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Cerebral Blood Flow During External Cardiac Massage[1,2]

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External cardiac massage in treatment of cardiac arrest was proposed in 1960 by Kouwenhoven, Jude, and Knickerbocker (1). Since then, many patients with cardiac arrest have recovered, without evidence of brain damage, after treatment by external cardiac massage. These empirical results have, until now, constituted the only evidence that this method is effective in supplying oxygenated blood to the central nervous system. The present experiments were designed to provide quantitative data on the degree of restoration of blood flow to the brain during cardiac arrest and external cardiac massage.

METHODS

1. Measurement of Cerebral Blood Flow

The rate of clearance of a radioactive inert gas such as krypton or xenon from a region into which it has been injected is proportional to the blood flow to the region (2). This principle provided the basis for the present study. The radioactive gases, krypton^{85} and xenon^{133} dissolved in 0.3 ml of 0.9 per cent sodium chloride solution, were injected into the internal carotid artery of the dog. The time course of radioactivity in the brain was measured by a collimated 3 inch crystal scintillation detector, placed beneath the superior surface of the animal's head. The dogs were anesthetized with pentobarbital and lay in a supine position. A gamma-ray spectrometer was used, together with a ratemeter with a time constant of one second.

The decrease in radioactivity following a single intraarterial injection of either Xe^{133} or Kr^{85} was a complex exponential but could be approximated by a single exponential function of time, described by the equation:

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$$C = C_0 e^{-kt}$$

where C_0 is the peak concentration (counts per minute) of the radioactivity after injection, and C is the concentration (counts per minute) at any time t (minutes) after the peak is reached. The value, k, or fractional clearance, is described by the equation:

$$k = F / V\lambda \tag{2}$$

where F = blood flow (ml/min); V = the volume of brain being perfused (ml); and λ is the partition coefficient of the gas between brain and blood. Since k is directly proportional to blood flow, it was used as an index of flow; in the present study V and λ remained constant during the period of measurement. The value, k, was obtained by measuring the half-time ($t_{\frac{1}{2}}$) of clearance, defined as the time required for the count rate to fall to one half C_o, and the relation:

$$k = -\frac{1n\ 2}{t\,\frac{1}{2}} = -\frac{0.693}{t\,\frac{1}{2}} \tag{3}$$

2. Cannulation of Internal Carotid Artery

The cerebral circulation of the dog is characterized by a massive network of anastomoses, the *rete mirabile*, between cerebral vessels and extracranial branches of the external carotid artery (3). During preliminary experiments the external carotid was ligated and the solution of radioactive gas was injected directly into the common carotid artery. As a result of retrograde flow through the *rete mirabile,* the temporalis and other muscles of the skull received as much radioactivity as the brain, and slow clearance rates were recorded. This problem was solved by inserting a small plastic catheter into the superior thyroidal artery against the direction of blood flow, threading it into the common carotid artery and then into the internal carotid artery (4). In this way blood flow and pressure in the external carotid artery were not greatly disturbed. The distribution of radioactive material injected by this route is shown in Fig. 1, where the distribution of radioactivity, determined by radioisotope scanning, is superimposed on an x-ray film of the dog's head. All of the radioactivity is within the brain. Injection of radio-opaque media by this route provided good x-ray visualization of the circle of Willis and its branches.

3. Fibrillation and External Cardiac Massage

The technique of external cardiac massage in dogs and human beings has been described by Kouwenhoven, Jude and Knickerbocker (5). In these experiments the dogs were massaged with vigorous manual pressure, at the rate of one compression per second, over the lower portion of the sternum. Ventricular fibrillation was induced by a four-second 110-volt AC shock across the chest. Defibrillation was achieved in all 14 cases by a 440-volt AC shock applied from base to apex of the heart.

4. Experimental Procedure

Each of six mongrel dogs, ranging in weight from 11.3 to 14.6 Kg, was anesthetized with pentobarbital (30 mg/kg) and placed in a supine position.

