generated. When considering that Eα discharge occurs in 2% of all RMN only, it is doubtful if these neurons are indispensable for bulbar rhythmogenesis. EI neurons are supposed to activate I units[10], I cells to excite IE neurons[9,11] and IE units to facilitate E cells[9]; if this mechanism is true, a relatively low level of EI and I neuron excitation is sufficient to initiate oscillation. The excitation level of EIα and β and Iα and β neurons at the end of the apneic pause covered a relatively wide range; the range of dma was in a comparable order of magnitude. Most Iβ units, however, were silent immediately after respirator arrest. In some RMN, rhythmic modulation of spd starts well before oscillation of the entire neuronal network, i.e. before the 1st expiration occurs; this is probably due to unequal thresholds for mutual inhibition within each phase type of RMN.

1 M.I. Cohen, J. Neurophysiol. *31*, 142 (1968).
2 G. Böhmer, R.A. Chaplain and M. Fallert, Pflügers Arch. *365*, 61 (1976).
3 R.A. Chaplain, H.R.O. Dinse and M. Fallert, Pflügers Arch. *365*, 49 (1976).
4 O.A.M. Wyss, Pflügers Arch. ges. Physiol. *244*, 712 (1941).
5 M. Fallert and B. Wassermeyer, Exp. Brain Res. *30*, 339 (1977).
6 R. von Baumgarten and E. Kanzow, Archs ital. Biol. *96*, 361 (1958).
7 H.L. Batsel, Exp. Neurol. *19*, 357 (1967).
8 R. von Baumgarten and S. Nakayama, Pflügers Arch. *281*, 245 (1964).
9 F. Bertrand, A. Hugelin and J.F. Vibert, J. Neurophysiol. *37*, 91 (1974).
10 R.A. Mitchell and D.A. Herbert, Brain Res. *75*, 345 (1974).
11 D.W. Richter, F. Heyde and M. Gabriel, J. Neurophysiol. *38*, 1162 (1975).

Cardiac output and regional blood flow studies in golden hamsters

O.P. Gulati and G. Ponard

Research Department, ZYMA S.A., CH-1260 Nyon (Switzerland), 14 November 1979

Summary. A method is described for the acute catheterization of the left ventricle of the heart and descending aorta combined with the use of the radioactive microsphere technique to study hemodynamic parameters in anaesthetized hamsters. The hemodynamic parameters studied include mean blood pressure, cardiac output, percentage distribution of cardiac output and regional blood flows in different organs.

Recently the hamster has been used as a model animal for the study of renal hypertension[1], microcirculation[2] and thrombosis[3]. Scanty data however, are available on hemodynamic aspects of this species. We attempted to study cardiac output, its distribution and regional blood flows in different organs using the modified radioactive microsphere technique of Malik et al.[4] in anaesthetized hamsters.

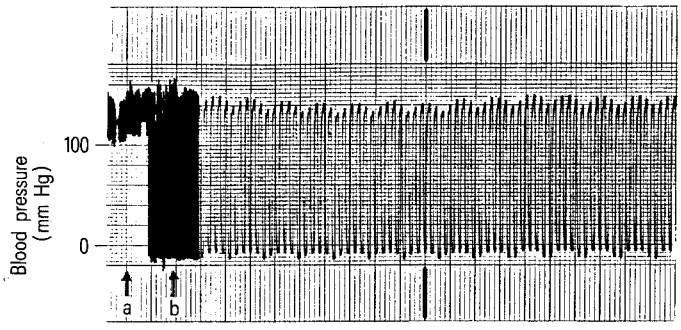
Materials and methods. 10 golden hamsters weighing between 90 and 110 (99 ± 3) g were used. They were anaesthetized with pentobarbitone 80 mg/kg i.p. A median incision was made on the ventral surface of the neck, tracheotomy was performed for free ventilation, and the right carotid artery was isolated from its position beside the trachea. The vessel was catheterized with PE-50 polythene tubing (inner diameter 0.58 mm and outer diameter 0.97 mm) connected to PE-10 polythene tubing (inner diameter 0.28 mm and outer diameter 0.61 mm). The catheter was filled with physiological saline containing heparin 50 IU/ml and attached at its proximal end (PE-50) to a pressure transducer (HP-1280C), which in turn was connected to a Hewlett packard multichannel recorder. The end to be inserted into the artery (PE-10) was marked approximately 3 cm from the tip to indicate when a sufficient length of the catheter had been inserted. A small incision was then made (under a microscope, magnification × 16) in the wall of the artery, and the catheter was eased down in the artery, as the recording of mean blood pressure was being monitored. At the point at which the catheter entered the left ventricle, the end diastolic pressure dropped to zero, whereas systolic pressure remained unchanged (figure). The regular pulse indicated that the catheter did not touch the internal wall of the ventricle. The catheter was then tied firmly in position by 2-3 ligatures placed around the catheter in the carotid artery to secure it. The exact position of the catheter in the left ventricle was verified at autopsy. The aortic catheter was inserted in the descending aorta about 5 mm above the bifurcation, through a median incision made on the ventral abdominal surface of the body. The other end of the aortic catheter (PE-50) was connected to a precalibrated withdrawal pump (B. Braun Melsungen AG), for collection of a timed reference blood sample.

