SPECIAL ARTICLE

Atherosclerosis
A Personal Overview

By Irvine H. Page, M.D.

SUMMARY
The effectiveness of the research endeavor in atherogenesis is searchingly considered because neither how to prevent nor how to cure atherosclerosis is known, and there is no decision about what atherosclerosis looks like.

In the overview one of the most serious problems is failure to see the whole problem. Systematic marshalling of detail is vital; yet there must be a longer look. The first broad suggestion is to curtail the divisive trends, view the blood vessels and heart as a whole, and declare unabashedly in favor of atherosclerosis as the prime interest no matter where it appears or under what guise. The time has come when those who study atherosclerosis and myocardial infarction should rethink their approach. Research excellence is the ability to select the few experiments most likely to get at the heart of the matter. An important question is, If the experiment is successful, will it contribute to the solution of the problems of atherogenesis?

There is urgent need to reduce the amount of repetitive, almost trivial, investigation and to seek more creative approaches. Several problems are suggested as examples: the neural component, the atherogenic mosaic, and the inextricable association of atherosclerosis with myocardial infarction. Even such sacrosanct rights as how to do research are briefly considered. This all constitutes an apologia of the author’s own failures in this pressingly important field.

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One of the great weaknesses of getting older is the belief in your own point of view and in the stupidity of others. This is the gap between the tired older generation and the tiresome younger one. To be specific, I am not happy about the effectiveness of our research endeavor in atherogenesis. As a result, I suspect the usual turn of events is occurring; the plumber surgeons are cutting in because we know neither how to prevent nor how to cure atherosclerosis. Indeed, we cannot even decide what atherosclerosis looks like.

Of course our management of myocardial infarct victims has improved, and several of the surgical treatments undoubtedly are helpful. But heart transplantation and artificial hearts will not be the answer to coronary vascular disease for many years, even if a Boston store advertises, “Used organs available.” We announce bravely through the
news media what we will be doing in the year 2000, knowing full well many of us won't be around to take the responsibility. This may keep the research dollars rolling in, but it deflects from the real problem, loath as we are to admit it. It is no fun to tell an eager Congressional committee how much we don't know and even less rewarding to give a panting reporter the reasons why the role that cholesterol plays is unclear. Especially is this so when dashing surgeons have just put the heart of a young girl into a man twice her age. This is really giving her heart to Daddy!

It is good clean fun to point out the faults of others, but we had best take a closer look at ourselves. What I have to say is very personal and comes from a long experience during which I have learned much less than I should have thought. But it is time that an overview be made by each of us to avoid exhibiting the neutrality of Brownian movement.

**Divisive Trends**

My first broad suggestion is that the divisive trends, unfortunately emboldened by the name, "Heart Disease, Cancer, and Stroke," be curtailed and the blood vessels and heart be viewed as a whole. Why should those investigators interested in strokes become separated from those trying to discover the cause and cure or prevention of coronary or renal artery disease? I understand about the union lines for picketing and protesting but, I suspect, we can all live comfortably together. There is a neurological aspect to stroke just as there is a surgical aspect to myocardial infarcts, but the mechanistic aspects of atherosclerosis belong in the same hat and we should all wear it.

It is a pity that atherogenesis does not have a strong enough chemotactic attraction to concentrate the majority of publications into a few journals. As things now stand, you are as likely to find something in the *Journal of the Oil Chemists* or *The New Yorker* as in *Circulation Research*.

Epidemiologists, the whirling dervishes of our trade, have contributed some of the most substantial pieces of knowledge. But they need fresh methods and ideas lest they tire of our fare and seek other interests. They should not become a separate union or be isolated from the uncertainties of our endeavor.

Then there are the statisticians, social scientists, anthropologists, and such like who participate in our big enterprises such as the "National Diet-Heart Study." We need them and heaven knows they need us! But we are only a very minor interest of theirs. If we were all that important such problems as the lack of atherosclerosis in Rosetta described by Stewart Wolf would not have been allowed to lapse unconfirmed.

What, then, I am suggesting is that we unabashedly declare in favor of atherosclerosis as our prime interest no matter where it appears or under what guise. The only thing I strenuously object to is calling it, "targeted" or "mission-oriented" research along with "task forces" and other suitable battlefield jargon. I don't like "assaulting" atherosclerosis with words any more than I like the Washington disease of expanding the smallest amount of thought into the greatest possible number of words.

