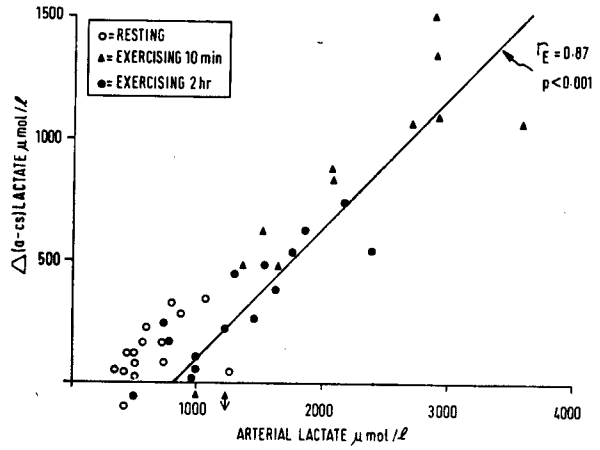

FIG. 6. Relationship between arterial blood lactate concentration and myocardial extraction (Δ(a-cs)) of lactate. Since concentration and extraction were significantly correlated only during exercise, regression line and correlation coefficient (r_R) have been calculated from these points (see Table 6).

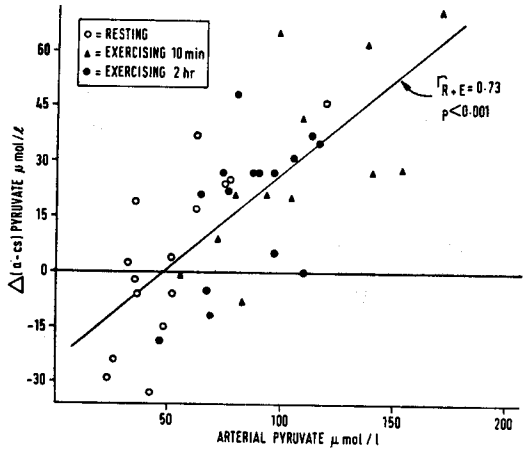

FIG. 7. Relationship between arterial blood pyruvate concentration and myocardial extraction (Δ(a-cs)) of pyruvate. Negative values of Δ(a-cs) indicate efflux of pyruvate into coronary sinus blood. Since neither parameter of linear regression equation relating arterial concentration and myocardial extraction at rest differed significantly from that during exercise, regression line and correlation coefficient (r_{R+E}) have been calculated from pooled data (see Table 6).

difference could lie between +1.2 and −6.0 counts/min per ml at rest and between +1.0 and −9.4 counts/min per ml during exercise. Expressed as a percentage of average arterial ^{125}I radioactivity these limits are +0.25 to −1.3% at rest and +0.2 to −1.9% during exercise. The only blood substrate for which this degree of hemodilution or hemoconcentration could materially affect fractional extraction is TG. Since the average (a-cs) difference in TG concentration was 1.7% of the average arterial TG concentration at rest and 1.4% during exercise (Table 2), undetected hemodilution could reduce these differences to 1.45 and 1.2%, respectively. Thus, within these confidence limits, the significant (a-cs) difference in TG concentration cannot be attributed to a degree of hemodilution which could not be detected by the ^{125}I radioactivity measurements. On the other hand, because of this error in the method, undetected hemoconcentration could mean that the actual average (a-cs) differences in TG concentration at rest and during exercise were as much as 3.0 and 3.3% of their respective arterial concentrations.

The significant increase in arterial ^{125}I radioactivity from rest to exercise of 15 counts/min per ml (Table 1) indicates that exercise was accompanied by arterial hemoconcentration of about 3%.

DISCUSSION

Effect of Exercise on Myocardial Oxygen Utilization

Figures 2 and 3 compare our findings for the relationship between *a*) coronary sinus oxygen saturation and heart rate (Fig. 2) and *b*) (a-cs) difference in oxygen content and heart rate (Fig. 3) with those of Pernow et al. (30) for femoral venous blood at rest and during supine leg exercise. In both our study and that of Pernow et al. heart rate is used as an index of the work performed by the particular muscle tissue under consideration. This is probably valid for leg exercise since there is a linear correlation between heart rate and work intensity (6). In the case of the heart, the tension developed per minute by the left ventricular muscle will depend on heart rate unless there are significant changes in ventricular volume or arterial blood pressure. Although both of these variables do alter during prolonged supine leg exercise, the changes are relatively slight (12).

