

## The production of hypertension and the effects of some antihypertensive agents in the conscious unrestrained cat

R.H. POYSER, J.H. SHORTER & R.L. WHITING\*

Beecham Research Laboratories, Medicinal Research Centre, Harlow, Essex

The conscious cat with a permanently-implanted arterial catheter has been shown by Day & Owen (1970) to be very suitable for studying the effects of drugs on the cardiovascular system. In view of this we decided to explore the feasibility of producing hypertension in the cat with the aim of obtaining a model which might be of use for testing antihypertensive agents. A few brief reports on the production of hypertension in cats have appeared (Page, 1939; Zanchetti, Guazzi & Baccelli, 1966; Cohn & Notargiacomo, 1969; Guazzi, Ellsworth & Freis, 1971) but a study comparing methods and administering drugs has not been described.

A total of 22 cats have so far been used to study three methods of producing hypertension. Ten cats (group 1) had their left kidneys wrapped in cellophane (method of Page, 1939). Eight cats (group 2) had a figure of 8 ligature applied to the left kidney (method of Grollman, 1944). Four cats (group 3) had 500 mg of deoxycorticosterone implanted subcutaneously and for the following five weeks received 1% w/v NaCl solution as drinking fluid (method of Selye, Hall & Rowley, 1943). In each case the right kidney was removed.

Aortic pressures were measured directly using implanted cannulae (Day & Whiting, 1972).

All three methods succeeded in raising the BP which attained a diastolic level of  $>105$  mmHg (1 mmHg = 1.33 mbar) in most cats. Generally the rate of increase of BP was steady at approximately 5 mmHg per week over the first few weeks. In addition, some cats within groups 1 and 2 showed a transient hypertension and tachycardia within the first 5-7 days. However in four cats (two each of groups 1 and 2) an early rise in BP became severe and resulted in death within two weeks. Apart from these deaths the cats in groups 1 and 2 were in good condition throughout, but those with implanted deoxycorti-

costerone became unwell and lost weight.

Some antihypertensive agents have been administered orally as single doses to those cats of groups 1 and 2 with a stable hypertension.

$\alpha$ -Methyldopa (100-400 mg/kg), clonidine (25  $\mu$ g/kg), guanethidine (30-100 mg/kg), hydralazine (10-20 mg/kg) and pempidine (2.5-5 mg/kg) all caused falls in BP of 30-50 mmHg at 1 to 5 h after dosing with recovery to pre-dose values within 24 hours.

This preliminary study has shown that it is possible to induce a sustained high blood pressure in the cat which may be lowered by only single doses of some antihypertensive agents. In view of the ease of using the conscious cat for direct BP measurement, these results give encouragement to explore further the potential of this species in studies of hypertension.

We would like to thank May and Baker Ltd. for their gift of Pempidine Tartrate.

### References

- COHN, J.N. & NOTARGIACOMO, A.V. (1969). Clinical application of a simple, specific bioassay technique for measuring renin activity. *Am. J. Med. Sci.*, **257**, 344-351.
- DAY, M.D. & OWEN, D.A.A. (1970). The effect of reserpine on the pressor responses to angiotensin in the conscious cat. *Br. J. Pharmac.*, **39**, 414-427.
- DAY, M.D. & WHITING, R.L. (1972). An improved technique for the continuous measurement of arterial blood pressure in the conscious unrestrained cat. *Br. J. Pharmac.*, **45**, 182P.
- GROLLMAN, A. (1944). A simplified procedure for inducing chronic renal hypertension in the mammal. *Proc. Soc. exp. Biol. Med.*, **57**, 102-104.
- GUAZZI, M., ELLSWORTH, O.T. & FREIS, E.D. (1971). Influence of the adrenergic system in renovascular hypertension. *Cardiovasc. Res.*, **5**, 71-80.
- PAGE, I.H. (1939). The production of persistent arterial hypertension by cellophane perinephritis. *J. Am. Med. Ass.*, **113**, 2046-2048.
- SELYE, H., HALL, C.E. & ROWLEY, E.M. (1943). Malignant hypertension produced by treatment with deoxycorticosterone acetate and sodium chloride. *Can. Med. Ass. J.*, **49**, 88-92.
- ZANCHETTI, A., GUAZZI, M. & BACCELLI, G. (1966). Influence of sleep on circulation in normal and hypertensive animals. In: *Antihypertensive Therapy. Principles and Practice. An International Symposium*. pp. 74-95. ed. Gross, F. Berlin: Springer.