*LETTER TO EDITOR*

## VASOPRESSOR RESPONSE TO ISOPRENALINE

(Received on October 20, 1980)

Sir,

Isoprenaline has a minor adrenoceptor agonistic activity and a limited vasopressor response to this drug does occur following large doses, after blockade of the prominent β-adrenoceptor mediated vasodilatation (1). We found that isoprenaline in relatively small doses, which normally produce vasodepressor response, can exhibit dose dependent vasopressor activity in dogs, provided the animals are pretreated with propranolol, guanethidine and cyproheptadine.

Mongrel dogs of either sex weighing between 7-20 *kgs* were anaesthetised with pentobarbitone sodium (35 *mg/kg.* ip). Right femoral vein was cannulated for drug administration. Right carotid artery was connected to a mercury manometer for recording blood pressure. A period of 30 min was allowed for stabilisation of the preparations.

Cyproheptadine (400 and 800 *μg/kg)* produced a mean fall in blood pressure of 17.7±7.20 (n=3) and 31. 5±6.0 (n=6) mm of Hg respectively. The fall was transient and resistant to propranolol (4 *mg/kg*, iv). Cyproheptadine (400 *μg/kg*) reduced the vasodepressor response to isoprenaline (1.0 *μg/kg*) to 42% (n=3). Guanethidine produced a biphasic effect on blood pressure, a primary transient fall being followed by sustained rise. Vasodepressor response to isoprenaline was hardly altered by guanethidine (n=3).

In dogs treated with propranolol, (4 *mg/kg* slow IV infusion) the blood pressure was hardly altered; response to isoprenaline was totally abolished. A subsequent injection of either guanethidine (1 *mg/kg)* or cyproheptadine (800 *μg/kg)* did not result in the appearance of any vasopressor activity to isoprenaline (n=6). However, when both drugs were administered serially in either of the sequences, isoprenaline produced a dose dependent vasopressor response (Fig. 1-A) in dose range of 0.125 to 0.5 *μg/kg.*

Subsequent experiments revealed that administration of propranolol after (n=3, Fig. 1-B) or in between (n=3) a serial administration of guanethidine and cyproheptadine

or cyproheptadine and guanethidine also resulted in the appearance of vasopressor responses to isoprenaline. Likewise, without propranolol, guanethidine and cyproheptadine failed to bring out the pressor responses to isoprenaline (n=3, Fig. 1-B).

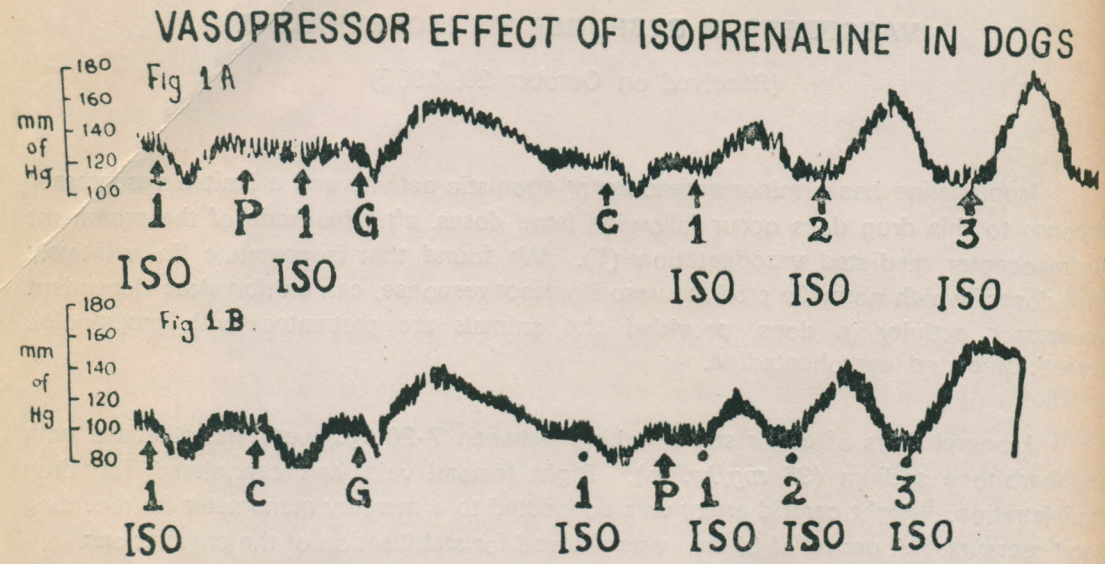


Fig. 1-A & B: Dog, pentobarbitone anaesthesia. Effect of isoprenaline (ISO), 0.125, 0.5 and 1.0 *μg/kg* (at 1, 2 & 3, respectively) on blood pressure before and/or after administration of cyproheptadine, 800 *μg/kg* (at C), guanethidine 1.0 *mg/kg* (at G) and propranolol, 4.0 *mg/kg* (at P). All injections were intravenous.

We concluded, that relatively small doses of isoprenaline can cause significant dose dependent vasopressor responses in animals pretreated with all three drugs, viz., propranolol, guanethidine and cyproheptadine. The experiments are in progress to seek explanation for roles played by guanethidine and cyproheptadine in this phenomenon.

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REFERENCE

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