It can be seen from Figs. 2 and 3 that skeletal muscle and cardiac muscle are behaving in a similar fashion from the point of view of the effect of work on venous oxygen saturation and arteriovenous difference in oxygen content across the organ, except that the work which is being performed by the myocardium at resting heart rates moves it down the curve relating oxygen saturation to heart rate and up the curve relating oxygen extraction to heart rate.

In both types of muscle these effects of exercise could result from: *a*) a redistribution of blood flow so that a larger proportion of the blood passing through the organ is coming into contact with muscle tissue or *b*) to an actual increase in the fraction of oxygen removed from that blood which is flowing past muscle tissue. It is clear, however, that the major part of the increase in myocardial oxygen consumption which occurs with exercise is being met by increased coronary blood flow and that the increased (a-cs) difference in oxygen content makes only a small contribution. In our subjects prolonged exercise almost doubled the average heart rate (Table 1), and such an increase in heart rate with exercise should be associated with a two- to threefold increase in coronary blood flow (17, 21). At the same time the average (a-cs) difference in oxygen content increased by about 21% (Table 5). If the average coronary blood flow during exercise had been twice the resting flow, then approximately 15% of the increase in oxygen uptake would be met by the increased (a-cs) oxygen difference. If flow had been 3 times the resting level, then the increased (a-cs) oxygen difference would have accounted for only about 8% of the increased oxygen uptake.

Effect of Prolonged Exercise on Relative Contribution of Substrates to Myocardial Oxidative Metabolism

Ten minutes after the beginning of exercise the average arterial lactate concentration had risen to more than 3 times

the resting level and the OER for this substrate had increased from 8 to 38% (Table 3). Previous studies have shown that arterial FFA concentrations fall below resting levels during the first 10–20 min of exercise (4) and that this is accompanied by a fall in the OER for FFA (23). In general the higher the rate of work, the greater is the early fall in FFA concentration (7) and the higher the rise in lactate concentration (6). Thus, during the early minutes of exercise it would appear that there is a shift in the relative contribution of blood FFA and lactate to myocardial energy metabolism (as assessed by the OERs) and that within limits the extent of this shift is dependent on the magnitude of the work load.

On the other hand, when exercise was prolonged for 2 hr, the arterial lactate concentration had fallen to only about twice the resting level and there had been a significant fall in glucose concentration, with an approximate doubling of FFA levels and no significant change in triglyceride concentration. At this time lactate extraction, although greater than at rest, was less than it had been at 10 min of exercise, FFA extraction had increased, and there was no significant change in glucose or triglyceride extraction. Myocardial oxygen extraction had increased 21%. The result of these effects on myocardial extraction of substrates and oxygen was that by the final minutes of the exercise period there was a fall in the glucose OER, the OER for lactate, although still greater than it had been at rest, had fallen from its level at 10 min, while the OERs of FFA (estimated chemically) and triglyceride had not changed significantly. Despite the fact that pyruvate extraction was about 6 times its resting level, the OER for this substrate was only 1%. Thus, in contrast to the early period of exercise, when exercise had continued for 2 hr, the relative participation of total blood carbohydrate and lipid substrates to myocardial oxidative metabolism did not differ from the pattern at rest.

