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# Differences Between Atrial and Ventricular Energy-Supplying Enzymes in Five Mammalian Species

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## Summary

The purpose of this study was to compare a pattern of 7 enzymes of energy-supplying metabolism in atrial and ventricular myocardium in some mammalian species. Tissue samples of right and left atria and ventricles were obtained from adult male rats, guinea-pigs, rabbits, dogs and pigs. The results clearly demonstrate significant differences in enzyme activities between the atria and ventricles in all these species. In the atria the activity of enzymes connected with aerobic and lactate metabolism (hydroxyacyl-CoA-dehydrogenase, citrate synthase, malate dehydrogenase and lactate dehydrogenase) was markedly lower than in ventricles. On the other hand, in rats, dogs and pigs glucose phosphorylation capacity (hexokinase) was approximately the same in atrial tissue as in ventricles. Right-to-left metabolic differences were much less expressed; conspicuous was only the higher activity of hydroxyacyl-CoA-dehydrogenase in the left atria and ventricles of guinea-pigs and rabbits indicating higher fatty acid utilization capacity in the left heart.

**Key words**
Heart - Atrium - Ventricle - Energy metabolism - Enzymes

## Introduction

Structural and functional properties of cardiac atria and ventricles differ considerably. Ventricular myocytes are organized into layers with a uniform direction; they are larger with closely interdigitating intercalated discs, more abundantly articulated T-tubules and mitochondrial matrices without granules. On the other hand, atrial cells form bundles of varying size; they are slender, less ramified, with specific atrial granules (Sartore *et al.* 1981, Gorza *et al.* 1982, Sommer and Jennings 1992). The atrial muscle contracts more rapidly; the rate of tension rise in isolated atrial strips is at least twice and the maximum shortening velocity three to four times higher as compared with ventricular muscle (Korecky and Michael 1974, Urthaler *et al.* 1975). This is in agreement with higher atrial levels of $Ca^{2+}$-activated myosin ATPase (Yazaki *et al.* 1977, Syrový 1987).

Much less is known about the differences between atrial and ventricular energy-supplying metabolism. Studies dealing with this topic were focused mainly on ventricular myocardial cells both in man and experimental animals (for review see Taegtmayer 1988, Piiper *et al.* 1988). Our previous studies (Bass *et al.* 1988, Šamánek *et al.* 1989) demonstrated significant differences between the enzyme activity pattern in the right atrial and ventricular myocardium of children operated for congenital heart disease. In the atrium, the activity of enzymes connected with aerobic metabolism and with glycolysis was markedly lower as compared with the ventricular tissue. On the other hand, glucose phosphorylation capacity in the atrium was higher than in the ventricle. These differences depend neither on the type of congenital heart disease nor on the reference value used. It was suggested that they also exist in healthy individuals.

The purpose of the present study was, therefore, to establish whether similar differences in atrial and ventricular energy supplying enzymes exist also in other mammalian species, often used for

experimental cardiological research. Since the myocardial sampling during cardiac surgery in man was for obvious reasons limited to the right heart, particular attention was paid to the possible right to left differences.

## Methods

Tissue samples (weighing 15 to 30 mg) of right and left atria and ventricles were obtained from adult male rats, guinea-pigs, rabbits, dogs and pigs. The samples were rapidly weighed, put into precooled homogenization tubes with 200 $\mu$l of 50 $\mu$mol/l Na-K phosphate buffer solution, pH 7.25, containing 10 $\mu$mol/l EDTA and 1 ml/l Triton-X-100. The samples were then adjusted up to a volume 20 times their mass with the same buffer solution, homogenized in the cold and centrifuged for 10 min at 15 000xg. The supernatant was decanted, the pellet rehomogenized and centrifuged as above. In the combined supernatants, the activity of seven enzymes was estimated by the photometric method (Bücher *et al.* 1964, Bass *et al.* 1968). The assayed enzymes were: lactate dehydrogenase (LDH; lactate uptake and/or formation; EC 1.1.1.27), triosephosphate dehydrogenase (TPDH; carbohydrate metabolism; EC 1.2.1.12), glycerol-3-phosphate: NAD dehydrogenase (GPDH; glycerol-P shuttle and metabolism; EC 1.1.1.8), hexokinase (HK; glucose phosphorylation; EC 2.7.1.1), malate: NAD dehydrogenase (MDH; tricarboxylic cycle TCC, reducing equivalent transport; EC 1.1.1.37), citrate synthase (CS, TCC; EC 4.1.3.7) and 3-hydroxyacyl-CoA-dehydrogenase (HOADH fatty acid breakdown; EC 1.1.1.35).

