

REPORT ON GEMINI LABEL TOXICITY TESTING

Summary

Ten Sprague-Dawley rats were exposed to a combination of reduced barometric pressure, pure oxygen, and Project Gemini labels glued with Minnesota Mining and Manufacturing Company's EC 583 applied with methyl ethyl ketone. These experimental animals showed toxicological symptoms not observed in control animals exposed to the same conditions without the Project Gemini labels. Further investigation is suggested before these labels are employed in manned space vehicles.

Apparatus, Subjects, and Materials

The AiResearch Department of Life Sciences small animal chamber was used in this work. This chamber is capable of withstanding both high and very low pressures; for this investigation it was plumbed to a vacuum pump for low pressure. The chamber has an internal volume of 12.5 cubic feet; it is not equipped with an airlock. The door, mounted on the top and side of the chamber, contains a large glass viewing port, and is opened and closed by an electric motor. A small high-speed fan circulates the air in the chamber. Both illumination and, to some extent, heating are provided by an externally controlled lamp in the chamber. Instrumentation to the chamber during this investigation consisted of a manometer and a copper-constantan thermocouple to measure temperatures near the animal cage.

The cage itself was 22" X 18" X 6" in size, and was made of half-inch mesh galvanized wire with a hinged top. It was fitted with four external water bottles with glass nipples reaching the inside of the cage. No food containers were employed. A large open waste tray was placed below

the cage to catch urine and feces.

No environmental control system was employed in this experimentation. Carbon dioxide was adequately absorbed by a flat tray containing soda lime treated with an indicator, and oxygen was continually replenished from an external bottle. A vacuum pump was used to lower the chamber internal pressure to 10.18 inches of mercury Absolute, and was kept running with the valve open slightly while oxygen was bled in; a balance was achieved so that the resultant of the gas continually pumped out and the oxygen bled in was 10.18 inches of mercury, or simulated 27,000 feet. This implied a bleed of slightly more than four liters per day of gas from the chamber.

The Project Gemini labels used with the experimental animals were fastened using standard techniques onto both sides of four stainless steel plates 30 X 45 cm. in size. Twenty-four labels per side were placed on these four plates; the labels were of various sizes and shapes, with their largest dimension or diameter of no greater than five centimeters. The adhesive used for these labels was Minnesota Mining and Manufacturing Company's EC 583 applied with methyl ethyl ketone. The four plates with the labels were placed around the animal cage in such a way that they did not interfere with gas circulation through the cage and soda lime. They were leaned against the chamber walls so that they could not be reached by the animals.

The subjects were twenty Sprague-Dawley albino rats, about six weeks in age, furnished by Simonsen Laboratories. The control and experimental groups involved ten animals each, with five males and five females per group. The animals had been raised on Simonsen Maintenance Stock Pellets, with fresh potatoes and carrots given intermittently. The rats were carefully observed for several weeks before the experimentation, and all were in excellent health. Individual animals were marked with

dots of methylene blue for identification.

Experimental Procedures

The animals were removed from their individual cages in the Life Sciences Vivarium and placed in the common chamber cage. Ten animals were employed, five males and five females. The chamber door was closed and the dump valve was opened, so that the chamber could be purged with oxygen. The purging was carried out for ten minutes at one inch of mercury above ambient barometric. It was considered that this oxygen tension for this length of time was not sufficient for the elicitation of oxygen toxicity symptoms.

After the oxygen purge, the dump valve and oxygen flow were closed and the chamber evacuated to 10.18 inches of mercury at the rate of 1.0 in. Hg/min. The chamber was leveled off with the vacuum valve and balanced at 10.18 in. Hg using the oxygen bottle. It was maintained at this simulated altitude (27,000 ft.) for twenty-four hours between openings. The total time at altitude was 98 hours, with daily interruptions during which the chamber was dumped to sea level and opened so that the animals' water and food could be replaced and the waste tray cleaned. The chamber was lowered in altitude by opening the dump valve to a descent rate of 1.0 inch of mercury per minute. The chamber was open to the surrounding atmosphere for no more than eight minutes per day; it is clear, however, that this time was sufficient to flush the chamber to a very low level of atmospheric contaminant. This daily opening was necessitated largely by the high evaporation rate from the water bottles at reduced pressure.

The temperature inside the chamber was generally about 24°C., which is also the mean Vivarium temperature. The temperature could be adjusted by means of the chamber light, although this seldom proved necessary. The maximum temperature (28°C.) was reached for short periods only during chamber repressurization.