Myocardial Energy Balance During Prolonged Exercise

Although the decrease in the total OER for blood energy substrates during prolonged exercise was not significant (Table 4) it is possible that during prolonged exercise some energy for myocardial metabolism is being derived from sources other than the blood substrates which we measured. Although plasma ketone bodies can provide about 5–7% of the heart's energy supply at rest (24, 33), their arterial concentration and contribution to myocardial oxidative metabolism fall during exercise (5, 24). The only other potential source of energy in the blood which might be of importance for myocardial metabolism is amino acids, and they do not appear to be extracted by the heart in amounts of significance for myocardial energy metabolism either at rest or during exercise (8). It is possible, therefore, that during prolonged exercise there could be some decrease in the total energy content of endogenous myocardial substrate stores, i.e., glycogen and TG fatty acids. However, as the fall with exercise in the total OER for blood substrates in our study was not significant and as the average OER during exercise did not differ significantly from 100%, it is clear that if, in fact, the myocardium does derive energy from endogenous stores during prolonged exercise in the fasting state, it is very much less dependent on these stores than is skeletal muscle, which under these circumstances may obtain as much as 70% of its energy from endogenous glycogen and TG fatty acids (5).

If the release of glycerol from the heart during exercise reflects increased lipolysis of stored myocardial TG (see below), this does not necessarily imply net loss of myocardial TG but only increased turnover of this lipid pool. Indeed, the fact that the total OER for blood substrates was close to 100% does suggest that, from the point of view of net balance, the heart's energy supply is covered by these substrates during prolonged exercise as well as at rest.

Relationship Between Arterial Concentration and Myocardial Extraction of Substrates

Figure 4 shows that during exercise the relationship between arterial FFA concentration and myocardial extraction of this substrate was altered so that myocardial extraction was independent of concentration—unlike the situation at rest when there was a significant linear relationship between the two variables. Since coronary blood flow also increases during exercise, it is possible that the rate of myocardial FFA uptake (extraction × flow) could still be dependent on arterial concentration if those subjects with higher arterial FFA concentrations also had higher coronary flow rates. This seems possible since arterial FFA concentration during exercise was highest in those subjects with the highest heart rates (Fig. 8), and it has been shown in man that there is a close relationship between increase in heart rate and increase in coronary blood flow during exercise (17, 21). If it is not the case that coronary flow is highest in those subjects with the highest FFA concentrations, and rate of FFA uptake is independent of concentration during exercise, this would suggest that either penetration of FFA into the myocardial cell or its utilization within the cell has become rate-limiting.

In the case of glucose, the relationship between arterial concentration and extraction is different (Fig. 5). Here there is a significant linear relationship between arterial concentration and extraction at rest, but not during exer-

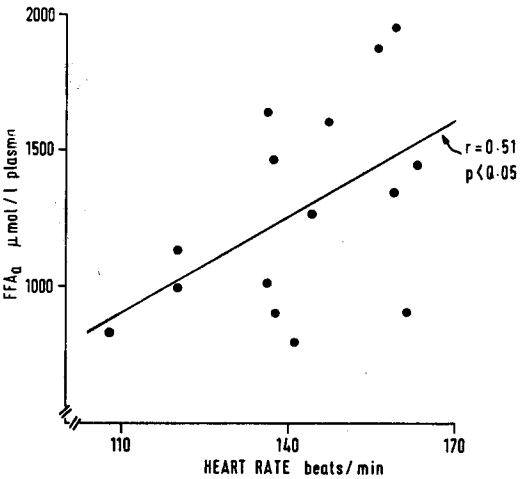

FIG. 8. Relationship between arterial plasma FFA concentration (FFA_a) and heart rate during final minutes of prolonged exercise (r = correlation coefficient).

TABLE 7. *Data from linear regression and correlation analyses comparing parameters obtained from measurements made at rest in present study with those of an earlier study (25)*

Arterial FFA Concn (x) and:	B	A	r	n	P
I. Glucose extraction (y)					
Previous study	−0.26	370	−0.51	28	<0.005
Present study	−0.36	420	−0.45	15	NS
II. Pyruvate extraction (y)					
Previous study	−0.04	29	−0.46	33	<0.005
Present study	−0.04	40	−0.30	15	NS
III. Lactate extraction (y)					
Previous study	−0.30	370	−0.62	32	<0.001
Present study	−0.28	310	−0.42	15	NS

$y = Bx + A$, where x is arterial FFA concentration and y is: *I*, myocardial glucose extraction; *II*, myocardial pyruvate extraction; and *III*, myocardial lactate extraction; r = correlation coefficient.

cise, and the values for exercise tend to lie close to or above the regression line for the values at rest. Since during exercise coronary blood flow has increased, for a given (a-cs) difference in concentration the rate of glucose uptake ((a-cs) difference × flow) must also be greater than at rest. In our subjects exercise was associated with a fall in arterial insulin concentration (M. L. Wahlqvist et al., unpublished data). Thus increased uptake of glucose during exercise could reflect either *a*) a stimulation, independent of insulin, of the process transferring glucose across the cell membrane, or *b*) a decrease in intracellular glucose concentration. The performance of work by the isolated perfused rat heart is accompanied by an analogous stimulation of glucose uptake (10).

