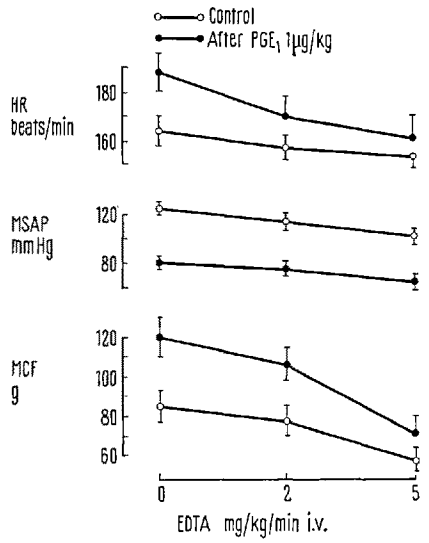
heart rate and myocardial contractile force in all dogs. The i.v. administration of EDTA decreased heart rate, mean systemic arterial pressure and myocardial contractile force essentially in proportion to the dose. As the dose of EDTA increased, the hemodynamic effects of the same dose (1 μg/kg) of PGE_1 decreased progressively except mean systemic arterial pressure. As seen in the Figure, the hypotensive effect of PGE_1 was not affected by the administration of EDTA.



Effects of the i.v. administration of PGE_1 (1 μg/kg) on heart rate (HR), mean systemic arterial pressure (MSAP) and myocardial contractile force (MCF) in 7 dogs before and during the continuous i.v. administration of disodium EDTA. Open and closed cycles denote the average values, respectively, before and after the administration of PGE_1. I-shaped bars denote standard errors of the means.

The present study shows that Ca chelation with EDTA causes decreases in positive chronotropic and inotropic actions of PGE_1. Presently, the precise underlying mechanisms of the effect of PGE_1 on the myocardial contractility are poorly understood. NAKANO and MCCURDY[3] found that the administration of propranolol did not modify the positive inotropic actions of PGE_1 in anesthetized dogs. The role of Ca on the pharmacodynamic actions of PGE_1 remains to be rather speculative at present. However, as described by COCEANI and WOLFE[1] on the gastric fundus strip preparations, this study also indicates that the cardiodynamic actions of PGE_1 could be influenced by the intracellular concentration or availability of Ca in dogs. In the present study, the administration of EDTA did not affect the hypotensive effect of PGE_1. The hemodynamic mechanism responsible for this cannot be explained satisfactorily. Since systemic arterial pressure is hemodynamically modified by 2 determinants, cardiac output and total peripheral resistance, it is conceivable that the 2 counteracting determinants may hemodynamically offset each other to possibly keep systemic arterial pressure unchanged in the present experiment. Further experimentations are necessary to elucidate the interaction between PGE_1 and Ca at subcellular levels.

Zusammenfassung. Die Wirkung des Dinatrium-EDTA auf die Kreislaufreaktionen des Prostaglandin E_1 (PGE_1) wurde an narkotisierten Hunden untersucht. Das Ausmass der positiv chronotropen und inotropen Einflüsse des PGE_1 war während der Infusion von EDTA bedeutend geringer als das des PGE_1 vor der EDTA-Gabe. Die Gegenwart oder das Einströmen von Kalziumionen scheint in der pharmakologischen Wirkung des PGE_1 eine Rolle zu spielen.

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On some Potassium-Like Qualities of the Thallium Ion

Univalent thallium compounds resemble potassium compounds in several respects. The chlorides of the 2 metals form mixed crystals. A number of minerals are known in which thallium can replace potassium. The ionic radii of the 2 metals are close to each other (K^+ 1.33 Å; Tl^+ 1.49 Å).

Though thallium had long been studied for its biological actions, it was only in the last decade that some of them could be convincingly shown to be potassium-like. MULLINS and MOORE[1] found that, similarly to potassium, thallium accumulated in muscle fibres and depolarized membranes. GEHRING and HAMMOND[2] produced evidence that thallium substituted for potassium in the same molar concentration activated adenosine triphosphatase. The present communication reports further investigations into the interrelations between thallium and potassium by examining their influence on muscular activity.

Isolated hearts mounted on Straub cannulas, and isolated rectus abdominis muscles of *Rana esculenta* were used. In the first few experiments using heart preparations, we worked with the poorly soluble thallium chloride; in all the others, with thallium nitrate dissolving readily in a Cl^--free medium. Two solutions were used: one contained NaCl, 6.43 g; KCl, 0.3 g; $CaCl_2$, 0.17 g; $NaHCO_3$, 0.36 g; glucose, 0.7 g, in 1000 ml of distilled water; the other was composed of $NaNO_3$, 9.35 g; KNO_3, 0.41 g; $Ca(NO_3)_2$, 0.25 g; $NaHCO_3$, 0.36 g; and glucose, 0.7 g, in 1000 ml of distilled water.

