The Anesthesiologist and His Position in Clinical Pharmacology

Clinical pharmacology is in an anomalous position relative to primary patient care. Since the specialty organization of patient care is largely along body-system lines (e.g. neurology, cardiology, gastroenterology, urology), the clinical pharmacist as such, who relates to all systems, finds himself in an inter-system discipline. Consequently, it is difficult for him to identify himself as a specialist responsible for primary patient care. A general clinical pharmacist in the hospital setting, rather than being in a natural position automatically supported and strengthened by reason of the institution's organizational structure, often finds himself more dependent on good interpersonal relationships than on his scientific capabilities. When he wishes to be responsible for primary patient care rather than acting solely in the capacity of a consultant, the clinical pharmacist automatically must compete with other specialists in medicine who consider themselves competent in the use of drugs; or, alternatively, he is relegated to caring for patients who are not cared for by other specialists in that particular institution.

The anesthesiologist—who is, in effect, a specialized clinical pharmacist—is in an enviable position. In the usual organizational structure of hospitals every patient who comes to surgery is automatically directed his way for therapy, and he becomes the primary attending physician for that component of medical care related to anesthesia. He is, in effect, in a direct line of referral, and he has a "captive audience" insofar as the patients are concerned. By the same token, the anesthesiologist assumes considerable responsibility, because he is obligated to treat every patient referred to him and he must give each patient definitive care irrespective of his knowledge or capability in any particular clinical field. He is not in a position to reject the patient or refer him to another physician because the medical problem is out of his area of expertise, although he might on occasion obtain consultative assistance.

Thus, when a patient has a disease or is receiving drugs that may complicate the management of anesthesia, the anesthesiologist must have sufficient background and training to determine the proper course of action. Some insight into the pathophysiology of disease is essential, since disease may influence the responses of patients to anesthetic agents and increase the possibility that complications may arise during anesthesia. I should like to give a simple example of how alteration of the physiologic state of a patient may sometimes be related to a complication observed during anesthesia, namely cardiac arrhythmias.

As a medical student I observed the standard experiment in which the myocardium of an animal was sensitized by cyclopropane anesthesia, arrhythmias were then produced by intravenous administration of epinephrine, and ventricular fibrillation ensued. It was a common observation that ventricular fibrillation usually did not occur when the animal was hypotensive. Why did hypotension protect against ventricular fibrillation?

A number of years later, Russell Huggins, a colleague working in the laboratory with me at Baylor, re-evaluated this problem using norepinephrine, which had just been made available for clinical investigation. We found consistently that reflex bradycardia occurred when blood pressure was increased to a certain level. The bradycardia could be blocked by atropine, indicating that it was largely a vagal response to the increase in blood pressure—i.e., carotid sinus stimulation. We also found that increases in blood pressure far in excess of the normal levels were associated with cardiac extrasystoles and, on occasion, more severe arrhythmias. The answer to our original question became apparent. The fatal ventricular fibrillation probably resulted from
the combination of the epinephrine effect on the myocardium and the subsequent increase in vagal activity, which decreased myocardial refactoriness. When the blood pressure was decreased below a critical level, reflex vagal activity was abolished, thereby eliminating the combination of events needed to induce fibrillation.

This same observation subsequently influenced clinicians in their use of vasopressor agents for treating hypotension secondary to myocardial infarction. In this situation it may be hazardous to increase systolic pressure above 100 to 110 mm Hg, since fatal arrhythmias may occur. Now, when vasopressor agents are administered to hypotensive patients after myocardial infarction reflex vagal stimulation is avoided by keeping the blood pressure as low as possible consistent with maintaining adequate tissue perfusion to the brain and myocardium. Appreciation that abnormal increases in blood pressure stimulate vagal reflexes, which in turn reduce myocardial refactoriness and predispose to arrhythmias, especially in the presence of excess catecholamines, enables us to establish better guidelines for the use of vasopressor agents in patients with myocardial infarctions, as well as in patients under anesthesia. The therapeutic interplay between the anesthesiologist and the clinical therapist is obvious.

Hypertensive patients who have been receiving antihypertensive drugs prior to operation present another challenging problem to anesthesiologists. It was once thought that patients receiving a drug, such as reserpine, which depresses the sympathetic nervous system are more susceptible to hypotension during surgery than healthy patients. We now know that this is not the case. Patients who have been taking reserpine are more responsive to vasopressor agents such as norepinephrine than are normotensive patients, since the neuroeffector site is not affected by the anti-hypertensive drug. When hypotension does occur in patients taking reserpine, hypovolemia or excessive depression from anesthetic drugs must be suspect. When the cause is hypovolemia, adequate infusion of fluids, and perhaps the temporary use of vasopressors, will usually correct the problem. When the patient is allowed to remain excessively hypotensive for an extended period of time he may become unresponsive to fluids or vasopressors and develop a state quite akin to irreversible shock.

Another group of drugs used in the treatment of hypertension that may cause serious problems with blood pressure or cardiac rhythm during anesthesia comprises the diuretic agents. Every patient who has been taking a diuretic (other than anti-aldosterone agents) as part of his antihypertensive medication has some deficit of total body sodium and potassium. An optimum concentration of these electrolytes at the neuroeffector site of blood vessels is necessary to maintain optimum transmission of sympathomimetic (vasoconstrictor) impulses. When this optimum concentration is decreased, vessels respond less effectively to stimulation by catecholamines. Thus, in the patient who has been receiving a diuretic, blood pressure may decrease excessively during anesthesia and operation and may not respond well to fluid therapy or vasopressor agents. Rapid correction of the total body sodium or potassium deficit is necessary before other types of therapy will be fully effective. Severe hypokalemia also predisposes to serious arrhythmias, including ventricular fibrillation. Treatment consists of rapid correction of plasma potassium levels through the parenteral administration of potassium.

It is evident that the anesthesiologist must have extensive knowledge of pathophysiology and know how abnormal physiologic states may affect responses to anesthetic drugs. His knowledge of the pharmacodynamics of drugs should embrace not only anesthetic agents but also drugs that might have adverse effects during anesthesia and drugs whose pharmacodynamics might be altered by anesthetics. To be a well-informed anesthesiologist is also to be a good clinical pharmacologist.

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