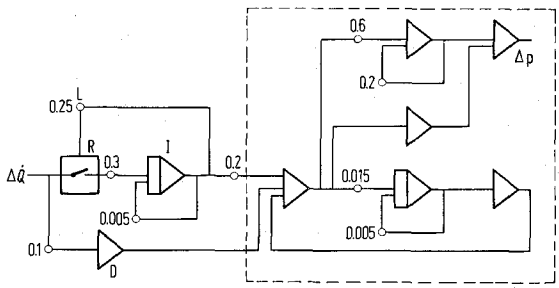

Fig. 2. Analog circuit to simulate the pressure response in the renal artery (Δp) to flow inputs ($\Delta \dot{Q}$). The dashed square represents the linear part of the transfer function; see eq. 1 in the text. The rest of the circuit represents the nonlinear element as explained in the text. The numbers refer to the potentiometer settings.

charged during the pulse and only slowly decharges after the pulse with a time constant of 200 sec (in the given example). The direct effect of the pulse goes via amplifyer D. When the integrator output (i.e. the 'activated state') reaches a certain level, provided by potentiometer L, relay R switches the input to the integrator off.

The simulation was performed on a TR 48 analog computer. The effect of the nonlinear element can be seen in the lower part of Figure 1. The first response corresponds to the summation of the pulse response and the response to the square input of the 'activated state'. If a 2nd pulse is provided before the 'activated state' has declined to Zero, the response will be much smaller. The 3rd pulse in Figure 1 (lower part) is still shorter after the previous pulse. Therefore, nearly no change in the 'activated state' is produced by the pulse and the reaction corresponds to the response which would be expected from the linear model. In a quite similar way, examining sinusoidal inputs, the results provide information only about the linear part of the system as long as the integrator (the 'activated state') continues to be fully charged.

The following conclusions can be drawn: 1. We have found a unique response to short flow pulses in the denervated renal arterial bed of anesthetized dogs. The response was found alike in kidneys left in situ, in autotransplanted and isotransplanted kidneys. 2. Although an explanation of the basic underlying mechanism cannot be given, a simple simulation suggests the generation by the pulse of an 'activated state' in the renal vascular bed, which might be a myogenic or humoral phenomenon. 3. The results are a step towards the explanation of long term effects of certain experimental procedures, and possibly of the influence of pulsatile pressure on the renal arterial bed[4].

Zusammenfassung. Die A. renalis von Hunden wurde mit arteriellem Blut mittels einer peristaltischen Pumpe durchströmt. Wir fanden hierbei eine bemerkenswerte Druckantwort auf kurze Strömungspulse, die spezifisch für die Niere zu sein scheint. Eine anschauliche Deutung der Reaktion konnte mit Hilfe einer einfachen Analogsimulation gegeben werden.

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Humoral Autoregulation of Blood Flow and Blood Pressure

In previous publications[1-3] we have shown that the reaction of the local arterial impedance of different arterial beds to changes in pressure or flow basically can be described as interaction between two processes. These were tentatively called autoregulation of flow and autoregulation of pressure[1]. To describe the interaction of both processes, which ususally have different time constants, we used the germ reciprocal autoregulation. In the following discussion we will show that besides by intrinsic mechanisms both autoregulation of flow and of pressure can be achieved by humoral mechanisms.

For a simplified explanation of this concept it may be assumed that no control or intrinsic autoregulatory mechanism exists in a local arterial bed, except for the presence of a vasoactive substance in concentration X in the arterial blood stream. In this example the input impedance Z (we prefer this symbol to the previously used R_i) of the arterial bed thus is a function of X only. p and $\dot{Q}$ are input pressure and flow, all variables are frequency dependent. The input impedance then is defined as

$$Z(X) = p/\dot{Q}\,. \tag{1}$$

Linearization of this equation yields

$$\frac{\partial Z}{\partial X}\,dX = dp/\dot{Q} - p\,d\dot{Q}/\dot{Q}^2. \tag{2}$$

With respect to the vasoactive substance the assumption is made that a constant amount per unit time is secreted or injected into the arterial blood stream. Thus the concentration of the substance decreases if the flow increases and vice versa.

$$dX = -k\,d\dot{Q}\,. \tag{3}$$

Inserting eq. 3 into eq. 2 yields the linearized input impedance

$$\frac{dp}{d\dot{Q}} = Z\left(1 - k\,\frac{\partial Z}{\partial X}\,\frac{\dot{Q}}{Z}\right) \tag{4}$$

[1] TH. KENNER and K. ONO, Experientia *27*, 528 (1971).
[2] TH. KENNER and K. ONO, Pflügers Arch. *324*, 155 (1971).
[3] TH. KENNER, Kybernetik *9* 215 (1971).

