males or of females ($P < 0.001$). A comparison between the values of the correlation coefficients and of the partial correlation coefficients, respectively, showed that, in groups which were subdivided according to the blood groups, the correlation coefficient in the blood group '0' was conspicuously low. Provided that the sex is not taken into consideration, it may be inferred that in the subgroups with the blood groups 'A', 'B', and 'AB' the dependence is statistically assured (in the groups 'A' and 'B' $P < 0.001$, in the group 'AB' $P \gtrsim 0.01 - 0.05$). In groups subdivided according to sex and blood groups, the dependence is not statistically assured if the groups consist of only a small number of subjects (females: groups 'B' and 'AB', males: group 'AB'). There is, however, reason to believe that even in these groups the dependence will prove to be significant if the number of subjects under investigation is increased. This assumption is based on the finding that a statistically significant dependence is observed when males and females of the same blood group are investigated as one group (i.e. when the number of subjects under investigation is increased). In the group of donors with the blood group '0', such a dependence could not be demonstrated, and, even if the number of subjects under investigation were increased, it could not be expected. The highest regressive coefficient of dependence of the values of bound hexoses on the values of total proteins was observed in the group 'AB'.

Discussion. It appears that the synthesis of the majority of plasma proteins, with the exception of glycoproteids, is accomplished in the liver[6-9]. It is assumed that under pathological conditions an increase in the level of glycoproteids in the serum is brought about by the liberation of a certain humoral factor which stimulates their synthesis[10]. It can reasonably be expected that under physiological conditions, the synthesis of the different fractions of plasma proteins and their penetration through the cytological membranes are determined by a certain law. One of the manifestations of this law is perhaps the dependence of the values of bound hexoses on the values of total proteins, which could be demonstrated in our experiments while carrying out in the first place an investigation of a whole group of blood donors, and then of its two subgroups – males and females. With regard to blood groups, such a dependence was observed only in the groups 'A', 'B' and 'AB'. From this it appears that in the group of blood donors with the blood group 'O', where such a dependence was not observed, the cause might have been a change either in the conditions of the formation of some protein fractions of the blood-serum (glycoproteids ?) or in the conditions of the penetration of these fractions through cytological membranes into the blood. A detailed report of these observations will be published elsewhere.

Zusammenfassung. Bei einer Gruppe von 400 Blutspendern wurde die Abhängigkeit gebundener Hexosen von Werten des Gesamteiweisses im Blutserum festgestellt. Einzig bei Blutgruppe «0» wurde keine solche Abhängigkeit beobachtet.

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Hyperemin, a New Vasoactive Substance which Regulates the Metabolic Responses of the Coronaries

In earlier investigations the metabolic adaptive capacity of the coronary vessels measured by reactive hyperemia (RH) was decreased after blocking the coronary vasoconstrictor tone and was interpreted as a consequence of decreased 'constrictor reserve' for the metabolic dilatation. However, in a number of cases the RH not only diminished but disappeared completely[1-3].

The present experiments succeeded in demonstrating that in this later case a substance was depleted from the heart which, when normally present, provides the coronaries with their ability to dilate in response to metabolic stimuli[4]. In the absence of this substance, no RH could be produced and other metabolic stimuli, such as adrenalin administration, also failed to produce a dilatation.

On 81 dogs with open chest under morphine-chloralose narcosis, the coronary blood flow (CBF) was measured by a rotameter, and RH was produced by clamping the inflow tube of the rotameter for 10 to 30 sec. To eliminate the RH, surgical or pharmacological blockade of the coronary vasoconstrictor tone was attempted, i.e. stelletectomy or intra-coronary administration of agents such as hexamethonium (C_6), dibenamine, or other procedures were performed, which had proved to be active in earlier investigations[1-3]. If stelletectomy or C_6 failed to eliminate RH, hypoxic periods were performed by incomplete occlusion of the inflow tube of the rotameter or cyanide (CN) was administered[4]. By this means RH was eliminated in 60% of the experiments. In all these cases CBF was not maximal; sometimes it did not change while in other cases it decreased. Blood pressure was often unchanged, but a drop as well as an elevation could equally often be observed. After stelletectomy, RH disappeared 5 sec to 1 h later. During the experiments RH was tested periodically and test samples were taken from the coronary sinus. The samples were centrifuged, and the plasma, or a portion of the plasma which was heated to 100 °C, was tested on a second dog heart or isolated rat heart (49

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hearts) for its ability to restore the disappeared RH or to alter normal RH.

In Figure 1, two samples from a 'donor' dog were tested on the RH of a second dog in which RH had been eliminated previously by DNP administration. Sinus samples 38/II–IV, which were taken from the 'donor' dog after stelletectomy, reestablished RH in the test dog. However, samples 38/V–VI did not contain the RH-influencing substance, for no effect was seen on the disappeared RH of the test animal.

