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BASIC CONCEPTS IN CARDIOLOGY

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Quantitative Structural Analysis of the Myocardium During Physiologic Growth and Induced Cardiac Hypertrophy: A Review

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The quantitative structural properties of the ventricular myocardium during postnatal physiologic growth are compared with those accompanying an increased load in the adult rat heart to determine whether induced cardiac hypertrophy is a pathologic condition or simply a form of well compensated accelerated growth. The expansion of the ventricular myocardium during maturation shows a remarkable degree of well balanced compensatory response, because the capillary microvasculature, parenchymal cells and subcellular components of myocytes all grow in proportion to the increase in cardiac mass. In contrast, the increases in myocyte diameter and length caused by pressure hypertrophy, volume hypertrophy and infarction-induced hypertrophy are consistent with concentric, eccentric and a combination of concentric and eccentric hypertrophic growth of the whole ventricle, respectively.

These cellular shape changes may represent a compensatory response of the myocardium at the cellular level of organization that tends to minimize the effects of an increased pressure or volume load, or both, on the heart. Cardiac hypertrophy, however, may also show alterations affecting capillary luminal volume and surface and the mitochondrial to myofibril volume ratio, which indicate an inadequate growth adaptation of the component structures responsible for tissue oxygenation and energy production. Thus, hypertrophy of the adult heart differs from that during physiologic growth, and the hypertrophied myocardium may exhibit structural abnormalities that can be expected to increase its vulnerability to ischemia.

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The expansion of cardiac mass during postnatal physiologic growth, as well as the expansion caused by an increased load in the adult rat, tends to accommodate changes in work demand by adaptations involving the myocyte population and the capillary microvasculature of the ventricular myocardium (1). Myocyte hypertrophy is the prevailing mechanism of cellular growth during development, and these cells possess the capacity for additional hypertrophy in response to an added work load (1,2). Cellular enlargement can be effected by an increase in myocyte diameter, length, or both; the cellular changes, in turn, are responsible for the gross changes in wall thickness and chamber volume of the hypertrophied ventricle (3). Changes in the dimensional properties of myocytes imply expansion of the subcellular components responsible for oxygen consumption and adenosine triphosphate (ATP) synthesis (the mitochondria) and those responsible for ATP utilization, that is, the contractile proteins assembled in the myofibrils (4). An equally relevant growth variable of the myocardium is the expansion of the capillary network, as new capillary units are necessary to maintain an adequate oxygen supply to the rapidly expand-

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This article is part of a series of informal teaching reviews devoted to subjects in basic cardiology that are of particular interest because of their high potential for clinical application. The series is edited by Arnold M. Katz, MD, FACC, a leading proponent of the view that basic science can be presented in a clear and stimulating fashion. The intent of the series is to help the clinician keep abreast of important advances in our understanding of the basic mechanisms underlying normal and abnormal cardiac function.

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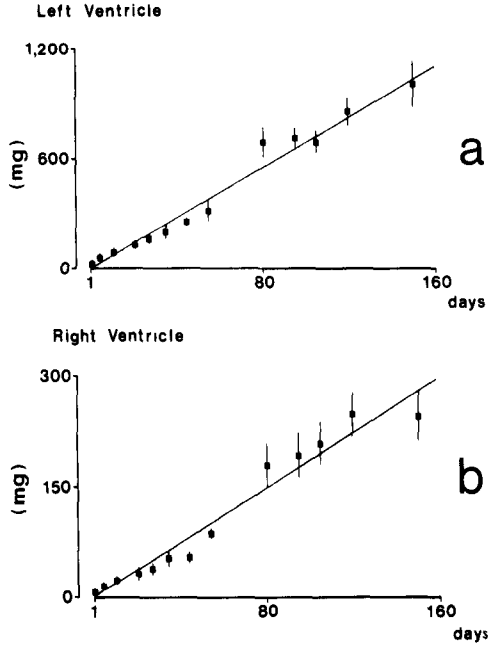
ing ventricular mass. The proportional or disproportional growth of the capillary microcirculation during enlargement of the myocyte compartment of the ventricle can be anticipated to preserve or alter capillary luminal volume and surface densities, and the average diffusion distance for oxygen, which are the structural properties of the capillary bed controlling tissue oxygenation (5).

This article reviews the quantitative morphologic characteristics of the ventricular myocardium in an attempt to evaluate whether physiologic growth differs from induced hypertrophic growth, and whether cardiac hypertrophy in response to an increased hemodynamic load is a pathologic condition or simply a form of well compensated accelerated growth.

