Anoxic Tolerance of Beating and Resting Heart During Perfusion at Various Temperatures. (23260)

FRANK GOLLAN AND INNES A. NELSON (Introduced by George R. Meneely)
Thayer Vet. Admin. Hosp. and Department of Surgery, Vanderbilt University School of Medicine, Nashville, Tenn.

The use of pump-oxygenators has brought such a rapid and vigorous advance of open cardiac surgery that in some instances successful clinical experiences outdistanced experimental observations. This seems to hold true for the degree of complete ischemia to which by-passed human hearts have been subjected and successfully resuscitated, although isolated dog hearts dilate rapidly when oxygen saturation of the arterial blood falls to 45%(1). The large coronary flow produced by efficient pump-oxygenators(2,3) defeats to some extent the purpose of the "bloodless heart." Therefore, attempts were made to stem the coronary tide by aortic occlusion for three(3), six(4) and even 25 minutes(5) or intermittently(6). The present study endeavors to determine the time limit of myocardial anoxia during perfusion experiments.

Methods. In heparinized dogs (3 mg/kg) pretreated with Quinidine (30 mg/kg slow i.v. drip) venous blood from the caval system was shunted by a finger pump* into a plastic chamber (Fig. 1) where it was oxygenated by bubbles, defoamed by a methylpolysiloxane† resin(7) and returned into the aorta. The volume of this oxygenator is 300 ml and its capacity tested in dogs is one l/min. A refrigeration coil replaces most of the volume and its surface serves to defoam and to cool and rewarm the oxygenated blood(8). The entire extracorporeal circuit is filled with mammalian Ringer's solution and circulation, oxygenation and cooling of the diluted blood is started simultaneously. After 15 to 30 minutes of differential hypothermia(9) the temperature in the deep oesophagus reaches the desired degree and the ascending aorta is clamped. In another series of experiments one to 2 ml of 25% potassium citrate(10) was injected into the coronary circulation to produce cardiac arrest. After the coronary occlusion period the heart rhythm, force of contraction and ability to maintain adequate blood pressure during and after extracorporeal circulation were observed for several hours.

Results. In 29 experiments in which the by-passed, but beating hypothermic heart was deprived of oxygenated blood (Fig. 2) the periods of aortic occlusion ranged from 4 to 33 minutes at temperatures ranging from 30 to 18°C. Occlusion of 25 minutes at 30°C, and for 15 minutes at 28°C proved injurious to the myocardium. When the clamp was removed these hearts fibrillated and although electric shock reestablished rhythmic contractions while their work load was carried by the pump-oxygenator, they reverted to ventricular fibrillation when the instrument was stopped and cardiac massage and repeated shocks were unable to overcome this condition. At temperatures from 26 to 20°C myocardial ischemia up to 33 minutes duration was tolerated without ventricular fibrillation or myocardial weakness. Although these periods of occlusion would be satisfactory for many intracardiac surgical procedures, they were too short to test the limits of anoxic tolerance. Ventricular fibrillation occurred in 3 cases but temperature or duration of ischemia did not seem to cause it as much as manipulation of the heart. Defibrillation was readily achieved and no ensuing myocardial weakness was discernible.

In 56 dogs the internal body temperature, as measured in the deep oesophagus, was lowered from 36° to 14°C and after clamping of the ascending aorta potassium citrate was injected into the coronary circulation to produce asystole ranging in duration from 14 to 77 minutes (Fig. 3). At 36°C an occlusion period of 27 minutes caused myocardial damage, whereas at 20°C one hour of ischemia

* Sigmamotor, Inc., Middleport, N. Y.

† Antifoam A, Dow-Corning Co., Midland, Mich.

