Stamler on CVD Epi Priorities at end of 1960s FB.

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J. Stamler to:

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Dear Fred:

Here, finally, are my comments on the draft of our Council Executive Committee statement:

I find myself in general agreement with virtually all points made in the draft. It has all the ideas in it that we need. However, I think it needs a sizeable editing job, to make it as effective and forceful as possible. I would like, therefore, first to make some general observations that I hope will be helpful to you as you tackle the difficult editing task. (I am painfully aware how difficult it is to edit one's own splendid words, based on helpful comments from good colleagues around the country! I have just been going through the process!!)

First of all, it was my distinct recollection -- I may be wrong in this regard -- that the statement was to limit itself to current priorities for epidemiological research in the cardiovascular field. I believe we discussed the matter of attempting to encompass community needs as well, and decided to consider incorporating our views on this in a separate statement. In reading over the draft, I am more than ever convinced that we would be speaking out much more clearly if we confine ourselves to the research question. I encompass in this all aspects of epidemiological research in the cardiovascular field -- including the gamut of descriptive-analytical studies, experimental studies (field trials), and use of the research modality for evaluation of community programs. I believe we should try to make a clear distinction between the needs in community programming *per se*, and the use of epidemiologic research to evaluate community programs undertaken. This statement, I think, should deal with the latter only.

My second general observation relates to our keeping in mind throughout, as we attempt to get a final draft, certain key questions: What is the background that led us to undertake this statement? What is our purpose in preparing it? To whom primarily is it addressed?

With respect to these key matters, you will recall that the proposal to write a statement came out of our Executive Committee meeting in the Fall of 1967. It was born -- I believe -- out of a recognition of two important phenomena: First, the recognition that the field was at a scientific turning point, based on the tremendous growth of activity since World War II, and the sizeable achievements, particularly on the epidemiology of atherosclerotic coronary heart disease. This recognition led us to the conclusion that there was need for a statement, which would attempt to indicate where we stand, and where the priority needs lay for epidemiological research in the cardiovascular field for the period ahead. The second factor leading to the proposal to draft a statement was the recognition of the increasingly tight budgetary situation, particularly in the National Heart Institute, with resultant threats to the further development of effective epidemiological research on the cardiovascular diseases. Both these developments, one largely positive, the other largely negative, compel more than ever before attention to priorities. Thus, one of our key purposes is to help define these priorities, as sharply as possible. To the extent that we are general and diffuse, and fail to do this, to that extent our statement will be restricted in its value. This is always a big problem, since we always want to "touch base" on every problem that exists, be complete, give recognition to all relevant research, etc. This matter bedeviled me in preparing the report of the Makarska meeting, and the criticism was made of my first draft that it lacked any clear statement whatsoever about priorities. I believe this was a correct criticism, and attempted to overcome this shortcoming in the later draft -- without violating the mixed views of the group, and without imposing my own thoughts (I hope). I believe we have the same problem for this statement.

As I believe we saw it when the project was launched, and when our subcommittee met, the basic purpose here is to indicate priorities clearly, so that there will be a persuasive statement of the need for continued healthy growth of epidemiological research on the cardiovascular diseases over the next decade or two. The field has not only accomplished much, it has much to contribute in the period ahead, of an indispensable nature -- if research generally in this area is to really progress, and not just "piddle". I believe our main purposes are to make these points as crystal clear as we can, i.e. we are stepping into the arena as active protagonists for research in this field, not because we are grinding our axes, but because objective reality compels recognition of the need for this research and attention to its priority problems at this juncture. In connection with this purpose, I believe we should avoid any apologetics. There really is no need for any. Our field, like all other aspects of research, has its strengths and weaknesses (both in regard to the method, and the achievements so far). We are the ones most keenly aware of these and we tend to be very critical, very alert about questions of design, statistics, etc., to the point at times of "beating our breats" about the problems in our field. I do not notice our colleagues doing clinical investigation, animal work, biochemistry and biophysics doing this in their public pronouncements. I see no reason why we should. Rather, our job is to explain repeatedly the fact that this research method has a legitimacy equal to that of all others, is indispensable for solving certain problems which no other can solve, just as it is unable to solve certain problems which only other methods can solve. This is a key question of the moment, when there is extensive confusion about what is "basic" in research, and a marked tendency to regard as fundamental only reductionistic approaches. As Dubos and others have emphasized, this is fundamentally wrong in terms of scientific methodologies, and this dysbalance needs to be fought, implicitly, if not explicitly. Unfortunately, at present the fight is taking place within a context of very tight budgets, and keen competition, in which those who have no understanding of epidemiology are readily persuaded to convert their lack of knowledge into hostility, thereby intellectually justifying further restriction of its support, so that the money can be funneled into other "basic" channels. This is part of the context in which we are writing. It relates to the figure you have mentioned of only four percent of research monies being allocated to epidemiological research in the cardiovascular field. It has a great deal to do with the difficulty of getting the needed mass field trials going. While we may not be explicit on some of these questions, we must always keep this context in mind as we write our statement, and understand its basic purpose in relation to this context.

