

in experiments on 6 rabbits. We determined the sensitivity of the animals to both substances previously. Then we used amounts of bradykinin and histamine which do not disturb the blood vessel permeability, mixed them, and injected them i.c. The summation of effects of both mediators was observed in these experiments (Figure 3).

Discussion. The investigations confirmed the high sensitivity of skin blood vessel permeability of rabbits, guinea-pigs and rats to bradykinin^{5,6}. More pronounced differences between the sensitivity of blood vessels to bradykinin and histamine found in our experiments are probably explained by the fact that we have taken for calculation the derangement of permeability appearing in 50% of the animals. The blood vessel permeability de-

range of short duration observed after the injections of bradykinin is in accordance with published data¹⁰. This mode of action of bradykinin appears to depend on high activity of the skin kininase. But our data do not rule out the possibility of the participation of kinin in the pathogenesis of inflammation where the conditions for continuous formation of kinins may exist. Lower sensitivity of vessels to histamine than to bradykinin and small taxyphylaxis to bradykinin are serious arguments favouring bradykinin as mediator of inflammation.

The observed summation of the effects of bradykinin and histamine on blood vessel permeability appears to play an important role in the first phase of inflammation where histamine is considered to be the main mediator¹¹.

Zusammenfassung. Es werden quantitative Vergleiche in 3 Spezies der Hautgefäß-Empfindlichkeit gegenüber Bradykinin und Histamin angestellt.

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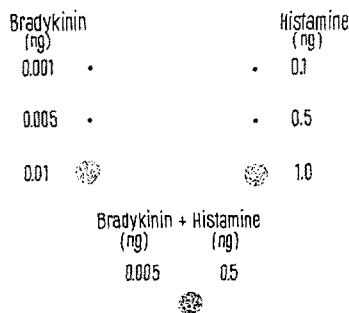


Fig. 3. Simultaneous actions of bradykinin and histamine on skin blood vessel permeability of rabbits.

¹⁰ G. P. LEWIS, in *Excerpta med. Int. Congr. Series 82*, Milan, 114 (1964).

¹¹ W. G. SPECTOR and D. A. WILLOUGHBY, *Bact. Rev.* 27, 117 (1963).

Does Acute Obstruction of the Common Bile Duct Produce Distension of the Rat Bile Tree?

During short periods of obstruction of the common bile duct in rats biliary secretion apparently continues¹. This leads to a rising intrabiliary pressure which is ultimately stabilized by biliary leakage (regurgitation). Sudden release of obstruction at this time is immediately followed by a gush of bile which may be recorded with a biliary cannula and drop counter. The increased flow rate subsides to the basal rate in a few minutes.

It is generally accepted that the bile tree distends in response to increased pressure resulting from acute obstruction, and that the gush of bile seen on release of obstruction is due to the rapid ejection of stored bile produced by the elastic recoil of the distended bile tree. However, the suggestion has been put forward that in order to continue secreting against a raised pressure the hepatic cells must accumulate extra substrate (i.e. accumulate substances which drive the secretory mechanism)². Release of acute obstruction would be expected to produce an increased secretory rate during the unloading of the excess substrate. This increased secretory rate could be wholly or partly responsible for the temporary increase in flow rate observed on release of obstruction.

The cause of this increased flow rate is of some importance in the measurement of the distended capacity of the bile tree by the dye method described elsewhere³. This method measures the volume of bile present in the tree (= capacity of bile tree) at the time of injection of a mar-

ker dye. The dye is injected i.v. and since its appearance in the collected bile is taken to indicate the arrival of bile secreted after the injection time, it follows that secretion of bile in the time period between dye injection and dye secretion represents an error of the method resulting in over-reading of true capacity. With normal bile flow rates in rats this error is probably small³ but could be significantly large if the secretion rate approximated to the bile flow rate seen at the time of release of obstruction.

The distensibility of the bile tree is important in other studies too, as, for example, in recent investigations on the dual origin of bile in dogs⁴.

One approach to this problem is to measure the bile tree capacity at raised intrabiliary pressures under conditions allowing substrate unloading, and to compare the results with measurements made at the same pressure and with the same animal but arranging matters so that substrate unloading cannot occur.

In the first experiment the cannula exit was kept at the level of the hilum of the liver and a side arm was attached to an adjustable constant level device which was set at the desired height. The cannula exit was obstructed

¹ G. BARBER-RILEY, *Am. J. Physiol.* 205, 1127 (1963).

² T. G. RICHARDS and J. Y. THOMSON, *Gastroenterology* 40, 705 (1961).

³ G. BARBER-RILEY, *Am. J. Physiol.* 205, 1122 (1963).

