wir in entsprechender Weise wie für Heparin auch den Einfluss von Glykogen bzw. Dextran (5%ige Lösung in einer der Badeflüssigkeit entsprechenden Tyrode; 0,1, 0,25, 0,5, 1,0 ml) auf die Wirkung von 5-HT *in vitro*.

Ergebnisse

Rattencolon. Zugabe konstanter Mengen von 5-HT-Kreatininsulfat zum Bad in regelmässigen Zeitabständen führt zu den bekannten Kontraktionen des Colons. Wird dem Bad vorgängig Heparin in der erwähnten Dosierung zugefügt, so bleibt die übliche, auf 5-HT-Zugabe folgende Kontraktion aus oder sie ist wesentlich abgeschwächt. Die Verminderung der Amplitude ist der zugefügten Heparinmenge proportional; die zur Aufhebung der 5-HT-Wirkung notwendige Heparinmenge ist von Präparat zu Präparat verschieden.

Wird nach diesen Heparinzugaben und dem Auswaschen 5-HT wiederum allein zugegeben, so sind die Amplituden der Kontraktionen bei einem Teil der Präparate deutlich kleiner als diejenigen der Ausgangswerte. In diesem Falle werden die ursprünglichen Amplituden erst nach drei bis fünf 5-HT-Gaben wieder erreicht. Die gleichzeitige Verabreichung von 5-HT und Heparin in einer Mischlösung hat dieselben Resultate ergeben. Auch hier lässt sich in jedem Versuch eine dosisabhängige antagonistische Wirkung des Heparins zum 5-HT erkennen.

Wird statt Heparin eine Glykogen- oder Dextranlösung in der erwähnten Dosierung verabreicht, so werden die nachfolgenden 5-HT-Kontraktionen in keiner Weise beeinträchtigt; vorgängige Zugaben von Tyrodelösung verändern die 5-HT-Wirkung ebenfalls nicht.

Rattenuterus. In allen geprüften Präparaten hat Heparin zu einer Hemmung oder Aufhebung der 5-HT-Wirkung geführt, währenddem Tyrode, Glykogen oder Dextran keine Veränderungen bewirkten.

Nach Drucklegung erhielten wir Kenntnis von der Arbeit von G. and A. N. SMITH [Surgery, Gynecology and Obstetrics *101*, 691 (1955)]. Diese Autoren fanden *in vivo* bei der experimentellen Lungenembolie der Katze und *in vitro* am Rattencolon ebenfalls einen Antagonismus zwischen Heparin und Serotonin.

R. KELLER

Institut für Hygiene und Arbeitsphysiologie der Eidgenössischen Technischen Hochschule, Zürich, den 10. Dezember 1956.

Summary

In the isolated rat colon and uterus, heparin caused inhibition or elimination of contractions occurring after the administration of 5-hydroxytryptamine. In contrast to this, neither Tyrode's solution, nor glycogen, nor dextran produced any change in the response of these organs to 5-hydroxytryptamine.

Investigation of the Physiologically Different Glycogen Fractions in Newborn Rabbits

There are numerous publications dealing with the physiological importance of the two glycogen fractions found in animal tissues. MERRICK[1], for instance, established a correlation existing between the glycogen level of the heart muscle, the distribution of the glycogen fractions and the resistance to anoxia in several specii of different degrees of phylogenetic development.

The resistance to anoxia definitely alters in the course of the ontogenetic development. It is a question whether the glycogen content of the tissues proves correspondingly different when assayed at an age exhibiting the greatest differences in resistance to anoxia. A comparison was made and in addition the effect of fasting and acute anoxia on the glycogen fractions was studied in rabbits, which species exhibits ten times greater resistance to anoxia in the newborn than in adults.

The total glycogen hydrolysable in KOH, the trichloracetic acid soluble free glycogen and the protein-bound residual fraction show the following changes:

The correlation described by MERRICK, existing between anoxic resistance and heart-glycogen may also be established to some extent, as the newborn rabbit disposes of much greater stores during the first 24–48 h of life than the adult. A higher glycogen level is found not only in the heart muscle, but in all tissues investigated with the exception of the liver, such as the m. long. dorsi, m. biceps femoris, m. abdominis and the lung. (see table). There are no appreciable changes in the percentual distribution of the fractions in the age-groups investigated. Consequently the characteristic adult level is reached by the simultaneous decrease of the two fractions from the higher newborn level. The amount of the protein-bound glycogen in the white muscle remains unchanged in the course of development.

After fasting, the mobilisation of glycogen changes as follows: the total glycogen decreases abruptly in the liver, diminishes somewhat less in the m. abdominis (red muscle) and in the m.l.dorsi (white muscle) and exhibits small changes in the heart and in the lung, both in the newborn and in the adults. Examining the individual fractions, we find the following results: in the adult the trichloracetic acid soluble fraction exhibits a great percentual decrease and there is an increase of the protein-bound glycogen; in the newborn, however, a similar decrease of the two fractions may be detected. Consequently there is no difference between the precentual distribution of the fractions in fasting and non-fasting newborn animals. In adults a shift occurs in the ratio of the two fractions.

Acute anoxia exerts the following effect on the tissue-glycogen of newborn rabbits: in the striated muscles it remains unchanged, in the liver a small but not significant variation occurs. In the lung, the simultaneous decrease of the two fractions causes a loss of 25%. In the heart-muscle 68% of the normal glycogen content disappears, which is the result of a break-down in both fractions, with relative increase of the protein-bound glycogen. MERRICK described a similar phenomenon in adults, with the exception that he found an increase in the absolute value of protein-bound glycogen as well.

