Historical note

The normal range and determinants of the intrinsic heart rate in man

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As Editors we are forced to look back at the paper of Jose and Collison [1] ourselves, because we were not successful in retracing Drs. Jose or Collison. Their study on the normal range and the determinants of the intrinsic heart rate in man was published in 1970. The study was performed in “healthy volunteers”: 80% of them were inmates of the New South Wales State Penitentiary. The other 20% were members of the hospital staff or medical students. The majority of subjects were male (73%), probably reflecting the ratio between male and female inmates. The paper did not receive much attention during the first 10 years after publication. The citation frequency was about two citations per year during that period. However, the citation frequency increased after 1980 leading to a total of 200 between 1971 and 1998 (see also Introductory Editorial [2]). We have analyzed the titles of 99 papers that cited the original paper by Jose and Collison between 1988 and 1999. We found that 33% of those papers either were on sinus node dysfunction or on sinus node function during some pathophysiological state (e.g. ischemia or atrial fibrillation). Another 20% of those citing papers dealt with syncope or autonomic balance. Aging contributed 17%, heart rate variability 9%, cardiac transplantation 7% and gender 4%. Interestingly, the studies on aging, heart rate variability and gender that cited the paper of Jose and Collison were more numerous during the second half than during the first half of this 1988–1999 time window, probably reflecting the increased awareness that (intrinsic) heart rate constitutes an important parameter for these research topics.

In retrospect the paper of Jose and Collison included an important piece of information that should have been incorporated in the title by the authors. They did not only study “intrinsic heart rate”, which they defined as the heart rate under the simultaneous presence of the nonselective β-adrenoceptor antagonist propranolol (0.2 mg/kg) and the muscarinic receptor blocker atropine (0.04 mg/kg), but they also established the inverse relation between age and intrinsic heart rate, both in males and females. The authors also demonstrated that the variability between individuals is of the same order as the effect of aging in the whole population. This might have been emphasized more by the authors, because this limits the significance of measurement of intrinsic heart rate to serial measurements in the same individuals.

The data of Jose and Collison [1] have later been confirmed by Alboni et al. in 1982 [3]. The youngest individuals in the study of Jose and Collison were 16 years. An extension to younger age has been provided by Marcus et al. in 1990 [4].

Again in retrospect it is of interest to note that the pharmacological concept of intrinsic heart rate had been raised by previous work of Jose published in 1966 [5] and of Jose and Taylor published in 1969 [6]. In those studies — directed to normal individuals as well as to patients with heart failure — it had already been established that heart rate becomes constant under the combined presence of atropine and propranolol. Jose and Taylor [6] showed that the intrinsic heart rate is much lower in class III/IV patients (77 beats/min) than in control patients (107 beats/ min). The averaged age of the two groups was 50 and 25 years respectively. Since age decreases the intrinsic heart rate by 0.57 beats/min according to the data of Jose and Collison [1], the age difference between the groups explained 14 beats/min of the difference between the normal group and the group with severe heart failure. In other words half of the difference could be explained by age rather than by the underlying pathophysiology. This
renders the measurement of intrinsic heart rate in patients with heart failure less attractive than it appeared at the time of the previous publications [5,6].

References