Finally, I think our purpose was to write a statement that could go to and influence policy makers. In other words, it is not primarily an inner-Council statement. Rather, it is to influence the American Heart Association overall, its Central Committee, its Research Committee, and even more important the National Heart Institute. Thus, it is basically a public statement. That too must be kept fully in mind as we write.

All these considerations make the writing task a tough one! I am glad you have the chore of trying to prepare the final draft, and not I!

Attempting to keep the foregoing in mind myself (!), I have the following comments on specific aspects of the text:

I think the title should be changed to delete the reference to community needs.

I think the <u>Introduction</u> should be shortened, and made to focus sharply on the background considerations -- the fact that we are at a scientific and social crossroads in this field -- that led to the statement. A good deal of the material in the first draft of the Introduction drifts away from this, e.g. the second and third sentence of the second paragraph, page 1.

With respect to item number 2 Research Needs, 2.1.1. Coronary Heart Disease, I have the following comments: First, I believe it is proper to speak of two major achievements, i.e. the tremendous accumulation of knowledge about the disease through international comparisions, and the work on risk factors, and I might add the delineation of the relationships between risk factors and different incidence and mortality rates observed internationally. I think the estimate of the contribution of the last two decades is markedly enhanced if we recognize both aspects. I believe it also gives us a clearer perspective on what remains to be done. In regard to the international comparisons, one needs only to mention the work of Keys and his collaborators, and that of the New Orleans group and their collaborators.

Given this estimate, I think the first matter that needs clear delineation is an evaluation of the role of descriptive-analytical prospective studies on CHD in the next five to ten years. I think it is appropriate first to note that the ongoing studies should be carried through to completion, to maximize their contribution, e.g. to permit extension of their findings beyond coronary disease to peripheral and cerebrovascular diseases of the atherosclerotic type. I believe that permitting them to finish their work is a priority task. It will greatly enhance ability to make the multivariate analyses we all want, as well as give insight into atherosclerotic disease in beds other than the coronary. Finally, it will permit clarification of certain risk factor questions that are still obscure. Thus, as I read the data, the prospective studies to date have been especially clear in pinpointing the relationship of serum cholesterol, blood pressure and smoking to risk. The matter of weight needs further clarification, particularly through multivariate analyses in which several variables are held constant. Similarly, more needs to be done on serum uric acid and plasma glucose levels and their relationship to risk. The latter variable has been looked at in the best way (based on glucose loading) only latterly, and time must pass to get decent prospective data. More information is also needed on the relationship between coffee consumption and risk, and vital capacity and risk, and personality-behavior and risk. I omit mention of the physical activity-fitness parameter, since I do not believe the prospective studies have the ability further to clarify this question. I hope I am being clear in what I am trying to say (I am not sure I am!). The foregoing is all part of the theme of completing the job that is already well along. It encompasses three thoughts, i.e. getting as much information as possible on risk factors for the coronary, cerebral and peripheral beds; completing the clarification (insofar as possible) of those risk factors as not yet fully clarified; and getting the richest body of data possible for multivariate analyses, both of the usual type (by multiple substratifications), and of new statistical analytical varieties. I think it appropriate to mention here the importance of the Pooling Project in this regard. I frankly would hesitate to make vague proposals about the desirability of discovering new tasks. I know of none looming on the horizon, and frankly believe that the main ones have already been discovered. Perhaps life will prove me dead wrong in this regard. However, I believe a statement on priorities should be as concrete as possible, and should avoid vague generalities and promissory notes. I honestly do not believe that sizeable investment in the search for specific lipid subfractions, etc. is at this point indicated. I would hate to see us go out on this sort of limb.