Postnatal Myocardial Growth

The growth of the heart from early postnatal life to adulthood is associated with the increasing circulatory demands of the rapidly growing animal and the rather abrupt changes in the patterns of blood flow and circulatory resistance that occur shortly after birth (6). The transition from the fetal to the adult circulatory system is accompanied by a progressive increase in volume load on both sides of the heart and a marked increase in the pressure load of the left ventricle (6). The latter induces a faster growth of the left ventricular myocardium, which leads to its relatively larger muscle mass in the adult heart. In male rats from 1 to 150 days of age, augmentation in weight of the left ventricle occurs at a rate of 7.1 g/day, which is 3.7 times greater than that of the right ventricle, which increases by 1.9 g/day (Fig. 1).

Figure 1. Increase in mass of the left (**a**) and right (**b**) ventricles during the first 5 months of postnatal life. Values are expressed as mean ± SD. Note that the value for the left ventricle on the ordinate is four times that of the right ventricle.



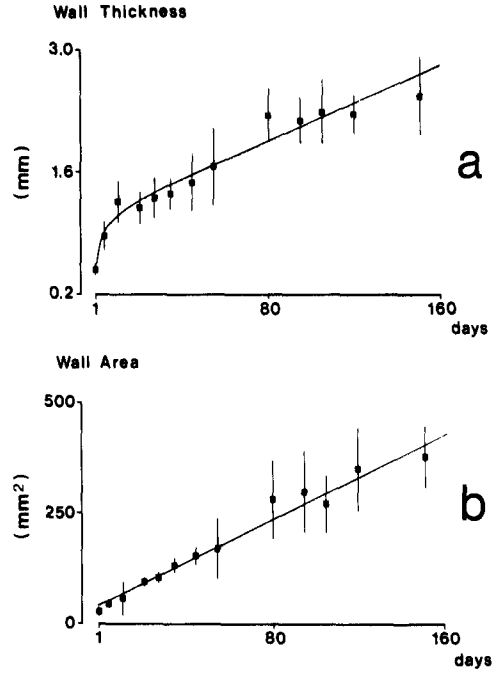


Figure 2. Changes in wall thickness (**a**) and wall area (**b**) of the left ventricle during the first 5 months of postnatal life. Values are expressed as mean ± SD.

Concentric and eccentric hypertrophy. Increasing pressure and volume loading of the left ventricle induces concentric and eccentric hypertrophy* in which wall thickness increases with chamber enlargement (7). Morphologic indexes of these growth patterns are seen in the measurements of change in wall thickness (Fig. 2a) and the respective increase in wall area (Fig. 2b). The calculation of ventricular wall area, which is obtained by dividing wall volume by wall thickness (8), assumes that the ventricular wall may be treated as a thin sheet. Thus, increases in wall area imply larger chamber volumes. The values for wall thickness versus the corresponding age period do not define a simple linear relation: instead, the best line is an initial hyperbolic curve followed by a straight line (Fig. 2a). This analysis indicates that the rate of ventricular thickening is greater up to the time of weaning, approximately 3 weeks after birth, during which time there is a nearly sevenfold increase in systemic arterial pressure (9,10). The subsequent, more moderate increase in blood pressure with maturation corresponds to the straight portion of the graph. It

*In this review, concentric ventricular hypertrophy is used to mean compensated pressure overload hypertrophy in which wall thickness increases without chamber enlargement, whereas eccentric ventricular hypertrophy corresponds to compensated volume overload hypertrophy in which chamber volume enlarges without a relative increase in its wall thickness.

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should be emphasized, however, that wall thickening is also influenced by the increasing volume load on the heart produced by the expansion in blood volume with growth. These factors characterize eccentric hypertrophy, in which chamber dilation is accompanied by proportional increase in wall thickness, so that the ratio of wall thickness to chamber radius remains constant (7). The progressive augmentation in chamber volume during postnatal development is shown by the positive linear correlation between left ventricular area and age (Fig. 2b).

Proliferation and increased size of myocytes. Myocytes in the rat heart continue to proliferate up to the age of weaning although the major increase in cell number occurs within the first few days after birth (1,3). The process of cellular hyperplasia leads to a marked increase in the number of myocytes across the ventricular wall that normalizes at approximately 3 weeks of age (Fig. 3a). In addition, myocyte diameter progressively increases (Fig. 3b) so that early wall thickening is caused by both these phenomena. When cellular enlargement rather than increased cell number becomes the main growth mechanism (2), lateral expansion of the myocytes is responsible for subsequent increases in wall thickness with age.

