Correp - Burchell

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611 Beacon Street S.E.
Minneapolis, Minnesota 55455
(612) 624-5400

May 31, 1989

TO: Howard Burchell

FROM: Henry Blackburn HB (nmf)

RE: Attached

Thanks for sending me your note to Franz Halberg. Though he is extremely intense, he is capable of "listening" to colleagues he respects. You should send it!

/nmf

Attachment

Henry - I did this as an exercise in reason, so you can give me a rating on that too - BUT, main reasons for asking your opinion, as per our conversation, are:
Should I think of sending it?
Would it do any good over-all to send it -

May 16, 1989 - Franz, as you know, has had cor. artery by-passes and also 'angioplasties' -

HB,

Franz Halberg, M.D.
Professor
Department of Laboratory Medicine
and Pathology
Box 609 - Mayo
Minneapolis Campus

HB → HBarchell.
See every occasion to send this. By all means! HB.

Dear Franz:

After enjoying the perusal of the brochure and struggling about its basic message, I thought a response might be attempted by constructing my comments in the format of a book review. I am sure you will have a good rebuttal or critical parts of it.

- -

The monograpph "Chronobiology of Human Blood Pressure", Fourth Edition, "The Sphygmochron; A Medtronic Seminar", authored by Franz Halberg, outlines the growth of knowledge of cyclic changes which have an inherent temporal periodicity, particularly as it may be applicable to varying levels of blood pressure.

The text is said to have been tailored for the "non-chronological" reader (presumably scientifically inclined), and it gives an historical perspective, and the developments in which the brilliant imaginative work of Dr. Halberg has played such a dominant part. Accepting the presence of temporal rhythms, which must have physiological significance, the reader may have qualms about accepting the level of importance implied in the text, but who should wish to inhibit some exaggeration to point up the past neglect of physicians and the impact ~~of~~ inherent biological rhythms should exert in medical practice.

The monograph does have some characteristics of a promotional brochure, whetting the interest of the reader in the public health problem of high blood pressure, with a focus on early identification of the to-be afflicted, the prevention, and early therapy. Such a laudable goal is outstanding and clear.

The brochure ~~inherently~~ develops (1) a defense of chronobiology as a separate science requiring its own language; (2) the importance of frequent blood pressure recordings over time (e.g. 48 hours), ~~and there is the suggestion of~~ a "sales pitch" for equipment available to do this; (3) and an implication that a proper understanding of (1), and implementation of (2), will substantially reduce or erase the burden of hypertension in any population.

In respect to (1) above, the author seemingly underestimates the attention given by many physicians to variations in blood pressure and their acquaintance with the time factor (delta △) in all physiological responses. He deprecates the concept of homeostasis, and, I believe he interprets this basic approach differently from many scientists, i.e., that the body has normal constants, rather than ~~it is~~ dynamically searching for some equilibrium.

Proper problem of labelling children at risk are not considered.

While osmotic levels, vascular volumes are held remarkably constant in health, and blood flows to some tissues can be regarded as primary homeostatic items; blood pressure and flow values may be regarded as secondary items.

The monograph includes a glossary of terms ~~which is overtly~~ helppful, but one wonders if all are necessary, and whether some possibly are obfuscating to a new reader. It has been said that scientists are "incorrigible wordsmiths, perhaps in part to name something, confers a title". One can wonder, without intending any umbrage, if physicians a decade hence, for example, will be familiar with the words "circasemiseptan" and "bathyriskdem"!

In respect to (2), that is the mechanical recorders, there is a lack of detail of validation of the blood pressure recordings, assuming this has been accomplished. There must have been comparisons with continuous direct recordings in patients in acute care areas. If there is to be a wide-spread application of the recorders, comparison of different types of apparatus, the costs, and the patient rights would be useful information.

In regard to (3), one can visualize real progress occurring regarding insights into the cardiovascular complications of intermittent hypertension; anecdotal evidence testifies it can be benign, but the overall burden remains unknown, and good records, well collected, with careful analyses with reports labelled "sphymochrons" will be useful, particularly with follow-up data.

One of the exciting amazing conclusions regarding blood pressure determinations in the newborn, was that the genetic predisposition to hypertension was evident in the first 48 hours. (This is the period when the ductus arteriosus has just closed and the morphology change in the right and left ventricle has begun, which is not discussed.)

In the graphs illustrating the 'circaseptan' feature of neonatal blood pressure (page 182), the meaning of ordinate units, systolic blood pressure "residuals", should be defined.

The monograph contains many well prepared figures which are helpful. Not particularly enjoyed by this reviewer are the cartoons, reminiscent of those in army service manuals, tailored to the least intelligent of the recruits. Some of the figures showing the automatically monitored systolic blood pressure ~~showing~~ wide ranges (e.g., 160 to 80) (page 75-76) are of special interest, and ~~one would like~~ to know the position of the body, the clinical story, and any medications being taken. In some of the charts, it ~~has been~~ was difficult for me to ascertain which circadian changes might be due to levels of activities and which are tied to inherent biological temporal templates.

An occasional illustration seems misplaced in a book on chronobiological rhythm, such as the individual taking Nardil (a monamine oxidase inhibitor) who had a hypertensive episode at night. The nature of his evening meal, or of possible medications, is not mentioned (page 96C). The graphs showing hypertension during sleep (page 96B) might be elucidated if the type of sleep had been recorded (e.g. REM).

