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PAUL EHRLICH*

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BY

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This week there was held, in Frankfurt-on-Main and in Marburg, a joint centenary commemoration of the births of Paul Ehrlich and Emil von Behring. They appear to have been born on successive days, March 14 and 15, 1854; but the combined celebration recognized also, of course, the fact that both had contributed to a great and historic achievement in medical science. Their direct association lasted, indeed, for only a few years; but their names will always be linked together by the fact that von Behring discovered the antitoxins against diphtheria and tetanus in the opening years of the 1890s, and that Ehrlich, in the immediately following years, was largely responsible for the rapid development of that discovery. Ehrlich's work, indeed, played a part of central importance, not only in the early production of the antitoxins as effective and exactly controlled remedial agents, but also in the rapid opening which ensued, of a new vista of fundamental knowledge concerning the nature and the mechanisms of the reactions of immunity in a much wider field.

An essential preparation for such a new science of immunology had, of course, been made earlier by the work of Pasteur, of Koch, and of those who immediately followed those great leaders—and even much earlier, perhaps, by the observations of Edward Jenner, nearly a century before that time. There can be no doubt, however, that the study of the nature of immunity to infections entered a new phase of rapid progress with the discovery and further investigation of the antitoxins. Von Behring himself was doubtless concerned to find an immediate application for his sera in practical treatment, especially of diphtheria. So far, however, he appears to have made little more than a qualitative and empirical, though a fundamentally

important, observation. His first sera cannot have contained, in a cubic centimetre, more than a fraction of what was later defined as a unit of antitoxin, and he had not discovered the appropriate technique for so raising the acquired immunity as to obtain an antitoxin of a therapeutically useful potency. Ehrlich, on the other hand, was already in possession of at least some of the knowledge required for this next and immensely

important step. In work on which he had already been engaged quite independently, on the specific immunity acquired by animals which had been given sub-fatal doses of the poisonous plant proteins, ricin and abrin, from castor-oil and jequirity seeds, he had discovered that this immunity could be raised by stages to a high level if a suitably spaced series of increasing injections were given.

Collaboration with von Behring

When von Behring's discovery of the diphtheria and tetanus antitoxins was announced, it was natural, then, for Ehrlich and his co-workers to apply their method of progressive immunization to the production of these, with potencies likely to make them practically effective in treatment, or in prophylaxis. Such records as are available suggest that the first serum of this kind to be used with a convincing

remedial effect, in human diphtheria, was one which Ehrlich had prepared in a sheep or a goat, at a time when von Behring's attempts had not yet produced an antitoxin with a recognizable therapeutic action; a result which, indeed, was to be expected, if we can accept Ehrlich's statement that the serum from his immunized goats already contained up to 100 units of antitoxin per ml., while von Behring's still showed less than one unit. It is certain, in any case, that von Behring invited Ehrlich's collaboration, and that, as the result of their work together, antitoxin of good potency was soon

Ehrlich in 1905.

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obtained from the horse—in all ways a more suitable animal—and was thus made ready for large-scale production in Germany, and then in other countries.

A position of this kind, in which one investigator has been responsible for a primary and fundamental though essentially an empirical discovery, and another for giving it a quantitative and scientific basis and thereby making it effective in practical therapeutics, must always be apt to cause some division of opinion on the proportion of credit due to each of these different contributions to a common result. We know that the collaboration between von Behring and Ehrlich did not last very long, and that misunderstandings of some kind arose between them. On an occasion like the present we may be well content, I think, to leave the matter of the personal relations between these great men of science where it was left some 20 years later by von Behring himself, when at the side of Ehrlich's grave he said :

Nun ruhest auch Du, Du lieber Freund . . .
Du hattest stets eine empfindliche Seele . . .
Und wenn wir Dir wehgetan haben—Verzeih !

