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STUDIES IN MUSCULAR ACTIVITY.

VII. Factors limiting the capacity for work.

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In a dog the energy reserve consists chiefly of carbohydrate and fat. For their utilization oxygen must be supplied and carbon dioxide eliminated. The maximum over-all efficiency is probably from 20 to 30 p.c., most of the energy appearing as heat. Hence, if a constant body temperature is to be maintained, provision must be made for heat dissipation. The experiments to be described indicate that, by suitably varying the conditions, inadequacy in any one of the three factors, fuel supply, oxygen supply or heat dissipation, may limit the capacity for work. In our experiments these three taken singly, or in combinations, are of primary importance, although factors of secondary importance no doubt exist.

Two dogs were trained to run on a motor-driven treadmill. Most of the experiments were carried out on Joe, an immature male of the fox-terrier type weighing 13 kg. Additional experiments were carried out on another dog, a mature female of the Irish terrier type and of the same weight. With the exception of a few early experiments the grade[1] was 17·6 p.c. The rates and other experimental conditions will be given in detail below. Observations were made of: (*a*) heart rate, using a cardio-tachometer previously described; (*b*) rectal temperature either with a thermocouple during exercise or with a clinical thermometer after it; (*c*) room temperature; (*d*) blood lactic acid by the method of Friedemann, Cotonio and Schaffer [1927]; (*e*) blood sugar by the method of Folin and Malmros [1929]; and (*f*) morphological properties[2] of the blood. Notes were made of the dog's behaviour, particularly during the onset of exhaustion. The nomenclature of Campos, Cannon, Lundin

[1] According to Tracy [1908] a grade of 1 p.c. is defined as "a rise or fall of 1 ft. measured *vertically* for each 100 ft. measured *horizontally*." This usage, generally accepted by engineers, has been adopted in our calculations although it is not always followed by physiologists, *e.g.* by Smith [1922].

[2] These will be described elsewhere.

and Walker [1929] will be followed in describing the degree of fatigue. The relative humidity was low in all cases, and with a few exceptions (all at low temperature) there was virtually no air movement.

The blood samples were all obtained from the saphenous vein as soon as possible after work stopped. Usually not more than a minute elapsed before the sample was withdrawn. Christensen [1931] suggests that such samples should be called recovery rather than work samples. He shows that the blood-sugar level in man may increase several mg./100 c.c. during the first few minutes of recovery. Three experiments may be cited which show that under the conditions of our experiments only a small change occurs during the first minute of recovery, and hence our values for blood sugar differ but little from work samples. In the first case, a cardiac puncture was made while the animal was running. As soon as blood was obtained, the dog was lifted from the treadmill and with the needle remaining in position a series of samples was collected. In each of two experiments on Joe, one in hypoglycæmia and another in a normal state, a series of samples was obtained during recovery. These results, assembled in Table I, show that changes in blood sugar during the first minute of recovery are unimportant from our point of view.

TABLE I. Change in blood-sugar concentration during recovery. Zero time corresponds to cessation of work.

Experiment 1		Experiment 2		Experiment 3	
Time (sec.)	Blood sugar mg./100 c.c.	Time (sec.)	Blood sugar mg./100 c.c.	Time (sec.)	Blood sugar mg./100 c.c.
-10	86	15	46	10	106
15	92	40	52	30	105
60	97	100	53	90	110
120	92	120	52	130	121
240	92	270	49	160	119
—	—	330	47	—	—
—	—	360	55	—	—

The experiments illustrated in Fig. 1 include several in which either the supply of oxygen or the dissipation of heat determined the work output. In one of these experiments the rate of oxygen supply certainly was the chief limiting factor. In this case, with a room temperature of 16° C., the energy output during work was 352 kg.m. per minute[1] for $7\frac{1}{2}$ minutes, a total of 2640 kg.m. At the end of work there was evidence of a large

[1] The energy output has been calculated from the data of Slowstoff [1903]. He found that the energy requirement for running on an inclined treadmill may be resolved into horizontal and vertical components. For dogs of 12–14 kg. weight the horizontal component is 0·64 kg.m. per metre, and the vertical component 2·92 kg.m. per metre. These are expressed in kilogram-metres per kilogram of body weight.

oxygen debt. The blood lactic acid concentration was high, 74 mg./100 c.c. The laboured and deep character of the respiration during recovery indicated that a high rate of oxygen intake was being maintained. There was confirmatory evidence of an indirect nature. Thus, the rectal temperature

