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An Easier Approach to Estimating Risk of Coronary Heart Disease and Stroke

To the Editor:

In their article, Wilson et al1 provide useful information that allows clinicians to predict coronary heart disease risk in patients without a history of heart disease. This is very much needed because primary care and specialist physicians typically overestimate patients’ absolute heart disease risk and the expected benefits of drug therapy given for primary prevention.2,3

To encourage clinicians to use this type of information, it must be easy to use and incorporate into a busy clinician’s practice.4 In addition, it should facilitate clinicians’ discussion of this information with their patients so that an informed decision about drug therapy or other risk reduction strategies can be made.

We recently developed5 a simple nomogram for estimating the risk of coronary heart disease and stroke in individual patients using the Framingham data from previous studies by these authors.6,7 Our method allows the clinician and patient to consider the impact of individual risk factors. In addition, it allows them to visualize the interplay between individual risk factors; easily add, remove, or modify risk factors; and observe the impact of changes on risk assessment.

Because modification of risk factors does not necessarily mean that cardiovascular risk will be reduced, we also provided clinicians with a table that provides examples of demonstrated risk reductions that allows the clinician to incorporate the evidence from well-designed clinical trials into the decision-making process.

We encourage the Framingham group to present their risk prediction information in a more visual format rather than as a score sheet. This type of format is faster and easier to use and does not require summation of risk factor points and transfer of this information to tables. It allows the clinician and patient to visualize the potential effects of a combination of risk factors on the chance of coronary heart disease and the expected benefits of drug therapy given for primary prevention.

James P. McCormack, BSc(Pharm), PharmD
Associate Professor
Faculty of Pharmaceutical Sciences
University of British Columbia
St. Paul’s Hospital
Vancouver, BC, Canada

Marc Levine, BSc(Pharm), PhD
Associate Professor
Faculty of Pharmaceutical Sciences
University of British Columbia
Vancouver, BC, Canada

Robert E. Rangno, MSc, MD, FRCP(C)
Associate Professor, Departments of Medicine and Pharmacology
University of British Columbia
Head, Clinical Pharmacology
St. Paul’s Hospital
Vancouver, BC, Canada


Three-Dimensional Imaging of Atrioventricular Node

To the Editor:

In your issue of July 7, 1998, Efimov and Mazgaley1 describe a very exciting new avenue for study of the AV node. If the new approach is to achieve its full potential, however, it is important that it be assessed in the light of what we already know concerning nodal architecture. Thus, the diagram used by Efimov and Mazgaley (their Figure 1) is simplistic and misleading. On the basis of reconstructions supplemented by microelectrode recordings, we already know that cells comparable to the bundle of His extend posteriorly through the length of the AV node.2 Recognition of this posterior extension of the “lower nodal bundle” is now the more important in the light of its very recent identification by Medkour et al3 as the slow pathway of the AV node. We are also aware that using the sensible criterion proposed by Tawara,4 only the areas upstream of the insulating connective tissue illustrated by Efimov and Mazgaley1 should properly be described as “node.” We were unaware of this criterion when making our earlier description,2 and it is of interest that Medkour et al3 do not discuss this feature. We now believe that if we are to make full use of techniques similar to those employed by Efimov and Mazgaley, we should follow Tawara’s lead and agree with him that when differentiating node from bundle of His, “I make the border at the place where the system penetrates the atrioventricular fibrous septum, because this place is easily determined anatomically.”5

Robert H. Anderson, MD
Pediatrics, National Heart & Lung Institute
Royal Brompton Campus
Imperial College School of Medicine
London, UK

Response

It might suffice to stress that the arm-chair drawing shown as an inset in Figure 1 of our article did not imply any morphological fidelity. Its sole purpose was to illustrate the dual-layer AV nodal structure as the proposed source of the multicomponent optical signals recorded in our experiments. Thus, as far as the essence of the discussed study is concerned, we do not feel that the reader would have been misled by the admittedly simplified drawing.

However, Dr Anderson’s criticism is broader and as such deserves special attention. A strict nomenclature related to the AV node and shared by both morphologists and electrophysiologists is clearly missing and needed. Although the fundamental AV nodal structure as the proposed source of the multicomponent optical signals recorded in our experiments. Thus, as far as the essence of the discussed study is concerned, we do not feel that the reader would have been misled by the admittedly simplified drawing.

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PA prevents spontaneous wave break, decreases the number of reentrant waves, and synchronizes fibrillating activity, thereby exhibiting antiarrhythmic effects unrelated, at least directly, to wavelength.

