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THE FUTURE OF SYPHILIS *

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YOUR honourable secretary has, with a graciousness that well befits the representative of a distinguished society, bidden me accept, within the domain of syphilology, the sky as my roof-tree, and infinity as my limit, and to discourse to you upon "Syphilis and Civilisation." I have sought to improve a bit upon the grandeur of his conceptions, and simultaneously to avoid even the implication of a pun, by changing the title to "Syphilis and the Future." For who can imagine a future without syphilis, and what syphilologist would dream of syphilis without a future?

To-day we stand in relation to this ancient and intriguing disease in a curiously paradoxical position. We seem to know a great deal, and yet we know very little. We seem to be armed at all points, yet we seem to make little headway. We seem to have made great progress,—back to the point from which we started. As one aspect of the situation is dragged into the light of knowledge another scuttles off into Stygian obscurity. I need not repeat before you perhaps the common slogans of our public health propaganda: that syphilis stands between first and fourth of all the causes of death that afflict mankind; that we ride beside it, eat beside it, too often sleep beside it, and yet that a statistical survey of the second million drafted men showed that in the population of our great northern cities it was present among young soldiers to the extent of less than one-half of 1 per cent. It is estimated that at any one moment not less than 1 per cent. of our national population is under active treatment for the disease, yet in the rural districts of the north-west only 1.5 per cent. of farmers have it, while Railroads are coming to recognise it as the chief factor in their disability and sick pension lists, and hospital populations are syphilitic to an extent

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ranging from 0·5 per cent. to 30 per cent., depending on race and social type. On the one hand, it is asserted that death from tabes and paresis is on the increase ; on the other, it is stated that there is a positive drop amounting to as much as 24 per cent. in the incidence of syphilis in such countries as Great Britain, in which prophylaxis by treatment has had its most thorough-going application. We find assertions of a high percentage of curability pitted against positive evidence of total and incomprehensible failure to cure. We see advocacy of *laissez-faire* by permitting early infections to progress to full-bloom secondaries set over against seemingly unescapable evidence of a loss of 25 to 35 per cent. of curability by such delay. On the one hand, the socially-minded plead that the individual patient's right to this shadowy and theoretical immunity development has no place when the prevention of dissemination of the disease by the early use of spirillicidal drugs is at stake ; on the other, it is argued that the failure of arsphenamines to develop individual resistance may convert patients treated before the blood Wassermann becomes positive into foci of relapse so dangerous that it may well be asked whether they do not in pernicious activity make up for the 25 per cent. of alleged additional cures gained by the earliest possible exhibition of these drugs. These are but random samples of the conflicts into which the inquiring mind is led in contemplation of the field of syphilology to-day ; and if the inquiring and allegedly expert mind is thus led into confusion, what will be the fate of those who must take information second-hand and be content only with a general rather than a special knowledge of the disease ?

But, fortunately, there is land beneath our feet ; and a few encouraging and valid principles may be dragged from the welter to form a framework and support for the syphilology of the future. These I lay before you under successive heads, beginning with the future of diagnosis.

The Future of Diagnosis.—The first and foremost issue of the day is to move all diagnosis of syphilis a notch ahead, to be anticipatory and preventive instead of dilatory and consequent. Inasmuch as diagnosis is the logical predecessor of treatment, and treatment is the great preventive of the spread of an infectious disease, early diagnosis with prompt treatment are the pivotal

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points of the entire movement against syphilis as a public health problem. This means that we should, as physicians, fasten our eyes upon the chancre and its immediate sequelæ, not upon the Charcot joint, the aneurysmal bulge, or the pelvis full of spleen. I always feel a vicarious sense of guilt in writing on the treatment of neurosyphilis, or even on the early diagnosis of syphilis of the heart and aorta. If all of us would turn to writing and thinking about chancres and their sequelæ, a generation or two might see the extinction of the disease. For, as Thomas Parran has well said, every syphilitic person comes to us from another with syphilis. The statistical records of the Public Health Service have shown us over a period of years that every hundred syphilitic persons is succeeded by just another hundred syphilitic persons. The disease is at least not on the increase. It apparently is on the decrease, but in this country as yet we cannot prove it. If we can bring it about, as Parran says, that every hundred persons with syphilis gives rise to only ninety-nine with syphilis, the end of the disease is in sight. How shall we cut that hundred to the ninety and nine? By concentrating on the chancre and its immediate sequelæ. The attack on the infectious lesion and its immediate and permanent sterilisation is the death-blow to syphilis.