In our previous study of myocardial metabolism in healthy men (25) we showed that there were significant, negative linear relationships between increasing arterial FFA concentration (x) and myocardial extraction (y) of glucose, pyruvate, and lactate. This suggested that FFA can suppress glucose extraction by the human heart at rest as it does in the rat heart (32, 34) and that, at least in part, this may be due to inhibition of pyruvate dehydrogenase. Although at rest these variables were not significantly correlated in the present study, it can be seen from Table 7 that the parameters for the various linear regression equations are very similar in the two studies. The lack of significance in the present study may be due to the fact that the number of observations was about half of that in the earlier study. During exercise, however, not only were the variables not significantly correlated, but the parameters for the regression equations differed greatly from those at rest. These findings suggest that during exercise there may be enhanced glucose uptake which is independent of both the fall in arterial insulin concentration and the rise in FFA.

Effect of Exercise on Entrance of Unlabeled Fatty Acids and Glycerol into Coronary Sinus Blood

In an earlier study of myocardial metabolism of blood lipid and carbohydrate substrates in fasting men at rest, using a continuous infusion of albumin-bound palmitate-^{3}H (25), we found that the specific activity of the subjects' coronary sinus FFA was almost always less than that of their arterial FFA, and concluded that this indicated the release into the coronary sinus of FFA of relatively low specific activity rather than the alternative possibility of selective uptake of palmitate. Although this FFA could have been released from plasma TG, epicardial adipose tissue or endogenous myocardial glycerides, we thought that the last of these possible stores was the most likely source. In addition, we interpreted our observation that the FFA which was released into the coronary sinus was not accompanied by free glycerol as meaning either that the FFA was derived from partial hydrolysis of endogenous glycerides, or that glycerol was metabolized within the myocardium.

In the present study, when our subjects were at rest our findings were very similar to those of the earlier study. In contrast, when the subjects were exercising, the specific activity of their coronary sinus FFA was only slightly less than that of their arterial FFA, and free glycerol was released into their coronary sinus blood.

Although glycerol release into the coronary sinus during prolonged exercise could indicate decreased myocardial reutilization of glycerol, it is more likely to be a reflection of an increased rate of lipolysis within at least one of the three glyceride stores mentioned above. On the other hand, the fact that the arterial and coronary sinus FFA specific activities were very similar during exercise indicates an apparent decrease in the rate of entrance of unlabeled fatty acids into the coronary sinus at this time.

The most likely source of the free glycerol which entered the coronary sinus during exercise would seem to be endogenous myocardial glycerides rather than plasma TG or epicardial adipose tissue. If plasma TG had been the source, there would have been an increased (a-cs) difference in TG concentration during exercise rather than the small decrease which actually occurred, and if the glycerol had come from epicardial adipose tissue, there should have been a concomitant efflux of FFA into the coronary sinus. Since the rate of incorporation of fatty acids into adipose tissue in the fasting, exercising state is probably relatively slow, it is unlikely that the specific activity of adipose tissue fatty acids would have reached that of the plasma FFA during exercise. Thus an increased rate of efflux of epicardial adipose tissue fatty acids would have tended to increase the difference between arterial and coronary sinus specific activities and not decrease it.