An endotracheal tube was inserted and connected to a motor-driven positive-pressure respirator, which remained in operation throughout the experiment. A cannula was inserted into a femoral artery and connected to a Statham Strain Gauge Pressure Transducer. Electrocardiographic leads were attached to the fore-legs. An internal carotid cannula was inserted as described above. Mean arterial pressure and electrocardiogram were recorded throughout each experiment.

At the beginning of each experiment a minimum of three separate control measurements of cerebral blood flow were made with the dog's heart in normal sinus rhythm. Thirty seconds after a fourth injection of the radioactive gas solution, ventricular fibrillation was induced. After one minute of fibrillation, vigorous manual massage was begun, and continued for four minutes. Five and one half minutes after the injection and five minutes after the onset of fibrillation, the dog's heart was defibrillated. In most dogs this entire procedure was carried out two or three times, with at least 30 minutes between fibrillations to allow for stabilization of arterial pressure.

RESULTS

A typical tracing depicting washout of Xe^{133} from a dog's brain during external cardiac massage is shown in Fig. 2. For the first 30 seconds, during

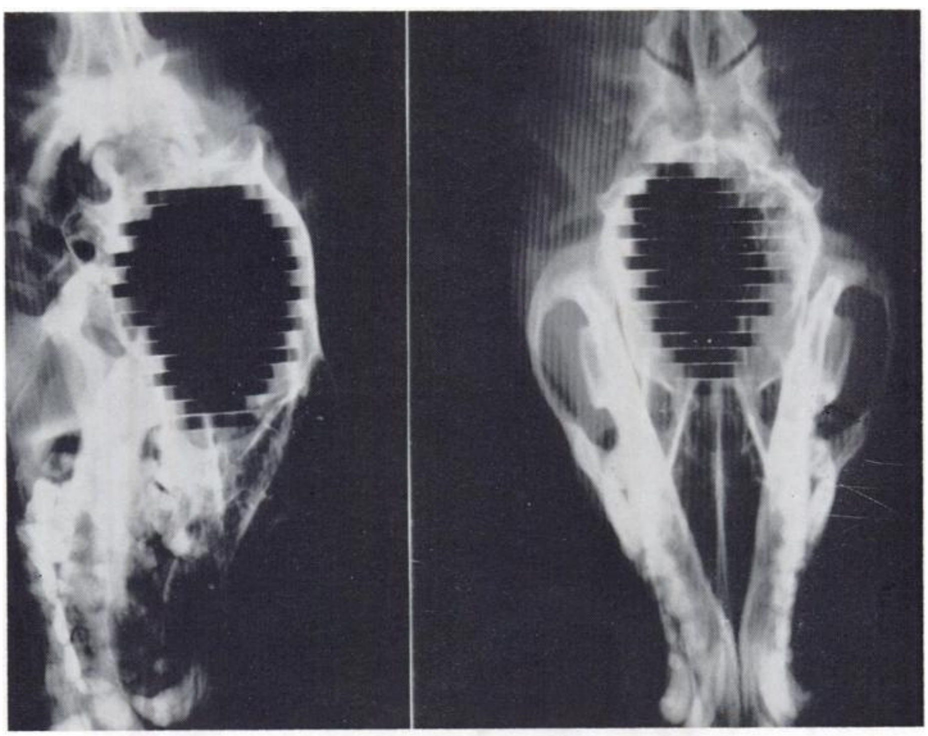

Fig. 1. Distribution of radioactivity in the brain of the dog following injection of radioiodinated macroaggregated albumin according to the technique of cannulation of the internal carotid artery described.

