throughout the body. We are not aware of any such determinations.

Since stools of dogs with biliary fistulae contain Co^{60} radioactivity, it is evident that labeled B_{12} or one of its degradation products passes into the lumen of the gastrointestinal tract from sources other than bile. Fecal radioactivity is obviously enhanced when the flow of bile to the intestines is uninterrupted. Whether Co^{60} in bile is still part of the Vit. B molecule and can be absorbed for reutilization has not yet been determined. Okuda *et al.* (7) have also independently demonstrated the presence of radioactive B_{12} in bile and stools of rats after injection of labeled B_{12} in rats and believe that fecal B_{12} has a biliary and an intestinal source.

Conclusions. 1. Following intravenous administration of 2.09 to 3.48 μc Co^{60} Vit. B_{12} to dogs between 2.6 and 6.6% of radioactivity was recovered in the bile. 2. In 3 of 5 dogs the 2-phased excretion pattern showed fast and slow components of 6.0 to 7.5 hours and 90 to 295 hours, respectively. 3. Fecal excretion of radioactivity in dogs with biliary fistulae was considerably less than in intact normal animals.

1. Grasbeck, R., Okuda, K., *Trans. 2nd Internat. Cong. Clin. Chem.*, Stockholm, August 1957, p96.

2. Miller, A., Corlius, H. F., Sullivan, J. F., *J. Clin. Invest.*, 1957, v36, 18.

3. Stiefel, G. E., Jasiuski, B., Frei, H., *Schweiz med. Wchaschr.*, 1956, v86, 824.

4. Grasbeck, R., Nyberg, W., Reizenstein, P., PROC. SOC. EXP. BIOL. AND MED., 1958, v97, 780.

5. Meyer, L. M., Bertcher, R. W., Cronkite, E. P., *ibid.*, 1957, v96, 360.

6. Cronkite, E. P., Henley, E., Meyer, L. M., Plasma clearance and excretion in human beings.

7. Okuda, K., Grasbeck, R., Chow, B. F., *J. Lab. Clin. Med.*, 1958, v51, 17.

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Oxygen Consumption of the Hypothermic Potassium Arrested Heart.* (24255)

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Cardiac arrest induced by intracoronary administration of potassium(1) or acetylcholine(2) has been found useful in cardiac surgery. However, revival of arrested hearts has not been completely satisfactory(3). Refractory ventricular fibrillation and inability of the previously asystolic heart to maintain an adequate cardiac output have been the principal difficulties. Previous studies(3) have indicated that the combination of cardiac hypothermia and potassium arrest resulted in the most rapid and complete post-arrest recoveries. The assumption was made that a reduction in myocardial oxygen requirement by cardiac hypothermia in the arrested heart was in large part responsible for these results and the present study was undertaken to test this asumption by quantitating the oxygen consumption of the normothermic and hypothermic arrested heart.

Methods. Fifteen technically satisfactory experiments were performed on open chest dogs anesthetized with sodium pentobarbital (30 mg/kg). The chest was opened bilaterally in the fourth intercostal space and the sternum transsected at this level. Following administration of heparin, the left coronary artery and the coronary sinus were cannulated. During control studies when the circulatory system was intact and the heart doing work, the source of blood for left coronary artery perfusion was either the dog's carotid artery or a pump oxygenator(4). When the pump oxygenator was used, blood was withdrawn from the right atrium at a rate

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equal to that of infusion into the left coronary artery. Blood from the coronary sinus was returned to the animal *via* the right jugular vein. Coronary blood flow was measured with an optically recording rotameter(5), and perfusion pressure with a Statham strain gauge. The oxygen content of coronary artery and coronary sinus blood was determined in duplicate by the method of VanSlyke and Neill (6). After coronary blood flow had been determined and blood samples for oxygen had been withdrawn in the normothermic working heart, the dog was placed on a complete cardiac bypass(4). The left coronary artery was supplied with oxygenated blood from the pump oxygenator at the same flow rate that existed during the control period. A catheter in the right atrium served to drain blood that returned by routes other than the coronary sinus. Potassium chloride was then infused into the tubing leading to the cannulated left coronary artery at a constant rate sufficient to produce and maintain left ventricular arrest. Since potassium has a coronary vasodilator or vasoconstrictor effect, depending upon dose employed(7,8), it was necessary to make careful adjustments of perfusion pressure and rate of potassium chloride infusion in order to keep coronary blood flow constant throughout the experiment. A small glass coil immersed in a water bath was interposed between the rotameter and the coronary artery cannula. Blood passing through the coil could be warmed or cooled by varying the temperature of the water bath. The temperature of coronary artery blood was measured at the coronary cannula and continuously recorded by a thermocouple connected to a Leeds and Northrop Speedomax. At the conclusion of each experiment the perfused portion of the heart was stained with India ink, excised, and weighed.

Results. The average coronary blood flow and oxygen consumption of intact working hearts were 73 and 9.18 ml/min/100 g of heart muscle, respectively (Table I). Cardiac arrest in the normothermic heart resulted in an average reduction in myocardial oxygen consumption to 2.08 ml/min/100 g of heart whereas cooling of the arrested heart to 21.5

TABLE I. Oxygen Consumption of Normothermic and Hypothermic Potassium Arrested Hearts.

