

the boy at a stage before the scrotal skin is so oedematous that the testis cannot be felt and untwisted. Sparks's work at Rugby School has established very clearly the value of prompt action on the part of the general practitioner.

How sad it is that even now young patients lose their testicles because of a supposed diagnosis of epididymitis. Epididymitis hardly ever occurs unless there is frank evidence of urinary infection or obvious urethritis, and in any case little harm is done by making an exploration whenever there is any doubt about the diagnosis. In all cases where the swelling is not confined to the epididymis and where there is no pus in the urine and no urethral discharge the swollen testicle must be explored.

We wish to thank Professor J. P. Blandy for his helpful advice and encouragement.

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Scientific Basis of Clinical Practice

Mechanism of Ventricular Ejection

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The basic mechanism of ventricular ejection is simple (Fig. 1). The muscle of the ventricular walls begins to shorten and the ventricular volume begins to decrease and deform. This produces a rapid and propagated rise in the pressure of the contained blood which leads to closure of the atrioventricular valves (a). The ventricle is then a closed space, and its continuing contraction is described as isovolumetric (b). During this phase the pressure rises very rapidly until it exceeds that in the aortic or pulmonary root. At this time the semilunar valves open and the ventricles begin to eject blood (c).

Initially, the pressure in the left ventricle is greater than that in the aortic root, but in the latter part of the ejection phase the pressure gradient reverses and ejection continues by virtue of the inertia that has been imparted to the blood. This reversal of the pressure gradient across the aortic valve causes closure of the valve as soon as the velocity of blood flowing through the valve orifice has fallen to zero. The ventricle is once again a closed chamber, and the phase of isovolumetric relaxation begins (d). As soon as the intraventricular pressure falls below that of the atrium the atrioventricular valves open and the ventricle fills, rapidly at first (e) and then more slowly (f). The contraction of the atrium (g) adds a small and variable amount of blood to the ventricular volume, and the cycle then repeats.

The simplicity of the sequence of events thus stated conceals the complexity of the individual processes, which is apparent on detailed study. We shall consider these processes in some detail before considering the characteristics of the heart as a pump and the extent to which it is adapted to its function.

Activation of Myocardial Contractile Mechanisms

Myocardial fibres have properties which are intermediate between those of skeletal muscle and those of visceral smooth

muscle. They share with skeletal muscle a striated appearance when seen under the light microscope, and a one-to-one relationship between action potentials and activation of the contractile mechanism. They differ from skeletal muscle in

