

Left and Right Ventricular Pressures in the Normal and the Cardiomyopathic Syrian Hamster (*Mesocricetus auratus*)¹ (35175)

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Among animal models of congestive heart failure, the cardiomyopathy of the Syrian hamster (1-3) is unique. This hereditary dystrophy-like myopathy, transmitted by an autosomal recessive gene, has a predictable incidence of 100% in inbred lines and, in most instances, is associated with congestive heart failure, which ultimately appears to be the cause of death. The histopathologic lesions in skeletal muscle resemble those of myotonia atrophica and Duchenne's dystrophy in man, also known to be associated with a cardiomyopathy (4). In order to permit utilization of this model for physiologic and pharmacologic studies of congestive heart failure, the development of methods of measuring pressures in the systemic as well as the pulmonary circulation would appear highly desirable. It is the purpose of this communication to describe such methods, and to report normal values of left and right ventricular pressures for the golden Syrian hamster (*Mesocricetus auratus*), as well as to examine the effect of congestive heart failure in the myopathic animal upon these measurements.

Material and Methods. Nine random-bred male Syrian hamsters (*M. auratus*), 34 weeks old, were used to establish normal values. Nineteen male hamsters with hereditary myopathy of the BIO 14.6 strain (2) (Bio-Research Institute, Cambridge, Massachusetts), 47 to 55 weeks old, were then studied in identical manner. All myopathic animals showed clinical signs of congestive heart failure, with distended neck veins and marked generalized subcutaneous edema. At subsequent necropsy, ascites, and pleural effusions

were generally evident, as was cardiac dilatation and hepatomegaly. Not infrequently, intra-atrial thrombi were encountered.

All animals were anesthetized with sodium pentobarbital 40-60 mg/kg given intraperitoneally approximately 10 min prior to study. Animals in advanced congestive failure were generally given the lower dosage. The electrocardiogram was recorded with needle electrodes applied to four extremities. A tracheotomy was carried out, and a cannula without dead space was inserted into the trachea. The animals were ventilated by means of a rodent respirator (Model 680, Harvard Apparatus Company, Inc., Millis, Massachusetts) at a tidal volume of 1.5-2.0 ml and rates ranging from 40 to 60/min. A modified thoracotomy was performed through a left intercostal incision. Right and left ventricular pressures were obtained by direct puncture of the exposed ventricular apices.

Left ventricular blood was sampled, generally 0.2 ml, and analyzed for pCO₂, pO₂, and pH by an ultramicro-gas analyzer (pH-blood gas analyzer Model 113-S1, Instrumentation Laboratory, Inc., Lexington, Massachusetts). The hematocrit was measured by the micromethod.

The manometric system comprised disposable 26-gauge needles, 12 mm in length, inserted into 8 to 12 cm long polyethylene catheters (id, 0.023 in.) and connected to a stopcock system permitting alternate flushing and measurement of left or right ventricular pressure. Pressures were measured with a fiberoptic manometer (American Optical Corp., Framingham, Massachusetts) and recorded on a multichannel photographic recorder (HP-568 Series, Hewlett-Packard Company, Palo Alto, California) at slow and fast paper speeds, ranging from 2.5 to 200

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TABLE I. Physiologic Measurements (mean \pm SD) in Normal and Myopathic Hamsters.

	Unit	Normal hamsters		Myopathic hamsters	Significance of difference <i>p</i>
<i>N</i>		9		19	
Body wt	g	106.7 \pm 5.2		157.5 \pm 15.9	<0.001
Hematocrit	%	46.4 \pm 1.3		33.1 \pm 7.6	<0.001
pH		7.37 \pm 0.06		7.45 \pm 0.07	<0.01
pCO ₂	mm Hg	45.0 \pm 9.8		51.2 \pm 10.0	NS
pO ₂	mm Hg	83.0 \pm 8.0		52.8 \pm 20.6	<0.001
Heart rate	beats/min	367.2 \pm 40.6		254.9 \pm 50.5	<0.001
Left ventricle					
Syst. pressure	mm Hg	124.3 \pm 15.1		78.4 \pm 14.0	<0.001
End-diast. pressure	mm Hg	8.2 \pm 2.5		17.1 \pm 5.5	<0.001
<i>dp/dt</i> max	mm Hg/sec	5184.9 \pm 1095.3		2918.3 \pm 848.7	<0.001
Right ventricle					
Syst. pressure	mm Hg	37.1 \pm 5.0		33.9 \pm 3.9	NS
End-diast. pressure	mm Hg	4.6 \pm 1.9		11.5 \pm 3.9	<0.001
<i>dp/dt</i> max	mm Hg/sec	1613.7 \pm 413.6		1073.3 \pm 313.4	<0.01

