PRESSURE REVERSAL OF ANESTHESIA REQUIRES WATER

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The pressure reversal of anesthesia, first reported by Johnson, Eyring and co-workers (1), is now firmly established. The mechanism of pressure reversal, however, remains in mystery. Although most of the high pressure anomalies in chemical reactions are observed above 1,000 bars, the reversal of anesthesia is complete less than 150 bars.

The ionic charges on the surface of proteins and cell membranes exert strong electrostatic forces upon the water dipole which amounts to about one million volts per cm. The attracted water molecules form a crystalline lattice structure. The water crystal is ice, but the ice formed around the electrical charges has different structure compared to the ordinary ice frozen at 0°C. The ice polymorphism under pressure is well known and the ice-I is the only structure that floats in water. All other ice structures are heavier than water, and the ice formed around the electrical charges has structure similar to ice-III which is about 15% heavier than water. Therefore, water molecules around the charges decrease its volume 15%, a phenomenon known as electrostriction.

We advocate that anesthetics induce conformational change of proteins and lipid membranes to expose the hydrophobic parts of these structures. As a result, ionic charges originally exposed to the interface in an awake state are displaced from the boundary and release the electrostricted water molecules, resulting in the expansion of the total volume. Due to this volume expansion, anesthesia is susceptible to the pressure according to the Brown-Le Chetelier principle.

Thus, anesthesia is a phenomenon occurring at the water-macromolecular boundary where the cluster of water molecules changes their structure cooperatively between the electrostricted compact awake state and the anesthetized expanded state. Presumably other water structures contribute to the volume change in a minor degree.

Our theory predicts that the pressure reversal of aneshtesia occurs only in the presence of water molecules. To test this hypothesis we used elastomers which responds to inhalation anesthetics by expansion.

White et al (2) reported that natural and synthetic rubbers expanded when they were exposed to anesthetic vapors. The expansion of rubber membrane by anesthetics was dose-dependent and reproducible. A commercial product (Draeger Narkotest Meter) has been in use to measure the concentrations of halothane on this principle.

We used a thin membrane of a silicone rubber (dimethylsiloxane) with a thickness of 0.1 mm. Stretching of the rubber membrane (80 mm x 5 mm) was controlled by a servomoter and a follow-up potentiometer and the created tension was measured by a Nihonkoden force-displacement transducer. The pressure-length diagram was recorded on an X-Y recorder from the output of the transducer and the potentiometer. The whole system was placed in an Autoclave pressure chamber with a custom made cover through which electric leads are wired. Following the administration of halothane vapor and an equilibrium of the rubber membrane tension was reached, pressure was applied with helium up to 140 bars. The gases inside the chamber were continuously mixed by a small electric fan.

Application of 7.2×10^{-2} bars halothane displaced the force-length diagram to the longer side in parallel to the control, and at 8 gm tension the membrane length was stretched by 0.91%. The application of helium pressure up to 140 bars reversed the stretching of the membrane only about 33%. The force-length diagram under pressure was parallel to the control.

Complete reversal of the expansion requires much higher pressure than those used for the in vivo studies. We postulate that the discrepancy of the magnitude of pressure reversal of anesthesia between the two is attributable to the absence of water molecules in the synthetic elastomer expansion by anesthetics.

References:

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2. White DC, Wardley-Smith B, Halsey MJ: Elastomer as analogues of anesthetic receptors: Brit J Anesth 44:1020-1024, 1972