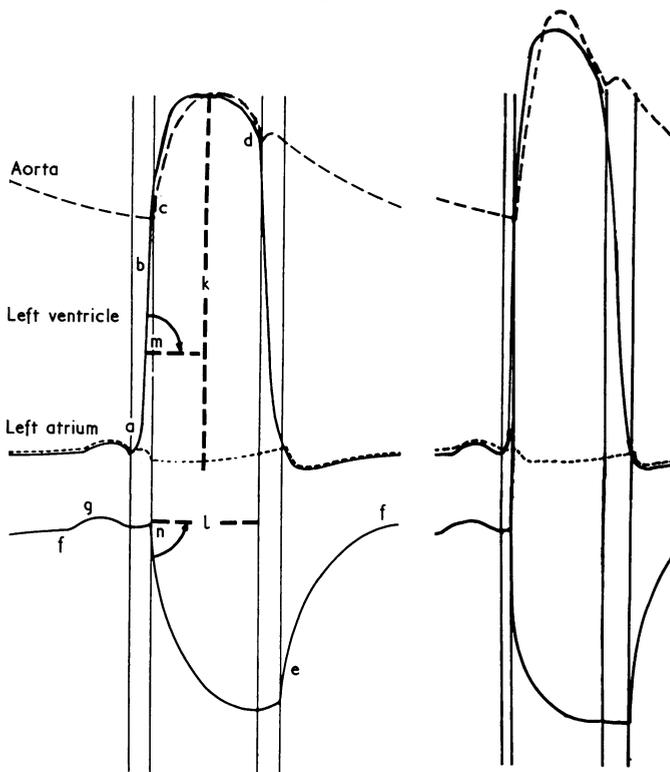


FIG. 1—Left. Diagram to show the aortic pressure, the left ventricular pressure, the left atrial pressure, and the intraventricular volume demonstrating: (a) the closure of the atrioventricular valve; (b) the phase of isometric contraction; (c) the opening of the aortic valve; (d) the closure of the aortic valve; (e) the phase of rapid ventricular filling; (f) the phase of reduced filling; (g) the effect of atrial contraction. The peak ventricular pressure; (k) the duration of ejection (l), the maximum rate of increase of the ventricular pressure, dP/dt max, (m) and the maximum rate of ventricular ejection (n) are indicated as measures which may be used to describe the changes produced by adrenaline, illustrated in the right-hand panel.

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that the fibres branch and have centrally placed nuclei and in that the action potentials are much longer (200 msec as opposed to 10 msec) and arise as a result of conduction from fibre to fibre rather than from activation of a receptor region by a motor nerve.

The mechanism of spread of depolarization from a cell or cells which act as a pacemaker to the remainder of the fibres is reminiscent of visceral smooth muscle, but the latter has a much longer latent period between the depolarization and the resultant contraction of the fibres. Because the refractory period of cardiac muscle is of similar duration to the contraction, the production of tetanus is not normally possible. It can be achieved under abnormal circumstances such as in cooled cat papillary muscle. The shortening of the contractile elements in a myocardial fibre leads to a shortening of the fibre as a whole, but the relation between the two requires further examination.

Activation of Contractile Mechanisms and Shortening of Muscle Fibre

Any attempt to make a model of the muscle fibre as a whole is bound to be defective, and the following simple model is intended only to illustrate the type of phenomenon involved in the relationship. In addition to being actively contractile, the actin-myosin has an elasticity, which is represented as an elastic component (E_p) in parallel with the active element. In addition, the active elements are effectively in series with other elastic elements, shown as a series elastic component E_s . Because the myocardium is doing work on a

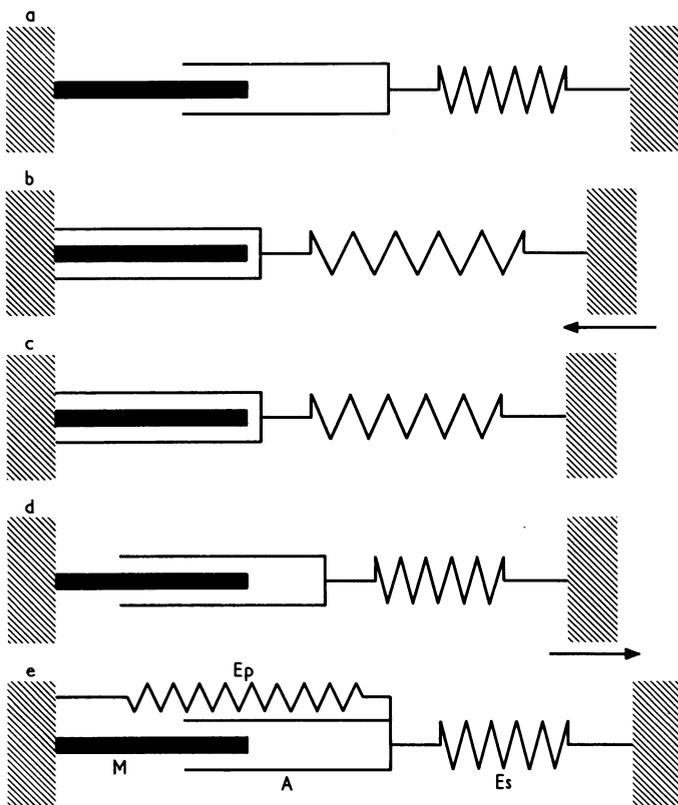


FIG. 2—Diagram to illustrate the length tension relationships of muscle fibres. The contractile mechanism, consisting of the thicker myosin filaments (M) and the thinner actin filaments (A), are in series with the series elastic components E_s . The parallel elastic component E_p is illustrated in panel e, but omitted in the other panels for the sake of clarity. (a) Shows the resting extended muscle fibre. In (b) the active shortening of the contractile component has finished, but the fibre as a whole continues to shorten with a diminishing tension as the series elastic component shortens until the end-systolic situation is reached at (c). Relaxation of the actively contractile elements in (d) results in a rapid fall in the fibre tension without appreciable increase in length, which can be achieved only by the application of an external force which will do work extending the series and parallel elastic components. This results in the end-diastolic situation illustrated in (e), in which there is a small tension dependent on the degree of passive stretch.