Most people are unaware that only a couple of decades ago a forlorn little group of us met in Atlantic City to start the American Society for the Study of Arteriosclerosis, which is now represented by the present Council on Atherosclerosis. Its beginnings were not auspicious chiefly because there wasn't much to talk about. Remember that a number of us knew Anitschow and Aschoff: Schönheimer was one of my warm friends. During my stay in Germany, I knew Windaus of digitonin fame. When I started work on cholesterol in 1919, it had no structure, and fats occupied about six pages in Matthews' textbook of physiological chemistry. About all we had as research equipment were petroleum ether and separatory funnels. Bromination, iodine numbers, a few color reactions, and digitonin precipitation were our total stock in trade. Feeding cholesterol to rabbits was the benchmark of our expertise. Knowing...
all this, I suggest that the field has done better than expected but nothing like as well as it should. This is especially so, when you realize that cardiologists, for what they were worth in those days, could hardly have cared less about atherogenesis. Neurologists were chiefly British trained, very elegant in manner—especially with a pin to elicit pain—and did not care to hear about cholesterol.

Thus, the field was initially chaotic, and when it started to move, it splayed out in a variety of channels, all leading away from the central theme. People in the field had about the same relationship to atherogenesis that the ornithologist has to the birds.

Our Current Research is Not Good Enough

Surely the time has come when we who study atherogenesis, myocardial infarction, and stroke should rethink our approach. There are many aspects, which while never exhausted, still are potentially much less productive than others. It is unwise to point the finger of scorn, but I think the discerning are aware of the desert areas which may best be characterized as neutral and expensive both in manpower and money.

Research excellence to me is the ability to select those few experiments most likely to get at the heart of the matter. This is not the place to attempt a blueprint of what to do, which I neither could nor should make, but rather to ask ourselves certain useful questions that will delineate good research.

Among the most important of these is, if the experiment is successful, will it contribute to the solution of the problems of atherogenesis? Has the work continuity with your own or previous efforts so that superficiality and scientific opportunism are avoided?

Why drop your current experiment to pile on the bandwagon of some new observation? It is good strategy to stay with a problem while others are in a headlong competitive race which has already been won by the originator. Could the research just as well have been planned and executed by a technician? In short, is truly creative thinking of a trained scientist necessary?

Does the problem merely fit the instruments and experience of the laboratory and the investigator? Far too many tailor their work to the kinds of equipment they possess. This is often a millstone around a young investigator’s neck. One of the great advantages of starting his research career in an essentially bare laboratory is that it helps to get at the bare facts. It reminds me of a press release: “Behind the Miniskirt—A Look at the Real Briton.”

Has there been a suitable period of butterfly-net thinking during which the mind lies fallow and cogitates on an approach that no one else has tried? I keep a file, which has grown large, of problems that at least at the moment seemed important, that are not now under investigation. Reviewing these now, I want to start my career all over again!

Lastly, I believe you should feel at home with a problem. It should fit your capacities and not require the services of a whole team unless it is team research you are undertaking. I am amazed at how many young investigators either quit or become stalemated because of this. They are always searching for someone else’s method and never seem to catch fire. A hallmark is the question they ask, “Is there a method for doing this?” It never seems to occur to them to develop their own method if one is not available.

I believe we need those who can clean up already identified roadways once and for all to obviate the endless reworking of unrewarding territory. This helps to sharpen the image of the main problem. Think of the amount of excess intellectual luggage we are currently carrying in such aspects as the morphology of atherosclerosis and the relationship to lipoproteins. This morass often overwhelms and discourages a young investigator so that he is years in finding out what has been properly, or often improperly, done.

The main function of such massive cooperative studies as the one on lipoproteins as an indicator of atherogenesis hopefully had as
their chief function clearing the air of uncertainty. I hate to think what would have happened if the original trend had continued unabated. Every hospital laboratory in the country would have had a $15,000 ultracentrifuge spinning out results that not one physician in a thousand could understand. But it did help pave the way toward simpler, more revealing patterns which should soon be reflected in more discerning control of the varied hyperlipemias.

I fully realize the impertinence of talking to an audience of peers on how to live rightly. I also know that these arguments have other sides to them. But I do strongly recommend critical reevaluation of much of our current research—not by committees or commissions but by that creative fellow who speaks in concord with the smaller inner voice. Take time to let him speak to you.

