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PATHWAYS OF MEDICAL PROGRESS[1]

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ON occasions such as this we gather together from laboratories and hospitals as disciples of scientific medicine. We assemble, primarily, for the purpose of exchanging views on problems which seem to have crystallized for each of us individually. Current reviews thus prepared by thoughtful minds and representing diverse perspectives afford those engaged in other fields an opportunity to keep in touch with the trends of contemporaneous research in specialized fields.

But these occasions have other functions, too. The frank exchange of opinions and the exposition of facts upon which they are founded serve to re-energize us, even if like opposite charges they outwardly seem to repel. As no effective electrical forces can exist without positive and negative charges, so no dynamic forces can be induced in research without a polarity of opinion. Furthermore, we who, despite earnest efforts, frequently become dissatisfied with our own contributions need to revitalize our faith occasionally by noting that the summation of modest efforts has contributed quite as much to medical progress as the occasional big discoveries.

However, impressive as the advance has been during the past quarter century, occasions such as this are opportune for reexamining our current methods and procedures with a view to planning still more efficient and economical means for accelerating it. I shall attempt to review the major pathways over which we have reached our present state of progress in medicine, and, as we proceed, shall stop occasionally to note the ruts in the road and obvious suggestions for their repair. Since this assembly is dominantly interested

[1] Address of the vice-president and chairman of the Section on Medical Sciences, American Association for the Advancement of Science, Columbus, December 28, 1939.

in cardiovascular problems, I may perhaps take the liberty of using illustrations in our field; and, as some of the reflections have grown out of personal experiences, I may be permitted to elucidate them by reference to some of my own work. However, the principles have obvious applications to other clinical fields and other laboratory sciences.

A First Pathway of Progress

Some thirty years ago a transition began to occur in the clinical attitude toward disease. Medicine had passed through the empirical, the descriptive, the nosological, the morphological and the bacteriological epochs of development and began to enter the physiological period. By this we mean that interpretation of disease no longer consisted solely in recognizing signs and symptoms, in grouping them into complexes or syndromes and, in the light of past experiences, in giving the disease a name. Rather, disease was regarded as an experiment which nature makes on man and animals, and the clinical objective changed to that of determining what kind of an experiment is going on. In short, the urge developed not merely *to see* but *to see through* the phenomena of disease. *This change in attitude constituted one important pathway for advance.*

Consider the irregular pulse. As long as clinicians were content to describe and classify irregular hearts and unsuccessfully sought correlations with autopsy findings, the subject remained in a state of chaos. As phrased by Mackenzie, "there seems to be a universal idea in the medical mind that something is very much amiss with the heart that presents an irregular rhythm. As to what that something is no one has any clear idea." As soon as information gained from physiological experiments was logically applied, our understanding of cardiac irregularities and the importance of different types became clearer.

A Second Pathway of Progress

It must not be supposed that this transition involved any abrupt change in the clinical approach toward disease or that no further advances occurred through processes that had dominated previous epochs. There was, and still is, ample opportunity for application of bacteriological and morphological sciences. Important contributions are still made through the processes of observation and description of disease. In fact, nothing can substitute for the power of accurate observation, either at the bedside or in the laboratory. But, during this era, clinicians recognized more definitely that many phenomena of health and disease can not be detected by our unaided senses or, if detectable, can not be adequately analyzed. With this came the greater appreciation that the microscope, the test-tube and—in the case of the heart and circulation—certain instruments developed and tested in physiology laboratories could translate these phenomena into forms that our minds can grasp. Through use of such instruments, our scope of observable phenomena increased tremendously; and, with this greater stock of facts, it became easier to interpret nature's experiments. We need only mention the aids thus gained in studying cardiovascular disease from introduction of pulse recorders, blood pressure apparatus, roentgen rays, electrocardiographs, phonocardiographs, etc. *The extension of observable phenomena through the use of instrumental laboratory aids therefore constituted a second pathway for advance.*

The clinician has employed these implements well; indeed, by their use he has not merely aided in the understanding of disease, but in many instances has extended our knowledge of physiological processes. However, it should not be overlooked that most of these valuable instruments were designed, tested and continuously improved by physiologists. In many cases, the information obtainable was elucidated by previous laboratory experimentation. I mention these facts, not to garner an unshared credit for physiologists, but to emphasize that a silent process of cooperation and correlation has existed for many decades.

