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Genesis and Development of a Scientific Fact

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Three The Wassermann Reaction and Its Discovery

For a long time I wondered how I could describe the Wassermann reaction to a layman. No description can take the place of the idea one acquires after many years of practical experience with the reaction. It is a complex, extremely rich field related to many branches of chemistry, physical chemistry, pathology, and physiology.

The procedure is based on five little-known factors, whose mutual effects are adjusted by means of preliminary tests and whose mode of application is secured through a system of controls. The most important reagent, the so-called "antigen" or, better, "extract," is used on the basis of numerous and varied preliminary tests as well as of comparisons with other previously tested extract preparations. Only a continuous, regular, and well-organized execution of the procedure for the reaction, always with many blood samples, several taken from each series for comparison with the next, will yield results of the necessary reliability. A clinical control of these results must of course also be carried out, involving a comparison of the laboratory results with the clinical results and an appropriate adjustment of the mode of procedure.

Despite every safeguard and mechanization, however, new and unexpected findings continually emerge. From time to time very promising relations and vistas open up, only to vanish again like so

many mirages. The reaction occurs according to a fixed scheme, but every laboratory uses its own modified procedure, which is based upon precise quantitative calculations; nevertheless, the experienced eye or the "serological touch" is much more important than calculation. It is possible to obtain a positive Wassermann reaction from a normal blood sample and a negative one from a syphilitic sample without any major technical errors. This was shown very clearly at the Wassermann Congresses held by the League of Nations, where the best serologists from various countries examined the same blood samples simultaneously but independently. It was shown then that the results did not completely agree either with each other or with the clinical aspect of the disease.

Yet the reaction is one of the most important medical aids used in thousands of medical establishments every day and about which many theoretical papers are written. Its importance is already apparent from the fact that the procedure is subject to official regulations and that in many countries only special laboratories are qualified to carry it out.

This field is a little world of its own and therefore can no more be fully described in words than any other field of science. Words as such do not have fixed meanings. They acquire their most proper sense only in some context or field of thought. This delicate shading of the meaning of a word can be perceived only after an "introduction," whether historical or didactic.

But neither approach is purely rational or intellectual per se. History cannot be logically constructed any more than a scientific event, if only because it involves the progress of vague and indefinable concepts which are about to crystallize. The more detailed and differentiated the description is for any field of thought, the more complex, interrelated, and mutually dependent in definition will be its concepts. They become a tangle impossible to unravel logically, an organic structure produced by mutual development and with interacting components. At the end of the development, the beginning cannot be understood any longer or even properly expressed in words. If at all, it will be understood and expressed differently than it was originally. It is therefore not possible to present the result of such a development as if it were a logical conclusion from past premises. Can the development of the concept of chemical elements from the early qualitative concept to the modern one mainly in terms of atomic weight be described in terms of formal logic? The meanings of the concepts of quality, weight, element, composition have changed completely during the course of time, although in harmonious reciprocity. No medieval chemist could understand a modern law of chemistry in the same way that we do today and vice versa.

Nor is the didactic or authoritative type of introduction purely rational, for the momentary state of knowledge remains vague when history is not considered, just as history remains vague without substantive knowledge about the momentary state. Any didactic introduction to a field of knowledge passes through a period during which purely dogmatic teaching is dominant. An intellect is prepared for a given field; it is received into a self-contained world and, as it were, initiated. If the initiation has been disseminated for generations as in the case of introducing the basic ideas of physics, it will become so self-evident that the person will completely forget he has ever been initiated, because he will never meet anyone who has not been similarly processed.

One could argue that, if there were such an initiation rite, it would be accepted without criticism only by the novice. The true expert must free himself from the shackles of authority and justify his first principles again and again until he establishes a purely rational system.

But the expert is already a specially molded individual who can no longer escape the bonds of tradition and of the collective; otherwise he would not be an expert. For the introduction, then, factors which are not subject to logical legitimization are also necessary, as well as essential both to the further development of knowledge and to the justification of a branch of knowledge that constitutes a science in itself.

We are now about to perform the rite of initiation into the field of the Wassermann reaction according to the German ritual. I have chosen the 1910 edition of the catechism by Citron, a student of Wassermann. As a textbook it is still rather useful, although already outdated by the most advanced research.

Dr. Julius Citron, *The Methods of Immunodiagnostics and Immunotherapy* (Leipzig 1910). First lecture: Introduction. The concepts of immunity and antibody. The law of specificity. The importance of control experiments.

Gentlemen: There are several approaches we can use to the diagnosis of infectious diseases. Besides clinical observation, which enables us to make the diagnosis through close observation of the temperature curve, changes in the organs, exanthema, and the biochemical processes, we were taught by etiological research to utilize the direct detection of specific causative agents, and by immunology to utilize that of the specific reaction products of the organism, in making the diagnosis. We know now that the progress of an infectious disease depends not only on the type, the quantity, and the virulence of the disease germ, but also on the behavior of the organism. *The disease must be seen from the viewpoint of the reciprocal effect arising from these two groups of factors, although it is impossible to determine in detail the specific effect of the causative agent and its products, and that of the reactive power of the organism.* Although the reaction of the organism varies widely in detail, it can be shown that in spite of all individual differences, well-characterized bacteria and their products are confronted with equally typical basic forms of defense measures serving the organism. For this purpose the body employs cellular and humoral means. It is possible to arrange infectious diseases in an order which shows cellular reactions dominating the picture at one end of the scale, humoral changes at the other, with every intermediate degree between these extremes. We thus find in the widely diversified picture of tuberculosis that the tubercular nodule occurs again and again as a typical cellular reaction product, whereas leprous and syphilitic infections induce the cellular changes that are typical of these diseases. More difficult to recognize, however, because they are invisible both to the naked eye and under the microscope, are those delicate biological reactions which occur in the body fluids during the course of infectious diseases. Special methods are necessary to detect and differentiate humoral changes found especially in the blood serum. But as we now know, humoral immunity reactions, like cellular ones, are not confined to the field of infectious diseases proper but are to a far greater extent expressions of physiological events, whether normal or pathological. With humoral reactions, the ingenious concept of Ehrlich's side-chain theory has enabled us to understand that the physiological manifestation of assimilation which functions in nutrition and energy consumption corresponds to events leading, in pathological conditions, to the formation of the anti-infectious reaction products. Metchnikoff has shown in a no less remarkable analogous achievement that the same group of cells originating in the mesenchyme, which the organism mobilizes against the bacterial enemy, fulfills a variety of physiological and physiological-pathological functions throughout the animal kingdom. They cooperate in the metamorphosis of the body structure of lower animals by their ability to make entire organs disappear. They also take part in the involution of the uterus after childbed, eat up nerve cells destroyed during senile atrophy of the nerve centers, and in the form of chromophages bleach the hair as a sign of advancing age. *The dividing line between the physiological and the pathological event cannot be biologically drawn with any precision.* It represents a whole chain of phenomena with various transitions.

Gentlemen: To make certain that we understand each other in what follows it is above all necessary that we agree on certain concepts, with which most of you are probably already familiar.

To begin with, the word "immunity" needs to be explained. You all know the strange phenomenon that after recovery from most infectious diseases the organism undergoes a change, detectable neither macroscopically, nor microscopically, nor chemically, which protects it against, or at least makes it less susceptible to, the same infectious disease. Because, as you will presently hear, we must distinguish between types of immunity, it is advisable to introduce certain attributes in the interest of facilitating understanding. We designate as "active immunity" the form in which the body immunizes itself by its own power in its fight against infection. You know that Jenner and Pasteur artificially produced this form of immunity, spontaneously acquired through recovery from a disease, for the purpose of protective vaccination and inoculation. Our knowledge about the nature of active immunity is as yet incomplete. All we can do is demonstrate that under active immunity the organism usually forms certain specific reaction products against the disease germs and their toxins. We call these reaction products, which circulate mainly in the blood serum, antibodies. These antibodies have different names according to their different

effects, and they vary in significance. The agglutinating and precipitating antibodies, designated as the agglutinins and precipitins respectively, probably have very little protective effect. But others undoubtedly serve to protect the organism either by directly neutralizing bacterial poisons and toxins (antitoxins), by killing bacteria (bacteriolysins, bactericides), or by changing the bacteria in such a way that they can be destroyed more easily by the cells (bacteriotropins, opsonins). Corresponding to these three main types we can speak of antitoxic, bactericidal and cellular immunity, of course with many possible intermediate types. It is very likely that other, still unknown types of immunity exist besides those already known. Above all it can be accepted as certain that cellular immunity can claim far greater importance than is usually accorded it on the basis of the facts known thus far. There is apparently also a type of cell immunity which is effective without the agency of any serum substances, and this is designated "histogenic" immunity and "tissue immunity."

By injecting antibody-containing blood serum obtained from immunized animals into healthy, nonimmunized ones, it is often possible to induce immunity against the associated infective agents. Here the organism thus protected has not produced its protective substances itself through cellular activity of its own but receives them in a prefabricated state. We therefore call this "passive immunity" to distinguish it from the previously discussed "active" form.

All the types of immunity described so far share in the fact that they are acquired only through certain reactions, whether this involves either spontaneous or artificial recovery from disease, or alternatively the transfer of antibodies. Besides such "acquired" immunity, there is also "natural immunity," by which we mean the fact that not every type of animal is susceptible to every infectious disease. Man, for instance, enjoys a natural immunity against a number of the most dreaded animal diseases such as chicken cholera and swine pox. Natural immunity is almost always of the cellular type. The most important natural defensive weapon is phagocytosis, which is the ability of the leucocytes to "eat" the bacteria.

In conclusion it should be pointed out briefly that we speak of a "local" and "general" immunity to express the difference that various organs of the same individual can show in their reaction to an infection. An immunity may be called "relative" or "absolute" to events, whether normal or pathological. With humoral reactions, the ingenious concept of Ehrlich's side-chain theory has enabled us to understand that the physiological manifestation of assimilation which functions in nutrition and energy consumption corresponds to events leading, in pathological conditions, to the formation of the anti-infectious reaction products. Metchnikoff has shown in a no less remarkable analogous achievement that the same group of cells originating in the mesenchyme, which the organism mobilizes against the bacterial enemy, fulfills a variety of physiological and physiological-pathological functions throughout the animal kingdom. They cooperate in the metamorphosis of the body structure of lower animals by their ability to make entire organs disappear. They also take part in the involution of the uterus after childbed, eat up nerve cells destroyed during senile atrophy of the nerve centers, and in the form of chromophages bleach the hair as a sign of advancing age. *The dividing line between the physiological and the pathological event cannot be biologically drawn with any precision.* It represents a whole chain of phenomena with various transitions.

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In conclusion it should be pointed out briefly that we speak of a "local" and "general" immunity to express the difference that various organs of the same individual can show in their reaction to an infection. An immunity may be called "relative" or "absolute" to denote quantitative differences, and a further distinction can be made between "permanent" and "temporary" immunity.

Gentlemen: The second important term we must discuss is the concept of the antibody. I have already explained to you briefly that by antibodies we mean all the specific reaction products formed by the organism against disease germs and their products. To complete the picture I must now add that antibodies are also formed when any foreign albumin of a nonbacterial type, for instance blood from a different type of animal or albumin from chicken eggs, is administered to an organism parenterally, that is in a manner other than stomachically.

To establish better understanding of the nature of antibodies, attempts have been made to prepare them in a chemically pure state. All these attempts, however, have thus far failed. The chemical nature of antibodies is unknown. We do not even know whether what we call antibodies constitute independent chemical structures at all. All we know is the serum effects. Thus antibodies represent only the mentally accomplished materialization of these serum effects. But for didactic purposes we shall henceforth speak of different antibodies such as antitoxins or agglutinins when we really mean the antitoxic or the agglutinating ability of the serum.