Germinal work in atherosclerosis is hard to find. I still have great faith that most of us middle-grounders will lay the foundations and slowly build an edifice of knowledge that will at least lessen the disasters resulting from myocardial infarction and stroke and may ultimately prevent them. We are not running, but rather leisurely walking. Fatty acids are not for sitting on but for the energy it takes to get up off of them!

The Overview

One of the most serious problems facing us is failure to see the whole problem in perspective. Systematic marshalling of detail is vital; yet there must be time for the longer look. You remember Will Rogers’ story. When asked how to combat the German U boat menace, he answered, “Boil the water in the ocean.” But how? “I’ll leave the details to you.”

Most current research is done in the middle area of creativity. Much of it is good and much bad, some in depth, but most the “one shot” kind. Much better would be the selection of a theme by an investigator and then a building by him of a body of knowledge that has some form and structure. In short, when an investigator hangs up his gloves, he should be able to look back and say, “See what I have wrought.” Instead, there has been a great deal of what I call “scientific opportunism” in which every new observation inspires workers to abandon their own leads to scramble for publication and reflected glory. This leads to fragmentation and instead of clearing up the byways so as to define the main thoroughfare, great uncertainty remains. For example, what functionally significant cells contribute to atherogenesis? Organ culture methods used to isolate intimal cells or “Intimocytes” in vitro and more recently, enzymatic intimection, are being used for the metabolic identification of cell types we might call “atherophils” involved in the initial stages of human atheroma. Evidence suggests that the rate of incorporation of extracellular lipids is very high in these intimal cells which in some ways morphologically resemble smooth muscle cells. Incorporation is low in others, such as the fibrophils. These functional differences may be independent of the cell origin: smooth muscle, blood monocytes, connective tissue macrophages, or even mast cells. We have to establish a new cell classification based on local function in the arterial intima, rather than depend upon conventional morphological identification using their resemblance to cells elsewhere.

Quite aside from problems that need research in depth, many old-timers have yielded interesting and possibly important results largely because the investigator refused to give up. For example, continued study of diet in animals would appear to have limited interest, and by and large this is only too true. But Malmros has done long-term studies which have again brought challenge into the field. You remember he showed that the amount of polyunsaturated fatty acids in the diet of rabbits fed cholesterol is crucial for atherogenesis and that saturated fatty acids, especially lauric, greatly augment it. He believes that the high rate of coronary disease in Sweden is, in part, due to the large intake of coconut oil by infants and adults. In rabbits but not in dogs and monkeys, feeding
a saturated neutral fat is enough to produce hypercholesterolemia and atherosclerosis. Why this great difference between rabbits and dogs? I thought once that it was due to inability of rabbit's liver to withhold and metabolize lipid, so most of it appeared in blood. In comparison, for example, with cat's liver, this insufficiency is striking. Whether human beings are more like rabbits or cats you must decide; reproductively, I suggest rabbits and emotionally, probably cats!

Sometimes it pays to be cheeky! I am fully aware of the imprudence of telling other investigators what to investigate. However, I am attempting just that because I believe many, both inside and outside the field, need to reexamine its state.

The demand "to do something" about atherosclerosis is becoming urgent and has grown ever since the vascular tree was pasted together again. Time was when the vessels in the brain were the property of the neurologist and neurosurgeon, those of the kidney, the urologist—who partly metamorphosed into the nephrologist—those of the heart, the cardiologist, and so on. Each was largely unaware of the problems of the other, but this is no more. It is fascinating and often unnerving to listen to these specialists discuss the problems of atherogenesis. The member of the only true union—The American Society for the Study of Arteriosclerosis—would find it diverting, to say the least. The urgent need is for those wholly occupied with research on atherosclerosis to reduce the amount of almost trivial, repetitive investigation and increase the number of fresh, creative starts. Corroborating others' results is safe and makes friends, but contributing new knowledge is what we are being paid for. I propose as examples to formulate a few problems to make the principles come alive, while knowing fully the dangers of misunderstanding in such a Jovian posture.

1. Emphasize the basic mechanism rather than concentrating on refinements of "clinical" methods because I believe strongly that the former is in great danger of being and, indeed, at present is being neglected at the expense of so-called more practical approaches. For instance, I too would like to localize precisely a lesion in the brain, heart, or kidney, but I would much rather avoid the lesion in the first place. Unfortunately, we do not have enough financial and manpower resources to do both kinds of exploration adequately. In our field there are not enough good workers to allow dissipation of their energies in peripheral pursuits.