A Third Pathway of Progress

A third pathway for clinical advance was opened when clinicians attempted to reinterpret observations —old and new, direct and indirect—by application of new physiological discoveries. This tendency was marked by the appearance of special texts on applied, clinical and pathological physiology and of monographs on special subjects. In some fields—in electrocardiography, for instance—new physiological discoveries were quickly applied clinically and have reaped a rich reward. Unfortunately, this has not been true in all branches; in far too many, the newer physiology has not been utilized as fully as it might have been. This is true quite generally in the consideration of the dynamics of the circulation, with the result that the dynamic changes concerned in valvular disease, cardiac failure, etc., are still explained in ways that are neither very deep nor very accurate. Too frequently clinicians neglect physiological knowledge altogether and invent various similes to clarify processes for themselves and others. While the adult mind continues to delight in kindergarten pastimes, their substitution for sound thinking in the realm of physics is scarcely in keeping with medical science of the present age.

The reason for the slow absorption and utilization of new physiological discoveries is obvious. Physiological phenomena are abstract; they do not appeal directly to our unaided senses. Generally, they require complicated apparatus and procedures for their elucidation. This involves the continual introduction of new techniques unfamiliar to the clinician. In order to describe or express facts so discovered, new words, terms and phrases need to be coined; indeed, in some instances, the thoughts are incapable of expression in words and need to be communicated through the medium of mathematics. For this reason, many an interesting discovery of useful knowledge remains in the cocoon stage because ideas can not be expressed in simple language. The slow metamorphosis that modes of expression undergo delays the birth of many physiological discoveries having a practical value.

May I illustrate the dormancy of laboratory discoveries of daily clinical importance in relation to the dynamics of mitral insufficiency—a topic which every competent clinician professes to understand. In 1922, Dr. Feil and I raised a number of interesting questions. Among them were the following: How, with a grossly incompetent mitral valve, can the left ventricle raise the pressure in its cavities with normal speed and to normal heights? What, indeed, prevents all the blood from being expelled from the ventricle into the auricle against a low pressure rather than partly into the aorta against a high pressure. I should be interested in the answer that competent clinicians would give to these questions to-day, *i.e.*, eighteen years after they were elucidated by modern experimental methods. Suffice it to-day if I stimulate your curiosity, but I may say that the physical conditions for minimal regurgitation are contingent upon a forceful ventricular beat; if the heart is extremely hypodynamic all the blood *does* regurgitate into the auricles. Obviously, such a type of research is fundamental in understanding (1) why myocardial insufficiency is of much greater significance in producing circulatory unbalance when the mitral valves are incompetent, and (2) why improvement in ventricular contraction, *e.g.*, that induced by drugs, reduces the percentile regurgitation and thus aids in compensation.

Delayed recognition of important physiological discoveries frequently continues untenable and wrong points of view. I offer a pertinent illustration! The clinician and the pathologist are concerned in explaining the frequent death following coronary thrombosis. The experimental physiologist finds it more difficult to understand why the patient so often lives. The clinician and pathologist invoke the existence of an adequate collateral circulation. This is certainly not the complete answer, for it happens also in normal dogs in which no functional collateral supply of any importance exists and in which Dr. Tennant and I showed that the entire ischemic area fails to contract within about one minute after ligation of a coronary branch. Indeed, after about thirty minutes, this appears to be irreversible.

With deletion of such a large contracting mass, the pressures within the ventricles and aorta may be expected to fall. However, as Dr. Orias and I demonstrated, the remainder of the muscle at once compensates by giving more vigorous contractions, owing to immediate operation of the fundamental laws of initial tension and initial length—first demonstrated for the frog's heart by O. Frank and extended to the dog's heart by Starling. Hence, if the animal or patient is fortunate enough to escape an initial fibrillation or irregularity and the remaining heart muscle is in good physiological condition, the chance for survival is good.

Apparently greater mutual efforts ought to be made by clinicians and physiologists for better dissemination, digestion and absorption of important physiological discoveries. Attendance at each other's meetings, interdepartmental conferences, reciprocal attendance at ward rounds and especially designed laboratory demonstrations serve to stimulate such interest. Real attainment of these ends can come only through individual effort. The physiologist owes a duty to make current knowledge easily available through current abstracts, annual reviews, special monographs and up-to-date text-books of physiology. The clinician must so arrange his life that time is set aside for serious study of such summaries of knowledge. Indeed, time should be as definitely allotted for such perpetual study as it is in every busy life, for music, art, movies, golf, hunting, baseball, etc. In fact, as Dr. Vaughan was accustomed to admonish us, "the busy individual can always find time to do what he wants to do."