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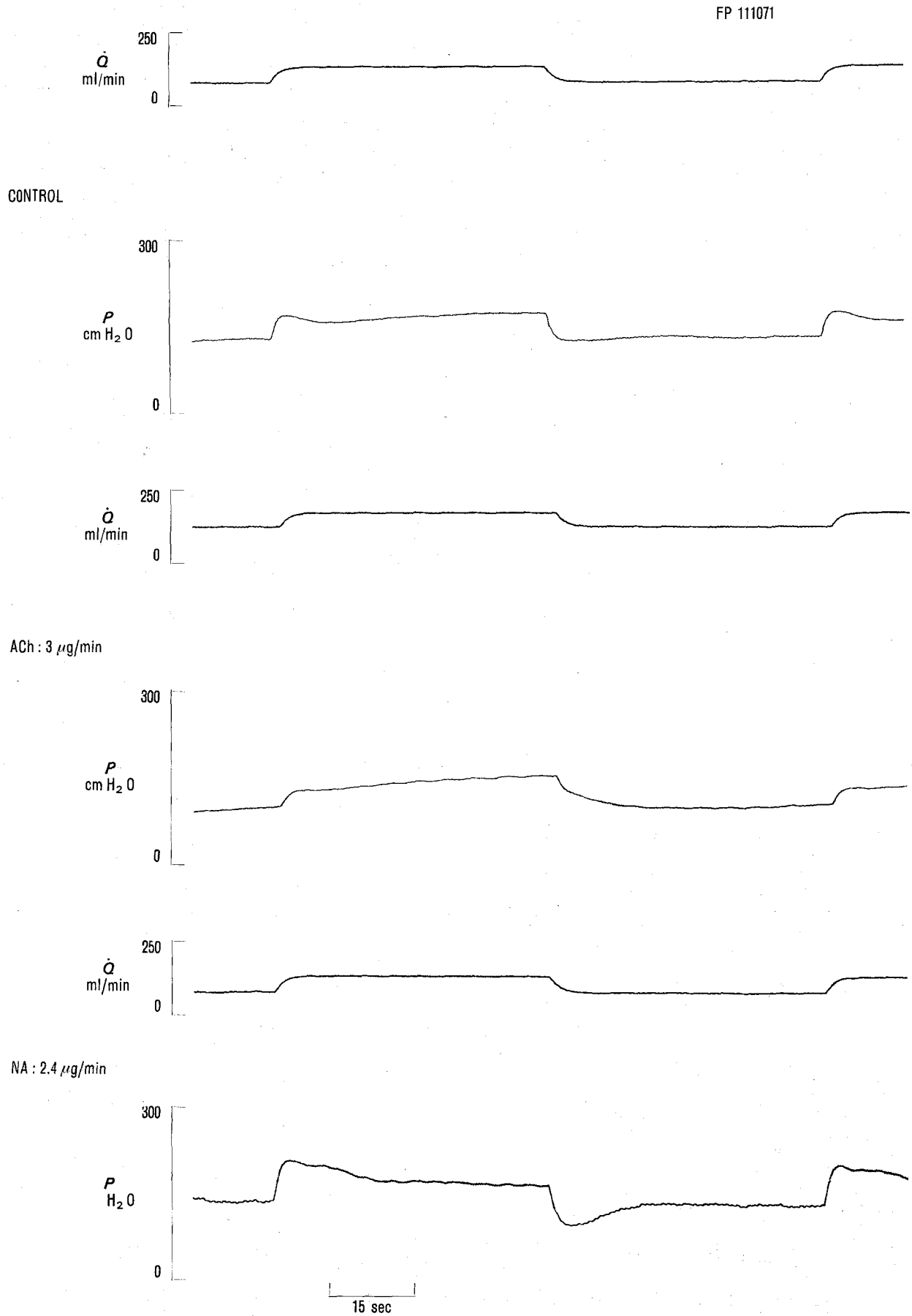
Arterial pressure (p) and flow ($\dot{Q}$) in the femoral artery of a dog. The flow is provided by a peristaltic pump (arterial blood). The reaction of the arterial pressure to flow step increases, and decreases, are shown. Upper tracing: control. Middle tracing: during constant rate intra-arterial infusion of Acetylcholin. Lower tracing: during constant rate intraarterial infusion of Noradrenalin.


FP 111071
250
Q̇
ml/min
0
CONTROL
300
P
cm H2 O
0
250
Q̇
ml/min
0
ACh : 3 µg/min
300
P
cm H2 O
0
250
Q̇
ml/min
0
NA : 2.4 µg/min
300
P
H2 O
0
15 sec

where $Z = p/\dot{Q}$ defines the set value around which small changes are examined. The second term in the brackets describes the influence of X on the impedance Z and thus may be called the transfer function of the vasoactive substance. This function is positive if the substance is a vacoconstrictor, and negative if it is a vasodilator.

