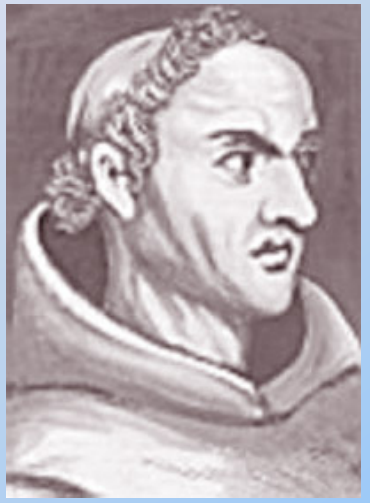


William of Occam.
14th century Franciscan friar

Occam's Razor

Shaves off unnecessary complexities.

When two solutions come to the same conclusion, the simpler solution is the better.

The Conventional Wisdom & Occam's Razor

Ventricular function usually and simplistically refers to *acquired* disease of a *two chambered heart* in which a morphologic *left ventricle* is in the *subaortic* position.

Is this an example of the principle of Occam's razor?

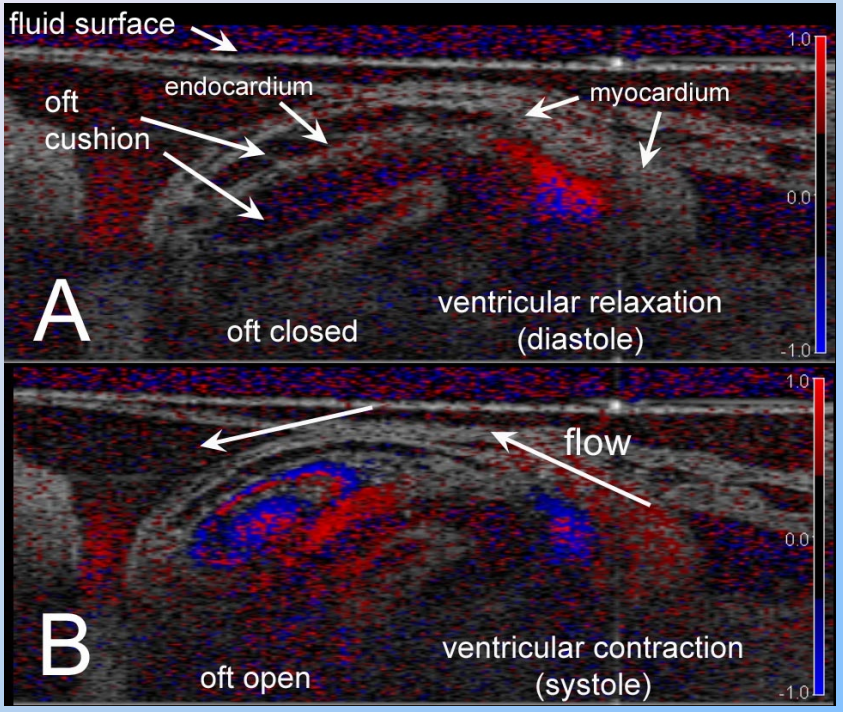
A Non-Occam Look at Ventricular Function

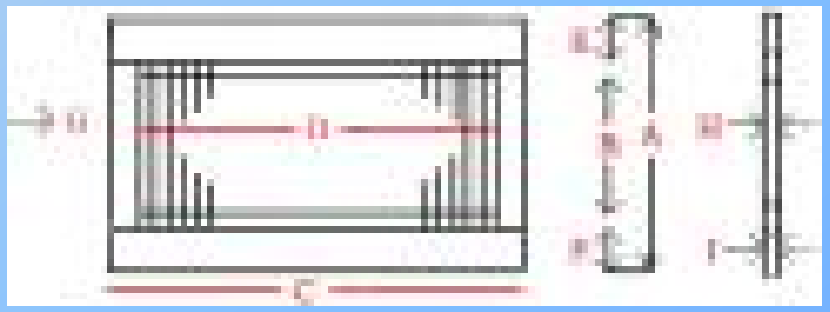
The Complex Determinants of Systolic & Diastolic Function in Congenital Heart Disease

The heart cannot function without beating.

But the heart can beat without functioning.

Fluid Dynamics in a 1 mm Chick Embryo

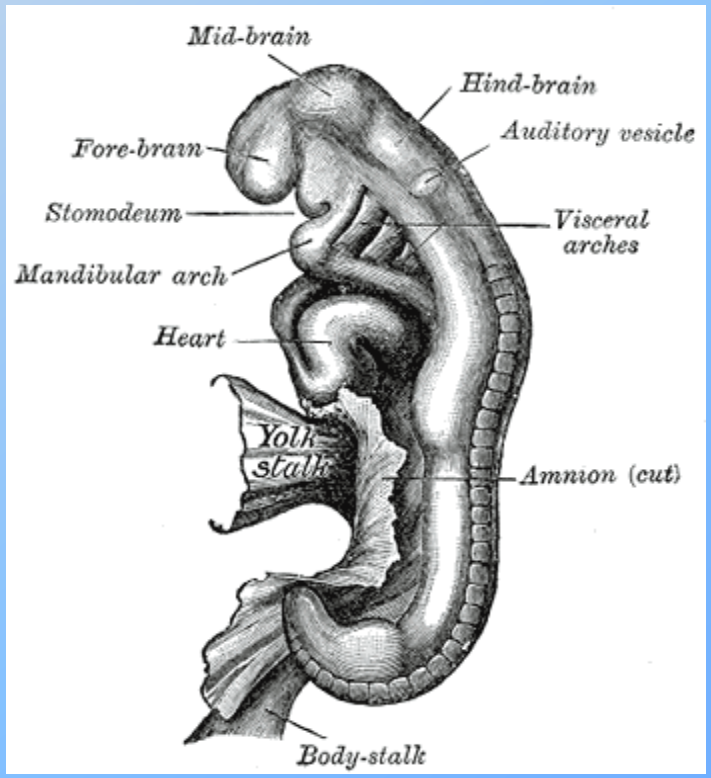




1mm scale

Perinatal Research Institute
Duke University Medical Center
Doppler Color Flow

The embryonic heart begins to beat 18 to 21 days after conception. At this stage, the heart is empty and therefore has no circulatory function. But if the beat stops, the embryo dies.



The Heart of a Human Embryo

- *Rhythmic beating of an empty embryonic heart serves to remodel the ventricles in anticipation of receiving the blood they are designed to pump.*

Variables That Determine Ventricular Function and Ventricular Mass

Cell type *–myocyte vs non-myocyte*

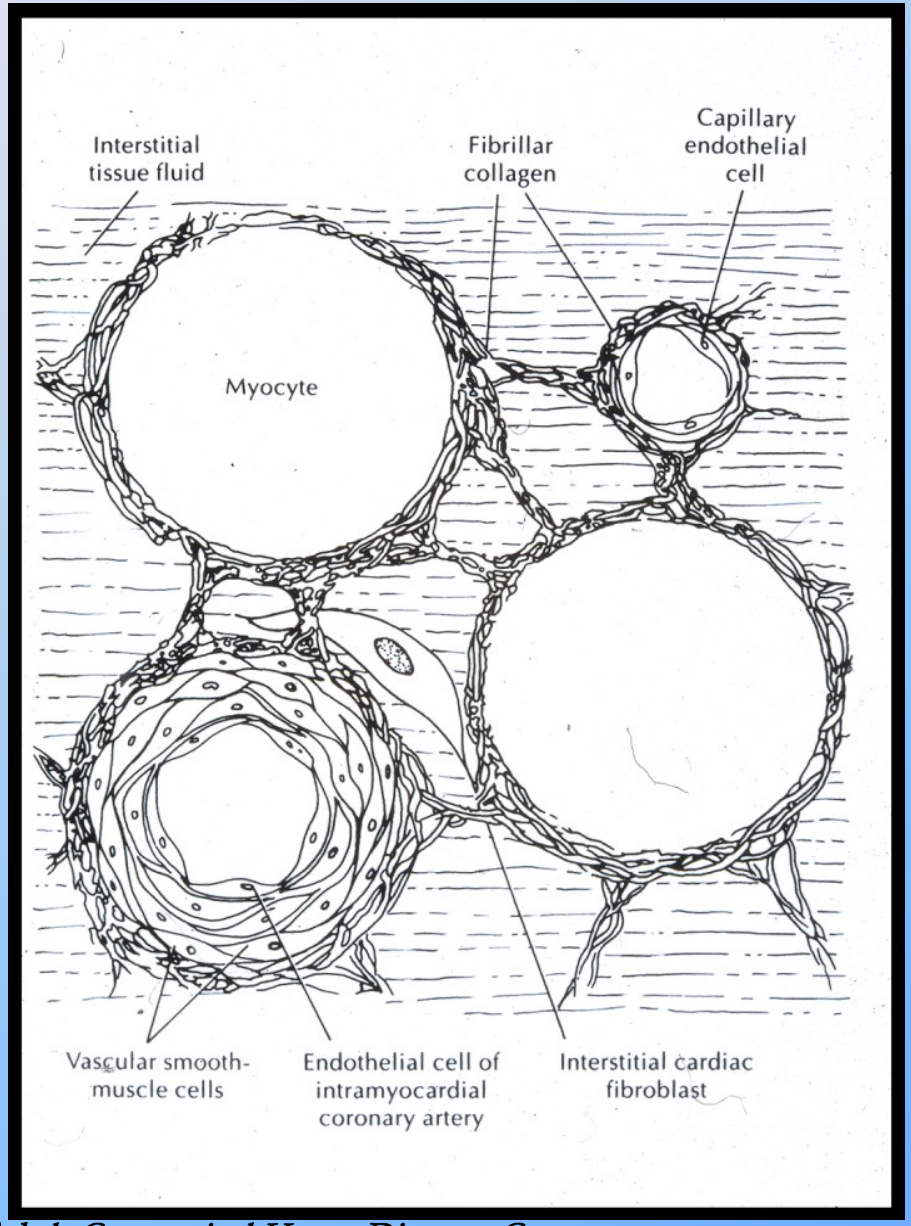
Genetic regulation *of cell populations*