viscous medium, the time course of shortening in the active component may be different from the time course of shortening in the muscle fibres as a whole. The time-tension diagram (Fig. 2) has repercussions in the development of ventricular pressure which are complicated by the fact that the muscle fibres are distributed in the wall or a more or less spherical chamber.

If the heart consisted of cylinders, each having a piston which was moved by muscle fibres orientated parallel to the direction of motion, then the pressure developed in the cylinder during the ejection stroke would be linearly related to the tension in the muscle fibres and the volume ejected would be a linear function of the change in length. Because the muscle of the heart is arranged in the wall of a hollow viscus, however, the relationships are much more complex. If for simplicity the ventricles are assumed to be thin-walled spherical cavities, then the volume displaced by a mean shortening of Δl when the radius of the sphere is r is given by

$$\Delta v = k r^2 \Delta l, \text{ where } k \text{ is a constant}$$

and when the myocardial tension is T , the intraventricular pressure (p) is given by

$$p = 2T/r, \text{ which is a statement of Laplace's law for a sphere.}$$

Thus, the myocardial fibre tension necessary to produce any intraventricular pressure is a linear function of the ventricular radius. Though the ventricular is not a thin-walled sphere, this effect is observed in modified form, and if it were not for other factors it would have a drastic effect on cardiac performance. Imagine a myocardium which is beginning to fail to eject an adequate stroke volume. The volume of blood remaining in the ventricle at the end of systole (the end-systolic volume) would be slightly greater than usual. This would lead to a slightly increased volume in the ventricle at the beginning of the subsequent systole (the end-diastolic volume). This would require a greater myocardial fibre tension than in the previous beat to raise the ventricular pressure to an adequate level. Because the myocardium is failing, this increase cannot occur, and ejection falls further leading to a vicious circle of cardiac dilation. Under normal circumstances such a sequence of events is prevented from occurring by regulatory mechanisms which are both intrinsic to the heart and dependent on reflex neural and hormonal effects.

Intrinsic Regulation of Cardiac Function

It has long been known that for skeletal muscle the tension developed on maximal stimulation is a function of the resting length of the muscle. This was shown also to be true for amphibian myocardium contracting isometrically by Otto Frank at the end of the last century. Ernest Starling generalized his observations on the mammalian heart contracting more or less isotonicly when he enunciated his Law of the Heart in his Linacre lecture of 1915. "The Law of the heart is thus the same as the law of muscle tissue generally, that the energy of contraction however measured is a function of the length of the muscle fibre."

This law has been the subject of much discussion ever since. The occasional failure of subsequent workers to observe his predictions has resulted from their failure to provide the experimental conditions required. Starling recognized clearly that the energy of contraction depended on the influence of nerves and hormones in the intact organism, and that intrinsic myocardial control is "the Central fortress of the system and under normal conditions is protected and to a large extent prevented from coming into play by the central nervous system and its servants. . . ."

Nevertheless, in relation to his experimental preparation (which was denervated and not subject to changes in hormonal influence) Starling stated that the sole factor in determining the increase in contractile stress set by each muscle fibre must be the greater dilatation of the ventricles. The Anrep effect—in which ventricular work is maintained despite change in ventricular filling—was known at that time and is

