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January 14, 1955

Mrs. Mary Lasker
Chrysler Building
New York 17, New York

Dear Mrs. Lasker:

I finally was able to corner Dr. Simon and Mahmud to discuss the cerebro-vascular problem and am outlining my general views of what could and should be done together with some tentative estimates of general cost range. I shall try to cover the subject with reference to the approaches in my letter to you of November, 1954.

I. The study of occurrence of de novo cerebro-vascular disease in people whose lipoproteins are already known.

This, as previously mentioned, should be a dividend of the large scale followup study under the auspices of the U.S. Public Health Service. There is nothing to do here but await followup coming in.

Estimated Cost: None, beyond what has already been spent in the Cooperative Study itself.

II. A study of the difference in lipoprotein levels between individuals with a documented episode of cerebral thrombosis versus clinically well individuals of the same age and sex.

This is the study which Dr. Wright, Mrs. Fordyce, you, and I discussed at lunch in New York. Dr. Wright has told me since then that he is definitely prepared to go ahead with this study as soon as it can be organized. I believe an effort should be made to have at least a series of 100 well-documented cases of cerebral thrombosis plus control cases. Whether Dr. Wright can collect an adequate series in 2 to 3 years I don't know for sure, but it may prove advantageous to have Dr. Marmorsten's colleagues also collect a series in Los Angeles both for numbers and for confirmation.

Estimated Cost per year:

(a) For Dr. Wright's part I don't know what costs may be entailed. He will have to estimate this and I shall ask him to let you know if there is any cost, and if so, how much.

(b) For shipping bloods, materials, ultracentrifugation, etc., in our laboratory. Several hundred analyses per year for 2 or 3 years - \$5000/year.

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File Code No.	<i>12-5-33</i>
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The Correlation of cerebral atherosclerotic changes with coronary atherosclerotic changes.

As discussed with you this study provides one way of getting at the relationship lipoproteins to cerebral vascular disease, independent of the other approaches. As, since we know lipoproteins are related to coronary sclerosis, it would be reasonable that a finding of a coronary versus cerebral relationship would mean correlation also between lipoproteins and cerebral atherosclerosis.

Best person to do this would be Dr. Malamud. He is interested in doing it, provided the pathological material can be made available to him. As with all cases of life, this momentarily may present a stumbling block because of lack of cooperation of some of the pathologists who control the State Hospital material would like to use for the study. However Dr. Simon, Dr. Malamud and I are going to try to break this block and I believe we can do it.

When the pathological material will be available for him, we can estimate the costs for Dr. Malamud's work.

Estimated Cost per year

(a) Pathologists technician	\$4000/year
(b) Materials, etc.	<u>2000/year</u>
Total	\$6000/year

There are some additional possibilities of getting this study done, if our State Hospital sources fail.

- (a) Dr. Marmorsten suggested she might be able to get pathologic material.
- (b) I am writing to Dr. Jesse Edwards at the Mayo Clinic who, I think, may be quite interested in doing it.

The measurement of lipoproteins during life with subsequent autopsy measurement of the degree of sclerosis of the cerebral arteries.

This study I believe Dr. Malamud plus ourselves can execute successfully, since the source of the material is assured. Part of the study is already in progress. Basically this involves the study of about 500-1000 people in State hospitals where a high death rate for such people exists. Bloods are taken at admission to the hospital for lipoprotein analysis and the results are to be correlated with the cerebral vessel changes in that fraction of the studied group which comes to autopsy within approximately a 2 year period of the blood study.

Estimated Cost per year

- (a) Blood studies ultracentrifugally on about 300 cases per year. \$4000/year.
- (b) Dr. Malamud's costs (none additional to those estimated in Section II).

The utilization of the Stockton State Hospital material for evaluation of therapeutic agents plus provision of clinical material of value in some of the above studies.

In our discussion I told you about the thyroid studies at Stockton. These and other very valuable studies for the cerebro-vascular program (and, incidentally the coronary disease program) could be very materially accelerated if physician and technical help assigned specifically for this work could be made available at

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the Stockton Hospital

<u>Estimated Cost per year</u>		
Physician (Resident Level) Responsible for the studies at Stockton		4600/year
Nurse-secretary combination to administer drugs, collect samples, etc.		<u>3600/year</u>
	Total	\$8200/year

Total Estimated Costs per year

I.	No. Cost	
II.	\$5000/year	
III.	\$6000/year	
IV.	\$4000/year	
V.	<u>\$8200/year</u>	
	\$23,200/year	

Not included here are (a) any costs Dr. Irving Wright might have associated with his participation, and (b) any costs Dr. Marmorsten might have if she or her colleagues participate.

Since a two or three year period should be considered as a minimum for any effective progress on the problem, the estimated costs would be:

For two year,		Total \$46,400
For three years,		Total 69,600

Knowing how research goes in general, even with enthusiasm and drive, our general inclination is to underestimate the time it takes to do a job. Therefore I would strongly advise consideration of the three-year prospect.

It is evident that some part of the program could be left out if a cost figure of roughly \$70,000 for the three years is not within the realm of consideration. The cost would be reduced accordingly, but of course some would the chance of covering the critical aspects of the problem.

I submit this to you, not as a formal proposal, but for your consideration, review, and suggestions. Please feel free to question any or all parts of it and give me your reactions.

With my best personal regards.

Sincerely,

John W. Gufman, M.D.

JWG:dip