Inciting stimulus *--overload/hypoxia*

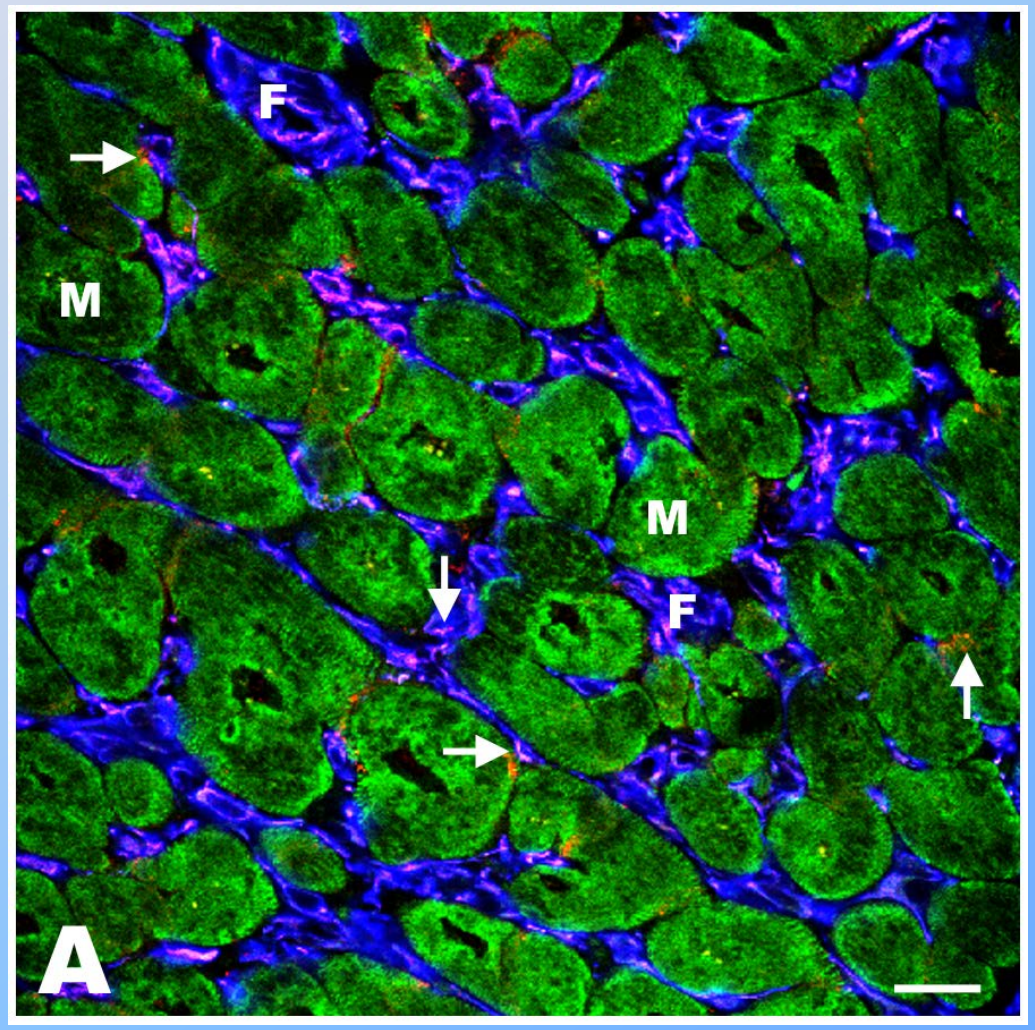
Timing of the stimulus -- immaturity vs maturity of cardiomyocytes

Hyperplasia vs hypertrophy

Myocardial Cell Types



Myocytes (M---green anti-myosin label).
Fibroblasts (F---blue anti-vimentin label).



Increased Ventricular Mass

The Inciting Stimuli

Pressure overload

Volume overload

Hypoxemia

Responses to the Inciting Stimulus

Ultrastructural:

a) *New sarcomeres in parallel*

b) *New sarcomeres in series*

Cellular:

a) *Hyperplasia* in the immature heart

b) *Hypertrophy* in the mature heart

Gross morphologic:

