procaine (2×10^{-4} g/ml) or by transmural stimulation at 10 Hz and 0·3 ms for up to 60 s or by storage at 4° C for 48 h.

Release of the material was related to sphincter tone. Incubation with amyl nitrite, 2,4-dinitrophenol, Ca^{2+} free Krebs solution, anoxia or stimulation with high pulse widths for long periods reduced tone and inhibited release of the active material. Output increased as tone increased after first mounting the tissue.

Estimates of prostaglandin content of the bovine iris give a very low level. The results, therefore, suggest that release of the prostaglandin-like substance in the present experiments is not a passive process.

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Effects of decaborane on gastric secretion in the Shay rat

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Decaborane ($B_{10}H_{14}$) was shown by Merritt & Sulkowski (1967) to be a potent inhibitor of aromatic L-amino-acid decarboxylase. More recently Medina, Londez & Foster (1969) showed that it is also a potent inhibitor of the specific histidine decarboxylase of the rat stomach, causing a reduction in histamine concentration in the stomach.

Rats were pylorus-ligated under ether 12 h after receiving decaborane (0, 15, 30, 45 or 60 mg/kg in vegetable oil 1 ml/kg intraperitoneally). Decaborane produced a dose-related reduction in the concentrations of total acid, free acid and K^+ ions and in the volume of gastric secretion. Na^+ ion concentrations were increased dramatically. All these effects were statistically highly significant ($P<0.01$). Sodium output was unchanged at 45 mg/kg. Pepsin concentration was unaffected. Gastric histidine decarboxylase activity was virtually abolished. Severe toxicity was seen with the two highest doses.

In vitro decaborane inhibited specific histidine decarboxylase and aromatic L-amino-acid decarboxylase, but it had no effect on peptic activity. Decaborane reacted rapidly with pyridoxal phosphate.

The results suggest that this compound preferentially inhibits the secretory mechanisms of the parietal cell in the rat.

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The use of neuromuscular blocking agents to investigate receptor structure requirements for histamine release

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The polymeric compound 48/80 has been used most frequently to demonstrate histamine release in experimental animals, but recent work has shown that the mechanism of the release from isolated rat peritoneal mast cells by tubocurarine was similar to that of 48/80 (Frisk-Holmberg and Uvnäs, 1969). It was of interest, therefore, to investigate several other neuromuscular blocking agents for their ability to release histamine, in an attempt to determine the molecular features necessary for histamine liberation.

Histamine release was measured in rat mast cells using a fluorimetric method (Frisk-Holmberg & Uvnäs, 1969), in the guinea-pig by a broncho-constriction test (Konzett & Rössler, 1940) and in isolated perfused cat paws, after the following clinically used neuromuscular blocking agents: tubocurarine chloride, dimethyltubocurarine chloride, C-toxiferine chloride, alcuronium chloride, pancuronium bromide (Buckett, Marjoribanks, Marwick & Morton, 1968) and dacuronium bromide (Buckett & Saxena, 1969). Neuromuscular blocking potency was also determined in anaesthetized cats and conscious mice after intravenous administration, but no correlation between muscle relaxation and histamine liberation was found.

Tubocurarine was the most potent releaser of histamine in all species, whereas pancuronium was almost inactive. For example, in rat peritoneal mast cell suspensions, tubocurarine (10^{-3}M) released 57·8% of total histamine content in contrast to the 2% liberated by pancuronium (Table 1).

The rank order of potency of the neuromuscular blocking agents in releasing histamine was similar for the three test situations, allowing the following conclusions to be drawn.

Methylation of the two phenolic hydroxyl groups of tubocurarine to dimethyltubocurarine reduced the ability to release histamine. Both C-toxiferine and alcuronium contain two primary hydroxyl groups, but the moderate histamine releasing

TABLE 1. *Release of histamine from rat peritoneal mast cells by neuromuscular blocking agents*

		Molar concentration			
Drug	*n*	10^{-4}	5×10^{-4}	10^{-3}	5×10^{-3}
Tubocurarine	(5)	16·33±1·69	40·50±3·58	57·80±5·01	64·50±1·97
Dimethyltubocurarine	(6)	7·66±1·56	20·00±0·54	33·17±1·79	37·67±1·16
Toxiferine-C	(4)	5·25±1·08	13·75±0·28	23·25±1·48	29·50±0·50
Alcuronium	(4)	2·00±0·20	6·75±0·08	15·25±0·88	20·25±0·88
Dacuronium	(4)	0	2·75±1·59	5·00±2·25	7·25±2·59
Pancuronium	(4)	0	0	2·00±0·25	4·00±0·25

The figures represent percentage release of total histamine content (±S.E. of mean) corrected for spontaneous histamine release (less than 1%); *n*= number of determinations.