In Vitro Studies of Human Cardiac Tissue

An important question that frequently confronts anesthesiologists concerns the effects of general anesthetics on the heart. For years, the safety of anesthetics has been dictated by the magnitude and nature of their effects on cardiac function. It is now clear that the response of the heart is the result of a complex interaction of factors, including reflex changes in activity of the autonomic nervous system, alterations in transmembrane electrical potentials, changes in myocardial contractility, and altered metabolic phenomena in cardiac fibers. In addition, there is little doubt that the response of the heart to anesthetics is determined to a substantial degree by the age of the patient, the presence or absence of pathologic changes, and drug interaction at receptor sites.

Most of our current knowledge of the principles involved in these phenomena has been derived from laboratory experiments (either whole animals or tissue preparations) and from data compiled from empirical clinical observations. In the practical application of anesthetic procedures and analysis of clinical data, the anesthesiologist certainly must question the extent to which the results of laboratory experiments are applicable to the patient. The problems of translating physiologic and pharmacologic responses from one species to another have been discussed many times. A related, but rather infrequently considered, problem highly relevant to anesthesia concerns the extent to which it is possible to extrapolate data from “normal” cats, dogs, and rats to human patients who are “abnormal” as a result of either premedication (e.g., with vagolytics, digitalis, sedative, or narcotics) or pathologic changes which modify, and perhaps seriously compromise, cardiac function, or both.

In most attempts to identify the mechanisms of the electrical and mechanical actions of drugs on the heart, it has been assumed that the same rules and limits apply to normal and to abnormal cardiac fibers, and that studies of normal fibers might be used to explain either abnormal activity or the mode of action of drugs. (The latter is particularly evident in studies of the mechanisms of cardiac arrhythmias and the responses to antiarrhythmic drugs.) With open-heart surgery and the consequent availability of samples of human cardiac tissue, it is now possible to test these assumptions and analyze cardiac drug response directly in the absence of the indirect factors inherent in the intact human heart.

In this issue of the Journal, Ko and Paradise describe the effects of halothane on myocardial contractile force and glucose metabolism in human atrial appendages isolated from 7-10-year-old patients undergoing cardiac surgery. This work is an extension of previous studies of a similar nature using isolated rat atria by Paradise and his co-workers, many of which have been reported in Anesthesiology. The data for human atria provided in the pres-
ent paper are essentially similar to those previously obtained from studies of the rat. In both tissues a halothane-induced negative inotropicism is accompanied by an interference with glucose metabolism prior to completion of the initial steps of glycolysis. This interference may be the result of impairment of glucose uptake by the cell or inhibition of glucose breakdown within the cell at an early point in the glycolytic pathway (prior to the phosphofructokinase step). The similarity of results from rat and human tissues is suggestive evidence that the presence of pathologic changes in the hearts from which these preparations were excised (not detailed by the authors but assumed) did not alter the basic response. At first glance this would seem to counter the argument presented earlier in this article. However, from my experience with isolated human preparations, and from the published data of others, I would predict that had their attention been focused upon transmembrane electrical phenomena in these preparations, or had Ko and Paradise used atrial appendages obtained from the adult rather than the child (in a study of either electrical or mechanical phenomena), the fit between the data obtained from human preparations and the laboratory analog would have been less convincing. This is not meant to be a criticism of their work, and I do not question the relevance of their findings. As Ko and Paradise have stated, it is much more difficult to do quantitative experiments on human (rather than animal) tissues owing to the difficulty in obtaining samples and their heterogeneity.

A major point that I would emphasize, and I am certain that Ko and Paradise would agree, is that if physiologic and pharmacologic studies of human cardiac tissue of this type ultimately are to be useful to clinicians, we must not permit the experimental designs to be rigidly limited by the problem of tissue heterogeneity. Rather, we must eventually undertake the difficult task of broad-spectrum analyses of detailed drug responses in each of the various types of cardiac fibers (i.e., the myocardium as well as specialized conducting tissues) under each of the various conditions presented clinically. It is probable that ultimately a large number of laboratory analogs will be employed to simulate human cardiac responses, for we can be almost certain, even at this preliminary point, that no single species can adequately serve as a model for man.

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Anesthesia

HEAT BALANCE The use of air conditioning in the modern operating theater to provide comfortable conditions for the surgical team has led to declines in the body temperatures of patients. Heat can be lost by radiation to surroundings, by evaporation from the wound, lungs and skin, and by the use of cold intravenous fluids. During lobectomies and pneumonectomies in 15 patients, the deep body temperatures decreased by 1.15 degrees C over three and a half hours, and the average surface temperature decreased by 2.6 C, corresponding with a total heat deficit of 78 kcal, or 21 kcal per hour. This deficit must be repaid later. The comfort of the patient is also affected by operative heat deficit. In the presence of cold stimuli from the surface, the recovering surgical patient will feel cold and shiver, and this discomfort often produces restlessness, which requires repeated doses of narcotic sedation. One of the results of observing central and surface temperatures is to emphasize the necessity for measuring both in all operations where heat balance is likely to be affected. (Vale, R. J., and Lunn, H. F.: Heat Balance in Anaesthetized Surgical Patients, Proc. Roy. Soc. Med. 62: 1017 (Oct.) 1969.)