a) *Magnified normal geometry*

b) *Spherical geometric enlargement*

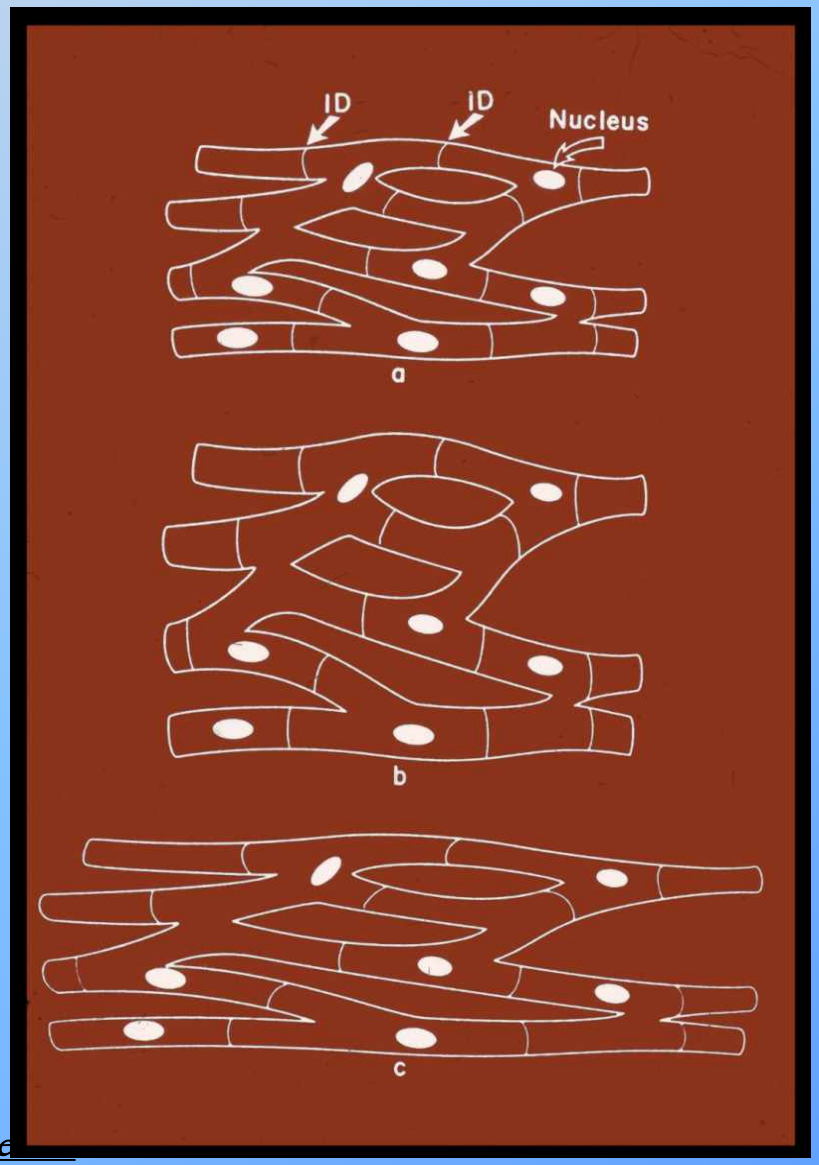
c) *Increased wall thickness*

Ultrastructural Responses to an Inciting Stimulus

Normal

New Sarcomeres
In parallel

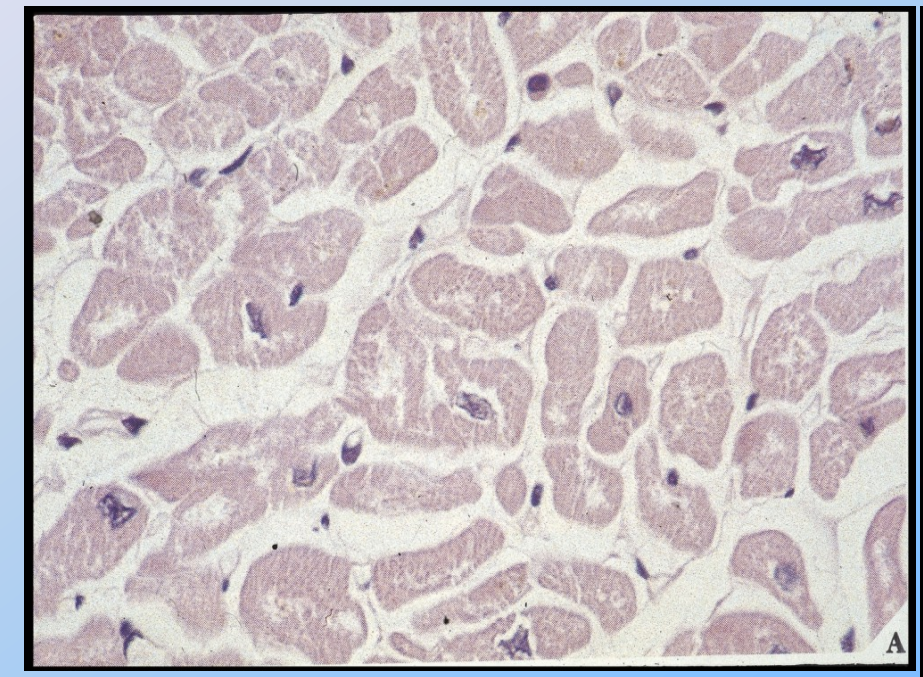
New Sarcomeres
In Series



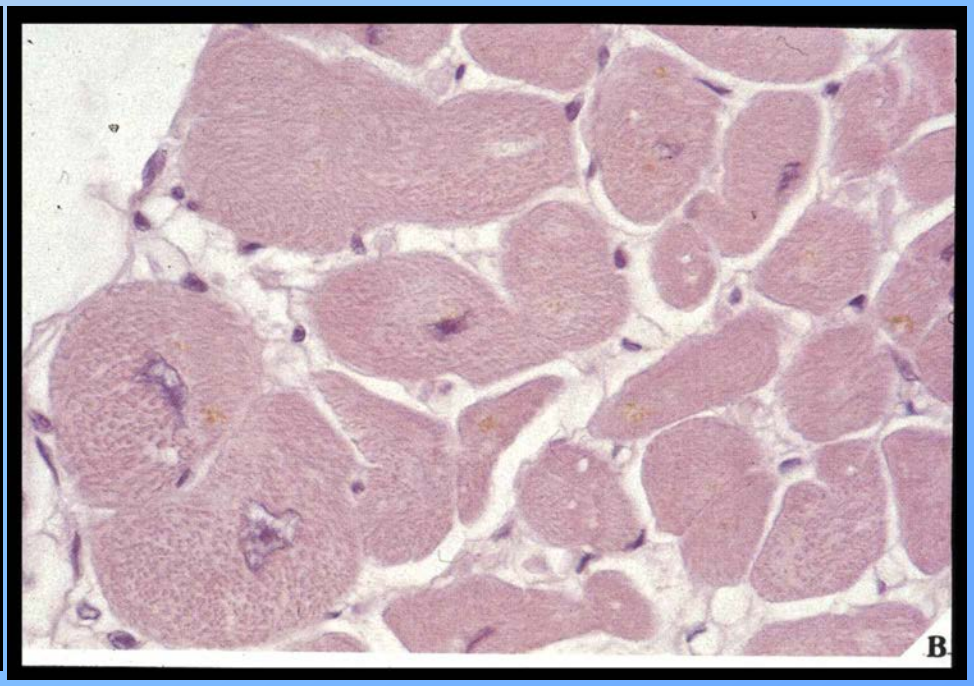
Cellular Responses to the Inciting Stimulus

- ***Immature cardiomyocytes*** *increase in number (mitotic replication, hyperplasia).*
- ***Mature cardiomyocytes*** *increase in size (hypertrophy) .*
- .

Hyperplasia
(*Increase in Cell Number*)



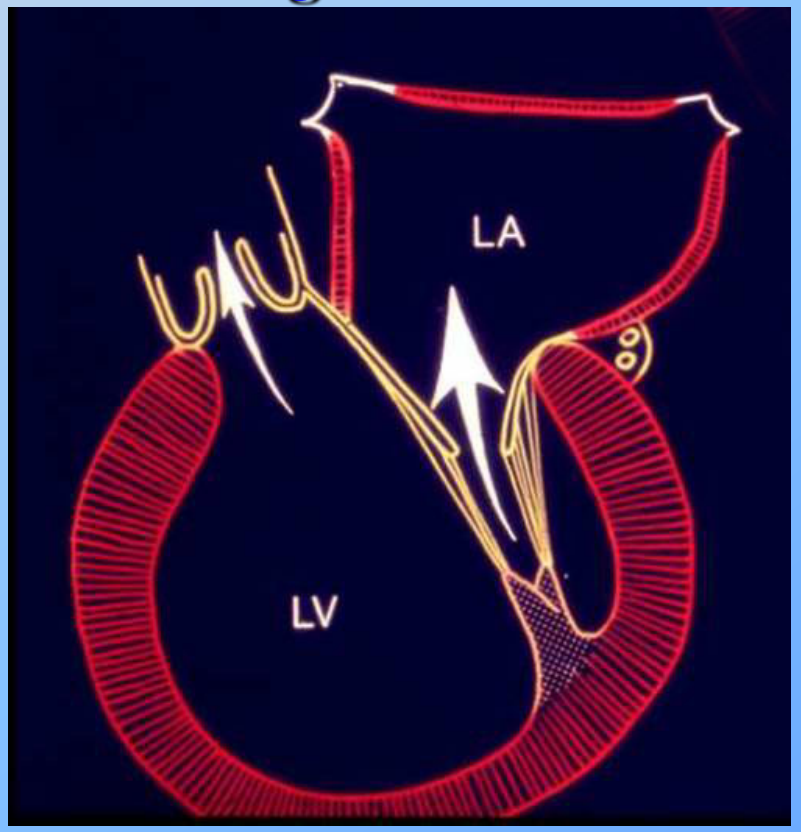
Hypertrophy
(*Increase in Cell Size*)