A Fourth Pathway of Progress

A fourth pathway for clinical advance, which many regard as the real avenue of progress, was the assumption of active investigation by clinicians themselves. A number of forces motivated clinicians in this new venture:

(1) While clinicians recognized that they were being assisted in the task of interpreting nature's experiments by application of physiological knowledge, this did not satisfy the growing urge to comprehend disease reactions fundamentally. Consequently, efforts were made to hasten an understanding, not only by investigation of patients, but by animal experiments in which clinical conditions were reproduced or simulated.

(2) At the time that such investigations were inaugurated, physiologists generally were concerned chiefly with the orderly solution of fundamental problems regardless of their immediate practical application, and, if interested in disease at all, were so only for the information it gave regarding physiological problems. The clinician, on the contrary, became interested in experimental work for the light it shed

on processes of disease and, being constantly confronted by these problems, naturally designed more pertinent types of experiments.

In 1930, Rufus Cole, in reviewing a quarter century of progress on the occasion of the twenty-fifth anniversary of the Harvey Society, pointed out that the constitution of that society in 1905 contained no provision for inclusion of clinical investigation in its programs; the reason being that no such science existed. During the three decades or more that have passed, clinical investigation has increased by leaps and bounds, so that the clinician without an active experimental laboratory attached to his wards is apt to be called *passé*. Through such activity, clinical medicine has advanced in many directions. New outlooks have been opened, and our range of vision has been extended; with beneficial results in the management and treatment of many diseases. In this forward march of progress, cardiovascular research in hospitals and associated laboratories has been in the front ranks. Consider the field of electrocardiography alone. Einthoven, a physiologist, had contributed not merely by designing the string galvanometer but in showing the uses of electrocardiograms in diagnosis of the simple arrhythmias, hypertrophy of cardiac chambers and changes in position of the heart. The experimental work of Sir Thomas Lewis, his pupils and disciples, extended the work to include curious ventricular beats and many obscure rhythms and sequences of the heart. Since these epoch-making experiments, the pendulum has swung across the Atlantic, and to-day leadership in cardiology rests in our midst. We need only recall the progressive advances in recognition of coronary obstruction by standard leads, the introduction of chest leads, etc. In other fields, such as heart failure, decompensation, hypertension, coronary obstruction, pericardial interference with cardiac action, injury of the heart and peripheral vascular disorders, American leadership stands out conspicuously. We are fortunate that many of the foremost contributors in their fields are with us to participate in our symposia. Under such auspices, it would be presumptive for your chairman to enlarge upon their contributions.

The discipline of science demands, however, that in the same breath that we pay tribute to our successes, we also examine our shortcomings and mistakes. Progress in any field of research is measured less by quantity than by quality of work. Quality is at least a three-dimensional attribute. It involves (1) length, as regards time spent in execution of the work and in its preparation for presentation, (2) breadth, as regards experience and vision in setting the problem, choosing proper and dependable methods, etc., and (3) depth, as regards caution in restricted interpretation of demonstrated facts and understanding in their integration with those previously established.

A perusal of current journals strongly suggests that improvement in quality of research has not kept pace with increase in quantity. Far too much is characterized neither by breadth of vision, depth of understanding nor restraint in generalization unwarranted by the facts. As Cushney phrased it well, "much base coin passes for legal tender."

This criticism applies to investigations emanating from laboratories of clinical as well as fundamental research. Nevertheless, an impartial evaluation of the yearly publications from these two sources reveals, I believe, a greater proportion of immature, uncritical investigation in the clinical field. Others have delicately hinted at such a situation—but no one has attempted to analyze the reasons.

I raise the issue, not with the motive of extolling the superior quality of research in fundamental medical sciences. I raise it with the conviction that, unless we enter the years before us either with greater increased financial support or with greater economy of effort in clinical research, our rate of progress will retard, not accelerate. I raise the issue because I feel that the mutual regard of laboratory and clinical investigators for each other is such that frank, respectful criticism is welcomed, not resented. And I raise the question particularly because the reason seems clear and the prognosis is good.

