de tissus leucosiques, rendus non-pathogènes par un séjour dans l'organisme du lapin a notablement inhibé la leucémogenèse spontanée chez ces animaux.

Tableau
Critère du χ^2
Cancer (mai 1958)

	Non traités	Traités	
Tumeurs	20	7	27
Pas de tumeurs	19	23	42
Total	39	30	69

χ^2 corrigé = 4,449*. χ^2 non corrigé = 5,561*.

Leucémies (août 1958)

	Non traités	Traités	
Leucémies	246	7	253
Pas de leucémies	45	12	57
Total	291	19	310

χ^2 corrigé = 23,951**

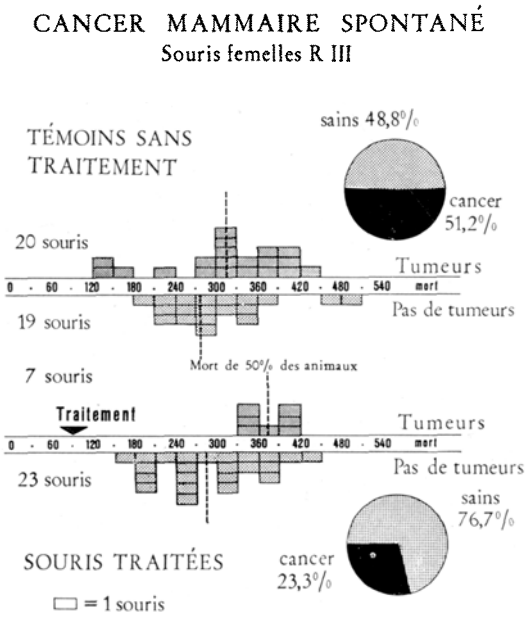

Fig. 2

Ces résultats se passent de commentaires (Figures 1 et 2) car l'inhibition est manifeste dans les deux cas étudiés. En ce qui concerne le mécanisme de cette inhibition, aucune hypothèse ne peut être proposée pour expliquer suffisamment ce phénomène, sinon le principe qui a servi de fil conducteur à ces expériences.

R. FISCHER et G. RUDALI

Centre de Transfusion Sanguine, Hôpital Cantonal, Genève et Laboratoire de Génétique, Fondation Curie, Paris, le 5 novembre 1959.

Summary

(1) After a 24-h passage in a rabbit, fragments of spontaneous isologous mammary carcinoma were implanted under the skin of young R III females. This procedure was found to prevent the appearance of spontaneous mammary tumours in a high percentage of these animals. The subsequent appearance of carcinoma was to be observed in only 23% of treated animals as compared with 51% in controls.

(2) After a 24-h passage in a rabbit, fragments of leukotic isologous tissue, implanted subcutaneously in young AkR females, reduced subsequent spontaneous leukomogenesis from 85 to 38%.

Local Constriction and Spasm of Large Arteries Elicited by Hypothalamic Stimulation

Large and medium sized arteries are generally assumed to show only minor degrees of vascular activity, and especially to be devoid of nervous control of any importance. This may seem true during normal 'resting' conditions, but contradictory evidence has been presented[1]. Of the consecutive vessels of different size in a vascular loop, the large arteries may even constrict more strongly than small vessels to local stimuli[2].

In this study the central nervous control of vasomotion in large arteries has been investigated. Special attention was paid to their interrelation to the cardiovascular system as a whole, and to selective vasomotor activation patterns.

Methods. — 96 rabbits under moderate pentobarbital or chloralose-urethane anaesthesia were used. Blood pressures were recorded with strain gauge manometers through polyethene catheters, inserted in suitable lateral branches to the main artery studied. For example, in the hindlimb, the great saphenous artery and contralateral iliac artery were cannulated, and the 'output' pressure characteristics from the saphenous were compared with the 'input' pressure values of the iliac artery. Pulse pressures at both ends of the artery, mean pressure gradients along it, and the arterial flow through the segment, were folowed. For comparison, diameter changes of the artery were observed with a dissection microscope, and venous outflow from the leg recorded. Electronic drop counters were used as flowmeters. Control experiments showed that changes in amplitude of the pressure pulse as it was transmitted along the segment, supplemented with evaluation of the other data, could provide a fair index of vasomotor reactions of the segment.

The radial artery of a forelimb, a branch of the inferior mesenteric artery in the splanchnic area, and the central ear artery were also cannulated for local pressure measurements. In addition, the electrocardiogram and heart rate were recorded.