Although the effectiveness of the individual antibodies differs widely, specificity is a common property of them all. This means that the typhus antibody, for example, can produce the various immunity reactions only with typhus bacteria and the cholera antibody only with cholera vibriones. This property of specificity is so important that we must not designate as antibodies any substances possessing all the other properties of an antibody yet remaining nonspecific. The law of antibody specificity does not apply, of course, in the extreme form I have just outlined to explain the term to you. We shall presently have the opportunity to discuss the nature of specificity in detail, and thus get to know its limitations. *For the time being, however, I would ask you to commit firmly to your memory the law that every true antibody is specific and that all nonspecific substances are not antibodies. The law of specificity is the precondition of serodiagnostics.* Correctly to diagnose typhus, for example, we must know that a patient's serum can produce immunity reactions with genuine typhus bacilli only if the patient in question really has typhus. When the specificity of a reaction becomes doubtful, its diagnostic utilization must accordingly suffer. For this reason, we must repeatedly discuss the question whether and to what extent any given reaction is specific and

ascertain true specificity in any way possible, especially by means of control tests. Permit me, even in this first lecture, to draw your attention to the importance of adequate control tests. At first you will find it perhaps pedantic that the controls demanded for seemingly very simple tests often require many times the effort involved in the actual test. You will be tempted perhaps to omit such controls if during the practical utilization of serodiagnostics you are able to obtain good results without the required controls, even in large series of tests. Nevertheless, gentlemen, I cannot impress upon you strongly enough never to operate without the necessary controls. You will thus protect yourselves against grave errors and faulty diagnoses, to which even the most competent investigator may be liable if he fails to carry out adequate controls. This applies above all when you perform independent scientific investigations or seek to assess them. Work done without the controls necessary to eliminate all possible errors, even unlikely ones, permits no scientific conclusions.

I have made it a rule, and would advise you to do the same, to look at the controls listed before you read any new scientific papers dealing with serodiagnostics. If the controls are inadequate, the value of the work will be very poor, irrespective of its substance, because none of the data, although they may be correct, are necessarily so.

What does this excellent introduction suggest? What elements do we find in it that cannot be justified? It will not be difficult to identify them, for we already have the rudiments of other views, even though these have not as yet found their way into the textbooks. The new views, of course, cannot be fully confirmed either, but because the forcefulness of the old views has diminished, we have acquired the possibility of a comparison.

1. *The concept of infectious disease.* This is based on the notion of the organism as a closed unit and of the hostile causative agents invading it. The causative agent produces a bad effect (*attack*). The organism responds with a reaction (*defense*). This results in a conflict, which is taken to be the essence of disease. The whole of immunology is permeated with such primitive images of war. The idea originated in the myth of disease-causing demons that attack man. Such evil spirits became the causative agent; and

the idea of ensuing conflict, culminating in a victory construed as the defeat of that "cause" of disease, is still taught today.

But not a single experimental proof exists that could force an unbiased observer to adopt such an idea. It is unfortunately beyond the scope of our discussion to examine all the phenomena of bacteriology and epidemiology one by one to show that the disease demon haunted the birth of modern concepts of infection and forced itself upon research workers irrespective of all rational considerations. It must suffice here to mention the objections to this idea.

An organism can no longer be construed as a self-contained, independent unit with fixed boundaries, as it was still considered according to the theory of materialism.[1] That concept became much more abstract and fictitious, and its particular meaning depended upon the purpose of the investigation. For the morphologist it has changed into the concept of genotype as the abstract and fictitious result of hereditary factors. In physiology we find the concept of "harmonious life unit," according to Gradmann, "characterized by the notion that the activities of the parts are mutually complementary, mutually dependent upon each other, and form a viable whole through their cooperation." Morphological organisms of the type which are self-contained units do not have this ability. But a lichen, for instance, whose constituents are of completely different origins, one part an alga, another a fungus, constitutes such a harmonious life unit. The constituents are closely interdependent and on their own are usually not viable. All symbioses, for instance, between nitrogen-fixing bacteria and beans, between mycorrhiza and certain forest trees, between animals and photogenic bacteria, and between some wood beetles and fungi form "harmonious life units," as do animal communities such as the ant colony, and ecological units such as a forest. A whole scale of complexes exists which, depending upon the purpose of the investigation, are regarded as biological individuals. For some investigations the cell is considered the individual, for others it is the syncytium, for still others a symbiosis, or, lastly, even an ecological complex. "It is therefore a prejudice to stress the idea of organism," in the old sense of the word, "as a special kind of life unit, a prejudice which is unbecoming to modern biology."[2] In the light of this concept, man appears as a complex to whose harmonious well-being many bacteria, for instance, are absolutely essential. Intestinal flora are needed for metabolism, and many kinds of bacteria living in mucous membranes are required for the normal functioning of these membranes. Some species exhibit for their vital functions an even greater dependence upon others. Their metabolism and propagation, indeed their entire life cycle, depend on a harmonious interference by other species. Some plants are pollinated by certain beetles; and malarial plasmodia depend for their life cycle upon their transmission by mosquito to man.

Now continuous biological changes, within any complex biological individual, so construed are based upon phenomena which can be divided into several categories. They constitute either (1) a kind of spontaneous so-called constitutional process within the genotypes, such as mutations and spontaneous gene changes, roughly comparable with spontaneous radioactive phenomena within an atom. Many a disease belongs to this category, such as the hemolytic icterus of Nägeli, and even the outbreak of certain epidemics might perhaps be included here. Or they are (2) cyclic changes, of which some are genotypically conditioned and others are the result of reciprocal action within the complex life unit. These include the life cycle of organisms (aging), generational change, and some of the dissociation phenomena of bacteria. Both serogenesis and immunogenesis must be listed here, as well as virulence as a life phase of bacteria and even some infectious diseases, such as furunculosis during puberty. Or, lastly, they are (3) pure changes within the constellation of reciprocally acting parts of the unit comparable, for instance, to the reaction among ions in a solution. Hypertrophy of one element of the biological unit at the expense of another is a change of this type, as is the imbalance either consequent upon phenomena of the first or second category, or caused by external physico-chemical conditions. Most infectious diseases belong to this latter class. It is very doubtful whether an invasion in the old sense is possible, involving as it does an interference by completely foreign organisms in natural conditions. A completely foreign organism could find no receptors capable of reaction and thus could not generate a biological process. It is therefore better to speak of a complicated revolution within the complex life unit than of an invasion of it.[3]

This idea is not yet clear, for it belongs to future rather than present biology. It is found in present-day biology only by implication, and has yet to be sorted out in detail.

So construed, the concepts "sickness" and "health" also become unsuitable for any exact application. What used to be called infectious disease or the spread of epidemics belongs partly to the first, partly to the second or even the third group of phenomena. Biologically, this also includes phenomena such as germ carrying, latent infection, the development of allergies, and even serogenesis. These have nothing directly in common with being ill, although they are very important to the mechanism of the disease. The old concept of disease thus becomes quite incommensurable with the new concepts and is not replaced by a completely adequate substitute.

2. *Hence, the concept of immunity in this classical sense must be abandoned.* A fundamental property of all biological events is modified reaction to a repeated stimulus. Sometimes this consists of a certain immunity, whether habituation to toxin, true immunity to disease, or even mechanical immunity such as that against scalding (thickening of the skin) or against bone fracture (callus formation). On other occasions, hypersensitivity occurs, sometimes even in the same cases just mentioned. With sufficiently refined methods it is in fact always possible to detect both together. In some respects there is increased power of resistance and in others increased sensitivity. Thus instead of the prejudicial concept of immunity, we have the general concept of allergy (changed mode of reaction), or according to Hirszfeld the absence of reaction and hyperreactivity. Instead of antibodies, we speak of reagins to stress the lack of direction of the effect, because reagins ensure not only that the irritant is decomposed and rendered harmless but also that it is effective in the first instance and possibly increased in strength or velocity of reaction.

Many classical concepts of immunology were evolved during the period when, under the influence of great chemical successes in physiology, misguided attempts were made to explain the whole, or almost the whole, of biology in terms of effects produced by chemically defined substances. Toxins, amboceptors, and complements were treated as chemical entities, with such adversaries as antitoxins and anticomplements. This primitive scheme based upon activating and inhibitory substances is being progressively discarded in accordance with current physico-chemical and colloidal theories in other fields. We now speak of states or structures rather than substances, to express the possibility that a complex chemico-physico-morphological state is responsible for the changed mode of reaction, instead of chemically defined substances or their mixtures being the cause.

3. *Many other habits of thought* that today cannot be objectively confirmed will also be found in Citron's textbook for serologists.

The division into *humoral* and *cellular* factors (the French stress the second, the Germans the first) cannot be confirmed any more than the concept of specificity in the distinctly mystical sense in which it is used here.

4. Citron's lecture also contains a *methodological initiation.* The novice is introduced as quickly as possible to the importance of "controls." These specifically biological comparison tests, which are to be performed parallel to the main ones, have already been mentioned. There is no universally accepted system of measurement in biology, and this is especially so in serology. The results of quantitative tests are read minimetrically with dilution to the limits of reactivity and comparison with standard reagents as well as their combinations. The effect produced by a combination of reagents is also compared with that of incomplete combinations from which just *one* reagent has been intentionally omitted. All these comparisons control the outcome and are therefore called "controls." Epistemologically it may not be the best method, but we have yet to find another one.

5. The lecture also contains *general precepts* in addition to these particular ones: Cognition should progress not through intuition or from empathy with the phenomena as a whole, but through clinical

and laboratory observation of the various constituent phenomena. The so-called diagnosis—the fitting of a result into a system of distinct disease entities—is the goal, and this assumes that such entities actually exist, and that they are accessible to the analytical method.

Such precepts form the thought style of the serologist's collective. They determine the direction of research and connect it with a specific tradition. It is perfectly natural that these precepts should be subject to continual change. To prevent misunderstandings it must once again be stressed that it is not the purpose of these pronouncements to play off earlier viewpoints against those of today, or those of leading research workers against textbook views. It is altogether unwise to proclaim any such stylized viewpoint, acknowledged and used to advantage by an entire thought collective, as *"truth or error."* Some views advanced knowledge and gave satisfaction. These were overtaken not because they were wrong but because thought develops. Nor will our opinions last forever, because there is probably no end to the possible development of knowledge just as there is probably no limit to the development of other biological forms.

Our sole purpose has been to demonstrate how even specialized knowledge does not simply *increase* but also basically *changes.* Yet we do not want to confine ourselves merely to some banal statement about the transience of human knowledge.

Every act of cognition means that we can first of all determine which passive connections follow of necessity from a given set of active assumptions. To investigate successfully how assumptions change requires research into thought styles. Thought style, suggested during even the earliest acquaintance with any science and extending into the smallest details of its specialized branches, calls for a sociological method in epistemology.

Neither the particular coloration of concepts nor this or that way of relating them constitutes a thought style. It is a definite constraint on thought, and even more; it is the entirety of intellectual preparedness or readiness for one particular way of seeing and acting and no other. The dependence of any scientific fact upon thought style is therefore evident.

Thus even Citron's presentation, which only about twenty years ago was considered to be at the very zenith of research, indicates a thought collective nexus of knowledge which manifests itself in a social constraint upon thought. In the course of our further discussion concerning the Wassermann reaction, this interaction among the individual, the collective, and the fact will be considered in detail.

If an animal, for instance a rabbit, is inoculated, that is, immunized with killed bacteria or with the blood of a different species, the serum of the animal in question (the immune serum) acquires the property of decomposing such bacteria or blood corpuscles. Serologists have, so to speak, materialized this property by giving the hypothetical, even "symbolic" substance in the immune serum the name "bacteriolysin" or "hemolysin." Bacteriolysis or hemolysis succeeds only with *fresh* serum taken from a *pretreated animal.* If allowed to stand for prolonged periods, or heated to 50–60°C for thirty to thirty-five minutes, the serum will lose this property, although not irreversibly. Serum deactivated by age or heat can be reactivated by the addition of *fresh* serum from a *not pretreated* animal, preferably a guinea pig, even though the latter serum on its own has no effect whatsoever on those bacteria or blood corpuscles. It merely supplements the bacteriolysins or hemolysins of the inactivated immune serum. This property was also materialized by the serologists. The name "complement" is given to this hypothetical substance present in the fresh serum and in whose presence lysis occurs. To induce bacteriolysis or hemolysis two "substances" are thus necessary: (1) the bacteriolysin or hemolysin, (2) the complement. They act only together. The bacteriolysin and the hemolysin respectively are heat-resistant, that is, they withstand heating to 56–60°C without damage. The complement is heat-sensitive. It is lost when heated to 56–60°C as well as during prolonged storage (aging) of the serum. In the symbolic language of the German serologists, which owes its origin to Ehrlich, the antibodies of the bacteriolysin and of the hemolysin type are called amboceptors, because they combine with and fix two substances: the one earmarked for immunization, called antigen, and the other, the complement.