normal sinus rhythm, radioactivity in the brain fell rapidly, but with the onset of fibrillation brain radioactivity remained constant as perfusion ceased. With the onset of external cardiac massage, the radioactivity began to decrease again. The degree of restoration of cerebral blood flow during external cardiac massage (ECM) was determined by comparing the clearance rate constants (k) during the period of ECM with the values obtained during control determinations made at the same time after injection in the same dog. The average k for three to five control determinations in each dog was taken as 100 per cent. As shown

TABLE I

Dog No.		*Experimental Condition*	*Clearance Rate Constant (K) Min⁻¹*	*Per Cent of Control*
1	Kr^{85}	Control (3)	0.601	100.
		ECM	0.354	58.9
2	Kr^{85}	Control (3)	0.751	100.
		ECM 1	.141	18.8
		" 2	.151	20.1
3	Kr^{85}	Control (5)	.626	100.
		ECM 1	.208	33.2
		" 2	.268	42.8
		" 3	.189	30.2
4	Kr^{85}	Control (4)	.644	100.
		ECM 1	.104	16.1
		" 2	.218	33.9
5	Xe^{133}	Control (5)	.654	100.
		ECM 1	.177	27.1
		" 2	.225	34.4
		" 3	.144	22.0
6	Xe^{133}	Control (3)	.746	100.
		ECM 1	.231	31.0
		" 2	.301	40.3
		" 3	.257	34.5
Mean				31.7%

in Table 1, external cardiac massage produced a 16.1 to 58.9 per cent restoration of cerebral blood flow, with an average of 31.7 per cent in 14 determinations. Corresponding arterial perfusion pressures during massage averaged 32.2 per cent (range: 7.6 to 58.8%) of control values.

In Fig. 3, the fractional clearance, *k*, is graphed as a function of mean arterial pressure in 23 control determinations (normal sinus rhythm) and 14 determinations during external cardiac massage and ventricular fibrillation, in the same six dogs. The same data are presented in Table II. A correlation coefficient of 0.81 was calculated for the regression line shown in Fig. 3.

DISCUSSION

In these experiments in dogs, external cardiac massage restored cerebral blood flow (CBF) to approximately one third that provided by the normally beating heart. Increased perfusion pressure resulted in increased CBF, in ap-