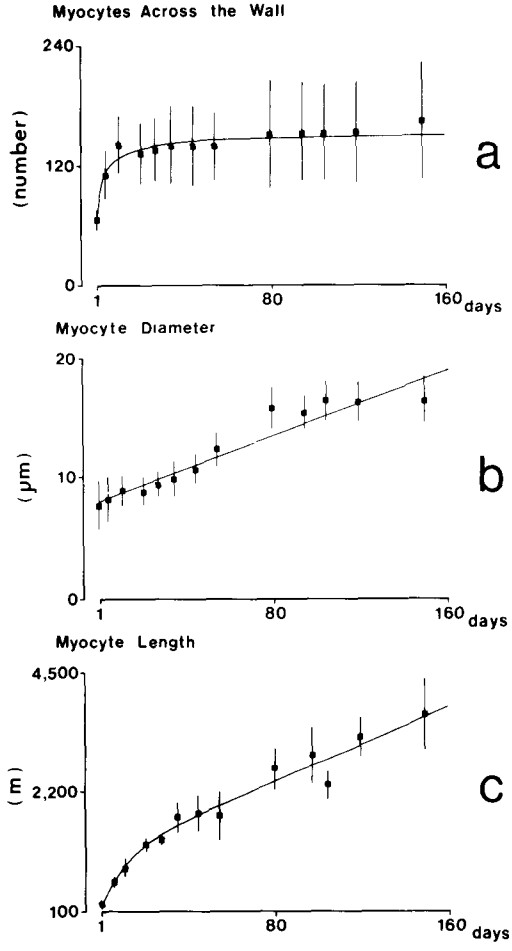

Figure 3. Changes in the number of myocytes across the wall (**a**), myocyte diameter (**b**) and total myocyte length (**c**) of the left ventricle during the first 5 months of postnatal life. Values are expressed as mean ± SD.

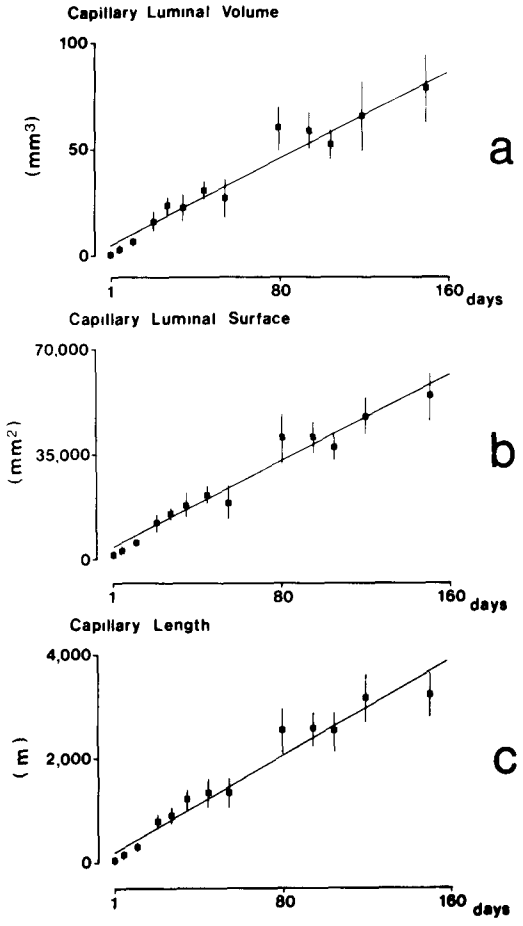

Figure 4. Changes in the aggregate luminal volume (**a**), luminal surface (**b**), and length (**c**) of capillaries in the left ventricle during the first 5 months of postnatal life. Values are expressed as mean ± SD.

The increase in myocyte diameter with maturation is also accompanied by lengthening of myocytes in the ventricle (Fig. 3c). The rate of aggregate myocyte lengthening is greater immediately after birth, when both myocyte hypertrophy and hyperplasia occur simultaneously (3). On the other hand, the straight portion of the graph appears to be related to myocyte enlargement alone. The apparent difference in the pattern of growth of ventricular area (Fig. 2b) and myocyte length (Fig. 3c) in the early stages of postnatal development most likely reflects the contribution of myocyte hyperplasia not only to the overall increase in myocyte length, but also to the process of wall thickening by the addition in parallel of new myocytes within the ventricular wall.

At a cellular level, the composition of myocyte cytoplasm changes rapidly after birth (4,11). Significant increases have been found in the volume fractions of mitochondria and

myofibrils, contributing to the maturation of muscle cell function (12). Adult levels are reached shortly after birth (4) and the greater concentration of myofibrils has been found to parallel the increased compliance of the myocardium during development (13).

Relation between myocardial blood flow and cell growth. The increasing work capacity of the myocardium during maturation, which results from a continuous augmentation in cardiac mass, requires an adequate oxygen supply to the muscle cells. Myocardial blood flow becomes progressively greater in the postnatal period (14), and the functional capacity of the tissue reaches adult values at approximately 3 weeks (4). Quantitative analysis of the structural variables of the capillary bed has shown that capillary luminal volume and surface increase linearly with age (Fig. 4a and b). These changes accompany the expansion of the myocyte compartment of the ventricle from 2 to 5 months of age, and maintain capillary luminal volume and surface per unit volume of myocytes nearly constant in the adult heart (15). In the first month of postnatal life, however, capillary growth exceeds myocyte growth (15).