Gross Morphologic Response to Volume Overload

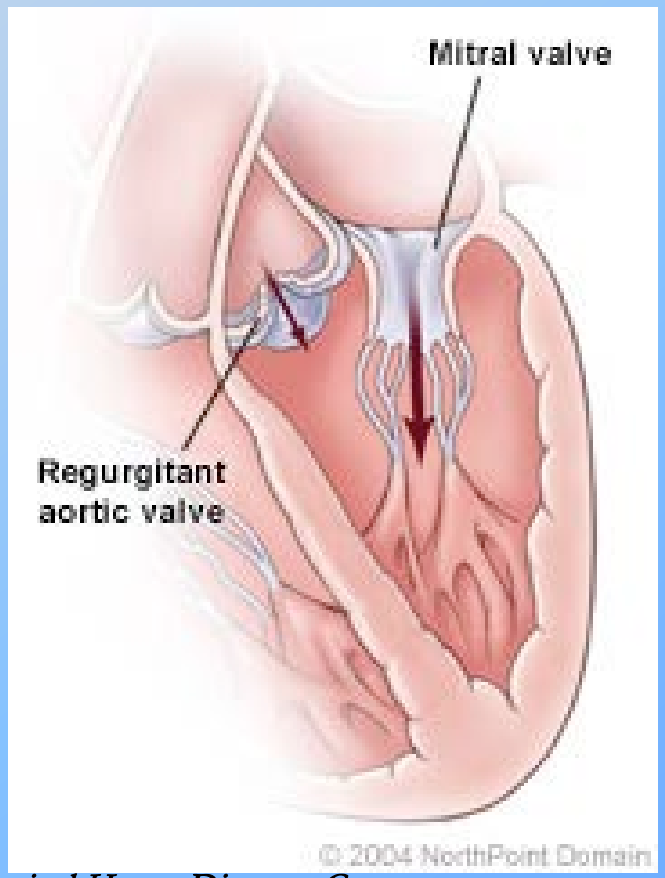
Mitral Regurgitation

Spherical Geometric Enlargement



Gross Morphologic Response to Aortic Regurgitation

Magnified Normal Geometry



Sarcomere Response to Pressure Overload

New Sarcomeres in Parallel

Increase in wall thickness

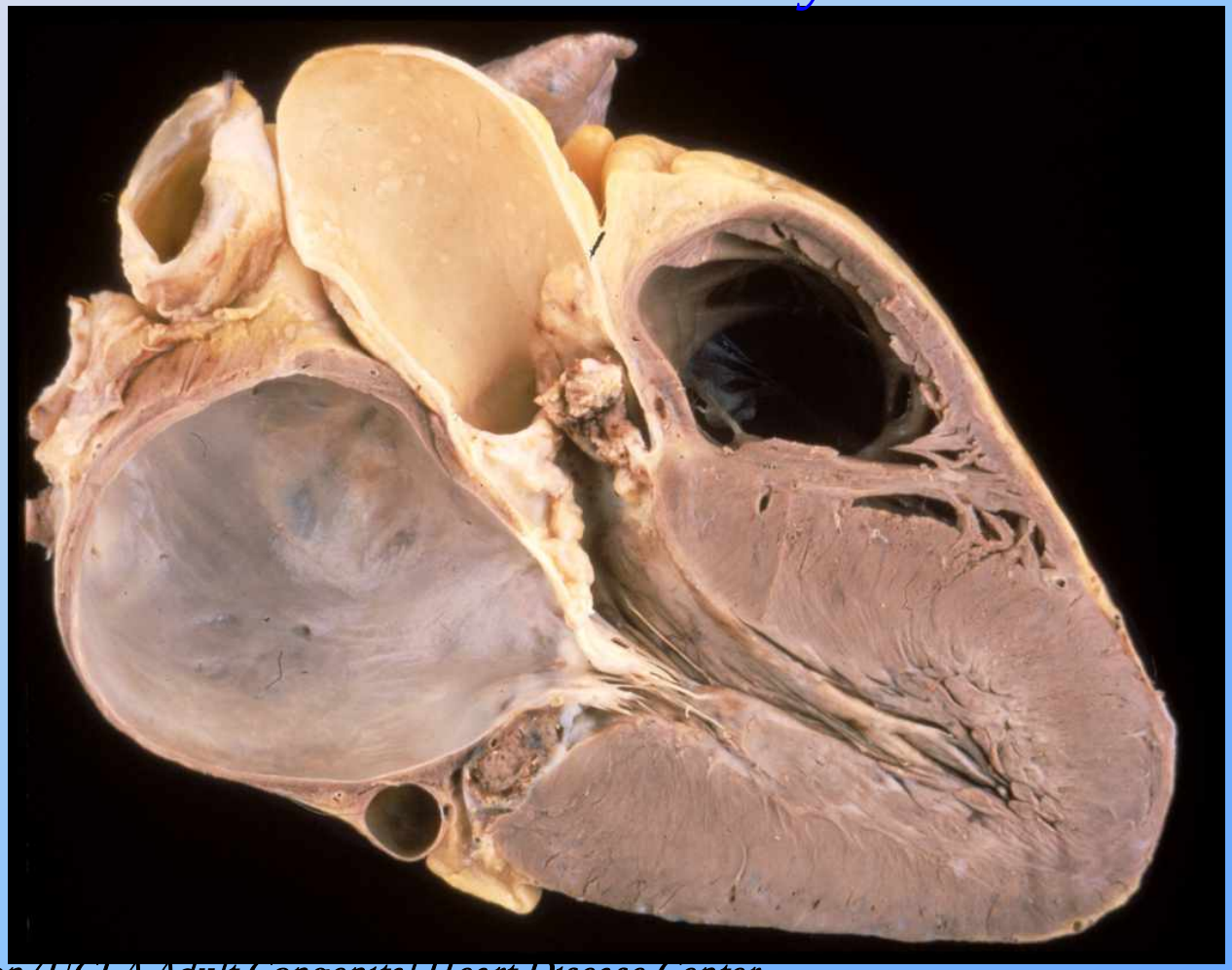
Decrease in cavity size

Pressure Overload

New Sarcomeres in Parallel

Increased Wall Thickness

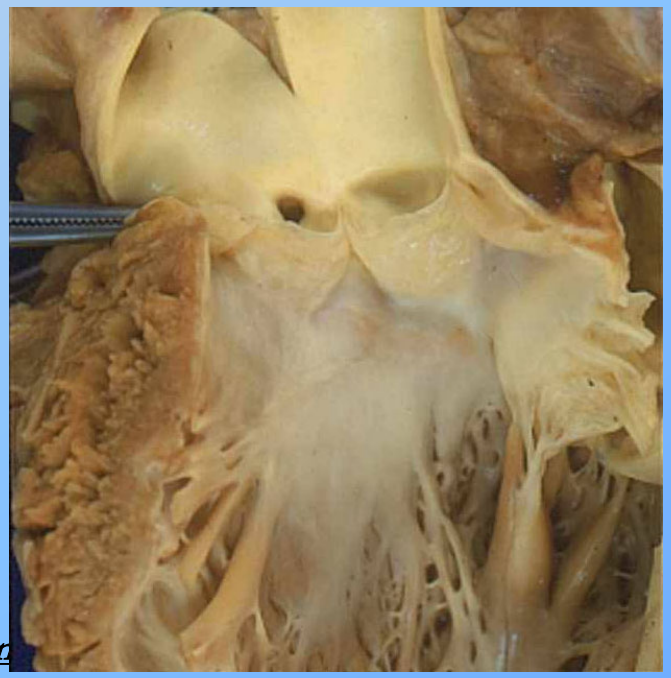
Decreased Cavity Size



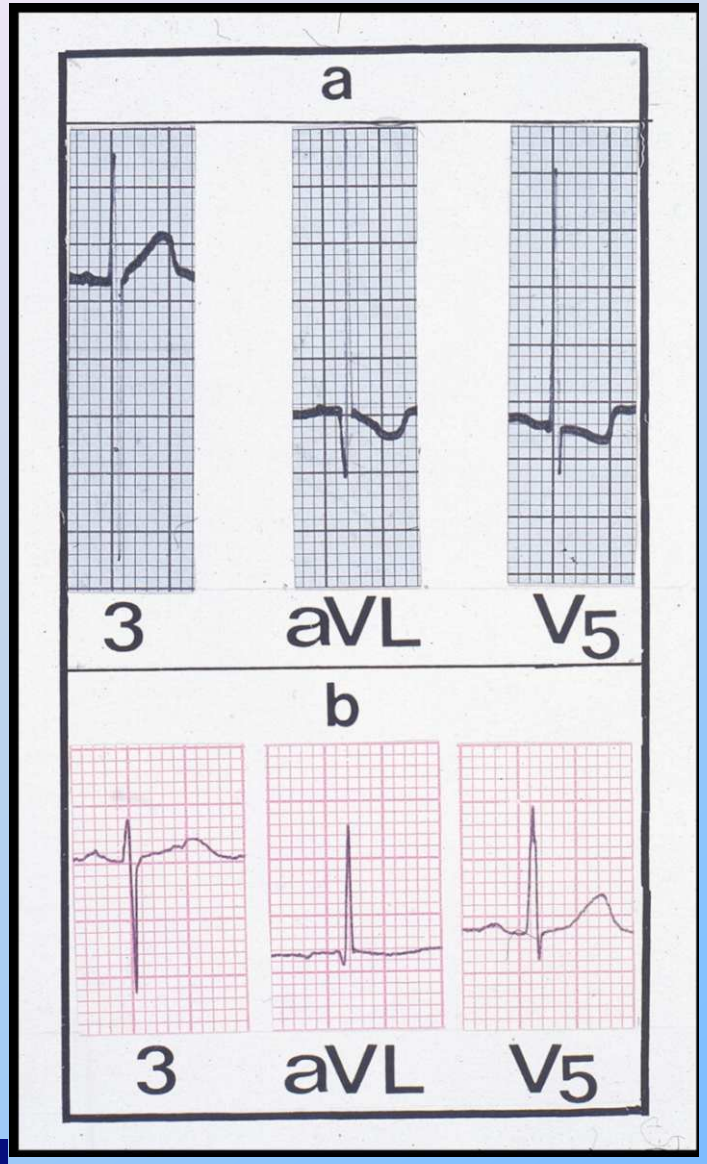
The Immature Heart
Cardiomyocyte Response to Hypoxemia

Congenital anomalies of the coronary arteries: Report of unusual case associated with cardiac hypertrophy. Am Heart J 1933