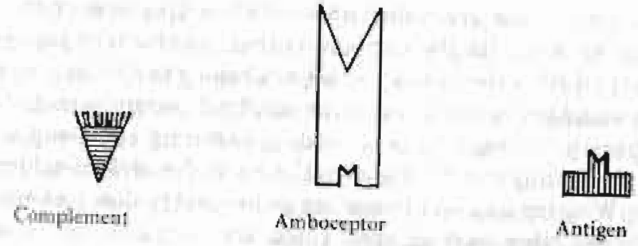
Ehrlich introduced very descriptive and mnemotechnically excellent symbols appropriate for the complex side-chain theory. The amboceptors are specific; their effect is confined to the particular antigen used in the immunization—being effective only on the blood corpuscles of a ram, only on cholera bacilli, etc. The complement is present in the normal serum and acts with any amboceptor.

It was at one time an open question whether a single uniform complement or several different complements existed in the same normal serum, one complementing the bacteriolysin, and the other the hemolysin. Ehrlich and his followers adopted the pluralistic view, but Bordet and Gengou proved the unitarian view in 1901 with the following experiment. If bacteria (antigen 1) are mixed with the corresponding inactivated immune serum (1) (that is, the bacteriolytic amboceptor), as well as with the complement, bacteriolysis will occur. If one now adds to this a mixture of blood corpuscles (antigen 2) and the corresponding immune serum (2) (that is, the hemolytic amboceptor), no hemolysis will occur, because the complement has been used up in the first process (bacteriolysis) and is no longer available for the second (hemolysis). This can be shown in the symbolic sign language as illustrated.*

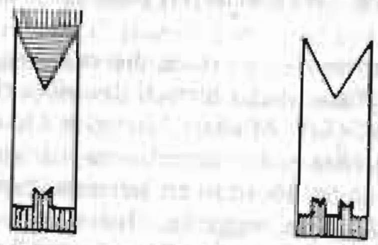
The complement is completely used up for bacteriolysis and none is left for subsequent hemolysis. This proves that no separate complement exists for hemolysis; that the complement is therefore uniform. The experiment must be conducted quantitatively, of course, which calls for special preliminary tests.

Because it is visible to the naked eye, hemolysis can be detected more easily than bacteriolysis, which requires microscopic examination. This complement fixation method has therefore become the most important instrument in serology, since according to this scheme the hemolytic system (the hemolytic amboceptor plus the corresponding blood corpuscles) can be used to indicate the occurrence of bacteriolysis, that is, whether the bacteriolysin used [is the "specific" one for, and thus]* reacts with the bacteria used. With this method, if the bacteria are known the bacteriolysin can be diagnosed. Conversely if the serum, that is the bacteriolysin, is known, the bacteria can be diagnosed. In the first case we have a method of recognizing, for instance in the serum of patients, the

*The bracketed portion of this sentence is our interpolation.—Eds.



Fixation of these three substances.



Scheme of the reaction, after Bordet and Gengou 1901. The complement has been used up in the first fixation; no second fixation (hemolysis) is therefore possible.

Figure 2

presence of certain antibodies upon which a diagnosis of the disease can be based. In the second we can determine with very great certainty whether the unknown bacteria belong to the same species as the standard bacteria used for artificial immunization. This complement fixation method according to Bordet and Gengou was soon successfully used by Widal and Le Sourd for abdominal typhus and by Wassermann and Bruck for abdominal typhus and meningitis. Many other workers used it later for such diseases as swine pox, cholera, and gonorrhea.

In 1906 "Wassermann and Bruck proceeded to utilize this reaction for the first time for the detection of antigens in human and animal organ extracts. With the aid of specific tubercle-bacillus immune sera, they demonstrated the presence of lysed tubercle bacillus substances (tuberculin) in tuberculous organs. With the aid of tuberculin, in turn, they demonstrated the occurrence of a specific antibody in the blood, namely antituberculin."[5] These experiments were not rated very highly. Weil expressly wrote of the "untenability of the experiments by Wassermann and his colleague in which specific antigen and antibodies in tuberculous foci, and, in a case of miliary tuberculosis, tubercle bacillus substance in the blood had apparently been successfully demonstrated."[6] Nor did these experiments have any direct major practical or theoretical impact. These results may not have been very solid; nevertheless they were the starting point for Wassermann's syphilis experiments.

It is very interesting to trace the stimulus for these syphilis experiments. Wassermann himself describes the situation as follows: "The head of the Ministry, Friedrich Althoff, asked me to his office when Neisser had returned from his first expedition,* and the French were far ahead in experimental biological research on syphilis. He therefore suggested that I work on this disease to assure that German experimental research have a share in this field."[7] Thus from the very beginning the rise of the Wassermann reaction was not based upon purely scientific factors alone. A

*To Indonesia for a suitable climate to conduct his experiments with monkeys.—Eds.

rivalry between nations in a field that even laymen consider very important and a kind of vox populi personified by a ministry official constituted a social motive for the work. The effort expended on this scientific project was correspondingly great. As with the discovery of *Spirochaeta pallida,* here again it was really an organized collective rather than any individual that brought it to completion. Even the lively polemics between, and personal protestations by, the various workers involved, which appeared in the *Berliner Klinische Wochenschrift* during 1921, do not help us to isolate from this community the one, sole discoverer. Owing to the controversy with Ehrlich, the instrument was supplied by Bordet and Gengou. Wassermann and Bruck perfected and expanded it. Because of rivalry with the French, Althoff mapped out the new territory and applied the necessary pressure. Neisser offered the pathological material and his experience as a physician. Wassermann as director of the laboratory was responsible for the plan, and Bruck as his colleague executed it.[8] Siebert prepared the sera. Schucht, an assistant of Neisser's, produced the organ extracts. These are the ones whose names we know. But there certainly were many suggestions concerning technical manipulations, modifications, and combinations from others whom it is impossible to list. Citron decisively improved the dosing. Landsteiner, Marie, and Levaditi, among others, published the first practical method of preparing the extracts. Skills, experience in the field, and ideas whether "wrong" or "right" passed from hand to hand and from brain to brain. These ideas certainly underwent substantive change in passing through any one person's mind, as well as from person to person, because of the difficulty of fully understanding transmitted knowledge. In the end an edifice of knowledge was erected that nobody had really foreseen or intended. Indeed, it stood in opposition to the anticipations and intentions of the individuals who had helped build it. For Wassermann and his co-workers shared a fate in common with Columbus. They were searching for their own "India" and were convinced that they were on the right course, but they unexpectedly discovered a new "America." Nor was this all. Their "voyage" was not straight sailing in a planned direction but an Odyssey with continual change of direction. What they achieved was not even their goal. They wanted evidence for an antigen or an amboceptor. Instead, they fulfilled the ancient wish of the collective: the demonstration of syphilitic blood.

The first paper entitled "A Serodiagnostic Reaction with Syphilis," which appeared on 5 October 1906, was signed by A. Wassermann, A. Neisser and C. Bruck. The purpose of this investigation, as can be gleaned from the contents, was to demonstrate, by means of the complement fixation method, *primarily* antigen in syphilitic organs and in syphilitic blood, and *secondarily* antibodies (cum amboceptors) in the syphilitic blood of patients. The primary aim was pursued with much greater vigor. The authors wrote: "The method consists in taking inactive serum from monkeys pretreated with syphilitic material and mixing it with substances such as organ extracts and serum obtained from syphilitic patients. After the addition of fresh, normal guinea pig serum as the complement, a certain time is allowed for fixation. By means of an inactive, specifically hemolytic serum and its related red blood corpuscles, a test is then performed to show whether the complement first added has been completely or only partially fixed. This manifests itself in the complete or partial failure of lysis of the red blood corpuscles or, in brief, in the degree to which hemolysis is inhibited.[9] It would be of the greatest diagnostic and therapeutic significance if one could succeed regularly in obtaining evidence of syphilitic substances or antibodies in the circulating blood of syphilitics. In a number of cases we have already succeeded in securing this evidence (examining extracts from defibrinated blood instead of the blood serum appears, incidentally, to be more suitable to produce this evidence), but in others we have failed. Obviously the strength of the immune serum has a decisive function here. It must therefore be our next task, which in our climate is perhaps impossible in view of the extreme sensitivity monkeys have in all experiments, to obtain a specific serum of the greatest possible strength against syphilis."[10]

The unbiased observer will consider the reaction described here still very primitive and quite different from what is called the Wassermann reaction today. What then was its most decisive characteristic, immune serum from monkeys, has altogether disappeared, as have extracts from defibrinated blood, because it is

not the antigen but only the amboceptors[11] that are required today.

It is important to note that, years later, Bruck, the author of this paper, saw its contents in a light quite different from that of an unbiased observer. He wrote in 1924: "During a discussion between Wassermann, Neisser, and Bruck, the latter was asked to deal with this question. He was able to obtain . . . positive results and so to demonstrate to Wassermann, his superior at the time, *the original method which remains fundamentally unchanged even today,*[12] and to record it officially. The first communication, entitled 'A Serodiagnostic Reaction with Syphilis,' with Bruck as the author and signed by Wassermann, Neisser, and Bruck, was published at the same time."[13] Retrospectively Bruck saw the ripe fruit already in the seed and hardly noticed that many seeds had not even taken. A similar attitude can be found in Wassermann too.

The second paper by the same authors together with Schucht and entitled "Further Observations on the Demonstration of Specific Syphilitic Substances by Complement Fixation" also appeared in 1906.[14] Evidence of specific syphilitic substances in organ extracts (that is, antigen detection) is again mentioned as being of principal importance, and the search for antibodies in the serum of syphilitics is only of secondary interest. The technique, the necessary controls, and the statistics of the results are each described in detail. Syphilitic antigen was detected in 64 out of 76 extracts from syphilitic organs, including 29 of 29 extracts from confirmed syphilitic fetuses. But not a single one was detected in 7 extracts from brains exhibiting progressive paralysis. Detection of amboceptors—the antibodies—was successful 49 times in 257 samples of syphilitic blood (or 19 percent). This second experimental setup (for amboceptor detection) thus yielded far fewer results than did the first (for antigen detection). It is therefore understandable why the authors should have mentioned antigen detection as of principal importance. Concerning the theory of this reaction, the authors are fully convinced "that it is a specific reaction between syphilitic antigen and syphilitic antibodies"[15] which indicates immunity against spirochaetes. This view was soon supported by the results of Bab and Mühlens which were meant to establish a correlation between the spirochaete count in the livers used for the experiment and the potency of extracts taken from these organs. But support aside, their view was later shown to be in error.

Citron soon showed that the conclusion could not be upheld that the blood corpuscle extracts contained syphilitic antigen, "because such extracts from healthy persons produced the same reaction, although more rarely." Thereafter, such detection of syphilitic antigen was generally rejected, although during the initial experiments it had actually yielded the "good" results and was particularly stressed.

The epistemologically most important turning point occurred with the detection of syphilitic antibodies (amboceptor detection). During the initial experiments it produced barely 15–20 percent positive results in cases of confirmed syphilis. How could it then increase to the 70–90 percent found in later statistics? *This turning point represented the actual invention of the Wassermann reaction as a useful test.* The theory of the reaction as well as the historical and psychological circumstances surrounding its conception are of less practical importance. *If the relation of the Wassermann reaction to syphilis is a fact, it became a fact only because of its extreme utility owing to the high probability of success in concrete cases.* The moment when this decisive turn occurred cannot be accurately determined. No authors can be specified who consciously brought it about. We cannot state exactly when it occurred nor explain logically how it happened.