Capillary proliferation is an important aspect of the adaptive development of the microvasculature. The augmentation of the aggregate capillary length in growing myocardium means that larger ventricles possess greater total capillary lengths (Fig. 4c). From the value of the slope it can be seen that there is an average capillary lengthening of 23 m/day during the time interval analyzed. It would be an oversimplification, however, to identify the changes in total capillary length with capillary proliferation (4), because the mean length of a capillary unit is unknown. Additional indexes of capillary proliferation during development have also been found by analysis of the changes in capillary density, capillary to myocyte ratio and the number of capillary profiles across the ventricular wall (1,4,15).

Pressure Overload Hypertrophy

Increasing pressure load in the adult rat heart induces concentric ventricular hypertrophy in which wall thickness increases without chamber enlargement (7). Different degrees of hypertrophic growth in the various layers of the free wall of the left ventricle, interventricular septum and papillary muscles have been reported after pressure overload hypertrophy (2). The papillary muscle, because of its easily dissectable elongated form and highly oriented histologic structure, is often used as a simplified model for the quantitative estimation of the structural mechanisms implicated in pressure hypertrophy (16).

Myocardial changes during pressure hypertrophy. Constriction of the abdominal aorta in rats leads, in 8 days, to a 51% increase in the mass of the papillary muscle that results from a corresponding increase in mean cross-sectional area with no change in length (Fig. 5a to c). This gross adaptation is accompanied by similar changes of the myocyte population in which a 53% cellular enlargement (Fig. 5d) is essentially identical to the 55% augmentation in average myocyte transverse area (Fig. 5e). This lateral

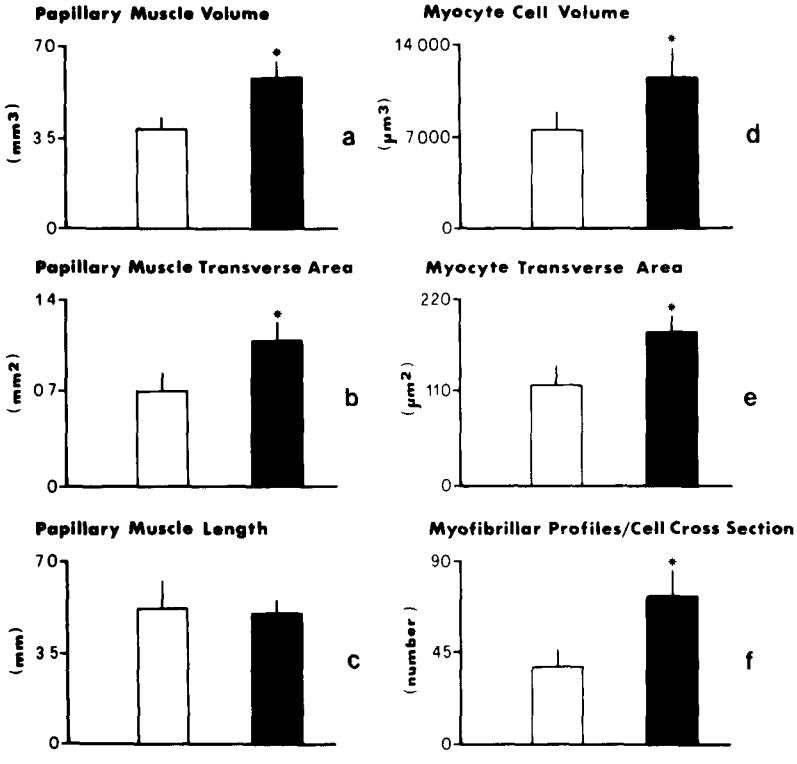

Figure 5. Effects of 8 days of aortic constriction on the dimensional properties of the papillary muscle and its myocyte population. Values are expressed as mean ± SD. **Bars** show the comparison between control rats (**white**) and experimental rats (**black**). *Statistically significant differences.

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expansion of myocytes is characterized by a significant increase in contractile material produced entirely by hyperplasia of myofibrillar units through the parallel addition of newly formed structures of approximately the same size (16). Thus, the number of myofibrillar profiles per cell cross section expands by 84% (Fig. 5f). It has been speculated that myofibrillar growth involves the accumulation of myofilaments at the surface of existing bundles (17) which subsequently split to form new myofibrils (18). The maintenance of myofibrillar size may be due to the existence of a critical perimitochondrial radius that is needed to supply ATP to the contractile proteins (19).

The pattern of myocyte growth in pressure hypertrophy is consistent with the concept of concentric hypertrophy in the intact ventricle. The adaptation in the dimensional properties of myocytes may be interpreted as a compensatory response of the myocardium at the cellular and subcellular levels of organization that tends to minimize the effects of an increased pressure load on the heart. According to the law of LaPlace, the greater myocyte diameter would produce a proportional thickening of the wall that should offset the higher peak systolic wall stress resulting from the elevation in pressure (7). Furthermore, the pattern of myofibrillar growth observed in papillary muscle myocytes supports the hypothesis that short-term increase in systolic wall stress produces a parallel replication of sarcomeres in the cell cytoplasm (7).