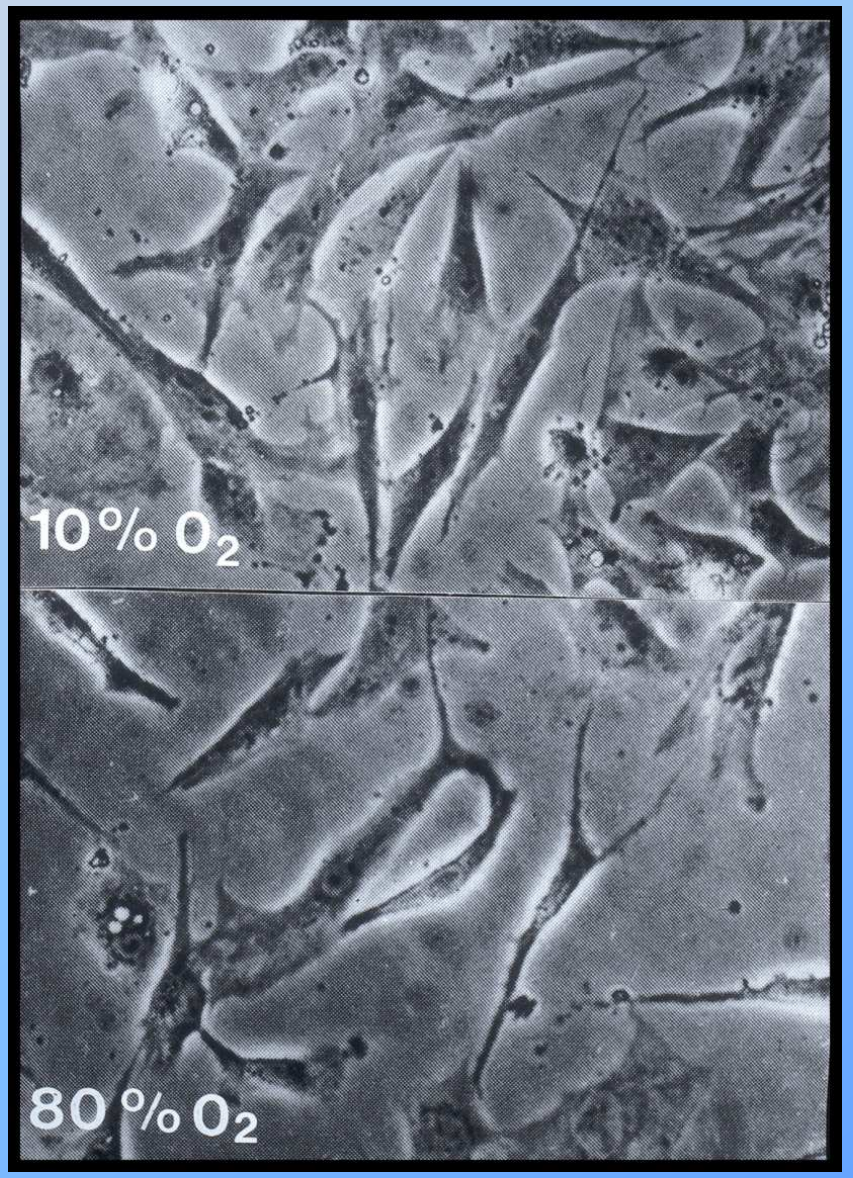
Bland, White, Garland



LCA from PT



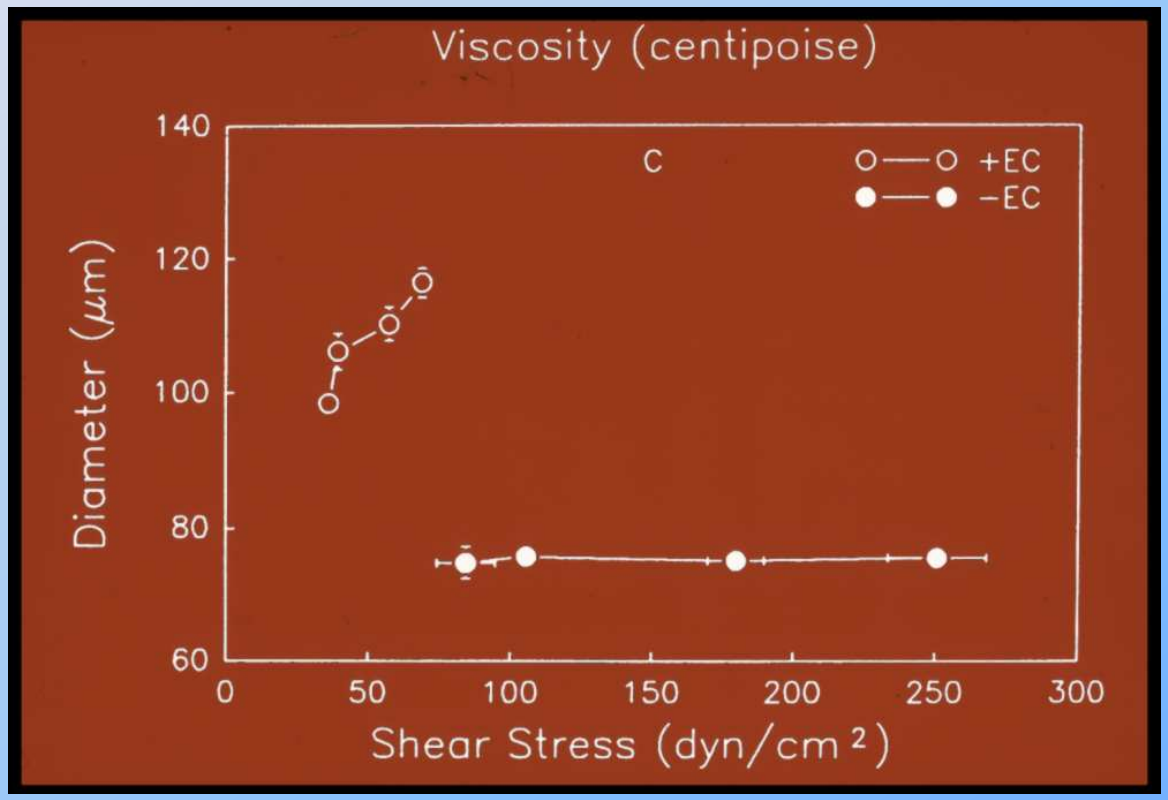
Cultured Chick Cardiomyocytes



The Coronary Circulation

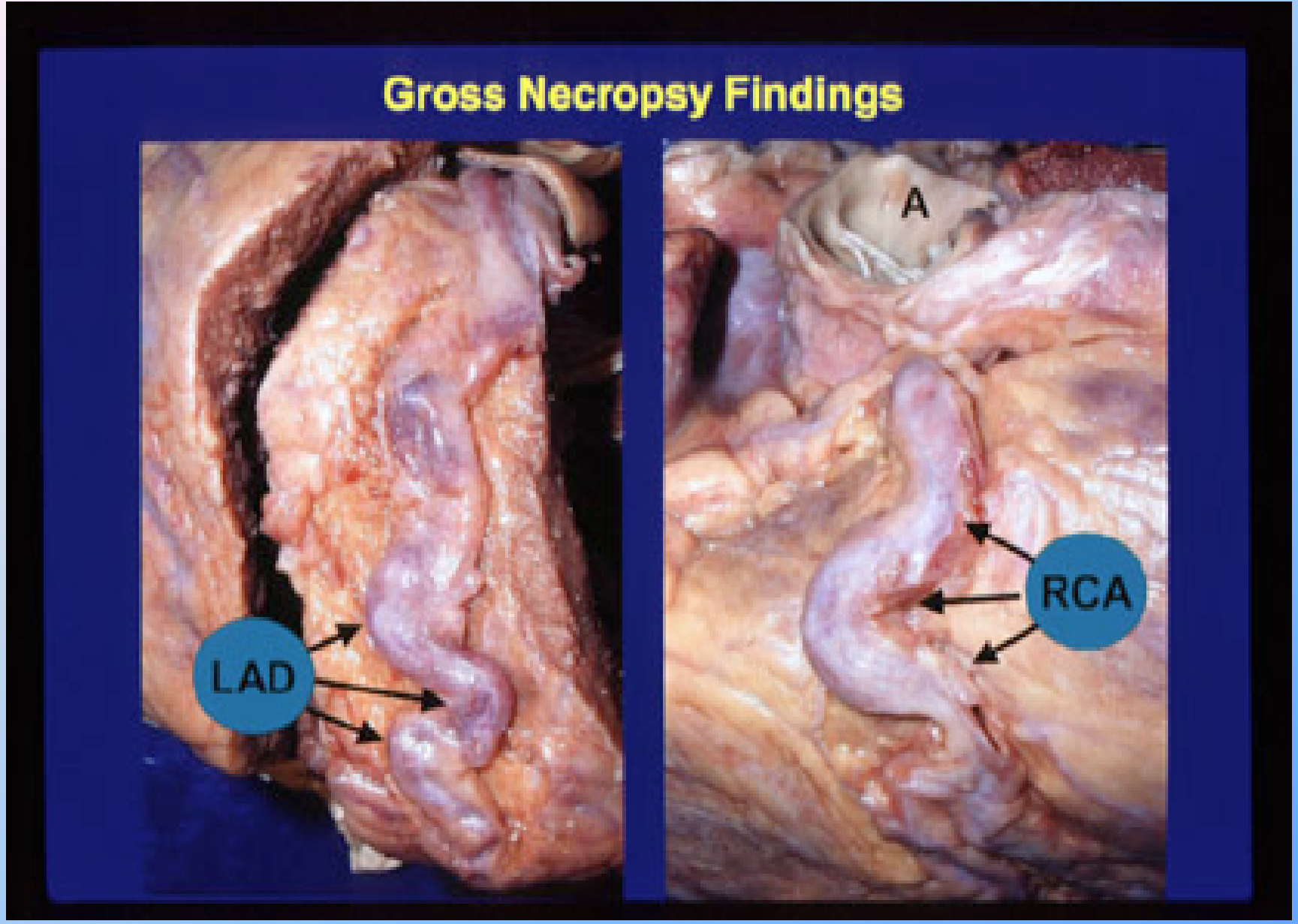
Kohler Experiment

Circulaton Research 1993



The viscous erythrocytotic perfusate in CCHD provokes an increase in endothelial shear stress and elaboration of NO which dilates the extramural coronary arteries.