For our present purpose I think that it is more important to recognize that the direct collaboration between men of such different aptitudes and ideals probably lasted as long as it could render its best service to science. It had left Ehrlich deeply engrossed for more than 10 years with the fundamental nature of the immunity reaction, and of the relation between the specific immune substances and the corresponding antigens, to the immeasurable gain of scientific immunology.

Von Behring, on the other hand, was less concerned with these deeper problems. His primary discovery of the antitoxins remained the only one of that status calling for a special centenary commemoration of his life and achievements. He made, indeed, in later years, another contribution to immunology which has acquired a comparable importance in practical medicine. This, however, may be regarded as an extension of the earlier one ; it was his recommendation, as a safe and effective inoculum for producing an active immunity to diphtheritic infection, of a suitable dose of diphtheria toxin combined with the amount of antitoxin required to neutralize it. In this case, however, I think that we are bound further to recognize that the mere trial of such a method would not have become practicable until Ehrlich's work had made clear the complexity of the factors concerned in this neutralization of toxin with antitoxin, and especially the presence in any toxin of "toxoid," combining specifically with the antitoxin and able to evoke its production, but free from the toxicity of the unmodified toxin. It would scarcely have been possible, indeed, until Ehrlich had further established, for diphtheria antitoxin, the first of all the biological methods for measuring the specific activity of a remedy, and probably still the most accurate of any. He had based it, as all later valid methods of biological standardization have been based, on the definition of a unit of activity as that of an exact weight of a permanently dried, stable, standard sample of the active substance, in this case of the antitoxin itself.

Ehrlich knew from the first, what one or another worker in quantitative biology from time to time forgets, and falls into trouble by forgetting, that a biological measurement, like any other measurement, has no real meaning unless it is made in relation to a fixed, invariable standard. And it may be noted yet further

that von Behring's contribution to the practice of active immunization against diphtheria did not extend much beyond the initial discovery and recommendation ; so that in any account of its practical and systematic application, now so widely successful, it would be necessary to mention also the names of a number of others who were responsible for its first trials on an extensive scale, for the methods of controlling its efficacy, or for the introduction, as the inoculum, of a toxoid prepared by treating the toxin with formaldehyde, and for the modifications of this which are now prevalently used, with greater success and safety than the toxin-antitoxin mixture which von Behring had suggested. I think, however, that we may be glad to have the opportunity which this occasion affords of saluting the memory of Emil von Behring, as a pioneer whose initiative played a very important part in the origin of an immunological therapeutics, which has now at its disposal the means for both passive and active immunization, used for a preventive or a curative purpose, with all that those resources mean for the effective control of infectious diseases, in any modern, scientifically developed community.

A Predominating Influence

In the case of Paul Ehrlich, whose personal and scientific career forms my real subject to-day, it seems to me that we are concerned with achievements of a different order, which for more than half a century have had a predominating influence upon almost every aspect of the medicinal treatment of infections, and upon its aims as well as its methods and materials. In 1896 Ehrlich was appointed to the directorship of a small "State Institute for the Investigation and Testing of Sera," in Steglitz, a suburb of Berlin ; and his progress there, with the fundamental study of problems arising more or less directly from the fulfilment of this official duty of control, was certainly but little checked by the relatively small dimensions and meagre equipment of the Steglitz Institute. It was from there, in 1897, the year following his appointment, that he published his famous memoir on "Die Wertbestimmung des Diphtherie-heilserums und deren theoretische Grundlagen" ("The Standardization of Diphtheria Antiserum and its Theoretical Basis"), which remains to this day the classical treatise on the subject. It laid the foundation, indeed, not only for all future work on the standardization of the diphtheria antitoxin, but for standardization in general by biological methods, in practically all of its now multitudinous applications. Even when the more imposing Royal Prussian Institute for Experimental Therapeutics in Frankfurt-on-Main was opened three years later, in 1899, with Ehrlich as its director, it was planned essentially for an extension of the work at Steglitz, though the change in title suggested a somewhat broader conception of its functions. Its first responsibility, however, to the Government which provided the money for its support, continued to be the organization and control of the testing of the new antitoxins, in order to give a public guarantee of the potency and safety of every batch which was issued in Prussia for practical use. To Ehrlich this was no merely tiresome obligation of routine, as many an investigator might have regarded it ; on the contrary, he eagerly seized the opportunity which it presented for new scientific enterprise in many directions.

