrhage and necrosis with slight fibroblastic proliferation. Very little phagocytosis of dust had occurred as yet. Ninety-six hours later, an occasional silica-bearing phagocyte was seen, and there was energetic fibroblastic activity not only immediately surrounding the injected dust, but at some distance from it. Hemorrhage, edema, and a number of acute inflammatory cells were still present.

An acute inflammatory exudate, but no actual areas of necrosis, surrounded the injected enamel at the end of forty-eight hours. The sections made at the end of ninety-six hours were unsatisfactory.

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A moderate inflammatory reaction was provoked by the atmospheric dust in forty-eight hours. An occasional fibroblast was noted. At the end of ninety-six hours, a few phagocytes and fibroblasts were present.

Forty-eight hours after injection, both acute and chronic inflammatory cells and about an equal number of dust-filled phagocytes were seen around the lamp-black deposits. Fibroblasts were surprisingly numerous. Although comparatively little carbon was seen in the section at the end of ninety-six hours, there was a moderately marked inflammatory reaction with a large number of fibroblasts. It was difficult to tell whether this response was provoked by the carbon or whether it was a distant reaction due to atmospheric dust, which was injected at the opposite lower quadrant of the abdomen.

The Intraperitoneal Lesions.

Gross Description.

Macroscopically, the nodules produced by G20, G21, and G22 did not show marked variations in appearance, except for the fact that those due to enamel could be distinguished by their characteristic bluish-gray color. Several features were common to all: intra-abdominal transportation of the dust, far from the original site of injection, evidently occurred rapidly; at the end of the first month the surface of practically every organ was studded with nodules. They varied in size from that of a millet-seed to that of a small lima-bean, and had a tendency to remain discrete, although a number of conglomerate forms were seen at the end of the second month. The anterior visceral peritoneum seemed to be the site of predilection, with the mesentery next frequently involved. The omentum was generally rolled up somewhere in the upper abdomen; dense bands of adhesions matted together

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many of the organs. As mentioned above, superficial nodules were found on most of the abdominal viscera; the diaphragm, liver, gall bladder, stomach, spleen, intestines, testes. None, however, were noted on the kidneys.

Microscopic Appearance.

The Silica Modules.

At the end of the first month, the nodule consisted of a central necrotic plug, surrounded by a zone of chronic inflammatory cells and a sharply circumscribing fibrous capsule. Attempted organization was shown by a number of new blood vessels seen most frequently peripherally; fibroblasts were numerous. Since it was difficult to recognize the injected dust in the stained sections, the extent of phagocytosis could not be judged. One month later, organization was much more advanced. The cellular zone around the central area of necrosis was broader, the capsule firmer, and a generous network of new blood vessels penetrated the greater part of the nodule.

The four-months old subcutaneous nodule was completely organized. Necrosis had disappeared and was replaced by numerous foreign body giant cells and new fibrous tissue. In sharp contrast, the carbon (peritoneal) nodule of the same age showed no cellular reaction whatever. Most of the carbon was contained within large foreign body giant cells, but there was no attempt at organization.

The Enamel Modules.

In the month-old nodule, the enamel was seen as a more or less amorphous, slightly refractile, greenish-bluish material interspersed with large, irregular, dark-blue, granular clumps. The center of the nodule was composed of this dust and cellular debris. Towards the periphery, however, large enamel-bearing phagocytes, and a number of

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new blood vessels were noted. Connective tissue proliferation was not marked and only about a sixth to a third of the distance from the periphery was organized.

Little change occurred in the nodule at the end of almost two months. A few collagenous fibrils were seen, but vascularization was not marked.

Section through a three-months nodule showed that most of the dust had been phagocytosed. Almost the entire nodule was vascularized, but the total amount of fibrosis was slight.

The Atmospheric Dust Nodules.

After one month, faintly luminous particles of a yellowish-greenish cast were seen both intra- and extra-cellularly. A chronic inflammatory reaction with marked fibroblastic proliferation surrounded the central coagulum. Indeed, there seemed to be more collagen in some of these nodules than in those caused by either silica or enamel.

Oddly enough, another month did not effect great changes in the nodule. The center was still largely necrotic and only at the extreme periphery was there a narrow cellular zone. Quite a little fibrosis surrounded this zone, however, and extended for some distance from the lesion.

Unfortunately, both the original and substituted animal died at the end of two months, so that three months old lesions caused by atmospheric dust could not be studied.

The microscopic appearance of the nodules produced by the above named dusts was very similar to the subcutaneous nodules described by E. H. Kettle².

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Conclusions

1. An attempt was made to estimate the relative harmfulness of two dusts, G20 (enamel) and G21 (atmospheric dust), by the Miller method of intraperitoneal injection, using a dust, G22 ("silica smoke") as control.
2. Widespread intra-abdominal nodules were produced by all three samples.
3. It was impossible to separate these samples into injurious and innocuous dusts by the appearance of the gross lesions alone.
4. The activity of each dust was judged by the speed with which it was engulfed by phagocytes and the ensuing cellular response, with particular emphasis on its capacity to excite fibrous tissue proliferation.
 - A. The most active excitant of fibrosis was the dust G22.
 - B. G21 provoked less fibrous tissue reaction than G22, but perhaps, a trifle more than G20.

Submitted by

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Approved

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Reference

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S-36-1065 G82 "Silica Smoke" 1 month

There was slight induration at the site of inoculation. On opening the peritoneum, several large nodules were seen. Most of them were discrete, but one large irregular one at the level of the umbilicus seemed to be the result of several coalesced nodules. They were military or sub-military to pea-sized, and distributed all over the abdominal cavity: a large one was found just under the left costal border; they were found on the omentum, the surface of the intestines, the liver, diaphragm, spleen, mesentery, peri-renal fat tissue and testes. A few were seen on the posterior abdominal wall.

S-36-1229 "Silica Smoke" 2 months

The peritoneum was adherent to almost all the abdominal viscera. The omentum was partially tucked under the spleen. A dense band of adhesions matted together the spleen and stomach; the gall bladder was attached to the xyphoid. There were numerous variously sized and shaped nodules, diffusely scattered all over the anterior abdominal wall, the surface of the spleen and liver, the mesentery, the fat tissue surrounding the kidneys and a few small ones on the posterior abdominal wall.

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