Differences between respective atria and ventricles were statistically evaluated by Student's t-test whereas differences between individual animal species by a non-parametric multiple comparison test.

## Results

The activities of enzymes of energy liberating metabolism (expressed as IU/g wet weight) in individual animal species are shown in Tables 1–5.

*a) Rats (Tab. 1)*

The activities of enzymes related to glycolysis and lactate uptake (LDH, TPDH), glycerolphosphate metabolism (GPDH), overall aerobic oxidation (MDH, CS) and oxidation of fatty acids (HOADH) were significantly lower in both right and left atria as compared with ventricular myocardium. The activity of HK, characterizing glucose phosphorylation capacity, exhibited no atrio-ventricular difference. Right-to-left differences were markedly smaller than the atrio-ventricular ones. As far as the atria are concerned, LDH and GPDH activities were significantly higher in the right side, whereas the activity of HOADH was higher in the left atrium. Right-to-left ventricular differences were even less expressed; the only significant one was the higher activity of HK in the left ventricle.

**Table 1**
Enzyme activities of right and left atria (RA, LA) and ventricles (RV, LV) in the rat.

| Enzymes | RA | RV | LA | LV |
|---|---|---|---|---|
| LDH | 259a* ±11 | 419 ±28 | 204* ±13 | 471 ±29 |
| TPDH | 185 ±12 | 202 ±9 | 171* ±9 | 215 ±12 |
| GPDH | 1.84* ±0.18 | 5.11 ±0.31 | 1.24* ±0.12 | 5.30 ±0.25 |
| HK | 4.37 ±0.34 | 4.32a ±0.21 | 4.64 ±0.21 | 5.16 ±0.29 |
| MDH | 744* ±58 | 1220 ±105 | 842* ±60 | 1425 ±121 |
| CS | 33.7* ±1.6 | 90.8 ±1.5 | 38.1* ±2.7 | 92.8 ±3.1 |
| HOADH | 10.4* ±1.0 | 46.9 ±2.5 | 15.5* ±1.3 | 49.1 ±4.0 |

Enzyme activities in U/g wet weight. Data are means ± S.E.M. (n=14). Significant differences ($p<0.05$): * – atria vs ventricles, a – right vs left parts.

*b) Guinea-pigs (Tab. 2)*

The activities of TPDH, GPDH, HK, MDH, CS and HOADH were significantly lower in the atrial myocardium as compared with ventricular tissue. There was no significant atrio-ventricular difference in the activity of LDH. Only one right-to-left difference was observed: the activity of HOADH was significantly lower in the right atrium and higher in the left ventricle than in the contralateral part.

*c) Rabbits (Tab. 3)*

All enzyme activities were significantly higher in ventricles as compared with atrial tissue; only TPDH from left atria and left ventricles did not differ significantly. The capacity of aerobic metabolism (CS) was significantly higher in the left atria and ventricles as compared with their right counterparts. Furthermore, the activity of LDH and MDH was significantly higher in the left atria than in the right ones.