And for more than 10 years, from 1893 onwards, the natural flow of his inventive and speculative genius followed the course thus given to it by the requirements of a public responsibility. It led him, in the first instance, into a detailed study of the diphtheria toxin itself, in which he recognized a series of components, with different affinities for the antitoxin, and contributing to different phases of the toxic action—components to which, characteristically, he liked to give a pictorial representation, in what he called

the "spectrum" of a toxin. This dissection of a toxin into its components was needed, of course, before a really scientific method could be elaborated for titrating against it the potency of an antitoxin, with an animal reaction to show the end-point. And such studies led Ehrlich naturally to examine the nature of immunity-reactions over a much wider range. In the later part of this period, and especially in conjunction with his principal colleague at that time, J. Morgenroth, Ehrlich extended these studies to the more complex immune lysins, formed in response to the injection of intact foreign cells, such as red blood corpuscles from an alien species, or bacteria; and in these lysins they found two components, both needed for the lytic action—a specific "amboceptor" and a non-specific "complement"—present also in normal serum. Bordet, who had studied the phenomenon independently and from a somewhat different angle, had also recognized these two components and had named them "substance sensibilatrice" and "alexine."

The Side-chain Theory

And when Ehrlich's brilliant scientific imagination had occupied itself actively for some years with the meaning of these variously complicated phenomena, the famous "side-chain theory" emerged. It would be far beyond the scope of my present purpose to deal with that theory in detail; it may be that some other contributor to this celebration will make it the main theme of his address. Others also will probably be noting that one principal feature of the theory, in which receptor-groups are pictured as forming side-chains of a protoplasmic macromolecule, figures also in Ehrlich's way of thinking about other reactions than those of immunity, and particularly about the specific localization of chemotherapeutic agents.

In no case, I think, could the side-chain receptors, in the form in which Ehrlich had conceived and pictured them, have retained all their first convincing appeal, or the stimulating influence on further investigations which they so long exercised. The theoretical background has, of course, since those early days been transformed by great advances in biochemical and physico-chemical knowledge. And Ehrlich's rather rigid conception of an immune antibody, with its closely specific affinity for a particular foreign substance, as originating from preformed side-chain receptors, kept ready, as it were, to combine with an antigen which they had never yet encountered, must surely have become more obviously inadequate as evidence accumulated. For it was soon to become clear that the cells of the body would produce these intensely specific antibodies in response to a practically unlimited variety of natural antigens. Landsteiner was later to show that a really unlimited number of artificial antigens could be prepared, by attaching pure chemical substances, natural or synthetic, by diazo-linkages to large-molecule proteins. And so it became clear that the antibodies must be formed, not from pre-existent receptors, but from some indefinitely adaptable cell constituent, which would respond to contact with any antigen by acquiring a new surface contour, conforming to that of the antigen with the detailed precision of a cast fitting into its mould. And, since all the immune antibodies appear to belong to the group of the gamma-globulins, Linus Pauling has pictured the long molecules of these as coiled into skein-like macromolecules, presenting surfaces which can be moulded to fit those of any number of different antigens. Such an ideal will obviously correspond more readily with the present state of knowledge than Ehrlich's diagrammatic conception in its original form.

Ehrlich's mind, however, though tenacious and combative in the face of criticism which he regarded as unfair, was readily receptive and versatile, eager to welcome any real illumination of his problems from sources outside the range of his own knowledge and experience. And I feel sure that, if he could have lived to survey all the evidence now available about the reactions of immunity, he would have

been ready to incorporate any new and more elastic interpretation of their meaning into the general structure of his own theory, and even to assume, perhaps, that this would involve a modification only in detail, and not in principle, of his own conception of the source of the antibodies. I myself believe, indeed, that there would be a substantial justification for such a claim. For there was another and by no means a less important feature of Ehrlich's original theory, which no more modern conception of the protoplasmic precursors of the antibodies has been able to replace, or even to modify. That was Ehrlich's application to the special case of an immunity reaction of a more general pathological principle, first propounded, as he was always proud to acknowledge, by his own distinguished cousin, Carl Weigert.

