ability of the former is reduced by allyl quaternization, the double bonds of which might form hydrogen bonds with the hydroxyl groups and thus reduce access of the latter to the receptor site. The weak histamine releasing power of dacuronium is practically abolished on acetylation of its 17-hydroxy group to give pancuronium. From this evidence it appears that one or more free hydroxyl groups, either primary, secondary or phenolic in nature, enhance histamine release. In addition, the interonium distance in these compounds may also play a critical part.

REFERENCES

BUCKETT, W. R., MARJORIBANKS, C. E. B., MARWICK, F. A. & MORTON, M. B. (1968). The pharmacology of pancuronium bromide (Org. NA97), a new potent steroidal neuromuscular blocking agent. *Br. J. Pharmac. Chemother.*, **32**, 671–682.

BUCKETT, W. R. & SAXENA, P. R. (1969). The pharmacology of dacuronium bromide—a new short acting neuromuscular blocking drug of non-depolarising type. *Abstr.* 4th *International Congress on Pharmacology, Basel*, p. 420.

FRISK-HOLMBERG, M. & UVNÄS, B. (1969). The mechanism of histamine release from isolated rat peritoneal mast cells induced by d-tubocurarine. *Acta physiol. scand.*, **76**, 335–339.

KONZETT, H. & RÖSSLER, R. (1940). Versuchsanordnung Zu Untersuchungen an der Bronchialmuskulatur. *Naunyn-Schmiedebergs Arch exp. Path. Pharmak.*, **195**, 71–74.

## The Schultz-Dale reaction in bovine pulmonary smooth muscles

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Calves 1–4 months old were sensitized by whole ovalbumin or horse serum (alone or with Freund's complete adjuvant), or ovalbumin-alum precipitate. At least 3 weeks after sensitization, animals were killed with pentobarbitone and the pulmonary artery, vein and bronchus taken from a lung with minimum delay. The blood vessels were cut spirally and the bronchus transversely into rings before mounting in a bath of 20 ml oxygenated Krebs solution at 35° C. Contractions were recorded isotonically on a pen recorder.

The pulmonary artery contracted to 5-hydroxytryptamine (5-HT; 10–20 ng/ml) and histamine (40–2,000 ng/ml). The pulmonary vein was at least 20 times more sensitive to these drugs; sometimes contracting to as little as 0·1 ng 5-HT/ml (Fig. 1). The bronchus, however, was 10–100 times less sensitive than the artery (confirming the observation of Aitken & Sanford, 1970).

Among sixteen "sensitized" calves, fourteen showed positive Schultz-Dale reactions in pulmonary veins to 50–500 $\mu$g ovalbumin or 0·1–1·0 ml horse plasma (Fig. 1). Plasma was used since serum contained enough 5-HT *per se* to contract the vein. Repeated antigen caused diminishing responses (desensitization). Of the fourteen animals giving positive pulmonary vein reactions, seven were also challenged in the artery and bronchus. Four such arteries and two bronchi gave feeble Schultz-Dale reactions. On two occasions strips of ileum were set up (Bywater, 1969) and these failed to contract to antigen.

The results support the contention that the lung is an anaphylactic shock organ of domesticated ruminants, but focus attention on the pulmonary vein rather than the artery or bronchus cited previously (Aitken & Sanford, 1969, 1970; Alexander, Eyre, Head & Sanford, 1970). We are presently making detailed studies of the Schultz-Dale phenomenon in cattle and have completed a similar study in sheep.

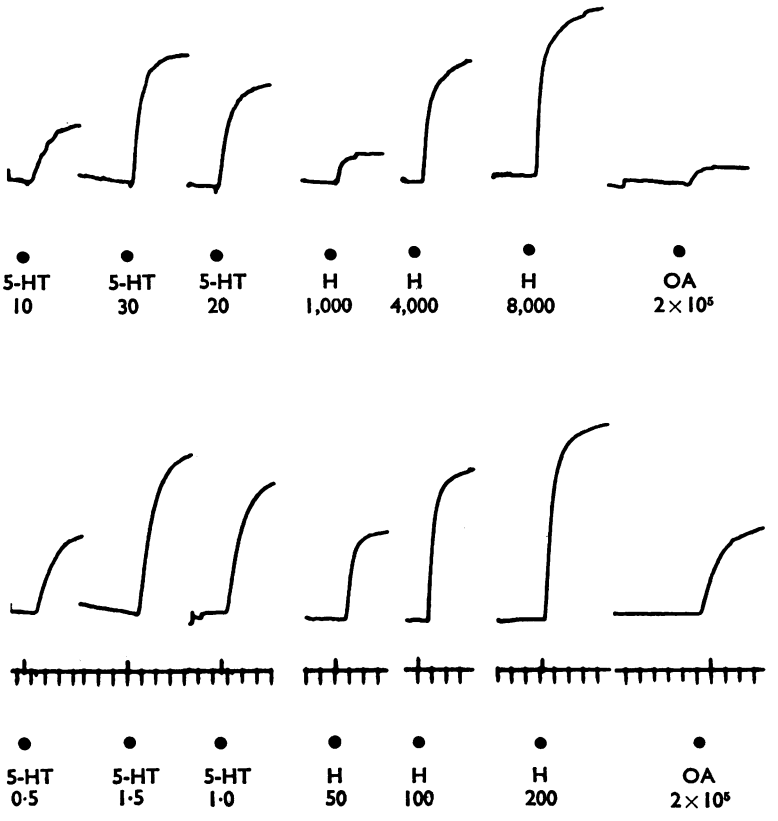


FIG. 1. Isolated spiral strips of pulmonary artery (upper tracing) and pulmonary vein (lower tracing) taken from a 6 week old Friesian calf sensitized with hen egg albumin (15 mg/kg intravenously). Tissues are contracting to 5-hydroxytryptamine (5-HT), histamine (H) and hen egg albumin (OA). Doses in ng/ml. The marker shows injection time and 30 s.

Supported by grants from the Ontario Department of Agriculture and Food, and the National Research Council of Canada.

REFERENCES

AITKEN, M. M. & SANFORD, J. (1969). Experimental anaphylaxis in cattle. *J. comp. Path.*, **79**, 131–139.
AITKEN, M. M. & SANFORD, J. (1970). The effect of drugs on bovine tracheobronchial and pulmonary vascular tissue. *Br. J. Pharmac.*, **38**, 443*P*.
ALEXANDER, F., EYRE, P., HEAD, K. W. & SANFORD, J. (1970). Effects of anaphylaxis and chemical histamines in sheep. *J. comp. Path.*, **80**, 19–30.
BYWATER, R. J. (1969). Some responses of bovine intestinal musculature to humoral agents *in vitro* and *in vivo*. *Archs int. Pharmacodyn. Thér.*, **179**, 459–468.

## Effects of azathioprine and phenylbutazone in rat adjuvant arthritis

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A single intraplantar injection of heat-killed tubercle bacilli in liquid paraffin (Freund's adjuvant) causes local and migratory peri-arthritis and other connective tissue lesions in rats (Pearson, 1956). This experimental arthritis can be suppressed to different degrees by various anti-inflammatory and immunosuppressive agents (Newbould, 1963; Ward, Cloud, Krawitt & Jones, 1964; Graeme, Fabry & Sigg, 1966). Piliero & Colombo (1967) showed that serum from rats treated with certain