In summary, higher glycogen values are found in the newborn in both fractions. The protein-bound glycogen of the newborn shows not such a degree of stability as in adults, which may be a result of the difference in the glycolytic processes.

Zs. N. GASPAR

Institute of Physiology, Veterinary Faculty, Budapest, October 2, 1956.

[1] A. W. MERRICK, Amer. J. Physiol. *176*, 83 (1954). – A. W. MERRICK and D. K. MEYER, Amer. J. Physiol. *177*, 441 (1954).

The glycogen content of the tissues of newborn and adult rabbits

Tissue	Glycogen fractions	Newborn			Adult		
		No.	mg/100 g wet weight	%	No.	mg/100 g wet weight	%
Heart muscle	Total glycogen	18	755 ± 57		6	398 ± 101	
	TCA soluble glycogen		578 ± 32	76		269 ± 55	67
	Bound glycogen		177	24		130	33
M. long. dorsi	Total glycogen	17	1468 ± 59		6	843 ± 142	
	TCA soluble glycogen		1181 ± 26	80		545 ± 96	65
	Bound glycogen		287	20		299	35
M. abdominis	Total glycogen	18	573 ± 31		6	280 ± 49	
	TCA soluble glycogen		364 ± 31	64		186 ± 36	66
	Bound glycogen		209	36		94	34
M. biceps femoris	Total glycogen	5	913				
	TCA soluble glycogen		720	79			
	Bound glycogen		193	21			
Liver	Total glycogen	14	917 ± 171		6	4042 ± 1165	
	TCA soluble glycogen		751 ± 68	82		3646 ± 1032	90
	Bound glycogen		166	18		396	10
Lung	Total glycogen	10	376 ± 16		5	99 ± 3	
	TCA soluble glycogen		228 ± 23	61		58 ± 7	58
	Bound glycogen		148	39		41	41

Zusammenfassung

Es wird das Verhältnis von gebundenem und trichloressigsäurelöslichem Glykogen in verschiedenen Muskeln, Leber und Lunge von neugeborenen und ausgewachsenen Kaninchen bestimmt und auf einen Zusammenhang zwischen Glykogenspiegel und Resistenz gegenüber Sauerstoffmangel hingewiesen; ferner auf Änderungen im Glykogenspiegel bei akutem Sauerstoffmangel und Hunger.

The Effect of Amphetamine on Food Intake in Rats with Hypothalamic Hyperphagia

The increasing evidence implicating hypothalamic centers in the regulation of food intake raises the possibility that these centers may be the site of action of appetite-depressing drugs. Recently, BROBECK *et al.*[1] reported increased electrical activity in the medial portion of the hypothalamus, but not in adjacent regions, following the parenteral administration of amphetamine derivatives in anesthetized cats. Utilizing the concept of a lateral feeding center and a medial inhibitory (satiety) center[2], these authors speculated that "amphetamine excites the medial portion of the hypothalamus which contains an inhibitory part of a 'feeding centre' ". If this is true, the appetite-depressing action of amphetamine should be lessened or abolished in animals made hyperphagic by the bilateral destruction of the ventromedian nucleus of the hypothalamus, which is generally considered to be the inhibitory center.

Methods.—The ventromedian nucleus was destroyed bilaterally in albino rats (Sprague-Dawley strain) by means of the Krieg stereotaxic instrument. Nine of 19 rats operated on became definitely hyperphagic as evidenced by a daily food intake in excess of 40 g per day at a time when the control animals were eating approximately 20 g per day. All animals were maintained in air-conditioned quarters on an *ad libitum* intake of food (ground Purina Laboratory Chow) and water. The hyperphagia had reached its peak and had begun to decline when the administration of amphetamine was started, but no decrease in the excessive rate of weight gain was in evidence.

Powdered amphetamine was thoroughly mixed in the ground food, by means of a Henry velocity mixer, in a dosage of 0·2 mg of drug per g of food. Rats were fed the amphetamine-containing food for a period of one week, preceded and followed by control weeks on normal food. In a second series of experiments, the drug was administered subcutaneously (5 mg/kg, at 5:00 P M daily) for one week in order to eliminate the possibility that the taste of the drug in the food might influence the food intake. The results were similar in the two series.

Results.—The results are summarized in the Tables I and II. It is apparent that the hyperphagic rats are hypersensitive to the action of amphetamine. Rat No. 5 refused all food for a period of 6 weeks following amphetamine injections and then gradually resumed eating. In addition, one hyperphagic animal (not included in the series) died after the subcutaneous administration of the drug for 5 days; no gross lesions were found at autopsy. The difference in sensitivity of the two groups of animals is especially marked when the drug is administered parenterally, probably due to the maintenance of drug dose despite declining food intake.

Discussion.—According to the concept of interacting lateral feeding and medial satiety centers in the hypothalamus, an agent which decreases food intake might do

[1] J. R. BROBECK, S. LARSSON, and E. REYES, J. Physiol. *132*, 358 (1956).

[2] B. K. ANAND and J. R. BROBECK, Yale J. Biol. Med. *24*, 123 (1951). – J. M. R. DELGADO and B. K. ANAND, Amer. J. Physiol. *172*, 162 (1953).