If endogenous myocardial glycerides are indeed the source of the free glycerol entering the coronary sinus during exercise, and if they are also the origin of the unlabeled or low specific activity fatty acids which are released into the coronary sinus at rest, then there are at least three possible explanations for the apparent decrease in this release which we observed during exercise: *a*) an increase with exercise in coronary blood flow, *b*) an increase in the specific activity of the FFA released into the coronary sinus relative to that of arterial FFA, and *c*) a decrease in the rate at which FFA is released into the coronary sinus. These explanations, which are obviously not mutually exclusive, are examined in turn below.

a) *An increase in coronary blood flow.* When our subjects exercised, the difference between the radioisotopic and chemical estimates of their FFA extraction (which is a function of the difference between the arterial and coronary

sinus specific activities and, therefore, a measure of the amount of unlabeled fatty acid entering the coronary sinus) fell to 10 μmoles/liter plasma from a resting value of 90 μmoles/liter. If the rate of entrance of fatty acids into the coronary sinus had remained constant during exercise, coronary blood flow would have had to increase ninefold to account for this fall. However, with the intensity of exercise performed by our subjects, which approximately doubled their resting heart rates, coronary blood flow would probably have increased only two-, or at the most, threefold (17, 21). It is unlikely, therefore, that the fall is explicable solely in terms of increased flow.

b) A relative increase in specific activity of FFA released into coronary sinus. When our subjects were at rest, the average specific activity of their arterial FFA was 1,852 counts/min per μmole (Table 2). However, when they had been exercising, the concentration of their arterial FFA rose, and its specific activity fell to 761 counts/min per μmole. Therefore, this in itself would have reduced any positive difference between the specific activities of the arterial FFA and any endogenous fatty acids which continued to enter the coronary sinus blood. The fact that the palmitate-^{3}H infusion had been in progress for a longer period would also have tended to increase the specific activity of an endogenous fatty acid pool.

c) A decrease during exercise in the rate of release of fatty acid into coronary sinus. This could arise from either a decreased rate of lipolysis within the glyceride pool or an increased rate of metabolism of fatty acids produced by lipolysis. As discussed above, increased rate of entrance of free glycerol into the coronary sinus with exercise makes the first of these possibilities seem unlikely. On the other hand, it is feasible that during exercise increased oxidation of this endogenous fatty acid could reduce its intracellular concentration and, therefore, its rate of efflux, although the fact that the total OER for blood substrates did not differ significantly from 100% makes this seem unlikely.

A possible unifying explanation for the exercise-induced changes which we observed in the metabolism of both glycerol and labeled palmitate is that at rest there is an appreciable, but relatively slow, turnover of an endogenous myocardial glyceride pool, with release into the coronary sinus of fatty acids with a specific activity lower than that of the arterial FFA. At rest this rate of turnover is less than the maximum rate at which the myocardium can reutilize glycerol. However, with exercise endogenous glyceride hydrolysis is accelerated, the production of glycerol exceeds the myocardial capacity for reutilization, and free glycerol appears in the coronary sinus blood. At the same time there may be either a continuing efflux from this glyceride pool into the coronary sinus of fatty acid which now has a specific activity very close to that of the arterial FFA, or, less likely, the intramyocardial oxidation of this fatty acid may be increased so that its rate of efflux falls. Either event would reduce the amount of unlabeled fatty acid entering the coronary sinus blood, so that the difference between radioisotopic and chemical estimates of FFA extraction by the heart would be smaller.

The albumin-^{125}I was kindly provided by G. Birke and L. O. Plantin, King Gustav V Research Institute, Stockholm, Sweden.

This work was supported by Swedish Medical Research Council Grant 19x-204-07 and 08. B. W. Lassers was a recipient of a Wellcome Swedish Travelling Fellowship and M. L. Wahlqvist a recipient of a Life Insurance Medical Research Fund of Australia and New Zealand Overseas Research Fellowship.

Present address of B. W. Lassers: Dept. of Medicine, The Royal Infirmary, Edinburgh, Scotland.

Address requests for reprints to L. A. Carlson, Dept. of Geriatrics, University of Uppsala.

Received for publication 14 September 1971.