Reduced mitochondrial to myofibrillar volume ratio. Reduction of the mitochondrial to myofibrillar volume ratio is a consistent subcellular alteration that occurs in myocytes after pressure overload hypertrophy (2,19). As the generation of ATP in the mitochondrial cristae represents the primary source of energy for myofibrils, the general decrease in the mitochondrial to myofibrillar ratio may impair energy supply and eventually compromise heart muscle function. Early in the hypertrophic response, however, mitochondrial growth exceeds myofibrillar growth, leading to a transitory elevation of the mitochondrial to myofibrillar volume ratio (20) that is associated with the prevailing synthesis of mitochondrial membranes (21).

Adaptations of the capillary bed in pressure hypertrophy. The work potential of muscle myocardial tissue is clearly dependent on its blood supply. Thus, the hypertrophic response of the myocytes must be related partly to the capillary microvasculature, as higher metabolic requirements are needed to meet the needs of enhanced cell growth and increased function. The principal structural variables of the capillary network that are functionally relevant to tissue oxygenation are the aggregate capillary luminal volume and surface within the tissue (5). The former is related to the total capillary blood volume available for gas exchange in the myocardium, whereas the latter represents the capillary area available for oxygen transport from the blood to the tissue.

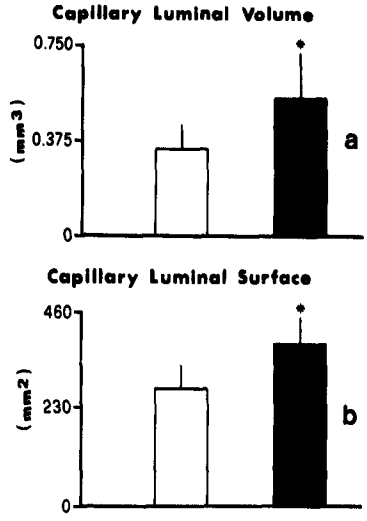


Figure 6. Changes in the total volume (**a**) and surface (**b**) of capillaries in the papillary muscle 8 days after aortic stenosis. See Fig. 5 for explanation of **open** and **solid bars.**

Adaptations of the capillary bed after pressure overload include significant increases in both capillary luminal volume and surface (Fig. 6) that are of the same order of magnitude as the expansion in myocardial mass (2,22). The determinants of these capillary variables are the length of the capillary network and the capillary mean cross-sectional area (10). Capillary length is not significantly affected by an increase in systemic arterial pressure, suggesting that capillary proliferation does not occur in pressure hypertrophy of adult myocardium (16,23). On the other hand, the average size of capillaries has been found to be consistently larger (2). This increase in the transverse luminal area of the average capillary compensates for the inadequate lengthening of the capillary microvasculature, and allows for the maintenance of capillary luminal volume and surface in the enlarged ventricle (2,16,23). These observations agree with measurements showing that coronary blood flow in cardiac hypertrophy increases in proportion to the mass of muscle and the work it must perform (24). An insufficient growth of capillaries, however, has been reported in renal and spontaneous hypertension (25,26).

Volume Overload Hypertrophy

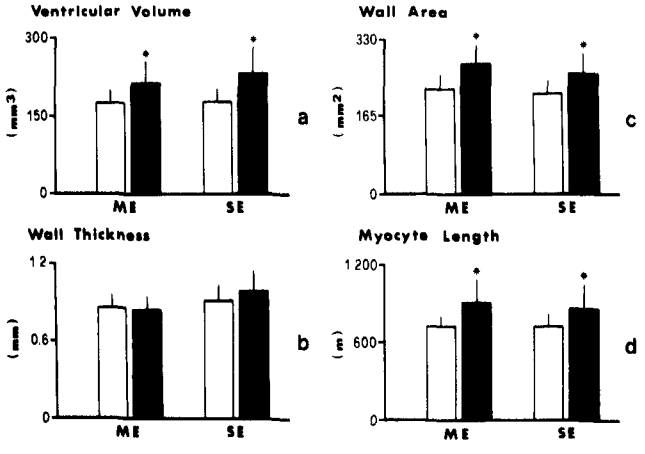
An increasing volume load of the heart induces enlargement of the ventricular chamber without a relative increase in its wall thickness, that is, eccentric hypertrophy (7). Adaptation to exercise is specific for a given model of physical activity (27) and events requiring dynamic exercise and endurance training are accompanied by an elevated preload, a functional condition that progresses into eccentric hypertrophy. In the last two decades, several studies have analyzed the morphologic changes in the myocardium after

exercise to determine whether the improvement in functional performance (28) is paralleled by corresponding adaptations of the structural variables of both myocytes and capillaries (8,29–33). In particular, the effects of moderate and strenuous running exercise on the rat heart are presented to demonstrate that this type of volume hypertrophy can be viewed as a form of induced growth in which components of incomplete compensation may constitute an interface between physiologic and pathologic hypertrophy. The significance of these morphologic changes can only be properly assessed by functional and metabolic correlated studies, in that the knowledge of length and size of the capillaries may not have a significant functional advantage or limitation.