2. Determine the controlling mechanisms of fibroplasia and the part played by growth of fibroblast as well as secretion of abnormal ground substance. Some believe it involves an initial inflammatory reaction.

3. Develop methods for measuring the deposition and resolution of fibrin.

4. Discover the role of platelets' sludging of red cells in atherogenesis.

5. Define the systems for the storage, transport, and degradation of lipids by intimal cells, all part of the broader study of the arterial wall itself.

6. Show the time sequence and responses of mucopolysaccharides in relation to atherogenesis.

7. Delineate the relationship of polyunsaturated fatty acids, hypertension, salt, and insulin to atherogenesis.

8. Devise procedures for the immunochromical approach to prevent invasion of cells or deposition of fibrin. Autoimmune hyperlipemia may have relevance.

9. Carry out much more penetrating studies of the effects of exercise, smoking, and diet on atherosclerosis. Again, get at fundamental mechanisms.

10. Determine the participation of chronic emotional fatigue on occurrence of myocardial infarction and atherogenesis in human beings.

11. Design methods for measuring intimal damage such as that due to hypoxia.

12. Continue search for anti-lipemic substances, those that decrease platelet adhesiveness, and reduce chronic emotional fatigue. The vast array of new drugs beginning to be studied is a most encouraging sign.

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The Neural Component of Atherogenesis

There is certainly no more controversial component of atherogenesis than neural participation. It ranges all the way from the indirect effects of catecholamines on lipid levels to control of fibrin deposition and lysis. Recently, Friedman and Byers have stated that they have shown how to anticipate myocardial infarction on the basis of emotional factors, and Raab bases preventive cardiology partly on emotional control. Oddly, psychiatrists have not put in their oar as deeply as they previously did in characterizing the hypertensive personality. The Russian school naturally promotes the Pavlovian conditioned reflex view. It is to be expected that many competent investigators will have none of it.

As is my custom, I remain in that awkward position of sitting on the fence with both ears to the ground. I am unable to decide whether it is atherogenesis we are discussing, or the resultant myocardial infarction. There are already enough leads to follow if there is a “verifier” who wants a lifetime job. And in this case the results of verification could be extremely important.

If we are confused, imagine that of the public as illustrated by this question: “How can a wife reduce tension and not give in to all the desires of her husband?”

The Atherogenetic Mosaic

As you know, I have made much of the notion that hypertension is a “disease of regulation”—the response of the hereditarily conditioned body to the internal and external environment to which it must submit. The “causes” of hypertension are many, and they elevate pressure by interfering with the equilibrated mechanisms which control the level of arterial pressure. Atherosclerosis also seems to me to be such a disease in which the tissues of the blood vessels live for the most part happily in a liquid environment periodically filled with lipid particles. In a sense the vessels are a filter bed of a quality selected by your parents. Some among the intimacyes are born to be atherocytes, others fibrocytes. If the environment brings too much lipid under too high a pressure, the atherophil becomes greedy and turns into an atherocyte or foam cell. Thus diet, endogenous lipid metabolism, and arterial pressure may be important factors upsetting the normal equilibria, so furthering atherogenesis.

The factors regulating fibrogenesis have barely begun to be studied, and we sadly need this knowledge. But there are many other facets such as how does diabetes increase atherogenesis? What part exercise and smoking have is almost wholly conjectural. Mental tension and fatigue and the social environment are recognized as vital factors without knowing why. There are certainly other factors we do not now recognize, and we must keep our minds open for their discovery.

The physical superiority of the female is a constant source of concern for the inferior male. He envisions the time when frozen sperm, the biological equivalent of automation, will make him useless except for the menial task of making money. Is it any wonder that he likes to think of himself as the head of the family, whereas in fact his only singular contribution may be spermatogenesis to be banked along with his dollars.

Note how among the “flower children” the male is becoming indistinguishable from the female; he is taking on a protective coloration and like small nations is becoming neutralized.

The one thing we most need to guard against is the facile acceptance of the notion that we are truly measuring the influence of any suspected factors simply by measuring blood levels of a substance or its excretion rate. These are, as you well know, no measure of dynamic equilibria. Tracers should long since have taught us this lesson, but we too often ignore it. Problems concerned with research in depth are almost unlimited and underscore the need to quit wasting so much research effort on superficial studies.

