SCHOOL OF PUBLIC HEALTH

CENTER FOR RESEARCH IN DISEASES OF THE HEART TECUMSEH HEALTH STUDY
130 SOUTH FIRST STREET

ANN ARBOR, MICHIGAN 48108

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Dr. Henry Blackburn Institut de Medecine Social et Preventive 12 Rue de Condolle 1205 Geneva Switzerland

Dear Henry:

I appreciate the opportunity to review your article on premature beats from the coronary drug project. It is a very important paper and answers many questions which have nagged all of us who are interested in this problem.

I have a number of comments about the paper. I hope they are helpful. First, the analysis of the data clearly indicates that ventricular premature beats are separate factors, which are apparently unrelated to other conditions that one might logically suspect as unfavorable prognostic traits. However, all the participants had a myocardial infarction, which seems to me to be a factor of overriding importance. We still do not know the role of VPB's in the sudden death of persons without prior evidence of CHD or whether the relationship of ectopic beats to risk factors is different in such "pre-event" individuals than in the survivor group. I think the mechanism of sudden death is similar, but survivors constitute a unique population. Some of your thoughts about these questions would be a valuable addition to the discussion.

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I also wondered if further elaboration about the increased mortality (but not sudden death) of persons with supraventricular premature beats would be desirable. Such beats are often precursors of atrial fibrillation, which tends to occur in those with incipient congestive heart failure in the absence of mitral disease or other obvious causes of AF. Did participants with SVPB's die of congestive failure? Their strong association with diuretic therapy would be compatible with such a mechanism.

Another item which caugh my attention was the site of the VPB's. I too was surprised that VPB's originating in the right ventricle seemed as bad prognostically as those from the left. I wonder if a reviewer may not question

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the high proportion of VPB's which were of indeterminate focus, particularly since the tracings were initially classified by trained lay personnel. It would be advisable to emphasize more forcefully that all questionable tracings were reviewed by an experienced cardiologist.

Although the details presented in the many tables and the annex are very convincing, I think they make the paper much too long and tedious for most readers. Those who have a special interest in this subject will work through it, but most readers would be put off by the "heavy going". Much of the detail adds nothing to the central theme and could be disposed of in a paragraph or two. Perhaps a very detailed version could be published as part of what I suppose will be a monograph on the results of the coronary drug project, but I hope that a streamlined version will appear soon in a cardiology journal.

The discussion, conclusions and summary need work. They repeat the information presented in the results instead of actually discussing the significance of the major points and proposing hypotheses. The review of previous work on this subject could also be more terse.

Finally, while I feel the same frustrations you do about the clinical application of this knowledge in the absence of an effective, safe and inexpensive oral antiarrhythmic drug for long term use. I cannot retreat into our comfortable platitudes about primary prevention as an acceptable alternative. I would like to believe that we could put the "plumber" surgeons, coronary care units and pill pushing physicians out of the CHD business by the application of current knowledge, but as I survey the scene in our population and sense the indifference to even such simple measures as weight control, abstention from smoking and reasonable exercise, I am much more pessimistic about primary prevention than about the development of a reasonably good antiarrhythmic pill. I think the evidence of CHD has a long future and my clinical half yearns for something that will help control the out of hospital sudden death.

I realize this is still a rough draft, so probably some of my comments are not appropriate. I greatly appreciate the opportunity to review this important article, which must represent a great deal of work on your part. It is really excellent and I look forward to seeing it in print.

If and when we have any new ECG articles of importance, I will avail myself of your kind offer to review them before submission to a journal.

I hope to see you in Anaheim in November.

Sincerely,

Leon D. Ostrander, M.D.

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P.S. I shall return the morninget to minnespelis under sefante error.