Beside this issue all other problems of syphilology become, in the broad social sense, of secondary importance. What does it matter, in the interests of human welfare, if, as is sometimes asserted, the number of late non-infectious neurosyphilitics temporarily doubles, or the chronologic onset point of such complications is moved ahead five or twenty years, if the transmission of the disease is even for fifty years throttled at the root? That I am not taking flight into fancy pure and simple has been apparently indicated by the effect of bismuth upon the incidence of syphilis in France, which adopted it patriotically in place of the arsphenamines. The figures may be questionable and are undoubtedly variously interpretable, but there can be no doubt that their trend is in keeping with the logic of the situation. Syphilis is apparently going up in France while it goes down among her neighbours, in part because bismuth is an inferior spirillicide, and leaves the early case infectious for a period from five to ten times as long as does the

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feeblest of the arsphenamines. In precisely the same way may we anticipate a similar rise in syphilis or a failure to reduce the incidence of the disease in the United States, if the advice of those Americans who advocate mercury by mouth until secondaries are well established be generally heeded.

To focus the gaze of medicine upon the infectious stages of syphilis: the chancre, the secondaries and their recurrences, and to secure their sterilisation at the earliest possible moment—this is, then, the first and great commandment of the syphilology of the future.

What stands between us and this great consummation? The woman's genital tract, for one thing, an invisible *cul de sac*, which in a single day can receive and implant upon an unknown proportion of as many as thirty to fifty males the *Spirochæta pallida*. It is a genuinely ominous thing when a comparative survey such as the recent study of Spindler, in Reval, indicates that chancroid, the index of professional prostitute activity, is dying out, and gonorrhœa and syphilis are taking its place, as prostitution, in his words, becomes promiscuity. The late syphilis of to-day is overwhelmingly the product of the typical prostitute activity of the past, the brothel, the street-walker, and the house of ill-fame, against which the efforts and machinery of much of the agency of reform are still being directed. Who can say this of the early syphilis of to-morrow, the gift of the "girl friend," the "flapper," the "college chum," and the industrially emancipated woman? Syphilis is not only tending to retreat into invisibility clinically, but it may be retreating into inaccessibility from the standpoint of the infectious carrier, the "single standard" man or woman, the *liaison* and the trial marriage.

My next remark *à propos* of chancroid draws added point from Spindler's survey. The diagnosis of chancroid still stands to an alarming degree between the wholesale suppression of syphilis by control of the infectious person and our conquest of the disease. You recall that Moore showed, in his studies of A.E.F. statistics, that the besetting error of the American doctor in the field was to diagnose as chancroid what English and French experts recognised as chancre. There are, of course, intricacies to this problem which do not appear on sight. But there

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are indications that chancroid is a disappearing disease under modern conditions. I think I am still right in saying that, while the diagnosis of chancre takes perhaps ten minutes, the diagnosis of chancroid should never take less than four months, which is the time required for the Wassermann follow-up of the genital lesion developing after sexual exposure. Such a follow-up should always be carried out, no matter what the appearance of the lesion may be. To induce the medical student of the future to refrain from diagnosing chancroid until syphilis has been completely and finally ruled out is a step forward into the syphilology of the future.