The turning point has often been discussed. But even the principal actors themselves can say no more than that the technique had first to be worked out. Sometimes Citron is credited with having brought about the turning point through his introducing increased serum dosage. Wassermann and his co-workers originally used 0.1 cc of patient serum, but Citron recommended 0.2 cc. Yet today even 0.04 cc of patient serum is ample, provided all the reagents are mutually adjusted with precision. Fundamentally it is this very reagent-adjustment, coupled with learning how to read the results, that made the Wassermann reaction useful.

Proper balance was difficult to achieve and the results tended to fluctuate. There were too many positive results even with non-syphilitics and too many negative ones even with syphilitics. The optimum intermediate position between minimum nonspecificity

and maximum sensitivity had to be gradually established. This, however, is entirely work of a collective consisting mostly of anonymous research workers, adding now "a little more," now "a little less" of a reagent, allowing now "a little longer," now "a little shorter" reaction time, or reading the result "a little more" or "a little less" accurately. Added to this were modifications in the preparation of the reagents and other technical manipulations, such as the controls and preliminary tests as well as titrations and matching. "Some authors," Citron wrote in 1910, "call only those test tubes positive in which complete inhibition of hemolysis has occurred. That this is a poor method is borne out by the statistics published by authors such as Bruck and Stern. A great many definite cases of syphilis are indicated there which react negatively where this extreme criterion is applied, although to all appearances they were positive."[14] This describes the situation in which the sensitivity was insufficient.

Ten years later, in 1921, Weil wrote: "It must be borne in mind in this context that at the time we conducted these experiments the technical development of the Wassermann reaction had not yet been completed. It proceeded in the direction of making the reaction less and less sensitive to obtain a clinically usable test for syphilis. It must also be mentioned that most of the reactions we produced were weakly positive. These were accorded great importance at the time, but later such weak results were no longer considered positive."[15] This describes the situation in which exaggerated sensitivity or nonspecificity was dominant.

Collective experience thus operated in all fields related to the Wassermann reaction until, with disregard for theoretical questions and the ideas of individuals, the reaction became useful. But this rewarding and tedious work of the collective was carried out only as a consequence of the special social importance of the syphilis question and of the problem regarding change in syphilitic blood.

As early as 1907, the many wide-ranging tests had shown that, to produce the antigen (spirochaete substance) required for the reaction, alcoholic or aqueous extracts from normal organs could be used unrelated to the specific antigen—that is, to *Spirochaeta pallida*—in place of extracts from confirmed syphilitic organs. Landsteiner, Müller and Pötzl, Porges and Meier, Marie and

Levaditi, Levaditi and Yamanouchi reported this almost simultaneously.

The belief of Wassermann and his co-workers "that a spirochaete antigen and a spirochaete amboceptor, that is, a specific antigen-antibody reaction, had been demonstrated" was therefore completely mistaken. This became all the more obvious after the experiments by Kroo, which proved that no positive Wassermann reaction could be produced in man through immunization with killed spirochaetes, although spirochaete antibodies could be detected. After all, the Wassermann reaction proves only a special change in syphilitic blood, and even today we do not know much more than this. In the place of the antigen conforming to some theory or scheme, alcoholic extracts from bovine or human heart are now used almost exclusively. To these, following the suggestion of Sachs, cholesterol may be added.[18] With such extracts syphilis serum produces flocculation, which is clearly visible under certain conditions and on which some special and very practical flocculation reactions are based. The precipitate resulting from the mixture of syphilis serum and organ extract has a special effect, which may be due to adsorption, which removes the complement from the hemolytic system consisting of ram blood corpuscles plus corresponding hemolytic amboceptor. This produces the inhibition of hemolysis, which indicates the positive Wassermann reaction.

According to another theory, namely the autoantibody theory of Weil, the Wassermann reaction is not an instability reaction involving hemolysis as a complex biological indicator, but an immunity reaction with true complement fixation of the Bordet-Gengou type, occurring, however, with decomposed-tissue products of syphilis rather than directly with *Spirochaeta pallida.* The organ extract from healthy persons corresponds to the decomposed-tissue products from patients, which explains its usability. There are other theories too, but, in any case, Wassermann's assumption was wrong.

Bruck himself wrote in 1921 about an "extraordinary stroke of luck" by which "during the practical execution of Wassermann's idea, a syphilis reaction was discovered, the nature of which is still not quite clear today."[19] Weil, also in 1921, claimed that the assumption from which Wassermann proceeded was false but

that a discovery of great practical importance was made by accident.[20] Laubenheimer added in 1930: "Although Wassermann and his co-workers were led to discover the method which for short is now called 'the Wassermann reaction' by reasoning which was subsequently proved wrong, the reaction has, during the twenty years of its existence, proved its worth in the diagnosing of syphilis by means of serum, so that even today it cannot be fully replaced by any other more recent method."[21] Plaut lastly comments in 1931 with the wisdom of hindsight. "In view of the current situation respecting serology in general and the Wassermann reaction in particular, some actually wanted to accuse August von Wassermann of having proceeded from false assumptions. If this should really be so—and the case is not yet closed—then it was a blessing that Wassermann did proceed from false assumptions. For had he wanted to wait for the correct ones, he would never have discovered his reaction, because even today, six years after his death, we still do not know the correct preconditions for the reaction. Now and again there have even been foolish suggestions that luck had played a part in the discovery of the Wassermann reaction. In the context of research of this kind we can speak of luck only if the discovery in question is a matter of pure chance. But here exactly the opposite happened. Wassermann found his reaction not by chance but because he looked for it, proceeding quite systematically, naturally on the basis of our then current knowledge. But shrewd ideas are frequently also fortunate ideas, and a skilled hand is often also a lucky hand. Precisely this is an inexplicable part of the nature of a brilliant research scientist's personality who, from the many possible ways to tackle a problem, intuitively chooses the one that leads to success."[22]

It is important to record what Wassermann himself thought about it later. "You will remember that, when I created the serodiagnosis of syphilis, I proceeded from the idea, and with the clear intention, of finding a diagnostically usable amboceptor, that is, a substance which has a fixation relation to an antigen and, after saturation of this affinity, fixes an added complement according to the laws established by Bordet and Ehrlich. With my co-worker C. Bruck I used as antigen the organs of syphilitic patients or of monkeys which Neisser had artificially infected with syphilis."[23]

An impartial judge cannot agree with him even with the best will in the world, because in his first experiments Wassermann was not looking for "a diagnostically usable *amboceptor.*" He was looking primarily for "syphilitic substances" which he thought were "dissolved substances of the micro-organisms," that is, *antigen*, and secondly for "specific antibodies vis-à-vis substances of the causative agent of syphilis," that is, the *specific* amboceptor. But it was later shown that (1) the demonstration of syphilitic substances (antigens) is altogether unsuitable for a diagnostic reaction and (2) the amboceptor indicated by the reaction, if it is an amboceptor at all, is at any rate not a specific amboceptor of the anticausative agent. The ultimate outcome of this research thus differed considerably from that intended. But after fifteen years an identification between results and intentions had taken place in Wassermann's thinking. The meandering progress of development, in all stages of which he was certainly deeply involved, had become a straight, goal-directed path.[24] How could it be otherwise? With the passing of time, Wassermann amassed further experience, and as he did so lost the appreciation of his own errors. It would no longer even be possible for him to "demonstrate 64 times the presence of specific antigen in 69 extracts from syphilitic tissue" and to obtain 14 negative control tests without exception.

The following facts are therefore firmly established and can be regarded as a paradigm of many discoveries. *From false assumptions and irreproducible initial experiments an important discovery has resulted after many errors and detours.* The principal actors in the drama cannot tell us how it happened, for they rationalize and idealize the development. Some among the eyewitnesses talk about a lucky accident, and the well-disposed about the intuition of a genius. It is quite clear that the claims of both parties are of no scientific value. Where a scientific problem is concerned, even one of little significance, these people would not dismiss it so casually. Are we then to maintain that epistemology is no science?

Epistemologically the problem is insoluble from an *individualistic* point of view. If any discovery is to be made accessible to investigation, the *social point of view* must be adopted; that is, the discovery must be regarded as a *social event.*

Early, prescientific ideas brought about a powerful prevailing social attitude toward the problems of syphilis. These were the idea of syphilis as carnal scourge, with strong moralistic connotations;[25] and the persistent idea—demanding justification—of change in syphilitic blood.

The attention, importance, and power of development that this research gained from the special moral emphasis on syphilis cannot be overestimated. For centuries tuberculosis had done far more damage, but it never received comparable attention because, unfortunately, it was not considered the "accursed, disgraceful disease" but often even regarded as the "romantic" one. No tepid rational explanations or statistics can help here. Tuberculosis research simply did not receive as powerful an impulse from society. There was no corresponding social tension seeking relief in research.* The success of our tuberculosis research is therefore not remotely comparable with that of the Wassermann reaction or Salvarsan. Rivalry between nations in the field of pemphigus research would surely be impossible. No head of a public health authority would be able to arouse enthusiasm in the nation's best research workers, because it is a socially unimportant disease. No hospitals, experienced directors, enthusiastic assistants, or public funds could be found. No community discussions, rivalry, or public acclaim would support research. The necessary high tension and feeling for the vital importance of such work would never be generated in a research scientist.

In addition to this prevailing attitude with respect to syphilis, a special one arose from the earlier idea of change in syphilitic blood. Had it not been for the insistent clamor of public opinion for a blood test, the experiments of Wassermann would never have enjoyed the social response that was absolutely essential to the development of the reaction, to its "technical perfection," and to the gathering of collective experience. Wassermann first worked on the serology of tuberculosis. Where then were all those "verifiers," the fortunate fellow-competitors [*amici hostes*], the countless variations made by caviling rivals? As a result, very little came of this work. Yet surely it was no "worse" than his two first papers on syphilis, which, after

*The first international conference on tuberculosis was held in 1902.—Eds.

all, were also very immature, even if they appeared perfect to the authors and their pupils in the light of their subsequent success.

It was the prevailing social attitude that created the more concentrated thought collective which, through continuous cooperation and mutual interaction among the members, achieved the collective experience and the perfection of the reaction in communal anonymity. The antigen demonstration was rejected, and the initial 15–20 percent of correct results was subsequently increased to 70–90 percent. The findings were stabilized and depersonalized. This thought collective made the Wassermann reaction usable and, with the introduction of the alcohol extract, even practical. It standardized the technical process with genuinely social methods, at least by and large, through conferences, the press, ordinances, and legislative measures.

That which can be explained—where it is assumed that work is exclusively individual—only in terms of accident or miracle, becomes easily understandable where collective work is assumed, as soon as a strong enough motive exists for it. It is an accident when a stone drops into a hole. But it is inevitable that dust should penetrate pores; it is blown about in the environment until it finally enters, but each individual particle comes to rest in its particular position only by accident.

Laboratory practice alone readily explains why alcohol and later acetone should have been tried besides water for extract preparation, and why healthy organs should have been used besides syphilitic ones. Many workers carried out these experiments almost simultaneously, but the *actual authorship is due to the collective, the practice of cooperation and teamwork.*

The problem of how a "true" finding can arise from false assumptions, vague first experiments, as well as many errors and detours, can be clarified by a comparison. How does it come about that all rivers finally reach the sea, in spite of perhaps initially flowing in a wrong direction, taking roundabout ways, and generally meandering? There is no such thing as the *sea as such.* The area at the lowest level, the area where the waters actually collect, is merely *called* the sea! *Provided enough water flows in the rivers and a field of gravity exists, all rivers must finally end up at the sea.* The field of gravity corresponds to the dominant and directing disposition, and water to the work of the entire thought collective.

The momentary direction of each drop is not at all decisive. The result derives from the general direction of gravity.

The origin and development of the Wassermann reaction can be understood in a similar way. Historically it too appears as the only possible junction of the various trains of thought. The old idea about the blood and the new idea of complement fixation merge in a convergent development with chemical ideas and with the habits they induce to create a fixed point. This in turn is the starting point for new lines everywhere developing and again joining up with others. Nor do the old lines remain unchanged.[28] New junctions are produced time and again and old ones displace one another. This network in continuous fluctuation is called reality or truth.

