the parasympathetic actions on the rat intestine, however, are not disturbed by possible ganglionic actions. Ganglionic actions may be observed in objects which are not sensitive to parasympathetic actions, as for instance the blood pressure of the atropinized cat. Parasympathomimetic and ganglionic activities were studied on the blood pressure of the cat; the results are collected in Table II. From this Table, it may be seen that the ganglionic activity of pilocarpine is actually extremely low.

The mode of action of pilocarpine, however, is still more complex since in high doses ($>1\ mM$) papaverine-like actions become apparent in the intestine. On the same object, papaverine is active in concentrations of $10^{-2}\ mM$. This implies that pilocarpine behaves both as an agonist and as a competitive antagonist in low doses, and as a non-competitive antagonist in high doses.

Pilocarpine is an example of a parasympathetic drug with a dualism in action. Its intrinsic activity varies for different organs and species. Hence pilocarpine is more muscarinic in its effect on certain organs but more atropinic on others.

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Zusammenfassung

Pilocarpin ist ein geeignetes Beispiel einer parasympathischen Substanz mit dualistischer Wirkung. Auf Grund der Variationen in der Eigenaktivität (intrinsic activity) des Pilocarpins an verschiedenen Organen und Arten tritt entweder die parasympathomimetische oder die parasympatholytische Wirkung in den Vordergrund.

Serum Glutamic Oxaloacetic Transaminase after Hepatic Artery Ligature

Serum glutamic oxaloacetic transaminase (SGOT) is a very sensitive index of acute necrosis of many tissues, including the heart, liver, kidneys, bowel, and lungs (Lionel *et al.*[1]).

Experimental destruction of liver tissue by carbon tetrachloride was investigated by Wroblewski and La Due[2]. The level of SGOT was found by these authors to be a highly specific index of hepatocellular injury: the height and duration of enzymatic activity was proportional to the amount of carbon tetrachloride, as well as to the extent of liver cell damage.

Ligation of the hepatic artery, which was introduced by Rheinhoff[3], is performed in Egypt in the treatment of advanced cases of hepatosplenomegaly with ascites. In view of the fact that the results are controversial and the mortality rate is as high as 20% (Shalaby[4]; Khairy[5]), the present work was undertaken to study the effect of this operation on the SGOT level in an effort to assess the extent of hepatocellular damage which accompanies such a procedure.

The operation was performed on six dogs weighing between 9 and 10 kg. The hepatic artery was ligated distal to the right gastric branch. The animals were divided into two groups of three.

Animals of group I received no antibiotics and animals of group II received 0·5 g of Achromycin daily, 2 days prior to the operation and through the post-operative period.

In a third group of animals (3 dogs), laparatomy was performed using the same technique applied to group I and II but without ligating the hepatic artery (control experiment). SGOT was estimated according to the method of Dubach[6].

As regards group III, no rise in enzyme level was detected.

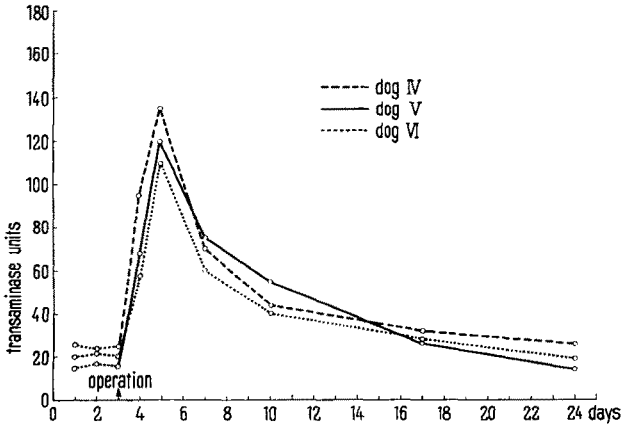
A review of these results indicates that hepatic artery ligature caused a rapid liberation of the enzyme from the anoxic liver cells into the blood stream. The enzyme level in the serum reached a maximum after 24 or 72 h. These results are in agreement with data obtained with other tissues like heart, kidneys, and lungs after ligation of their arterial supply (Lionel *et al.*[7]).