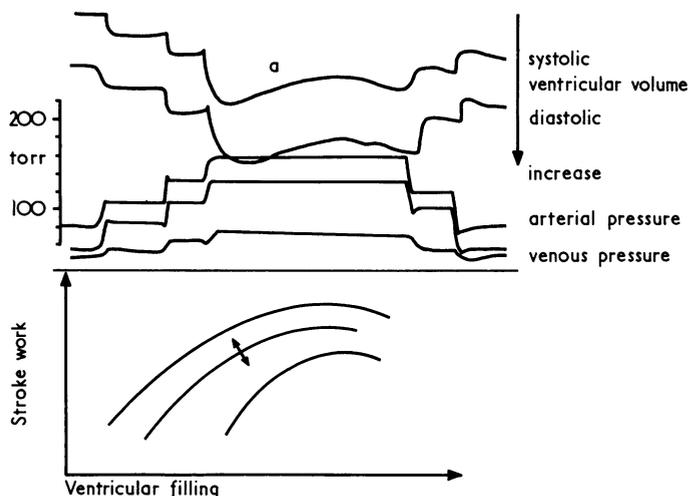


FIG. 3—Illustration of the type of effect observed by Starling. Upper panel. The work of the left ventricle of the isolated heart was artificially increased by increasing the arterial resistance. To achieve this, the volume of the ventricle increases, indicated by downward displacement of the ventricular volume trace, and the mean right atrial pressure increases. Notice that the difference between the systolic and diastolic volumes remains nearly constant, an indication of the way in which the heart maintains its output against a varying load. At (a) the ventricular volumes begin to decrease, and the venous pressure falls despite the maintained increase in stroke work. This is the Anrep effect, and is discussed in the text. The lower panel illustrates the sort of relationship that exists between the stroke work and ventricular filling. The curve is displaced upward and to the left by an increase in myocardial contractility, and downward and to the right by a decrease.

illustrated in Fig. 3 (a). This effect was regarded by Starling as a result of the condition of the myocardium having been improved by an increased blood flow resulting from the increased aortic pressure. It was not until fifty years after this observation that it was shown that the energy of contraction was not only related to the initial length of fibres (pre-load), but also to the resistance offered to myocardial shortening (after-load). Starling was thus "at fault" in not being fifty years ahead of his time. However, his erroneous explanation indicates that he had a clear concept of myocardial condition or tone (his terminology) or contractility (in more recent terminology).

CONTRACTILITY

The term contractility used in relation to the heart means more than the ability to contract. It means the ability to contract measured by the energy of contraction at a particular initial fibre length. In other words, contractility determines the position of the curve relating energy of contraction to the initial length of the fibre.

Contractility has come to be regarded as a property of the myocardium which must have some physical representation that is independent of initial fibre length, since contractility is independent of initial fibre length. This is an error of logic which has led to the investigation of many features in pursuit of such a representation. It remains true that cardiac contractility can be increased by the action of the cardiac sympathetic nerves, by inotropic agents such as adrenaline and isoprenaline, and by drugs such as digoxin, but this increase has representation only in the displacement of the Starling curve.

In the failing heart its progressive dilation is prevented by an increase in the energy of contraction, resulting both from an increase in initial fibre length and from an increase in contractility. The latter is produced reflexly by increased activity in the cardiac nerves resulting from a fall in blood pressure produced by the reduction in stroke volume. Only when the contractility of the heart cannot be further increased by these means does progressive dilatation occur. Thus the disadvantages inherent in a hollow muscular walled pumping chamber are overcome by a combination of built-in

non-linearity in the contractile element and an extrinsic "feed-back" type of control of contractility.

Arrangement of Ventricular Myocardial Fibres

The musculature of the walls of hollow viscera is usually described in terms of layers, bundles, fascicles, etc., and the heart has been described as comprising named muscles, such as the superficial and deep bulbospiral muscles. Earlier writers envisaged that contraction of these muscles produced tension in the connective tissue linking them and that this tension accounted for the rapid dilatation of the ventricles after their active contraction had finished (for the myocardium has no active antagonist). This interfascicular tension was held to account for the ability of the left ventricle apparently to suck blood from the atrium into its cavity. More recent studies have shown, however, that there is probably no such organization of the muscle, but rather that the orientation of the muscle fibres at a particular place on the ventricular wall changes smoothly across the thickness of the wall. Thus interfascicular tension is no longer a suitable term. Even so, the ventricular wall is a viscoelastic structure, and work done deforming it is converted into heat and elastic potential energy. The latter is recoverable and will tend to cause the ventricle to resume its diastolic form and dimensions. We may thus more properly speak of interlamellar tensions.

