Fractionation of the Cardiac Output of Rats with Isotopic Potassium

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A single injection of K42 given intravenously is initially distributed among the organs in proportion to the blood flow through them. By determining the organ content of K42 after such an injection the cardiac output may be fractionated. The conditions and limitations of the method are discussed and values are given for the fractional distribution of the cardiac output in the rat.

FOREIGN substance, after a single intravenous administration, will be distributed initially to the organs in proportion to their blood flow. The substance will then be carried away from the organs by their venous drainage. For a certain period of time, however, the venous drainage will be negligibly small compared to the arterial delivery. During this time the fractional distribution of the substance among the organs will correspond to the fractional distribution of the cardiac output among them.

In the case of a substance which is incompletely transferred from the blood to the tissues, or one which has a small volume of distribution within the tissues, the time during which the venous drainage is small will be short. The time will be greatest for substances which are completely transferred from the vascular system to the tissues with least hindrance and which have a large volume of distribution within the tissue. The radioactive isotope of potassium, K42, is such a substance.

The studies described here indicate that the venous drainage of K42 is negligible compared with its initial deposition in the organs of the rat for at least 1 min. after a single intravenous administration of the isotope. It is therefore possible to estimate the fractionation of the cardiac output of the rat by determining the distribution of K42 in the organs of the animal killed within 1 min. after intravenous injection of the isotope. This has been done for the kidneys, splanchnic viscera, heart, brain, skin and carcass of anesthetized rats.

METHODS

Forty fasting adult male rats were anesthetized with intraperitoneal sodium pentobarbital 44 mg./Kg. A femoral vein was exposed and 0.50 ml. of high specific activity K4 (about 200 mc./Gm.) containing 5–10 microcuries was injected rapidly. This injection was followed at times ranging from 5 to 1200 sec. by the intravenous administration of saturated KCl which produced cardiac arrest within 2 to 5 sec.

The organs, including the skin, were removed, drained of blood, weighed, and digested in hot 6X HCl. The carcass, including all organs not specifically taken for analysis, was ground in a meat grinder, and an aliquot taken for acid digestion. The K4 content of each digest was determined on a 1 ml. aliquot using an end window Geiger-Muller tube. All organ counts were referred to the arithmetic average of two counts of a standard K4 solution which bracketed them closely in time.

RESULTS

Table 1 shows the results in 40 consecutive measurements. The first 17 rats used were from a different group than the last 23 and had significantly smaller hearts and kidneys in relation to their body weights. There were corresponding but greater differences in the uptake of K4 by these organs and the data are therefore presented separately. No explanation is available for the large difference in heart and kidney K4 uptakes in the 2 groups.

The scatter of the results from animal to animal, even within each group, is considerable. Nevertheless, there is no evidence of a trend.
either upwards or downwards in the K\textsuperscript{42} uptake of any organ for at least 1 min. Unmistakable evidence of a downward trend appears first in the kidney after 3 min.

The average values during the first minute of 18.1 per cent for kidney, 14.3 per cent for the portal system, 6.6 per cent for the liver, 2.6 per cent for the heart, 6.3 per cent for the skin and 38.8 per cent for the carcass are therefore believed to describe the fractions of the cardiac output distributed to each organ. In the case of the liver, the fraction detected is only that which has not previously been through another vascular bed. The total hepatic blood flow fraction is the sum of the "liver" and "portal system" fractions.

Of the injected K\textsuperscript{42}, 93 per cent was accounted for in those experiments in which skin and carcass determinations were made. Ninety seven per cent of the mass of these animals was recovered.

### DISCUSSION

The present method is based on the principle that for a short time after any foreign substance enters an organ by way of the arterial circulation it does not appear in the venous circulation. During this time the extraction ratio is 1.00. Consequently, the clearance of the substance by each organ will be equal for a short time to its blood flow. Since the clearance may be described as the ratio between organ uptake and arterial concentration, and since the arterial concentration is presumably constant in all organs, the uptakes will be divided among the organs in proportion to their flows.

With the passage of time a sufficient quantity of measuring agent will accumulate in each organ to force a significant re-entry into the venous circulation. This will occur most rapidly in organs with perfusion rates which are high in relation to their capacity to contain the agent. Since the re-entry is not a simultaneous event for all organs, the extraction ratios will become different from 1 and unequal. The deposition of the measuring agent will now yield false values for flow. In the case of organs with high perfusion rates the apparent fractional flow will become falsly low; organs with low perfusion rates will yield fractional flows which are correspondingly high.