I agree very much with the concrete questions posed on the top of page 3 concerning carbohydrate-lipid interrelationships, multiple predictive functions incorporating variables hitherto overlooked, and approaches to the thrombogenesis question.

With respect to the last sentence in the discussion of risk factors, on the middle of page 3, this gets into the area of community needs, and as important as it is, I think it should be left for a separate statement -- although I agree with it completely, as you know.

With respect to the material on the bottom of page 3 and top of page 4, I think this should be put earlier in the statement, i.e. I think the <u>Introduction</u> should state clearly that our purpose is not to prepare a guide line for a specific research project. As to that material on mechanisms, I think the critical importance of a good deal of the risk factor work is that it has clarified mechanisms. Thus, the international studies since World War II have not only been important because they have given us a greatly enriched body of knowledge on the differences in occurrence of the disease in different parts of the world and their relationship to differences in the mode of life, but have in a major way indicated pathogenetic pathways (e.g. via differences in serum lipids particularly). I do not believe we need to imply that epidemiology contributes to knowledge of mechanism only when it is linked to clinical research studies. However, I do believe that a most important point is contained there, namely that an inter-linkage among epidemiological, clinical and laboratory research is very fruitful. Again, to cite an example, the metabolic ward studies of the Laboratory of Physiological Hygiene group on dietary components and serum lipids have dovetailed very nicely with their field studies, the one enriching the other. I do believe it would be appropriate somewhere in the statement, perhaps at the end, or at the end of the section dealing with atherosclerotic diseases, to make the point that much more encouragement should be given to the tackling by clinical investigative and animal experimental means of cardinal problems posed by epidemiology. My only concern in this regard is with the problem of writing too vague a statement on this, and yet I hesitate to deal at length with areas where this might be particularly fruitful.

With respect to the next to the last paragraph on page 4, the implication of my earlier discussion is that international research should be mentioned in the statement, and its achievements highlighted as one of the key contributions. I do not think we should make this beyond the scope of our statement.

With respect to environment and heredity, I think it would be good if we pinpointed more clearly what are the priority considerations. From both a practical and theoretical point of view, I regard as especially valuable the sorts of data that you have generated in/ Tecumseh indicatin a relationship between findings in parents and children, thereby permitting development of the practical concept that the upper end of the distribution in youth -- even though it is within normal range for such parameters as blood pressure, cholesterol, glucose -- is in fact abnormal and indicative of future risk (as supported by family history data). The question is, what are priorities for next work along these lines?

I think the paragraph on page 5 dealing with the study of social groups in transition is very important, and should be made a priority paragraph. It applies equally to hypertensive and to atherosclerotic disease.

With respect to the section on preventive trials, I of course believe that this must be one of the priority emphases. All of the developments in the descriptive-analytical work, as well as in the clinical, pathologic and animal-experimental laboratories, point to the possibility of prevention, and the need for field trials. You may perhaps want to lift material out of the Makarska report dealing with this whole question. I think we should put the argument in as many documents as possible, with every barrel we can fire. Unfortunately, I do not believe your first sentence is correct. The need and high priority of trials are <u>not</u> recognized, Quite the contrary, as a long day in Bethesda recently further taught me.

Further, I think we should commit ourselves to priorities on the types of trials needed. I think we should emphasize the need for primary prevention, in high risk persons, both in closed and open populations, to permit both the advantages of single factor-double blind design (closed population study), and to clarify the key question explicit in multifactorial mode of life studies (open population): Can we really prevent the disease in the general population? I believe the Makarska report goes a way toward dealing with these priority problems, and I think we should here to. Otherwise, the statement will have no real impact in this regard.

With respect to myocardial factors (page 6), I think it might not be amiss to say something about a priority for further research on sudden death. This perhaps should go into the earlier section dealing with priorities for further work from the prospective-analytical studies. My concern with this statement as it now reads is that it is too vague. A statement encouraging the pinpointing of risk factors for sudden death would be very explicit, and would clearly indicate a priority item.