Let us examine the situation. Those familiar with contributions of clinical investigation will probably agree that the really outstanding ones emanate (1) from departments in which the chief is better known as an investigator than as a diagnostician or therapeutist, or (2) from departments in which the chief, though not necessarily an experimentalist by training, organizes and inspires a group of investigators each with some specialized training. Such a happy combination of a capable clinician and laboratory-trained investigators gives a well-directed impulse to the investigation of disease and assures a reliability in the execution of the experiments. Such alliances ought to be encouraged. However, the plan is costly and, if universally adopted, would strain the supply of investigators trained in laboratories.

The bulk of clinical investigation is carried out in departments which, for lack of large financial support, can not be organized in these ways. In such departments investigative work is either attempted by older men who have achieved eminence in clinical practice or is delegated to younger men who aspire to higher academic posts through the medium of clinical research. Unfortunately, both groups often fail to realize that research requires more than the ability to formulate questions and the zeal to master difficult techniques. They forget that training and practice are fully as important in laboratory experimentation as in bedside diagnosis. They forget the injunction of

Claude Bernard that "we must be brought up in laboratories and live in them to appreciate the full importance of all the details of procedures in investigation which are so often neglected or despised by false men of science calling themselves generalizers."

Let us compare the routes over which most of these young medical men enter research with the approach of those who enter laboratory research *via* a doctorate in philosophy. Two young men, conveniently called Ph.D. and M.D., with approximately equal mentality, ability, and zeal, graduate together from college at the age of 21 years. Both aim to enter experimental fields but choose different approaches. Upon attainment of their respective doctorates at 25, Ph.D. has had about two years of research apprenticeship to his credit; M.D., of course, has had none. Ph.D. obtains an academic post and, if alert and wise, will find means to continue investigation for the next two years. During these times opportunity arises for displaying his initiative and inventiveness, but the methods he employs, the interpretation of results and particularly their publication still require guidance. The medical graduate, still with the urge to pursue a research career, might of course also enter a laboratory field, as was considered good and even noble practice in my day. But wisely or unwisely, this is no longer considered quite regular and in some states, unlawful. At any event, usually upon advice of his clinical professors, he elects to complete two intern years, during which he is exposed to no investigative work. Thus at 27 years, Ph.D. is already well launched upon a research career, whereas M.D. has not even started. M.D. realizes that he must either attain research equivalence four years later than his laboratory friend or adopt some short-circuit method. If he chooses the latter—and he too generally does—the danger begins. With the misguided concept that acquisition of laboratory technique and research procedure are easily acquired, he plunges into the turbulent waters of clinical investigation. Generally he is left to his own resources, on the theory that one learns best through experience. Guidance and training in precision of execution, caution in continually mistrusting apparent answers yielded by experimentation are generally wanting. Through industry and zeal, results and conclusions are forthcoming. These appear of mountainous significance to him. They are published and praised in local circles; they may be quoted and requoted in uncritical reviews, and he is acclaimed an investigator of promise. But a critical perusal of his work will generally reveal the inadequacy of training and immaturity of judgment of which I have spoken. He fails to realize that, while experiments generally give answers to questions asked, they do not always yield the correct ones. Now it may fairly be asked how an individual with two years of unguided research can hope to compete with another having six years of guided experience. This is the status of M.D. and Ph.D., both engaged in research, at the age of 29 years. This inequality of opportunity to gain experience in experimentation and the venture to short-cut the training is responsible for the mediocrity of much clinical research. Given equal mentality, ambition and zeal, the clinical investigator is at a serious disadvantage. Not infrequently he realizes the situation, and, with the mounting family and social obligations that inevitably enter, he abandons research to enter the practice of medicine. True, his experience is not lost; he is the better practitioner in consequence. But he is lost to clinical research at the beginning of an investigative career, and the results of his immature publications remain forever to confuse the literature.

A number of plans could be devised by which greater equality of opportunity could be achieved. I offer one suggestion that seems to have worked in some instances. The scheme involves encouragement of a few medical students with inclinations for an investigative career to break their medical course at the end of the second year and to assume a fellowship in an experimental laboratory. This should carry a stipend sufficient to defray the cost of the extra year. The work should be so organized that the student gains a year's apprenticeship in laboratory research. After completing his medical studies, a two-year medical internship should be reserved, in which provision is made for participation in a well-organized clinical or laboratory investigation for half of the time. If then he continues in a clinical post which offers ample time for research for another two years, he would, at the age of 29 years, have gained four years of research training and be well launched to undertake independent investigation.