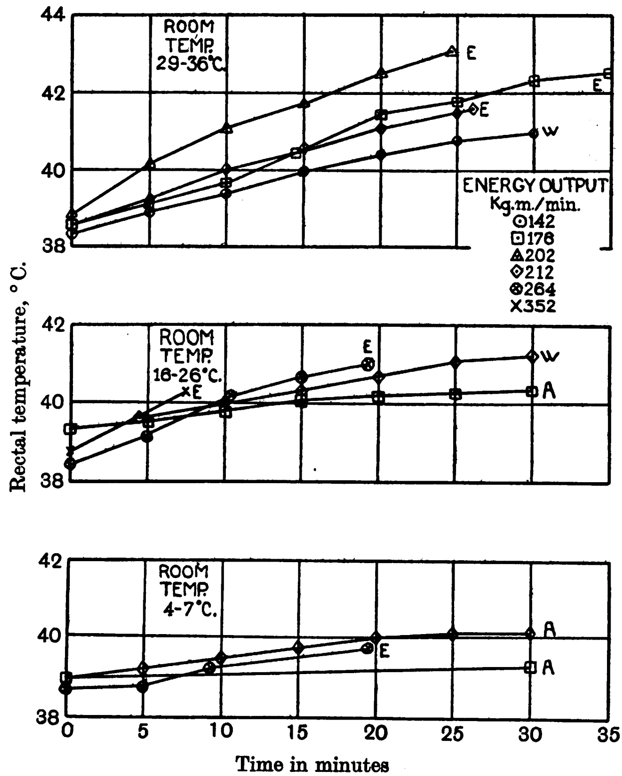

Fig. 1. Rectal temperature in relation to duration of work, intensity of work and room temperature. Exercise was continuous, temperatures being observed with a rectal thermocouple. The degree of fatigue is indicated by the notation of Campos, Cannon, Lundin and Walker [1929]. *A* = Active; ready to continue running. *W* = Weary; panting, but easily able to continue running. *E* = Exhausted; panting most heavily with head down, drops to platform and refuses to rise.

was raised only 1·5° C., an increase which is small in comparison with changes in other experiments shown in the same figure. Furthermore, the blood sugar remained at a high level, 119 mg./100 c.c. Failure was not because of high temperature or lack of fuel. In view of the direct evidence and since no other cause for exhaustion is known, it seems probable that this dog cannot transport enough oxygen to remain in a steady state at this rate of work. Energy reserves were utilized anaerobically, resulting in accumulation of unoxidized end products. It may be noted in passing that lactic acid accumulation alone is inconclusive evidence of oxygen deficiency in the dog. This subject will be referred to below.

In some of the experiments illustrated in Fig. 1, conditions were adjusted so that inadequate heat dissipation was the primary limiting factor. One of the necessary conditions for this is that the demand for oxygen shall not exceed the transport capacity. While the maximum rate of energy output which this dog can maintain in a steady state has not been determined, a single experiment may be cited which proves that his working capacity is not less than 212 kg.m. per minute. He maintained this output without interruption for 112 minutes, the linear velocity being 187 metres per minute and the grade 17·6 p.c. The room temperature ranged from 4° to 7° C. and at the end his rectal temperature was 39·3° C. A sample of blood drawn within a minute after work stopped was found to contain 105 mg./100 c.c. of sugar and 12 mg./100 c.c. of lactic acid. Apparently, in respect of body temperature, blood sugar and blood lactic acid he remained within the limits which are normal for the resting state, notwithstanding the fact that his oxygen intake was perhaps 15 times the resting level.

This experiment was repeated with all conditions the same except room temperature. At 20° C. he ran for 29 minutes with the rectal temperature rising gradually to 41·3° C. Although weary at the end, he could have gone farther. At 33° C. he ran to exhaustion in 27 minutes with a final temperature of 41·6° C. With a somewhat higher room temperature, 35° C., but with easier work, 176 kg.m. per minute, he ran for 34½ minutes to exhaustion with a terminal temperature of 42·5° C.[1] The highest rectal temperature reached, 43·1° C., was at a room temperature of 29° C. with an energy output of 202 kg.m. per minute for 24 minutes. This was an early experiment with a rate of 233 metres per minute and a grade of 8 p.c. These results prove that work which is easy at low temperatures is difficult at moderate temperatures. As the external temperature is increased, the length of time a given rate of energy output can be maintained diminishes.