Narcis Tribulova, PhD  
Institute for Heart Research  
Slovak Academy of Sciences  
Bratislava, Slovak Republic

Mordechai Manoach, PhD  
Department of Physiology and Pharmacology  
Tel-Aviv University Medical School  
Tel-Aviv, Israel


Response

We appreciate the comments of Drs Tribulova and Manoach. Very interestingly, the authors found that similar to its effects on canine ventricular fibrillation (VF), procainamide also decreases the complexities of VF in smaller hearts (rat and guinea pig) by a mechanism that is also independent of wavelength prolongation. The proposed mechanism(s) of procainamide-induced increase of cell-to-cell coupling as a basis for the prevention of spontaneous wave break is interesting, but we do not think that this is a unique mechanism for the prevention of wave break. We have shown in an in vitro swine model of stable VF (ie, perfusion maintained during the VF through the coronary artery) that in spite of good perfusion, procainamide reversibly regularized VF by preventing spontaneous wave break. We think that active regenerative cellular properties, including dynamic action potential duration (APD) restitution, may be involved. Although the wavelength (product of APD and conduction velocity) remains unchanged after procainamide, the drug tends to flatten the APD restitution curve and prevents the generation of action potentials with short duration during VF. Our working hypothesis is that activation with short APD is intrinsically a weak stimulus that undergoes block (wave break). By preventing the initiation of activation with shorter APD, procainamide might prevent spontaneous wave break. We therefore think that in addition to the possible passive mechanism (increased intercellular coupling resistance) of wave-front breakups, as proposed by Drs Tribulova and Manoach, there also exists the distinct possibility of active cellular properties (APD restitution properties during VF) that act in concert to either prevent or promote spontaneous wave breaks.

Evidence for a Link Between Adipose Tissue Interleukin-6 Content and Serum C-Reactive Protein Concentrations in Obese Subjects

To the Editor:

We read with interest the editorial by Tracy on inflammation in cardiovascular disease (CVD). Serum concentrations of C-reactive protein (CRP) were demonstrated to be related to increased risk of CVD, which underlines the potential inflammatory nature of human atherosclerosis. Interestingly, an unexpected association between CRP and body mass index (BMI) was found in several population studies without any explanation.

The production of CRP is regulated by cytokines, principally interleukin-6 (IL-6), and serum CRP levels reflect IL-6 activity in humans. It was demonstrated that IL-6 is released in vivo by subcutaneous adipose tissue and is thereby able to have systemic effects, particularly in obese subjects. Thus, we hypothesized that adipose tissue may play a role in the regulation of serum CRP concentrations via IL-6 production.

To test this hypothesis, we measured CRP and IL-6 in both blood and adipose tissue from 13 fasting obese subjects (2 men, 11 women) aged 44±2 years (BMI, 39.1±1.3 kg/m²; percent fat mass, 44.3±2.4%). CRP concentrations were determined with a BNII nephelometer analyser (Behring). IL-6 concentrations were determined by ELISA (Quantikine, R&D Systems). Body composition analysis was carried out by dual x-ray absorptiometry (QDR 1000, Hologic).

Serum CRP and IL-6 concentrations were 4.49±0.7 mg/L and 2.77±0.31 pg/mL, respectively. In adipose tissue, IL-6 concentrations were 12.81±1.28 pg/g fat, whereas CRP was undetectable. Serum CRP concentrations were significantly correlated with BMI (r=0.633, P<0.05), body fat mass (r=0.718, P<0.05), and percent fat mass (r=0.872, P<0.005) but not with lean body mass (r=−0.435, P=0.13). A strong correlation was found between serum CRP concentrations and adipose tissue IL-6 content when expressed as picogram per total fat mass (r=−0.757, P<0.01) but not as picogram per gram of fat (r=−0.446, P=0.12).

These data are consistent with the role of human adipose tissue in the regulation of blood circulating CRP concentrations via IL-6 production in obesity. In addition, the higher IL-6 production from adipose tissue...
seems to be more related to the increase of total fat mass than an overexpression of IL-6 in adipose tissue. Because CRP was proposed as a predictive marker of CVD risk, whether slightly elevated concentrations of CRP are the consequence of adipose tissue secretion, an inflammatory process, or both remains to be established.

Jean-Philippe Bastard, MD, PhD
Claude Jardel, PhD
Jacques Delattre, PhD
Bernard Hainque, PhD
Service de Biochimie B
Eric Bruckert, MD
Service d’Endocrinologie-Métabolisme
Flavien Oberlin, MD
Service de Rhumatologie
Groupe hospitalier Pitié-Salpêtrière AP-HP
Paris, France

Is the Antiarrhythmic Effects of PA Related to Wavelength?
Narcis Tribulova and Mordechai Manoach

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