

CONFIDENTIAL

August 25, 1948

Bob,

I am grateful for your fair and careful formulation of the purposes of the Laboratory. It shows me among other things that I have been remiss in not keeping you better informed of my activities here. I am looking forward to the privilege of talking these matters over with you as you suggested. I am taking the liberty of outlining briefly my interpretation of my behavior and motivation, without waiting for the time of the discussion, for the problem is so complex that I fear I might miss something if I tried to present all the aspects of the situation verbally, and I am anxious that we understand each other before we discuss the detailed plans for the future. For it seems to me that I can be of great value to you and to industrial health, and that I would find the responsibilities accruing from such a position most satisfying.

In the complex field of industrial health my principal interests and training have developed in the broad aspects of respiratory physiology and experimental methodology. I include in respiratory physiology not only diseases of the lungs and circulatory system, but such conditions as hemoglobin inactivation, tissue utilization of oxygen, and enzyme inhibition, so the pertinent conditions extend from silicosis to lead poisoning. Under methodology I include the design and evaluation of experiments, and this extends from estimating the parameters of the dosage-mortality curve for animals to the clinical evaluation of the therapy of lead poisoning in man. I recognize that I am trained as a clinician and clinical investigator, and do not pose as a physiologist, a biometrician, an industrial physician or a consultant internist, not because such activities would not be admirable, but because I can't be expert in all fields. I freely acknowledge my debt to these disciplines, and even feel that I can contribute to the advancement of knowledge in these fields.

To avoid loss by too wide diffusion of such time and abilities that are available to me, I have studied intensively in the years I have been here certain specific problems with which I have come in contact. What I want to do now is to increase my effectiveness by guiding the efforts of others in these same fields, for there is too much for me to do alone.

I would like to outline briefly three examples of these efforts to date. The first, and what seems to me of the most immediate importance (although the least fruitful as yet) has been a study of the data obtained from

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men exposed to lead, over the last five years. It soon appeared to me that if I was to make any contribution to your work in this field that I needed to know more than I did at that time about the measurement of variation and concomitant variation. I subsequently found, and my experience with decompression sickness confirmed this observation, that while my own knowledge was limited, others too had not known enough to completely resolve this problem of the measurement of variation. I feel now that I do know enough to finish the work I have been trying to do for five years, and agreed to finish this year: present, with your help, the efficiently analyzed and correlated data with a discussion of the inferences that may be drawn safely therefrom. My apparent withdrawal into an ivory tower has not been from ignoring the problem but from attempting to master it. It has required me to criticize J.C.I. manuscripts and such work as Mirsky's and Broh-Kahn's, but this has been a specific criticism along these very lines. Incidentally, the latter's paper presents some of the method of analysis in a quite similar fashion to the way it might be applied in the study of lead poisoning.

The second example is the study of ethyl vanillate and ethyl fluoroacetate. Here I found my principal limitation in this type of research was again my limited knowledge of biological variation. I soon found that others too were investigating in this field without a true understanding of efficient methods of research. Early I attempted to formulate a dosage schedule based on the known behavior of animals, along the same lines taken by Deichmann and LeBlanc. After my discussions with Deichmann he generously offered to include me as a co-author of his paper. With all due respect to both of the authors and acknowledgement of my debt to them, I felt their paper was limited first by the dosage schedule they used, and second by the failure to present a way of estimating the errors of the estimates. It has been this study which led mainly to the delay in the finishing of the ethyl vanillate paper, for that paper depended upon that very method of vertical dose stratification for its validity. Finally we had to finish the paper anyway. At the moment I am still engaged in trying to estimate these errors, for I am not satisfied with that study in its present state. I think that if I am successful that this will be an important contribution to pharmacology and to the specific methodology of this laboratory.

The third example is my private practice. You are well aware that I persisted in my efforts to practice clinical medicine, even though it cost me and my family (and still does), a considerable financial sacrifice, largely because I felt the study of patients was an absolute essential to my retaining and enhancing my clinical skill, and because I was unable to practice here or at the Holmes. There were other reasons for practicing, of course; one of them was the uncertainty that I would be successful as a clinical investigator. I am still convinced that practice is essential

for my type of research. Of course, I would like to pick and choose my cases, but that time has not yet come; so in order to get established I have had to see patients suffering from non-cardiac and non-respiratory conditions. However, a part of my work consists of the survey of several groups of executives, and I believe that these studies in their scope and objectivity compare favorably with those that anyone else has done or will be able to do. A great deal of the time I spend in my office is purely in order to be available to patients, and I do much of my research there. Possibly for the sake of my family I have been unwise in not trying harder to get known; I have preferred to use my free time working nights and early in the morning here, studying lung gas exchange and the methods of measurement of lung disease. I have used my private patients to this end. A superior method of doing BMR's, and a study of the relative importance of pCO_2 , pO_2 and lung volume on the stimulus to breathe, are the most important immediate problems that are near solution.

I have a burning desire to master these fields and contribute to the advancement of science. As I see it, I am limited now less by lack of knowledge than help and support. It seems essential that I delimit the field of my interests so as not to dissipate my energies, for the problems I would like to study are so vast as to be insoluble by my partial and unassisted efforts. I have suggested a separate laboratory not to disengage myself from others here, but to allow of the formal recognition that this is a field which is being studied productively and authoritatively by experts. Of course, it needs the active support and interest of the other members of the laboratory; their knowledge and skill is invaluable. I would want to be responsible for the teaching of the Fellows in the fields of respiratory physiology and clinical methodology; if they wanted to help in our research I would be more than pleased. But just as Cholak is responsible for his men and his equipment, so I would expect to be of mine.

It is not to my interest to have these problems independent of your review - the program includes formal approval and I should hope for your active interest. I need in addition rank such that I am recognized as a responsible investigator in order to have the respect, authority and prestige to carry out this work with facility and help my associates in their subsequent careers. I have observed that an investigator works best when the men under him are responsible solely to him, and if those to whom he is responsible trust in large degree in his wisdom in heeding the advice, desires and criticism of others in his choice of the problems to be studied in the field in which he is expert. I would expect to have referred all problems in these fields that come to the attention of the laboratory and to be given facilities to adequately study them. I feel that a study of such patients would be essential to keep me and my

fellows oriented in the practical problems of industrial health, just as my practice keeps me oriented in the problems of the diagnosis and treatment of lung disease, for in the final analysis it is toward helping these men that all our efforts would be devoted.

I have deeply appreciated the privilege of working under your aegis and the faith you have shown in me in allowing me to be governed largely by my own judgment in the selection of the problems which have occupied my time. I hope that you will find that your trust has been justified despite the discouragingly small output I may have had so far. I strongly feel that I now know enough, and the problems I have studied show promise enough, to have it worth my while to continue in clinical investigation. I cannot think of a possible alternative to working here that would anywhere near meet its advantages to me. Whether it would be worth it to you is not for me to decide. No matter how it turns out, there will certainly be no question in my mind of your devotion to your ideals which have come so close to realization, and of my indebtedness to you for what I have learned under your direction and for the whole-hearted support I have always received.