Gross Necropsy Findings



Myocardial Flow Reserve

Maximal dilatation of extramural coronary arteries in CCHD implies that basal blood flow is maximal and cannot increase further.

Does the increase in basal flow encroach upon flow reserve and compromise ventricular function?

The Coronary Microcirculation

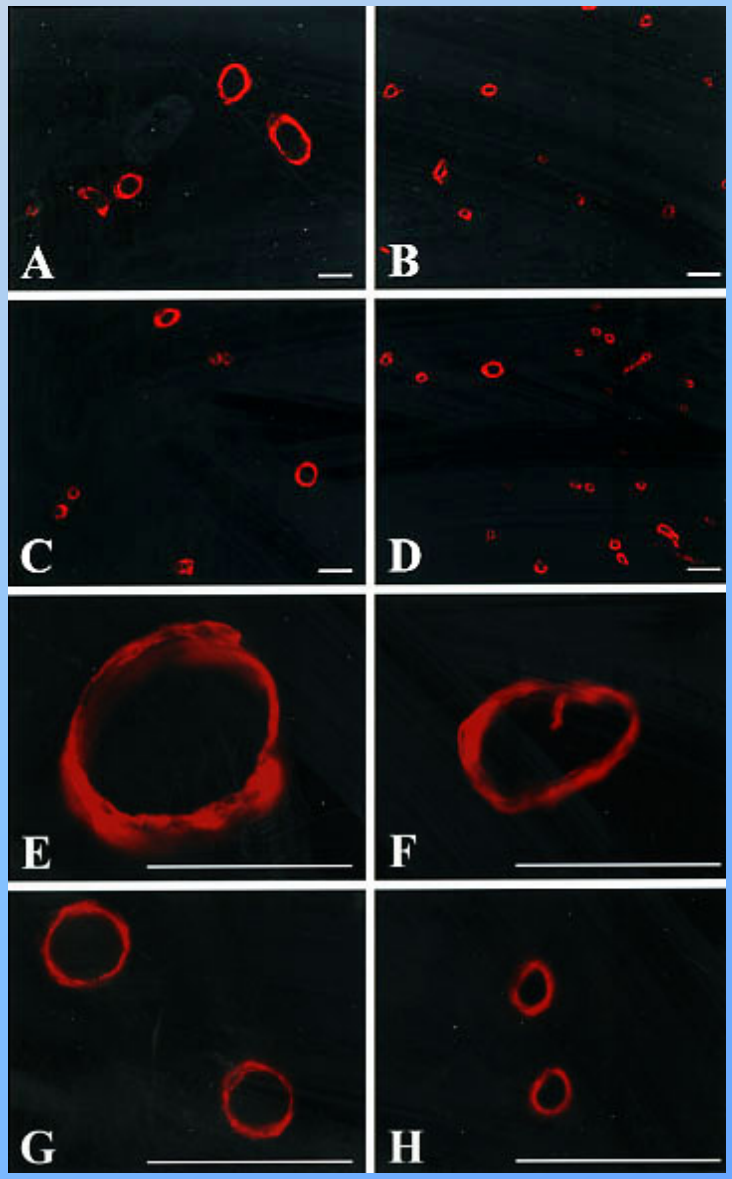
Because the extramural coronary arteries in CCHD are maximally dilated, and because myocardial oxygen extraction is maximal or nearly so, we hypothesized that preservation of flow reserve must reside in the coronary microcirculation.

Dedkov, Perloff. Circulation 2006

Morphometric Analyses of the Coronary Microcirculation in CCHD

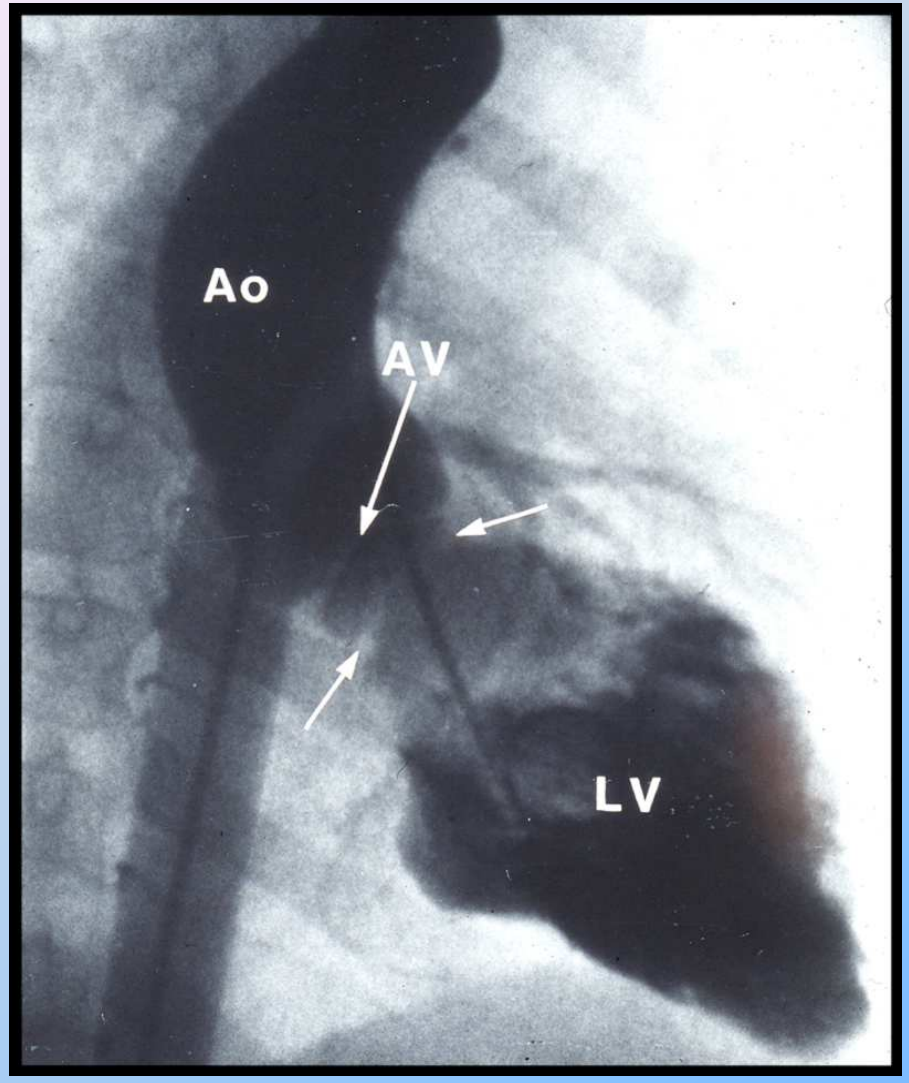
In Eisenmenger hearts (AC), terminal arterioles are fewer in number compared to hypertrophied but structurally normal hearts (BD), but have greater diameters (EG vs FH).

The decrease in length, volume and surface densities and the increased diameters indicate *remodeling of the microcirculation*.

