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May 5, 1936

Owens Illinois Glass Company
Toledo, Ohio

Attention: Mr. W.G. Hazard

Gentlemen:

I submit the following report of an investigation of the biological activity of glass wool undertaken at your request in the Saranac Laboratory.

To determine whether particles of glass wool are capable of producing reaction in the tissues, suspensions of finely ground plain and oiled wools were injected into the ear veins of rabbits and the peritoneal cavities of guinea pigs. Experience in this laboratory and elsewhere has demonstrated that these methods are adequate to demonstrate the capacity of a mineral dust to produce fibrosis. Investigation of over 20 different types of dust has indicated that if no reaction occurs in organs other than the lungs, it will not occur in the respiratory tract and that conversely dusts like silica and asbestos that are known to produce fibrosis of the lungs also cause fibrosis in other tissues when injected in sufficient quantities. Neither plain or oiled glass wools have caused fibrosis or any chronic progressive reaction by injection and therefore it is a reasonable assumption that their inhalation would likewise fail to produce such effects.

Glass wool cannot be classified as an inert dust for although it causes no progressive fibrosis nevertheless injection of large amounts into the peritoneal cavity of the guinea pig usually produces immediate death. Apparently this is due to the presence of sodium silicate which has a similar action. Animals surviving this immediate effect develop no chronic changes. This action of the glass could hardly occur in the lungs of a person inhaling it because the concentration could never be great enough to produce such an effect.

To determine whether the ingestion of glass wool particles is capable of injuring the stomach and intestines guinea pigs were fed 2.5 cc. of a 20 per cent suspension of glass particles mixed with their grain 6 days a week, over a

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period from 4 to 17 weeks, with proper precautions that all of the material was consumed. Another group received two doses totaling from 0.575 to 0.8 gm. of glass particles, in water suspension, by stomach tube before the morning feedings. When the animals were killed, 4 to 17 weeks later, no trace of the glass or injury produced by it could be discovered in any part of the alimentary tract. Therefore it is concluded that the ingestion of even excessive quantities of glass wool particles 100 microns or less in diameter, produces no injury.

The details of these various experiments are summarized as follows:

Preparation of dusts

Both plain wool and oiled glass wool containing 11 % oil were crushed in an agate mortar and then ground with water in a porcelain ball mill for 432 hours. It was then nearly dry; more water was added and the milling was continued for another 408 hours. The material removed from the mill was placed in a large beaker and allowed to stand over night. Examination of the supernatant fluid showed a high concentration of particles 1 to 3 microns in diameter. With the oiled glass some of the oil had separated in the process of grinding and this had to be discarded but examination showed considerable oil in the suspension that was subsequently prepared. The concentration was adjusted with water to 1% and sufficient sodium chloride was added to make the suspension isotonic with the body fluids.

Intravenous injections.

- a) Plain glass wool - 4 rabbits received 1 gram of 1 to 3 micron particles in 20 injections of 5 cc each, administered bi-weekly.

Rabbit #14 died, probably of cerebral embolism, on the day following the last injection. Such accidents are not uncommon in this type of injection. Autopsy showed no gross evidence of disease. In microscopic sections, collections of dust containing phagocytes were found in the lungs, spleen and liver. Frequently these cells were of the giant variety and they contained masses of glass fragments. There was no evidence of inflammatory change about them.

Rabbit #13 was killed 15 days after completing the injections. There were no gross changes and the microscope revealed identical reactions to those in #14, except that dust cells now occurred in the lymph node draining the liver.

Rabbit #12 was killed after 182 days. The picture was no different from that in #13.

Rabbit #11 was killed after 259 days. There was absolutely no gross evidence of reaction to dust. Microscopic sections have not yet been made as the animal was not killed until yesterday.

- b) Oiled glass wool - 4 rabbits received 1 gm. of 1 to 3 micron particles in 20 injections of 5 cc. each, administered bi-weekly.

Rabbit #1 was killed 143 days after completing the injections. There were no gross changes and the microscope revealed a reaction indistinguishable from that in rabbit #13.

Rabbit #2 was killed after 181 days - the picture was the same.

Rabbit #3 was killed after 285 days. Like #1, the animal showed absolutely no gross evidence of disease. Microscopic examination will not be completed in time to be included in this report.

Rabbit #4 is still alive and apparently well. It will be allowed to live for one year but there is no reason to suspect that it will develop further reaction.

These results are in every way comparable to those observed with inert dusts. Aluminum oxide, feldspar, fluorspar and 3 types of sericite have all shows similar reactions. Uncombined silica, on the other hand, produces acute inflammations followed by progressive fibrosis in the various organs. The liver shows a massive fibrosis that reduces the organ to a distorted mass of scar and the spleen is enlarged and studded with nodules. No microscope is necessary to discover the results of the injections which begin to be manifested before all the silica has been injected.

Intraperitoneal injections

a) Plain Wool

Four guinea pigs were injected into the peritoneal cavity with 2 cc of a 10% suspension of the 1 to 3 micron particles described above.