The item on the bottom of page 6 relates to my earlier discussion on the matters of peripheral and cerebrovascular disease. This is in part a matter of the organization of the statement. As I indicated, again with my concern for priorities, one of the items I believe is key is to get all the data we can from these ongoing studies on the key epidemiological correlates of peripheral and cerebral disease, as well as coronary disease. By itself, I find it difficult to think of generating any excitement about correlation among lesions in different beds.

At this point in the dictation, I recall my one concern with the statement Irv Page prepared for the Second National Conference on needs for research on atherosclerotic disease. It was indeed comprehensive. It missed nothing. It mentioned everything. In this sense it was very erudite. Looking over the list of all the things that needed to be done, however, one could easily get the impression that nothing was known, that everything needed still to be done, and that the tasks were endless. Amidst the detailed enumerations, absolutely no priorities emerged. It is precisely this kind of problem that I want us to avoid. I honestly do not believe that the kind of thing done in that Second National Conference document could have had any real impact, and I do not believe it has had any real impact.

As to hypertension (page 7), I think we should first note that we are on a rising curve of fruitful work on the epidemiology of this disease, and -- in view of limited knowledge in this area, and concerning its etiology generally -- this should be a very high priority item. As you know, in my overview of cardiovascular epidemiology generally, it is my strong conviction that a major shift should be effected, to an emphasis and priority for research on the epidemiology of hypertensive disease. I think this must be part of the perspective, based on the achievements to date of descriptive-analytical studies on atherosclerotic disease, and the unsolved problems of hypertensive disease. This of course is based on my view that the main aspects of the etiology and pathogenesis of atherosclerotic disease have been generally delineated, in contrast to the situation in hypertension, which is clearly the other major disease process. Perhaps you and the other members of our subcommittee, and the Executive Committee of the Council are not prepared to make a bold statement in this regard. I would hope that we would do so, and that it would include an emphasis on "milking" the current prospective studies to get from them the masses of data on the epidemiology of hypertension still lying buried in their files and data tapes. I also believe we should encourage more investigators to tackle this field from every aspect, including the complex methodological ones (e.g. ways to measure habitual salt intake, habitual tension, etc.). Work is going on in these directions, at an increasing rate, and it should be encouraged.

I think we should clearly separate sections dealing with this matter of basic epidemiological research on hypertension from the matter of further preventive trials. Obviously, in that latter area the key need is to delineate consequences of controlling "mild" hypertension, diastolics in the range of 90-115 mm.Hg.

I doubt that reference to the section we wrote in the book on the epidemiology of hypertension will result in many readers looking at it. Therefore I think we have to lift the essential material and put it here, if this is to be an effective section. It should include the importance of exploring the obesity question, the salt question, the personality question, the Negro-white difference question, etc. I would not hesitate to plagiarize and stick it right in here so that this is a major forceful section of the document, clearly indicating central priorities, within an overall priority area.

Again, in line with the general thought, discussion of community programs should be deleted -- but pointed reference made to the importance of including in the design of pilot, developmental and new public health programs ample epidemiological techniques for evaluation. My inclination would be not to include this in every section, as something of a pious statement, but to have a general section at the end highlighting this as a special area for the use of epidemiological research tools in the present changing public health scene. The present section on community needs could be boiled down or rather converted into that section, and the whole matter of our thoughts on programming in this area saved for a separate statement. I share with you the belief that we need such a statement, and perhaps this could be on the Executive Committee agenda for discussion. I am about to have the interesting experience of appearing before a Welfare Council meeting here in Chicago to discuss strategy in this area for the city. This is a monthly leadership gathering in the health field, and I go into it with great curiosity as to the intellectual response, and the actual results in practice! I have also found it very stimulating serving on a couple of Illinois Regional Medical Program committees dealing in this area. There are signs of potential progress -- but they are indeed feeble! Thus, we need to be heard!

I share your conviction that pulmonary heart disease is today the third major form of adult heart disease in our country. However, I must confess to inability to pinpoint priority areas for epidemiological research on this. Perhaps that reflects my ignorance. I think the first key here is the smoking question -- but that is not a research matter, but rather an issue of applying knowledge to public health control -- i.e. the subject for our other statement. I have nothing significant to contribute concerning priorities for research in this area. Again, I think we should say something only if we can give a clear priority indication.