There are many indications that exhaustion resulting from work at high temperature is a complex phenomenon. One notes the increase in

[1] In an experiment to be described below (Protocol I), this rate of energy output was maintained for 17 hours with the room temperature near 15° C. and with fuel and water supplied during half-hourly rest periods. A difference of room temperature of 20° C. determines the difference between a steadily increasing body temperature ending in exhaustion and a constant slightly elevated temperature with virtually tireless performance.

effective area from which heat is dissipated and simultaneous increases in salivary flow, respiratory rate and respiratory volume. These changes call for a greater oxygen supply both for the muscles involved in breathing and for the heart. With a rate of oxygen supply already near the

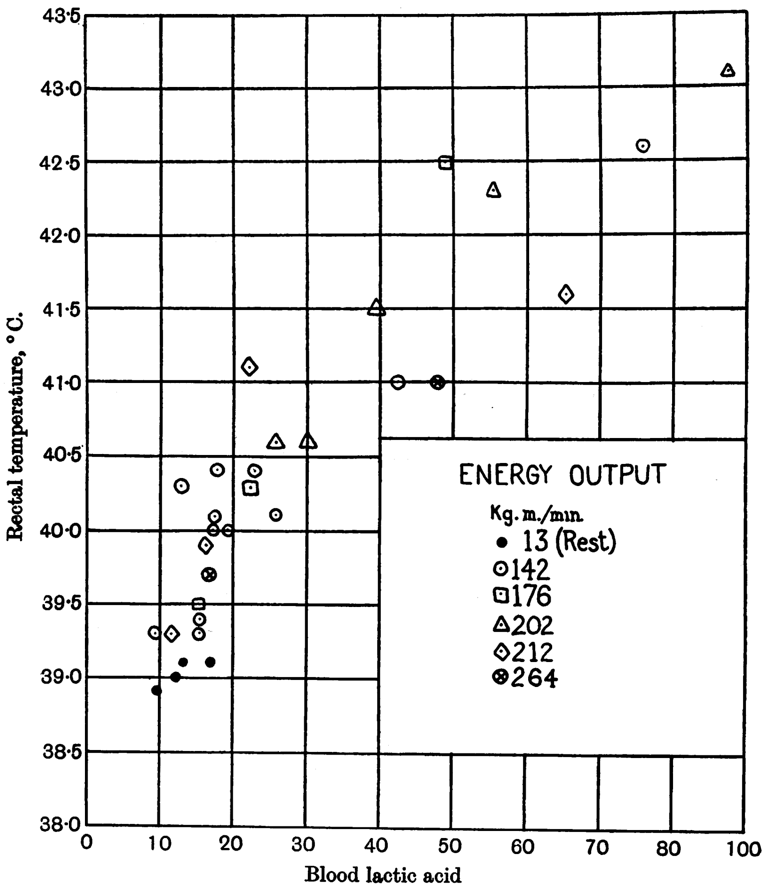

Fig. 2. Blood lactic acid in relation to rectal temperature. The blood sample was drawn at the end of a work period of at least 15 minutes' duration and rectal temperature was observed simultaneously.

upper limit, this further demand may result in breakdown. Under such conditions, before the rectal temperature has reached a high value, exhaustion may come as a consequence of anaerobic production of mechanical energy for dissipating heat. At present the evidence for this statement must remain indirect since, as intimated above, lactic acid concentration is not an infallible measure of oxygen debt in the case of the dog.

The highest rectal temperatures have been reached with rates of oxygen intake well below the maximum. In such cases, as body temperature rises, polypnœa and related changes become more pronounced. This forced breathing removes CO_2 faster than it is formed. Under similar conditions Rice and Steinhaus [1931] have observed CO_2 pressures in blood as low as 10 mm. While the results of Bock, Dill and Edwards [1932] indicated that men do not readily respond to overventilation by forming lactic acid, it seemed likely that the dog might do so. The experiments of Knudson and Schaible [1931] suggest that such is the case with resting dogs. It is therefore of interest to enquire whether in the dog, as part of the response to work at high temperature, formation of lactic acid occurs.

The results presented in Fig. 2 show that lactic acid concentration does not increase until rectal temperature exceeds 40° C., but that between the limits of 40° C. and 43° C. and over a wide range of metabolic rates, it increases with rectal temperature. This result is in harmony with Knudson's observations on dogs at rest. It appears that lactic acid accumulation in the dog is not necessarily due to anoxemia. If the work is hard enough lactic acid may accumulate directly from oxygen lack as in man, and if the temperature is normal its concentration is more or less proportional to the oxygen debt. In rest, however, or even in moderate work, it may accumulate as part of the response of the heat dissipative mechanism[1]. In such a case a high concentration of lactic acid should not be considered as indicating incapacity for transporting more oxygen even though in recovery removal of lactic acid is accomplished as usual, viz. by aerobic resynthesis.