On the following morning two were dead. Their abdomens were distended and on opening them the peritoneal surfaces were inflamed. particularly in the region of deposits of the glass dust that were scattered here and there over the different organs. The small intestine was pale and dilated with gas.

The experiment was repeated and again 3 of 4 animals were dead within 24 hours, showing similar reaction. The three animals that survived at first showed

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abdominal distention but this disappeared within a week. They were killed later while apparently well.

#18, killed after 23 weeks, showed 3 minute grey-white patches on the surface of the peritoneum that the microscope revealed to be clumps of phagocytes containing particles of dust. There was no fibrosis.

#6 and #8, killed after 34 weeks, showed no gross evidence of reaction but in microscopic sections a few compact collections of dust cells could be found on the surface of the omentum.

b) Oiled Wool

Four guinea pigs were injected into the peritoneal cavity with 2 cc. of a 10% suspension of the 1 to 3 micron oiled glass particles described above. On the following morning all were dead with the same evidences of an acute poisoning described in the plain glass group.

The test was repeated on 4 more guinea pigs. This time only one animal was dead the next day but another died on the third day and the other two on the fourth. All showed the same evidences of acute poisoning in the peritoneal cavity.

To control this experience two guinea pigs were injected intraperitoneally with the same quantity of finely powdered sodium silicate. They likewise died within 24 hours and exhibited the same type of reaction in the peritoneal cavity. Unpublished data from another laboratory corroborates this effect of intraperitoneal injection of sodium silicate.

This reaction is unusual and has not been observed after the injection of other types of dust which include a variety of silicates. Furthermore the introduction of a smaller dose of pure sodium silicate directly into the lungs has not produced this result. In 1923 a group of 16 guinea pigs was given intratracheal injections totaling 13 mgms. of sodium silicate and none of them showed any adverse symptoms. The conditions in this experiment were different from those in the present one as the dose was divided and administered in 7 injections during a period of approximately a month. No animal received more than 2 mgms. at any one time. Nevertheless, it seems not unlikely that if this silicate were poisonous when administered directly into the lungs some of the animals might have shown symptoms. Certainly it can be concluded that a human being would not be likely to inhale toxic quantity of sodium silicate in the form of glass wool dust.

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Ingestion Experiment

These tests were performed with plain glass wool only as previous tests had indicated that the oiled material did not act differently.

Four fasting guinea pigs were injected by stomach tube with from 1.5 to 6 cc. of a 5% suspension of glass wool ground in a mortar so that the particles were 100 microns and less in diameter. None showed any ill effects so the injections were repeated after 23 days. This time doses of 2 and 5 cc of a 10% suspension were employed and again there were no symptoms. The total doses for the 4 animals were as follows:

#4. . . . 1.5 cc (575 mgm)	#3. . . . 4 cc (700 mgm)
#1. . . . 2.0 cc (600 mgm)	#2. . . . 6 cc (800 mgm)

(Note that these totals were incorrectly reported in the preliminary statement of Jan. 28, 1936)

Since there was no apparent reaction to these injections, it was decided to continue the administration of the glass, using a 20% suspension mixed with a small portion of grain fed to the animals before they were given their regular morning ration. These 4 guinea pigs and 6 other ones were therefore fed 0.5 gm. of glass 6 days a week until they were killed. The following table summarizes their treatment:

Animal No.	Glass by Stomach Tube		Glass with Food	Total Dose	Duration of Feeding
	1st Feeding	2nd Feeding			
2	0.3 gm.	0.3 gm.	13.0 gm.	13.9 gm.	32 days
3	0.2 gm.	0.5 gm.	26.5 "	27.2 "	33 "
1	0.1 "	0.5 "	26.5 "	27.1 "	63 "
4	0.075 "	0.5 "	39.5 "	40.75 "	94 "
5			13.0 "	13.0 "	30 "
7			26.5 "	26.5 "	61 "
6			39.5 "	39.5 "	92 "
8			51.0 "	51.0 "	119 "
9			51.0 "	51.0 "	119 "
10			51.0 "	51.0 "	119 "

As these animals were killed their intestinal tracts were washed and carefully examined for gross evidence of inflammation. None were found in the mouth, esophagus, stomach, small or large intestine. Representative pieces of each portion of the tract and of the mesenteric lymph nodes were removed for microscopic section. Examination failed to disclose evidence of the glass fragments or any injury inflicted by them.

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One may therefore conclude that the ingestion of as much as 51 grams of finely powdered glass wool, administered in divided doses, will not cause injury in 4 months time. In the absence of any reaction at all it would hardly seem essential to continue the investigation further.

The general conclusion that both oiled and plain glass wools are incapable of exciting progressive fibrosis in the tissues is warranted from these observations in view of the wide experience in this laboratory with these methods of testing the biological activity of inorganic dusts.

Trusting that these findings may allay any scepticism as to a theoretical hazard involved from the handling of glass wool, I am

Very truly yours,

Leroy U. Gardner, M.D.
Director

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Rabbit #3 - killed after 365 days
" #4 - " " 285 "

They showed no further change.

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