Thinking of atherogenesis as an equilibrated mosaic provides room and order for all
the prejudices and bias each of us has. Remember that if we did not have these lacks of emotional balance, we probably would not do research, at least good research. The mosaic over the years has to some degree kept the peace among investigators of hypertension, and I hope it may be similarly useful to those in atherosclerosis.

Atherosclerosis and Myocardial Infarction

These two conditions become inextricably associated as well as confused for the very good reason that they are almost closely associated enough for one to be an expression of the other. Some believe that the former is the invariable substrate of the latter, but good evidence suggests that perhaps as many as 20% of the patients do not exhibit enough atherosclerosis to justify a cause and effect relationship.

It is important to stress, as has Fredrickson, that there is a vast difference in the occurrence of premature deaths from myocardial infarction in Sweden and Japan as compared with that in the United States. After about the age of 75 years, the rates are about the same. The difficulty lies in the definition of "premature."

If we accept fibrin deposition as the beginning of atherogenesis, with lipid deposition coming only later, interest shifts from lipid metabolism to blood clotting factors. Thus, the more important action of clofibrate may be its fibrinolytic activity, and the same might be true of phenformin plus ethylestrenol. The association of defective fibrinolysis, implying an ominous prognosis, may be one of our primary concerns.

In animals it is claimed that sexual frustration and restrained aggression are potent causes of myocardial infarction. Let that be a lesson to you all! The growing evidence of a behavioral pattern characterizing coronary-prone individuals needs increasing attention. "Run for your life," or jogging if you will, now has the important sanction of the world of fashion. I am not sure how many persons actually exercise even though they may be dressed for it. At least the costume has the advantage that cars don’t stop to pick you up under the illusion that you are in a hurry!

It is not wholly clear why some elderly persons can have extensive coronary atherosclerosis without ischemic heart disease. Perhaps the best explanations are (1) the narrowing of the lumen occurs slowly enough to allow collateral circulation to develop and (2) much of the atherosclerosis in older people is of the calcific variety, usually associated with widening rather than narrowing of the lumen.

Platelets have been a source of endless curiosity. At one time they were derogated as mere "blood dust," but with the discovery of their ability to form clots, they have taken on a new interest. They also are small packets of neurohormons much like the synaptic vesicles in nerve tissue. They release serotonin, histamine, and lysosomal enzymes and aggregate when stimulated by ADP, AMP, collagen, and thrombin. It is conceivable that their increased stickiness and aggregation to form a white clot could occur under a variety of circumstances not uncommon in our lives. They may be an important precipitating factor in myocardial infarction and deserve the most careful study.

You will note that in all mass studies on people the endpoint used is the occurrence of myocardial infarction, which almost unconsciously becomes interchangeable with coronary atherosclerosis. Diet and drugs are the only two aspects now under systematic study, but it is only a matter of time before the other risk factors will be measured. Such studies will become increasingly more difficult because of the great interest of the public and its proclivity to "do it yourself."

Two other factors are suspect, but no one is sure to what degree. Raab has for years believed in the primary importance of the catecholamines, myocardial hypoxia, and the resultant myocardial necrosis. He is a strong advocate of physical exercise as a preventive measure. More puzzling is Schroeder’s observation that the purer the drinking water in terms of solutes, the higher the cardiovascular death rate.
Clearly there is no lack of things worth studying, but there is some lack of the spirit of adventure and steadfastness to see some of these important problems to their solution.

Automated Research

But getting back to how to do our research, if we don't declare our own priorities, there are those who are willing and able to do it for us. Many businessmen and legislators have become impatient with our research efforts. They believe we should use the methods of what Washington likes to call "targeted, or mission-oriented research." This naturally requires a staff of planners and generally follows what is known as systems analysis which then becomes "big" science with big money. The news media have taken this approach to their bosoms under the heading of a "superplan" purporting to pretty much guarantee the desired result with no nonsense about it. An offshoot is the "Convergence Technique" in which there is "funneling in," to make multiple projects "zero in" on a single objective.

The originators put it this way. "Basically, the technique involves the formulation of a series of flows and arrays depicting major research program elements in a hierarchy of phases, steps and individual projects, sequentially ordered on the basis of research logic, and graphically represented by a matrix which relates research performance to resources required (including personnel, materials, equipment and facilities and funds). The completed matrix is called a convergence chart."...

Plans such as these doubtless have their application at some reasonably advanced stage of research but, I fear that such thinking in the field of atherosclerosis would be costly and unproductive—a very unpopular thing to say, I fully realize.