REFERENCES

1. Boberg, J. Separation of labeled plasma and tissue lipids by thin-layer chromatography. *Clin. Chim. Acta* 14: 325–334, 1966.
2. Boberg, J., L.A. Carlson, and U. Freyschuss. Determination of splanchnic secretion rate of plasma triglycerides and of the total and splanchnic turnover of plasma free fatty acids. *Acta Univ. Upsaliensis*, 105, 1971.
3. Bücher, T., R. Czok, W. Lamprecht, and E. Latzko. Pyruvat. In: *Metoden der enzymatischen Analyse.* Weinheim: Verlag Chemie, 1962, p. 253.
4. Carlson, L. A., J. Boberg, and B. Högstedt. Some physiological and clinical implications of lipid mobilization from adipose tissue. In: *Handbook of Physiology. Adipose Tissue.* Washington, D.C.: Am. Physiol. Soc., 1965, sect. 5, chapt. 63, p. 625–644.
5. Carlson, L. A., L.-G. Ekelund, and S. O. Fröberg. Concentration of triglycerides, phospholipids and glycogen in skeletal muscle and of free fatty acids and β-hydroxybutyric acid in blood in man in response to exercise. *European J. Clin. Invest.* 1: 248–254, 1971.
6. Carlson, L. A., and B. Pernow. Studies on the peripheral circulation and metabolism in man. I. Oxygen utilization and lactate-pyruvate formation in the legs at rest and during exercise in healthy subjects. *Acta Physiol. Scand.* 52: 328–342, 1961.
7. Carlson, L. A., and B. Pernow. Studies on blood lipids during exercise. II. The arterial plasma-free fatty acid concentration during and after exercise and its regulation. *J. Lab. Clin. Med.* 58: 673–681, 1961.
8. Carlsten, A., B. Hallgren, R. Jagenburg, A. Svanborg, and L. Werkö. Myocardial metabolism of glucose, lactic acid, amino-acids and fatty acids in healthy human individuals at rest and at different work loads. *Scand. J. Clin. Lab. Invest.* 13: 418–428, 1961.
9. Chernick, S. S. Determination of glycerol in acyl glycerols. *Methods Enzymol.* 14: 627, 1969.
10. Crass, M. F. III, E. S. McCaskill, and J. C. Shipp. Effect of pressure development on glucose and palmitate metabolism in perfused heart. *Am. J. Physiol.* 216: 1569–1576, 1969.
11. Ekelund, L.-G. Circulatory and respiratory adaptation during prolonged exercise in the supine position. *Acta Physiol. Scand.* 68: 382–396, 1966.
12. Ekelund, L.-G., A. Holmgren, and C. O. Overfors. Heart volume during prolonged exercise in the supine and sitting position. *Acta Physiol. Scand.* 70: 88–98, 1967.
13. Häggendal, J., J. H. Hartley, and B. Saltin. Arterial noradrenaline concentration during exercise in relation to the relative work levels. *Scand. J. Clin. Lab. Invest.* 26: 337–342, 1970.
14. Harris, P., R. F. Fletcher, J. Gloster, and M. Gotsman. The metabolism of glycerol and free fatty acids during exercise in patients with rheumatic heart disease. *Clin. Sci.* 28: 343–356, 1965.
15. Harris, P., J. H. Jones, N. Bateman, C. Chlouverakis, and J. Gloster. Metabolism of the myocardium at rest and during exercise in patients with rheumatic heart disease. *Clin. Sci.* 26: 145–156, 1964.
16. Hjelm, M. Enzymatic determination of hexoses in blood and urine. *Scand. J. Clin. Lab. Invest. Suppl.* 192: 85–98, 1966.
17. Holmberg, S. Koronarcirkulation och myokardmetabolism vid angina pectoris. In: *Nordiskt Symposium, Angina Pectoris*, edited by