These last statements must not, however, be taken to mean that the Wassermann reaction can be reconstructed in its objective entirety simply from historical factors along with those of individual and collective psychology. Something inevitable, steadfast, and inexplicable by historical development is always left out of such attempts. It can, for instance, be explained from the collective psychological standpoint that, after the initial work by Wassermann on syphilis serology, many others made it their business both to verify and to "technically perfect" it. The achievement of a positive result and its objective content, however, cannot *in the first instance* be explained through factors of historical development. A very large number of combinations were tried by these "verifiers," but not all were found to be equally good. Only one could be regarded as the best, or at least, only a few could be regarded as good. Which ones are to be so selected cannot be determined from these same factors alone.

The same applies to the problem of the extracts. From the psychological aspect of the collective, it is clear that alcoholic extracts would also be tried besides aqueous ones. But that they are actually suitable cannot in the first instance be explained on the basis of either historical or psychological factors, whether collective or individual. This relates to the problem of active and passive elements in knowledge as broached earlier. The introduction of the alcoholic extract was an active element. Its utility, however, is an inevitable outcome and a passive element with respect to this isolated act of cognition.

We shall presently deal with this problem in greater detail and show that *this compulsion becomes resolved only by comparative epistemological considerations and is explained as an intrinsic constraint imposed by thought style.*

We must first report the historical situation. The early idea of change in syphilitic blood did not cease with the Wassermann stage as described. The Wassermann reaction is far too complex and not clear enough theoretically to have such an effect. The attempts to "replace the complement fixation reaction by other and, if possible, simpler methods are divisible into four large categories. First, attempts were made to produce reactions of both complement fixation and precipitation with the aid of pure lipoids and soaps, whose importance in the serodiagnosis of syphilis became increasingly recognized. In this context we must mention the experiments by Porges-Meier with lecithin, by Sachs-Altmann with cholesterol plus sodium oleate, by Elias, Porges, Neubauer, and Salomon with sodium glycocholate, and by Hermann-Perutz with sodium glycocholate and cholesterol. A second series of experiments concerned the possible practical usability of globulin precipitations. Also in this category are the investigations of Klausner with precipitations by distilled water, as are those of Bruck with precipitations of nitric acid, alcohol, and lactic acid. A third group tried to replace the complement fixation reaction with other chemical and biological methods. The methods introduced by Schürmann (H_2O_2-phenol-ferric chloride), by Landau (iodine oil), and by Wiener-Torday (auric cyanide) among others must be mentioned on the one hand, and those by Weichardt (epiphanin reaction), by Ascoli (meiostagmin reaction), by Karvonen (conglutination), and by Hirszfeld-Klinger (coagulation reaction) on the other. Lastly, with the aid of the organ extracts associated with the complement fixation method, a fourth group of workers attempted the diagnostic utilization of flocculation instead of the complement fixation phenomenon. Here the fundamental investigations by Michaelis, Jacobsthal, and Bruck-Hidaka as well as the methods suggested by Meinicke, Sachs-Georgi, Dold (turbidity reaction), Hecht, Bruck, and others must be mentioned. These reactions must be accorded great practical importance as valuable supplements and controls for the method of complement fixation."[27]

Various modifications and simplifications of the Wasserman

reaction must not be forgotten either. In the so-called active methods of Stern, Noguchi, and others, complement contained in human serum is required instead of that in guinea pig serum. In Bauer's method no hemolytic amboceptor, in the original method obtained from the serum of an immunized rabbit, is added; the one normally found in human serum is used instead. Mutermilch added neither amboceptor nor complement. In yet another method, Sciarra claimed that not even antigen and possibly no addition of extract is necessary, because the antigen is said to be already present in syphilitic blood. There are also a great many modifications concerning the method of inactivating the patient's serum, the use of the complement, the preparation of the extract, the hemolysin production, the mode of using the blood corpuscles, and the conservation of the reagents, etc.

The size of the avalanche that the Wassermann reaction set in motion can be estimated from a general paper on the "serodiagnosis of syphilis." In 1927 Laubenheimer cited in it about fifteen hundred papers on this subject, although he restricted himself to more recent work.[28] If foreign-language and little-known contributions are added to these, as well as the clinically-oriented reports, which were not fully considered by Laubenheimer, the number can be estimated today at about ten thousand, including those published since 1927. There certainly cannot be many similar specialized problems which have had so many papers devoted to them.

Four Epistemological Considerations Concerning the History of the Wassermann Reaction

1. General Conclusions

If we compare the description of the history of syphilis with that of the Wassermann reaction, we note that the latter requires a much greater number of technical expressions. More basic preparation in the form of greater reliance on expert opinion is necessary, for we are moving away from the world of everyday experience and are entering more deeply into that of scientific specialization. At the same time we are coming into closer contact with the persons involved in such cognition, both collectively and individually. More names must be mentioned.

This is a general phenomenon. The more deeply one enters into a scientific field, the stronger will be the bond with the thought collective and the closer the contact with the scientist. In short, the active elements of knowledge increase.

with specialization

A parallel shift occurs. The number of passive and inevitable connections produced increases as well, because for every active element of knowledge there corresponds a connection that is passive and inevitable. We have already mentioned a few such linkages, for instance, that the mere use of alcohol in preparing extracts is an active element of knowledge, whereas the actual usefulness of such extracts is a passive one and therefore a necessary consequence.

The same spectacle can be observed in other scientific dis-

Active vs. passive

ciplines. To describe the history of the chemical elements, for instance, we would have to distinguish between two great stages: that of the so-called prescientific theory of the elements and that of scientific chemistry. Active and passive elements of knowledge exist in both. The concepts of the element and of the atom can thus be constructed very effectively from historical factors as well as from those of the thought collective. Such concepts are derived, one might say, from the collective imagination. But the usefulness of these concepts in chemistry is a circumstance which is really independent of any individual knower. The origin of the number 16 for the atomic weight of oxygen is almost consciously conventional and arbitrary. But if 16 is assumed as the atomic weight for O, oxygen, of necessity the atomic weight of H, hydrogen, will inevitably be 1.008. This means that the ratio of the two weights is a passive element of knowledge.

The situation we want to demonstrate consists in the fact that, during the first stage of its history, both the active and the passive elements of knowledge are smaller in number than in the second. Every rule and every chemical law can be divided into an active and a passive part. The more deeply we penetrate into a field, the greater will be the number of *both parts* and not just of the passive ones as might be expected at first glance.

For the time being we can define a scientific fact as *a thought-stylized conceptual relation which can be investigated from the point of view of history and from that of psychology, both individual and collective, but which cannot be substantively reconstructed in toto simply from these points of view.* This expresses the inseparable relation between active and passive parts of knowledge as well as the phenomenon that the number of both these parts of knowledge increases with the number of facts.

Another phenomenon must be noted. The more developed and detailed a branch of knowledge becomes, the smaller are the differences of opinion. In the history of the concept of syphilis we encountered very divergent views. There were far fewer differences during the history of the Wassermann reaction, and as the reaction develops further, they will become even rarer. It is as if with the increase of the number of junction points, according to our image of a network (on page 79), free space were reduced. It is as if more resistance were generated, and the free unfolding of ideas were restricted. This is very important, though it belongs no longer to the analysis of fact but to the analysis of error.

2. Observation, Experiment, Experience

Observation and experiment are subject to a very popular myth. The knower is seen as a kind of conquerer, like Julius Caesar winning his battles according to the formula "I came, I saw, I conquered." A person wants to know something, so he makes his observation or experiment and then he knows. Even research workers who have won many a scientific battle may believe this naive story when looking at their own work in retrospect.

At most they will admit that the first observation may have been a little imprecise, whereas the second and third were "adjusted to the facts." But the situation is not so simple, except in certain very limited fields, such as present-day mechanics, in which there are very ancient and widely known everyday facts to draw upon. In more modern, more remote, and still complicated fields, in which it is important first of all to learn to observe and ask questions properly, this situation does not obtain—and perhaps never does, originally, in any field—until tradition, education, and familiarity have produced *a readiness for stylized (that is, directed and restricted) perception and action;* until an answer becomes largely pre-formed in the question, and a decision is confined merely to "yes" or "no," or perhaps to a numerical determination; until methods and apparatus automatically carry out the greatest part of our mental work for us.

Wassermann and his co-workers experimented according to the method of Bordet-Gengou, trying to detect the presence of the syphilitic antigen in organ extracts and of syphilitic antibodies in the blood. From the early work we glean far more of hope than of concrete results. Successful experiments are discussed along with those that were unsuccessful, without the reason for failure being accurately known to the authors. It is certain that they were on the wrong track concerning the significance of the titration level with the immune serum from monkeys. In the second experiment the number of successful tests, which means those yielding the expected result, had already risen sufficiently for statistics to be published. Of 76 extracts from syphilitic organs, the syphilis antigen was detected in 64 cases. Of the 76, 7 were from progressive-paralytic brains, all of which were unsuccessful, and Weil had his own ideas about this. If these 7 cases using brain extracts are ignored, the success rate is almost 93 percent. All 14 control tests with confirmed nonsyphilitic extracts were negative; that is, they conformed 100 percent to expectations.

But today we know that such results are beyond all reasonable expectations. First, antigen detection in organ extracts is difficult, and even with the best technique yields only very irregular results. Second, extracts from organs which are definitely nonsyphilitic can also fix the complement with syphilis serum. The control tests with negative results are therefore unintelligible, and the high percentage of positive results is very fortuitous. At any rate, the first experiments by Wassermann are irreproducible.

His basic assumptions were untenable, and his initial experiments irreproducible, yet both were of enormous heuristic value. This is the case with all really valuable experiments. They are all of them uncertain, incomplete, and unique. And when experiments become certain, precise, and reproducible at any time, they no longer are necessary for research purposes proper but function only for demonstration or ad hoc determinations. To understand Wassermann's first experiments, we must imagine ourselves in his position. He had a complete plan and felt certain of the result. But the method was still very crude. It seriously disturbed him, for instance, that he had to use human syphilis material for the immunization of most of his monkeys, since pure cultures of *Spirochaeta pallida* could not yet be produced at the time. There were of course control animals which were inoculated with monkey material. But quite a large number of his monkeys yielded a serum which in addition to syphilis antibodies also contained antibodies against human albumin. The complement fixation with this serum was therefore not always specific to syphilis. Furthermore, titration of the extracts and all other preliminary experiments had not yet been perfected. Hence, the reagents were not yet precisely matched. Moreover, it was not yet known what degree of hemolysis inhibition was to be regarded as positive and what as still negative (see chap.

3 at notes 16 and 17). It is therefore clear that the indicators of the experiments were not well defined. The results of some were ambiguous, and it often had to be decided whether the result of an experiment should be considered positive or negative. It is also clear that from these confused notes Wassermann heard the tune that hummed in his mind but was not audible to those not involved.[1] He and his co-workers listened and "tuned" their "sets" until these became selective. The melody could then be heard even by unbiased persons who were not involved. Who could define the moment when this became possible for the first time? The community of those who made the tune audible and of those who listened increased steadily. It is not appropriate to speak of either correctness or incorrectness in these first experiments, because something very correct developed directly from them, although the experiments themselves could not be called correct.

If a research experiment were well defined, it would be altogether unnecessary to perform it. For the experimental arrangements to be well defined, the outcome must be known in advance; otherwise the procedure cannot be limited and purposeful. The more unknowns there are and the newer a field of research is, the less well defined are the experiments. Once a field has been sufficiently worked over so that the possible conclusions are more or less limited to existence or nonexistence, and perhaps to quantitative determination, the experiments will become increasingly better defined. But they will no longer be independent, because *they are carried along by a system of earlier experiments and decisions*, which is generally the situation in physics and chemistry today. Such a system could then become a self-evident law unto itself. We would no longer be aware of its application and effect. And if after years we were to look back upon a field we have worked in, we could no longer see or understand the difficulties present in that creative work. The actual course of development becomes rationalized and schematized. We project the results into our intentions; but how could it be any different? We can no longer express the previously incomplete thoughts with these now finished concepts.