^a NS = not significant.

mm/sec. This manometer system, previously reported from this laboratory (5), in the present application was found to have a natural frequency of 175 Hz, with a damping ratio of 0.25. The maximal value of the first derivative (*dp/dt*) of the ventricular pressure was obtained with an electronic differentiator circuit built around an operational amplifier. The time constant of the circuit was 1 msec.

The significance of differences in measurements was analyzed using Student's *t* test.

Results. The physiologic measurements in normal and cardiomyopathic hamsters are summarized and compared in Table I. The myopathic hamsters significantly exceeded the healthy hamsters in body weight. Whereas the mean hematocrit of the control animals was 46.4%, the hamsters in congestive heart failure had a significantly lower hematocrit at 33.1%. Left ventricular blood of normal hamsters had a mean pO₂ of 83 mm Hg, pCO₂ of 45 mm Hg, and pH 7.37. In contrast, the myopathic hamsters had a significantly lower arterial oxygen tension at 52.8 mm Hg and a slightly but significantly higher pH at 7.45.

The myopathic hamsters were characterized by relative bradycardia of 255 beats/min, 31% below the normal mean heart rate

of 367 beats/min. Congestive heart failure was associated with a significantly depressed left ventricular systolic pressure of 78 mm Hg, 37% below the control value, and an elevated end-diastolic pressure of 17.1 mm Hg, over twice the normal control of 8.2 mm Hg. Right ventricular end-diastolic pressure similarly exceeded the normal value by 150% at 11.5 mm Hg, whereas right ventricular systolic pressure was within normal limits. The first derivative of ventricular pressure, *dp/dt* max, was significantly depressed below normal for both ventricles. Examples of left and right ventricular pressure tracings and their first derivative *dp/dt* are shown in Figs. 1 and 2.

Discussion. *Measurements in healthy hamsters.* The mean hematocrit fell somewhat below the normal values summarized by Desai (6). No previous measurements of pH in whole arterial blood have come to our attention. The mean pH value of 7.37 approaches the value of 7.39 reported for venous plasma in 13 anesthetized hamsters by Lyman and Hastings (7), who calculated a venous pCO₂ of 60 mm Hg, compared to 45 mm Hg for arterial blood in the present series. The present values for pH and pCO₂ would seem to indicate that the animals were adequately ventilated. This appears confirmed by the

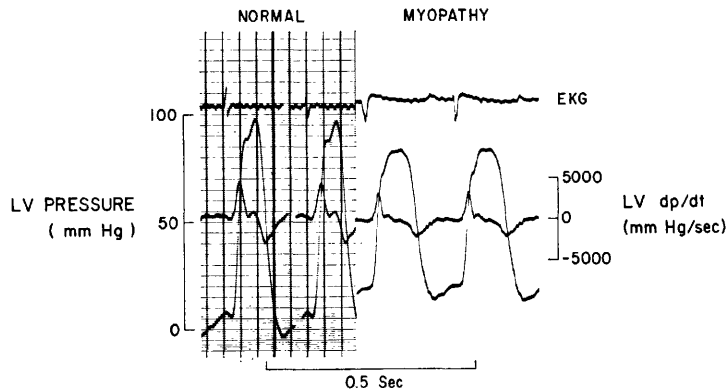


FIG. 1. Representative tracings of left ventricular pressure and its first derivative, dp/dt , in a normal hamster (left) at a heart rate of 315 beats/min, and in a cardiomyopathic animal in congestive heart failure (right) at a heart rate of 276 beats/min. The cardiomyopathic hamster manifests bradycardia, decreased systolic and elevated diastolic pressure, and depressed dp/dt max.

left ventricular pO_2 of 83 mm Hg, which, according to the oxygen dissociation curve determined for the golden Syrian hamster by Ulrich and collaborators (8) corresponds to a saturation for oxygen in excess of 97%.