Weigert had drawn attention to the regular tendency of a living tissue, in its repair of the effects of an injury, to produce new cells, and eventually new tissue, in excess of what is required for mere replacement; and Ehrlich conceived that the cell constituents—the protoplasmic side-chains, as he pictured them—which were first occupied and put out of action by specific combination with an antigen, would then, in accordance with Weigert's principle, be reproduced in such an excess that they would be shed freely into the body fluids as circulating antibody. And whatever more modern conception may now be acceptable to account for the initial specific union with the provocative antigen, the idea which would attribute to such a reparative overproduction, not only the first appearance of the antibody as a freely circulating constituent of the blood plasma, but also the rapid rise of its concentration there, in response to successive, appropriately spaced and graded injections of the antigen, seems to me to have lost none of its original validity. That idea was an original component, a central feature indeed, of Ehrlich's side-chain theory of the immunity reaction. And even to-day, after more than half a century, it still provides the only interpretation yet available for an essential aspect of the complex reaction of immunity, and still retains its power as a stimulus to further experimental inquiry. Will anybody yet discover, we may ask, why the metabolism of the body cells, when once it has been thus constrained to the overproduction of a protein with such a newly imposed specificity, should continue indefinitely to produce such a specific antibody, though in a diminishing quantity, even without further antigenic provocation? It is a question, I feel, which would have been congenial to Ehrlich's own alert and ingenious imagination.

And it seems to me that, whatever permanence we may be inclined to predict for the details of some of his theories and speculations, Paul Ehrlich's manifold permanent achievements in this field alone would give us an abundant justification for commemorating the centenary of his birth.

Although, however, the joint commemoration with that of von Behring has led me thus to deal first with Ehrlich's work on problems of immunology, and although this had, as we have seen, a great and intrinsic significance of its own, it had no such primacy of importance in his total scientific achievement. If we take a longer view of his scientific career as a whole, this concentration of his interest during a middle period on the phenomenon of immunity, and on its practical applications in therapeutics, assumes the appearance rather of a diversion, made first in response to a call of public duty, from the line of the researches which he had been following till then on his own natural initiative, and to which he was to return with an undiminished enthusiasm, and with an augmented equipment of knowledge and ideas, when this immunological phase was coming to an end. To obtain a more comprehensive and balanced appreciation, therefore, of Ehrlich's work in the medical sciences as a whole, we ought at this stage to go back to the beginning, so that we may consider his researches and his contributions to knowledge in relation to his life and career, and in their natural, chronological sequence.

Early Activities in Research

We should note then, in the first place, how early Ehrlich's activities in research began, and how, from the very first, he was led by the natural line of his interest to study the way in which chemical substances become distributed in the body, in accordance with their varying affinities for the different tissues. From a statement made by Ehrlich himself, in a still unpublished address which he delivered at the opening of the Georg-Speyer Haus in Frankfurt in 1906, we learn that his attention was first attracted to such problems during his first year as a student of medicine in Strasbourg, under Waldeyer, when at the age of 19 he read a book by Heubel on lead-poisoning. This described the distribution of lead in the body, as revealed by chemical analyses of the different organs. The young Ehrlich evidently began then to think of the possibility of following the unequal distribution of other substances in the body, due to their varying fixation by organs and tissues having different affinities for them. Lack of chemical methods for their detection would make an investigation of such distributive variations impracticable in the case of many substances. The distribution of dyestuffs, however, could be followed by direct observation, either with the naked eye or under the microscope; and the German industrial production of synthetic dyes, then in its early stages, gave the young enthusiast his opportunity.

