first experiment, when the inhibitory effect is evident, no histologically demonstrable necrotic lesions have been observed; furthermore, during a severe experimental necrosis, even quite early, an increase in thymidine incorporation into DNA has been noted[6]. The data of JENSEN et al.[1] and the present results can be related to the early observations of HADDOW[7] on inhibition exerted by carcinogenic hydrocarbons on growth of normal and neoplastic tissues. The mechanism of this effect is not yet clear. Some recent data can be quoted as providing some work hypotheses. BOYLAND and GREEN[8] and LIQUORI et al.[9] have reported the solubilization of benzo(a)pyrene and related compounds by dilute solution of DNA, and considered their results as providing evidence for the intercalation of the planar hydrocarbons between the base pairs of DNA; GIOVANELLA et al.[10] consider these data as the result of a non-specific adsorption. An in vivo binding of 1,2,5,6-dibenzanthracene to mouse skin DNA was reported by HEIDELBERGER and DAVENPORT[11], but subsequently MCKINNEY and HEIDELBERGER (unpublished data, quoted in [10]) did not confirm this result.

Table II. Specific activity of DNA (as c.p.m./mg) of regenerating rat liver

	No. of rats	Specific activity	% difference
Mean value of control animals	4	4375	100
Mean value of treated animals	5	1767	40

See Table I. The difference is highly significant.

Riassunto. L'idrocarburo cancerogeno 7,12-dimetilbenz(a)antracene somministrato con iniezione endoperitoneale inibisce l'incorporazione della timidina nel DNA del fegato normale e del fegato rigenerante di ratto.

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[6] M. C. LEEVY, Ann. N.Y. Acad. Sci. *104*, 939 (1963).
[7] A. HADDOW, Nature *136*, 868 (1935).
[8] E. BOYLAND and B. GREEN, Br. J. Cancer *16*, 507 (1962).
[9] A. M. LIQUORI, B. DE LERMA, F. ASCOLI, C. BOTRÉ, and M. TRASCIATTI, J. molec. Biol. *5*, 521 (1962).
[10] B. C. GIOVANELLA, L. E. MCKINNEY, and C. HEIDELBERGER, J. molec. Biol. *8*, 20 (1964).
[11] C. HEIDELBERGER and G. R. DAVENPORT, Acta Un. int. Cancr. *17*, 55 (1961).

Effect of Synthetic Vasopressins on the Myocardial Contractile Force in the Isolated Guinea-Pig Atria

It has been known for some years that pitressin constricts coronary arteries and decreases coronary blood flow in dogs[1–3]. Very recently, WANG[4] observed that synthetic 2-phenylalanine-8-lysine vasopressin (PLV-2) decreased coronary arterial blood flow, thereby reducing myocardial contractility in dogs. However, it remains uncertain whether synthetic vasopressin per se would possess the direct negative inotropic action of the heart. The present study was undertaken to investigate the comparative effect of three synthetic vasopressins, i.e. 8-arginine vasopressin, 8-lysine vasopressin and 2-phenylalanine-8-lysine vasopressin, on the myocardial contractility in the isolated guinea-pig atria.

Guinea-pigs of either sex weighing approximately 500 g were killed by cervical dislocation. Their hearts were removed immediately and the atria excised. The atria were washed twice with and suspended in a bath containing oxygenated Ringer-Locke solution (32°C) through which 95% O_2 and 5% CO_2 (pH = 7.35) was bubbled[5]. The frequency of atrial contraction was kept constant at a rate of 90/min using a Grass stimulator (Model S4). The force of atrial contraction was measured and recorded continuously using a Grass force-displacement transducer (FT-03) and a Grass polygraph (Model 5), respectively. 45 min after the preparation was completed, the effect of the three vasopressins in concentrations between 10 and 320 mU/ml on the myocardial contractile force was examined.

The results of the effect of the three vasopressins in the isolated guinea-pig atria were consistent in all experiments and are summarized in Figure 1. Tracings of representative experiments are illustrated in Figure 2. It was found that concentrations of less than 10 mU/ml of the three synthetic vasopressins in the isolated bath caused essentially no change in the myocardial contractile force. However, higher concentrations (more than 20 mU/ml) of the vasopressins decreased contractile force in proportion to the concentration. In no instance was any increase in the force of myocardial contraction observed. There was no essential difference in the magnitude of the decrease in contractile force between 8-arginine vasopressin and 2-phenylalanine-8-lysine vasopressin. However, the decrement in contractile force by these two vasopressins was slightly greater than that by 8-lysine vasopressin.

From the present study, it is evident that small doses of the three synthetic vasopressins did not show any

[1] E. BULBRING, J. H. BURN, and J. M. WALKER, Quart. J. Med. *18*, 73 (1949).
[2] H. E. ESSEX, R. G. E. WEGRIA, J. F. HERRICK, and F. C. MANN, Am. Heart J. *19*, 554 (1940).
[3] H. D. GREEN, R. WEGRIA, and N. H. BOYLE, J. Pharmacol. exp. Therap. *76*, 378 (1942).
[4] H. H. WANG, Fed. Proc. *23*, 565 (1964).
[5] S. GARB, Am. J. Physiol. *182*, 601 (1955).

change in contractile force of the isolated guinea-pig atria, whereas the larger doses of the vasopressins decreased contractile force in proportion to the dose given. Qualitatively similar observations were also made on synthetic oxytocin given to the isolated guinea-pig atria and dog atrial strips[6]. It can be said that larger doses of vasopressins may depress myocardial contractile force through its direct negative inotropic effect and also indirectly through its coronary vasoconstrictor effects in dogs and possibly in man[7].

