JACC Vol. 5, No. 2
February 1985:363–5

EDITORIALS

Atrioventricular Conduction Versus Heart Size From Mouse to Whale*

FRITS L. MEIJLER, MD, FACC

Utrecht, The Netherlands

In normal sinus rhythm, the atrioventricular (AV) conduction system introduces an appropriate delay between atrial and ventricular excitation and contraction (1,2). This delay, the AV or PR interval, increases with the size of the animal and, thus, of the heart (3,4). This increase, however, is relatively small in comparison with the difference in the sizes of the body and the heart. For instance, the PR interval is only twice as long in mammals such as the elephant or the whale as it is in human beings (4,5). Comparison of the AV nodal electrophysiologic properties with the size of the heart in a number of mammalian species raises rather interesting questions regarding the functional properties of the AV conduction system.

Comparative Function of the AV Node-His System

The behavior of the AV node-His bundle system has been studied systematically using conventional programmed atrial stimulation in rats, dogs and human beings (6–12).

1. AV conduction time or delay after atrial premature stimulation can be described by an exponential function of the coupling interval between the last normally conducted R wave and the stimulus (10,11).
2. Adaptation of AV conduction delays to stepwise atrial rate changes is a phenomenon dependent on time rather than on the number of cardiac cycles (10–12).
3. Atrial rate-induced changes in AV conduction time show a short time constant (10–12) or memory, with memory being the time the AV conduction system needs to adapt to changes in PP (AA) intervals (10). For example, in human beings, AV memory does not normally persist beyond one or two cardiac cycles.
4. The ratios between normal AV conduction time (atrial-His interval or PR interval) during sinus rhythm and the durations of the AV memory in rats, dogs and human beings are roughly similar (10).
5. Species-dependent differences in AV conduction delay during sinus rhythm and AV conduction adaptation after pacing-induced atrial rhythm changes are small, taking into account the differences in relative sizes of the respective animals and their hearts.

Comparative Morphology of the AV Node-His System

Despite differences in detail, the overall architecture of all mammalian hearts is essentially similar. One familiar with the anatomy of the heart of one species will have no great difficulty identifying cardiac structures in other mammals. Nature has used the same "blueprint" for all mammalian hearts, be it mouse or whale. This similarity applies generally to the morphology of the mammalian AV node-His system as well. Although differences such as the blood supply or the presence of an os cordis do exist between the AV nodes of, for instance, rabbits, dogs and human beings on the one hand and cattle on the other, the fact remains that the known similarities significantly outweigh the differences (13–15). The overall configuration of the mammalian AV node-His system from the AV region to the bundle branches is also similar among the smaller (16) and larger (17–19) mammals.

Although most studies tend to stress the differences, the microscopic and electron microscopic characteristics of the mammalian myocardial and AV nodal cells in the species studied to date show remarkable similarities (20). For the electron microscopist, it is difficult to differentiate between myocardial or AV nodal cells derived from the rabbit, dog or human subject (21). It is reasonable to expect that this is also true for the horse, elephant and whale. Thus, macroscopically and microscopically, the structural arrangement of the mammalian AV conduction system tends to be similar, if not uniform, while the size of the heart varies greatly from species to species.

*Editorials published in *Journal of the American College of Cardiology* represent the views of the authors and do not reflect the views of JACC or the American College of Cardiology.

From the Department of Cardiology, University Hospital, Utrecht, The Netherlands. This work was supported by the Wynand M. Pen Foundation, Utrecht. Manuscript received June 18, 1984, accepted September 6, 1984.

Address for reprints: Frits L. Meijler, MD, Department of Cardiology, University Hospital, Catharijnesingel 101, 3511 GV Utrecht, The Netherlands.

0735-1097/85/$3.30

JACC Vol. 5, No. 2
February 1985:363-5

Size Versus Function of the AV Node-His System

According to Schmidt-Nielsen (3), the weight of the mammalian heart is about 0.6% of the body weight. From comparative anatomic studies (13,22), it appears that the size of the mammalian AV node increases with the size of the heart, although not proportionally. For instance, the ratio between the weight of the heart of a rat, a human being and a medium-sized whale is approximately 1:300:60,000. When we accept the PR interval of the mammalian species (4,5) as a measure of AV conduction time and plot these values against the body mass (3), we find a gross disproportion between these two sets of data (Fig. 1). This presents a most interesting and still unexplained discrepancy between size and function of the mammalian AV conduction system.

Conduction Velocity in the AV Node-His System

Living systems must function at relatively uniform temperatures and pressures (23). The mammalian biologic system functions at about 37°C. Cardiac muscle is composed of individual cells that tend to be uniform in diameter, approximately 10 to 15 μm, whether the source is the mouse or the whale (24). This small range of mammalian myocardial fibers may reflect an optimal relation between cell volume and diffusion rate (25). From present knowledge, it is reasonable to assume that the same physicochemical conditions are applicable to mammalian conduction fibers. From the rabbit to the elephant, the metabolic rate per gram tissue decreases only slightly (26). Conduction velocity depends largely on cell (fiber) diameter (27,28). Assuming a more or less constant cell to cell resistance, it is unlikely that with increasing length or diameter of the His bundle and bundle branches, the known conduction velocity of approximately 2.5 m/s (29) will increase significantly.

