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Curt + Chris
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M E M O R A N D U M

TO: Dr. Curtis L. Meinert

FROM: Dr. Henry Blackburn

In reviewing my notes on the last Data Monitoring report, I find nothing consequential.

I was surprised at Dr. Levy's quotes of "authority" on the use of DT4 and his plea for its discontinuance based on dogma rather than data; or does he have access to the data?

There was a remark in the minutes that arrhythmias had a bad influence on prognosis in the VA study. I hope that the Natural History group can have regular access to any exchanges of information you are setting up with that study. What arrhythmias, for example, are important in our analyses.

I am increasingly bugged by the use of the analyses by "risk" group, because "risk group" confuses others, because it increasingly conflicts with terms we are using in writing up risk prediction in the Natural History series, and because it is a composite class. If the number of infarcts really makes up most of the class, and accounts for most of the excess risk, I'd like to consider using that term.

I request again that we set someone to search the early design meetings of CDP and to extract statements which show an awareness of the known hazards of administering thyroid or estrogen to cardiac patients. Chris's statement in the last minutes could be interpreted in a very damaging way that "stratification by risk class was made because of expectation of different death rates, not because of expected difference in drug effects." I simply cannot conceive of these matters not being thoroughly discussed by the clinicians who were well aware of the metabolic effects of thyroid and estrogen. If such considerations were <u>not</u> given to risk stratification, and if there is no clear statement of understanding the risks, and of reasons for excluding class III patients, etc., we are indeed sitting ducks for criticism and for legal action. Surely the possible risks of precipitating angina, myocardial

irritability and heart failure, etc., were carefully weighed against the possible benefits of lipid lowering. I see no evidence in the 1966 consent form that subjects are informed of risks of any of the drugs, or of estrogens and DT4 in particular, and wonder if it would not now be regarded as an inadequate form. There should be full disclosure of these early discussions and a rediscussion of our position.

I sort of helped start this subgroup analysis business which is bugging you, I guess. I don't find it troublesome that people who have more heart damage, more past infarcts, etc., respond differently to drugs. This is inherent in all approaches to therapy and is one reason why we individualize (or stratify) treatment.

Two minor comments on the minutes. Why are old ECG A-G and H-Q classes used when we have baseline readings to use. It doesn't really matter but I wondered?

Why is the coronary sudden death endpoint considered "suspect." The combination requirements of (a) clinical judgment of definite coronary death, (b) one or more documentary findings backing this judgment, (c) the use of CDP defined endpoint criteria, (d) last July 1970 documentation which revealed that 91% of interim infarcts had hard documenting criteria, and (e) the very explicit requirement of 60 minute lapsed time, all suggest that the coronary diagnoses are pretty strong, including the sudden death class.

HB:meb