THE MILD ANESTHETIC PROPERTIES OF
SULFUR HEXAFLUORIDE † ‡

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The recent report by Cullen and Gross (1) on the anesthetic properties of argon and xenon stimulated the thought that other inert gases might have anesthetic properties. Sulfur hexafluoride has been described as being as inert as nitrogen, unaffected by heated potash, and unchanged at the softening temperature of hard glass, as well as being used commercially as an insulating agent for an electrostatic generator with applied potentials up to 5,600,000 volts (2). The inertness of sulfur hexafluoride is, in all likelihood, associated with the fact that fluorine is the most electronegative of all the elements and that fluorine has a marked tendency to evoke the highest covalency of which an atom is capable (3). The special (inert) position of sulfur hexafluoride among the nonmetallic halides is comprehensible since the coordination maximum of the central atom is already attained (4).

Cullen and Gross found no signs of anesthesia when xenon was used with rats but found that when used with human beings, it did have anesthetic properties. Shelanski (5) tested rats, guinea pigs and dogs with sulfur hexafluoride and observed no effects. Lester and Greenburg (6) used 80 per cent sulfur hexafluoride with rats and confirmed Shelanski’s observations. Specht and Brubach (7) confirmed Shelanski’s observations but also reported that “after some twenty to thirty breaths at a normal rate and volume, a slight to marked vertigo was experienced” (by the authors). It was, decided, therefore, to use sulfur hexafluoride with human subjects. Preliminary trials of breathing this gas produced definite subjective sensations of mild analgesia, so further experiments were carried out.

METHODS

Comparisons of analgesic effects of 79 per cent sulfur hexafluoride and 30 per cent nitrous oxide were made, using the Wolff-Hardy-Goodell apparatus. Twenty young adults were used as subjects. It was found

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that “black face make-up” provided a more uniform coating on the forehead than the India ink usually used, so that consistent control values were more easily obtained. The concentration of sulfur hexafluoride inhaled was determined as follows: using a closed circle absorber of an anesthetic machine and emptying the bag frequently, the subject inhaled pure oxygen until the nitrogen in his system had been replaced by oxygen as shown by the Beckman oxygen analyzer. Sulfur hexafluoride was then slowly introduced into the system until the oxygen concentration dropped to 21 per cent, where it was kept for five minutes before beginning the tests. The same technic of measuring the concentration of sulfur hexafluoride was used in the operating room with a 36 year old patient who was having a cervical biopsy. She had been premedicated with 10 mg. of morphine sulfate and 0.4 mg. of scopolamine hydrobromide, both given ninety minutes previously.

For comparative purposes, the subjects whose analgesic responses to sulfur hexafluoride had been measured were also allowed to breathe 30 per cent nitrous oxide in oxygen, using the inhaler from an anesthetic machine equipped with a rotameter. A breathing period of ten minutes was allowed for equilibration before measurements were made.

Results

The average elevation of pain threshold using 30 per cent nitrous oxide was 22 per cent. With the same subjects, the average elevation of the pain threshold breathing 79 per cent sulfur hexafluoride was 19 per cent. The earliest subjective sensations occurred when the sulfur hexafluoride concentration averaged 55 per cent. The sensations observed included analgesia when the subject pulled the hair on his own wrist, sleepiness, and a deepening quality of the voice of all subjects. Sulfur hexafluoride produced no metallic taste, as did nitrous oxide. Sulfur hexafluoride did not produce tinnitus or “buzzing” that was experienced with nitrous oxide. A few of the subjects were sleepier with sulfur hexafluoride, but some also were sleepier with nitrous oxide. Recovery when sulfur hexafluoride had been given was faster than with nitrous oxide. Four of the subjects felt slightly dyspneic. The observers also noted a definite deepening of the quality of the voice, which had been noted by the subjects.

Sulfur hexafluoride did not provide sufficient anesthesia for operating room use although it rendered the patient unconscious with premedication. Supplementation with pentothal (325 mg.) allowed the operation to be done satisfactorily. It might be noted here that 79 per cent nitrous oxide usually requires supplementation also.

Comment

These results give further support to the concept that definite chemical groups may not be essential for anesthetic action. Sulfur
hexafluoride is chemically similar to the inert gases xenon and argon, so its activity would seem to be due to physical rather than chemical properties. Its relative impotency may be ascribed to its extremely low solubility in water and hence in plasma, namely, 0.1 volume per cent at standard conditions. The corresponding value for helium is 0.87 volume per cent. The question arises as to why sulfur hexafluoride shows anesthetic properties and helium does not. The answer may lie in the fact that the oil solubilities of the two gases are quite different. The solubility of sulfur hexafluoride in olive oil is "less than 21 volumes per cent" (8), while that for helium is only 1.4 volume per cent. The oil-water ratio for helium is less than 2, while that for sulfur hexafluoride is about 200. It is conceivable that sulfur hexafluoride would have more potent anesthetic properties if its partial pressure were higher. The total atmospheric pressure in Denver is about 630 mm. of mercury so that partial pressure of sulfur hexafluoride used in this experiment was about 500 mm. of mercury. At sea level, 21 per cent oxygen could be maintained and a partial pressure of 600 mm. of mercury of sulfur hexafluoride would be obtained.

**Summary**

Sulfur hexafluoride, a chemically inert gas, has mild anesthetic properties when used with human beings.

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**References**

8. Data supplied by S. I. Hodson, of the General Chemical Division of the Allied Chemical and Dye Corporation.