Chromium-51 (Cr^{51}) labelled microspheres (15 µm in diameter) suspended in physiological saline (NEN Chemicals GmbH) were used. 0.1 ml of a suspension of microspheres (containing approximately 4×10^4 microspheres and a total radioactivity of $9.3 \times 10^4 \pm 0.5 \times 10^4$ cpm) was injected into the left ventricle of the heart. The total radioactivity injected into the system was determined by calculating the difference between the radioactivity taken in to the syringe at the start and that retained in the syringe, needle and catheter after the injection of the microspheres. Microspheres were injected over a 30-sec period, while the reference sample was being withdrawn from the aortic catheter beginning 10 sec before the start of the microsphere injection and continuing for more than 1 min. The blood was withdrawn into a heparinized syringe at the rate of 0.187 ml/min. At the end of the experiment, the animals were sacrificed using a large dose (500 mg/kg) of pentobar-

Percentage distribution of cardiac output and absolute blood flow in different organs in anaesthetized hamsters

Organ	Percentage of cardiac output per organ	Blood flow (ml/min/g)
Heart (ventricles)	17.62 ±2.75	10.40 ±1.31
Lungs	0.94 ±0.19	0.29 ±0.08
Liver (arterial)	0.46 ±0.15	0.035±0.003
Spleen	0.57 ±0.12	1.36 ±0.33
Right kidney	9.44 ±0.68	3.91 ±0.50
Left kidney	9.94 ±0.94	3.90 ±0.48
Front paws	0.53 ±0.11	0.079±0.012
Right cheek pouch	0.073±0.012	0.039±0.007
Left cheek pouch	0.091±0.017	0.047±0.013

Values are represented as mean ± SEM (n = 10).



Typical left ventricular pulse after acute catheterization of the left ventricle of the heart through the right carotid artery. *a*, catheter in the right carotid; *b*, catheter in the left ventricle.

bitone. The heart (free from the atria and big vessels) lungs, kidneys, spleen, liver, front paws, and cheek-pouches were removed and weighed. A reference blood sample drawn up into the plastic syringe was placed in a counting tube. The syringe was rinsed with physiological saline 3 times and each rinse placed in an individual counting tube. The activities of the reference sample and the rinse samples were added for the purpose of calculation. The organs were placed in individual counting tubes and the radioactivity was measured in an MR-252 gamma counter for 5 min.

The flow to the organs was determined from the equation:

$$\text{Organ blood flow} = \frac{\text{Radioactivity in the organ}}{\text{Radioactivity in the reference blood sample}} \times \text{Reference blood sample flow rate (0.187 ml/min)}$$

The cardiac output was determined by the equation:

$$\text{Cardiac output} = \frac{\text{Total radioactivity injected}}{\text{Radioactivity in the reference blood sample}} \times \text{Reference blood sample flow rate (0.187 ml/min)}$$

Percentage distribution of the cardiac output in a particular organ was calculated by the equation:

$$\text{Percentage distribution of cardiac output} = \frac{\text{Radioactivity in the organ}}{\text{Total radioactivity injected}} \times 100$$

The values in the text and table are given as mean values $\pm$ SEM.