These assumptions suggest that in a large mammalian heart, such as that in the elephant (30) or whale (31), the contribution to the AV conduction delay by each component of the AV conduction system must be different from that of the heart in smaller mammals such as the human being, dog or rabbit. For example, in the adult blue whale having bundles that are likely 1 m or more in length from their origin at the AV node to their terminal ventricular ramifications and a conduction velocity of about 2.5 m/s, it will require at least 400 ms for the impulse to cover that distance. The PR interval in the elephant or a small whale does not exceed 400 ms (30–32). Even in the largest whales, the PR interval will not be much longer than 500 ms (Fig. 1). Therefore, the AV node, although anatomically present in large mammals, would not be expected to impose a significant delay on AV conduction during normal sinus rhythm, even if the conduction velocity was greater than 2.5 m/s.

During atrial fibrillation or flutter, however, the presence of the AV node may yet be vital in large mammals to protect the heart against an unduly rapid rate of ventricular responses (33,34). This may be especially true in large mammals with large stroke volumes because they need sufficiently long RR intervals for adequate diastolic ventricular filling.

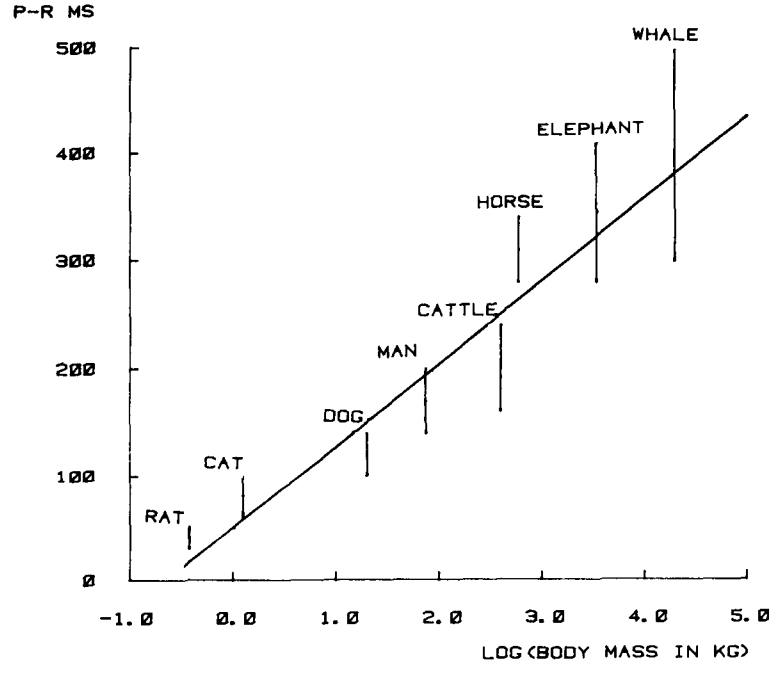

Figure 1. Approximation of the relation between body mass in kg (**abscissa**) and PR intervals in ms (**ordinate**) according to: y = 52.5 + 77.5 × log (x). In mammals smaller than 200 g, this formula may not be applicable.

Implications

An important lesson from a comparative biologic point of view seems to be that nature has maintained in all mammals the anatomic macro- and microstructure of the heart and its conduction system, but has adapted the function to enable the heart to meet the hemodynamic demands under normal as well as abnormal conditions. The tendency has been to study biologic functions in animals smaller than human beings. Had we studied larger species, our concepts about the form and function of the human AV conduction system in health and disease might have been quite different (35). A more general conclusion may also be drawn, namely, that evolution may be represented by form and structure of the mammalian heart, but survival of the species depends on proper adaptation of the function of the heart in health and disease.

The help, encouragement and criticism of many colleagues are highly appreciated. This paper would never have materialized without their active support.

