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Correspondence

Histamine, *d*-Tubocurarine, and CSF Pressure

To the Editor:—I congratulate Drs. Tarkkanen, Laitinen, and Johansson on their excellent article (ANESTHESIOLOGY 40:247–251, 1974), which documents increases in cerebrospinal fluid (CSF) pressure after 0.6 ± 0.1 mg/kg *d*-tubocurarine and relates this change to the cardiovascular effects of the drug.

May I offer the following comments:

1) The hypotensive action of *d*-tubocurarine in animals and in man is well known to be due to a combination of autonomic ganglionic blockade and histamine release.[1,2,3] It is not known which of these factors is the more important in man.

2) Histamine release secondary to *d*-tubocurarine and other agents is more prominent after large intravenous bolus dosage than following incremental dosage.[4]

3) Prominent features of the histamine-release response are: sudden hypotension with delayed onset, approximately 60–90 seconds after drug administration; occasional brief antecedent hypertension (15–30 seconds); tachycardia peaking during the recovery phase of the hypotensive "dip"; occasional hypertensive "rebound"; tachyphylaxis.[4]

4) The initial hypotensive phase during histamine release is due to the direct arteriolar-dilating action of histamine and possible other vasoactive polypeptides released from vascular mast cells together with histamine.[4]

5) The time course of the above responses increases with the severity of the histamine release, but after a moderate reaction, 5–10 minutes is typical.[4]

6) Histamine has been shown to cause increases in CSF pressure in man.[5]

I make the above points in order to indicate that the increases in CSF pressure described by Tarkkanen *et al.* are probably due to histamine release, and thus are secondary effects of the action of histamine, not the result of a direct action of *d*-tubocurarine on the cardiovascular system. Figure 1 in the article beautifully shows the coincidence of the time courses of all the above responses, the classic "delayed depressor response" described by Paton.[4]

What is the clinical lesson to be learned in view of the above evidence and discussion? Simply that, as we all know, it is safer to administer *d*-tubocurarine, and probably any other drug, in incremental fashion rather than as a large single bolus, if we desire to avoid unwanted side-effects.

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