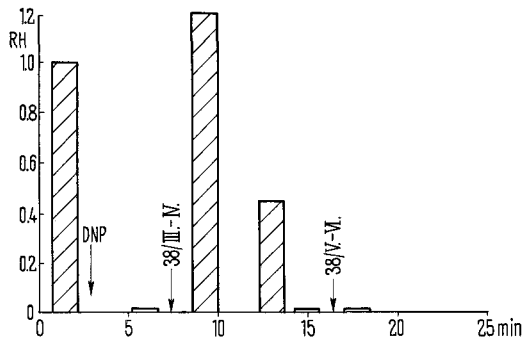

Fig. 1. Demonstration of the presence of RH-influencing substance by re-establishing disappeared RH of a test dog. – The diagram illustrates the RH changes of one test dog during several periods of the experiment. Columns: magnitude of RH on test dog following 20 sec of clampings of the left coronary artery. (The magnitude of RH was characterized by hyperemic peak flow × duration of RH, control value taken as a unit.) – After the control RH, 30 mg DNP was given into the coronary artery, which caused a 150% increase in flow. Blood pressure did not change; it remained 125 mm Hg. After turning back the flow to norm, RH disappeared. 3 ml of III–IV sinus sample of No. 38 donor dog containing the effective material reestablished RH; samples V–VI (3 ml of each) do not contain the effective material: they were ineffective in reestablishing disappeared RH.

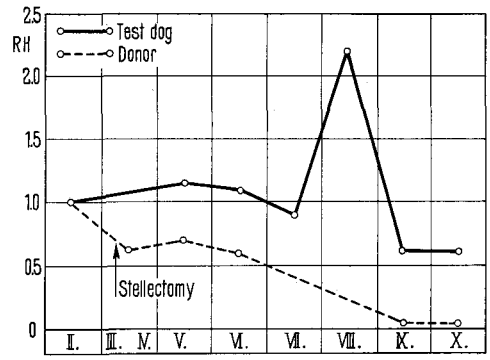

Fig. 2. Relationship between the disappearance of RH and the appearance of an RH-influencing substance in the sinus blood of one dog. The diagram illustrates the changes in donor RH during the period when the several sinus samples were collected and the changes of the test dog RH after administration of these samples. The numbers on baseline (II–X) represent time periods for donor and test dogs in which samples were taken from the donor and the periods when the same samples were administered for the test dog. The ordinate represents changes of magnitude of RH for donor and test dog, respectively. (Magnitude of RH, see Figure 1.) – After the control period (sample II), the donor was stelletectomized. After a steady state (III–VI), RH began to fall. During periods IX and X, RH completely disappeared. Note that only sample VIII of the donor, taken before RH completely disappeared, increases RH of the test dog. (Blood pressure of the donor dropped initially from 115 mm Hg to 80 mm Hg after stelletectomy, but turned back again before sample IX was taken.

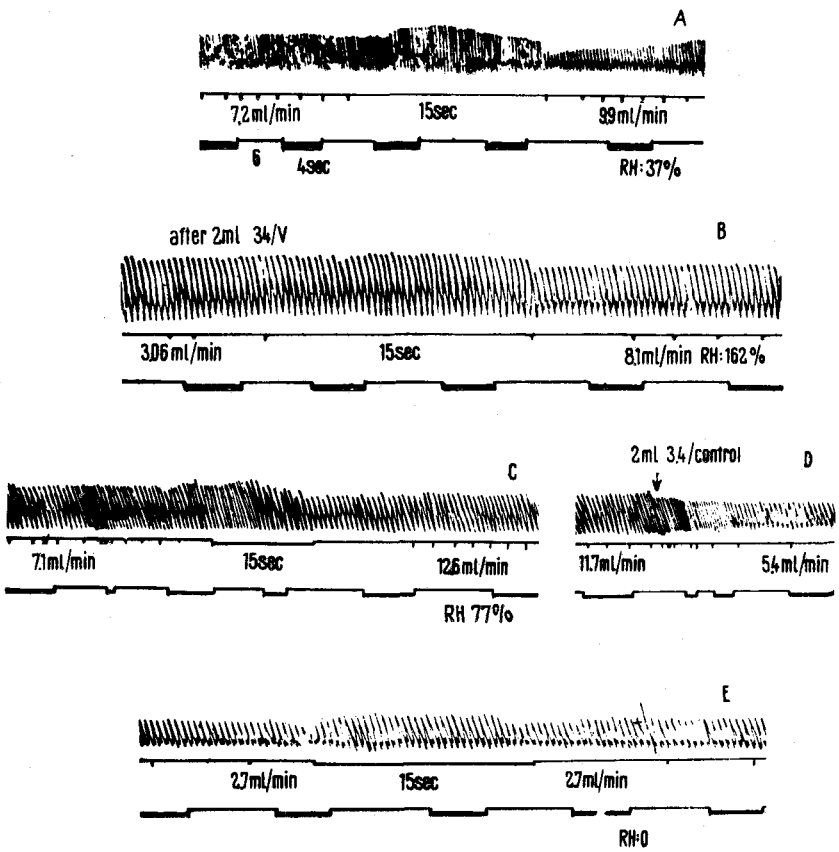

Fig. 3. The effect of RH-influencing substance on an isolated rat heart. Upper base line: coronary flow in ml/min. Lower base line: time signal. *A*, In the control period after a 15 sec arrest of coronary flow, RH was 37%. *B*, 2 ml of the sinus sample of the donor dog containing the effective material (34/V) causes a negative chrono- and positive inotropic effect. Flow diminished from 7.2 ml/min to 3.06 ml/min. 15 sec. arrest of the flow resulted in 162% flow increase. *C*, The RH still augmented. Also, the hyperemic peak flow exceeds the control value (12.6 ml/min). *D*, Control sample causes constriction from 11.7 ml/min to 5.4 ml/min. *E*, After administration of the control sample, RH disappeared. (Coronary flow was recorded by a special flowmeter[6]).