Effect of running and strenuous exercise on ventricular growth. A moderate exercise running program and a more strenuous physical regimen result in 22 and 31% hypertrophy of the right ventricle , respectively, after 8 weeks (Fig. 7a). The weight of the left ventricle also increases by 7 and 12%, respectively (8,31). The differential growth rate between the ventricles may be explained by the fact that when the primary stimulus is volume overload, the elevation in diastolic wall stress per unit volume of tissue will be relatively greater in the right ventricle because of its smaller total number of myocytes, lesser mass and thinner wall (8,31,32).

Ventricular growth occurs without a significant change in wall thickness (Fig. 7b), which results in an approximate 20% expansion of ventricular area in both moderate and strenuous exercise (Fig. 7c). Chamber enlargement appears to be brought about through lengthening of myocytes by replication of sarcomeres in series (7). This is strongly suggested by the 22% average increase in the aggregate length of these cells (Fig. 7d) with only slight variations in cross-sectional area and no change in sarcomere length (8,31,32). Lengthening of myocytes would counteract the greater end-diastolic wall stress (7) by contributing to the enlargement in chamber volume that would otherwise have occurred by spatial rearrangement or lateral slippage of myocardial fibers within the wall, or both. Slippage of myocardial fibers with alteration in the layering of myocytes may be implicated in the dilation of the ventricular chamber in the failing heart (34,35). A similar mechanism has been shown to account for thinning of the wall produced by increasing filling pressure of the ventricle in vitro (36). The sequence of structural events that characterize the transition from compensated hypertrophy to overt cardiac failure with enlargement of the ventricular chamber remains to be determined quantitatively.

Figure 7. Effects of exercise on the volume (**a**), wall thickness (**b**), wall area (**c**) and total myocyte length (**d**) of the right ventricular myocardium. Values are expressed as mean ± SD. **Bars** show the comparisons between sedentary rats (**white**) and exercised rats (**black**). ME = moderate exercise; SE = strenuous exercise. *Statistically significant differences.



Effect on mitochondrial to myofibrillar ratio. The volume fractions of mitochondria and myofibrils remain nearly constant with exercise (8,31). The maintenance of a constant mitochondrial to myofibrillar volume ratio has been repeatedly shown in several models of volume overload hypertrophy (2), although there is one report in which the volume percent of mitochondria was found to be decreased after aortocaval fistula in dogs (37). The changes in the dimensional properties of myocytes with a commensurate growth of the cytoplasmic structures responsible for energy production and utilization may constitute the morphologic counterpart for the normal or improved contractile (38) and relaxation (39) properties of the myocardium in volume overload hypertrophy.

Effect on capillary network. In contrast to the balanced growth adaptation of myocytes after exercise, the capillary network may not expand in proportion to the muscle mass. A relative deficiency in capillary luminal volume and surface in the ventricle has been found after aortocaval fistula or intense physical training (8,33,40). On the other hand, a moderate exercise regimen and pacing of the heart both produce a significant increase in capillary concentration within the myocardium, resulting in augmentations of capillary volume and surface that exceed ventricular growth (31,41). Moderate exercise hypertrophy is associated with increases in total capillary volume, surface and length (Fig. 8). The increases in surface and length are greater than ventricular growth (22%) (Fig. 7a). In contrast, after strenuous exercise capillary luminal volume remains nearly constant and the absolute increases in capillary surface and length are less than the 31% overall growth of the ventricle (Fig. 7a).

The morphometric differences in the capillary vasculature after moderate and strenuous exercise can be explained by the presence or absence of capillary proliferation, as shown by corresponding changes in the length of the capillary bed. The increased endothelial luminal surface after moderate exercise suggests that this form of physical activity may have a protective effect against ischemic episodes as insertion of new capillaries among myocytes increases the

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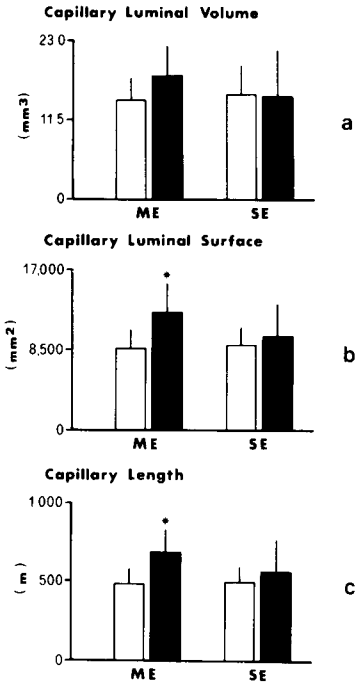