Research by the Individually Gifted

My life has spanned two vastly important phases in problem solving. The modern one with which most of you are familiar is that of the research team, with as much personal anonymity as good grantsmanship will allow. You remember the footnote in a paper which said, "Since this paper was written one of us has died,"—anonymity in its most sophisticated form. This phase of research method has also spawned that most prolific of all authors, "et al.," not to mention the specter of "empire building" and the provision of sufficient travel funds to insure that gifted young investigators can spend the better part of their research time listening to the airline stewardesses tell them how much they have enjoyed serving them or chuckling over the sign in the hotel room that says, "Put the curtain in the tub before bathing."

Despite all the diversionary tactics of Washington and the great principle of consensus, much good research is being accomplished; probably more than ever before, although per capita, I suspect less.

But if only for reasons of nostalgia, I invite you to look back to the days of my youth, when research was very thinly populated, and even more sparsely paid. In general, you had to be a kook or a near genius to elect to spend your life in it. But it produced an amazing array of scientific giants, all with remembered names and accomplishments.

I doubt that the Oslers, MacKenzies, and Ehrlichs in medicine, the Habers, Willstätters, and Warburgs in chemistry, and the Rutherfords, Bohrs, and Heisenbergs in atomic physics will soon be forgotten. But today, except for the Nobel Prize winners, it is hard to select such a list, even though substantial research achievements are there. Almost no one remembers that Oswald Avery started the DNA story. Everyone remembers Watson and Crick because of the Prize and the controversial book, "The Double Helix," and the rest are pretty much an anonymous blur.

The important thing, however, is whether there is still a place for the highly personal leadership that characterized the former era? Can our present impersonal system be as productive as one in which personal enthusiasm, experience, and leadership prevailed? A great deal of derogation has been heaped on what is sneeringly known as "the Geheimrat

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System." But before we forget it altogether, I would remind you of the many difficulties the Russians are having with their Academy-directed and planned research. Now ourselves are beginning to run into the same road blocks.

Our field is still in the bumbling phase, but the direction we should take is clear. Most of us are something less than geniuses, but the bidding for our research services is growing at an extraordinary rate. Atherosclerosis is just being discovered by the public, and government is reacting by demanding action, and action to them means money. Money badly spent can only hurt the research endeavor. I am not suggesting that we immediately ask for planning grants—indeed, I strongly object to any master plan because I so strongly believe in diversity in research—but rather I suggest that as individuals we take an overview of what we are trying to do and how we are trying to do it. If the object of our affection is the understanding and prevention of atherogenesis, I humbly suggest that we can all do better. This is the brunt of what I have been trying to say. We cannot wait for a genius to appear among us, but this does not mean a crash program or a mass "attack" is an alternative. What we must do is recognize new research approaches as they appear and make sure they are adequately developed. Even better is to open new vistas ourselves, and I have no doubt this can be done if we ask these two basic questions: (1) Is the problem to be solved unique and capable of being integrated into the existing body of knowledge, and (2) Could it as well be done by a technician as by a trained scientist? We have been held back too long by "over confirming" and attention to extraneous and often irrelevant sidelines. We must not overplan and overpromise. The unfettered mind is a wonderful thing, especially when coupled with an energetic body. Add a touch of skepticism and moderate amounts of money, and you have the recipe for achievement. I think we had better get at it before a "committeeized, targeted, task force" starts an "attack." Victory will, I suspect, be announced quietly from the working laboratory and clinic rather than the White House Rose Garden, with "instant reporting" by newspapers and television. Perhaps we can behave wisely now that most of the alternatives have been exhausted.

As I look back, I realize that almost concurrent with the birth and adolescence of first the American Society for the Study of Arteriosclerosis, then the Council on Atherosclerosis, giant steps have been taken. Most of us have lived too closely with them to appreciate their growth. Lipids have become substances that not only can provide tenure but are exciting. Blood lipids and the varied lipemias interest even the most dedicated stethoscopic cardiologist. Epidemiologists are deadly serious if often obscure in persuading the public of their errant ways. Even doctors are giving up smoking and eating eggs apologetically. Some day we may even realize that it is vastly more important, if not glamorous, to prevent atherosclerosis rather than repair the damage after it is done. Yes, we are living through a revolution started by a small band of the ill-paid and unglamorous "men for all seasons." There were no others interested. Despite my stricture and carping I hold these colleagues in deep respect and affection. Others later will see what they have wrought.
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