This active substance influences the normal RH too by increasing its magnitude. Figure 2 shows that the only active sample of the donor was taken while its RH was disappearing, i.e. when the substance required for normal RH was being released in the coronary venous blood. Here, RH disappeared in the donor 30 sec after stelletectomy. Samples II-VII, taken before RH began to decline, did not alter the normal RH responses of the test dog. Sample VIII, which was taken while RH was disappearing and while the active substance was being released, increased the RH of the test animal considerably. On the other hand, samples IX and X, taken after RH had disappeared in the donor, had again no effect on the test animal's RH, for the active material had been previously depleted.

Figure 3 shows the typical actions of the RH-influencing material on the isolated rat heart. Besides its strong action on RH, an increase from 37% to 162%, the administration of the active substance caused a constrictor effect too. (Flow dropped from 7.2 ml/min to 3.06 ml/min.) This constrictor response was regularly present in dog hearts also, although to a smaller degree (under 10%). As the Figure shows, control plasma induces coronary constriction on the isolated rat heart too; but instead of being increased, RH disappeared after its administration. The negative chronotropic and the positive inotropic action seen in this Figure are characteristic for this material only in larger doses; in more moderate doses no effect on the heart could be observed, whereas the coronary effects were still very pronounced.

On isolated rat hearts, RH and heart beats are restored after DNP or CN poisoning by the substance described. The active substance has a positive inotropic effect on the dibinamine-treated Straub's hearts. Boiling did not alter these effects. Vasopressin, angiotensin, ATP, ADP, IMP, adrenalin, noradrenalin, metanephrine, bradykinin, serotonin, $CaCl_2$, and $MgCl_2$, were found not to simulate the characteristic action of the active substance described. Therefore, a new name, hyperemin, is suggested for this new vasoactive substance.

Considering the fact that the release and depletion of hyperemin does not take place immediately after stelletectomy, it is understandable why some authors, neglecting these circumstances, were unable to find the disappearance of RH after stelletectomy[5]. On the other hand, the release of hyperemin may be continuous without any complete depletion which can maintain a good state of reactive hyperemia for a longer period after stelletectomy or C_6 administration.

Zusammenfassung. Unter bestimmten Bedingungen gelang im Koronarsinusblut der Nachweis einer Substanz, welche eine normale reaktive Hyperämie der Koronargefässe vergrössern und eine gewichene reaktive Hyperämie wiederherstellen kann. Diese Substanz hebt DNP- und CN-Effekte auf und scheint mit bisher bekannten gefässaktiven Substanzen nicht identisch.

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Denervation Atrophy: Enzyme Changes in the Control Muscle

It is generally accepted that nerves exert a trophic influence upon the muscles that they supply. Transection of the nerve is followed by muscle atrophy which differs, in many respects, from the muscle wasting resulting from lack of use. Many experimental studies have been concerned with the morphological and biochemical changes that take place in the denervated muscle. In these studies, it is a common practice to sever a nerve, in one extremity, and to use as control the contralateral, normally innervated limb, from the same animal. However, it is known that muscles undergo hypertrophy and morphological changes in response to increasing work demands[1]. Denervation of one limb must place a greater work load on the contralateral muscles. Thus, using these muscles as controls may not be entirely adequate. Our study of lactic dehydrogenase (LDH) in denervated and contralateral soleus, using intact animals as controls, shows that changes in the activity of this enzyme do occur in the contralateral muscle.

The enzyme LDH is known to exist in at least two principal forms, each being a tetrameric molecule containing four polypeptide subunits. These two forms have been found in different proportions in several tissues. They have received the names of muscle (M) and heart (H) LDH[2]. In general, M LDH predominates in muscles with high glycolytic and low oxidative activity, whereas H LDH is higher in muscles with the opposite metabolic pattern. We chose to study these two forms because of their characteristic changes in denervated muscle[2].

The present study involved twelve adult white male rabbits. Six of these underwent unilateral transection of the sciatic nerve, high in the thigh, with removal of one piece of the nerve about 1 cm long. The remaining six rabbits (normal controls) underwent no surgery. Both groups were similarly fed and housed. Two months after surgery, they were killed by a blow on the head followed by exsanguination. In the operated group, the soleus from both legs was removed and dropped in liquid nitrogen. In the control group, the soleus from one leg was similarly obtained. Each specimen was homogenized in the cold,

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