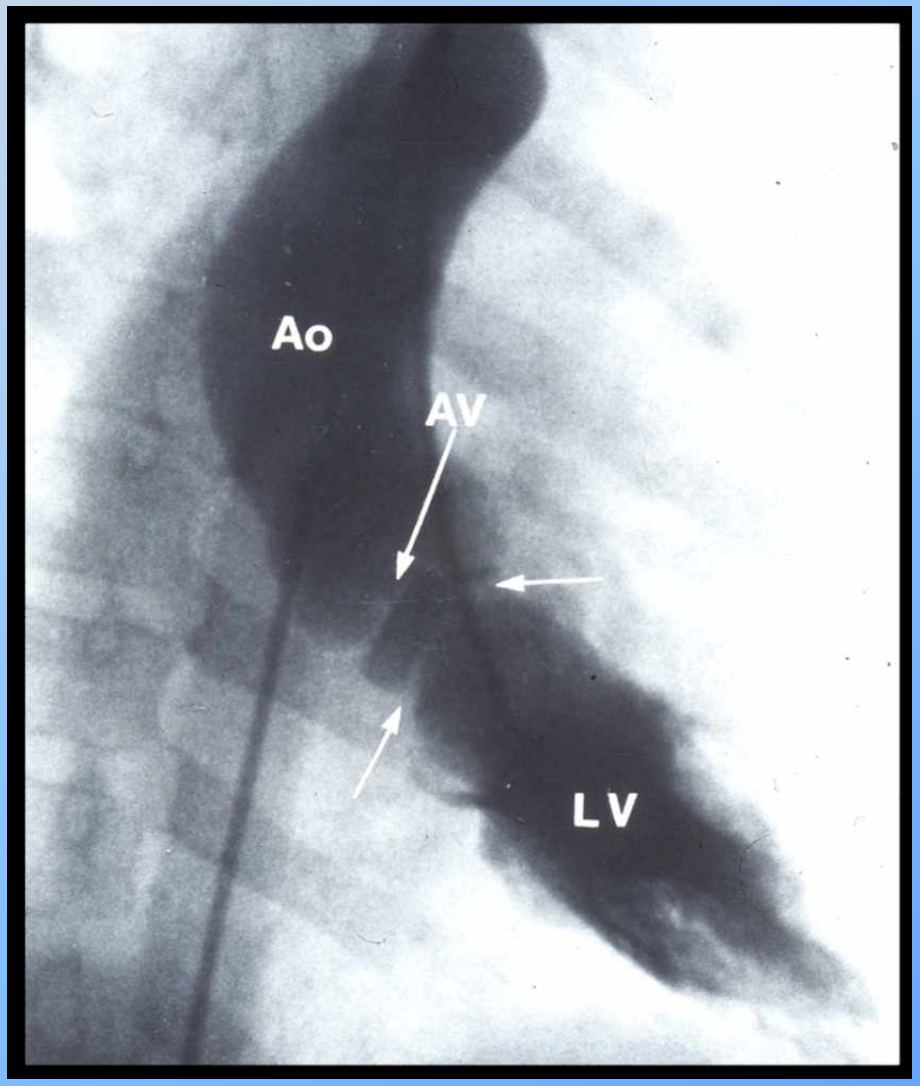


A,C,E,G Eisenmenger hearts.
B,D,F,H structurally abnormal hearts with ventricular hypertrophy

Supranormal Left Ventricular Function



Diastole



Systole

Supranormal Ventricular Contractility

Myocyte hyperplasia with capillary angiogenesis preserves capillary density.

Postoperative regression of ventricular mass leaves increased numbers of smaller myocytes with increased capillary density that result in supranormal contraction.

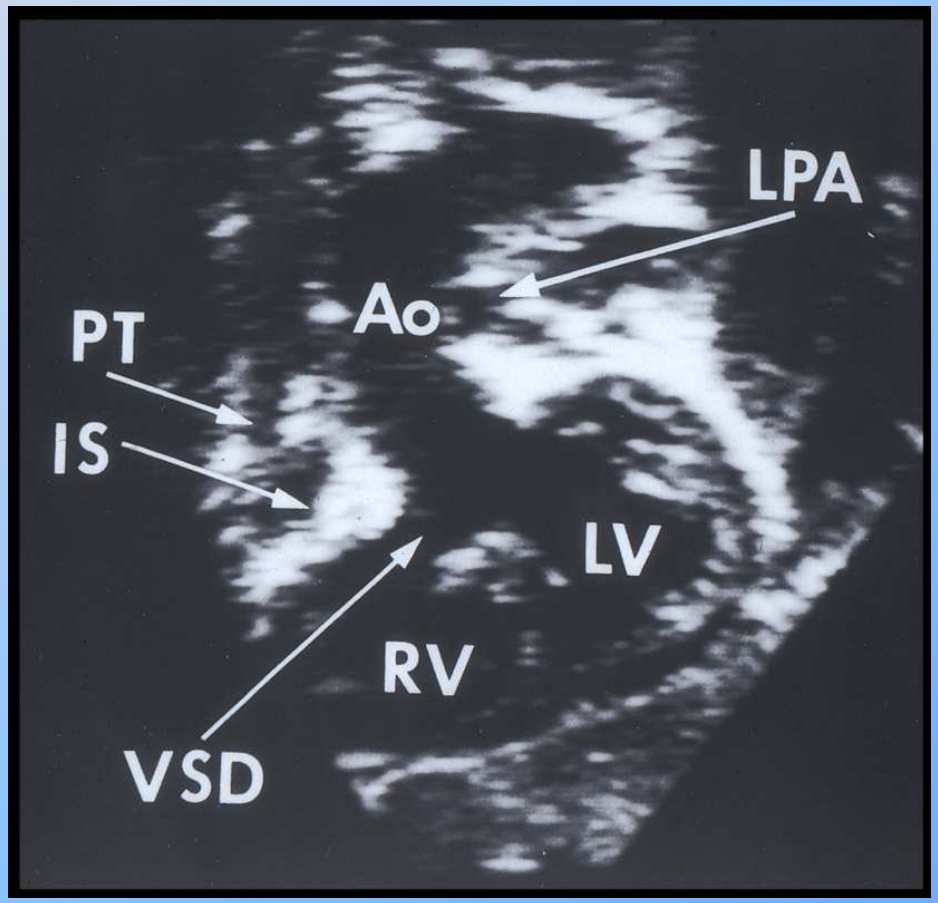
The ***right ventricle*** is a "recent" evolutionary adaptation that appeared beneath the conus arteriosus during the Jurassic Period. This development was a crucial adaptation for air-breathing land-living mammals, reptiles and birds.

However, the right ventricle evolved to function as a lung pump, and it can never function otherwise irrespective of its location or the physiologic circumstances.

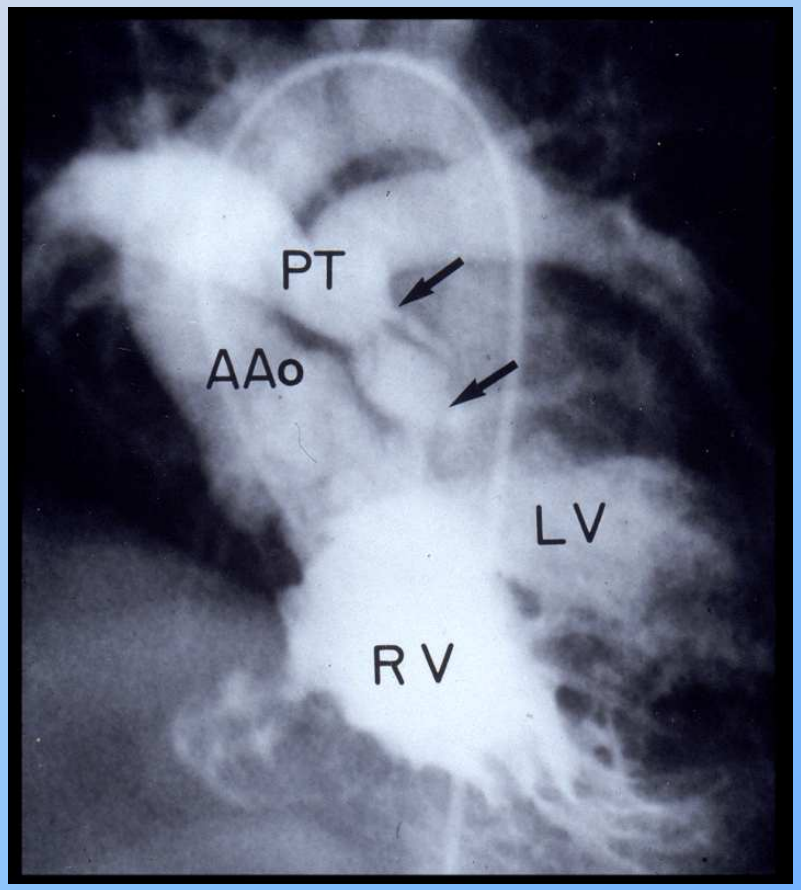
Two hearts that beat as one.
Magdi Yacoub

The right and left ventricles develop from the same heart tube during morphogenesis, but evolve into structures with such different characteristics that that they can be regarded as two different organs that function as one.

In Fallot's tetralogy, the systemic right ventricle functions without failing for two reasons: *first*, it is supported by the left ventricle.