Results and discussion. These hamsters had a mean blood pressure of 119 ± 8 mm Hg and cardiac output 19.2 ± 1.9 ml/min (193 ± 17 ml/min/kg). Percentage distribution of cardiac output and blood flow in various organs are represented in the table. The technique fulfils many of the assumptions for blood flow measurements as described by Heyman and his colleagues[5]. The similar or closely similar percentage distribution of cardiac output and blood flow in the kidneys and cheek-pouches of the left and right sides (table) validates homogeneous mixing of the microspheres in the heart and their even distribution in different organs. The presence of radioactivity in the lungs represents arterio-venous shunting of the microspheres and bronchial arterial circulation. A generally accepted satisfactory limit is a value less than 4% of the total radioactivity injected[6]. Distribution of cardiac output of 0.9 ± 0.2% in the lungs, as observed in the present studies, validates minimum arterio-venous shunting.

The values for percentage distribution of the cardiac output (17.62 ± 2.75) in the heart (ventricles) appear to be high as compared to the respective values reported in rats[4] (4.23 ± 0.26) and in cats[6] (6.7 ± 0.3). We cut open the hearts of 2 of the animals and rinsed them in normal saline before counting their radioactivity. The values of radioactivity counts in these 2 hearts were not different from those obtained in other hearts. Although the possibility of microspheres being trapped in myocardial pouches is less, it cannot be ruled out. We have further observed that the ratio between the weight of the heart (ventricles) and the total body weight was 17.45% more in hamsters (0.323 ± 0.009, $n = 10$) than in rats (0.275 ± 0.003, $n = 10$). This could partially explain the high coronary flow fraction in the hamsters. The values given for liver blood flow only represent hepatic arterial blood flow, since the organs for the portal system were not taken for the study.

The criterion of having 384 microspheres in the organ, as described elsewhere[5], is not achieved in the cheek-pouch. To fulfil this criterion, we would require a larger dose of radioactive microspheres, which in turn could lead to the formation of long chains in the capillaries and thus obstruct blood flow to the distal vascular bed as has been recently shown by Wiedeman[7] in the hamster cheek-pouch and the bat wing. It appears that the values of cardiac output (34.1 ± 74 to 40.1 ± 12.9 SD ml/min) and mean blood flow to the cheek-pouches (7.9 ± 2.8 to 11.8 ± 4 SD ml/100 g b.wt/min) as reported by Svensjö et al.[8] are higher than the respective values obtained by us. However, the percentage distribution of the cardiac output (0.1%) in the cheek-pouch as determined by these authors is not very far above the values presented (0.07–0.09%). Apparently, their hamsters were heavier, which could account for their higher values for cardiac output. They used PE-10 tubing and catheterized the femoral artery for withdrawal of a reference blood sample, and further, they used the cardiac puncture technique for the injection of 2×10^6 microspheres. All these technical factors could explain the discrepancy between their results and the present data.

1 R.L. Click, J.P. Gilmore and W.L. Joyner, Circulation Res. *41,* 461 (1977).
2 E. Svensjö, S. Renlund and E. Sjödin, Microvasc. Res. *15,* 116 (1978).
3 D. Bergqvist, E. Svensjö and K.E. Costa, Upsala J. med. Sci. *83,* 123 (1978).
4 A.B. Malik, J.E. Kaplan and T. Saba, J. appl. Physiol. *40,* 472 (1976).
5 M.A. Heyman, B.D. Pyne, J.I.E. Hoffman and A.M. Rudolf, Cardiovasc. Dis. *20,* 55 (1977).
6 B.M. Johnston and D.A.A. Owen, Br. J. Pharmac. *60,* 173 (1977).
7 M.P. Wiedeman, Microvasc. Res. *17,* 98 (1979).
8 E. Svensjö, K.E. Arfors, G. Arturson and G. Rutili, Upsala J. med. Sci. *83,* 71 (1978).