Table I. Animals of group I, SGOT units per ml

	h after operation						
	0	6	12	24	48	72	96
Dog I	25	28	42	65	125	132	Died
Dog II	10	10	35	50	160	Died	
Dog III	15	17	28	55	115	145	Died

Table II. Animals of group II, SGOT units per ml

	Days before operation		Operation Day	Days after operation						
	2	1		1	2	3	4	7	14	21
Dog IV	26	24	25	95	135	100	70	44	32	26
Dog V	15	17	16	68	120	95	75	55	26	14
Dog VI	20	22	20	58	110	80	60	40	28	19



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Using SGOT activity as an index of acute liver destruction, it is concluded that there is evidence of liver necrosis which is almost of the same magnitude in animals of group I and II. Biopsy and histological examination of the livers of animals of group I showed definite focal necrosis similar to that found in the livers of animals of group II, whereas biopsy taken after the 4th week (when the enzyme level is normal) showed no evidence of residual liver damage suggesting that the damage caused by hepatic artery ligature was not progressive but recoverable.

The fact that the height of the enzyme level was of the same order in animals of group I and II shows that Achromycin did not alleviate the necrosis caused by this operation. It is therefore suggested that the role of Achromycin is to inhibit the growth of microorganisms which in all probability are responsible for the death of animals of group I.

Stimulated by these results, a similar study on SGOT activity was undertaken in patients undergoing hepatic artery ligature. Preliminary findings in 2 cases showed a rise in enzyme level similar to that obtained with experimental animals.

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Zusammenfassung

Bei Hunden verursacht die Ligatur der Arteria hepatica einen starken Anstieg der Serum-Glutaminsäure-Oxalessigsäure-Transaminase-Werte mit Maxima am dritten oder vierten Tag. Der Anstieg wird auf die bioptisch feststellbare Nekrose von Leberzellen zurückgeführt, die mit und ohne Verabreichung von Achromycin gleich stark ausgeprägt war.

Die Wirkungsweise des Achromycins wird diskutiert und auf Parallelergebnisse an Patienten hingewiesen.

Release of Noradrenaline from Adrenergic Transmitter Granules by Tyramine

It was observed in 1932 by BURN[1] that tyramine is devoid of vasoconstrictor action when tested on the denervated foreleg of the cat, but that addition of adrenaline restores its constrictor action. The effect has later been interpreted by assuming that tyramine releases noradrenaline from the stores[2–4]. These are presumably chiefly located at the terminal parts of the adrenergic axones[5]. According to FLECKENSTEIN and STÖCKLE[6], the inhibitory action of cocaine on the action of tyramine is due to the blocking of noradrenaline release.

Very little is known about the releasing action of tyramine on the adrenal medulla and other chromaffin cell groups, or whether tyramine can exert this action on decentralized or denervated organs.

Recently SCHÜMANN[7] has reported that tyramine releases noradrenaline from isolated chromaffin cell granules when added in concentrations of 15–300 µg per ml. It is also stated that tyramine releases noradrenaline from isolated adrenergic nerve granules.

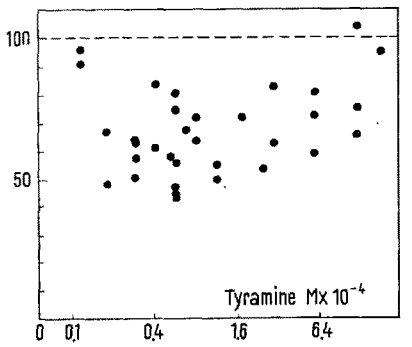
The effect of tyramine and 3-hydroxytyramine (dopamine) on the release of noradrenaline from isolated adrenergic nerve granules will be described in the present report.

Methods. Granules from splenic nerves were prepared according to the technique of EULER[8] and EULER and LISHAJKO[9]. After resuspension of the sediment in 0·08 *M* potassium phosphate at pH 6·7–7·0, it was incubated at 20°C for 30 min with a solution of tyramine hydrochloride at the same pH. After incubation, the suspension was resedimented by centrifugation at 30000 × *g* for 30 min. Noradrenaline was estimated by the fluorimetric technique of EULER and LISHAJKO[10] in the supernatant and in the sediment after releasing the noradrenaline by addition of 1 ml 1% metaphosphoric acid.

Similar experiments were made with 3-hydroxytyramine and with 4-hydroxyphenyletanolamine (octopamine).

Results. The Figure shows the amount of noradrenaline in the sediment after incubation for 30 min at pH 7·0–7·4 and recentrifugation, in % of the control value. As seen from the Figure, tyramine causes a release of transmitter when present in concentrations of 3–100 µg per ml. The effect is most conspicuous in the concentration range of 3–20 µg/ml but there is no sharply defined maximum. The maximal effect observed during the prevailing conditions was a lowering of the amount present in the sediment to about 40–50% of that in the controls.

No certain effect was obtained with 3-hydroxytyramine or octopamine in the same concentration range (3–300 µg/ml).



Effect of tyramine on the release of noradrenaline from granules isolated from bovine splenic nerves during incubation at + 20°C for 30 min. *Ordinate.* NA in sediment in % of controls.

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