The discussion relating to the general properties of length-tension/pressure-volume relationships in muscular walled spherical viscera has to be modified to take into account the static and dynamic aspects of ventricular anatomy.

While the left ventricular cavity is roughly elliptical in form (and therefore bears some relation to the argument given above), the right ventricular cavity is crescentic in section. The arguments relating radius of curvature, muscular tension, and intraventricular pressure apply equally well to a portion of a spherical surface as to a whole sphere. Nevertheless, probably the right ventricle works as much by contracting those parts of its wall that are at right angles to the interventricular septum so as to draw the major part of the wall which lies parallel to the septum closer to it. If this is the case, then the right ventricle functions more like the hypothetical ventricle in which a piston is moved by muscles orientated parallel to the direction of motion of the piston, or like bellows.

So far the discussion has assumed that the whole ventricular wall contracts instantaneously. While it is true that the ventricles have a specialized conducting system to reduce the time over which they begin to contract, inspection of the beating heart shows that contraction is far from instantaneous and its progression from the apex towards the base of the heart, which can be mapped by exploring electrodes, confers a peristaltic or "milking" action, which considerably helps ejection. This also prevents the outflow tracts of the ventricles being narrowed until the contraction is nearly complete.

The Heart as a Pump

A motor of any given power might be furnished with a fan, or with a crank connected to a piston, each acting as a pump. The pumps would, however, have very different properties.

The motor and fan would not be able to develop great pressures, but would be able to pump large quantities of fluid at a relatively low pressure. Since the fluid is never enclosed and then displaced, the pump works by imparting inertia to the fluid. This is useful for such functions as exchanging or circulating room air. The pressure produced by a pump of this type is low, but relatively independent of flow. Such a pump can have its outflow occluded without damage. The piston pump, on the other hand, encloses fluid and displaces it. Its output is low in volume but the flow output is relatively independent of the resistance offered to its output. By analogy with sources of electric current, the former may be called a low impedance pump the latter a high impedance pump.

The anatomy of the heart suggests that its ventricles are displacement pumps, and this is certainly the case with the left ventricle. This chamber can maintain its output in the face of aortic stenosis, systemic hypertension, and other cases of increased pressure load. Nevertheless, when faced with an increased volume load, even at a lower than normal mean pressure (as in patent ductus arteriosus), the left ventricle immediately becomes less able to cope and has a much reduced reserve. The right ventricle, however, is well able to cope with the increased volume load which it faces in atrial septal defect, and it is only the advent of pathological changes leading to high resistance in the pulmonary vasculature which causes this ventricle to fail.

The susceptibility of the right ventricle to fail under pressure loads with normal or subnormal flow outputs is illustrated by the early onset of right ventricular failure in mitral stenosis. Thus it appears that the right ventricle, though its structure is that of a displacement pump, functions in some respects like an inertial pump. It is noteworthy that the development of tricuspid insufficiency in right ventricular failure does not lead to a sudden deterioration in its function. Such a leak in a high impedance pump, on the other hand, would be severely disabling.

For efficient energy transfer, the impedance of a pump and of the pipes connected to its outflow have to be matched. Possibly the process of adaption to a slow change in the impedance of the left ventricle, such as produced by mitral insufficiency, is a change in the impedance of the vascular system. A sudden alteration in the ventricular impedance caused by the surgical replacement of such a diseased valve could give rise to a ventricle of supranormal impedance coupled to a vascular system of subnormal impedance. This, apart from the well-known reaction to surgery, may be of significance in causing a prolongation of the period of improvement, for maximum benefit would result only after there had been a regression of myocardial hypertrophy and an increase in the vascular haemodynamic resistance. How far such adaption takes place is not known, but investigations of this type of phenomenon with modern methods of pressure and flow measurement are likely to increase considerably our understanding of cardiac function.