**Table 2**
Enzyme activities of right and left atria (RA, LA) and ventricles (RV, LV) in the guinea-pig (n=8).

| Enzymes | RA | RV | LA | LV |
|---|---|---|---|---|
| LDH | 247 ±8 | 244 ±29 | 218 ±14 | 229 ±17 |
| TPDH | 105* ±16 | 132 ±5 | 96* ±5 | 134 ±8 |
| GPDH | 1.66* ±0.11 | 2.33 ±0.18 | 1.39* ±0.08 | 2.27 ±0.18 |
| HK | 10.0* ±0.4 | 13.5 ±0.7 | 11.2* ±0.5 | 13.5 ±0.5 |
| MDH | 730* ±74 | 972 ±13 | 680* ±54 | 1119 ±97 |
| CS | 37.3* ±2.8 | 66.8 ±5.2 | 38.8* ±2.1 | 65.6 ±5.4 |
| HOADH | 29.2*a ±1.2 | 24.0a ±1.0 | 13.9* ±0.7 | 30.1 ±1.4 |

Legend as in Table 1

**Table 3**
Enzyme activities of right and left atria (RA, LA) and ventricles (RV, LV) in the rabbit (n=12).

| Enzymes | RA | RV | LA | LV |
|---|---|---|---|---|
| LDH | 119* ±10 | 281 ±22 | 177* ±16 | 272 ±23 |
| TPDH | 86* ±7 | 129 ±14 | 104 ±9 | 139 ±16 |
| GPDH | 2.21* ±0.31 | 4.36 ±0.20 | 2.36* ±0.17 | 3.99 ±0.22 |
| HK | 3.80 ±0.24 | 5.91 ±0.38 | 4.20* ±0.28 | 6.15 ±0.39 |
| MDH | 450* ±34 | 933 ±82 | 636* ±59 | 1003 ±97 |
| CS | 18.8*a ±0.7 | 43.2 ±1.5 | 24.0* ±1.4 | 49.9 ±2.3 |
| HOADH | 6.7* ±0.9 | 25.4 ±2.2 | 9.1* ±1.1 | 23.1 ±1.7 |

Legend as in Table 1

**Table 4**
Enzyme activities of right and left atria (RA, LA) and ventricles (RV, LV) in the dog (n=10).

| Enzymes | RA | RV | LA | LV |
|---|---|---|---|---|
| LDH | 134* ±12 | 253 ±14 | 135* ±8 | 271 ±19 |
| TPDH | 162* ±14 | 219 ±16 | 183 ±11 | 206 ±15 |
| GPDH | 4.78* ±0.63 | 9.99 ±0.96 | 5.29* ±0.29 | 10.3 ±0.7 |
| HK | 5.81 ±0.52 | 5.14 ±0.23 | 4.86 ±0.48 | 5.76 ±0.32 |
| MDH | 664* ±44 | 1018 ±58 | 708* ±45 | 1185 ±105 |
| CS | 29.0 ±2.9 | 34.1 ±2.5 | 23.6* ±2.2 | 37.3 ±2.4 |
| HOADH | 9.9* ±1.0 | 14.7 ±1.0 | 9.9* ±0.74 | 17.5 ±1.6 |

Legend as in Table 1

**Table 5**
Enzyme activities of right and left atria (RA, LA) and ventricles (RV, LV) in the pig (n=16).

| Enzymes | RA | RV | LA | LV |
|---|---|---|---|---|
| LDH | 172 ±12 | 183 ±13 | 183* ±13 | 216 ±12 |
| TPDH | 105* ±8 | 171 ±12 | 128* ±10 | 168 ±12 |
| GPDH | 7.45* ±0.46 | 10.7a ±0.9 | 4.63* ±0.41 | 13.6 ±1.0 |
| HK | 4.11* ±0.20 | 3.56 ±0.15 | 4.53* ±0.23 | 3.79 ±0.15 |
| MDH | 771* ±59 | 914 ±76 | 791* ±60 | 1046 ±80 |
| CS | 43.2 4 ±3.0 | 8.2 ±2.8 | 38.3* ±2.6 | 51.5 ±2.5 |
| HOADH | 16.1* ±1.7 | 22.6 ±2.4 | 14.4* ±1.2 | 23.3 ±2.4 |