CBF	Myocardial oxygen consumption		
	Beating heart	K-arrested warm	K-arrested cold
	cc/min./100 g heart		
78	7.12 (34.0)*	.23 (34.0)*	<.20 (25.0)*
58		1.01 (37.0)	.64 (25.0)
83	10.61 (37.5)	1.08 (36.5)	.75 (23.0)
84		3.75 (36.5)	.39 (23.5)
67	9.51 (37.5)	2.41 (37.0)	1.27 (22.0)
117	8.42 (36.5)	3.74 (37.0)	.47 (23.0)
54	8.01 (36.5)	3.10 (36.5)	2.84 (22.5)
60	7.38 (36.5)	<.20 (36.5)	.48 (24.0)
72	11.01 (38.0)	2.00 (37.0)	<.20 (22.0)
51		1.53 (38.0)	<.20 (25.0)
50		2.65 (38.0)	.77 (22.0)
78	4.68 (36.5)	.94 (38.0)	<.20 (23.0)
† 124	14.87 (35.5)	2.17 (37.5)	.38 (22.0)
† 45		2.49 (36.0)	.65 (22.0)
† 83		4.05 (37.0)	1.11 (21.5)
Avg			
73	9.18	2.08	.66

* No. in parentheses denotes temperature of blood perfusing left coronary artery in degrees centigrade.

† 2-4 separate determinations on the same heart.

Arterial oxygen content avg 20 vol % and in none of the experiments was it less than 17 vol %.

to 25°C produced an average myocardial oxygen consumption of 0.66 ml/min/100 g of myocardium. In only one experiment (#8) was oxygen consumption of the cold arrested heart greater than that of the warm arrested heart. In this experiment, however, the myocardial oxygen consumption of the arrested heart was less than 0.2 ml/min at 36.5°C.

Discussion. Oxygen consumption of the normothermic potassium arrested heart in the present study was 2.1 ml/min/100 g of perfused heart. This is equivalent to 23% of oxygen consumption of the intact beating heart. These figures are in good agreement with those of McKeever *et al.*(9) who found oxygen consumption of the potassium arrested heart to be 2.2 ml/min/100 g of myocardium, which was between 16 and 32% of the oxygen consumption of the working ventricle in their studies. The values for oxygen consumption of the warm arrested heart in the present study are also in reasonable agreement with those of Berglund *et al.*(10). According to rough calculations from Fig. 2 of their paper, the average cardiac oxygen consumption for

6 experiments was 1.4 ml/min/100 g of heart, which was about 18% of the oxygen utilization of the working heart.

Cooling the blood perfusing the arrested heart reduced myocardial oxygen consumption to about one-third of that observed at normal body temperature and to 7% of the oxygen consumption of the intact working heart. These observations indicate that the rapid post-arrest recovery of the cold arrested heart is most likely due to its very low oxygen requirement. The possibility cannot be excluded, however, that the beneficial effects of cold in the arrested heart are not related to the reduction in myocardial oxygen consumption, but to some specific effect of low temperature on the metabolic characteristics of the myocardium. Application of these data to surgical situations in which cardiac arrest is necessary, suggests that coronary blood flow can be interrupted about 3 times longer in the hypothermic than in the normothermic arrested heart.

Summary. Oxygen consumption of the potassium arrested heart averaged 2.1 ml/min/100 g of perfused heart at normal body temperature, and 0.66 ml/min/100 g of perfused heart at 21.5 to 25°C.

1. Melrose, D. B., Dreyer, B., Bentall, H. H., Baker, J. B. E., *Lancet,* 1955, v2, 21.

2. Lam, C. R., *J. Thorac. Surg.,* 1956, v32, 370.

3. Berne, R. M., Jones, R. D., Cross, F. S., *J. Applied Physiol.,* 1958, v12, 431.

4. Cross, F. S., Berne, R. M., Hirose, Y., Jones, R. D., Kay, E. B., PROC. SOC. EXP. BIOL. AND MED., 1956, v93, 210.

5. Shipley, R. E., Wilson, C., *ibid.,* 1951, v78, 724.

6. Van Slyke, D. D., Neill, J. M., *J. Biol. Chem.,* 1924, v61, 523.

7. Katz, L. N., Lindner, E., *Am. J. Physiol.,* 1938, v124, 155.

8. Driscol, T. E., Berne, R. M., PROC. SOC. EXP. BIOL. AND MED., 1957, v96, 505.

9. McKeever, W. P., Canney, P. C., Gregg, D. E., *Fed. Proc.,* 1957, v16, 86.

10. Berglund, E., Monroe, R. G., Schreiner, G. L., *Acta, Physiol. Scand.,* 1957, v41, 261.

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Significance of Circulating Phenols in Anemia of Renal Disease.* (24256)

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Anemia is a frequent complication in patients with chronic renal disease. The degree of anemia is roughly proportional to the level of azotemia, but the exact mechanism whereby anemia is produced is still unsolved. The most widely supported theory is that anemia results from a suppression of erythropoiesis by "toxic" metabolic products retained in the blood(1-5). Recent reports also stress the importance of increased erythrocyte destruction associated with inadequate bone marrow response(1-5) The hemolytic process is thought to be extracorpuscular, but no definite mechanism has been set forth. Evidence has appeared to suggest that phenol and/or its derivatives are hematopoietic poisons(6, 7). Conceivably they could be implicated either as bone marrow "toxins" or hemolytic agents. Most earlier work suffered from lack of specific analytic reactions employed to detect blood phenols(6). Using one such nonspecific reaction, the xanthoprotein index, Bock and Thedering(7) reported that elevated xanthoprotein levels were seen in anemic patients with renal insufficiency, and suggested that these substances might be implicated in production of anemia of these patients. Schmidt, *et al.*(8) applied a more specific technic for detection of blood phenols

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