Electrical stimulation of the forebrain, hypothalamus, and mesencephalon was performed through steel needle electrodes inserted stereotaxically. Rectangular pulses, 0·5–2·0 V, 1–500/s, 1–15 ms pulses, independently variable, were used. Electrode positions were verified by the Prus-

[1] A. SCHRETZENMAYR, Klin. Wschr. *15*, 625 (1936). – J. M. BARNES and J. TRUETA, Brit. J. Surg. *30*, 74 (1942). – J. B. KINMONTH and F. A. SIMONE, Brit. J. Surg. *39*, 333 (1951). – F. J. HADDY, Minnesota Med. *41*, 162 (1958).

[2] F. J. HADDY, M. FLEISHMAN, and D. A. EMANUEL, Circ. Res. *5*, 247 (1957).

sian blue method[3], comparing frozen serial sections of the brains with the brain atlas of SAWYER, EVERETT, and GREEN[4].

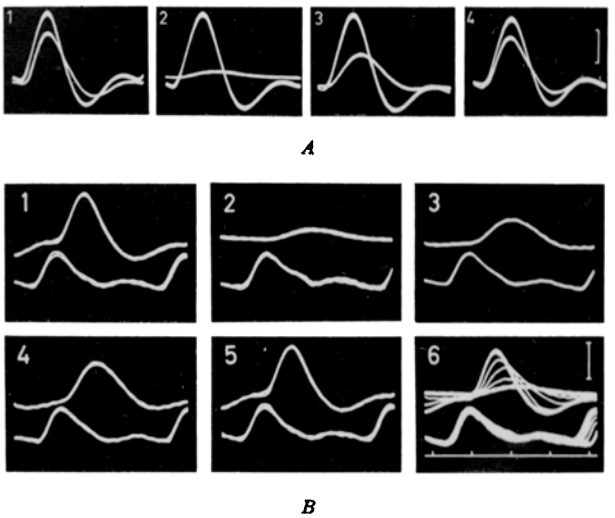

Fig. 1. – Consecutive records of single pressure pulses. *A*. Rabbit 3·0 kg. Chloralose. Superimposed tracings of iliac (larger) and saphenous (smaller) pulse waves, before (1), during (2), and after (3, 4) hypothalamic stimulation. Calibration to the right, vertical bar 20 mm Hg. Note reduction of pulse pressure due to constriction of the femoral artery. *B*. Rabbit 3·4 kg. Nembutal. Upper tracing saphenous, lower tracing central ear artery pressure pulses. Before (1), during (2), and after (3, 4 and 5) hypothalamic stimulation. Stimulation repeated (6), but serial pressure pulses now superimposed. Vertical bar 30 mm Hg. Note ear artery pulse uninfluenced during marked reduction of femoral pulse pressure. Time 0·1 s.

[3] W. R. HESS, *Beiträge zur Physiologie des Hirnstammes. I.* (G. Thieme, Leipzig 1932).

[4] C. H. SAWYER, J. W. EVERETT, and J. D. GREEN, J. comp. Neurol. *101*, 801 (1954).

Results. – By stimulation of circumscribed subcortical regions, the pulse pressure in the arteries investigated could be reduced so that the output pulsations were barely perceptible (Fig. 1 *A*). At the same time, the pressure gradient along the segment usually decreased; sometimes this was followed by a secondary increase. The arterial flow through the segment decreased markedly and even stopped. If the femoral artery was exposed, inspection showed a considerable constriction starting at the level of the proximal third of the artery and increasing distally. These arterial responses could occur independently of pressor or depressor reactions. By selecting electrode sites and stimulus parameters, almost maximal constrictions of the femoral arteries could be induced without any change in mean aortic blood pressure or heart rate. Moving the electrode, sometimes as little as 0·5 mm, would change this response into a pressor or depressor reaction, without concurrent large artery constriction.

The arterial response had a latency of about 5 s, after which the degree of constriction usually reached a value that was proportional to stimulus intensity and frequency and maintained for several minutes of stimulation. After stimulation, the artery usually relaxed and pre-stimulatory values were restored within 1 min. Long or intense stimulations, on the other hand, caused a short post-stimulatory increase of pulsatory amplitude followed by a post-stimulatory constriction of the artery for several minutes (Fig. 2, *3*). Repeated short stimulations seemed to summate and cause a longlasting constriction. After continuous stimulation for about 5 min (Fig. 2, *5*), the vasoconstriction of the femoral artery persisted for 20 to 30 min. These post-stimulatory 'vasospasms' could be abolished by a small additional dose of pentobarbital (Fig. 2, *6*). After repeated or prolonged constriction, the artery sometimes dilated spontaneously, pulsated forcibly, and did not respond with constrictions any more.