2–8 washings with a potassium-free solution arrested the activity of the isolated frog heart and 1 or 2 subsequent washings with a solution containing 4 m*M* of potassium restarted it. It could also be restarted with a solution in which 2 m*M* of thallium took the place of potassium. 4 m*M* of thallium in the solution stopped the heart beating. With potassium, 8 m*M* were not enough; a 12 m*M* concentration was required to arrest cardiac activity. The toxic effect both of potassium and thallium was found to

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be reversible: bathing the heart in a solution containing 4 mM of potassium restored its activity.

Potassium nitrate and thallium nitrate had the same effect on contractions of the rectus abdominis muscle. The concentration-effect curves ran parallel courses. Based on the average values obtained in 11 experiments, the mean active concentrations of the 2 ions (the 50 mm isotonic contraction recorded by the kymograph at 1:25 transmission) may be regarded as identical (K^+ 11.1 mM/l, S.D., 2.36; Tl^+ 10.3 mM/l, S.D., 1.66).

The foregoing findings raise the question why potassium restarts the arrested frog heart; that is, which of its qualities is the one that accounts for its biological actions. ZWAARDEMAKER[3] still believed that it might be the radiation of the ^{40}K isotope. Although the frog heart arrested with potassium-free solution can be restarted with external irradiation[4], it seems certain that the very weak radiation of the active isotope can have no role to play in the effect of potassium. As the Table shows, in our experiments the inactive solution containing $^{39}K^+$ restarted the arrested frog heart in the same manner as did the Ringer in general use which contains $^{40}K^+$. Thallium also is devoid of radiation effect.

Work is now in progress in these laboratories to find out whether the potassium-like actions of thallium are due to the close proximity of the ionic radii alone[1] or in combination with other atomic properties (field strength), and how these actions are brought about by radiation energy; further, to lay clear the causes underlying the antimitotic[5] and radiomimetic[6] activities of thallium.

Effects of potassium and thallium ions on the isolated frog heart

K^+ concentration mM/l	Tl^+	Anion	Tested	No. of hearts: Restarted after arrested with K^+-free solution	No. of hearts: Arrested while working with Ringer containing K^+	Washings to achieve effect
4[a]	–	Cl	15	15		1–2
–	2	Cl	9	7		1–2
–	2	NO_3	14	11		1–2
4	2	Cl	5		5	1–2
–	4	NO_3	12		9	1–2
4	4	NO_3	10		9	1
8	–	NO_3	9		0	4
12	–	NO_3	12		10	1

[a] $^{39}K^+$ employed.

Zusammenfassung. Thallium ist am isolierten Froschherz und M. rectus abdominis von kaliumähnlicher Wirkung. Es setzt das mit kaliumfreier Lösung in Stillstand gebrachte Froschherz in Bewegung, bei erhöhter Konzentration führt es zum Herzstillstand. Am rectus-Muskel verursacht Thallium eine Kontraktur. Seine Aktivität am Froschherz übertrifft jene von Kalium, während am isolierten rectus-Muskel ihre Aktivität gleichwertig ist.

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Further Contribution to the Effect of Diazoxide on the Thyroid Gland in Rats

In 2 previous papers[1,2] we reported the effects of the i.v. injection of 5 mg of diazoxide on the thyroid gland in rats. We found a significant decrease in the 4 h uptake of radioiodine after diazoxide injected just prior to the ^{131}I. However, the blood flow through the thyroid gland at time intervals up to 3 min after the application of diazoxide was elevated. In this paper, we present further results elucidating the relation between the blood flow and radioiodine uptake in the thyroid gland after diazoxide.

Methods. Male Wistar rats weighing 175–210 g fed standard laboratory diet (Larsen) and water ad libitum were used. Methods were the same as described in previous papers[1,2]. The uptake of radioiodine was measured 4 h after an i.p. application of 0.2 μCi ^{131}I. The organ blood flow was indicated by the tissue uptake of radioactive rubidium ^{86}Rb, measured 40 sec after i.v. injection of 10 μCi ^{86}Rb (according to SAPIRSTEIN[3]) and expressed in % of the dose in 1 g of the tissue. 5 mg of diazoxide (Hyperstat Schering) in 0.33 ml of original solution was injected in the tail vein just prior to the application of radioiodine and at different time intervals before the radioactive rubidium (we are grateful to Schering Comp., Bloomfield, New Jersey for kindly supplying the diazoxide).

Results and discussion. The results of the tissue uptake of ^{86}Rb in the thyroid gland at 90 sec, 15 min, 30 min, 1 h, 2 h and 4 h intervals are presented in the Figure. At 90 sec interval after diazoxide, a temporary increase in ^{86}Rb uptake was noted (in agreement with our previous findings[2]). However, at further time intervals the values decrease rapidly, reaching the minimum 62% of the mean control value at 30 min and returning to the initial level at 4 h intervals. The 95% confidence intervals indicate the significance. Radioiodine uptake in the thyroid gland was decreased after diazoxide also in this series of experiments,

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