References

Baba, W. I., Smith, A. J. & Townshend, M. M. (1967). *Q. Jl exp. Physiol.*, **52**, 416–421.
Civan, M. M., Kedem, O. & Leaf, A. (1966). *Am. J. Physiol.*, **211**, 569–575.
Finn, A. L., Handler, J. S. & Orloff, J. (1967). *Ibid.*, **213**, 179–184.
Leaf, A. (1965). *Ergbn. Physiol.*, **56**, 216–263.
Martin, D. W. (1964). *J. cell. comp. Physiol.*, **63**, 245–251.
Martin, D. W. & Curran, P. F. (1966). *Ibid.*, **67**, 367–373.
Orloff, J. & Handler, J. (1967). *Am. J. Med.*, **42**, 757–768.
Steinbach, H. B. (1933). *J. cell. comp. Physiol.*, **3**, 1–27.
Ussing, H. H. & Zerahn, K. (1951). *Acta physiol. scand.*, **23**, 110–127.

Adrenergic receptors in the ruminal wall of sheep

SIR,—Ruminants suffering from infectious diseases often show a reduction in rumen motility, especially during the fever period. This effect can also be observed after injection of infusion fluids contaminated with pyrogens, or purified lipopolysaccharide from Gram-negative bacteria (Miert, 1966). We considered the possibility that the reduction in rumen motility after an injection with lipopolysaccharide is the result of sympathetic stimulation or adrenaline release (Miert, 1968). This led to a study of the adrenergic receptor in the rumen.

We know from the literature (summarized by Habel, 1956), that in the unanaesthetized ruminant with intact vagi, adrenaline inhibits rumen motility. In unanaesthetized vagotomized sheep it caused a single slow contraction of reticulum, rumen and abomasum. An intravenous injection of adrenaline in the anaesthetized goat results also in a contraction of the rumen.

Adrenaline on isolated strips of ruminal wall inhibited or stimulated the contractions (Dussardier & Navarro, 1953; Sanford, 1958). Duncan (1954) noted that the most characteristic effect of adrenaline on strips from the rumen abomasum and omasum of sheep was brief inhibition followed by contractions. With low doses, inhibition was the main effect, with high doses only strong contractions were observed. Dussardier & Navarro (1953) gave particular attention to the effects of adrenaline on strips of the abomasum. They noted that contractions from adrenaline could not be suppressed by atropine in concentrations which were sufficiently high to antagonize the action of acetylcholine. The adrenergic blocking agent 883F [2-(diethylaminomethyl)-1,4-benzodioxan], however, inhibited the motor effect of adrenaline.

For our experiments, strips of 7 × 2 cm were taken from the dorsal ruminal sac of sheep, immediately after slaughtering. These were transported in cooled Tyrode solution. In the laboratory, the serosa and mucosa layers were removed and the muscular layer placed in a bath with 50 ml of Tyrode solution without glucose, at 37° and aerated with an oxygen 95% and carbon dioxide 5% mixture. Recordings of the contractions were made isotonically on a kymograph (Stücklin, 1951). For specific α-receptor stimulation we chose oxymetazoline hydrochloride (Mujic & Rossum, 1965; Rossum & Mujic, 1965), and for specific β-stimulation we used isoprenaline hydrochloride, both at a concentration in the bath fluid of 0·2 μg/ml. Other agents were adrenaline hydrochloride (0·2 μg/ml), dibenamine hydrochloride (2 μg/ml), pronethalol hydrochloride (8 μg/ml) and Du 21445 [1-isopropyl-amino-3-(2-methylthiophenoxy)-propanol-2], also a strong β-blocking agent (2–4 μg/ml). The time intervals between the drug administration was usually about 30–40 min. After each response the bath fluid was renewed several times.

Results. Only about 10% of all strips showed spontaneous activity after a short incubation time, which subsided in a few hours as the experiment progressed. The activity usually consisted of monophasic contractions occurring 8 to 10 times/min.

Isoprenaline always gave a reduction in tension and very often a decrease of amplitude. This effect could be blocked by pronethalol, but not by dibenamine. Oxymetazoline caused always a sharp rise in tone, sometimes with a reduction of the amplitude. This effect could be blocked by dibenamine, but not by pronethalol. Some strips reacted with a strong contraction, others with a relaxation after exposure to adrenaline. The rise in tone could be blocked by dibenamine; thereafter, a second dose of adrenaline gave a relaxation, which in turn could be blocked by pronethalol. Strips which reacted first with a relaxation, gave a contraction to a second dose of adrenaline after pronethalol. Dibenamine added next, blocked this type of reaction. After Du 21445, oxymetazoline still gave a contraction, while the effect of isoprenaline was completely inhibited.

From these results, we conclude, that in ruminal smooth muscle preparations, there exist α-stimulatory and β-inhibitory receptors.

It is of interest that in the gastrointestinal tract of most species, both α- and β-receptor stimulation results in inhibition of contractions ((Ahlquist & Levy, 1959; Bucknell & Whitney, 1964; Rossum & Mujic, 1965; Takagi, Osada & others, 1967). Some exceptions, where motor effects of adrenaline were observed, have been listed by Dussardier & Navarro (1953) and recently by Christensen & Daniel (1968). In the ruminal wall, apparently the stimulation of α-receptors characteristically gives contraction.

Acknowledgement. We are grateful to N.V. Meattrading, Breukelen, The Netherlands for their assistance and to N.V. Philips Duphar and Merck Darmstadt A.G. for gifts of Du 21445 and oxymetazoline respectively.

Institute of Veterinary Pharmacology and Toxicology, University of Utrecht, The Netherlands.

A. S. J. P. A. M. VAN MIERT
E. A. HUISMAN

March 26, 1968

References

Ahlquist, R. P. & Levy, B. (1959). *J. Pharmac. exp. Ther.*, **127**, 146–149.
Bucknell, A. & Whitney, W. (1964). *Br. J. Pharmac. Chemother.*, **23**, 164–175.
Christensen, J. & Daniel, E. E. (1968). *J. Pharmac. exp. Ther.*, **159**, 243–249.
Duncan, D. L. (1954). *J. Physiol., Lond.*, **125**, 475–487.
Dussardier, M. & Navarro, J. (1953). *J. Physiol (Paris)*, **45**, 569–595.
Habel, R. E. (1956). *Cornell Vet.*, **46**, 555–628.
Miert, A. S. J. P. A. M. van (1966). *Tijdschr. Diergeneesk.*, **91**, 1485–1494.
Miert, A. S. J. P. A. M. van (1968). *Vet. Rec.*, in the press.
Mujic, M. & Rossum, J. M. van (1965). *Archs int. Pharmacodyn. Thér.*, **155**, 432–449.
Rossum, J. M. van & Mujic, M. (1965). *Ibid.*, **155**, 418–432.
Sanford, J. (1958). *J. Physiol., Lond.*, **143**, 82P.
Stücklin, K. (1951). Thesis, University of Zurich.
Takagi, K., Osada, E., Takayanagi, J. & Taga, F. (1967). *Archs. int. Pharmacodyn. Thér.*, **168**, 212–219.