is presynaptic, there is probably an impairment of the noradrenaline uptake into the adrenergic nerves. Cocaine and surgical denervation inhibit the uptake of noradrenaline but they also seem to sensitize the isolated vas deferens by a "deformation" of the receptor area, thus altering receptor kinetics to allow increased receptor utilization.

Department of Pharmacology and Therapeutics S. DE MORAES
Faculty of Veterinary Medicine, F. V. CARVALHO
University of São Paulo, Brasil. R. D. WEHRLE

April 8, 1970

REFERENCES

AXELRED, J., HERTTING, G. & POTTER, L. (1962). *Nature Lond.*, **194**, 297
BARNETT, A., GREENHOUSE, D. D. & TABER, R. I. (1968). *Br. J. Pharmac. Chemother.*, **33**, 171–176.
BIRMINGHAM, A. T. (1967). *J. Physiol. Lond.*, **190**, 16P-17P.
BURGEN, A. S. V. & IVERSEN, L. L. (1965). *Br. J. Pharmac. Chemother.*, **25**, 34–49.
CARVALHO, F. V., MARTINS, M. C. & de MORAES, S. (1970). *Ibid., in the press.*
DE MORAES, S. & CARVALHO, F. V. (1968). *Pharmac.* (Basel), **1**, 129-134.
DRASKOĆZY, P. R. & TRENDELENBURG, U. (1968). *J. Pharmac. exp. Ther.*, **159**, 66–73.
FURCHGOTT, R. F., KIRPEKAR, S. M., RIEKER, M. & SCHWAB, A. (1963). *Ibid.*, **142**, 39–58.
HÄGGENDAL, J. & HAMBERGER, B. (1967). *Acta physiol. scand.*, **70**, 277–280.
HUKOVIĆ, S. (1961). *Br. J. Pharmac. Chemother.*, **16**, 188–194.
LANGER, S. Z. & TRENDELENBURG, U. (1969). *J. Pharmac. exp. Ther.*, 167, 117–142.
REIFFENSTEIN, R. J. (1968). *Br. J. Pharmac. Chemother.*, **32**, 591–597.
VARMA, D. R. & MCCULLOUGH, H. N. (1969). *J. Pharmac. exp. Ther.*, 166, 26–34.
WHITBY, L. G., AXELROD, J. & HERTTING, G. (1960). *Nature, Lond.*, **187**, 604–605.

Pentazocine and nikethamide antagonism

Pentazocine, a benzomorphan derivative, is in increasing use for the relief of pain. Like all analgesics it is capable of producing respiratory depression in man and possibly in some other species also. Because pentazocine is itself an opiate antagonist, respiratory depression produced by it cannot be reversed by nalorphine. It therefore seemed worth while to examine the possibility of using nikethamide to reverse the respiratory depression produced by pentazocine.

The respiratory minute volume of rabbits was measured with the aid of the Gaddum Respiration Recorder by methods described previously (Hunter, Pleuvry & Rees, 1968).

In a preliminary trial, pentazocine, 4 mg/kg, produced in rabbits significant respiratory depression in most animals. The administration of nikethamide, 25 mg/kg, produced a sharp increase in respiratory minute volume and a less distinct increase in respiratory rate in animals given 4 mg/kg of pentazocine 7 min previously (Table 1). The simultaneous administration of nikethamide and pentazocine produced significantly less depression of respiratory minute volume, but not of rate, than pentazocine alone. A dose of nikethamide of 25 mg/kg was also capable of producing an increase in respiratory minute volume and rate of respiration in an animal depressed by morphine (Table 1).

These findings point the way to the treatment of an emergency in which the administration of pentazocine produces an unexpectedly severe depression of respiration in the human subject.

Since this work was begun Kallos & Smith (1968) showed that naloxone can reverse the respiratory depression produced by pentazocine in human volunteers, and this finding is amply backed by experimental evidence in animals. Until naloxone

Table 1. *The effect of nikethamide* (25 mg/kg) *on the respiratory depression produced by pentazocine* (4 mg/kg) *and morphine* (8 mg/kg). Figures are means and standard errors of means, recorded immediately before and after the injection of nikethamide.

Drug	No. animals	Respiratory minute volume (% control) Before nikethamide	After nikethamide	Significance of difference *P*	Respiratory rate (% control) Before nikethamide	After nikethamide	Significance of difference *P*
Pentazocine	5	86 ± 3·2	110 ± 4·9	<0·01	79 ± 5·1	104 ± 4·8	<0·01
Morphine	5	16 ± 1·8	69 ± 10	<0·01	22 ± 1·6	35 ± 4·6	<0·05

Table 2. *The effect of giving nikethamide simultaneously with pentazocine.* Figures are means and standard errors of means.

	No. animals	Respiratory minute volume (% control) With nikethamide	Without nikethamide	Significance of difference *P*	Respiratory rate (% control) With nikethamide	Without nikethamide	Significance of difference *P*
7 min after injection	5	105 ± 2·4	92 ± 4·0	0·05	89 ± 3·0	91 ± 3·2	N.S. >0·05
15 min after injection	5	105 ± 2·9	93 ± 3·9	0·05	98 ± 2·3	96 ± 6·5	N.S. >0·05

becomes available for use in the United Kingdom, nikethamide remains a convenien antagonist should respiratory depression arise after the administration of pentazocine.

We are indebted to Dr. R. A. P. Burt for reading this text, to Mrs. H. R. Lane for help with the statistical analysis, and to the Sterling-Winthrop Research Division for generous supplies of pentazocine.

Department of Anaesthesia,
Royal Infirmary,
Manchester, U.K.

A. R. HUNTER
C. T. MAJOR

January 23, 1970

REFERENCES

HUNTER, A. R., PLEUVRY, B. J. & REES, J. M. H. (1968). *Br. J. Anaesth.*, **40**, 927–935.
KALLOS, T. & SMITH, C. (1968). *J. Am. med. Ass.*, **204**, 180.