The heart rate of the golden Syrian hamster has been reported to average 450 beats/min under ether anesthesia (9) and 400 ± 25 (SD) beats/min under pentobarbital anesthesia, 30 mg/kg (10). Under somewhat deeper anesthesia, a slightly lower heart rate was obtained in the present series.

Left ventricular pressure has not been measured in the hamster heretofore. The average peak systolic pressure of 124 mm Hg obtained in the present series compares favorably with the average mean systolic pres-

sure measured in the cannulated carotid artery of golden hamsters under secobarbital anesthesia (11), which was 111 mm Hg. No previous measurements of right ventricular or pulmonary arterial pressures, nor of the first derivative of right or left ventricular pressure are available for comparison.

Measurements in myopathic hamsters. Hamsters in gross congestive heart failure weighed significantly more than the control animals. The 48% increase in weight was associated with a 29% decrease in hematocrit, probably largely a dilution effect. Although the significantly elevated pH of 7.45 suggests adequate ventilation, the significantly lowered arterial oxygen tension of 43 mm Hg, corresponding to an arterial oxygen satu-

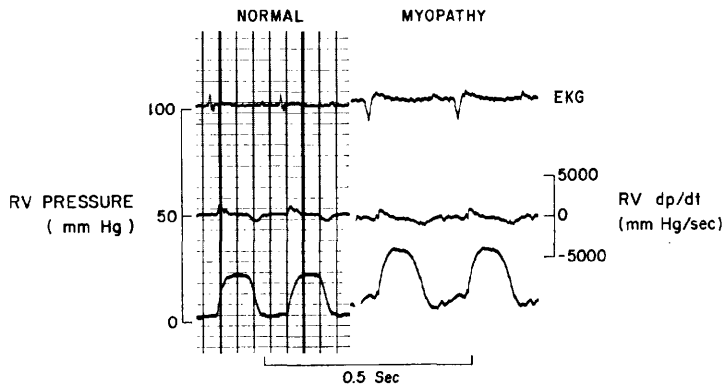


FIG. 2. Right ventricular pressure and dp/dt in a normal (left) and a cardiomyopathic hamster (right). In the myopathic animal illustrated, both systolic and diastolic right ventricular pressures are elevated, while dp/dt is depressed.

ration of about 87% (8), indicates inadequate oxygenation, probably related to pulmonary congestion (3) and/or thoracotomy.

A significantly lowered heart rate and left ventricular systolic pressure describe the hypodynamic state of the circulation associated with advanced cardiomyopathy, reflected also in the markedly lowered maximal dp/dt . The significantly increased left ventricular diastolic pressure, in the face of a decreased pressure load, probably reflects failure rather than decreased compliance of the left ventricular myocardium. Notwithstanding the increase in left ventricular filling pressure, right ventricular systolic pressure was not increased, suggesting that cardiac output might be decreased. In keeping with the clinical picture of biventricular heart failure, right ventricular end-diastolic pressure was also significantly increased, and right ventricular dp/dt significantly decreased.

This predictable and stable model of a chronic cardiomyopathy appears to be suitable for physiologic and pharmacologic studies of congestive heart failure.

Summary. By means of a high fidelity fiberoptic manometer system, right and left ventricular pressures and their first derivatives have been measured at thoracotomy in 9 anesthetized and artificially ventilated golden Syrian hamsters, and are reported along with normal values for pH, pCO_2 , and pO_2 .

Nineteen Syrian hamsters of the BIO 14.6 strain, with hereditary cardiomyopathy and clinical signs of congestive heart failure were studied in similar manner. At mean arterial pH of 7.45, significant hypoxemia was demonstrated, associated with hemodynamic evidence of depressed left and right ventricu-

lar function. Biventricular heart failure was characterized by significant bradycardia, elevation of left and right ventricular filling pressures, decrease in left ventricular systolic and maintenance of right ventricular systolic pressure.

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