Title : DESTRUCTION OF INTERFACIAL WATER STRUCTURE AS A CAUSE OF VOLUME EXPANSION BY ANESTHETICS

Authors : S. Kaneshina, Ph.D., H. Kamaya, M.D.,Ph.D. and I. Ueda, M.D.,Ph.D.

Affiliation: Department of Anesthesia, University of Utah College of Medicine, Salt Lake City, Utah 84132 and Veterans Administration Medical Center, Salt Lake City, Utah 84148

It is established that anesthetics expand cell membranes and a high pressure antagonizes it. It is generally assumed that the membrane expansion by anesthetics is attributable to the phase transition of the phospholipid, in which the lipid tails of the phospholipid change from the all-trans conformation (small volume) to the gauche rotation (large volume). The interfacial actions of anesthetics are grossly ignored except by Shieh et al (1) who reported that the inhalation anesthetics did not penetrate deep into the lipid core of the phospholipid bilayer vesicles. Eyring et al (2) and Ueda et al (3) emphasized the importance of the state of water molecules, hydrogen-bonded to the membrane surface, for the volume expansion induced by anesthetics. Our theory is often confused with the Pauling-Miller microcrystal theory, but the two are completely opposite. The microcrystal theory advocates the formation of the Ice-I-like structure, and our theory postulates the destruction of the Ice-III-like structure.

An aqueous solution of nonionic surfactants becomes suddenly turbid on being heated to a critical temperature, known as the cloud point, and the solution separates into two phases. This phase separation is caused by the partial dehydration of the hydrophilic surface of the surfactant micelles and accompanies with the volume expansion. This volume expansion is cuased mainly by the destruction of the high-density hydrogen-bonded water structure at the hydrophilic surface and not by the disordering of the lipid core. It will be shown that inhalation anesthetics decrease the cloud-point temperature of aqueous solution of a nonionic surfactant and increase the apparent molal volume due to the release of the hydrogen-bonded water molecules.

METHODS: Homogeneous hexa(oxyethylene) dodecyl ether was obtained from Nikko Chemicals (Tokyo, Japan). Its purity was checked by gas chromatography and found to show a single peak. Water was purified by triple distillation, once from alkaline potassium permanganate solution. The cloud points of nonionic surfactant solutions under high pressure were determined by a Hitachi 139 UV-visible spectrophotometer with the high pressure cell with sapphire windows, which was described in a previous study. The densities of the surfactant solutions with or without anesthetics were measured as a function of temperature by using Pyrex glass pycnometers with a capacity of about 10 cm^3. The error in measurements was less than $\pm$ 2x10^{-5} g/cm^3. The temperature was controlled within $\pm$ 0.01°K.

RESULTS: The cloud-point temperature of 1.0% (w/w) surfactant solution was 49.8°C, which was in good agreement with the value in the literature. The cloud-point temerature decreased linearly with the increase of the concentration of anesthetics. The concentrations of methoxyflurane, halothane and enflurane to depress one degree C in the cloud-point temperature were 0.51, 0.71 and 0.78 mmolal, repectively. Hydrostatic pressure increased the cloud-point temperature in the absence and presence of the anesthetics. The change of the apparent molal volume at the cloud point was estimated to be 2.2 cm^3/mole (larger at higher temperatures) in the absence of anesthetics. This value decreased in the presence of anesthetics, dose-dependently.

DISCUSSION: At the cloud point, two phases are in equilibrium. From the dependence of the cloud-point temperature upon the pressure, the Clausius-Clapeyron equation describes the ratio of the changes between the molal volume and entropy. The apparent molal volume changes were measured by pycnometry and the entropy changes were estimated from the quation. They are listed in the next table.

	$(\partial T/\partial P)$ °K/bar	ΔV cm^3/mole	ΔS J/°K·mole
Without Anesthetic	1.32x10^{-2}	2.2	16.9
Methoxyflurane 2.4 mmolal	1.37x10^{-2}	2.0	14.8
Enflurane 3.5 mmolal	1.53x10^{-2}	1.7	11.3

The volume change at the cloud point is reduced by the presence of anesthetics. Since partial dehydration of the hydrophilic group is the major change which takes place at the cloud point, the reduction of ΔV by anesthetics indicates that the association of the anesthetics to the surfactant micelles favors the destruction of the structured water at the interface. That is, the hydrogen-bonded water, which should be released at the cloud point is likely to be released in advance by the presence of anesthetics. The positive volume change is also caused by the elimination of hydrocarbon-water contact. But the contribution of the hydrophobic hydration to the phenomenon of cloud point is considered to be minor.

REFERENCES:

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