be limited by the lesser of the two gene frequencies, in this case q. Hence the frequency of Aa is $2q$, while that of AA is $1-2q=p-q$. When sex-linkage is involved the distribution becomes, obviously, ♀ ♀ $(\overline{p-q}AA:2qAa)+$ ♂ ♂ $(pAY:qaY)$, and the ratio of female carriers to male exhibitors is $2q:q=2:1$, rather than $2pq:q=2p:1$ as in the Hardy-Weinberg distribution.

Application of the Hardy-Weinberg law to determining primary distribution of genotype frequencies requires not only that the population be indefinitely large, panmictic, and with gene frequencies equal in both sexes, but also that the relation between the population number N (breeding population) and the gene frequency q be such that $q \geqq N^{-0.5}$. Whether a Hardy-Weinberg or a "limiting" distribution obtains actually depends upon this relation between q and N, rather than upon the absolute size of either (Dahlberg [1] and Hogben [3] have discussed a similar though not identical situation). It follows that, on the average, the point in the possible values of q at and above which the Hardy-Weinberg distribution applies, and below which it does not, is given by log $q=0.5$ colog N. When log $q<0.5$ colog N, genotype frequencies take the form of a limiting distribution, the Hardy-Weinberg distribution then being a probability distribution but not a frequency distribution, with respect to the pertinent genotypes.

The consequences of this relation between population size and gene frequency are at present being worked out for a number of different genetic conditions.

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A Simple Pulsating Perfusion Apparatus

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Descriptions of a number of perfusion devices are available in the literature. Many of these are highly complex, adapted to special purposes, or inefficient. We have found that a very satisfactory perfusion apparatus can be simply prepared using a Sterling Automatic Pipette.

The most important parts of a pulsating perfusion device are the valves to control the direction of flow of the blood, and a mechanism to simulate the pumping of the heart. The delivery mechanism of the automatic pipette effectively embodies both these features. The pipette used by us was a Sterling Automatic Pipette, Model 4-3 M (Ivan Sorvall, New York). The amount of perfusate delivered per stroke can be regulated from 0.5 ml to 3.0 ml by adjustment of the stroke regulator. In order to control the rate of pulsation we attached the delivery mechanism of the pipette, by means of a reduction gear, to a variable speed motor. We have found, however, that the perfusion pressure can be adequately adjusted by means of the stroke regulator when delivery rate is 50 strokes per min.

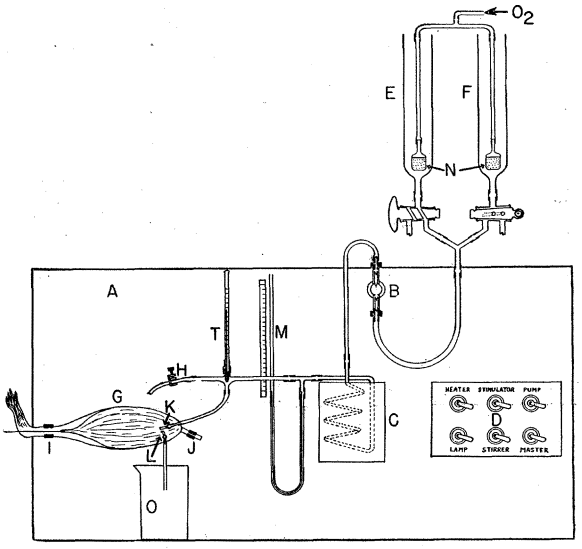

FIG. 1.

Fig. 1 presents diagrammatically a successful adaptation of this pump for the perfusion of an isolated dog hind leg, using defibrinated blood. The leg was prepared as described by Huston, Martin, and Dille (*1*). The leg was kept in good condition for several hours during investigations of the effects of certain drugs on the somatic neuromyal junction.

The tubing and clamps for the leg are attached to a perpendicular board, A. The motor for the pump and the apparatus for the constant temperature water bath are placed behind the board. Just the head of the pipette, B, and a small chamber of the water bath, C, protrude through holes in the board. In this way the work area is kept free of apparatus. The electrical equipment is controlled by switches on plate D.

The blood is stored in two reservoirs, E and F; one is for normal and the other for experimental blood. Oxygenation is accomplished by bubbling oxygen through small Mandler-type filters in the reservoirs. A two-way stopcock at the bottom of each reservoir provides a bypass.

The blood passes from the reservoir to the pump, B, and to the leg, G, through a coil in a constant temperature water bath, C. The perfusion pressure is recorded on a manometer, M; and the temperature on the thermometer, T. H is a bypass for rapid withdrawal of blood from the system.

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