November 6, 1972

MEMO TO: Doug and Marc

FROM: Dr. Blackburn

Had I discussed the enclosed with you? It represents some possibility of our looking at fixed coupling (re-entry) versus automaticity (parasystole). Do we still measure R-R' or just T-R'? The point here would be to measure R-R' or T-R' variations between multiple PVCs and relate the variability to sudden death. This is an exciting and fundamental question. We will explore it in CDP and in the International Data.

HB/rs

c.c. S. Tominaga

In considering the natural history of angina pectoris complicated by infarction on purely clinical experience, one would suggest that different forms of angina behave differently i.e. unstable angina is often relieved by infarction and the angina in that instance is presumably a manifestation of a pre-infarction state; whereas chronic stable angina is seldom alleviated by infarction. The third category, that of patients who develop angina for the first time after infarction, is not relevant to this discussion.

The unstable angina question has probably been answered adequately by clinical experience alone, where pre-infarction angina terminating with infarction without further sequelae is very well recognized. It is unlikely that the CDP resource could add any information to this question.

On the other hand, the epidemiologic approach to the chronic angina situation could be very informative. However, the CDP resource has been pre-empted by the recent report form Framingham (Kannel and Feinleib, American Journal of Cardiology, Feb. 1972), in which that question has been examined directly. The results, showing disappearance of angina in only 4 of 29 men (15%) and 0 of 8 women post-infarction, a rate lower than the spontaneous rate of loss of angina, is again consistant with clinical experience. It is therefore debatable whether an analysis of the CDP data would add to the problem, although I personally would favor such an analysis, since our numbers are larger and the natural history of angina in the CDP does not seem quite as depressing as in the Framingham study.

Regarding the premature beat paper, my personal opinion is that the paper is beautifully organized and presented, and I have nothing to add to its style or content. In fact, I have borrowed liberally from this work in my paper on ventricular ectopic beats, a copy of which has recently been sent to the Editorial Revue Board. I hope you will regard this as a compliment. I gather from Tomie that the statisticians were harsh in their revue, but the statistical aspects are beyond my understanding.

There is, however, one new analysis that I think would really be worthwhile, and that is a comparison between VPB's with and without fixed coupling with respect to sudden death. Let us examine the hypothesis that automatic rhythms do not degenerate into ventricular fibrillation, whereas other types of dysrhythmias eg. re-entrant rhythms do. Clinical support for the hypothesis comes from 1) our observations on parasystole 2) the rarity of ventricular fibrillation in accelerated idioventricular rhythms and parasytolic ventricular tachycardia 3) some unpublished experimental observations by Neil Moore's group that rapid electrical stimulation does not produce ventricular fibrillation. Against this view is the digitalis toxicity experience, since digitalis induced-rhythms are generally considered to be automatic rhythms. However, the digitalis question is a rather complicated one because it induces multifocal areas of activity. Equally complex are other known automatic rhythms such as artificial pacemaker rhythms. Ventricular fibrillations does occur with pacemaker rhythms in certain circumstances but these are rare.

Since it is difficult at a clinical level to differentiate between automatic and re-entrant ectopic beats, one can either take a rigid view of automatic rhythms i.e. that only clearcut parasystolic or escape rhythms are due to automaticity; or a broader view i.e. that any ectopic beat showing even slight variations in coupling times are likely to be automatic. Since the standard ECG data in the CDP does not lend itself to accurate diagnosis of parasystole, it might be worth examining the data with respect to fixed versus variable coupling. I cannot give any precise definition of variable coupling interval. Perhaps we could take 0.04 seconds as one cutoff point, 0.08 seconds as another cutoff point. I do, however, think that the question is worth examining in detail in those records containg at least several VPB's i.e. the group with 10 or greater per 100 beats.

I would appreciate your views on this matter.

With warmest personal regards,

Sincerely yours,

Bernie

Bernard Tabatznik, M.D.