Effect of Strophanthus on Coronary Blood Flow and Cardiac Oxygen Consumption of Normal and Failing Human Hearts

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The action of strophanthus preparations on the coronary blood flow and the oxidative metabolism of the normal and failing human heart has been studied by coronary sinus catheterization. It has been found that strophanthus preparations have no effect on the coronary flow or oxidative metabolism of either the normal or failing heart. This agrees with the concept that the oxidative metabolism (energy production) of the failing heart in vivo is not abnormal. The results indicate that this drug is responsible for causing more effective conversion of oxidative energy into work.

The effect of various digitalis preparations on the circulation of patients with and without cardiac failure has been studied by a large series of investigators. Quantitative measurements of the effect of digitalis on cardiac oxygen consumption and efficiency of the human heart in vivo have not been published to date because of difficulties in the methods involved. Catheterization of the coronary sinus in man in conjunction with the nitrous oxide method has now made it possible to determine cardiac oxygen consumption and coronary blood flow in man, and to study quantitatively the effect of digitalis on the energy metabolism of the normal and failing human heart in vivo. This report deals with the effect of strophanthus preparations on the coronary blood flow and cardiac oxygen consumption of patients with and without cardiac failure.

Methods

The coronary sinus was catheterized according to a method previously described. Coronary blood flow was determined by means of the nitrous oxide method. Cardiac output was measured with the direct Fick principle, the mixed venous samples being obtained from the right ventricle or the pulmonary artery by means of an intracardiac catheter. Peripheral arterial pressures were optically recorded with strain gauges or obtained with the sphygmomanometer.

Coronary blood flows and cardiac oxygen consumption were obtained for 100 Gm. of cardiac tissue. These values may be considered accurate. Because of difficulties in defining accurately that portion of cardiac muscle which has its venous drainage into the coronary sinus and because of inaccuracies in calculating the heart weight from height and weight of the patient, figures for mechanical efficiency and energy cost of the heart must be considered only approximations. However, since major variations in the distribution of coronary venous drainage are unlikely during the short period of the test, changes in cardiac efficiency and energy cost produced by the drug are quantitative and therefore significant. In the calculations of cardiac efficiency it was assumed that the tributaries of the coronary sinus drain primarily the left ventricular muscle. Consequently, the work-energy cost relationship was calculated for the left ventricle only. Recent observations of Gregg indicated that better correlations between results derived from the nitrous oxide method and direct determinations of flow can be obtained if the combined weights of the left auricle and ventricle are used. However, in evaluating the effect of strophanthus preparations, only the relative changes from the control values are of importance.

In general, the procedure outlined in a previous report was followed. After the first measurement of cardiac output, coronary flow and cardiac oxygen consumption, strophanthus K (0.65 mg. Burroughs Wellcome Co.) or strophosid (0.5 mg. Sandoz Chemical Works) were slowly injected intra-arterially through a manifold. After a 10 minute interval, the nitrous oxide mixture was again administered over a period of 12 minutes. Following this, coronary blood flow, cardiac oxygen consumption and cardiac outputs were again determined.

Cardiac work was expressed in kilogram meters per minute. It was calculated from the formula:
STROPHANTHUS AND CORONARY BLOOD FLOW

### Table 1.—Effect of Digitalis on Coronary Blood Flow in Normal Subjects

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### Table 2.—Effect of Digitalis on Coronary Blood Flow in Patients with Cardiac Failure

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Work (Kg. meters/min.) = cardiac output (cc./min.) × mean aortic pressure (mm. Hg) × 15.6

To express the oxygen consumption of the left ventricle in the same units as left ventricular work the oxygen consumption was multiplied by the work equivalent of oxygen at a respiratory quotient of 0.82 (cc. oxygen = 2.059 Kg. meters). The following equation was used for the calculation of left ventricular efficiency:

Mechanical efficiency of left ventricle (percentage) = \( \frac{\text{work of total left ventricle (Kg. meters/min.)}}{\text{oxygen consumption of total left ventricle (Kg. meters/min.)}} \times 100 \)
Coronary vascular resistance was calculated according to the equation:

\[
\text{Coronary vascular resistance} = \frac{\text{mean aortic pressure (mm.Hg)}}{\text{coronary blood flow cc./100 Gm./min.}}
\]

Consequently, the units for this resistance are expressed in mm.Hg/cc./100 Gm./min. The resistance calculated in this manner refers to that portion of the coronary vascular bed only which drains into the coronary sinus.

