June 29, 1941.

Dear Noel:

Will at least start this tonight. As usual I am far behind in my correspondence debt to you. Thanks for your tolerance about it.

I am returning herewith Michael's letter and thanks for letting me read it. Strange to say, I had received a good long letter from him just a few days earlier.

His problems and yours, so far as cyclo is concerned are so much the same, in my opinion, that they could be discussed together from the fundamental standpoint. The difference is that he is dealing with lung surgery and you are using it mostly on abdomen.

Your capitalized remark as to "Why use cyclo when ether is so much easier." Not just those words but that was the thought I got from it. I mentioned you in my reply to Michael's letter as having had the same sort of experiences. I should have made a copy of that letter for you and saved some writing now.

This "Arm Chair" research is a bit better than I had thought it could be. Given enough time, a fellow can piece together various parts of his former experiences and the reports of experiences from friends, as you and Michael, for example, and sometimes get a picture. Often it is not a complete picture, and often when it is complete it is not correct but the making of them helps the maker and probably hurts no one else, so it is worth continuing.

My ideas, vague as they are and probably wrong, about your cyclo and Michael's, might be rendered into a classification by a more active mind than mine. I gave them all to Michael in a letter just finished and am briefing them here for you, hoping that one of you may be able to fit the pieces together. To me it seems just out of reach but keeps bobbing up as if giving me the horse laugh.

All of our depressant drugs—at least all that I can think of—have a period of "Stimulation" on their way down to their depressant action. Stimulation it is called in the books but that word doesn't fit well. I would rather call it a period of increased irritability of the nervous mechanism which is later to be depressed by the drug. The degree of increase in irritability and its duration before depression is accomplished depends of course upon a number of things, and varies with each individual as well as with different conditions in the same individual. Thus a fast induction, although possibly more likely with some agents to invoke active induction delirium, is more quickly through the stage and to its desired depth, with shorter period of irritability. And active reflex manifestations during the irritability period are proportionately more likely as the metabolic rate or conscious irritability before anesthesia, is high.

The action of different anesthetic agents in the matter of degree of irritability before the desired depression is achieved, varies a great deal. Cyclo is, I believe by far the most active agent in this respect. It seems to produce not only a more active reflex response to stimulation than other agents but the period of its activity in this respect is longer.
The comparison of Cyclo with Ether in this respect is interesting.

Ether is a respiratory stimulant and although much slower in its action than cyclo, ether produces but little period of descending irritability. The fact that it is a decided respiratory stimulant is here important. And now I must repeat an old belief of mine which is that inspiratory inhibitory reflex response to direct irritation of any part of the external respiratory neuro mechanism is largely proportionate to the need for respiration at the time. If the need is great - high CO2 - the inhibitory watch dogs grow lenient and will tolerate a considerable degree of direct irritation before interfering with inspiration. If the need is small - low CO2 - inhibitory inspiratory reflex activity is much more marked. Or if the physiological appreciation of the high need for respiration, even in the unconscious patient, is blocked by depression of the respiratory centers, (Cyclo) the reflex response stopping or interfering with inspiration is about the same as if the need were low. Thus ether has it on cyclo in this activity in promoting better respiration in the presence of the direct irritation of inspired vapors, or of debris etc.

Cyclo is one of the most potent respiratory depressants in anesthesia and this fact lowers the appreciation in the patient of any high need for respiration that might be present. Cyclo, to repeat, produces about the most active and longest stage of reflex irritability among our anesthetic agents. Call it sensitization to adrenin if you will. Probably is so. But whatever the mechanism might be, the activity is there. So we have with cyclo, a stage of hyper-irritability of entire automatic nervous system with respiratory difficulties outstanding, probably because of the blocking of appreciation of the greater need for respiration which might be present. Greater need is certainly present pretty shortly after reflex glottis closure.

Again we must recall the relationship between Threshold and Stimulus in respiration as well as in all nervous activity and, if you can imagine the "Ouija" board, the positions of these two factors will be quite different with ether than with cyclo.