Figure 8. Effects of exercise on total volume (**a**), surface (**b**) and length (**c**) of capillaries in the right ventricle. Abbreviations as in Fig. 7.

ratio of capillary profiles to myocyte profiles (30,31) and effectively decreases the average diffusion distance for oxygen from the capillary wall to the surrounding tissue (31). On this basis, the inadequate compensation of the capillary bed after strenuous exercise results in alterations of the structural properties of the microvasculature that may impair oxygen availability, diffusion and transport (8,32,33). Thus, excessive volume overload hypertrophy may lead to a conditioned state that leaves the myocardium more susceptible to ischemia.

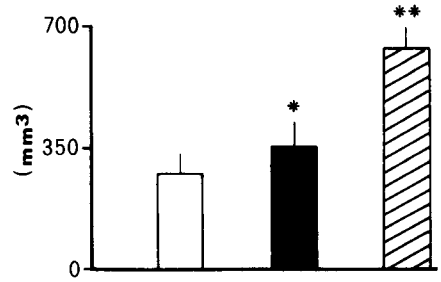
Reactive Hypertrophy

Reactive hypertrophy occurs in a large variety of myocardial conditions, such as ischemic cardiomyopathy or acute myocardial infarction (42), in which muscle cells are lost in a diffuse or focal manner. In contrast to volume and pressure hypertrophy, reactive ventricular hypertrophy during or after recovery from infarction cannot be estimated on the basis of tissue weight or volume measurements alone. Scar formation, the contraction of necrotic tissue with time and cellular hypertrophy in the surviving myocardium all represent dynamic processes that continuously change the proportions of viable and nonviable myocardium in the ventricle (43–45). These limitations have recently been resolved by a new morphometric methodology that allows the estimation of infarct size through the measurement of the percent loss of myocyte nuclei in the infarcted ventricle (43–45). Because the number of nuclei within the surviving myocytes does not change in adult rats (1,43), the fraction of nuclei lost from the whole ventricle is a valid measure of the fraction of tissue destined to become necrotic after coronary occlusion. Thus, from the original volume of the ventricle, this fraction defines the initial volumes of infarcted and spared myocardium from which their subsequent changes in volume can be calculated (43–45).

Effects of myocardial infarction. With this approach it has been demonstrated that infarction affecting 50% of the left ventricle evokes an immediate reaction in the spared myocardium that results in a 29% tissue hypertrophy in 3 days (Fig. 9), despite the presence of heart failure (44). However, a substantial residual deficit in muscle volume is still present at this time, because the magnitude of hypertrophic growth in the spared myocardium is significantly less than the muscle volume of noninfarcted animal hearts (Fig. 9). Ventricular hypertrophy progressively increases during the evolution of the healing process, but because compensation for these large infarcts cannot be achieved by the surviving myocardium (43), heart failure persists (46). In humans, infarcts involving 40% or more of the left ventricle lead to cardiogenic shock and irreversible myocardial dysfunction (47). Compared with the rat heart, the more limited tolerance of the human heart may be found in a coexisting vascular disease that may impair the ability of the viable tissue to offset the large destruction in muscle mass.

Until recently, it was unknown whether myocardial infarction leads to concentric or eccentric hypertrophy of the unaffected portion of the ventricle. Because alterations in ventricular geometry after infarction are produced by progressive thinning and bulging of the necrotic region (48),

Figure 9. Changes in the volume of viable myocardium after acute myocardial infarction. Values are expressed as mean ± SD. **Open bar** shows the volume of myocardium destined to survive after coronary artery ligation. **Solid bar** shows the volume of surviving myocardium 3 days after coronary artery ligation. **Shaded bar** shows the volume of myocardium in noninfarcted animal hearts. The difference between **black** and **white bars** represents the magnitude of hypertrophic growth that occurred in the spared myocardium of the infarcted rat hearts (*$p < 0.05$). The comparison between **shaded** and **black bars** gives the residual deficit of myocardial tissue in the infarcted animal hearts (** $p < 0.05$).



the anatomic criteria of chamber size and wall thickness cannot be directly applied in the analysis of factors contributing to the increase in mass of the viable tissue. On the other hand, estimation of changes in the dimensional characteristics of muscle cells provides an alternative approach for the evaluation of the structural processes implicated in the adaptive growth of the heart after myocardial infarction. On a cellular basis, hypertrophy in the infarcted left ventricle has been found to be accomplished by cellular shape changes in which increases in myocyte diameter and length both participate in the growth of the average myocyte throughout the healing process (44,49).