Cognition modifies the knower so as to adapt him harmoniously to his acquired knowledge. This situation ensures harmony within

the dominant view about the origin of knowledge. Whence arises the "I came, I saw, I conquered" epistemology, possibly supplemented by a mystical epistemology of intuition.

This exemplifies the effect of the harmony of illusions (or, as we can now call it, the intrinsic harmony of thought style), which makes the scientific results applicable and generates a firm belief in a reality existing independently of us. Rational epistemology, however, is based upon the acceptance of the *threefold function of cognition* and the reciprocal relations between cognition and its three factors. It necessarily leads to the investigation of thought style as its proper object.

Our remarks about experiment apply to an even greater degree to observation, for experiment is observation directed in a certain way. Let us consider some observations which I recently published in the area of bacterial variability. These were new to me, at any rate.[2]

We grew a streptococcus from the urine of a female patient. Its unusually rapid and profuse growth attracted our attention, as did pigment formation, which is very rare with streptococci. I had never seen streptococci producing such intense pigment and remembered only vaguely having read about them. I therefore wanted to find out about the germ in greater detail. I had intended to grow regular nutrient cultures and perform animal inoculations, as well as a few serological experiments and especially a chemical analysis of the pigment. But the project turned largely into a study of variability. How could this have happened?

A few months previously, at the request of some colleagues, I had prepared a comprehensive survey on the concept of species in bacteriology, which brought me into close contact with the phenomena of variability in bacteria. The colityphus group, difficult to systematize because of its special variability, particularly attracted my attention. I collected details about such factors as mutation, habitat modifications, and so-called germ transmission and saw that without order in the field of variability no consistent concept of species would be possible. Such order, however, could not be established without a fundamental discussion of the concept of the individual, which brought me into contact with the relevant work of Van Loghem's school.

This was the psychological foundation for the observations on streptococcus. Now streptococcus habitually reminds laboratory scientists of staphylococcus. I remembered having read of the splitting off of staphylococcus colonies of different colors. I therefore suggested to my colleague that she find out whether our strain split into lighter and darker colonies. I received the answer the next day. Such a dissociation had just occurred. In addition to the hundreds of ordinary yellowish, transparent colonies, a few very small, white, and more opaque ones nad grown. We next carried out an entire series of experiments with several generations of the streptococcus to determine: (1) whether the few small colonies belonged to our strain, (2) the extent to which these differed from the others.

The answer to the first question was positive because these colonies contained organisms that were morphologically, biochemically, and zoopathologically identical with those of the typical colonies. The second part of the investigation called both for many exploratory tests to select the method and for many reformulations of the problem. We could not even claim with any certainty and assurance that a real problem existed at all. Were the new colonies definitely different from the old ones? Differences noticed initially, such as the small size, the lighter color, and the opacity all became unstable in subsequent generations. Strangely, however, a difference remained which at first could not even be clearly understood—the difference between the offspring of the special colonies and that of the others. Not only did it persist, but it in fact increased with the transfers, by the partly subconscious selection of the most divergent colonies during inoculation. All attempts to formulate this difference had to be dropped right after the next reinoculations; until at last, after we had gained comprehensive experience, a formulation crystalized. We were dealing with splitting off not of variants more strongly or weakly pigmented but of colonies with a different structure, although of the same color. In other words, the structural variations of the colonies were much more marked than those of color intensity. Moreover, structural variants were produced which, unlike the color variants, could be perpetuated through transfers. Inoculation of these different colonies finally produced what we later called the smooth

type (type G) of streptococcus colony in contrast to the curly type (type L).

The smooth types arising later were always more transparent than the curly ones. The more opaque colonies, which were noted in the initial observations on dissociation and which formed the starting point of the investigation, were therefore not identical with them. Was it, then, a dissociation phenomenon at all? This question must remain undecided, for our first observations are irreproducible. We cannot even describe them clearly, because the descriptive terms and concepts which developed during the work are inadequate for unconditioned observation.

This description of our limited experiment with streptococci can serve as an epistemological example. It shows (1) the material offering itself by accident; (2) the psychological mood determining the direction of the investigation; (3) the associations motivated by collective psychology, that is, professional habits; (4) the irreproducible "initial" observation, which cannot be clearly seen in retrospect, constituting *a chaos;* (5) the slow and laborious revelation and awareness of "what one actually sees" or *the gaining of experience;* (6) that what has been revealed and concisely summarized in a scientific statement is an artificial structure, related but only genetically so, both to the original intention and to the substance of the "first" observation. The original observation need not even belong to the same class as that of the facts it led toward.

Consequently it is all but impossible to make any protocol statements [*Protokollsätze*] based on direct observation and from which the results should follow as logical conclusions. This can be done only during the subsequent confirmation of a finding [*eines Wissens*] but not while making the effort of acquiring it. The results can be no more expressed in the language of the initial observations than, vice versa, the first observations in the language of the results.

Every statement about "First Observations" is an assumption. If we do not want to make any assumption, and only jot down a question mark, even this is an assumption of questionability, which places the matter in the class of scientific problems. This is also a thought-stylized assumption.

One might think that the statement, "Today one hundred large, yellowish, transparent and two smaller, lighter, more opaque colonies have appeared on the agar plate," could in our case be regarded as a description purely of what is observed, devoid of any assumptions. But the statement contains much more than "pure observation" and much more than could in the first instance be claimed with certainty. It anticipates a difference between the colonies, which could actually be established only at a later stage of a long series of experiments. The difference of course—and this is very important—was ascertained as of quite another kind than that anticipated.

No two completely identical colonies were found. We therefore had 102 differently structured colonies. First of all it was necessary to determine whether this or that difference was *important enough* to enable us even to speak of different colonies, and whether such a distinction was scientifically worthwhile. We still had to determine *whether* and *how* common *types of colony* could be established from such different colonies. That these two colonies could constitute something different from the other hundred, and that they somehow belonged together, was not "pure observation" but already a hypothesis, which may or may not prove to be true or, alternatively, from which another hypothesis may evolve.

For all practical purposes, the knower is initially unaware of the hypothetical nature of his assertion. Although the statement mentioned here does not describe a "pure observation," it might well be taken to express a "direct observation" or what a *trained person* would see without difficulty when looking at our agar plate. An expert or specialist in variability phenomena of bacteria, for example, would not be in the least misled by the various forms of all the colonies. He would not stop at "unimportant differences" but would recognize the two types of colony at first glance, without any analysis or hypothesis.

One could, however, argue that, although a "pure observation, that is, one without assumptions" does not occur psychologically, it is logically possible and even necessary as a subsequent construction for the confirmation of a finding. Specifically in our case, such an expert would immediately identify the two different colonies among the 102 but neglect the accidental and unimportant differences among the other 100. This ability, acquired through experi-

ence, of immediately drawing a conclusion, during observation, from a long series of comparisons and combinations could, and in fact must, also be carried though very strictly and in detail. The corresponding procedure would be to investigate *all* 102 colonies as to *all* their properties and their theoretically possible combinations and in this way to find the various types of colonies according to their *complete* nature. This is what one might find:

I.	Colonies of 5-6 mm diameter	30
	4-5 mm "	60
	3-4 mm "	10
	½-1 mm "	2
		102
II.	Colonies of color 100 (arbitrary scale)	70
	" 80 (lighter)	25
	" 70 "	5
	" 5 "	2
		102

Then the procedure would be repeated for transparency and for *all* other properties. If one were to compare the data in the two tables with each other and to place the relevant colonies beside one another, tabulated according to their ranking, one would find that very light color, together with other conspicuous properties, occurs only in the two very small colonies. Furthermore, the differences between these two colonies and all the others far exceed the fluctuations among the properties of the others when they are compared with one another. They would therefore constitute a distinct type of colony, which was the point to be demonstrated and which would thus have been demonstrated without any assumptions having been made.

This description contains some gross errors, which are committed by many theoreticians. *First*, assumptions are already incorporated within the choice and limitation of the object of investigation. With 102 undoubted colonies, there are certain to be a few doubtful features such as grains or dots that might be regarded as colonies or even as accidental structures, depending upon the assumptions.

Second, it is altogether pointless to speak of *all* the characteristics of a structure. The number of characteristics can be as large as desired, and the number of *possible determinations of characteristics* depends upon the habits of thought of the given scientific discipline; that is, it already contains directional assumptions. Accordingly such mechanical combinatorial analyses are either arbitrary or actually conditioned by thought style.

Third, new discoveries cannot be carried out by such tabulations and mechnically exhaustive combinations any more than, for instance, a poem can be composed by means of combining letters mechanically.

Observation without assumption,[3] which psychologically is nonsense and logically a game, can therefore be dismissed. But two types of observation, with variations along a transitional scale, appear definitely worth investigating: (1) *the vague initial visual perception*, and (2) *the developed direct visual perception of a form*.

Direct perception of form [*Gestaltsehen*] requires being experienced in the relevant field of thought. The ability directly to perceive meaning, form, and self-contained unity is acquired only after much experience, perhaps with preliminary training. At the same time, of course, we lose the ability to see something that contradicts the form. But it is just this readiness for directed perception that is the main constituent of thought style. Visual perception of form therefore becomes a definite function of thought style. The concept of being experienced, with its hidden irrationality, acquires fundamental epistemological importance, which will presently be discussed in detail.

By contrast, the vague, initial visual perception is unstyled. Confused partial themes in various styles are chaotically thrown together. Contradictory moods have a random influence upon undirected vision. There is a rivalry among visual fields of thought. Nothing is factual or fixed. Things can be seen almost arbitrarily in this light or that. There is neither support, nor constraint, nor resistance and there is no "firm ground of facts."

All empirical discovery can therefore be construed as a supplement, development, or transformation of the thought style.

Why did bacteriologists for a time almost fail to see the phenomena of variability? At first there was a period of controversy,

involving unconnected details, when variability was too much taken for granted. Billroth, for instance, firmly believed in a universal coccobacterium septicum, which could transform itself into all possible forms. This was followed by the classical Pasteur-Koch period. The all-persuasive power of practical success and personalities created a rigid thought style in bacteriology. Only a strictly orthodox method was recognized, and the findings were accordingly very restricted and uniform. For example, cultures were reinoculated generally for only twenty-four hours. Very fresh cultures (two to three hours) or very old (about six months) ones were not even considered worth examining. As a result, all secondary changes in the cultures, which were the starting point for the restyled theory of variability, escaped attention. Whatever failed to conform completely to the standard scheme was regarded as a "form of involution," a kind of pathological phenomenon, or an "artificial" modification caused by external conditions. The harmony of illusions was thus preserved. Species were fixed, because a fixed and restricted method was applied to the investigation. The thought style, developed in this particular way, made possible the perception of many forms as well as the establishment of many applicable facts. But it also rendered the recognition of other forms and other facts impossible. Now things are turning around. The notion of variability was never quite extinct, but the successors of the classical school regarded any such observations as technical mistakes to be simply passed over in silence or rejected. The first detailed observation of variation to be taken somewhat seriously was made in 1906 by Neisser and Massini. This concerned the so-called bacterium *Coli mutabile*. It could not very well be suppressed, because it was couched throughout in terms of the current thought style and was expressly revolutionary in only one point. The authors used the classical method with only a *single* modification. They examined* the cultures not only after twenty-four hours but again after several days. Had they introduced several modifications all at once, they would have had to wait much longer for a consideration of their findings. They found that after a few

*"Examined" here renders *untersucht*, but further reinoculation (*Umimpfen*) was presumably involved; otherwise the desired contrast with traditional method is lacking.—Eds.

days buds containing modified germs were growing within the colony. Reinoculation of these buds and with them also other secondary growth phenomena within the bacterial colonies soon became popular topics for investigation. The spell cast by the harmony of illusions was thus broken, and the conditions were created without which many discoveries would have been impossible. It is typical that the new theory of variability found roots in a country other than that of classical bacteriology. It thrived in America with its paucity of tradition and was attacked most strongly in Koch's native country. It is also typical that this did not constitute a simple regression to the age of transformation of species. The very concept of species as well as many other concepts now became construed in a manner different from that in the past. What is involved here is neither mere accretion of knowledge nor a simple link-up with the period before Koch, but a change in thought style. It is also characteristic that during this change in thought style, or learning by experience, the observation of Neisser and Massini, which was its first stimulus, remained outside the new field. Today it is not considered "classical" variability (the word "classical" can already be used in such a context) but as a bacteriophage effect.