Legend as in Table 1

*d) Dogs (Tab. 4)*

The activities of LDH, GPDH, MDH and HOADH were significantly higher in both ventricles as compared with the atria. In TPDH was such an atrio-ventricular difference significant in the right ventricle only, in CS in the left ventricular wall. The activity of HK did not exhibit any atrio-ventricular difference. No significant right-to-left differences were found.

*e) Pigs (Tab. 5)*

The activities of TPDH, GPDH, MDH and HOADH were in both right and left ventricles significantly higher than in the respective atria. This trend, although not significant, was present also in the activity of LDH on both sides and MDH and CS in the right heart. On the other hand, the activity of HK was in both atria significantly higher as compared with the ventricular myocardium. The right-to-left differences were less expressed; they concerned only GPDH, which was significantly higher in the right atria and left ventricles.

*Atrio-ventricular ratios*

The atrio-ventricular enzyme ratios (atrial – ventricular activity) in individual animal species compared with those of the human myocardium (Bass *et al.* 1988) are summarized in Fig. 1a-e. Generally, most enzyme activities in atrial musculature are lower as compared with the ventricular tissue in all species studied. Nevertheless, in the rat, dog and pig heart, similarly as in man, atrial hexokinase activity reached the ventricular values indicating relatively increased capacity for glucose metabolism.