In most cases, the magnitude of the arterial responses to brain stimulations were proportional to the frequency

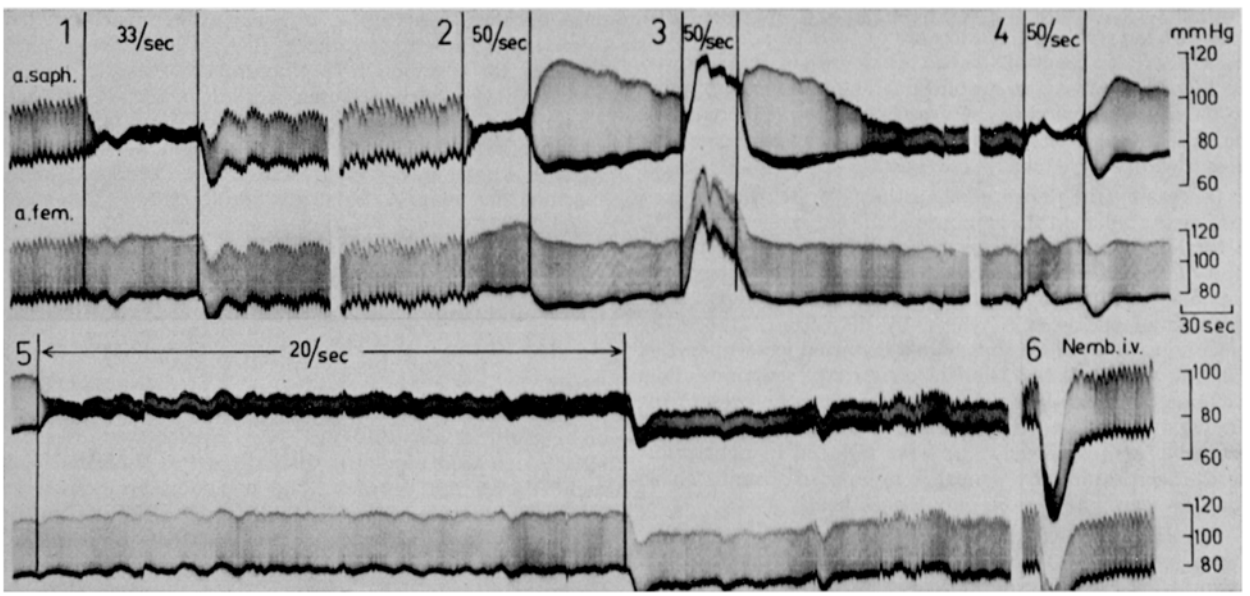

Fig. 2. – Rabbit 3·2 kg. Nembutal-chloralose. Pairs of records of saphenous and contralateral femoral blood pressures. Calibrations in mm Hg to the right. Between signals hypothalamic stimulations of a site at stimulus frequencies indicated. Intensity 0·8 V, except for record *3*, where it was 1·0 V. In record *6* 10 mg Nembutal. Note constrictor responses increase with increasing stimulus frequency (*5*, *1*, *2*). Post-stimulatory increase of amplitude is related to frequency and intensity (compare *1*, *2*, and *3*). Post-stimulatory constriction (*3* and *5*) is correlated to strength and duration of stimulation. This constriction is temporarily abolished after a subsequent stimulation (*4*) and after injection of Nembutal (*6*). Between *5* and *6* there is an interval of 10 min.

used and then followed an S-shaped curve approaching maximal values at 50–100 pulses/s. The post-stimulatory dilatation and consecutive constriction showed a similar relation to the stimulus frequency.

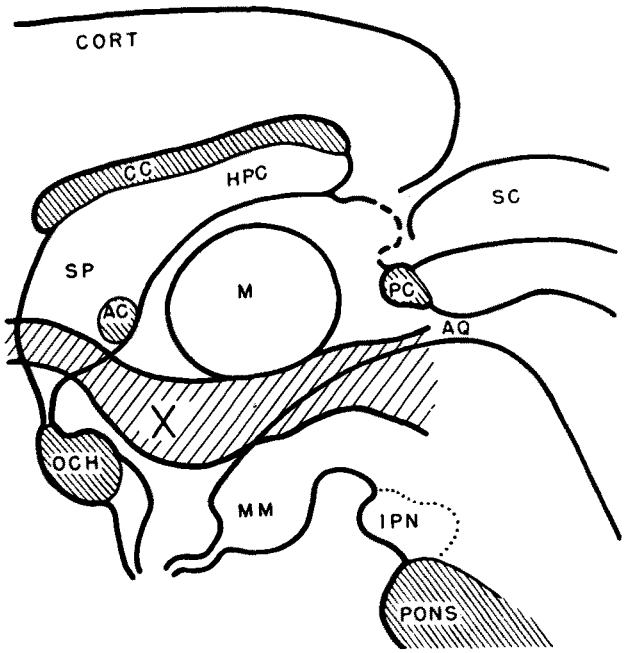

Fig. 3. – Schematic mid-sagittal reconstruction on rabbit brain stem of the region (*X*), from which large-artery constriction has been elicited.

