dently be predicted. Nevertheless, although recovery from a dual block is slow it is always steady, and in the vast majority of patients it is far better to go on ventilating the patient adequately and to rely on patience!

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Connecting Links to Solve Discrepancies of Actions of Pressor Drugs

About five years ago, the cardiovascular effects of some commonly used pressor amines were reviewed in the Journal. The review article ended as follows: “It is important to emphasize the fact that the available information on the mechanism of cardiovascular effects of pressor agents has been derived from two types of preparations: anesthetized animals and unanesthetized human subjects. The connecting link of studies on anesthetized subjects would be a welcome addition that might help resolve some of the existing discrepancies.”

It is pleasant to note that elsewhere in this issue, one “connecting link” is offered to resolve the discrepancies regarding the cardiovascular effects of one pressor drug, mephenetermine. Li, Shimosato and Etsten report the hemodynamic effects of mephenetermine in human subjects under spinal anesthesia. The three conclusions and the significance of each are as follows:

(1) The hemodynamic responses following the administration of mephenetermine to hypotensive subjects under spinal anesthesia consist largely of a combined increase in cardiac output and total peripheral vascular resistance. The increase in cardiac output is to be expected because of the known positive chronotropic and inotropic actions of mephenetermine. The simultaneous increase in total peripheral vascular resistance is surprising because, hertofoe, mephenetermine has been shown to be free of any local vasoconstrictor action when tested in various preparations, with the exception of two abstracts describing a local vasoconstrictor action. Two possibilities remain to explain the increase in peripheral vascular resistance, other than a local vasoconstrictor action. First, is the release of circulating catecholamines when mephenetermine is administered intravenously, a possibility demonstrated in the isolated heart perhaps readily tested in the patient by measurements of blood levels. Secondly, is a stimulation of the medullary vasoconstrictor centers by mephenetermine, a likely explanation requiring direct proof.

(2) The simultaneous occurrence of increase in blood pressure, cardiac output and peripheral resistance reported to occur following the administration of mephenetermine in subjects under spinal anesthesia has been previously described for norepinephrine in human subjects with either atropine or gangliiceps blocking drugs. A hemodynamic change in which all three measurements simultaneously increase cannot be elicited by any pressor drug if the autonomic nervous system is not blocked. For example, mephenetermine in normotensive individuals, initially increases output and later increases peripheral vascular
resistance but not both simultaneously. Nor-
epinephrine, in the absence of autonomic
blockade, causes an increase in vascular re-
sistance but a decrease in cardiac output. As
long as the autonomic nervous system is intact
the baroreceptor reflexes can automatically com-
penstate for a primary increase in output or
peripheral resistance by a secondary decrease of
the other.

(3) The hemodynamic response of the hu-
man subject under spinal anesthesia to meph-
entermine depends upon the initial circulatory
status prior to the administration of the drug.
When the initial cardiac output values are low, there is a significant increase of the car-
diac output following the administration of mephentermine, but when the initial output
values are high, the changes in output are
minimal. Li and his collaborators emphasized that such a pattern of response obeys the
law of initial values which states that "the intensity and direction of the response of any
function of the organism to the stimu-
lus depends to a great extent upon the initial value (level) of that function at the moment of
the stimulus." The observations supporting the law would have been more convincing
if they were based on multiple observations in the same individual, each one with two or
more hypotensive levels of blood pressure and cardiac output, rather than single observa-
tions from several individuals. Specifically, meph-
entermine could have been tested under two levels of spinal anesthesia and hypotension in
the same individual. In the anesthetized dog, the increase in cardiac output during anox-
emia was compared at various levels of cardiac
output. When cardiac output was inten-
tionally reduced by bleeding, the percentage
increase during anoxemia was about two times
greater than that encountered in the same ani-
mal prior to bleeding. These observations, derived from each of a group of dogs, support
the law of initial values. On the other hand,
not all cardiovascular responses follow such a
pattern. For instance, when the common car-
rotids are temporarily occluded, the pressor
response is less intense if the control level of
blood pressure is reduced. The law of initial
values will require direct proof in each situ-
tion.

The above comments should not detract
from the scientific value of the article under
consideration. The most significant feature of
the article is the availability for the first time
of a complete study of the hemodynamic
effects of a drug directly on hypotensive pa-
ients. The results have served the purposes of
identifying which of the known actions of
the drug are of primary importance clinically
and also of raising additional questions which
require further studies.

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