Cardiac Filling

Fig. 2 (d and e) shows how an external force must be applied to myocardial fibres to extend them. This force consists of the interlaminar tensions and the hydrostatic intraventricular pressure. It has to do work against the frictional resistance offered by the viscous myocardium. Because the actively contractile elements in muscle fibres behave as if they have a weak spring in parallel with them, work is also done in extending this parallel elastic component. Since this can be done only by developing tension in the series elastic component, work is done extending this as well, though the amount of extension is much smaller. It is well known that certain substances, such as adrenaline, can increase the rate at which the ventricles fill at a given filling pressure. This must imply an increase in the interlaminar tensile forces or a decrease in the strength of the parallel elastic component or a decrease in the myocardial viscosity. The usual interpretation is that the myocardial viscosity is decreased, though it is difficult to envisage the physical changes which might account for such a rapid reduction. Possibly under certain circumstances the interlaminar forces could be sufficiently great for the ventricle to be dilated even with a negative transmural pressure—that is, that the ventricle may be able to “suck”; such suction has been observed.

The shape of the ventricular volume curves (Fig. 1) shows how the diastolic period can be considerably reduced without much decrease in the passive ventricular filling. Because the diastolic period can shorten very considerably when the heart rate is high (since the duration of systole is governed by the

duration of the myocardial action potential and is much more nearly constant), this ensures that ventricular filling is not unduly prejudiced by tachycardia. The effect of atrial contraction is greater in proportion to passive filling at high heart rates.

Indices of Ventricular Effectiveness

In the assessment of the effectiveness of the ventricle as a pump, various clinical observations are helpful. A good exercise tolerance; an adequate blood pressure; warm, well-perfused extremities; a moderate heart rate; and absence of the signs of pulmonary oedema or raised central venous pressure are indicative of good function. Nevertheless, these observations may be misleading, and direct measurement of cardiac function is preferable.

Cardiac output is probably the most important single measurement of cardiac function. More significance can be attached to the maximum value which can be achieved in exercise. Indicator dilution techniques are the easiest to employ, and heat is the most useful indicator as it permits repeated measurements to be made. Recently, electromagnetic flowmeters and Doppler velocity meters have been developed which can be placed around the aorta or the pulmonary artery. These enable direct phasic measurements of cardiac output and permit instantaneous computation of stroke volume and stroke work. (Stroke work may be calculated by integrating the product of intraventricular pressure and aortic or pulmonary root flow over the period of one heart cycle. If stroke work is calculated by multiplying the stroke volume by the mean arterial pressure, the result is very approximate because it takes no account of the pulsatility of the heart.)

Observations of the changes in the ventricular pressure trace or of the aortic root flow enable qualitative descriptions of the change in form produced by adrenaline or by sympathetic stimulation. An attempt can be made to quantify certain aspects of these changes. Thus the peak intraventricular pressure, the time over which ejection takes place, the steepness of the pressure rise in the phase of isovolumetric contraction, and the maximum rate of ejection may all be used as indices of the inotropic effects of sympathomimetic agents. The steepness of the isovolumetric pressure rise is usually measured by its maximum value, dP/dt max. (Fig. 1). This and other values have from time to time been claimed as indices of contractility, but they are all to some extent dependent on ventricular filling pressure. Nevertheless, they may be useful in making comparisons of cardiac function over short time intervals.

True information about contractility as formerly defined can be obtained only by observing a shift in the Starling curve. Myocardial fibre length cannot be measured directly, but because of the parallel elastic component in the muscle the inactive tension measures fibre length, and also determines the intraventricular pressure. Thus the end-diastolic pressure is often taken as an index of ventricular filling and the initial fibre length. Complex hybrid computing circuitry is necessary to derive this automatically from a signal representing intraventricular pressure, and it is laborious to measure it directly from a pressure trace. Left atrial pressure (or central venous pressure in the case of the right heart) is commonly taken as an index which is more readily obtainable, and is plotted against stroke work or one of the inotropic measurements referred to above. The use of such indices in diagnosis and monitoring is likely to become commonplace within comparatively few years.

This article is based on a lecture given in the Birmingham course under the title “The Scientific Basis of Clinical Practice” (see B.M.J., 27 November 1971, p. 510).

Further Reading

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