Since, in the present experiments, the first minute failed to reveal a systematic decline in the apparent perfusion rates of well perfused organs.
organs or a systematic increase in the apparent perfusion rates of poorly perfused organs, it must be concluded that entering K\textsuperscript{21} is, so to speak, “trapped” for this time by all the organs studied. It is possible that the brain represents an exception to this situation, and that the decline in brain potassium occurs with such extraordinary rapidity that it is essentially complete before the 5 sec. period at which the first observation was made. This would occur if the cerebral blood flow were exceedingly large in relation to the cerebral “sink” for potassium. A small reservoir of exchangeable potassium in the brain has been observed by others.\textsuperscript{1} The possibility cannot, however, be excluded that the cerebral blood flow is correctly measured in these experiments and that it is much lower than is ordinarily believed to be the case. If the cardiac output of the rat is taken as 210 ml./Kg./min.\textsuperscript{2} then the values given here represent a flow of about 0.1 ml./min./Gm. of brain tissue. Although this value is much smaller than that reported in other species (about 0.5 ml./min./Gm.) it may not be unreasonably small for the deeply anesthetized rat.

The sum of the fractional values indicated for the hepatic arterial (liver) flow, and the hepatic portal (portal system) flow is the hepatic blood flow fraction. The fraction (20.9 per cent of the cardiac output) is somewhat higher than that ordinarily accepted, although the distribution between the arterial and portal flows is consistent with that previously reported.\textsuperscript{3} The discrepancy in total flow may be explained by a species difference; on the other hand, it is possible that the accepted values, based upon hepatic venous catheterization are falsely low.\textsuperscript{4}

The cardiac uptakes of K\textsuperscript{21} differed radically in the 2 experimental groups. In the first group, the heart received 1.8 per cent of the isotope; in the second it received 3.3 per cent. These values correspond to flows of 1.5 and 2.6 ml./min./Gm. of heart. Such values exceed those found in the dog by the nitrous oxide method\textsuperscript{6} considerably. Whether a species difference is involved or whether the nitrous oxide method is inapplicable to the heart\textsuperscript{4} is not clear. It may be noted at this time, however, that the present method cannot yield falsely high values for an organ with a high perfusion rate, so that the value found here represents a minimum coronary flow.

The value for renal blood flow found in the first group of animals was about 3.5 ml./min./100 Gm. rat. In the second group of animals, the value was about 5.9 ml./min./100 Gm. rat. Assuming a 50 per cent hematocrit, both values give renal plasma flows well within the ranges reported for normal rats.\textsuperscript{7}

The blood flow through the skin, about 6 per cent of the cardiac output, for an organ making up some 20 per cent of the body mass, may be typical only of the deeply anesthetized animal in a relatively cool (26 C.) environment.

The carcass, consisting primarily of bone and muscle, received almost 40 per cent of the cardiac output, and made up 66 per cent of the mass of the animals.

**Summary**

Intravenously injected K\textsuperscript{21} is distributed among the organs of rats in the first minute after injection in the following manner: kidney, 18.1 per cent; portal system, 14.3 per cent; liver, 6.6 per cent; heart, 2.6 per cent; brain, 0.3 per cent. These values remain essentially constant between 5 and 60 sec. after injection, suggesting that the early distribution of isotopic potassium reflects the distribution of the cardiac output.

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**Summario in Interlingua**

Injectiones intravenose de K\textsuperscript{21} es distribuite inter le organos del ratto durante le prime minuta post le injection in le sequente maniera: Ren—18,1 pro cento; sistema portal—14,3 pro cento; hepate—6,6 pro cento; corde—2,6 pro cento; cerebro—0,3 pro cento. Iste valores remane essentemente stabile ab 5 a 60 secundas post le injection. Ergo il pare que le distribution precoce de kalium isotopic reflecte le distribution del rendimento cardiae.
Recommendations of Committee of National Academy of Sciences on Loyalty in Relation to Government Support of Unclassified Research

On the basis of their findings the Committee appointed by the National Academy of Sciences to counsel with the Government regarding the question of loyalty criteria in the award of Government grants and contracts for unclassified scientific research recommends that the Government adhere to the following policy:

1. The test in the award of grants and contracts for unclassified research should be the scientific integrity and competence of the individuals responsible for carrying out the research, and the scientific merits of their program.

2. When an official of the Government comes into possession of evidence which in his opinion indicates the possible existence of disloyalty in violation of law, he should promptly refer that information to the Federal agencies of law enforcement established to deal with such matters.

3. An allegation of disloyalty should not by itself be grounds for adverse administrative action on a grant or contract for unclassified research by scientifically competent investigators; if the indications of disloyalty appear sufficiently serious to warrant any action at all, the Government in the opinion of the Committee has no other course than to bring formal charges and to produce the evidence in open hearing before legally constituted authority.

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