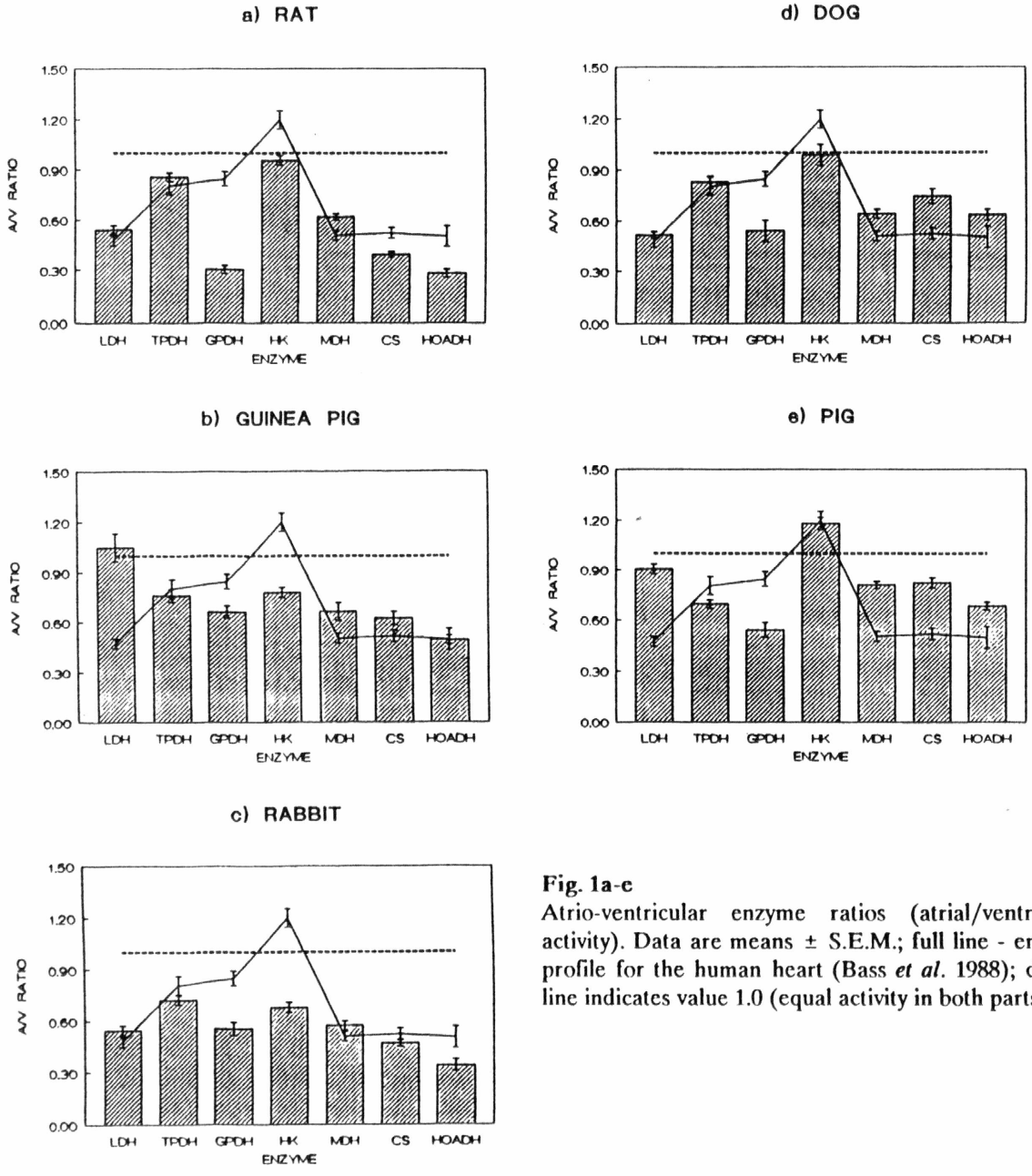


**Fig. 1a-e**
Atrio-ventricular enzyme ratios (atrial/ventricular activity). Data are means ± S.E.M.; full line - enzyme profile for the human heart (Bass *et al.* 1988); dotted line indicates value 1.0 (equal activity in both parts).

## Discussion

Our results clearly demonstrated significant differences in the enzyme activity pattern between the atrial and ventricular myocardium in all mammalian species studied. In the atrium the activity of enzymes connected with aerobic and (with the exception of the guinea-pig) lactate metabolism was markedly lower as compared with the ventricular tissue. On the other hand, in the rat, dog and pig, similarly as in man (Bass *et al.* 1988), the glucose phosphorylation capacity was at least the same as in the ventricle. In these species aerobic glucose catabolism thus seems to be the dominant source of energy in the atrial myocardium.

Comparable data in the literature are surprisingly scarce. Gross biochemical analysis of both cardiac compartments showed no differences in water content or in glycogen concentration, but atria were found to have a higher lipid content (Arminger *et al.* 1984) and concentration of collagenous proteins (Pelouch *et al.* 1993). Furthermore, Plattner *et al.* (1970) have found a lower activity of succinate dehydrogenase (an enzyme of tricarboxylic acid cycle, functionally comparable to our CS) in the atrium of guinea-pigs, mice and cattle. On the other hand, they did not observe any atrio-ventricular difference in cytochrome oxidase activity, a part of the respiratory chain. It seems, therefore, that cytochrome oxidase is not the factor limiting aerobic metabolism in the atrium. Similarly Frič *et al.* (1971) in dogs and Schultheis *et al.* (1981) in guinea-pigs have observed lower activity of H-isozymes of lactate dehydrogenase in the atrial musculature.

Right-to-left metabolic differences were much less expressed and no significant differences were found in the dog and pig hearts. The higher activity of HOADH in the left atria of rats, rabbits and guinea-pigs and left ventricles of rabbits and guinea-pigs indicated a higher fatty acid utilization capacity in the left heart.