What further hinders us in our throttling of syphilis at its onset? The practitioner's fear or rejection of the dark-field. Across the river from me an old friend of mine uses a cardioid substage dark-field condenser, with "Bitukni" binocular eye-pieces and an apochromatic objective—a lovely thing, costing into the hundreds and showing spirochætes as you have dreamed they should be. His writings elevate the dark-field identification of *Spirochæta pallida* to the dignity of a science. No wonder the practitioner turns from it in awe. On this side of the river I set up my old-fashioned supra-stage dark-field attachment, costing all told less than fifty dollars, on an instrument of the vintage of 1909, and pick out spirochætes, thus far quite as unerringly, I believe, as he. My only luxury is an arc lamp: I love its hum; yet the first *Spirochæta pallida* that greeted me at the Mayo Clinic swam into the light from a common 75-watt bulb in the commonest of common desk fixtures. The man in practice who is waiting for modern syphilology to develop a differential stain for *Spirochæta pallida* as satisfactory as the Gram for gonococci will let much early syphilis slip through his hands because he does not diagnose by the identification of the organism instead of by the Wassermann or Kahn test. But it is at least to be hoped that the syphilology of the future will give us an adequate differential stain for office use, a local precipitation procedure performed on the chancre serum with highly accurate results, and a means of transporting chancre fluids to properly equipped laboratories, even at a distance, for expert dark-field examination and authoritative reports.

Relapse is, I believe, though I cannot prove it, the

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source of as much transmitted syphilis as is the original undiagnosed and untreated infection. From the diagnostic standpoint we do not as yet fully understand or appreciate relapse. A specious sense of infallibility, a false confidence in modern treatment, has lulled our perceptive senses into dangerous repose. As I intimated, there is good reason for questioning whether the incidence of relapse in the inadequately treated or uncured early case is not so high as to have counteracted much of the good effect of the arsphenamines in controlling the infectiousness of the sero-negative primary case. So far as effect on general incidence of the disease is concerned, there is nothing more dangerous than the patient with early syphilis turned loose, after a few arsphenamine injections and a little mercury of bismuth, to relapse with a new chancre, delayed secondaries, or other infectious recurrences, and to distribute infected semen to his female contacts, without control of any kind, under the delusion that he is cured. It might almost be conceived that two years of pills, cheerfully and consistently taken by the patient in the knowledge that he is infectious, is a better remedy for syphilis in the aggregate than the care-free mental state of the majority of dispensary-treated patients whose half-dozen "shots" and vanished symptoms leave them with the impression that they can no longer transmit the disease. The syphilology of the future, then, will study the morphology and mechanism of relapse; its inevitability will be impressed upon the medical student side by side with the best machinery for prevention, and he will be taught to look for it, and to warn his patients against it, throughout the course of the disease and throughout life.

The future of diagnostic syphilology contains many other items for stimulating speculation. With the retreat of syphilis into the invisible, paper syphilology, with the record of year after year of diagnostic tests in place of visible lesions, of which I have so often spoken, comes to the front as a new field for interpretation. "What will become of the Wassermann test?" students often ask. "Is the Kahn replacing it?" Leaving names out of the issue, we are witnessing now in diagnostic syphilology a most interesting battle between serologic sensitivity and specificity. On the sensitivity side the laboratorians serenely compare results too often without

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reference to clinical controls. In a number of reports aggregating more than a hundred thousand comparative Wassermann and Kahn tests published during the past year in one of our leading medical journals, the claim of the laboratorians that the Kahn test is the more sensitive, and hence the better, was scarcely relieved by a single chirp from a clinician on the subject of its specificity. Specificity is an issue for the clinic, not the laboratory, and it comes home hard, not to the laboratorian, secure behind his test-tube racks, but to the physician in the consulting-room, who faces the patient, to tell him that he has or has not syphilis. Let us be slow, then, to run with the crowd to take up any new test, forsaking the old and tried. Let the test-tube men have their way and set their world on end. Meanwhile let the clinically wise insist on both a Wassermann and a precipitation test in the serologic reports on which they must make a critical decision. The Supreme Court in such issues sits in the clinic. Wait, then, in final judgment for the voice of the clinician.

