counteracts or enhances the facilitatory action of Reserpine on Metrazol induced seizures.

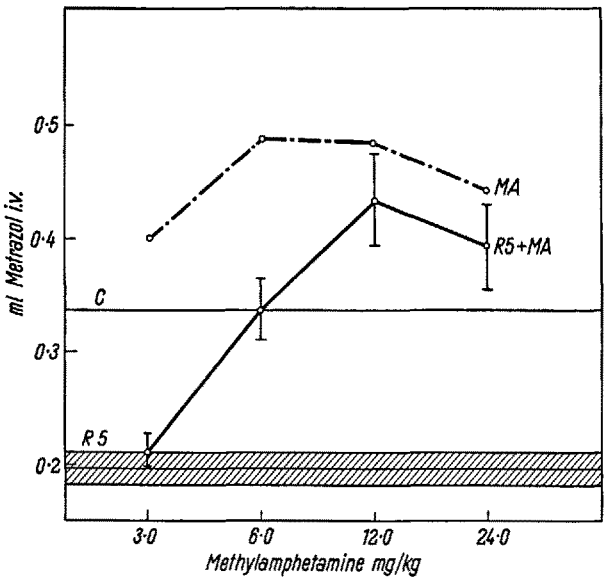

Fig. 2.—*Mean threshold (± s.e.m.) for tonic-extensor seizures on mice induced by Metrazol.* Metrazol was injected 15 min after various doses of Methylamphetamine(abscissa). *MA* = Methylamphetamine (each point, $n = 15$). *R5 + MA* = Reserpin 5 mg/kg injected 150 min before Methylamphetamine (each point, $n = 15$). *C* and *R5* same as in Figure 1. No normal frequency distribution was obtained for *C* and *MA*.

Metrazol-convulsions were induced in white mice (20–21 g) by infusion of a 0·5% solution into a tail vein at the rate of 0·05 ml every 10 sec until the occurrence of maximal tonic-extensor seizures (ORLOFF, WILLIAMS, and PFEIFFER[4]). (+)-Methylamphetamine hydrochloride was injected intraperitoneally $2^1/_2$ h after a constant dose of Reserpine (5 mg/kg intraperitoneally).

Reserpine considerably lowered the threshold for tonic extensor seizures (Fig. 1, 2). When Methylamphetamine 12 mg/kg was injected after Reserpine, the animals woke up a few minutes later from their somnolent, motionless state, and at the same time the low extensor seizure threshold was raised (Fig. 1). This action reached its maximum 15 min after the injection of Methylamphetamine. Thereafter various doses of the latter were injected after Reserpine and the Metrazol test was carried out 15 min later. Figure 2 demonstrates that Methylamphetamine in doses between 3 and 24 mg/kg raised the extensor seizure threshold of Reserpine pre-treated mice, the logarithm of the dose and the action showing approximately a linear relation within the dose range of 3 and 12 mg/kg. Methylamphetamine alone was followed by a marked elevation of seizure threshold; a complete abolition of tonic extensor seizures, as described by CHEN and BOHNER[5], could not be observed after the Methylamphetamine doses used in these experiments.

From the fact that substances like Iproniazid and Methylamphetamine both antagonize the sedative action of Reserpine[6] and abolish its CNS facilitatory action (Iproniazid[7]), it can be concluded that the state of alertness and spread of seizure discharge are closely connected.

W. KOBINGER

LEO – Pharmaceutical Products, Pharmacological Laboratory, Copenhagen (Denmark), May 20, 1958.

Zusammenfassung

Die durch Reserpin herabgesetzte Schwelle für tonische Streckkrämpfe, ausgelöst durch Metrazol (Cardiazol), konnte durch Methylamphetamin erhöht werden. Methylamphetamin ist ein wirksamer Antagonist der sedativen Wirkung des Reserpins.

[4] M. J. ORLOFF, H. L. WILLIAMS, and C. C. PFEIFFER, Proc. Soc. exp. Biol. Med. *70*, 254 (1949).

[5] G. CHEN and B. BOHNER, Fed. Proc. *15*, 408 (1956).

[6] K. TRIPOD, M. J. BEIN, and R. MEIER, Arch. int. Pharmacodyn. *96*, 406 (1954). – B. B. BRODIE, A. PLETSCHER, and P. A. SHORE, J. Pharmacol. *116*, 9 (1956).

[7] W. KOBINGER, Arch. exp. Path. Pharmakol. *233*, 559 (1958).

Paradoxical Effect of Quinidine upon Coronary Flow of the Isolated Heart at Different Temperatures

According to the few experimental data available, quinidine does not affect the coronary flow either in the dog heart-lung-preparation (BODO[1]), in the perfused dog heart (ELEK and KATZ[2]), or in the revived human heart perfused by the Langendorff method (KOUNTZ[3]).

In our experiments, isolated rabbit hearts perfused by the Langendorff method and subjected to experimental ventricular fibrillation (rectangular impulses of 10 ms duration and 30 Hz frequency) were used. In an other series, the hearts were allowed to beat spontaneously. The isolated hearts were perfused with warm (38°C) and cold (26°C) Locke solution alternately. In all experiments, quinidine has been administered in form of single injections of 2 mg drug in 1 ml Locke solution. Injections were given to the region of the orifice of the coronary vessels through a thin catheter placed in the aortic cannula.

