One of the most obvious results of arterial occlusion is the arterial hypoxia distal to the occlusion. Krogh (1) found that decreasing the oxygen tension of the blood with low oxygen ventilation caused vasodilatation in the rabbit's ear and the abdominal muscle of cat. It thus appears that reactive hyperemia may be initiated either directly or indirectly by the lack of oxygen. The purpose of these experiments is to inquire into the relationship between the deficit of oxygen resulting from occlusion of arterial flow and its repayment during the hyperemia and the time course of the return to normal of blood flow as related to the return to normal of arteriovenous oxygen difference and rate of oxygen utilization.

METHODS

The venous blood flow of the gracilis muscle of the dog was measured with an electronic drop recorder (fig. 1) filled with oil. The blood was collected in successive small samples under oil and was analyzed for O₂ content by the Van Slyke-Neil procedure as modified for 0.1-cc samples. The arterial-venous O₂ difference was determined and the time course corrected for the dead space of the collecting tube. The O₂ consumption was computed as the product of the A-V O₂ difference and the blood flow. All figures for rates of blood flow or oxygen consumption are in terms of a unit wet weight of muscle. This was possible since dye or India ink injection showed a homogenous perfusion of the muscle. The arterial blood supply to the muscle was occluded with a hemostat on a small polyethylene through-cannula in the artery to the muscle.

RESULTS AND DISCUSSION

The time course of the change of the rate of blood flow following a period of arterial occlusion is plotted (fig. 24) for a typical experiment. On termination of the occlusion the rate of blood flow attains a maximum in a very short time, usually within the time of the first 0.2 cc blood flow. The hyperemia decreases rapidly and in 16 of 17 experiments for short occlusions the hyperemia decreased below the control blood flow (ischemia). If the time course were extended, there appears to be an oscillation about the mean until a normal small fluctuation is attained.

If sufficiently small successive blood samples are collected, the first one will show little or no change in the A-V O₂ difference from the control value. This is probably the blood present in the collecting tubes and large veins during the occlusion. The increased A-V O₂ difference of the next samples, though decreasing, continues usually from 10 to 40 seconds. At least a portion of the increased A-V O₂ difference may be a result of flushing the stagnated capillary blood. How the venous, capillary and arterial blood finally mix before being sampled is not known at this time.

Considering the data from all experiments on short periods of occlusion, an increased A-V oxygen difference and blood flow follows the release of the occlusion. There is a mean increase of 2.7 volumes % (range, 0.2-6.4) over the control value (mean, 8.3 volumes %; range,
From Vein of Muscle

Oil Reservoir

Teflon Tip

Electrodes to Electronic Drop Recorder

Test Tubes

FIG. 1. Apparatus for counting and collecting blood drops under oil.

5.7-14.5). The mean increase in the blood flow is 7.4 cc/min/100 gm (range 3.3-14.1) above the control value (mean, 2.4 cc/min/100 gm; range, 0.9-5.6).

The product of the rate of blood flow and the A-V oxygen difference is used for the average oxygen consumption from the blood. The time course of the typical experiment is plotted in figure 9C. During the occlusion, O₂ consumption ceases and ‘demand’ builds up. This is accompanied by dilatation so that as soon as the artery is opened, the flow is very rapid and O₂ uptake is very rapid. As the demand begins to be satisfied, constriction occurs and both flow and O₂ consumption diminish. The period of hyperemia for the short periods of occlusion (30-60 sec.) is always followed by a period of ischemia in which the blood flow, A-V oxygen difference, and oxygen consumption are below normal.

It would seem from these considerations that there is a distinct parallelism between blood flow and A-V oxygen difference, although in one experiment flow increased so much that the A-V difference remained fairly constant. It is obvious that if the flow were not to increase, the venous O₂ tension and hence that of the pericellular fluid would be low, perhaps to the detriment of the cells.

Occlusion of the arterial supply will result in a deficit of blood and oxygen supply. The blood deficit is taken as the amount of blood that would have flowed during the period of occlusion had the control rate of flow been maintained. In only 4 of 16 experiments was the blood deficit made up (within 10%) during reactive hyperemia. In 6 of the 16 experiments the blood deficit was not made up during reactive hyperemia, and in the other 6 it was more than rapid. The range was from 45% - 196%. The average was 109%. This is to be compared with the work of Freeman (2), showing that the blood debt for short periods of occlusion is repaid during reactive hyperemia. It must be concluded that in this preparation, the repayment of the blood deficit is highly variable.

For convenience only, we assume that the O₂ demand remains unchanged during cessation of flow and is set by the rate of O₂ consumption during the control period. This may be too high a figure because certain evidence indicates that O₂ consumption is reduced at low O₂ tensions. Thus it is found that, in certain specific systems, respiration is reduced at low ranges of O₂ tension (3-5). Confirmatory evidence is seen in that the temperature of the hind leg decreases during occlusion (6). On the other hand, the resting O₂ consumption may be too low a figure. If anaerobic metabolism had supplied the energy
requirements of the muscle at the control rate, anaerobic metabolites, releasing less energy in anaerobic breakdown than in oxidation, would accumulate in large amounts requiring a large amount of oxidative energy for their resynthesis. On this basis one might expect a larger oxygen deficit than that computed from an extension of resting oxygen consumption. As a matter of fact, the O_2 consumption of the muscle during the reactive hyperemia was 1.32 times the computed O_2 deficit. This is not unreasonable when it is recalled that the muscle may have been releasing energy at a lower level when anoxic and that some of the unoxidized metabolites may have been washed out of the vascular field with return of circulation.

Another relationship comes out of our data which is difficult to evaluate. As indicated in figure 2 the blood flow, A-V difference and O_2 consumption are all reduced below control value for a short period after the reactive hyperemia. When the O_2 deficit is computed as above for the longer period, including the phase of hyperemia and ischemia, it is found that the overpayment of O_2 deficit is reduced and in fact, that the repayment is on the average nearly exact (fig. 3).

It is impossible to speculate profitably upon the mechanism by which the flow after occlusion—both the hyperemic and ischemic phase—is governed. The fact that there is a rough parallel between flow and A-V oxygen difference implies that chemical mechanisms related to anoxia play a role. The roughly quantitative agreement between the deficit and repayment has the same implication but the fact that the larger blood flow deficit resulting from longer occlusion (2) is not made up indicates that relations are complex enough to deserve further study. Whether there may be a specific dilator substance or whether the dilation is due to a low O_2 tension (1, 7, 8) in the tissues cannot be speculated upon from the evidence presented.

REFERENCES