There can, however, be no question that, if a precipitation test can be brought to the same level of sensitivity and specificity as the best of the Wassermann modifications, it will largely, if not entirely, supersede them. The move toward diagnostic simplification, so desperately needed in modern syphilology, demands it. How soon, however, we shall see a reliable vest-pocket, portable, cover-glass diagnosis of syphilis made by a precipitation procedure in an alcove, as a hemoglobin is taken, no one can say; but I believe we are moving toward it. In the meanwhile it is unwise to cherish delusions about the simplicity and ready technical availability of any new or modified test. It is always more difficult than it seems and bristles with factors of errors that one never suspects until he has upset his world with his mistakes. Serology is still a field for the expert, and will be for many years to come.

One of the really important serologic, or perhaps rather clinical, problems of the present day, on which the future must pass a verdict, is the too common practice of diagnosing syphilis on partial and weak positive serologic tests, whether by Wassermann or precipitation technique. Herbert Mitchell has directed the attention of the profession in the United States to this particularly

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serious abuse of modern serology. Hardly a day passes on which the clinical expert is not called upon to reverse the judgment of some physician who took a doubtful Wassermann or an 012 or even a 123 Kahn reaction as evidence that the patient had syphilis, and instituted treatment, thus permanently fastening the diagnosis of syphilis on his patient, with almost no hope of ultimate correct solution of the question. Partial positive serologic tests are never diagnoses. They are merely interrogation points; and the day will come when, unless the laboratorian knows he is talking to a clinical expert, he will not even report the numerals or pluses, but will return a report marked "Questionable" or "Indeterminate." This, fortunately, is becoming the practice of the larger and better laboratories, but is not given the weight by the practising physician that it should. It is so little regarded that it was even possible within the past few weeks for a published report of the substitution of the Kahn for the Wassermann test in the diagnosis of the chancre to appear without even a reference to the grade of positiveness accepted as clinching a diagnosis. Fortunately, in dealing with the chancre, less harm is done by treating as syphilitic a dozen or even fifty sexually exposed persons with non-syphilitic genital lesions, than by failing to identify one person with genuine primary syphilis. But in the later stages of the disease, and in the general medical investigation of a patient, the complete substitution of a clinically unevaluated test like the Kahn for one that has had the years of study given to the Wassermann, without prolonged cross-checking and the side-by-side performance of both procedures *under clinical control*, is diagnostic impressionism of the worst sort. It should call forth sharp criticism upon laboratories that have done so from those who appreciate the problems of diagnostic syphilology.

The past has seen the day of the hypo-suspicious physician in the diagnosis of syphilis. There are signs that the future may see the swing toward the hyper-acute diagnostician, who sees syphilis in everything. Conspicuous examples of the frame of mind have been seen among some of our foreign friends, and when they have been able to speak *ex cathedra*, their pronouncements have precipitated reaction and discredited rather than furthered the cause of diagnostic syphilology. Let us, however, re-

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member that the tendency is toward inertia rather than progress, and that we can at present better afford a few syphilophiles than a universally apathetic and under-suspicious profession. If in the future the physician over-ready to diagnose primary syphilis will treat the patient with the thoroughness that his perhaps mistaken diagnosis demands, we shall see a decrease in syphilis in the aggregate; and that in the end serves the best interests of the race, albeit with some travail to the individual. In later and fully established infections, presumably past the infectious stage (first five years), let us, however, be reasonably sure as the result of a genuine study of the patient, and not just his blood serum, that he has syphilis, before we begin to treat.