Myocardial metabolism of homoiotherms is almost exclusively aerobic. The principal substrates utilized by the cardiac muscle are free fatty acids, glucose, lactate and pyruvate. Free fatty acids supply approximately 70 percent of the total energy used by the heart, glucose 20 to 30 percent, lactate 10 to 20 percent and pyruvate about 1 percent. To some extent, the myocardium can also use triglycerides, ketone bodies or amino acids (for review see Opie 1989). There are, however, significant species differences in myocardial energetics related to cardiac efficiency (Gibbs and Loiselle 1978, Loiselle and Gibbs 1979, Loiselle 1987).

This view may be supported by our findings showing striking differences in energy-supplying metabolism in mammalian species including man. The heart muscle of man had the lowest enzyme activities with the exception of HK, suggesting that glucose phosphorylation plays an important role not only in atria but also in the ventricular myocardium. Similar high activity of HK in both parts of the heart was observed in guinea-pigs. The metabolic pattern of the rat heart is completely different. Particularly in the ventricle, high metabolic capacity of lactate (LDH), fatty acids (HOADH) and overall aerobic metabolism (MDH, CS) predominates. The only similarity with the human heart is the high activity of HK in the atrial musculature. Our results support the view of Loiselle and Gibbs (1979) that the capacity of energy-supplying metabolism is not simply related to the body size and heart rate of individual species.

Species differences in myocardial metabolism in healthy (control) individuals can be even more pronounced under different pathological conditions. Our observations in the chronic hypoxaemic heart may serve as an example; in rats exposed to chronic hypoxia an increase of HK and decrease of HOADH activities was observed, indicating a shift from fatty acids to glucose metabolism (Bass *et al.* 1989). Similar results were obtained in guinea-pig hearts (Barrie and Harris 1976). On the other hand, in children with congenital cardiac malformations producing hypoxaemia (Šamánek *et al.* 1989) only CS was decreased while HOADH and HK were unchanged. In this connection it is interesting to note that the hypoxia-induced changes were significantly more pronounced in the human atrial tissue samples.

In conclusion, our results demonstrate significant atrio-ventricular and species differences in myocardial energy supplying metabolism. This fact should be taken into consideration in all experimental studies dealing with myocardial energetics.

## References

ARMINGER L.C., SEELYE R.N., MORRISON M.A., HOLLISS D.G.: Comparative biochemistry and fine structure of atrial and ventricular myocardium during autolysis in vitro. *Basic Res. Cardiol.* **79:** 218–229, 1984.

BARRIE S.E., HARRIS P.: Effect of chronic hypoxia and dietary restriction on myocardial enzyme activities. *Am. J. Physiol.* **231:** 1308–1313, 1976.

BASS A., BRDICZKA D., EYER P., HOFER S., PETTE D.: Metabolic differentiation of distinct muscle types at the level of enzymatic organization. *Eur. J. Biochem.* **10:** 198–206, 1968.

BASS A., OŠŤÁDAL B., PROCHÁZKA J., PELOUCH V., ŠAMÁNEK M., STEJSKALOVÁ M.: Intermittent high altitude-induced changes in energy metabolism in the rat myocardium and their reversibility. *Physiol. Bohemoslov.* **38:** 155–161, 1989.

BASS A., ŠAMÁNEK M., OŠŤÁDAL B., HUČÍN B., STEJSKALOVÁ M., PELOUCH V.: Differences between atrial and ventricular energy supplying enzymes in children. *J. Appl. Cardiol.* **3:** 397–405, 1988.

BÜCHER T., LUH W., PETTE D.: Einfache und zusammengesetzte optische Tests mit Pyridinnukleotiden. In: *Handbuch der physiologisch- und pathologisch-chemischen Analyse.* Hoppe-Seyler/Thierfelder, Springer Verlag, Berlin, 1964, IV. A, pp. 292.

FRIČ P., LOJDA Z., VAŠKŮ J., BEDNAŘÍK B., ŠTĚPÁNEK V., URBÁNEK E.: The heterogeneity of lactate dehydrogenase in the myocardium of the left atrium and ventricle of the dog (in Czech), *Čas. lék. čes.* **48:** 1125–1128, 1971.