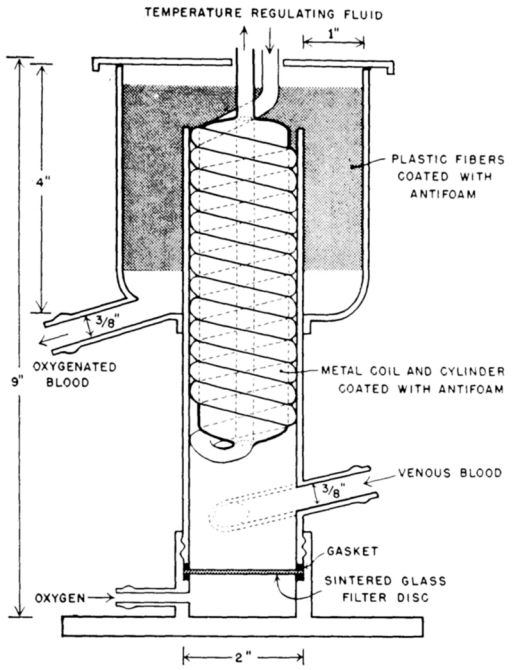
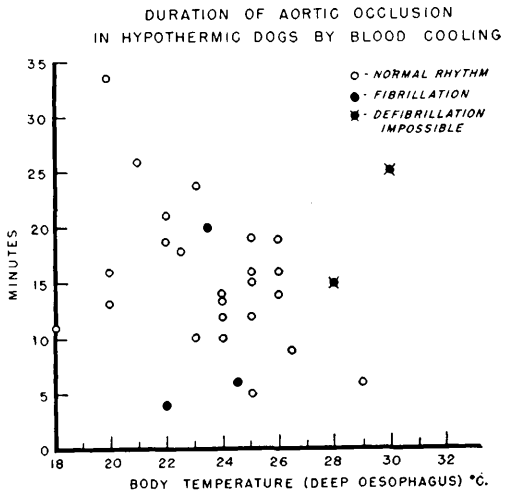


FIG. 1. Diagram of blood oxygenator.

was tolerated without ill effect. Many points indicating recovery or failure are very close and many more experiments at temperatures of 25°C and below 20°C would be needed to establish a rule, instead of just giving fairly well defined ranges of tolerance of the perfused, hypothermic, resting heart to complete ischemia. In 6 experiments ventricular fibrillation was observed during rewarming, but neither temperature nor duration of ischemia seemed to be related to it and sinus rhythm could be easily reestablished.

Discussion. These experiments were undertaken to explore the conditions under which open operations in the left side of the heart could be undertaken without the present limitation in time due to myocardial anoxia. Assuming that thorough exploration of the anatomy, delicate plastic surgery or excision of a nonfunctioning valve, choice of an eventual prosthesis, evacuation of air and closure of the incision may last one hour or longer, the aim of these and of previous investigations was to establish the essential prerequisites for such a procedure: occlusion of the ascending aorta to stop coronary flow and a myocardium undamaged by anoxia. Extracorporeal circulation and oxygenation at normal body temperature fulfills these requirements up to 25 minutes(5), whereas slow recovery and poor cardiac action follows coronary occlusion for 40 minutes(11). If myocardial metabolism and heart rate are reduced by blood-cooling to 21°C the coronary flow can be safely stopped for at least 25 minutes(12) and for at least one hour during asystole at about the same temperature as the present study shows. Prolonged exposure of the



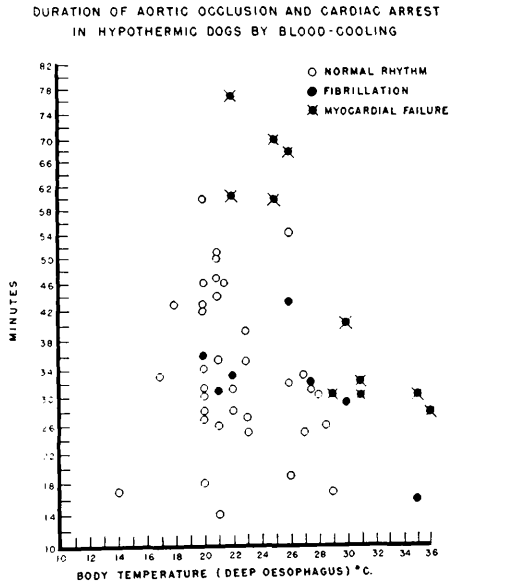


FIG. 2 (top). Anoxic tolerance of by-passed, hypothermic and contracting hearts.