To demonstrate a simple example a first order transfer function may be assumed; to be inserted into eq. 4:

$$k \frac{\partial Z}{\partial X} \frac{\dot{Q}}{Z} = \frac{G}{1 + \tau s}. \quad (5)$$

Using the Laplace transform technique, the time response of the arterial pressure $\Delta p(t)$ to a flow step increase $\triangle \dot{Q}$ can be derived from eq. 4

$$\triangle p(t) = Z \triangle \dot{Q} \left[1 - G\,(1 - e^{-t/\tau})\right]. \quad (6)$$

As mentioned above G is positive if the vasoactive substance is vasoconstricting. In this case the vascular bed tends to reduce the pressure closer to its previous value after a flow step increase, an effect which may be called humoral autoregulation of pressure. If the substance is a vasodilator, G is negative. According to eq. 6 in this case the pressure will continue to rise after a flow step increase. This reaction is characteristic for a system which tends to regulate blood flow at a certain level and may, therefore, be called humoral autoregulation of flow. Intuitively explained, the pressure rise after a flow increase represents the attempt to reduce the flow to the former value by increasing the resistance.

The Figure shows an experimental example. The femoral arterial bed of an anesthetized dog was perfused with arterial blood using a peristaltic pump. The inflow was recorded by an electromagnetic flowmeter. Into the arterial cannula drugs could be infused by a piston pump. The results were reproduced in 5 different animals.

The upper tracing of the Figure (control) shows the intrinsic autoregulatory response of the femoral arterial bed to a step flow increase. The middle tracing shows the continuing pressure increase after a flow step which is characteristic for the autoregulation of blood flow, during acetylcholine infusion. The lower tracing shows the response of the pressure to a flow step during noradrenalin infusion which is typical for the autoregulation of pressure.

In other words, it can be shown experimentally that a vasoconstricting substance released at a constant rate into the arterial blood stream is able to stabilize the blood pressure in the presence of perturbations of the blood flow. A vasodilating substance, on the other hand, would tend to stabilize arterial flow values in the presence of perturbations of the arterial blood pressure.

The following conclusions can be drawn from this discussion: 1. There exists a phenomenon which may be called humoral autoregulation. We were able to demonstrate this fact under artificial experimental conditions. 2. Certain effects which usually are ascribed to intrinsic autoregulation actually may be due to humoral autoregulation. 3. As can be seen in the Figure intrinsic (nonhumoral) and humoral autoregulation. may interact. As mentioned elsewhere[3] interactions of this type may under certain circumstances lead to instability and vascular autooscillations[4].

Zusammenfassung. Vasoaktive Substanzen im arteriellen Blut können charakteristische Reaktionen des lokalen Strömungswiderstandes hervorrufen. Die einfachsten Beispiele dieser humoralen Autoregulation können durch intraarterielle Infusion von Acetylcholin (Autoregulation der Strömung) oder Noradrenalin (Autoregulation des Drucks) demonstriert werden. Es wird angenommen, dass der humoralen Autoregulation Bedeutung bei der normalen und pathologischen Kreislaufregulation zukommt[5].

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[5] The experiments were performed in the Division of Biomedical Engineering, University of Virginia, Charlottesville, USA.
[6] Recipient of NIH research career development award No. HE 50288-01.

Correlation of Ammonia Liberation and Calcium Deposition by the Avian Egg and Blood Ammonia Levels in the Laying Hen

We have previously noted that unfertilized eggs removed from the reproductive tracts of laying hens liberate ammonia in vitro and have suggested that ammonia may function in vivo to cause the dissociation of bicarbonate thereby providing carbonate for egg shell calcium carbonate formation[1]. In this report, we show that there is a negative correlation between the amount of ammonia liberated by eggs and the amount of calcium deposited as calcium carbonate. We also show that there is an increase in the plasma ammonium ion content during the laying cycle that may be due, in part, to the addition of ammonium ion to the blood by the shell gland during eggshell formation.

Materials and methods. White Leghorn laying hens were kept in individual cages under a 14 h light: 10 h dark photoperiod and were fed Purina Eggena (Ralston Purina Co., St. Louis, Mo., USA). The stage of eggshell formation was estimated from the time of the preceeding oviposition. The hens were killed and the eggs removed from the reproductive tract and placed in all-glass metabolic chambers. Ammonia liberation was measured continuously for 24 h as previously described[2]. At the end of this time, the egg shell or outer membrane was separated and ashed at 1300° for 24 h. The ashed residue was dissolved in a minimal amount of concentrated hydrochloric acid (3 to 5 ml), diluted with water and its calcium content determined by a fluorometric method[3].

An enzymatic method[4] was used to determine plasma levels of ammonium ion; readings were normally made within 20 after withdrawing a blood sample and the

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