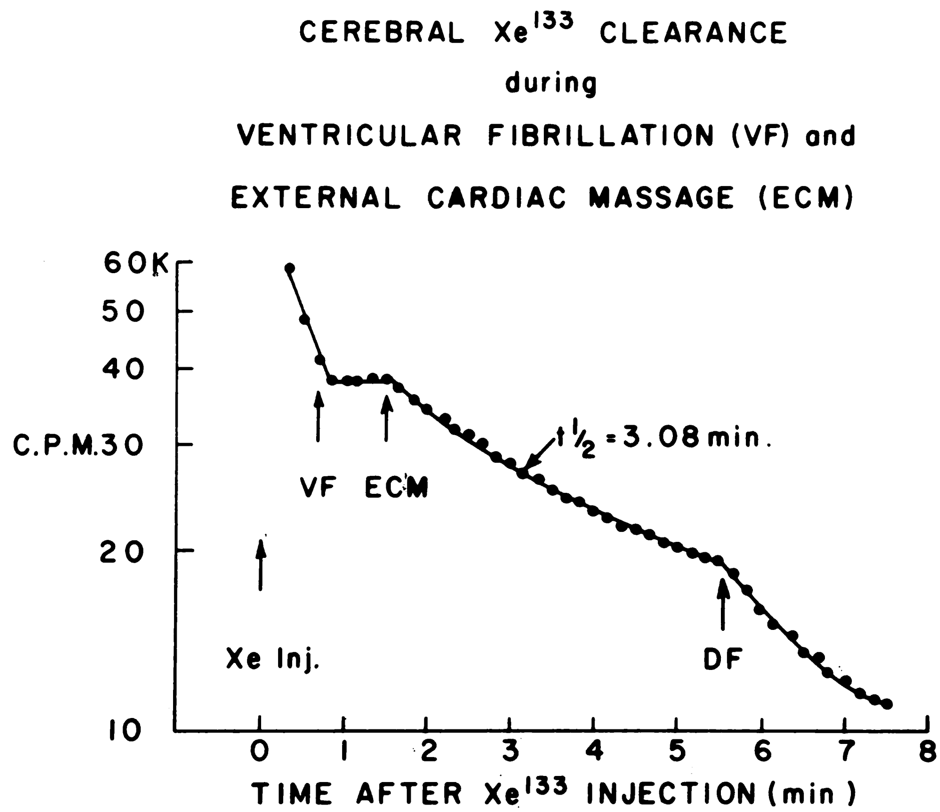

Fig. 2. Time course of radioactivity in the brain of the dog during a typical study. At point VF, ventricular fibrillation was induced. At point ECM, external cardiac massage was begun. At point DF, defibrillation was accomplished by a second electric shock.

proximately linear fashion (Fig. 3). Such a direct linear relationship indicates that over a wide range of pressure in these anesthetized dogs, there was no significant increase in cerebral vascular resistance. This result is consistent with the results of Kety (6) (in human beings) and of Sagawa and Guyton (7) (in dogs), who reported that the cerebral vascular bed, unlike most of the systemic vasculature, does not respond to hypotension by vasoconstriction. On the contrary, Kety showed that cerebral vascular resistance (in man) actually decreases in hypotension, possibly as a consequence of hypoxia or hypercapnia.

In the present study we found no evidence of autoregulation of the type that preserves CBF (in man) remarkably constant at perfusion pressures greater than 50 mm Hg. In a review of 376 determinations of CBF in unanesthetized humans by seven different investigators, Lassen (8), found that CBF did not

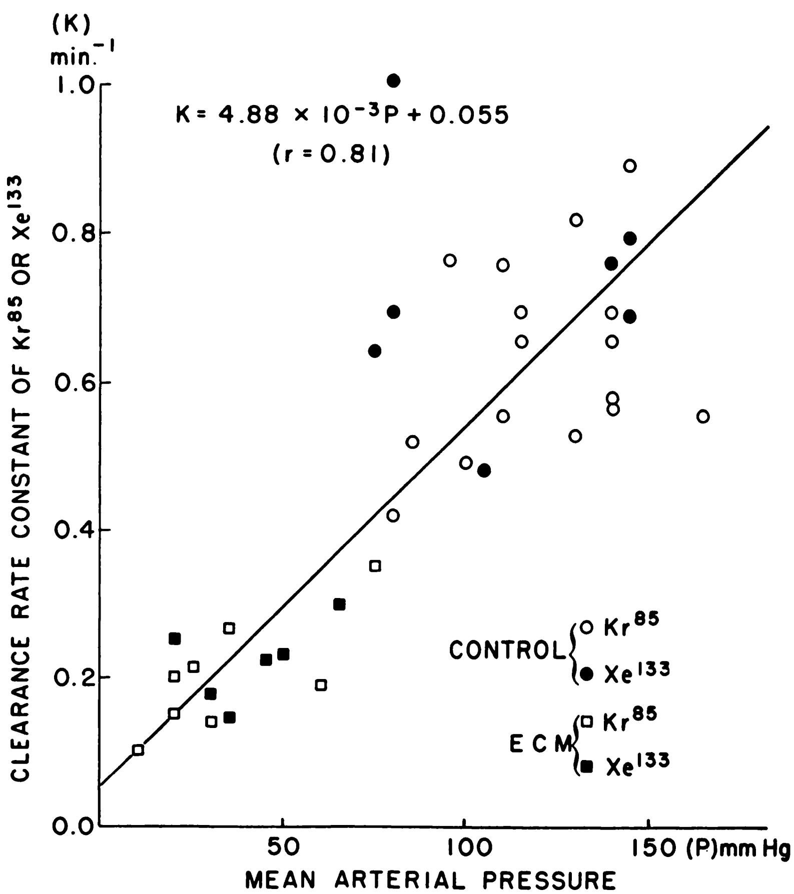

Fig. 3. Relationship between mean arterial pressure and fractional clearance (k) of Kr^{85} and Xe^{133} from the dog's brain. ECM refers to values obtained during cardiac arrest and external cardiac massage.