FIG. 3 (bottom). Anoxic tolerance of by-passed, hypothermic and resting hearts.

mitral valve can also be obtained by hypothermic asystole at about 10°C at a very reduced systemic and coronary rate of blood flow(13) and because of the continuous oxygenation of the heart and all other organs left cardiotomy is not limited in time. For open surgery on the aortic valves the coronary flow has to be discontinued and asystole during hypothermia of about 20°C by cooling of oxygenated blood appears to be a desirable condition.

Summary. Hypothermia was produced in dogs by circulating, oxygenating and refrigerating venous blood in a small, plastic pump-oxygenator. The by-passed, contracting, hypothermic heart could be safely deprived of coronary flow for 15 minutes at 28°C and for at least 33 minutes at 20°C. During cardiac arrest induced by intracoronary injection of potassium citrate the safe period of myocardial ischemia could be prolonged to at least one hour at 20°C.

1. Gremels, G., and Starling, E. H., *J. Physiol.*, 1926, v61, 297.

2. Dennis, C., Spreng, D. S., Jr., Nelson, G. E., Karlson, K. E., Nelson, R. M., Thomas, J. V., Eder, W. P., and Varco, R. L., *Ann. Surg.*, 1951, v134, 709.

3. Helmsworth, J. A., Clark, L. C., Jr., Kaplan, S., and Sherman, R. T., *J. Thor. Surg.*, 1953, v26, 617.

4. Clowes, G. H. A., Jr., Neville, W. E., Hopkins, A. Anzola, J., and Simeone, F. A., *Surgery*, 1954, v36, 557.

5. Clowes, G. H. A., Jr., and Neville, W. E., *Surg. Forum*, 1954, p39, W. B. Saunders Co., Philadelphia, 1955.

6. Warden, H. E., Cohen, M., Read, R. C., and Lellehei, C. W., *J. Thor. Surg.*, 1954, v28, 331.

7. Clark, L. C., Jr., Gollan, F., and Gupta, V. B., *Science*, 1950, v111, 85.

8. Gollan, F., Blos, P., and Schuman, H., *Am. J. Physiol.*, 1952, v171, 331.

9. Peirce, E. C. II, and Polley, V. B., *Ann. Surg.*, 1953, v67, 521.

10. Melrose, D. G., Dreyer, B., Bentall, H. H., and Baker, J. B. E., *Lancet*, 1955, July 2, v2, 21-22.

11. Burroughs, J. J., and Donald, D. E., *Proc. 29th Scient. Sessions Am. Heart Assn.*, 1956, p23.

12. Gollan, F., and Kory, R. C., Abstracts XIX, Int. Physiol. Congress Montreal, 1953, p398.

13. Gollan, F., Grace, J. T., Schell, M. W., Tysinger, D. S., and Feaster, L. B., *Surgery*, 1955, v38, 363.

Received April 30, 1957. P.S.E.B.M., 1957, v95.

Age Related Changes in Plasma Cholesterol of the Chicken.* (23261)

HAROLD S. WEISS (Introduced by R. P. Reece)
Department of Poultry Science, Rutgers University, New Brunswick, N. J.

The incidence of spontaneous atherosclerosis in the chicken is reported to increase with age(1). Since atherogenesis can be stimulated in the chick by hypercholesterolemia(2), the role of plasma cholesterol in spontaneous atherosclerosis, particularly in relation to changes of plasma cholesterol with age, becomes a matter for speculation. Data from a number of sources can be organized to suggest that plasma cholesterol increases rapidly with age in the hen. Thus 58 three-year-old hens(3) yield average value of 257 mg %, and combined data on 55 two-year-old hens (4,5) give 197 mg %. For 41 pullets between 6-9 months, grouped results(6,7,8) average 121 mg %. On the other hand, Kaishio(9) found no change in plasma cholesterol of hens between 9 and 81 months of age, but his average value of 80 mg % is considerably lower than most other published data. In males, there are no changes in plasma cholesterol up to 15 months of age(10), apparently the oldest birds studied.

Considering that plasma cholesterol is highly variable, particularly in the female, and may be affected by breed, diet, season, and reproductive state, as well as by analytical technic, it seemed desirable to restudy the problem under more uniform conditions.

Procedure. Male and female White Leg-

* Journal Series, N. J. Agri. Exp. Station, Rutgers University, State University of N. J.