This example also exhibits three stages: (1) vague visual perception and inadequate initial observation; (2) an irrational, concept-forming, and style-converting state of experience; (3) developed, reproducible, and stylized visual perception of form.

This description demonstrates how a finding originates. Many a research scientist will certainly recognize an analogy here with his own method of research. The first, chaotically styled observation resembles a chaos of feeling: amazement, a searching for similarities, trial by experiment, retraction as well as hope and disappointment. Feeling, will, and intellect all function together as an indivisible unit. The research worker gropes but everything recedes, and nowhere is there a firm support. Everything seems to be an artificial effect inspired by his own personal will. Every formulation melts away at the next test. He looks for that resistance and thought constraint in the face of which he could feel passive. Aids appear in the form of memory and education. At the moment of scientific genesis, the research worker personifies the

totality of his physical and intellectual ancestors and of all his friends and enemies. They both promote and inhibit his search. The work of the research scientist means that in the complex confusion and chaos which he faces, he must distinguish that which obeys his will from that which arises spontaneously and opposes it. This is the firm ground that he, as representative of the thought collective, continuously seeks. These are the passive connections, as we have called them. The general aim of intellectual work is therefore maximum *thought constraint with minimum thought caprice.*

This is how *a fact* arises. *At first there is a signal of resistance in the chaotic initial thinking, then a definite thought constraint, and finally a form to be directly perceived.* A fact always occurs in the context of the history of thought and is always the result of a definite thought style.[4]

It is the aim of all empirical sciences to establish this "firm basis of facts." Two points are important in epistemology. *First,* this work is continuous. It has no demonstrable beginning and is open-ended. Knowledge exists in the collective and is continually being revised. The store of facts also changes. What has previously been classed with the passive elements of knowledge may later join the active ones. The ratio between the atomic weight of oxygen and that of hydrogen, 16:1.008, for instance, we explained as a proportion resulting passively under given conditions. If, for instance, it were possible to split O into two elements, this proportion would be accounted for by the inadequacy of the earlier method and would have to be replaced by another ratio.

Second, however, it is impossible to exhibit the passive elements of knowledge on their own, as has already been pointed out.

The passive and the active elements cannot be separated from each other completely either logically or historically. Indeed, it is not even possible to invent a fairy tale which does not contain some inevitable connections. Myth differs from science in this respect only in style. Science seeks to include in its system a maximum of those passive elements *irrespective* of inherent lucidity. Myth contains only a few such passive elements, but they are artistically composed.

The necessity of being experienced introduces into knowledge an irrational element, which cannot be logically justified. Introduction to a field of knowledge is a kind of initiation that is performed by others. It opens the door. But it is individual experience, which can only be acquired personally, that yields the capacity for active and independent cognition. The inexperienced individual merely learns but does not discern.

Every experimental scientist knows just how little a single experiment can prove or convince. To establish proof, an entire system of experiments and controls is needed, set up according to an assumption or style and performed by an expert. The state of being experienced [*Erfahrenheit*], as it will here be designated, consists in just such factors as (1) the ability to make assumptions and (2) both manual and mental practice together with a research scientist's entire experimental and nonexperimental fund of knowledge, including features clearly conceived, those that are uncertain, and those that are "instinctive." The summarized report about a field of research always contains only a very small part of the worker's relevant experience, and not even the most important. Missing is that which makes the stylized visual perception of form possible. It is as if the words of a song were published without the tune.

Wassermann's reports about his reaction contain only the description of the relation between syphilis and a property of the blood. But this is not the most important element. What is crucial is the *experience* acquired by him, by his pupils and in turn by theirs, in the practical application and effectiveness of serology. Without this *experience* both the Wassermann reaction and many other serological methods *would not have become reproducible and practical.* Such a *state of experience* became general only slowly and had to be practically acquired by each initiated individual. A state of this kind is what the first critics of the Wassermann reaction lacked. The roots of this state in Wassermann and his co-workers have already been described. But, even today, anybody performing the Wassermann reaction on his own must first have acquired comprehensive experience before he can obtain reliable results. Only through this experience will he participate in the thought style, and it is experience alone that enables him to perceive the relation between syphilis and blood as a definite form.

We might also mention some cases where such experience involving the irrational "serological touch" is specifically needed.

1. The preparation and titration of the organ extracts perhaps calls most for experience. Here the need is not confined to theory but includes the skill of preparing uniform dilutions of the extract. An inexperienced individual obtains irregular results through having diluted the extract either too rapidly or too slowly. In this respect the Wassermann reaction is particularly sensitive. It can be confirmed now and again that the kind of extract dilution determined by a given individual does not always automatically work with another person. Psychological and physical differences among the performers of this serological test lead to appreciable differences in the degree to which the colloidal solution from the alcoholic extract disperses. The solution must thus be freshly prepared for each test.

2. The matching of all the five required reagents, so as to maximize the effect of the reactions and ensure that the results are as clear as possible, requires experience. Even quasi-*orchestral practice* is needed if, as is usual, the test is performed by a team. Change in personnel often produces a disturbance in the progress of the reaction, even if the new member of the team had worked well with other associates. This explains the poor results obtained even by excellent research workers at the previously mentioned Wassermann conferences held under the auspices of the League of Nations.

3. Obviously, general competence is also necessary in the elementary operations such as measuring, pipetting, storing of the sera, washing of the vessels, etc.

We can summarize as follows our theory of the recognition of the relation between the Wassermann reaction and syphilis. The discovery—or the invention—of the Wassermann reaction occurred during a unique historical process, which can be neither reproduced by experiment nor confirmed by logic. The reaction was worked out, in spite of many errors, through socio-psychological motives and a kind of collective experience. *From this point of view the relation between the Wassermann reaction and syphilis—an undoubted fact—becomes an event in the history of thought.* This fact cannot be proved *with an isolated experiment* but only with broadly based experience; that is, by *a special thought style* built up from earlier knowledge, from many successful and unsuccessful experiments, from much practice and training, and—epistemologically most important—from *several adaptations and transformations of concepts.* Without this experience the concept of syphilis and that of serum reaction could not have been established and research workers could not have been *trained* to practice accordingly. Error and the failure of many experiments are also part of the building materials for a scientific fact. The perfection of the Wassermann reaction can be seen from this point of view as the solution to the following problem: How does one define *syphilis* and set up a *blood test,* so that after *some experience* almost any research worker will be able to demonstrate a *relation between them* to a degree that is adequate in practice? The collective character of this finding readily manifests itself in such a formulation of the problem; it is based on the need to obtain indispensable experience by comparing working methods with those of other workers, as well as on the need for some kind of connection with the traditional and incomplete concept of syphilis and that of the blood test.

The factuality of the relation between syphilis and the Wassermann reaction consists in just this kind of solution to the problem of minimizing thought caprice, under given conditions, *while maximizing thought constraint.* The *fact* thus represents a *stylized signal of resistance in thinking.* Because the thought style is carried by the thought collective, this "fact" can be designated in brief as the *signal of resistance by the thought collective* [*denkkollektives Widerstandsaviso*].

3. Further Observations Concerning Thought Collectives

The preceding chapter tried to show how even the simplest observation is conditioned by thought style and is thus tied to a community of thought. I therefore called thinking a supremely social activity which cannot by any means be completely localized within the confines of the individual.

Teamwork can take two forms. It can be simply additive, as when a number of people join together to lift something heavy. Alternatively it can be collective work proper—not merely the summation of individual work but the coming into existence of a special form, comparable to a soccer match, a conversation, or the playing of an orchestra. Both forms occur in thinking and especially in the act of cognition. How could the performance of an orchestra be regarded as the work only of individual instruments, without allowance for the meaning and rules of cooperation? It is just such rules that the thought style holds for thinking. *All paths toward a positive, fruitful epistemology lead toward the concept of thought style,* the varieties of which are mutually comparable and can each be investigated as a result of historical development.

Like any style, the thought style also consists of a certain mood and of the performance by which it is realized. A mood has two closely connected aspects: readiness both for selective feeling and for correspondingly directed action. It creates the expressions appropriate to it, such as religion, science, art, customs, or war, depending in each case on the prevalence of certain collective motives and the collective means applied. We can therefore *define thought style as* [the readiness for] *directed perception, with corresponding mental and objective assimilation of what has been so perceived.* It is characterized by common features in the problems of interest to a thought collective, by the judgment which the thought collective considers evident, and by the methods which it applies as a means of cognition. The thought style may also be accompanied by a technical and literary style characteristic of the given system of knowledge.

Because it belongs to a community, the thought style of the collective undergoes social reinforcement, as will shortly be discussed. Such reinforcement is a feature of all social structures. The thought style is subject to independent development for generations. It constrains the individual by determining "what can be thought in no other way." Whole eras will then be ruled by this thought constraint. Heretics who do not share this collective mood and are rated as criminals by the collective will be burned at the stake until a different mood creates a different thought style and different valuation.

But every thought style leaves remnants. First, there are the small, isolated communes which adhere unchanged to the old style. This explains the existence even today of astrologers and magicians: eccentrics who associate with the uneducated of the lower social classes or become charlatans because they do not share the community mood. Second, every thought style contains vestiges of the historical, evolutionary development of various elements from another style. Probably only very few completely new concepts are formed without any relation whatsoever to earlier thought styles. It is usually only their coloring that changes. Just as the scientific concept of force originated from the everyday concept of force, so also the new concept of syphilis descended from the mystical.

A historical connection thus arises between thought styles. In the development of ideas, primitive pre-ideas often lead continuously to modern scientific concepts. Because such ideational developments form multiple ties with one another and are always related to the entire fund of knowledge of the thought collective, their actual expression in each particular case receives the imprint of uniqueness characteristic of a historic event. It is, for instance, possible to trace the development of the idea of an infectious disease from a primitive belief in demons, through the idea of a disease miasma, to the theory of the pathogenic agent. As we have already hinted, even this latter theory is already close to extinction. But while it lasted, only one solution to any given problem conformed to that style. (See chap. 2, sec. 4, on Schaudinn's "causative agent" versus that of Siegel.) *Such a stylized solution, and there is always only one, is called truth.* Truth is not "relative" and certainly not "subjective" in the popular sense of the word. It is always, or almost always, completely determined within a thought style. One can never say that the same thought is true for A and false for B. If A and B belong to the same thought collective, the thought will be either true or false for both. But if they belong to different thought collectives, it will just *not* be *the same* thought! It must either be unclear to, or be understood differently by, one of them. Truth is not a convention, *but rather (1) in historical perspective, an event in the history of thought, (2) in its contemporary context, stylized thought constraint.*

Even unscientific statements contain compulsory connections.

Consider a myth, such as the Greek myth of Aphrodite, Hephaistos, and Ares. Aphrodite cannot but be the wife of Hephaistos and the lover of Ares. As any poet knows, a web of fantasy spun for long enough always produces inevitable, "spontaneous" substantive and formal connections. In a romance about chivalry, for instance, one cannot simply write "horse" instead of "steed," although these words are logically synonyms differing only in style. There are consequential links in musical imagination too, which correspond to the example: "Assuming O = 16 then H = 1.008." An artistic painting also exhibits its own constraining style. This we can easily demonstrate by placing part of a second painting over a good painting executed in a definite style. The two parts would clash with each other, even if the two paintings were matched in content. Thus every product of intellectual creation contains relations "which cannot exist in any other way." They correspond to the compulsory, passive links in scientific principles. These relations can be, as it were, objectivized and regarded as expressions of "beauty" or "truth." There actually are special individual and collective conditions which favor just such objectivization.