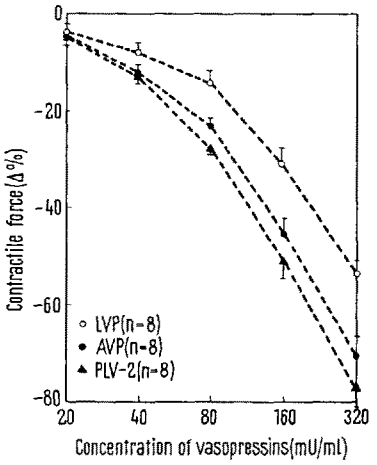

Fig. 1. Effect of 8-lysine vasopressin (LVP), 8-arginine vasopressin (AVP) and 2-phenylalanine-8-lysine vasopressin (PLV-2) on the myocardial contractile force in the isolated guinea-pig atria. Mean ± S.E.

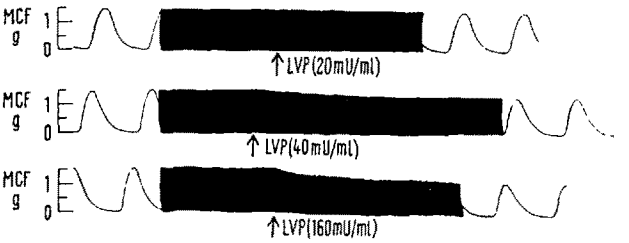

Fig. 2. Effects of 20, 40 and 160 mU/ml of 8-lysine vasopressin (LVP) on the myocardial contractility in the isolated guinea-pig atria.

Zusammenfassung. Niedrige Dosen von 8-Arginin Vasopressin, 2-Phenylalanin-8-Lysin Vasopressin und 8-Lysin Vasopressin (unter 10 mU/ml), haben keinen Einfluss auf die Myokardkontraktion des isolierten Meerschweinchen-Atriums. Grössere Dosen dieser Peptide (über 20 mU/ml), führen zu einer dosisabhängigen Kontraktionsverminderung.

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March 3, 1965.

[6] J. NAKANO and R. D. FISHER, J. Pharmacol. exp. Therap. *142*, 206 (1963).

[7] This work was supported in part by research grants from the US Public Health Services (HE 08057 and HE 07334). The authors are indebted to Dr. R. BIRCHER of Sandoz Pharmaceuticals, Hanover (N.J., USA)for generous supplies of vasopressins.

Sekretorische Aktivität des Flexural- und Subcommissuralorgans bei frühen Entwicklungsstadien von *Triturus alpestris* Laur.

Die augenfälligste sekretorische Tätigkeit des Subcommissuralorgans (SCO) besteht in der Bildung des Reissnerschen Fadens (RF) (OLSSON[1], HOFER[2] und OKSCHE[3]). Bei Untersuchungen an Embryonen niederer Vertebraten (bes. *Salmo* und *Esox*) findet OLSSON[4] im Neuralrohr einen gut entwickelten RF, während ein SCO noch nicht nachzuweisen ist. Cranialwärts lässt sich der Faden bis in die Region der Plica ventralis encephali verfolgen. Diesen Ursprungsort des RF in den frühen ontogenetischen Stadien bezeichnet OLSSON als Flexuralorgan (FO). Im weiteren Verlaufe der Entwicklung übernimmt das SCO die Bildung des RF, wobei zunächst das FO noch tätig ist, später aber seine Aktivität einstellt.

In der vorliegenden Arbeit wurden Embryonen und Larven von *Triturus alpestris* auf dieses Phänomen hin untersucht. Als äusserst störend erwies sich dabei zunächst das im gesamten Embryo massenhafte Auftreten eines Melaninpigmentes. Es erschien nach Färbung mit Chromhämatoxylin oder Aldehydfuchsin gleich tingiert wie die Sekretgranula im FO oder SCO. Erst durch eine verlängerte Vorbehandlung mit H_2O_2 gelang es, klare Bilder zu erzielen. Als beste Färbemethode erwies sich das Aldehydfuchsin ohne jede Gegenfärbung. Parallel dazu wurden fluoreszenzoptische Untersuchungen mit Pseudoisocyanin (STERBA[5]) durchgeführt. Die Einteilung der Embryonalstadien der Molche erfolgte nach KNIGHT[6].

Ein erstes Auftreten des RF ist schwierig zu datieren, da der Faden sehr dünn und dadurch seine Farbqualität kaum zu erkennen ist. Auch das Vorkommen verschiedenartiger Koagulationsprodukte kompliziert die Beurteilung. Im Neuralrohr der Knight-Stadien (KS) 22–24 (Länge der Embryonen ca. 3–4 mm) ist eine äusserst dünne, fadenartige Bildung zu erkennen, deren craniales Ende im Bereich des FO liegt. Die Zellen sind hier noch relativ niedrig. Ausser einigen kleinen Granula und einer schwach violetten Färbung in den apikalen Zellbereichen zeigen die Regionen von FO und SCO keine auffällige Sekretion. Die Aktivität verstärkt sich etwas in den KS

[1] R. OLSSON, *The Subcommissural Organ* (Stockholm 1958).
[2] H. HOFER, Verh. dtsch. zool. Ges., Frankfurt a. M. (1958). Zool. Anz., Suppl. *22*, 202 (1959).
[3] A. OKSCHE, Z. Zellforsch. mikrosk. Anat. *54*, 549 (1961).
[4] R. OLSSON, Acta zool. Stockh. *37*, 235 (1956).
[5] G. STERBA, Z. Zellforsch. mikrosk. Anat. *55*, 763 (1961).
[6] F. C. E. KNIGHT, Wilhelm Roux Arch. Entw.-Mech. Org. *137*, 461 (1938).