Up to this point the limiting factors considered have been oxygen supply and heat dissipation. What happens if the work is moderate and the temperature low? First of all the animal must have water; provided water is supplied, what determines the capacity for work? The limiting

[1] The results of Rice and Steinhaus [1931] indicate a reduction in alkali reserve during work accompanied by increase in rectal temperature. It is possible with certain assumptions to calculate the decrease in alkali reserve (the total CO_2 of oxygenated blood when $pCO_2 = 40$ mm.) from their data. Thus in their Fig. 1 the pCO_2 was reduced from 40 to 10·5 and the ($BHCO_3$) from 24 to 6·7 mM/litre. Assume the same oxygen content and an oxygen capacity of 20 volumes per cent. in these blood samples. On the basis of these assumptions and the known properties of dog blood [see Dill, Edwards, Florkin and Campbell, 1932] the reduction in alkali reserve was about 7 mM. Since the pH was nearly constant such a change in alkali reserve implies an increase in blood lactic acid of about 60 mg./100 c.c.

factor seems to be merely the quantity of easily available fuel; the principal evidence for this is found in Fig. 3. These experiments were carried out according to a uniform plan. The run began either after a 36 hours' fast or 1 hour after a heavy carbohydrate meal. In the first case, exercise was carried on to exhaustion; in the second case, fuel was

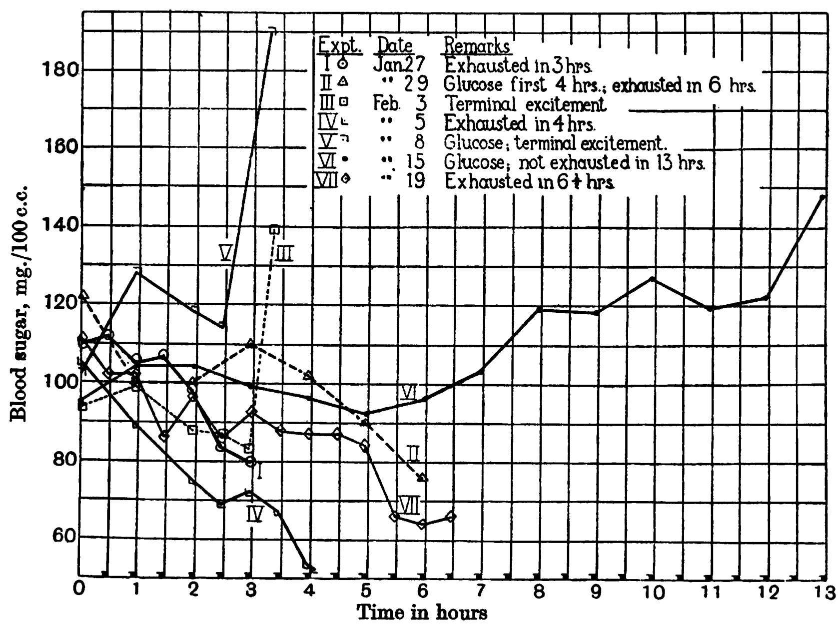

Fig. 3. Performance in relation to blood sugar. Observations were made at 30-minute intervals during rest periods of 5 minutes' duration.

supplied at intervals[1]. In either case the schedule called for 25-minute runs with intervening periods of 5 minutes for withdrawing blood, observing rectal temperature, supplying water and, in some cases, fuel. The

[1] The fuel used (except in one case when sterile glucose was injected and in a second case when glucose was given by stomach tube) was a candy referred to as glucose candy. Analysis was made after the experiments were concluded and it was found to contain 16 p.c. glucose and 72 p.c. sucrose + polysaccharide. According to the manufacturer it also contained citric acid and artificial colour and flavour. It contained by analysis 0·17 p.c. ash and less than 1 mg. of combined phosphorus per 100 g. The dog is able to utilize this fuel alone during long periods of exercise, indicating that added phosphate is unnecessary, contrary to the suggestion of Dische and Goldhammer [1932]. Furthermore, in order to utilize sucrose the secretion of digestive juices is necessary. For this purpose it is particularly important to maintain a low temperature. Nausea and vomiting are likely consequences of running a dog with a full stomach, if the temperature is high.

dog ran 50 minutes of each hour, putting out in each of these experiments 142 kg.m. of energy per minute while running.