His cousin, Carl Weigert, shared to some extent his interest in the new dyes, but was more concerned with their uses as conventional stains for microscopical specimens. Ehrlich appears from the first to have had in view the possibility of using them as selective, histochemical reagents; and there are incidents on record which suggest that he was apt to arouse comment from his teachers, by the amount of time which he spent on experiments of this kind with the new dyes, to the detriment of his studies of the more normal subjects of a medical curriculum, on which he would presently have to face his examiners.

Already in 1877, as an undergraduate of 23, he published a paper on the use of staining with aniline dyes in microscopical technique; and in the following year, 1878, he presented his graduation thesis to the medical faculty of the University of Leipzig. This has never yet been published, but, most fortunately, a copy of it in typescript has been preserved. It is entitled: "Beiträge zur Theorie der histologischen Färbung" ("Contributions to the Theory of Histological Staining"); and it is full of precocious speculations concerning the meaning of the selective staining of different tissue elements. Little imagination, indeed, is required to detect in this thesis by the 24-year-old Ehrlich the germs of nearly all the ideas which were to guide his scientific activities, and to lead him eventually to his great discoveries, during the whole of his active career.

By the next year, 1879, he had begun to use the dyes to classify the wandering white cells of the blood and the tissues, by the different and chemically significant staining-reactions of their granulations; and he had thus opened the way for his classical series of researches on the anaemias and the leukaemias, extending from then onward over many years, through which he became one of the principal founders of the modern science of haematology. As a student of physiology, I myself first heard of Ehrlich as the discoverer of the different types of leucocytes, with their oxyphil, basophil, and neutrophil granulations. In 1883, while holding a clinical appointment in Berlin, he discovered the acid-fast staining property of Robert Koch's then recently discovered tubercle bacillus, and the colour-reaction given by the urine in certain diseases with diazo-benzene-sulphonic acid.

And then, in 1885, came his remarkable treatise entitled: "Die Sauerstoffbedürfniss des Organismus" ("The Avidity of the Organism for Oxygen"). This is truly a precocious classic of functional biochemistry, in which the comparative avidities for oxygen, of the still normal cells of the different organs of a living animal, are measured by their

power of converting one, both, or neither of two dyes with different reduction-potentials, indophenol blue and alizarine blue, into the corresponding, colourless reduction products. Even to-day, when oxidation-reduction potentials and the intracellular systems of oxidizing and reducing enzymes are matters of daily experiment and discussion in so many laboratories, this little book remains full of stimulating suggestions, and many have found in it, again, the germs of ideas which were to be given more definite form in the side-chain theory.

Work on Methylene Blue

In the same year, 1885, Ehrlich published his first observations on the biological uses of methylene blue, which was to play such an important part in more than one phase of his further investigations. He had observed that it also was readily reduced by some tissues to a colourless leucobase, and that it showed a selective affinity for nerve cells and nerve-fibre endings. Three years later, in 1888, he was experimenting with Leppmann on its possible use to interfere with nerve conduction, and thus to act as an analgesic. And from about this time, or more probably two years later—after his return from a longish absence due to a threat of tuberculous infection—there are undated copies of letters which he wrote to leading dyestuff chemists, inquiring about the possibility of obtaining analogues and derivatives of methylene blue for trial, and even suggesting the details for a possible synthesis of a cyano-derivative, with an astonishing knowledge of chemistry in this range for one who had had no formal training in any kind of chemistry beyond the mere rudiments.