**RESULTS**

The results obtained in normal individuals are illustrated in table 1. It may be seen that the cardiac output fell in every instance. This is in agreement with the findings of Cohn and Stewart and McMichael and Sharpey-Schafer. The arterial pressure remained constant. As a result of the fall in cardiac output, the left ventricular work decreased.

The coronary blood flow per 100 grams and the coronary arteriovenous oxygen difference also showed no significant change following the injection of the glycoside. Therefore, the cardiac oxygen consumption remained constant. Because of the fall in the work of the heart, the left ventricular efficiency decreased.

In failure due to arteriosclerotic heart disease or to mitral stenosis and insufficiency the initial cardiac output was low (table 2). The coronary arteriovenous oxygen difference and the left ventricular coronary blood flow were within normal limits. These results are in agreement with those previously published from this laboratory. Table 2 illustrates that following the injection of strophanthus preparations, the cardiac output rose. Similar findings were obtained by Ahmed and associates, Stead and Bloomfield and co-workers. The coronary blood flow and the coronary arteriovenous oxygen difference remained at the previous level. Therefore, the left ventricular efficiency rose following the injection of strophanthus preparations.

**DISCUSSION**

The results published in a previous report show that the output of the heart in failure is reduced, while the oxygen consumption is normal. Similar results were obtained in this series in patients with failure. This indicates that while there is no defect in the utilization of the oxidative energy of the failing human heart in vivo, the heart is defective in converting oxidative energy into effective work. This is in agreement with the finding of Goodale and associates that the aerobic oxidation pattern of the failing heart in vivo is normal. In line with this is the observation that strophanthus has no effect on the oxygen consumption of the failing heart but aids in a more effective conversion of oxidative energy into effective work. Thus, strophanthus increases the efficiency of the failing heart only by increasing the output. These findings contrast with those obtained by Starling and Visscher, and by Gremels and Moe and Visscher. In all patients in cardiac failure in this series there was radiologic evidence of cardiac enlargement. The finding of cardiac enlargement existing in conjunction with normal cardiac oxygen consumption raises further doubt concerning the validity of Starling and Visscher's postulate that the total energy set free by the heart beat is solely a function of the diastolic volume.

In the normal, strophanthus causes a decrease in the work of the heart, by reducing its output. The finding is in agreement with that of Stead and McMichael. As the energy cost remains unchanged, the efficiency decreases.

The effect of strophanthus on the resistance of the coronary vascular bed is illustrated.
in table 3. It may be seen that changes in coronary vascular resistance following strophanthus are small. This indicates that the drug has no direct action on coronary blood vessels.

**Summary**

The effect of strophanthus preparations on coronary blood flow, cardiac oxygen consumption and efficiency has been measured in a series of patients with and without cardiac decompensation.

Strophanthus lowers the efficiency of the normal heart by reducing the cardiac output. The oxygen consumption of the heart is not affected. The oxygen consumption of the failing heart per 100 grams of muscle is normal. Strophanthus increases the efficiency of these hearts by elevating the cardiac output. Again the cardiac oxygen consumption remains unchanged.

Strophanthus has no significant effect on coronary vascular resistance, indicating that the drug has no direct action on coronary vessels.

The findings illustrate that there is probably no defect in the utilization of oxidative energy of the failing human heart in vivo, but the failing heart is defective in converting oxidative energy into effective work. Strophanthus aids in this conversion.

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Circulation. 1950;2:513-516
doi: 10.1161/01.CIR.2.4.513

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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