Under these conditions the best performance recorded in Fig. 3 when working without fuel was a run of 6½ hours to complete exhaustion. Four days before this, when fuel was supplied, the same dog ran for 13 hours and was not exhausted at the end. The room temperature was 15° C. in each case, the rectal temperature remained between 39° and 40° C. and blood lactic acid concentration remained near the resting level. There is every reason to believe that exhaustion came from depleted fuel in the 6½-hour run and that the administration of easily available fuel in the 13-hour run resulted in twice the output of energy without exhaustion at the end and with the blood-sugar level maintained at or above the resting level. The actual energy outputs in these two cases were 46,150 kg.m. and 92,300 kg.m. per kg. of body weight.

PROTOCOL I. Record of a 17-hour run.

Energy output, 176 kg.m. per minute or a total of 150,000 kg.m.; a 5-minute rest period each half-hour was used for making observations and supplying water and fuel.

Time (hr.)	Remarks	Temperature Room (° C.)	Temperature Rectal (° C.)	Intake Water (c.c.)	Intake Fuel (g.)	Blood sugar mg./100 c.c.
0	Start	15·5	38·7	—	—	—
0–1	—	15·0	39·5	340	40	—
1–2	—	14·7	39·5	250	40	112
2–3	—	15·5	39·6	180	40	131
3–4	—	15·8	39·7	330	40	—
4–5	Defæcated	16·0	39·6	270	40	127
5–6	Refused candy	15·6	39·9	270	0	132
6–7	Urinated	14·8	39·8	120	40	—
7–8	Defæcated	14·8	39·8	30	40	120
8–9	—	14·0	39·7	180	20	111
9–10	—	12·9	39·6	50	20	—
10–11	—	15·7	40·0	105	20	107
11–12	Refused candy	14·4	39·6	215	0	—
12–13	Refused candy	13·6	40·0	100	0	103
13–14	Glucose by stomach tube	13·6	39·8	295	42	—
14–15	Glucose by stomach tube	13·4	39·7	355	50	94
15–16	Refused candy	14·0	39·7	100	0	—
16–17	Tired but not exhausted	13·7	39·5	100	0	101

Three later experiments, not illustrated in Fig. 3, may be referred to briefly. With the treadmill running at the same rate, our second dog, with fuel supplied, ran for 9 hours. By that time she was becoming tired and her temperature had risen to 41·3° C. At this time the rate was decreased to 92 metres per minute, with the result that rectal temperature soon returned to normal and she was able to run easily for 15 more hours. At the end of 24 hours she was not exhausted notwithstanding an energy output of 64,000 kg.m. during the first 9 hours and 79,000 kg.m. during the succeeding 15 hours, a total of 143,000 kg.m.

In the next experiment, detailed in Protocol I, Joe was used as a subject with the rate of work output one-fourth greater than in the experiments of Fig. 3. This higher rate of work output, 176 kg.m. per minute, is approximately the same as that which Rice and Steinhaus [1931] used. Under their experimental conditions, "rarely can a dog run continuously for 30 minutes." Joe had already maintained a still higher work output for 112 consecutive minutes (as already stated), and in this case he ran for 17 hours with fuel supplied and was not exhausted at the end. The total work output was 150,000 kg.m.

In the final experiment conditions were the same except that no fuel was supplied until after $4\frac{1}{4}$ hours' work. As may be seen in Protocol II,

PROTOCOL II. Record of a run demonstrating the effects of withholding and supplying fuel.

Conditions as in Protocol I except that food had been withheld for 36 hours and none was supplied until the onset of exhaustion. Then (during a rest period of 8 minutes instead of 5) 40 g. of candy restored the animal to an active state and simultaneously brought the blood sugar to its normal level. The experiment was discontinued when it appeared that the dog had returned to a steady state.