In lung surgery, the depth of anesthesia is governed more by the requirements for holding quiet under the irritation of the trachea, larynx or bronchi by the endotracheal or bronchial catheter, than by the requirements of the surgical procedure. This means that we are likely to play along, in the cyclo anesthesia, in the hyper-irritability stage instead of above or below it. Above is impossible; below seems unnecessary. Therefore we have respiratory difficulties. For example Michael tells of a case in which, with endo-bronchial tube in place properly under cyclo, there was so much reflex spastic fixation of skeletal respiratory muscles that he could not push gases into the lungs by bag pressure. But when he changed to ether in this case, respiration was satisfactory.

I have seen that spastic fixation in cases intubated too early - as have you - under ether or cyclo. If the tube were not in place there would undoubtedly be glottis closure or other inspiratory reflex inhibition. If and no need for skeletal spasticity in the protective effort of nature.
Anesthesia with cyclo must be—often, or at least much more often than with any other agent,—either very light or very deep. The in-between-stage begets trouble. And, it is that possibility which is the only one that I can imagine, causing you the roughness in your cyclo abdomens. I would not insult you by implying that you are not going deep enough. But there is SOMETHING different about your way and my way of handling cyclo in belly surgery. Either it is that or I do not know how to give ether, and all joking aside, the latter is possible. At any rate, I have always been able to produce better bellies with cyclo than with ether. By always I mean since we have started using the deeper technique and refer to the usual case. I don't mean that every case is perfect, or even good, with cyclo. The average is higher since the L.V. barbiturate inductions. But my results with cyclo in belly work, (practically always below apnoea and with C.R.) have been much better and more easily secured than with ether.

With you it is the reverse. It makes me wonder about myself as well as about you.

Started this June 29th. This is July 1st and hardly started.
Good night.)))

July 2nd. 10:00 P.M.

Seems like now that I have less to do, I have not enough time to get it done. Have just re-read the above. It is the skinniest sort of a skeleton outline but I believe that YOU will get what I have tried to say. There is more to it but, as I have said, it seems just out of reach, but coming nearer. Maybe you can gather it in.

I am glad that the Foreword is all straightened out and I am sorry if my crude exposition led to the misunderstanding. Good luck with it.

As for your giving credit in writing, I did not mean to offer any criticism of you in that policy. It happened that I mentioned the discovery of cyclo in Ralph's letter and sent that copy to you. You must be the one to govern that thing and criticism would be presumptuous unless it were specifically asked for. You know; in that matter I have been governed myself, by "My religion"—the Golden Rule—which is the only religion that I have. I try to mention everyone who has been connected with the development of such a thing, whenever it is possible, and to give credit, sometimes when it seems a bit forced. But I don't like to hurt people's feelings and mine have been hurt so many times by exactly that thing, that I know what it means. Of course that is only my idea. Maybe it is not academic. If it is not, then I prefer to be non academic in that matter. No criticism of you from me at all on that score. That is yours.

It is Bill Shuman who has gone into the Army service. Jack, his father, I am afraid is so close to the age limit that he is likely not to be called; and besides, they are not calling many Colonels from the Reserve Corps. My other son in law is with the Navy. Just now he and his family are with us while he waits for transportation to someplace in the Pacific,—probably Honolulu. His family will remain with us.

I can appreciate how glad you must be that the monograph is rounding into shape. You would not be so glad if you had slighted it.
It is the well earned holiday that is most appreciated.

It seems that someone is always just moving away from our house, during the past two years. John Hart had started practice here and had bought his furniture which, when he went into the service, was stored here. He sold it and it was moved away today. Has been but a short time since Shuman (Bill) and his wife and son left us for a station north of San Francisco. However it is likely that my sister will be with us shortly and that will keep the vacancy filled. No cabin in the country for us this summer. Possibly for a short time this fall.

Good luck to you Noel. Hope the above pseudo scientific Arm Chair report does not bore you. I believe it might lead to a valuable teaching classification. Have given it to Nosworthy and now to you. Perhaps one of you will either build it up or tear it down.

But very little writing nowadays. I seem to get along as well and my friends, better. Most of the days spent in the garage work shop, which institution has been given many names by us, depending upon the circumstance at the time. Reparatorium; Inventatorium; Restatorium; Escaporium, which my family does not care for; and since I took some books out there a few days ago my family have referred to it by the very common and undecorative name of Studio. But it is quiet and cool there. Surprising how rapidly the days pass.

And now to finish this installment letter. Time to mail it.

Good night.

As ever yours.

[Signature]

Your bound T.S.S. is attracting much attention among callers and I am proud to have it.