References

1. Rushmer RF. Cardiovascular Dynamics. 4th ed. Philadelphia: WB Saunders, 1976:87–8.
2. Dagget WM, Bianco JA, Powell WJ, Austen WG. Relative contributions of the atrial systole-ventricular systole interval and of patterns of ventricular activation to ventricular function during electrical pacing of the dog heart. Circ Res 1970;27:69–79.
3. Schmidt-Nielsen K. Animal Physiology, Adaptation and Environment. 2nd ed. Cambridge: Cambridge University Press, 1979:99–112.
4. Clark AJ. Comparative Physiology of the Heart. Cambridge: Cambridge University Press, 1927:49–51.
5. Altman PL, Dittmer DS. Biological Handbooks: Respiration and Circulation. Bethesda, MD: Federation of American Societies for Experimental Biology, 1971:278.
6. Meijler FL. Atrial fibrillation. A new look at an old arrhythmia. J Am Coll Cardiol 1983;2:391–3.
7. Heethaar RM, Robles de Medina EO, Meijler FL, et al. Response of AV nodal conduction to rate changes in rat, dog and man (abstr). Circulation 1981;64:IV-645.
8. Van Capelle FJL, Du Perron JC, Durrer D. Atrioventricular conduction in isolated rat heart. Am J Physiol 1971;221:284–90.
9. Harms FMA, Heethaar RM, Robles de Medina EO, Meijler FL. Atrioventricular nodal "memory" studied by random atrial stimulation (abstr). Am J Cardiol 1980;45:459.
10. Meijler FL, Heethaar RM, Harms FMA, et al. Comparative atrioventricular conduction and its consequences for atrial fibrillation in man. In: Kulbertus HE, Olsson SB, Schlepper M, eds. Atrial Fibrillation. Mölndal, Sweden: Astra Cardiovascular, 1982:72–80.
11. Heethaar RM, Denier van der Gon JJ, Meijler FL. Mathematical model of AV conduction in the rat heart. I. Cardiovasc Res 1973;7:105–14.
12. Billette J. Short time constant for rate-dependent changes of atrioventricular conduction in dogs. Am J Physiol 1981;241:H26–33.
13. Truex RC, Smythe MQ. Comparative morphology of the cardiac conduction tissue in animals. Ann NY Acad Sci 1965;127:19–33.
14. James TN. Anatomy of the sinus node, AV node and os cordis of the beef heart. Anat Rec 1965;153:361–72.
15. James TN. Structure and function of the AV junction. Jpn Circ J 1983;47:1–47.
16. Kawamura K, Urthaler F, James TN. Fine structure of the conduction system and working myocardium in the little brown bat, myotis lucifugus. In: Kobayaski T, Ito Y, Rona G, eds. Recent Advances in Studies on Cardiac Structure and Metabolism. Cardiac Adaptation. Baltimore: University Park Press, 1978:81–91.
17. Bishop SP, Cole CR. Morphology of the specialized conduction tissue in the atria of the equine heart. Anat Rec 1967;158:401–15.
18. King RL, Burwell CS, White PD. Some notes on the anatomy of the elephant's heart. Am Heart J 1938;16:734–50.
19. White PD, Kerr WJ. The heart of the sperm whale with especial reference to the A-V conduction system. Heart 1917;6:207–10.
20. Sommer JR, Johnson EA. Ultrastructure of cardiac muscle. In: Berne RM, Sperelakis N, Geiger SR, eds. Handbook of Physiology–The Cardiovascular System I. Bethesda, MD: American Physiological Society, 1979:113–86.
21. Virágh S, Challice CE. The impulse generation and conduction system of the heart. In: Challice CE, Virágh S, eds. Ultrastructure of the Mammalian Heart. New York, London: Academic, 1973:43–84.
22. Lev M. The conduction system. In: Gould SE, ed. Pathology of the Heart. 2nd ed. Springfield, IL: Charles C Thomas, 1960:132–65.
23. Eckert JR, Randall D. Animal Physiology, Mechanisms and Adaptation. San Francisco: WH Freeman, 1983:49.
24. Sommer JR, Johnson EA. Comparative ultrastructure of cardiac cell membrane specializations. A review. Am J Cardiol 1970;25:184–94.
25. Black-Schaffer B, Grinstead CE II, Braunstein JN. Endocardial fibroelastosis of large mammals. Circ Res 1965;16:383–90.
26. Schmidt-Nielsen K. Energy metabolism, body size, and problems of scaling. Fed Proc 1970;29:1524–32.
27. Jack JJB, Noble D, Tsien RW. Electric Current Flow in Excitable Cells. Oxford: Clarendon, 1975:292–6.
28. De Mello WC. Passive electrical properties of the atrio-ventricular node. Pflügers Arch 1977;371:135.
29. Durrer D, Janse MJ, Lie KI, Van Capelle FJL. Human cardiac electrophysiology. In: Dickinson CJ, Marks J, eds. Developments in Cardiovascular Medicine. Lancaster: MTP Press, 1978:53–75.
30. White PD, Jenks JL, Benedict FG. The electrocardiogram of the elephant. Am Heart J 1938;16:744–50.
31. King RL, Jenks JL, White PD. The electrocardiogram of a Beluga whale. Circulation 1953;8:387–93.
32. White PD, King RL, Jenks J. The relation of heart size to the time intervals of the heart beat with particular reference to the elephant and the whale. N Engl J Med 1953;248:69–70.
33. Cohen SI, Lau SH, Berkowitz WD, Damato AN. Concealed conduction during atrial fibrillation. Am J Cardiol 1970;25:416–9.
34. Meijler FL, Kroneman J, Van der Tweel I, Herbschleb JN, Heethaar RM, Borst C. Nonrandom ventricular rhythm in horses with atrial fibrillation and its significance in human patients. J Am Coll Cardiol 1984;4:316–23.
35. Brock TC. Why study large animals? New Scientist 1983;100:193–6.