At 38°C temperature, quinidine, after a possible slight increase of 30–60 s duration, consistently depressed the coronary flow in fibrillating hearts, whereas at 26°C the same doses increased it markedly. The same was found to hold for hearts beating spontaneously.

Table Ia summarises the maximal changes in the coronary flow in fibrillating hearts at different temperatures. 'Maximal flow' means the highest value of coronary flow observed during the drugs action, expressed in ml/min.

Table Ib gives the changes in the total flow during drug action. 'Total flow' indicates the amount of Locke solution in ml, flowing through the coronaries from the onset of drug action until the evanescence of the latter. 'Changes in the total flow' means the difference between the above value and the flow observed in the absence of the drug during a corresponding control period.

Table IIa and IIb represent the corresponding changes in the spontaneously beating heart.

L. SZEKERES and G. LÉNÁRD

Institute of Pharmacology, Medical University, Pécs (Hungary), April 28, 1958.

[1] R. BODO, J. Physiol. *64*, 365 (1927).

[2] S. R. ELEK and L. N. KATZ, J. Pharmacol. exp. Ther. *75*, 178 (1952).

[3] W. B. KOUNTZ, J. Pharmacol. exp. Ther. *45*, 65 (1932).

Table I.—The action of quinidine upon coronary flow in the perfused fibrillating rabbit heart at 38° C and 26° C temperatures

a) Maximal changes in coronary flow

n	26° C			% change	*n*	38° C			% change
	Coronary flow ml/min					Coronary flow ml/min			
	Initial	Treated	Change			Initial	Treated	Change	
10	24·80 ± 1·73	3·50 ± 2·63	+ 8·75 ± 1·65 $t = 5{\cdot}30$ $p < 0{\cdot}001$	+35·3	10	37·60 ± 2·96	26·40 ± 2·50	− 11·20 ± 1·65 $t = 6{\cdot}80$ $p < 0{\cdot}001$	−29·8

b) Changes in the total flow

n	26° C			% change	*n*	38° C			% change
	Total coronary flow ml					Total coronary flow ml			
	Initial	Treated	Change			Initial	Treated	Change	
10	78·70 ± 9·67	92·60 ±14·22	+13·90 ± 3·76 $t = 3{\cdot}7$ $p > 0{\cdot}001$ $p < 0{\cdot}01$	+17·7	10	264·10 ±25·16	218·35 ±19·32	−45·75 ± 8·61 $t = 5{\cdot}32$ $p < 0{\cdot}001$	−17·3

Table II.—The action of quinidine upon coronary flow in the perfused spontaneously beating rabbit heart at 38° C and 26° C temperatures

a. Maximal changes in coronary flow

n	26° C			% change	*n*	38° C			% change
	Coronary flow ml/min					Coronary flow ml/min			
	Initial	Treated	Change			Initial	Treated	Change	
10	25·90 ± 2·42	35·75 ± 3·07	+ 9·85 ± 1·34 $t = 7{\cdot}35$ $p < 0{,}001$	+38·0	10	30·70 ± 3·47	23·05 ± 2·26	− 7·65 ± 1·47 $t = 5{\cdot}21$ $p < 0{\cdot}001$	−24·9

b. Changes in the total flow

n	26° C			% change	*n*	38° C			% change
	Total coronary flow ml					Total coronary flow ml			
	Initial	Treated	Change			Initial	Treated	Change	
10	91·80 ± 4·66	104·90 ± 5·02	+13.10 ± 2·04 $t = 6{\cdot}42$ $p < 0{\cdot}001$	+14·5	10	159·35 ±15·35	142·32 ±11·94	−17·03 ± 4·55 $t = 3{\cdot}75$ $p > 0{\cdot}001$ $p < 0{\cdot}01$	−10·9

Zusammenfassung

Nach Langendorff wird am isolierten Kaninchenherzen gezeigt, dass die Temperatur der Durchströmungsflüssigkeit sowohl an spontan schlagenden wie auch an elektrisch gereizten Herzen bei Kammerflimmern die Koronarienwirkung des Chinidins grundsätzlich abzuändern vermag. Bei 26°C Temperatur wird der Koronardurchfluss durch Chinidin ständig erhöht, während bei 38°C Chinidin die Herzkranzgefässe verengert.

Die Wirkung von synthetischem Oxytocin (Syntocinon) und Acetazolamid auf die Ausscheidung von Wasser, Natrium und Kalium

Ein Extrakt der Neurohypophyse (NH), der reich an Oxytocin, aber fast frei von Vasopressin ist, verstärkt die Wirkung des Acetazolamids (ACA) auf die Wasser-, Natrium- und Kaliumdiurese. Da die Wirkung von 100 mE Oxytocin und die für die Hemmung der Carboanhydrase nötige maximale Dosis von ACA sich summieren, besteht die Möglichkeit, dass der Wirkungsmechanismus des NH-Präparates von der Carboanhydrase unab-