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In reply:—Molecular models of anesthetic drug action: Read the music before playing the song.

The statement of Dr. Hanukoglu that "In Trudell's model the basic principle is that anesthetic drugs fluidize membrane lipids" betrays a complete misunderstanding of the concepts I have described in diagrams and text.[1] A lateral phase separation in a biological membrane conveys to integral membrane proteins properties that are entirely different from those resulting from membrane fluidity. In fact, in my model the suggestion that anesthetic agents destroy lateral phase separations in membranes means that the environment of the protein becomes *more rigid* with respect to lateral expansion.

Historically, around 1970 a number of workers, including Seeman, Bangham, Hubbell, Metcalfe, Burgen, Smith, and myself, observed that various anesthetic agents increase the internal fluidity of membranes in several model systems. In general, neither the investigators mentioned nor other researchers were able to relate the small anesthetic-induced increase in membrane fluidity to a molecular mechanism of anesthesia. That is, we could not explain how a slight change in membrane fluidity would affect the sodium channel or the components of synaptic transmission. This frustration led others to study the direct interaction of anesthetic agents with protein, and Hill, Jain, and myself, and several others to study the effects of anesthetic agents on the phase behavior of synthetic membranes.

The direct binding of anesthetic agents to proteins, as well as modification of protein function, has been well documented. The possibility remains that this direct drug–protein association is the primary effect of anesthetic agents. On the other hand, I have shown that an anesthetic agent produces more than a one-hundred fold greater effect in a part of a membrane containing a lateral phase separation than in a homogenous membrane. I have used this amplification effect of phase separations to suggest molecular details for the mechanism of action of anesthetic agents. Careful reading will demonstrate that my model is very different from that of Lee, which suggests that local anesthetics may fluidize the phospholipids that form the immobilized halo around membrane proteins.[2] My model is somewhat like that proposed in the Ph.D. Thesis of Browning,[3] although he focuses on membrane asymmetry produced by local anesthetics, rather like that suggested by Sheetz and Singer in 1974.[4]

Through a misinterpretation of my model, Dr. Hanukoglu stated: "Trudell suggests that the increased fluidization would result in an inhibition of fusion . . ." and went on to say that this conflicts with experimental evidence. In fact, I presented the evidence of others that the existence of lateral phase separations are important for vesicle fusion. I then reasoned that since anesthetic agents destroy lateral phase separations, the exocytosis process may be modified. Indeed, it is likely that calcium acts as a trigger for exocytosis by means of lateral phase separations.

Finally, the ability of various investigators to detect positive,[5] biphasic,[6] or no[7] effect of anesthetic agents on membrane fluidity depends on: 1) their estimation of drug concentration in a membrane exposed to a clinically-used concentration of a particular anesthetic; 2) the model system they investigate; 3) the ability of their measurement technique to detect small changes. The sum of these effects has been reviewed recently by Miller.[8] I know of no investigator who has failed to detect a change in lateral phase separation properties with a low concentration of an anesthetic agent.

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Location of CVP Catheters

To the Editor:—Drs. Burgess, Marino and Peuler[1] are not correct in their claim that the effects of head position on the location of venous catheters had not been previously reported. We published our findings from a randomized trial in 46 patients in 1975.[2] In contrast to Dr. Burgess and his co-workers, we found that there seemed to be no benefit from turning the patient's head towards the side of insertion. Neck compression provided a quick and simple method for detecting a malpositioned catheter tip in the internal jugular vein, an increase in the recorded pressure of 10 cm H_2O or more being seen when pressure was applied to the root of that side of the neck.

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Topical Anesthesia Lessons Sore Throats from Tubes

To the Editor:—Dr. Menias,[1] in discussing the article by Loeser *et al.*,[2] speculated that the use of lidocaine, 5 per cent, ointment might have been responsible for the appearance of the sore throats reported in that study. He cites his clinical impression that the use of non-anesthetic lubricants has decreased the incidence of postoperative sore throat in his patients. In 1965, Lund and Daos[3] reported data that do not support Dr. Menias' supposition. They examined the incidence of postoperative sore throat in a series of 1,025 patients whose tracheas were intubated during general anesthesia. Patients were assigned to one of five treatment groups in which the endotracheal tubes were coated with: 1) nothing; 2) a heavy viscous base; 3) a heavy base containing lidocaine, 5 per cent; 4) a light foamy base; or 5) a light foamy base with pramoxine, 1 per cent. The incidences of sore throat in groups 2, 4 and 5 were virtually the same as that in the control group (about 22 per cent). Sore throat was significantly less frequent (6.6 per cent, $P < 0.001$) only in group 3. Available evidence indicates that lidocaine, 5 per cent, ointment decreases, not increases, the incidence of postoperative sore throat.

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