GIBBS C.L., LOISELLE D.: The energy output of tetanized cardiac muscle: species differences. *Pflügers Arch.* **373:** 31–38, 1978.

GORZA L., SARTORE S., SCHIAFFINO S.: Myosin types and fiber types in cardiac muscle. II. Atrial myocardium. *J. Cell Biol.* **95:** 838–845, 1982.

KORECKY B., MICHAEL L.H.: Regional differences in contraction of mammalian hearts. In: *Recent Advances in Studies on Cardiac Structure and Metabolism.* N.S. DHALLA (ed), University Park Press, Baltimore, 1974, 4: 77–78.

LOISELLE D.S.: Cardiac basal and activation metabolism. In: *Cardiac Energetics.* R. JACOB, H. JUST, CH. HOLUBARSCH (eds), Steinkopff Verlag, Darmstadt, 1987, pp. 37–50.

LOISELLE D.S., GIBBS C.L.: Species differences in cardiac energetics. *Am. J. Physiol.* **237:** H90–H98, 1979.

OPIE L.H.: Substrate and energy metabolism of the heart. In: *Physiology and Pathophysiology of the Heart.* N. SPERELAKIS (ed), Kluwer Academic Publ., Boston, 1989, pp. 327–360.

PELOUCH V., MILEROVÁ M., OŠŤÁDAL B., ŠAMÁNEK M., HUČÍN B.: Protein profiling of human atrial and ventricular musculature: the effect of normoxaemia and hypoxaemia in congenital heart diseases. *Physiol. Res.* 1993 (in press).

PIIPER H.M., SIEGMUND B., SPAHR R.: Energy metabolism of adult cardiomyocytes. In: *Myocardial Energy Metabolism.* J. W. DE JONG (ed), Martinus Nijhof Publ., Dordrecht, 1988, pp. 171–180.

PLATTNER H., TIEFENBRUNNER F., PFALLER W.: Cytomorphometric and biochemical differences between the muscle cells in atria and ventricles of the guinea-pig heart. *Anat. Rec.* **107:** 11–16, 1970.

SARTORE S., GORZA L., BORMIOLI S.P., DALLA-LIBERA L., SCHIAFFINO S.: Myosin types in cardiac muscle. I. Ventricular myocardium. *J. Cell Biol.* **88:** 226–233, 1981.

SCHULTHEISS H.P., BISPINK G., NEUHOFF V., BOLTE H.D.: Myocardial lactate dehydrogenase isoenzyme distribution in the normal heart. *Basic Res. Cardiol.* **76:** 681–689, 1981.

SOMMER J.R., JENNINGS R.B.: Ultrastructure of cardiac muscle. In: *The Heart and Cardiovascular System.* FOZZARD *et al.* (eds), Raven Press, New York, 1992, pp. 3–50.

SYROVÝ I.: Properties of atrial and ventricular myosin in mammals of various size. *Gen. Physiol. Biophys.* **6:** 249–254, 1987.

ŠAMÁNEK M., BASS A., OŠŤÁDAL B., HUČÍN B., STEJSKALOVÁ M.: Effect of hypoxaemia on enzymes supplying myocardial energy in children with congenital heart disease. *Int. J. Cardiol.* **25:** 265–270, 1989.

TAEGTMAYER H.: Principles of fuel metabolism in heart muscle. In: *Myocardial Energy Metabolism.* J. W. DE JONG (ed), Martinus Nijhoff Publ., Dordrecht, 1988, pp. 17–34.

URTHALER F., WALKER A.A., HEFNER L.L., JAMES T.N.: Comparison of contractile performance of canine atrial and ventricular muscles. *Circ. Res.* **37:** 762–771, 1975.

YAZAKI Y., UEDA S., NAGAI R., SIMANDA K.: Cardiac atrial myosin adenosine triphosphatase of animals and humans. *Circ. Res.* **45:** 522–527, 1977.

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