Time (hr.)	Remarks	Temperature: Room (°C.)	Temperature: Rectal (°C.)	Intake: Water (c.c.)	Intake: Fuel (g.)	Blood sugar mg./100c.c.
0	Start	13·5	38·5	—	—	78
0–1	—	14·8	39·8	120	0	88
1–2	—	16·6	40·0	120	0	82
2–3	—	16·0	39·7	140	0	71
3–4	Fan started	17·0	39·5	155	0	50
4–$4\frac{1}{4}$	Exhausted	16·0	39·6	10	0	46
$4\frac{1}{4}$–$4\frac{2}{5}$	Rest period; candy supplied	—	—	—	40	—
$4\frac{2}{5}$–$5\frac{2}{5}$	Ran easily	15·8	39·8	420	20	127
$5\frac{2}{5}$–$5\frac{4}{5}$	Ran easily	14·3	39·8	100	0	106

he was unable to run longer without fuel. He was revived by 40 g. of candy and was able to resume work within 8 minutes. The experiment was discontinued $1\frac{1}{2}$ hours later, for the dog seemed to be in good condition and able to continue for hours with fuel supplied.

A study of the reasons for exhaustion in these experiments naturally leads to a consideration of the heart rate. The importance of the cardiotachometer for this purpose is revealed by Fig. 4. The rapid decrease in heart rate during recovery shows that counts made in the usual way at the end of work may be 100 beats per minute too low. One rarely reads of a heart rate greater than 150 or 160 in the dog after work stops.

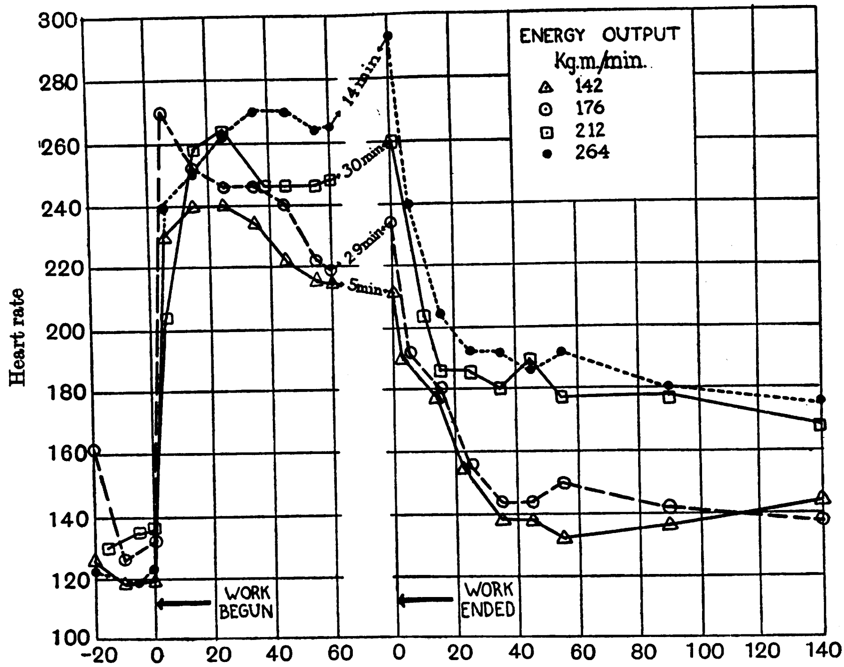

Fig. 4. Heart rate during work and recovery.

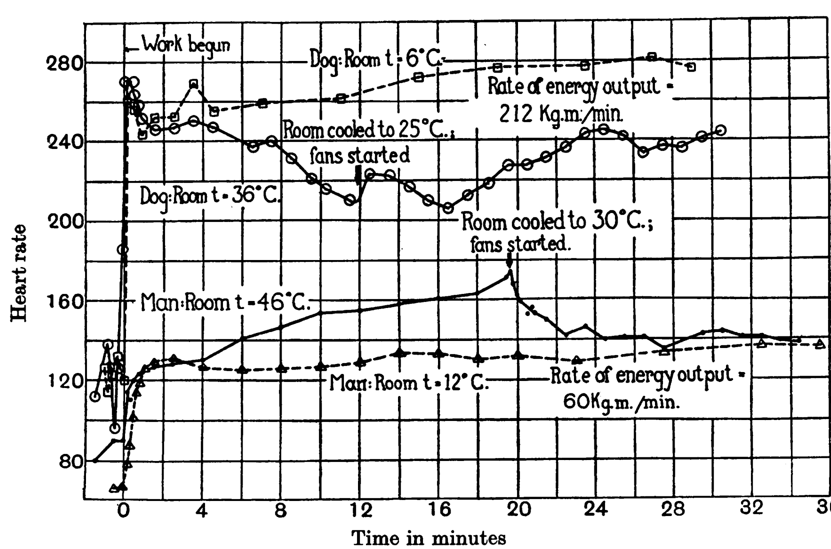

Fig. 5. The relation of heart rate to external temperature. With the onset of exhaustion during work in a hot room the heart rate of the dog decreases, that of man increases. As work continues after the room is cooled, the heart rate of the dog increases, that of man decreases.