To summarise, then, the practitioner of the future will be marked by the following attitudes with respect to the diagnosis of syphilis. As a medical student he will have been trained to gain an inch and a minute on the disease at every turn. He will concentrate his diagnostic resources on early syphilis, and will treat every chancre and secondary case to a maximum, and keep it under observation throughout life. He may treat a few patients on suspicion, but if he does, it will be with the vigour of a confirmed diagnosis. In this way he will, as our fathers did with typhoid, and as every good physician should, cut the throat of much of the syphilologic practice of his day and leave a mark upon the spirochæte from which it will never recover. What a misfortune it is that we cannot as yet vaccinate against syphilis! There seems no immediate likelihood that we ever can, unless by such a scheme as the discovery of a chemical constituent of the organism that confers immunity. In the second place, he will stand resolutely against the single procedure diagnosis of syphilis except where, as in the chancre, the issue of infectiousness is at stake. He will restore to the clinic the judicial rights filched from it by the laboratory man, and will draw on many-sided procedure in the clinic for syphilis, and not merely on a single blood test in a laboratory, to make the final decision in cases which overtax his diagnostic acumen and resources. And, finally, he will stand for the routine serologic test for syphilis as part of every medical examination of every patient everywhere. This is the finger pointing toward the hiding place, the entering wedge of exploratory

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syphilology, the nose of the ferret. As he examines the patient syphilis will stand as near the forefront of his mind as tuberculosis, and nearer, because its serologic test is more trustworthy. The routine Wassermann *and* precipitation test, or a reliable simplification, will rank with the urine and the hæmoglobin estimation in his diagnostic approach.

The Future of Treatment.—I have already touched on the most critical issue of the future in my remarks on the need for a drug that will absolutely control infectiousness. Conceive of a therapeutic technique which within the first twenty-four hours of an early infection could so bottle the disease within the patient that it would become from that moment absolutely non-transmissible. Far-fetched though this speculation sounds, we are on the way toward its realisation. We can already end infectiousness within twenty-four hours, but it returns. To-day we must employ two or three cumbersome, slow and painful methods to prevent that return, and only with partial success. The future of the public health campaign depends more than on any other one thing upon the development of a technique for ending the infectiousness of a patient within an hour after the first treatment, and keeping it ended, simply, briefly, painlessly. Once we reach this point, the rest is mere detective work and police power, not medicine. The contraceptionists have held out an equally alluring bait. If an absolute contraceptive, as Dickinson has suggested, could be combined with an absolute, instantaneous and penetrating spirillicide, and the factors which distort all contraceptive techniques eliminated, such as intoxication and stupidity, we should have a weapon of attack upon syphilis which would rival the efficacy of an absolutely effective system of treatment. Leaving the contraceptive problem out of consideration, where do we stand to-day? We have quick surface sterilisation, with relapse in an unknown proportion of cases. The procedure for preventing relapse, failing absolute extinction of the infection in the patient, is to-day a long and complicated affair of building up resistance by excluding rest intervals, and by the continuous employment of one or another of those drugs, like mercury, which are conceded to be inferior spirillicides, but good stimulants to the fighting powers of the patient. We stand, then, after twenty years with our

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half-effective weapons, still upon that most ancient battleground of therapeutics, fighting the battle of the resistance of the patient *versus* the specific effectiveness of our drugs. The arsphenamines have failed us in absolute specificity, but they have gone part way in the quick suppression of infectiousness. We piece out with various combinations and permutations of mercury, bismuth, iodides, the frayed edges of our spirillicidal hopes. Our aim must be to develop either simpler, shorter combined techniques, or methods of giving all the needed drugs in a single, easily tolerated preparation.

With his hope set on the spirillicidal attack of the arsphenamines, imagine, then, the alarm of the syphilologist when he encounters the inveterate arsphenamine-fast relapser. Picture his dismay when he meets, as I have in the past year, a patient whose spirochætes are totally resistant to, and in fact thrive on, what to all tests is a thoroughly potent arsphenamine. There is more than casual evidence that *Spirochæta pallida* is not sitting around waiting for us to kill it. It, too, is a living organism, intent on making a living and reproducing its kind. Klauder and his predecessors have shown that it is definitely adaptable to the environment into which we are trying to force it with our spirochæte-destroying drugs. It can be taught to like arsphenamine and mercury and bismuth mixed with its meat and drink. Reports are now gathering from the clinical side directing attention to the increasing resistance of syphilitic infection in the aggregate to what at the outset seems to have been effective treatment. The fixed positive Wassermann problem is but one aspect of it. Just as we witness the elastic recoil and the comeback of epidemic influenza between generations of partially immunised individuals, so I suspect we are going to see more in the future of the elastic recoil of the spirochæte from our fanfare of arsenic. The problem of the chemotherapy of the future will, then, be one of ingenuity and variety as well as infallibility, several good drugs rather than one single perfect drug. And it must take on, if I am not mistaken, a resistance-building turn. What is resistance, and how is it built? Of the answer to this most significant question we know almost nothing. It is part of the intimate mechanism of the cell, on whose physico-chemical threshold we have not as yet gained