With respect to the section on methods (page 9), I think particular care should be taken to avoid apologetics. Let me cite the second and third sentence as examples. As in other field of research, there are precise and clear methodological problems, and we should mention them, while avoiding any tendency to exaggerate our difficulties. The items mentioned in the second paragraph are indeed excellent. I think we should include in the list the matter of resolving the methodological problem of getting more accurate data on habitual salt intake.

The questions in the area of methods are two-fold, I believe: First what are the most important methodological problems we face at the present juncture, and second what is the atmosphere for encouraging work in this area to solve them? I think this section should be greatly shortened to focus on these two questions. With respect to the latter, I think it can be correctly said that one is not readily encouraged to put forward a lot of energy on methodological questions, since support for sustained efforts along these lines is not readily obtained. This is bad, and should be corrected, and we should say so.

I agree that one important priority area is that of improving methods for assessing aspects of personality and behavior. I think that we should note the important work going on in this area, and the need to encourage it. I believe that much of the material on page 10 needs careful editing, since it tends -- I think -- to divert from our central purposes in this statement, and tends to be overly negative and apologetic (see my xerox of page 10 and the marginal notes, which I hope are comprehensible).

With respect to the whole matter of facilities, I am not quite sure what our priority considerations are in this area. I personally have nothing precise to propose. I think we should delete the general and rather vague statement on the bottom of page 11 that a reassessment of prerequisites and requirements for the most efficient and economical conduct of prospective studies is needed. I would be strongly inclined to delete this. In general, I found myself not being fully able to grasp the point being made in the first paragraph of item 2.3. on facilities.

The material on the top of page 12 deals very well with the matter of the role of epidemiological research in assessment of aspects of medical care delivery. As I have already indicated, all of this should be put into a separate section, as the third facet of our contribution (#1 is work on etiology and pathogenesis, #2 is work on trials).

With respect to registries, having had my considerable experiences with them, I think we should give them a priority only if there is very clear reason for having them, including not only research but also service aspects. In only a few instances familiar to me, have registries served any purpose when set up for reasons other than service. We do have such a chronic bronchopulmonary disease registry here, but its research role is very clear, in regard to effect of air pollution on illness rates in members of the registry. At a recent meeting, I heard talk about an attempt to set up a registry for all the persons with a history of previous myocardial infarction in a given city. No precise reason was given for doing this. This obviously would be a huge undertaking. I am in favor of it only when the reasons are very clear. For example, it might be of great value to get information on prognosis nowadays after myocardial infarction and care in intensive care units. This would be a very specific aspect of epidemiological intelligence surveillence, in relation to the changing natural history presumably resulting from changes in survival because of coronary care unit impact. I do not offer this necessarily as a priority suggestion, but rather to make my point about qualifying our support for registries. I think we need to select priority items in the epidemiological surveillence area, and would mention such things as the effects of mass detection programs to identify coronary prone people, influences of trends of antihypertensive therapy, influences of trends of antidiabetic therapy, influences of trends of use of antihyperlipidemic drugs, influences of the coronary care units, influences of various levels and qualities of medical care service on prognosis for hypertensives (with particular concern for poverty versus nonpoverty sectors of the population, whites versus blacks, etc.). These are more or less immediate thoughts. I think perhaps we need a little pinpointing and refining in this area. I do not believe we have really talked about all this enough so far. We also need epidemiological surveillence on trends of certain habits in the United States. For example, what is actually happening to the diet? We need nutritional surveillence teams to get representative samples and give us information in this regard. I have reason to believe that there may be changes going on sufficient to produce modest reduction in the serum cholesterol levels for middle-aged men, but I'm not sure. It would be valuable to know. Other secular trends of the population need monitoring -- e.g. smoking habits, exercise habits. I believe this would be a very important part of the epidemiological research relating to evolving public health programs. It is these kinds of items that should be boiled out of the last few pages, for this statement on research, reserving the rest for our separate statement on priorities in medical care, or whatever we want precisely to call it.

Well, this has been a long and meandering discussion as you can see! You stimulated the thought processes! I will read this over after I get it off the tape, make whatever changes I can in short order, so that it is not delayed, and send it off -- unless it all sounds so unsatisfactory as to lead me to junk it, in the belief that it will not really help you very much. Let us see.

My commiserations for your task in this regard!

The very best, as always.

Cordially,

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Executive Director

JS/nd