Actually the rate after a steady state is reached is closely proportional to the rate of energy output and may be as high as 300 beats per minute.

It is not proposed at this time to present detailed observations on the heart rate during all these experiments. Two other sets of records will be presented briefly. The first of these, given in Fig. 5, shows the difference in response of man and dog to heat. As man approaches exhaustion at a high external temperature his heart rate rises and commonly the point of exhaustion coincides with the attainment of his maximum heart rate.

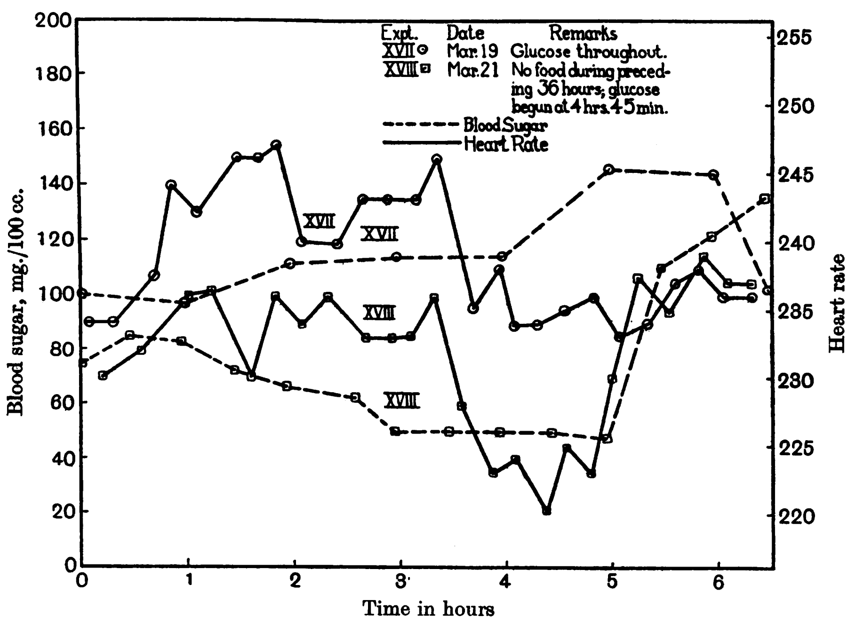

Fig. 6. Heart rate and blood sugar. Rest periods were interposed as described in the legend of Fig. 3.

In this case, fans were turned on the man and the room was cooled suddenly. Work was continued at the same rate, the heart rate decreased 30 to 40 beats per minute and within 3 minutes the subject had passed from a state of exhaustion to one of comfort. The dog, on the other hand, showed a decrease in rate with the onset of exhaustion, and after the room was cooled recovery (which was slower than in man) was accompanied by an increase in heart rate. Similar observations have been made on other occasions; evidently the control of the heart rate under these conditions is different in the two species.

Fig. 6 shows simultaneous observations of heart rate and blood sugar in two experiments. While there are large changes in heart rate which are not parallel to the observed changes in blood sugar concentration, it is nevertheless a fact that in the experiment in which no fuel was given until the onset of exhaustion the minimum heart rate was reached shortly before candy was given. As the blood sugar increased from 50 to 100 mg./100 c.c., the heart rate increased from 220 to 235 beats per minute. Further experiments on this subject are planned.

The experimental results are of such a character that little discussion is necessary. The literature has been reviewed recently by Rice and Steinhaus [1931], by Campos, Cannon, Lundin and Walker [1929], and by Dische and Goldhammer [1932]. The experiments of Rice and Steinhaus indicated that the energy output of a dog in treadmill running might be limited by inadequate heart dissipation. Our experiments confirm this and show that by decreasing the external temperature the working capacity can be greatly increased. They were mistaken, however, in supposing that man possesses better facilities for heat regulation than the dog. The significant difference, at least in ordinary environmental conditions, is that the dog can produce heat at a much greater rate than man. We have found that an athlete running on a horizontal treadmill at the rate of 233 metres per minute with a room temperature of 22° C. and virtually no air movement could not dissipate heat quite as fast as its rate of production. At the end of 80 minutes he was exhausted; his rectal temperature was 40·6° C. His energy output as calculated from the oxygen intake and respiratory quotient was about 100 kg.m. per minute per kg. of body weight. The dog Joe was able to maintain a constant temperature with an energy output greater by at least 50 p.c. with the same environmental conditions. This represents a greater rate of energy output than can be attained by any athlete. We have made a comparison of the working capacity for short periods of this dog with that of a trained runner. Joe ran at the rate of 311 metres per minute on a grade of 17·6 p.c. for 7½ minutes to exhaustion. A mile runner, able at the time to run a mile in 4 minutes and 30 seconds, was exhausted with the treadmill at the same grade after 6 minutes at the rate of 125 metres per minute. Evidently this dog has a capacity for expending energy which is 2½ times greater than that of an athlete. It is not surprising, therefore, that heat dissipation is a more common limiting factor than with man[1].