⁴ H. O. WHEELER and P. L. MANCUSI-UNGARO, *Am. J. Physiol.* 210, 1153 (1966).

until the dye was injected, at which time continuity was switched from the constant level device to the cannula exit. The volume of clear (dye free) bile collected in this way included bile stored in the distended tree and also bile secreted by the hepatic cells before the arrival of the injected dye.

In the second experiment on the same animal the level of the cannula was permanently fixed to give the same intrabiliary pressure as in the previous experiment. There was no side arm and no constant level device, nor was the cannula exit obstructed. After a short delay, presumably due to bile tree distension or substrate accumulation, bile flow became constant. In this experiment the volume of clear bile collected after the time of dye injection included the bile stored in the distended bile tree, but since there was no change in intrabiliary pressure no spurt in bile secretion due to substrate unloading could occur.

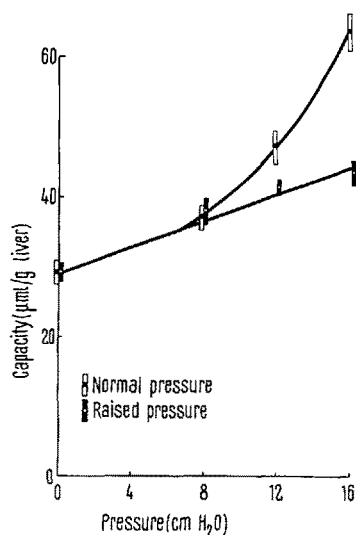


Fig. 1. Pressure/volume curves obtained by the 2 methods described in the text. Means (\pm S.E.), 20 experiments.

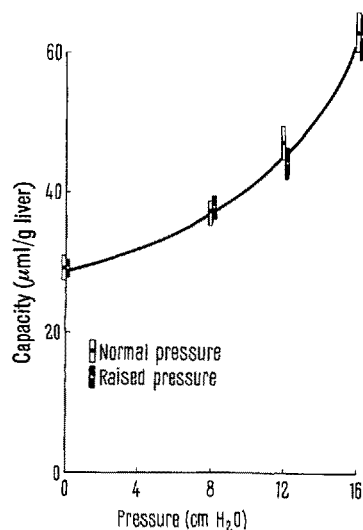


Fig. 2. Pressure/volume curves obtained by the 2 methods described in the text after applying a correction for bile loss due to regurgitation. Means (\pm S.E.), 20 experiments.

In both experiments the marker dye used was bromsulphthalein (BSP).

Measurements of capacity were made at pressures of 0, 8, 12, and 16 cm water in a series of 20 rats. The means and standard errors after correcting for cannula dead space are shown in Figure 1. There was no significant difference (at 5% level) between the capacities measured by the 2 methods with zero pressure, as would be expected, since both methods were applied to the same animal. Similarly at 8 cm water pressure there was no significant difference, suggesting that the effect of any substrate unloading by the hepatic cell was negligible on the measurement of bile tree capacity. At the 2 higher pressures significant differences were observed in capacity measurements, suggesting that the effect of substrate unloading was here significant.

However, it has been shown^{1,5} that in rats biliary regurgitation is significant at an intrabiliary pressure of 12 cm water, total regurgitation occurring at pressures in excess of about 16 cm water. It therefore follows that the volume of clear bile collected with the permanently raised cannula would be less than the true capacity of the bile tree at these pressures since leakage from the bile tree would occur during collection.

As the biliary secretion rate is either unchanged by the pressures recorded in these experiments, or is able to return to normal on accumulating sufficient substrate², a simple correction may be applied for the bile loss due to regurgitation. This is based on the known secretion rate (= flow rate with zero pressure) and observed steady flow rate at raised pressure. Thus, for example, if the observed steady flow rate falls to half when the cannula is raised to a certain height, then it is assumed that the true capacity equals twice the volume of clear bile collected. When this simple correction is applied to the previous data there is no significant difference (at 5% level) between the results of the 2 sets of experiments (Figure 2).

From Figure 2 it would appear that substrate loading does not significantly affect the measured capacity of the distended biliary tree and that the spurt of bile seen on release of obstruction is probably due to collapse of the distended bile tree. With the higher intrabiliary pressures this conclusion clearly depends upon the validity of the applied correction. This simple correction would appear to be satisfactory under conditions where the advancing column of dye-stained bile has a flat front and regurgitation takes place only at the lower end of the bile tree. In fact conditions are such that coning almost certainly occurs, and there is some evidence that regurgitation sites are distributed evenly throughout the bile tree¹. Errors introduced by these 2 factors cannot be measured at present but are opposite in sign and therefore should tend toward mutual cancellation.

Zusammenfassung. Der Gallenausfluss, der bei akuter Verstopfung des Hauptgallentraktes beobachtet wird, scheint durch den elastischen Nachreflex des ausgedehnten Gallentraktes verursacht.

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⁵ O. HARTH and F. WALDECK, *Klin. Wschr.* 42, 118 (1964).