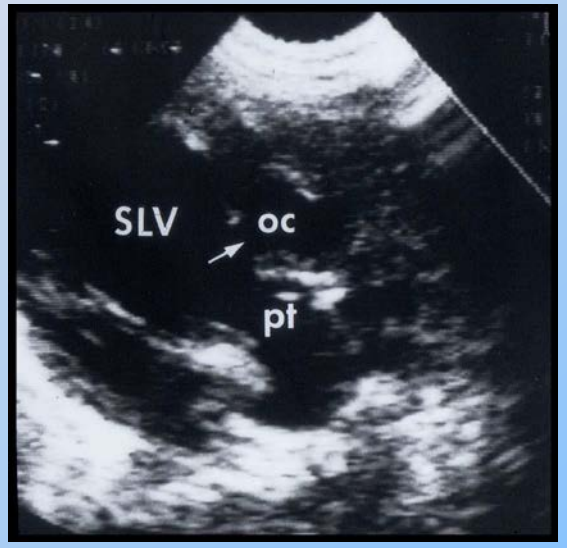
And *second*, it benefits from hyperplasia of its myocytes and its myocardial capillaries, so capillary density is normal.



Ventricular-Ventricular Interaction

*In a **biventricular heart**, the free wall of each ventricle affects the contralateral ventricle because a single myofiber band originates at the RV outflow tract and extends to the left LV outflow tract. RV function supports LV function, and LV function supports RV function.*

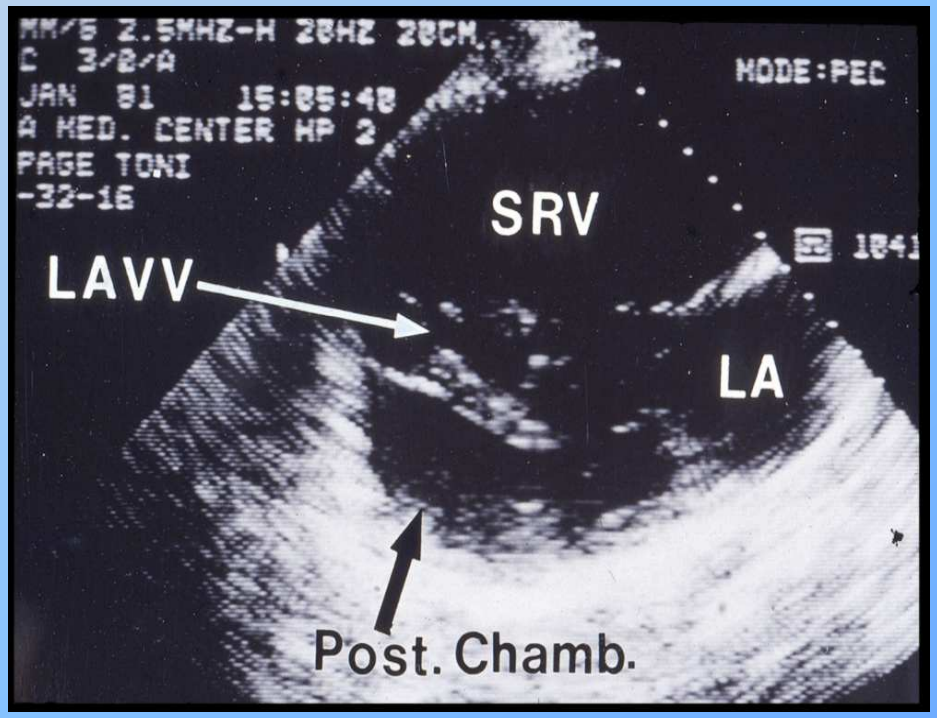
Single Left Ventricle



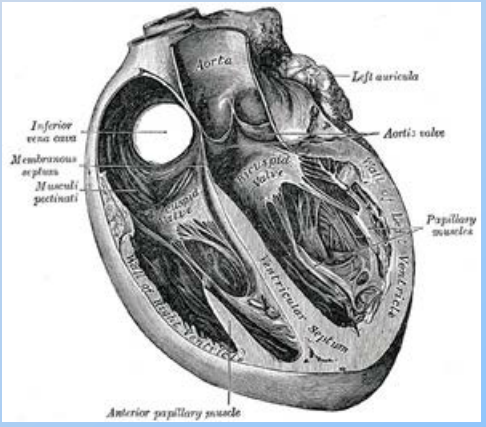
There is no second ventricle to provide ventricular/ventricular interaction and support.

A Single Right Ventricle is Doubly Beset

When the single ventricular chamber is a morphologic right ventricle, inadequate mass relative to volume results in poor adaptation to overload. In addition, there is no second ventricle to provide ventricular/ventricular interaction and support.



Function of the Septum



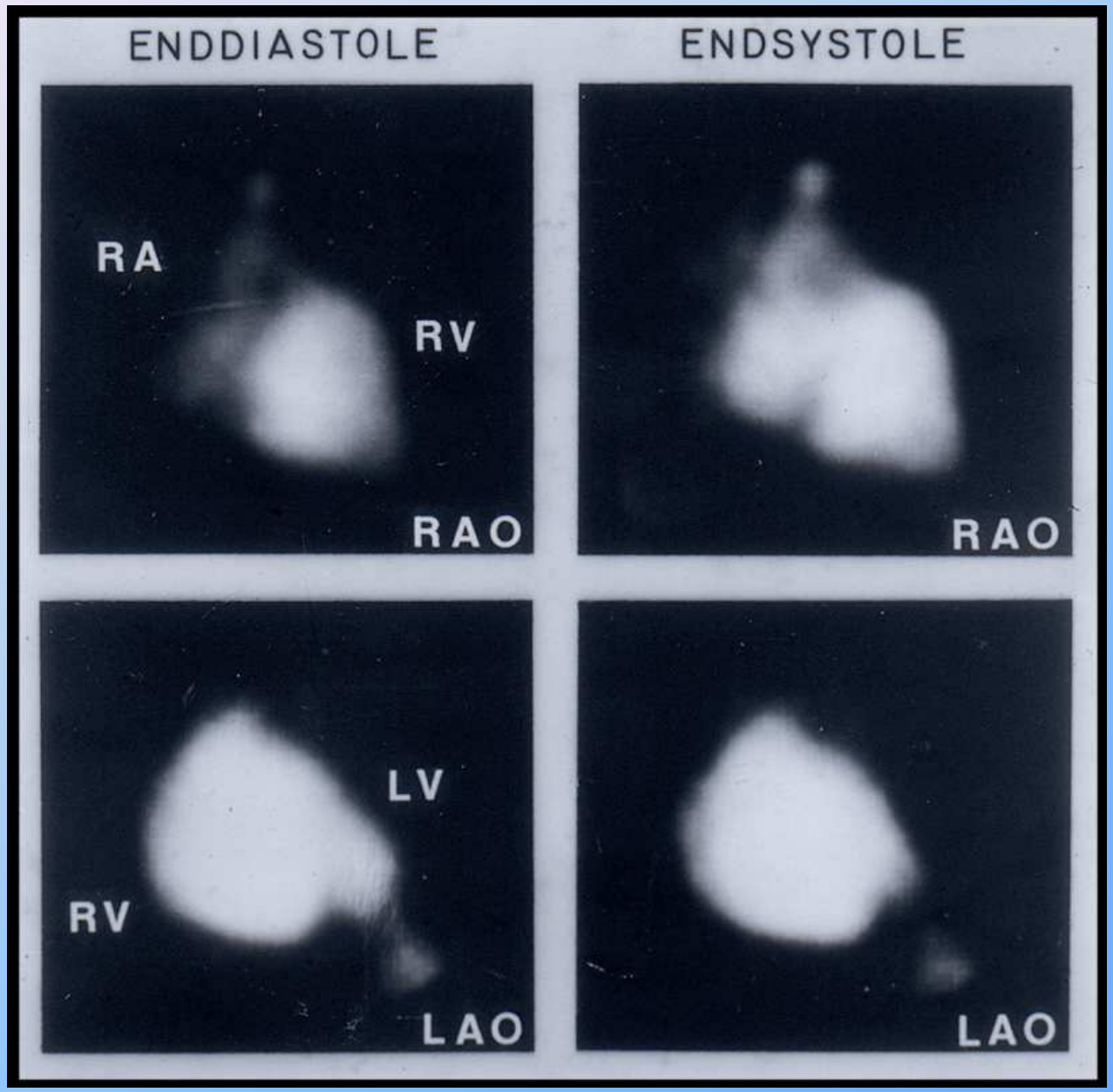
Paradoxical motion of the ventricular septum serves as a right ventricular mechanical assist in:

Uhl's anomaly

Atrial septal defect

Ebstein's anomaly

Uhl's Anomaly



Myocyte shape, remodeling, and ventricular function.

Myocyte shape interests me especially regarding
the relationship between shape and remodeling in the beating but empty embryonic heart.