The experiments of Eagle and Britton [1932] showed that the

[1] Dogs no doubt differ greatly in heat dissipating capacity. Perhaps Joe has a greater than average ability to dissipate heat on account of his small size and short hair. The dogs used by Rice and Steinhaus were twice as large and possibly were handicapped on this account.

administration of their cortico-adrenal extract to normal dogs increased their capacity for work. We are indebted to Dr Eagle for supplementary information regarding their experimental conditions. No water was given to their dogs during exercise and the room temperature was about 25° C. They report some decrease in blood sugar, although this was not simply related to degree of exhaustion. The total energy output before cortico-adrenal extract was about 15,000 kg.m. and from 20,000 to 25,000 after. The work output was at a lower rate, but even with cortico-adrenal extract the total output was only one-sixth as great as in our 17-hour experiment on Joe. The rate was the same and the total work output about two-fifths as great as in the 9-hour experiment on our second dog. The most reasonable interpretation of the effect on working capacity of cortico-adrenal extract is that it is indirect, possibly helping in mobilizing fuel, possibly eliminating unpleasant sensations arising from thirst, hunger and overheating. The same may be said of the similar effect of adrenaline on working capacity. In the most successful experiment of Campos, Cannon, Lundin and Walker [1929] in demonstrating the effect of adrenaline, the rate of work output was four-fifths as great and the total work output one-third as great as in our 17-hour experiment. Neither extraneous adrenaline nor cortico-adrenal extract *per se* is necessary even when the exercise is of long duration.

Summary.

A study has been made of three factors which may limit the capacity of a dog for work—external temperature, supply of oxygen, and supply of fuel. A fourth factor perhaps of equal importance is the supply of water. The water intake has been observed in all these experiments, but the limiting effect of inadequate water intake has not been studied.

With external temperature low and oxygen supply adequate and when fuel and water are supplied, the performance of a dog is virtually tireless. In one case a dog ran for 17 hours with 5-minute rest periods each half-hour. In the 17 hours he ran 132 km. (82 miles) and climbed 23 km. (14 miles) with a total energy output of 150,000 kg.m. per kg. of body weight. His working capacity was increased more than three times by supplying fuel. His energy output in this run was three times greater than in any recorded experiment showing the influence of adrenaline injections on working capacity, and six times greater than in similar experiments with cortico-adrenal extract. Evidently the dog does not require an extraneous supply of either of these hormones for work of many hours' duration.

REFERENCES.

Bock, A. V., Dill, D. B. and Edwards, H. T. (1932). *J. clin. Invest.* **11**, 775.

Campos, F. A., Cannon, W. B., Lundin, H. and Walker, T. T. (1929). *Amer. J. Physiol.* **87**, 680.

Christensen, E. H. (1931). *Arbeitsphysiol.* **4**, 128.

Dill, D. B., Edwards, H. T., Florkin, M. and Campbell, R. W. (1932). *J. biol. Chem.* **95**, 1.

Dische, Z. and Goldhammer, H. (1932). *Biochem. Z.* **247**, 8.

Eagle, E. and Britton, S. W. (1932). *Science*, **75**, 221.

Folin, O. and Malmros, H. (1929). *J. biol. Chem.* **80**, 115.

Friedemann, T. E., Cotonio, M. and Schaffer, P. A. (1927). *Ibid.* **73**, 335.

Knudson, A. and Schaible, P. J. (1931). *Arch. Path.* **11**, 728.

Rice, H. A. and Steinhaus, A. H. (1931). *Amer. J. Physiol.* **96**, 529; (1929) **90**, 529.

Slowstoff, B. (1903). *Pflügers Arch.* **95**, 158.

Smith, H. M. (1922). *Publ. Carnegie Instn.* 309.

Tracy, J. C. (1908). *Plane Surveying.* John Wiley and Sons, New York.