Other plans, of course, are satisfactory. For example, many young doctors after completion of their regular intern years find it feasible, despite the pursuing years, to return to laboratories of fundamental science for methodical training in research. Those of us who direct such departments should make every effort to assist these earnest men. I have made it a practice for some years to keep two salaried places on my staff on a rotational basis for the purpose of training suitable candidates of this type. The results have proved mutually beneficial. But many years the number of applicants exceeds the places available. Foundations desirous of aiding clinical research by starting young men properly in such careers are unable to help all that are worthy of such assistance. More fellowships for the explicit purpose of training promising medical men in the *technique of research* are still urgently needed. In experimental physiology these fellowships should be for a period of two years, since this is the minimal time in which an adequate training can be acquired.

A Fifth Pathway of Progress

In our discussion, it has become apparent that physiology has contributed in various supplementary ways to the success of clinical progress, and several other ways in which it could be of further service have been indicated. What other rôles can experimental physiologists as a class properly play in accelerating the advance of medical science. Physiologists as individuals will probably give different answers. A considerable group still hold, as one current textbook states in the preface, that "the greatest service which physiology can render modern medicine is to continue to solve fundamental problems which are not necessarily of immediate practical concern." Another group, of which I am one, believes that, while the orderly solution of fundamental problems should remain a dominant aim, physiology and clinical medicine are aided simultaneously by researches of a more practical sort carried out by physiologists.

It happens frequently, certainly in cardiovascular research, that data and observations gained through clinical studies need to be referred back to laboratories of physiology, because the fundamental premises involved in their interpretation are not sufficiently understood. All too often, clinical research is not concluded until such additional knowledge is available. May I illustrate by a reference that falls within my field of experience? It concerns the dynamics of aortic insufficiency. Sound physiological teaching has assigned to the aortic valves the function of preventing backflow into the ventricle during diastole. Clinicians therefore arrived at the *a priori* conclusion that a large backflow of blood must necessarily occur when these valves become incompetent. Now, ever since Corrigan in 1832 described the typical peripheral pulse of aortic insufficiency which bears his name, the rapid collapse was attributed to such diastolic regurgitation. In 1908, clinical investigations on patients brought forward a serious difficulty, *viz.*, that the rapid drop in radial sphygmograms precedes the dicrotic wave and therefore seems to come during systole. Supplementary experiments on animals *by clinicians* then apparently demonstrated (1) that the volume of regurgitation is apparently not large, and (2) that the collapse of the pulse is due to reflex vasodilation which simultaneously explains the capillary pulse. In 1914, I restudied the question experimentally by more advanced methods. It was found (1) that a similar collapse occurs during aortic insufficiency in an artificial circulation machine when the peripheral resistance is *not* altered, (2) that in dogs the characteristic changes in the pulse occur in the first beat after production of a lesion and therefore must be of central origin, and (3) that the collapse is partly systolic and partly diastolic in time, shifting more toward the systolic side, the larger the leak becomes. The cause of the systolic collapse remained an enigma for many years because certain fundamental reactions of the heart were not understood. By continued study of the problem in a physiological atmosphere, it gradually became clear that the overloaded ventricle contracting against a low aortic resistance empties fairly completely during the first half of systole and ejects little blood during the latter half. The peripheral escape of blood from the central elastic reservoir is responsible for the systolic collapse.

Experimental physiologists should continue to participate in the solution of practical questions because their background often enables them to see problems which are not obvious to clinicians. May I illustrate my thoughts with reference to the dynamics of hypertension, a subject to which clinical investigators have contributed in large measure? Physiological research had rather firmly established that an elevation of blood pressure may be due to increases in heart rate, in systolic discharge, in peripheral resistance or in viscosity. Clinical investigations on hypertensive patients excluded all these factors except peripheral resistance; hence, by elimination, the conclusion was drawn that the fault lies in the peripheral arterioles. No one, however, has submitted visual, photographic or other direct proof of the occurrence of such narrowing, except in the retinal vessels. In 1938, I pointed out, using published clinical data, that even the magnitude of the increase in resistance can be gauged by applying hemodynamic formulae. However, the magnitude of the increase did not correspond to the elevation of pressure in different patients. Furthermore, the relative increase in systolic and diastolic pressures found in clinical and experimental hypertension are not those anticipated, either on dynamic principles or experiments from increase in peripheral resistance alone. The suggestion both by clinical investigators and physiologists that an aortic factor must be concerned led to further experiments in which Dr. Wegria and I showed that acute hypertension produced in dogs by humoral or nervous constriction of blood vessels is accompanied by alteration both in the size and elasticity of the aorta. Thus the hint was relayed back to the clinicians that changes in aortic elasticity, previously suspected to occur in hypertension, need not necessarily be demonstrable as histological or elastic changes of the aorta obtained post mortem, but may represent a reactive functional state during life only.