E. Vernauskas and L. Werkö. Göteborg: Lindgren & Söner, 1969, p. 20.
18. HOLMGREN, A., AND K.-H. MATTSSON. A new ergometer with constant work load at varying pedalling rate. *Scand. J. Clin. Lab. Invest.* 6: 137–140, 1954.
19. HOLMGREN, A., AND B. PERNOW. Spectrophotometric measurements of oxygen saturation of blood in the determination of cardiac output. A comparison with the Van Slyke method. *Scand. J. Clin. Lab. Invest.* 11: 143–149, 1959.
20. HUNTER, W. H., AND M. Y. SUKKAR. Changes in plasma insulin levels during muscular exercise. *J. Physiol., London* 196: 110P–112P, 1968.
21. JORGENSEN, C. R., K. KITAMURA, F. L. GOBEL, H. L. TAYLOR, AND Y. WANG. Long-term precision of the N_2O method for coronary flow during heavy upright exercise. *J. Appl. Physiol.* 30: 338–344, 1971.
22. KESSLER, G., AND H. LEDERER. Fluorometric measurement of triglycerides. In: *Automation in Analytical Chemistry*, edited by L.T. Skeggs. New York: Mediad, 1966, p. 341.
23. KEUL, J. Myocardial metabolism in athletes. In: *Muscle Metabolism During Exercise*, edited by B. Pernow and B. Saltin. New York & London: Plenum, 1971, p. 447.
24. KEUL, J., E. DOLL, H. STEIM, U. FLEER, AND H. REINDELL. Über den Stoffwechsel des menschlichen Herzens. III. Der oxydative Stoffwechsel des menschlichen Herzens unter verschiedenen Arbeitsbedingungen. *Arch. Ges. Physiol.* 282: 43–53, 1965.
25. LASSERS, B. W., L. KAIJSER, AND L. A. CARLSON. Myocardial lipid and carbohydrate metabolism in healthy, fasting men at rest: studies during continuous infusion of ^{3}H-palmitate. *European J. Clin. Invest.* In press.
26. LEES, R. S., AND F. T. HATCH. Sharper separation of lipoprotein species by paper electrophoresis in albumin-containing buffer. *J. Lab. Clin. Med.* 61: 518–528, 1963.
27. LUNDHOLM, L., E. MOHME-LUNDHOLM, AND N. VAMOS. Lactic acid assay with L (+) lactic acid dehydrogenase from rabbit muscle. *Acta Physiol. Scand.* 58: 243–249, 1963.
28. NIKKILÄ, E. A., P. TORSTI, AND O. PENTTILÄ. Effects of fasting, exercise and reserpine on catecholamine content and lipoprotein lipase activity of rat heart and adipose tissue. *Life Sci.* 4: 27–35, 1965.
29. OPIE, L. H. Metabolism of the heart in health and disease. II. *Am. Heart J.* 77: 100–122, 1969.
30. PERNOW, B., J. WAHREN, AND S. ZETTERQUIST. Studies on the peripheral circulation and metabolism in man. IV. Oxygen utilization and lactate formation in the legs of healthy young men during strenuous exercise. *Acta Physiol. Scand.* 64: 289–298, 1965.
31. PRUETT, E. D. R. Plasma insulin levels during prolonged exercise. In: *Muscle Metabolism During Exercise*, edited by B. Pernow and B. Saltin. New York & London: Plenum, 1971, p. 165.
32. RANDLE, P. J., P. B. GARLAND, C. N. HALES, AND E. A. NEWSHOLME. The glucose fatty-acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. *Lancet* 1: 785–789, 1963.
33. RUDOLPH, W., D. MAAS, J. RICHTER, F. HASINGER, H. HOFFMANN, AND P. DOHRN. Über die Bedeutung van Acetacetat und beta-Hydroxybutyrat im Stoffwechsel des menschlichen Herzens. *Klin. Wochschr.* 43: 445–451, 1965.
34. SHIPP, J. C., L. H. OPIE, AND D. CHALLONER. Fatty acid and glucose metabolism in the perfused heart. *Nature* 189: 1018–1019, 1961.
35. SJÖSTRAND, T. Changes in the respiratory organs of workmen at an ore smelting works. *Acta Med. Scand. Suppl.* 196: 687–699, 1947.
36. TROUT, D. L., E. H. ESTES, AND S. J. FRIEDBERG. Titration of free fatty acids of plasma: a study of current methods and a new modification. *J. Lipid Res.* 1: 199–202, 1960.
37. WAHLUND, H. Determination of the physical working capacity. *Acta Med. Scand. Suppl.* 215: 1948.