increase in hypertensive or decrease in hypotensive individuals in the range of 50 to 170 mm Hg. Below 50 mm Hg, however, this regulatory mechanism did not function, since there was a precipitous drop in CBF. Different results, similar to those of the present study, were reported by Sagawa and Guyton (7), whose experiments in anesthetized dogs showed a linear relationship between

TABLE II

MEAN ARTERIAL PRESSURE (MAP) AND CLEARANCE RATE CONSTANT (K)

		Control		*External Cardiac Massage*	
Dog No.	*Gas*	*MAP* *mm Hg*	*K* min^{-1}	*MAP* *mm Hg*	*K* min^{-1}
1	Kr^{85}	140	0.659	75	0.354
		140	.577		
		140	.568		
2	Kr^{85}	145	.899	28	.141
		130	.532	20	.151
		130	.823		
3	Kr^{85}	115	.659	20	.208
		115	.693	35	.268
		95	.769	60	.189
		85	.521		
		100	.488		
4	Kr^{85}	165	.554	10	.104
		140	.693	25	.218
		110	.769		
		110	.558		
5	Xe^{133}	105	.484	30	.177
		80	.419	45	.225
		75	.642	35	.144
		80	1.03		
		80	.693		
6	Xe^{133}	145	.796	50	.231
		140	.769	65	.301
		145	.672	20	.257

CBF and perfusion pressure at levels from zero to 160 mm Hg. While species differences might be important, of perhaps greater significance is the effect of anesthesia in depressing autoregulation of cerebral blood flow.

SUMMARY AND CONCLUSIONS

(1) Cerebral blood flow was measured in anesthetized dogs by determining the rate of clearance of radioactive inert gases (Kr^{85} and Xe^{133}) from the brain after injection into the internal carotid artery.

(2) External cardiac massage during cardiac arrest restored cerebral blood flow to approximately one-third of that measured during normal cardiac action in the same animals.

(3) In the anesthetized dog, over a pressure range from 15 to 150 mm Hg, cerebral blood flow increased in an approximately linear fashion as arterial pressure increased.

REFERENCES

1. Kouwenhoven, W. B., Jude, J. R., Knickerbocker, G. G.: Closed Chest Cardiac Massage, *J.A.M.A.* **173**:1064, 1960.
2. Ingvar, D. H. and Lassen, N. A.: Regional Blood Flow by External Collimation Following Intravenous Injection of Radioisotopes, *Acta Physiol. Scand.* **54**:325, 1962.
3. Barnett, C. H., Marsden, C. D.: Functions of Mammalian Carotid Rete Mirabile, *Nature* **191**:88, 1961.
4. Shoji, T., Saigusa, M., Uei, I.: Studies on the Cerebral Circulation by Dilution Method, *Resp. & Circulation* **5**:931, 1957 (in Japanese).
5. Jude, J. R., Kouwenhoven, W. B., Knickerbocker, G. G.: Cardiac Arrest, *J.A.M.A.* **178**:1063, 1961.
6. Kety, S. S. and Schmidt, C. F.: Nitrous Oxide Method for the Quantitative Determination of Cerebral Blood Flow in Man, *J. Clin. Invest.* **27**:476, 1948.
7. Sagawa, K. and Guyton, A. C.: Pressure Flow Relationships in Isolated Canine Cerebral Circulation *Am. J. Physiol.* **200**(4):711, 1961.
8. Lassen, N. A.: Cerebral Blood Flow and Oxygen Consumption in Man, *Physiol. Rev.* **39**:183, 1959.