The reference list is long, seemingly up-to-date, articles as late as 1987 being noted. Eighty-eight references are to papers on which Dr. Halberg was the author or the first author. From the list of credits given, Dr. Halberg has had many eminent authorities in the field of hypertension who have given him their counsel.

I think most physicians attempting to master Dr. Halberg's monograph will find it a formidable task. However, some acquaintance with the massive information and conclusions is overtly a requirement for the practitioner, epidemiologist, physiologist, teacher and administrators of research agencies. Some may wish to avoid or delegate the task. A concise editorial in a major clinical journal might better disseminate the concept, while referring more serious students to this excellent monograph.

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Corresp-Burchell

October 17, 1989

Howard Burchell
Professor Emeritus
260 Woodlawn
St. Paul, MN 55105

Dear Howard:

I had barely seen and appreciated your memo but had put it aside undigested. There is no question in my mind that Cherne Enterprises is misleading the public. Richard Crow resigned from them many months ago because they actually submitted an abstract with his name on it that he had not approved. They are making claims on the basis of data that he cannot accept. The post doc fellow involved was basically fired from his fellowship for failing to meet academic standards.

If you have any of the actual information in which our name was being exploited, I would appreciate having copies of it. Richard Crow has decided not to seek action against them. I even entertained, when I saw that they were artificially building up the value of their stock and selling out large amounts of stock (Cherne's wife) about informing the SEC of their practice. We decided not to take any action but formally removed ourselves from any association. I appreciate your note and am sorry that I didn't respond more promptly. I believe Jon Murray is a consultant.

Cordially,

Henry Blackburn, MD
Professor and Director

Corresp-Burchell

Henry - To keep you acquainted with my peregrinations with Franz
H.

UNIVERSITY OF MINNESOTA
TWIN CITIES

Department of Surgery
Medical School
Phillips-Wangensteen Building
516 Delaware Street S.E.
Minneapolis, Minnesota 55455

July 11, 1989

Corresp

Franz Halberg, M.D.
Professor
Department, Lab. Medicine and Pathology
Box 609, UMHC

Dear Franz:

I enjoyed listening to the presentations given at the symposium - "Chronobiological Approach for Disease Preventions,Diagnosis and Treatment" (June 25, 1989), and in accord with our brief discussion, send you this short critique.

It is of concern to me, that the varied studies on hypertension appear to be proceeding, as independently of one another, for instance, those of the chronobiologist, the behaviorist, the epidemiologist and the practitioner, despite the overlapping flow of data therefrom. White debate was encourage by you, it never became active partly because the schedule ran behind, and any antagonists were too polite with issues often ill-defined. I was very favorably impressed with Dr. Tamura's work and presentation giving objective evidence of the "hypertension load" and the development of hypertrophy. I though Dr. Zachariah's talk was clear, though a little dogmatic and was surprised that it did not generate more discussion. Maybe the clarity to me might be, in part related, that there was a dearth of the new chronobiological terminology.

Dr. Schmitt's exposition, Dr. Lindern's and Dr. Bingham's talks werebeyond my comprehension related to my very limited mathematical background.

I had thought chronobiology was basically related to "inherent biological clocks" and; could have a debate been staged whether the hourly variations in blood pressure have a strong intrinsic modulation or, the pattern with the morning increment be related to overall activity, morning tensions, eating, working, etc. The person who has been vocal in support of the latter is Dr. Pickering. His most recent essay challenging the existence of an intrinsic rhythm in blood pressure is in the chapter in the new book that I happened to see on the new book table this past week in the Diehl library - edited by Elbert, et al entitled "Behavioral Medicine inCardiovascular Disorders". I

had hoped there would be more discussion on the patterns of blood pressure in the newborn.

The chronobiologist's claim to expertise in the diurnal incidence of sudden death and onset of acute mycardial infarction was of interest and their analyses of the data should be helpful, although the reasons for the patterns may be more likely to come from epidemiological techniques. When I looked at time of death in cardiac patients in hospitals, the incidence of death was slightly higher in the late evening (18:00-24:00). (I was looking for evidence that the pattern of medication, physician and nursing staffing might be responsible for any deviation from a flat 4.17/hour rate.) With the large number of cases of sudden death, I think the hourly rate might be more informative than the 6 or 8 hour period.

Incidentally, you have probably seen the reports that beta-blocker therapy obliterates the diurnal variation of sudden death and frequency of ischemic attacks in patients with coronary disease. As you would know, a number of investigators have attempted to fit the occurrence of coronary events, within the context of the "new" science of chaos which seems like fun and games to me) without having the necessary mathematical knowledge to criticize it.

The papers on the varying lethal dose of digoxin in mice (?) according to time of day, have become so much a classic reference for chronobiologists that I should study them in detail. Were they carefully blinded and well controlled? Do you have copies of papers that you could lend me? Is the difference in lethal dosage present in other species, too? - etc.

About a dozen years ao, I gave an after-dinner talk on delta-t which was a complete "flop". I happened to run across a copy, cleaning out my files, and I enclose it for your possible bemusement.

Sincerely,

Howard B. Burchell, M.D., Ph.D.
Emeritus Professor of Medicine
Cardiovascular Division

HBB:fmw
encls