Frequent observations were made on the animals by a trained biologist. These were made both through the glass view port and at closer range when the chamber was brought down. After the 98-hour sequence, the animals were given a more thorough examination and were placed in individual cages for detailed observation. The examinations employed were those used by the Toxicity Screening Branch of the Chemical R & D Laboratories at Edgewood Arsenal. The animals were not sacrificed.

Results

In general, it can be said that the experimental animals showed symptoms of toxicity, while the control animals did not. These symptoms were noted after the first day of exposure, and continued undiminished or increased until after removal from the chamber; they were universal among the experimental animals, and not specific as to sex.

These symptoms included:

1. Breakdown in grooming habits, evinced by matted, discolored fur and general extreme untidiness
2. Blotchy skin coloring, particularly on tail. This symptom has persisted.
3. Severe eye irritation which caused some animals to keep one or both eyes closed.
4. Periodic subconvulsive jerking of the limbs
5. Excessive lassitude, with occasional fits of extreme running excitement
6. Excessive urination; volume almost doubled. This symptom increased noticeably as the test continued.
7. Loose and excessive stool, which increased through the test to almost twice normal size
8. Loss of weight, with slow subsequent recovery

The "running excitement" generally took place on descent and upon opening the chamber; at this time, all experimental animals took part in it. Individual animals showed this symptom at seemingly random times, while the other animals remained quiet.

The glue material was easily detectable by smell when the chamber was opened, and was of very strong and disagreeable odor. In comparison, the usual urine and feces smell was almost pleasant.

Discussion

The etiology of the observed symptoms is uncertain, although it appears obvious that the symptoms are results of some physiological effect of the adhesive material. It is probable that the toxic materials involved entered through the pulmonary tree, although some could conceivably have been dissolved in the water or absorbed by the food. The pulmonary route is the most likely.

The breakdown in grooming habits indicates only a general malaise; rats normally spend about half of their waking hours cleaning themselves. The blotchy skin color could indicate an irritating surface effect of the glue material, especially since the bare tails were particularly affected. This could also have caused the eye irritation, although the high oxygen tension could have contributed to this. The lack of such an effect in control animals may simply indicate the irritating effect of the atmospheric contaminant, or it could imply a synergistic reaction of the contaminant with pure oxygen at an elevated tension. The convulsive effects, and the gastrointestinal-genitourinary symptoms, indicate some internal dysfunction of uncertain physiological genesis.

The primary defect of this experiment was the necessity to interrupt the experimental sequence for bringing the animals "down" for fresh water and waste removal. For this reason, the results obtained are considered

conservative. The atmosphere was completely refreshed each time the chamber was open. Also, the system was continually diluted with pure oxygen at the rate of over four liters per day. Nor were the labels ever heated above the moderate chamber ambient; they were placed well clear of the electric lamp and fan motor. Furthermore, half of the labels rested very close to the chamber walls, where the air circulation was at a minimum. Thus the symptoms observed occurred despite several ameliorating experimental artifacts.

Conclusion and Recommendations

From the above discussion, it is apparent that the Project Gemini label adhesive is toxic under the conditions of oxygen atmosphere and reduced barometric pressure (10.18 in. Hg A). It is impossible to determine whether this toxicity would be greater or less to human subjects than with rats. It is safe to assume that some toxic effects would be observed with humans, although the degree of these effects is uncertain. The humans involved in this experiment can only relate that the "chemical" smell of the adhesive compound is very noisome and unpleasant. To ascertain more exactly the probably toxicological effect on humans, more testing should be done.

This testing should involve more than one species of animal in addition to further testing with rats. A common reaction among animals of several species enables a confident prediction of the effect on humans to be made. The chamber should be modified to permit continuous exposure without interruptions of the sort made in this preliminary work; this could be accomplished with a plumbing system for water, a waste flushing and disposal system, and an arrangement for the exposure of more soda lime to the atmosphere. Instrumentation should be employed (gas chromatography, mass spectroscopy, etc.) to monitor contaminant

levels, humidity, carbon dioxide concentrations, oxygen levels, and area temperatures. Instrumentation and apparatus, such as spirometers, body temperature sensors, and voluntary activity wheels, should be installed to detect physical and behavioral changes. The experimental animals should be sacrificed and subjected to a thorough post-test pathological examination, so that sites and degrees of organ damage could be ascertained.

The work discussed above must be interpreted as a definite danger signal. It is imperative that further investigation be carried out to determine the exact effects of this adhesive material.

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