HARVARD UNIVERSITY

SCHOOL OF PUBLIC HEALTH

TEL. (617) 734-3300
(617) 734-3311 (AFTER HOURS)
CABLE ADDRESS: NUTHARV, BOSTON

DEPARTMENT OF NUTRITION
665 HUNTINGTON AVENUE
BOSTON, MASSACHUSETTS 02115

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pcopy to S. Tonninger

Henry Blackburn, M.D.
Laboratory of Physiological Hygiene
School of Public Health
University of Minnesota
Minneapolis, Minnesota 55455

Dear Henry:

Your manuscript and letter finally have caught up with me in my vacation hideaway in Maine. I am pleased that I was able to read the preprint. It is a most important communication and thrilled me no end. I have not been as excited about a medical article in a long time. For the past five years, I have tried to organize an investigation that will demonstrate the prognostic implications of ventricular ectopic activity. At first, I attempted to do so in Boston and then with HIP in New York, but could not persuade the N.I.H. of the importance of such an endeavor. I am pleased that you have carried out these important correlations and done so in such a masterly fashion.

Let me first respond to your ciriticisms:

1) I am not clear to what mortality you are referring. I agree a time base is essential to make such a statement meaningful.

2) "The mere presence" refers to the finding of a rare VPB on prolonged, namely, 10-hour monitoring period. Since about 60% of patients with CHD exhibit some ectopic activity, it is unlikely to define risk. It seems reasonable that if monitoring were extended to a still longer duration, perhaps 80% or more, patients would demonstrate VPB's. It is unreasonable to surmise that the mere occurrence of a variable at this order of frequency has prognostic implications. Of course this does not apply to the recognition of VPB's on a single electrocardiographic recording, which provides less than one minute of monitored information. The finding of even a single VPB, therefore, would in our classification designate these as frequent. In fact, you make the same point on p.24, and continue with the thought, "this suggests that the excess risk of occasional isolated VPB must fall off rapidly to insignificant levels." I concur entirely.

3) You object to my formulation, "the decisive factor does not inhere alone in the VPB." On rethinking your criticism, I again conclude that this formulation is biologically sound. a) VPB's carry the highest risk of sudden death during the first 24 hours after myocardial infarction; thereafter, their prognostic implications diminish exponentially. The reason, of course, is the presence of electrical instability in the heart with probable reduction in vulnerable period threshold which is short-lived; b) patients who have VPB during episodes of angina pectoris have a greater predisposition to sudden death; c) many patients with CHD have multiple VPB's over many years without apparent deleterious effect; d) the patients you identify with many VPB's, 70% survived 30 months. The reason is that there are vpb's and VPB's. (See enclosed article on "Pathogenesis, Prevention, and Treatment of Arrhythmias in Myocardial Infarction.") It is my view that when VPB's occur in association with ischemia, they carry a more dire prognosis then when developing in the absence of ischemia. Furthermore, when a patient has VPB's, an ischemic episode becomes more hazardous by the possible accidental triggering of more advanced degree of electrical instability.

Let me now turn to a few random comments about your paper, though I would have welcomed much more the opportunity to discuss this subject with you directly. -- The introduction is poorly formulated and thereby detracts from your important data. The implication presented is that you merely confirm what has already been established. This, of course, is not the case. Neither Tecumseh nor Hinkle present persuasive data. At best they suggest a possibility. -- The body of the paper is repetitive. This is an important communication that needs to be widely read. I am anxious that in its present format, it will be merely skimmed. -- It is not clear what was the mechanism of death of those who did not die suddenly and why the correlation with VPB's. There is no discussion why SVPB's carry the same mortality as VPB's and especially why the drop off in the percentage of deaths when they equal or exceed 10/100 beats (Fig.2). -- The TR' measurement is less precise than the Q-T. Why introduce a new ratio when the $\frac{Q\text{-}R'}{Q\text{-}T}$ is already in use? -- Page 37, the discussion of my view on secondary risk factor misses the point. Incantation against atherosclerosis seems out of place in this important document. You state a number of oft repeated truisms, but do not address yourself cogently to the fact that many CHD deaths are accidental, i.e., sudden, and for which we already have the means of prevention, if the victim could be precisely identified.

Predictor of total death not entirely explained by sudden death.

Rel. risk sudden & all deaths & non-sudden? same.

My congratulations to you and the participants in the CDP who have provided us with these vital findings.

On the way back from Geneva, how about stopping over in Boston?

Warm regards,

Bernard Lown

Bernard Lown, M.D.

BL/sla
Encs.
N.B. I enclose a copy of the Conner Lecture. This is a more carefully thought out document than the lecture itself of which you have a copy. I also enclose a preprint of Kosowsky's paper which is to appear in Circulation. In the three enclosed papers you have many of the essential references.

CC: J. Stamler, M.D.

Signed in Dr. Lown's absence.