It seems to me that such shuttling of problems between clinical and laboratory investigators, each in turn attacking problems from his respective point of view, offers one of our greatest hopes for understanding the ultimate mechanisms that produce disease.

A SIXTH PATHWAY OF PROGRESS

Finally, the physiologist can frequently link his talents with those of a clinical investigator in the pursuit of collaborative research. Such interdepartmental research is particularly valuable when investigators have interests in similar problems but possess different talents required in their solution. Obvious benefits accrue from such cooperative efforts in the science of research as in the science of warfare. It is important that a feeling of mutual understanding and fellowship exist and, above all, that both parties be ready to disregard self and self-interest. The individual must be subservient to the progress of the research.

Such interdepartmental investigation must necessarily be so ordered that the primary duties of each participant to his own calling do not suffer. Each must be careful to limit his interest. For example, the physiologist who becomes so enamored of clinical problems that he neglects his interest in orderly fundamental studies may be popular with clinicians but soon loses standing among his colleagues.

Older physiologists should ever be ready to assist younger clinical investigators in technical methods, new ways of approach and, if competent to do so, even in suggesting new lines of investigation. Having started a line of investigation and assisted the clinical investigator in the technique of special methods, the physiologist should gracefully withdraw, leaving the field to his clinical associate. In this way, his time becomes free again for other duties or for helping others, but, what is more important, the clinical investigator left with a method as well as a problem is given an opportunity to test his own ability and develop his resourcefulness.

SUMMARY

During the three decades that have passed, medical science has ascended to a high plateau of achievement. The climb has involved several pathways; among them: (1) the physiological approach toward disease as experiments which nature performs on organisms, (2) the more intelligent interpretation of the functional reactions of the body in disease in accordance with latest discoveries in physiology, (3) the supplementation of observable phenomena through use of laboratory instruments, (4) the assumption of active investigation both on patients and experimental animals by clinicians themselves, (5) the shuttling of problems between clinical and experimental laboratories and (6) correlated research in clinical and physiological departments.

As we look down from the heights we have reached, we have reason to be pleased with our progress; but when we look ahead we become aware that there are still high mountain ranges to be climbed. We realize that their ascent can not be accomplished by employing merely the methods, equipment and strategy that have proved successful so far; we must improve the application of principles that are old and well established, and evolve others that are new. Above all, we from laboratories and clinics must join hands to help each other climb; and through correlated teamwork overcome the great obstacles that jealous nature places in our way.

I have ventured to suggest a few directions which such mutual help may take. They include (1) means by which new fundamental discoveries can be utilized more quickly by clinicians and practitioners of medicine; (2) plans by which younger clinical investigators can be given approximately the same opportunity for training in research technique as their colleagues entering experimental sciences; (3) pleas that the shuttling of problems between hospitals and laboratories of fundamental science may continue in order that the ultimate significance of clinical results may be better understood and that the applicability of fundamental discoveries to nature's experiments may be tested; (4) judicious combination of talents of laboratory and clinical workers, whenever this leads to greater economy of effort and does not infringe upon the primary duties of each participant to his calling.

The spirit of correlation which is involved in all these plans of advance is a silent force which grows not only through mutual interest in each other's problems but also through frank respectful criticism of each other's trends. With such a spirit of correlated effort science marches on.

THE SYNTHESIS OF VITAMIN K_1[1]

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I HAVE a story to tell to-night about the naming of a cat. This was by no means a simple matter, for it involved a fully pedigreed Siamese aristocrat requiring an appropriate and dignified name. Fortunately, it took all summer to conclude the various arrangements involved in getting the cat born, for this gave time for deliberation on a suitable name for the prospective offspring of Oriental Nanki Pooh and his dam

[1] From an address before the Boylston Chemical Club, Harvard University, October 24, 1939.