The same letter, to Professor A. Bernthsen, contains a request of particular significance. Bernthsen had earlier supplied a specially purified sample of methylene blue, and Ehrlich reports that this has all been used by him with Leppmann in the clinical trials of its efficacy in neuralgia; and he now asks for a further supply, "which is again to be used for therapeutic experiments, but in this instance they are to be extended in a new direction." There can be little doubt of the nature of the new experiment which he had in view. As Ehrlich recalled in later years, in a paper dealing with his chemotherapeutic experiments with trypanosomes, Leopold Landau had already recommended him, about 1880, to try methylene blue as an internal antiseptic, since Ehrlich had himself shown it to be a specially good stain for bacteria. It was not, however, until his experiments with Leppmann had further encouraged him that he decided to try it on human malaria—the malaria parasites having also, of course, a strong affinity for methylene blue, as could be seen in a stained blood film. This clinical trial was actually carried out in 1891 with Professor Guttman, who had a patient suffering from malaria under his care; and the result was not, in itself, at all discouraging. Methylene blue appeared to have a definite remedial action on the malarial paroxysms, but not better than that of quinine, and not certainly even as good.

This clinical trial of methylene blue as an antimalarial remedy seems to me, however, to have been one of the decisive events in Ehrlich's scientific career, and one of the principal landmarks in the history of modern therapeutics. For it appears to have been the very first occasion on which an artificial substance, or, indeed, a medicinal substance of any kind, was made the subject of a deliberate test of its power to cure an infection by a direct action upon the infecting organisms. Here, then, Ehrlich adopted for the first time what he later claimed to be a new principle in therapeutic research, and called "chemotherapy"—a quest for remedies which would specifically kill or eliminate the parasitic organisms responsible for infectious diseases, without detriment to the patients; in contrast to the then current pharmacology, which only concerned itself, as he alleged, with the symptomatic or toxic effects which a supposed remedy produced on the patient or on an

experimental animal. Ehrlich's effective campaign on these new lines was not to begin till some 12 years later; but the delay is not to be attributed to disappointment with the result of this first trial. Methylene blue had shown, in fact, sufficient promise as a specific antimalarial agent to have qualified it for use as the starting-point of a systematic attempt to find better ones. And when, many years later, and long after Ehrlich's death, the research staff of the Bayer Company undertook such a campaign, using the transmissible malaria-like infections of birds to test their synthetic products, and were thus led to discover plasmoquine and atebirin (mepacrine), their starting-point was, in fact, methylene blue rather than quinine. There is even evidence on record of a successful use, as recently as 1946, of methylene blue itself for the treatment of certain cases of chronic malaria.

A Diversion

Ehrlich, then, abandoned further attempts at chemotherapeutic research for the time being, not because the result with methylene blue was unpromising, but rather because the experimental requirements were not yet available. He could not wait for opportunity on the chance of encountering another case of human malaria, or test an indefinite series of new compounds on human patients for curative efficacy and toxicity. The effective opening of his chemotherapeutic campaign had therefore to wait till the opportunity was presented by Laveran and Mesnil's discovery that trypanosome infections could be transferred to rats and mice, and maintained indefinitely in series by subinoculations.

We must remember, moreover, that it was not long after the trial of methylene blue in malaria that Ehrlich's activities were diverted, and fully occupied then for more than a decade, by the enlistment of his interests in the production and standardization of the new antitoxins, and by his eager pursuit of the fundamental problems of immunity with which he thus came into contact. I doubt, indeed, whether Ehrlich himself would have regarded this interlude as a diversion. For him, I believe, the antitoxins and other immune substances would already have presented themselves as the ideal chemotherapeutic agents: with maximal specific affinities for the parasites and their poisons, and none for the tissues of the host, they must surely have been for him the perfect realization of the "magic bullets" which had figured in his therapeutic dreams.