Changes in myocytes in infarction. Figure 10 illustrates the changes in myocyte cell volume, mean cross-sectional area, and length of the average myocyte 3 days after coronary artery occlusion. The 28% increase in myocyte volume, which is the result of a 12% increase in cross-sectional area and a 14% lengthening of the cell, is characteristic of a combination of pressure and volume overload hypertrophy. Mitochondria and myofibrils have been found to grow in proportion to the cell with the maintenance of a constant mitochondrial to myofibrillar volume ratio (45).

Loss of cardiac cells in the ventricle can be expected to result in a greater stress on the remaining viable myocytes that is proportional to the amount of myocardial cell loss. To reduce the magnitude of systolic stress, myocytes would tend to hypertrophy by increasing their mean diameter (42). In addition, physiologic studies performed over several weeks in the dog heart have shown a progressive increase in end-diastolic segment lengths in the normal regions of infarcted ventricles (50). Similar adaptations have been observed in chronic volume overloaded left ventricles (51), in which lengthening of myocytes contributes to the enlargement in chamber volume (7).

Capillary vasculature response to infarction. Recent morphometric studies have analyzed the growth response of the capillary network in infarction-induced hypertrophy to determine whether the increase in muscle mass is accompanied by an adequate expansion of the capillary microvasculature (45,52). It was shown that the greater work load sustained by the ventricle is not supported by an equivalent expansion of the capillary bed either immediately (45) or at the completion of the healing process (52). Capillary luminal volume, surface and length did not expand in 3 days, demonstrating a lag in the adaptive growth of the microvasculature with respect to the myocytes (Fig. 11). Because of these alterations, the hypertrophied infarcted ventricle can be expected to be more vulnerable to subsequent ischemic episodes, a condition commonly present in humans.

Conclusions

Physiologic growth of the rat myocardium represents a combination of concentric and eccentric hypertrophy in which the capillary microvasculature, parenchymal cells and the subcellular components of myocytes all grow in proportion

Figure 10. Changes in the dimensional properties of spared myocytes 3 days after coronary artery ligation. Values are expressed as mean ± SD. **Bars** show the comparison between sham-operated control rats (**white**) and animals with infarction (**black**). *Statistically significant differences.

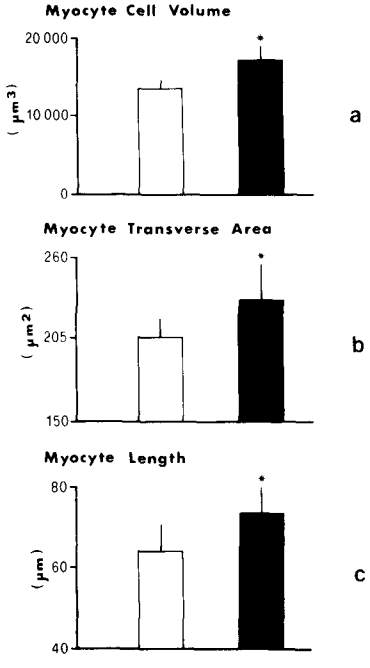
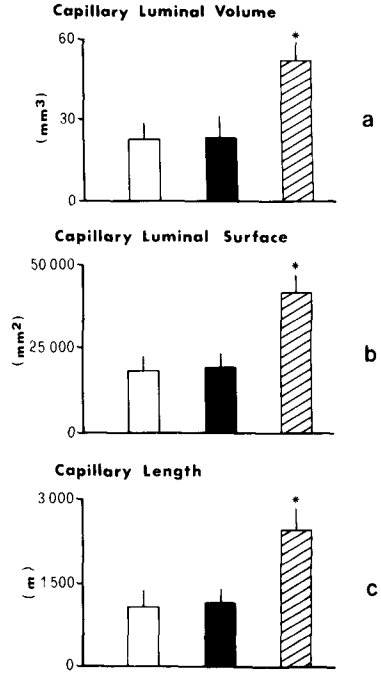


Figure 11. Adaptation of the capillary microvasculature in the spared myocardium 3 days after myocardial infarction. *Statistically significant differences.



to the expansion in cardiac mass. In contrast, experimental cardiac hypertrophy of the adult rat heart shows disproportionate growth adaptations that may involve either the capillary network, the myocyte population, or both. In exercise-induced hypertrophy there is a greater hypertrophy of the right versus the left ventricle because in volume overload there is greater effect of increased wall stress in the lesser mass and thinner wall of the right ventricle.

Capillary proliferation is not a consistent adaptive mechanism of the enlarging heart in pressure overload hypertrophy, severe volume overload hypertrophy and in the reactive hypertrophy associated with myocardial infarction. In contrast to the developing heart, the inadequate growth of capillaries may cause alterations of the structural properties of the capillary network responsible for tissue oxygenation that could increase the vulnerability of the hypertrophied myocardium to ischemic episodes.

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