Arterial vasoconstrictions could be elicited bilaterally in the ear, forelimb and hindlimb with only minor changes in mean systemic pressure. Unilateral hypothalamic stimulation sufficed for bilateral responses. The constriction of the ear arteries had the lowest stimulation threshold, constriction of the forelimb arteries demanding the highest voltage. The splanchnic arteries reacted only to those stimuli that evoked considerable pressor responses. During constrictor reactions in the other vessels, they showed an increased pulsatory amplitude. This was probably due to passive distension of the vessels, as similar increases of pulsations was seen in other arteries when the tone of the vessel wall was reduced.

Increasing the depth of anaesthesia, or heating the animal, first abolished the response of the ear artery (Fig. 1 *B*). A further injection of anaesthetics depressed the constriction of the forelimb arteries. This extinction of response was accompanied by an increase of the local pulsations. Trauma of the vessels caused by dissection, anoxia, or mechanically induced spasm also favoured loss of nervous control, and abolished the vasoconstrictor reactions. This was one of the main reasons for adopting the present indirect method of study. Minor vasoconstrictions also occurred 'spontaneously', or were induced in lightly anaesthetized animals by 'arousing' or noxious stimuli. These changes were not seen in deep anaesthesia.

The arterial constriction was abolished by appropriate nerve sections and after ergotamine. The nerves to the femoral artery were found to run in the femoral nerve. Stimulation of the lumbar sympathetic trunk or the femoral nerve in curarized preparations, provoked responses similar to those obtained by central stimuli. From 1 to 10 pulses/s (the latter maximal), the response was proportional to stimulus frequency, though the strict relation was an S-shaped function. Increasing frequency beyond 20/s, usually led to a decrease of response. Relaxation responses, or secondary constriction after stimulation, were not found in these postganglionic stimulation experiments.

Conclusions. A central nervous control of vasomotor activity in large arteries has been found. It resembles the well-known vasoconstrictor innervation of small vessels with respect to activation, neural structures, and neuroeffector characteristics. It usually operates concurrently with the vasoconstrictor control of smaller vessels, thus producing a homologous response in consecutive parts of a vascular loop. However, in case of prolonged activation, the large arteries maintain constriction far better than small ones and show evidence of arterial spasm. This is particularly true when the system is stimulated at the diencephalic level. It then seems capable of producing independent, isolated constrictions, at least as judged by the overall vasomotor patterns. Probably central functional patterns and local peripheral conditions interact to create the powerful regional vasospasm.

The mean systemic pressure was constant, even during generalized constriction in the limbs, and this may be partly ascribed to a redistribution of flow to visceral areas, as evidenced by the concurrent distension of splanchnic arteries. Such a vasomotor pattern could be of importance for centralization of pressure in pathological emergency situations, e.g. shock.

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N. Weckman

Nobel Institute for Neurophysiology, Karolinska Institutet, Stockholm (Sweden), October 8, 1959.

Zusammenfassung

Die nervöse Kontrolle der Femoral-, Brachial-, zentralen Ohr- und Mesenterialarterien wurde am Kaninchen untersucht. Es konnten durch elektrische Reizung eines Gebietes im lateralen Hypothalamus abgestufte Gefässverengerungen hervorgerufen werden. Ohne wesentliche Änderung des Aortenmitteldruckes und der Herzfrequenz konnten sogar maximale Kontraktionen hervorgerufen werden. Lange Reize verursachten anhaltenden Gefässspasmus, der in der A. femoralis am stärksten ausgeprägt war.

Untersuchungen zur intrazellulären Lokalisation der Renin- und Hypertensinase-Aktivität

Trotz zahlreicher Untersuchungen ist es bis heute noch nicht geglückt, die Bildungs- bzw. Speicherorte des Renins in der Niere eindeutig festzulegen[1–3]. Während Versuche dieser Art beträchtliche methodische Schwierigkeiten bieten, schien uns die Frage nach der Lokalisation des Renins in der Zelle mit Hilfe der Differentialzentrifugierung lösbar zu sein. Wir bestimmten deshalb die Reninaktivität in den einzelnen Fraktionen von Nieren-

[1] A. Bohle, Habilitationsschrift Heidelberg (1953); Verhandlungen der Deutschen Gesellschaft für Pathologie (1959), im Druck.
[2] J. Bing and B. Wiberg, Acta path. microbiol. scand. *44*, 138 (1958).
[3] F. Gross, Klin. Wschr. *36*, 693 (1958).