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even a secure footing. We are literally in a race with the adaptive cellular mechanism of the spirochæte, pitting against it the fighting power of our individual cells and the fertility of our intellects. Let us in all humility remember that the race is not always to the swift or the battle to the strong.

From the problem of controlling infectiousness by an ideal combination of spirochæte-destroying and resistance-building chemicals let me turn your attention sharply toward another problem of the future, that of technical procedure. The whole structure of syphilotherapeutics to-day is top-heavy with difficult, dangerous and esoteric procedures. The mere change from oral to intravenous administration of a drug means something more than the mere difference in effect and reactivity between the two routes. It means the raising of a whole new generation of physicians and of patients, willing and able to think in terms of the vein and the blood stream instead of the mouth from the technical standpoint. Here the modern treatment of syphilis meets a tremendous static resistance. The cream imagines that all the world is fat, like itself, and gives intravenous arsphenamine and intramuscular mercury and bismuth. But underlying it is five times the depth of lean old skimmed milk, the administration of mercury and iodide by mouth, a sacred tradition of doctors and of patients for generations. It follows, then, that every new method and every new drug faces not only the problem of evaluation of its intrinsic worth, colossal though it is, but the adamant surface of human inertia toward its adoption. Here many a brilliant scheme has perished. What is it that ails the best modern technique for the treatment of syphilis, the one we believe to-day can bring about the extinction of most of the disease in fifty years? The general practitioner of to-day can't handle it, and the patient of to-day won't follow it. In a few clinics, under inspired leadership, it goes over, yet even they lose their hundreds in collecting the dozens on whom they can prove their results. In the "sticks," the backwoods, in even the unaided doctor's office, such schemes are paper and ink, nothing more. A new generation of medical men and patients must be trained to make them really effective.

Is it all so hopeless as that? Not at all, if the problem is simultaneously approached from the other side.

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Instead of glorying in the development of a new and esoteric procedure like the malarial therapy of paresis, which only a few can use, and that, moreover, at the wrong end of the disease, let us apologise for it, use it regretfully, and give ourselves to thoughts of simplification. Let us set clearly before ourselves the basic ideals, such as the immediate control of infectiousness, and move with a will to make them quickly, easily and perhaps even pleasantly possible. Instead of pyramiding upon three or four drugs a vast structure of interwoven courses, with complex preparation and complex methods of administration, years tall, let us strive for a low, flat, earthquake-proof structure with the smallest number of the simplest parts, simply put together, and of small spread. Remember that the nearer we can bring the control of the transmission of syphilis to a single, painless, non-toxic act, the sooner the disease goes out of existence. Thus I have ventured to herald as an advance the combining of the administration of bismuth and arsphenamine in a single injection, and that an intramuscular instead of an intravenous one. Thus I keep "dinging" at the manufacturers to take the pain out of it, to concentrate on making it acceptable to the patient as well as fatal to the spirochæte. A year ago, in a conference of specialists, I was gravely reproached by an eminent man for suggesting that we would see the day when the treatment of syphilis would have completed a cycle and returned to mouth administration of some drug. Yet "spiricid" and "stovarsol" are but the crudest stepping-stones; and within a year of my rebuke I am invited to consider the therapeutic testing of what is alleged to be the most advanced of all syphilotherapeutic agents, still in the experimental stage—the congener of Bayer 205, for mouth administration with curative results. While we struggle with the problem of popularising the already-known good, let us, as Colonel Russel said a few days ago, keep up our research. And in the treatment of syphilis let it be in the direction of simplification. The hope of single dose cure may be gone, for personally I believe that the whole immunology and pathologic physiology of syphilis is against it. The disease must be, as I have often said, worn out rather than knocked out. But there remains the hope of reducing effective treatment and control of infectiousness

