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 pharmacologist 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 pharmacologist 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 pharmacologist 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 pharmacologist—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 vaga! activity, which decreased myocardial
refractoriness. When the blood pressure was
decreased below a critical level, reflex vaga! activity was abolished, thereby eliminating the
combination of events needed to induce fibril-
lation.

This same observation subsequently influ-
enced 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 arrhyth-
mias may occur. Now, when vasopressor
agents are administered to hypotensive pa-
tients after myocardial infarction reflex vaga! 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 ab-
normal increases in blood pressure stimulate
vaga! reflexes, which in turn reduce myo-
cardial refractoriness and predispose to ar-
rhythmias, 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 anesthesi-
ologist and the clinical therapist is obvious.

Hypertensive patients who have been re-
ceiving antihypertensive drugs prior to op-
eration present another challenging problem to
anesthesiologists. It was once thought that
patients receiving a drug, such as reserpine,
which depresses the sympathetic nervous sys-
tem are more susceptible to hypotension dur-
ing 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, hypov-
olemia or excessive depression from anes-
thetic drugs must be suspect. When the
causes 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 ex-
cessively 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 treat-
ment of hypertension that may cause serious
problems with blood pressure or cardiac
rhythm during anesthesia comprises the di-
uretic agents. Every patient who has been
taking a diuretic (other than anti-aldosterone
agents) as part of his antihypertensive medica-
tion 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 trans-
misson of sympathomimetic (vasoconstrictor)
impulses. When this optimum concentration is
declined, vessels respond less effectively to
stimulation by catecholamines. Thus, in
the patient who has been receiving a diuretic,
blood pressure may decrease excessively dur-
ing 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 seri-
ous arrhythmias, including ventricular fibril-
lation. Treatment consists of rapid correction
of plasma potassium levels through the paren-
teral administration of potassium.

It is evident that the anesthesiologist must
have extensive knowledge of pathophysiology
and know how abnormal physio!ogic 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 pharma-
codynamics might be altered by anesthetics. To
be a well-informed anesthesiologist is also to
be a good clinical pharmacologist.

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