Systematic Chemotherapy

But when Laveran and Mesnil showed that trypanosome infections in small laboratory animals could be made available in any numbers required for experimental treatment, Ehrlich seized the opportunity to return to his study of the remedial effects of artificial substances, and in the first place of synthetic dyes, and thus to make an effective beginning of his systematic chemotherapy. For this he obtained the co-operation of Dr. Shiga, known to all the world for his work on bacillary dysentery, who was on a visit to the Frankfurt Institute from Japan; and they began to explore the possibilities of finding a synthetic dyestuff with the desired selective affinity and the consequent high toxicity for the infecting trypanosomes, and relatively little for the tissues of a mouse. Ehrlich's friend, Dr. von Weinberg, of the Cassella dyestuffs firm, was ready to place its resources at the disposal of the new enterprise; and when I myself was working in the Frankfurt Institute for a short period, in 1903-4, Ehrlich and Shiga had just reached an initial success with the discovery that trypan-red, a sulphonated benzidine dye, would definitely cure an artificial trypanosome infection in mice. In the event, it was not found to be similarly effective in the natural trypanosome infections of man and the larger animals, as they occur in tropical Africa; but its discovery had shown the potentialities of the chemotherapeutic approach to the problem and given great encouragement to further explorations by the same method.

All the world knows about Ehrlich's discovery of salvarsan, which has even been made the subject of a popular

film; and it has, indeed, a proper claim to such wide recognition, as the first great practical success of chemotherapy, and one which brought new hope of an effective campaign against what had been one of the most resistant of the microbial enemies to human health in all the world. But it seems to me that the debt of medicine, and of humanity, to Ehrlich's dedicated genius would have been but little diminished if he had never discovered salvarsan, or any other chemotherapeutic remedy with a comparable importance for practical treatment. For there are other important practical successes, achieved by Ehrlich's methods long after his death, the origins of which can be traced in fairly direct line to pioneer observations which he had made many years before, without any such directly practical results. We have seen already how the scientific pedigree of the first artificial remedies for malaria can thus be traced to Ehrlich's trial of methylene blue; and, similarly, trypan-red, though it was not itself effective as a practical remedy, can be recognized as the founding ancestor of the line leading to germanin (suramin). I am sure that other examples of such particular derivations could be found; but in addition to them all, and surpassing them by far in its claim upon our grateful recognition, we should remember how large a part of all the great and still expanding advance in the direct and specific treatment of infectious diseases can be traced at its beginning to the inspired vision, the brilliant initiative, and the invincible scientific enthusiasm of Paul Ehrlich.

An Unusual Personality

Paul Ehrlich was a man not only of rare scientific genius but of a very unusual personality. His waking thoughts and attention were concentrated upon his scientific activities and speculations with a burning intensity. Any visitor, if he could be thought to have some kind of contact with such interests, was likely to find himself abruptly plunged into a flood of enthusiastic and exclamatory exposition, though he could hardly fail to retain some stimulus and inspiration from the immersion. Within his special range Ehrlich's knowledge was profound and comprehensive, and his memory prodigious; but beyond the sharply drawn limits of that range he made no secret, but rather a parade, of the astonishing completeness of his ignorance. Anything electrical, for example, was entirely beyond his ken, and he would confess to, or boast of, his inability to remember the direction of the earth's rotation. Apart from his unremitting concentration on his scientific work, his small remainder of interests and activities had a remarkable simplicity.

He seemed to read very little outside his own scientific range. I have heard him speak with enthusiasm, indeed, of the Sherlock Holmes stories, and a portrait of Conan Doyle hung on his study wall; but that was because he prided himself on a supposed resemblance between Holmes's detective methods and those of his own researches. His tastes in the fine arts were those of a child; and there were many other child-like aspects of his character. He had no trace of the pomposity which men of his eminence in the Germany of those days were apt to display; and his freedom from many normal inhibitions could be endearing or exasperating, according to the circumstances. He seemed to be generous and petty, open-hearted and secretive, culpably careless of his own interests, and fiercely, explosively resentful of anything which he felt as an encroachment, or even as unfair criticism—all in turn and unpredictably. His character seemed, indeed, to have a heavy dose of what is commonly called the artistic temperament, but without any faculty of artistic appreciation.

With it all, nobody who had the privilege of knowing him, and of working at any level under his stimulating influence, can have had any doubt of his essential greatness. The world has abundant reasons of gratitude for his achievements and his inspiration, and for celebrating the centenary of the birth of one of its great benefactors.

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