heart. This seems to supply additional evidence that beta receptor inhibition is responsible for the benefit of these drugs in angina and not some other non-specific property.

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Cardiovascular actions of glucagon and secretin

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It has been suggested (Robison, Butcher & Sutherland, 1967) that adenyl cyclase is the β-receptor for catecholamines and that the cardiac effects of catecholamines result from myocardial cyclic 3',5'-AMP accumulation. Glucagon also causes cyclic AMP accumulation in certain tissues and produces cardiac chronotropic and inotropic responses. It seemed of interest to determine the peripheral vascular effects of glucagon and to compare them with isoprenaline. The actions of secretin, which closely resembles glucagon in structure, were also examined.

Cats were anaesthetized with pentobarbitone sodium. Arterial blood flows were measured with non-cannulating electromagnetic flowmeters and drugs were given by close intra-arterial injection, or infusion.

Rapid injections of glucagon (1–10 μg) produced dilatation of mesenteric resistance vessels, constriction of the hepatic arterial vascular bed and no effect on the renal and femoral vasculature. Rapid injections of secretin (1–10 μg) produced dilatation of the mesenteric and femoral vasculature, constriction of the hepatic arterial bed and no effect on the renal vessels. Glucagon and secretin appeared to act directly on the resistance vessels, since the responses developed within a few seconds and were unaffected by appropriate denervation. Their vasodilator actions were unaffected by pre-treatment with propranolol.

Isoprenaline dilated the mesenteric, hepatic and femoral vasculature and was without effect on renal vessels.

Since the pattern of vascular responses induced by glucagon and secretin differed from that of isoprenaline, the vasomotor changes induced by these hormones were probably not mediated by β-receptors.

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The excretion of hydroxyphenyltrimethylammonium in bile

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The biliary excretion of quaternary amines varies greatly from compound to compound. For example, benzomethamine and procainamide ethobromide are

excreted in high concentrations, and as much as 30% of the dose may be detected in bile (Levine & Clark, 1955; Schanker & Solomon, 1963). Tetraethylammonium, hexamethonium and decamethonium, however, are present only in trace amounts in bile (Levine, 1960; Schanker, 1962; Luthi & Waser, 1965). The results reported here were concerned with the biliary excretion of hydroxyphenyltrimethylammonium; this compound has been shown to be the principal metabolite of neostigmine (Roberts, Thomas & Wilson, 1965). Wistar rats were anaesthetized with urethane and the common bile duct was cannulated through a mid-line abdominal incision. Trimethyl-^{14}C-(*m*-hydroxyphenyl)-trimethylammonium iodide (specific activity 10·2 μc/μM; 2 μM/kg) was injected intravenously over a one-minute period, and hepatic bile was collected at hourly intervals for 4 hr.

The amount of radioactivity detected in bile represented less than 3% of the dose. Thus the elimination of hydroxyphenyltrimethylammonium in bile is quantitatively similar to the excretion of neostigmine (Calvey, 1966).

Four main peaks of radioactivity were resolved by paper chromatography of bile in a mixture of *n*-butanol, ethanol, acetic acid and water (Somani, Roberts, Thomas & Wilson, unpublished). Two of these peaks had similar R_f values to concurrently run authentic standards of hydroxyphenyltrimethylammonium and hydroxyphenyldimethylamine. The two remaining peaks were both eliminated by previous incubation with β-glucuronidase, and were tentatively identified as the glucuronides of these two compounds. These two peaks accounted for most of the radioactivity in bile.

On the basis of these results it is suggested that hydroxyphenyltrimethylammonium is mainly excreted in bile as the glucuronide of the parent drug and the glucuronide of its demethylated metabolite. Similar metabolic pathways may well be involved in the biliary excretion of neostigmine.

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A possible explanation for the varied effects of sulphonic acid diesters on spermatogenesis

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The different antifertility effects in male rodents produced by simple members of a series of methane sulphonic esters (busulphan (Myleran) homologues, n=1–9) is