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to a far simpler, shorter and less painful business than it is to-day. Undoubtedly there are those among both physicians and patients who think a simple procedure trivial and not exciting enough, and who will not follow it. Let the raw internes do their lumbar punctures, and let calomel, the impressive drug, be their intramuscular companion. But for most of mankind the simplification and shortening of treatment will be popular, practised by doctors and followed by patients with large gains in ultimate results.

And now let us turn our faces in still one other direction. What do we really know about the end result of so-called modern methods as applied to man? We know painfully little. Here is a truly herculean task for the future: the evaluation of these hectic two decades of "curing" human beings of syphilis with "606." One criterion after another has undergone the fire of criticism and been driven from the field. There is no way now to show clinically that a patient is cured. The more persistently we search, the more closely we comb the patients who have had the disease, the more we find that a disconcerting proportion of them are merely arrested, not cured. We do not even have as yet a real perspective on the meaning of what might be called functional or physico-chemical scars, such as the persistent, asymptomatic positive Wassermann reaction. Does this mean that all our effort has been in vain? Not a bit of it. It demands only a stay of judgment. Within fifty years we shall know whether we cured syphilis in these days. We shall know *granted the proper correlation and co-ordination of research*. The thing that appals the clinician to-day is the tremendous waste of informative material and the frustration of effort at evaluation that marks the treatment of syphilis. The best modern treatment of the disease is an unknown quantity outside a few clinics and a few specialists' offices. When, as a result of huge effort and expenditure, it is finally evaluated, what can we say of the multitudes who have not been followed, and who have not been treated by high standards? How shall we get the practising doctor to apply what we know? Here again our hope must be in averages and in the training of the student, and the proof of our success in the evidence of the mortality and morbidity tables. But meanwhile let every pathologist search his material

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for the patient who has had syphilis and been treated with the arsphenamines. This material is the crude ore of a research that can yield fine gold. Let such autopsy material be collected, prepared, studied, under the direction of experts, in the effort to find out whether, as Warthin found, the symbiosis between man and the organism of syphilis is not almost too perfect to break. And coincidentally let the follow-up mechanism of clinics and the records of the clinical expert be drawn upon to differentiate the clinical from the pathologic cure, the lifetime of non-transmission and of freedom from symptoms as distinguished from the total extirpation of the germ. Just as we are all tuberculous, but few transmit it, so it is conceivable that we are expending enormous effort on the treatment of the truly latent patient, whose infection has no public health bearings and no real personal significance for himself. A re-adjustment of our energy distribution toward the detection of the infection distributor rather than the mere carrier may greatly simplify and improve the outlook for extinguishing the disease.

In summarising the treatment situation, then, let us dedicate the future to research in new and preferably simpler methods, to the simplification and popularisation of what we now have available, and to the evaluation of results. And now let me turn to the future of research.

The Future of Research.—I have never forgotten a conversation I had some ten years ago with Folin, at the time I was looking for a research chemist to attack certain problems in dermatology. He protested against the glibness with which the clinician could mouth and propound problems, leaving to the investigator that immeasurably more difficult task of reducing them to a practicable research basis. I have never forgotten his commentary, and as my experience with the mere clinician has grown I have myself come to appreciate the fact that the proposing of problems, like the concocting of conundrums, is the lowest order of achievement in an investigative field. The facile propounding of problems for other men to study is the work of the armchair syphilologist. The Croix de Guerre goes to the man who makes ideas take form with a *method*, and who gives to notions the touch of reality. How priceless such men are can only be realised by those who are called upon year after year

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to pan the human student material that goes through their hands in the search for that speck of gleaming gold that means the truly investigative mind. Upon that and its detection must rest all the really basic hope for progress in research. Organisation can do something to help it once it is found, but it cannot create it. As the chairman of a committee seeking to direct the first large available fund in the United States into international research in syphilis, I am beginning to realise the distance that separates the proposal of a problem from even the first step in the getting of a result. Co-operative research is a modern slogan, and we hope to apply it to the study of syphilis. The first step proposed was to get perhaps six clinics to agree to follow a concerted plan over a period of years, employing similar checks and tests criteria in the evaluation of selected methods of treatment. It all sounds amazingly easy, and should not cost much. Yet how many co-operative mountains have laboured and brought forth mice. The very first issue that glimmers through the mist is the definition of a clinic that can produce trustworthy results, this to be followed by the bringing of six clinics up to that level in all particulars. In one, for example, inexperienced dermatologists labour to identify aortic lesions without adequate consultant direction. In another the material is vast, the follow-up ineffective or non-existent. The first move must be an appraisal, then a selection of the likeliest candidates, then a proper distribution of funds to bring each to the desired level, without rancour and recrimination. Tentative investments may be made in a promising young brain, heavier ones in a brain that is at its prime. Mistakes will be made, and a large fund that should have been concentrated about a single brilliant unit may be unwisely dispersed in raising a general average to something distinctly short of a high degree of productiveness. On the other hand, too large an investment in a single brain may, like marriage to a rich and socially climbing wife, put darkness and indolent ineptitude where there once was fire and light. Co-operative research in syphilology is on the way, though travail may mark its progress. The application of animal immunity studies to man, the testing of drugs in the clinic before their curative virtues are bruited abroad in the advertising circular, the evaluation of the laboratorian's results by the touch-

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stone of clinical syphilology, and the practical decisions as to the range and type of ammunition to be used for the day's barrage in the attack on syphilis in the field, all demand a combined intelligence and an orderly and cohesive massing of forces. Fortunately, there are brilliant examples of such organised attack shining in the firmament of to-day to guide us. Many of them are in the fields of industrialised science rather than purely medical research, for the individualism and the humanistic subjectivity of the medical man tends less to qualify him for such plans than does the detachment of the scientific mind and the one aim practicality of the business concern. But somehow through all these pessimistically portrayed obstacles research manages to worm its way, blunderingly and with effort, but none the less with progress. Some of the important directions which a mere clinician conceives it may profitably take have been sketched in the course of these remarks.

Conclusion.—You who have followed me thus far will hardly be content without a glimpse behind the final veil. Shall we there find the altar on which the sacrificial monster of syphilis shall be immolated to the glory of medicine and the exaltation of the public health? Or, the last veil rent, the last turn turned, shall we not see stretching before us still another alley, leading away to still another turning point in the unending struggle of man with his parasitic enemies? Personally, I declare for faith in the conquering virtue of human intelligence. "There will come a time," reads my confession of faith—for it is no more—"when, as with small-pox in Germany and yellow fever in the United States, the last endemicity focus of syphilis shall have been wiped out, not only in any country, but in all the world. So also may it be," reads on the prayer of the chronicler, "with gonorrhœa and with all the venereal group. They too shall be dragged down the long corridor of time to meet extinction at the altar's foot." But what is that? A veil behind the altar? As we follow the vista of the diseases associated with the sex life of man, and reach the point in human progress where their crimes have been expiated in a man-devised extinction, we confront another veil, another altar, and another turn. We meet the sex ethics of coming generations, freed by medical science from fear of disease and from disease itself, and from the biologic and reproduc-

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tive consequences of a sexual act. Upon that ground another battle will be fought, carrying the evolution of man still higher into the intellectual levels as distinguished from the mere earthy materialism of drugs and germs. For the day of that issue it is not too soon to be preparing ourselves by straightforward, sincere and lucid thinking, by organisation, by trial and error, and by research. I present it to you as a corollary of the future of syphilology and as an inseparable companion to all forward-looking thought on the problems of syphilis in the medicine of to-day that you give heed to these larger things.