In the field of cognition, *the signal of resistance* opposing free, arbitrary thinking is called a *fact.** This notice of resistance merits the adjective "thought collective," because every fact bears three different relations to a thought collective: (1) *Every fact must be in line with the intellectual interests of its thought collective,* since resistance is possible only where there is striving toward a goal. Facts in aesthetics or in jurisprudence are thus rarely facts for science. (2) *The resistance must be effective within the thought collective. It must be brought home to each member as both a thought constraint and a form to be directly experienced.* In cognition this appears as the connection between phenomena which can never be severed within the collective (see chap. 3 at note 26). This linkage seems to be truth and conditioned only by logic and content. Only an investigation in comparative epistemology, or a simple comparison after a change has occurred in the thought style, can make these inevitable connections accessible to scientific treatment. The principle of immutability of species characteristics was

*Cf. chap. 4, sec. 2, at note 4 and end of section.—Eds.

valid for classical bacteriology, according to the interpretation of the time. If a scientist of that time had been asked why the principle was accepted or why the characteristics of species were conceived in this way, he could only have answered, "Because it is true." Only after a change in thought style did we learn that the opinion was constrained mainly by the methods applied. The passive linkage between these principles was transformed into an active one (cf. the definition in chap. 1, p. 8).[5] (3) *The fact must be expressed in the style of the thought collective.*

The fact thus defined as a "signal of resistance by the thought collective" contains the entire scale of possible kinds of ascertainment, from a child's cry of pain after he has bumped into something hard, to a sick person's hallucinations, to the complex system of science.

Facts are never completely independent of each other. They occur either as more or less connected mixtures of separate signals, or as a system of knowledge obeying its own laws. As a result, every fact reacts upon many others. Every change and every discovery has an effect on a terrain that is virtually limitless. It is characteristic of advanced knowledge, matured into a coherent system, that each new fact harmoniously—though ever so slightly—changes all earlier facts. Here every discovery is actually a recreation of the whole world as construed by a thought collective.

A universally interconnected system of facts is thus formed, maintaining its balance through continuous interaction. This interwoven texture bestows solidity and tenacity upon the "world of facts" and creates a feeling both of fixed reality and of the independent existence of the universe. The less interconnected the system of knowledge, the more magical it appears and the less stable and more miracle-prone is its reality, always in accordance with the thought style of the collective.

The communal "carrier" of the thought style is designated the thought collective. The concept of the thought collective, as we use it to investigate the social conditioning of thinking, is not to be understood as a fixed group or social class. It is functional, as it were, rather than substantial, and may be compared to the concept of field of force in physics. A thought collective exists whenever two or more persons are actually exchanging thoughts. This type of

thought collective is transient and accidental, forming and dissolving at any moment. But even this type induces a particular mood, which would otherwise affect none of the members and often recurs whenever these members meet again.

Besides such fortuitous and *transient* thought collectives there are *stable* or comparatively stable ones. These form particularly around organized social groups. If a large group exists long enough, the thought style becomes fixed and formal in structure. Practical performance then dominates over creative mood, which is reduced to a certain fixed level that is disciplined, uniform, and discreet. This is the situation in which contemporary science finds itself as a specific, thought-collective structure [*denkkollektives Gebilde*].

A thought community [*Denkgemeinschaft*] does not fully coincide with the official community. The thought collective of a religion comprises all true believers, whereas the official religious community includes all the formally accepted members, irrespective of their way of thinking. It is thus possible to belong to the thought collective of a religion without being formally accepted as a member of that congregation, and vice versa. The internal structure and organization of a thought collective also differs from the organization of a community in the official sense. The intellectual leadership and the circles that form around it do not coincide with the official hierarchy and organization.

A closer investigation of thought style and of the general social characteristics of thought collectives in their mutual relations can be made by concentrating upon stable thought collectives. Such stable (or comparatively stable) thought communities, like other organized communes [*Gemeinden*],* cultivate a certain exclusiveness both formally and in content. A thought commune becomes isolated formally, but also absolutely bonded together, through statutory and customary arrangements, sometimes a separate language, or at least special terminology. The ancient guilds, for instance, are examples of such special thought communes. But even more important is the restricted content of every thought

*Gemeinde: often used for the smallest administrative district of local government in some European countries.—Eds.

collective as a special realm of thinking. There is an apprenticeship period for every trade, every religious community, every field of knowledge, during which a purely authoritarian suggestion of ideas takes place, irreplacable by a "generally rational" organization of ideas. The optimum system of a science, the ultimate organization of its principles, is completely incomprehensible to the novice. Yet this is the only valid yardstick for the expert. We have already described this situation in the case of the closure of thought within serology, which has only a traditional and not a "rational" initiation.

Every didactic introduction is therefore literally a "leading into" or a gentle constraint. The history of science is pedagogically helpful, because long-established concepts have the advantage of less thought specialization and are therefore more easily understood by the novice. Furthermore, the public at large, and therefore many an apprentice, are already familiar with them. The initiation into any thought style, which also includes the introduction to science, is epistemologically analogous to the initiations we know from ethnology and the history of civilization. Their effect is not merely formal. The Holy Ghost as it were descends upon the novice, who will now be able to see what has hitherto been invisible to him. Such is the result of the assimilation of a thought style.

The organic exclusiveness of every thought commune goes hand in hand with a stylized limitation upon the problems admitted. It is always necessary to ignore or reject many problems as trifling or meaningless. Modern science also distinguishes "real problems" from useless "bogus problems." This creates specialized valuation and characteristic intolerance, which are features shared by all exclusive communities.

Corresponding to any thought style is its practical effect or application. Any thought can be applied. Even the confirmation or refutation of conjectures calls for mental activity. Verification is therefore just as much bound by thought style as is assumption. Thought constraint, habits of thought, or, at least, a definite aversion to alien thinking that does not conform to a given thought style all help to guard the harmony between application and thought style. Guild associations are communities that are clearly directed to practical aims. It is instructive to see how differently,

depending on the nature of the trade, similar practical problems are solved. A crack in the wall plaster, for instance, presents a painter with a problem different from that which a bricklayer has to face. The painter sees only the surface damage and treats it accordingly. But the bricklayer worries about the wall structure and is likely to "work in depth." The way in which their thinking is stylized is revealed by the way it is applied.[*]

Independently of the possible organization in form and content of a stable collective, such as has been noted for the organization of a church community or a trade union, there are also structural characteristics shared by all such communities of thought. The general structure of a thought collective consists of both a small esoteric circle and a larger exoteric circle, each consisting of members belonging to the thought collective and forming around any work of the mind [*Denkgebilde*], such as a dogma of faith, a scientific idea, or an artistic musing. A thought collective consists of many such intersecting circles. Any individual may belong to several exoteric circles but probably only to a few, if any, esoteric circles. There is a graduated hierarchy of initiates, and many threads connecting the various grades as well as the various circles. No direct relation exists between the exoteric circle and that creation of thought [*Denkgebilde*] but only one mediated esoterically. Thus most of the members of the thought collective are related to the works produced by the thought style [*Gebilde des Denkstiles*] only through trusting the initiated. But the initiated are by no means independent. They are more or less dependent, whether consciously or subconsciously, upon "public opinion," that is, upon the opinion of the exoteric circle. This is generally how the intrinsic self-containment of the thought style with its inherent tenacity arises.

The esoteric circles thus each enter into a relation with their exoteric circles known in sociology as the relation of the elite to the masses. If the masses occupy a stronger position, a democratic tendency will be impressed upon this relation. The elite panders, as it were, to public opinion and strives to preserve the confidence of the masses. This is the situation in which the thought collective of science usually finds itself today. If the elite enjoys the stronger position, it will endeavor to maintain distance and to isolate itself from the crowd. Then secretiveness and dogmatism dominate the life of the thought collective. This is the situation of religious thought collectives. The first, or democratic, form must lead to the 2 development of ideas and to progress, the second possibly to conservatism and rigidity.

Individuals too take up special mutual positions in the communication of thoughts within a collective. If there exists a relation of definite mental superordination and subordination between two individuals, as between teacher and pupil, it is really not a relation between individuals but between elite and masses. On the one hand there is basically trust, and on the other, dependence on public opinion and "commonsense." Between two members of the same thought collective on the same mental level, there is always a certain solidarity of thought in the service of a superindividual idea which causes both intellectual interdependence and a shared mood between the two individuals. No question, once raised, can remain totally without effect. Each is pondered and has a place within the thought style. This comradeship of mood can be sensed after only a few sentences have been uttered and makes true communication possible. Without it, the speakers are at cross purposes. A special feeling of dependence therefore dominates all communication of thought within a collective. The general structure of a thought collective entails that *the communication of thoughts within a collective, irrespective of content or logical justification, should lead for sociological reasons to the corroboration of the thought structure* [*Denkgebilde*].* Trust in the initiated, their dependence upon public opinion, intellectual solidarity between equals in the service of the same idea, are parallel social forces which create a special shared mood and, to an ever-increasing extent, impart solidity and conformity of style to these thought structures [*Denkgebilde*].** The greater the distance in time or space from the esoteric circle, the longer a thought has been conveyed *within the same thought collective,* the more certain it appears. If

*In this context the ambiguous "thought structure" is selected, since an indirect reference to the patterns of thought *may* be implicit in this direct reference to the products of thought.—Eds.

**Thought products and the thought style under which these arise are both of them socially constrained. Cf. Preface.—Eds.

the bonds consist in mental training during childhood years or, better still, in a tradition several generations old, they will be indissoluble.

At a certain stage of development the habits and standards of thought will be felt to be the natural and the only possible ones. No further thinking about them is even possible. But once they have entered personal consciousness, they can also be regarded as supernatural, a dogma, a system of axioms, or even a useful convention. In this context it would be of interest to compare the history of science or the history of sports from semireligious practices in antiquity to the health-oriented sports of our own day.

The complex structure of modern society results in multiple intersections and interrelations among thought collectives both in space and time. We see professional and semiprofessional thought communities in commerce, the military, sports, art, politics, fashion, science, and religion. The more specialized a thought community is and the more restricted in its content, the stronger will be the particular thought nexus among the members. It breaks down boundaries of nation and state, of class and age. Compare the social role of sports or of spiritualism. Special terms such as *match, foul,* and *walkover* in sports; *demarche* and *exposé* in politics; *Saldo* [balance], *Konto* [account], *hausse* [bulls], and *baisse* [bears] on the Stock Exchange; *staffage* [props] and *expression* in the arts, each within its own thought collective, are used even across the barriers of national languages. The printed word, film, and radio all allow the exchange of ideas within a thought community. They also make possible the connection between the esoteric and the exoteric circles even across long distances and in spite of little personal contact.

A good example of the general structure of the thought collective is provided by the thought community of the world of fashion, as long as we examine only the common mental outlook of the followers of fashion and disregard either the general economic and social factors or the special professional and commercial factors of that field. What is of interest is fashion consciousness as such, independent of the content of fashion. The special mood of the thought collective of fashion is constituted by a readiness immediately to notice that which is fashionable and to consider it of absolute importance, by a feeling of solidarity with other members of the collective, and by an unbounded confidence in the members of the esoteric circle. The most dedicated followers of fashion are found far out in the exoteric circle. They have no immediate contact with the powerful dictators forming the esoteric circle. Specialized "creations" reach them only through what might be called the official channels of intracollective communication, depersonalized and thus all the more compulsive. Nothing is motivated in petty style; they are simply told "ce qu'il vous faut pour cet hiver" [what you need for this winter], or "à Paris la femme porte" [in Paris, women are wearing], or "Lancé au printemps par quelques jeunes femmes de la société parisienne" [presented to the public in the spring by several young ladies of Parisian society]. It is coercion of the strongest kind, because it appears in the guise of a self-evident necessity and is thus not even recognized as a coercive force. And woe to the true believer who does not or cannot conform. She feels cast out and branded, because she knows full well that every fellow member of the collective immediately notices her act of treason. For the esoteric members the coercion is much reduced. They can permit themselves many a new-fangled idea, which does not become a "must" until subsequent communication has taken place throughout the thought collective. But they too are held by the style of their own creations to particular "obligatory matchings": baroque sleeves may not be worn with an Empire waistline, to name only one example.

If we compare various thought styles, we can easily see that the differences between two such thought styles can be greater or smaller. The thought style of the physicists, for instance, does not differ all that much from that of the biologists, unless the latter happen to adhere to the thought style of the vitalists. There is a much greater difference in style between the physicists and the philologists, and a much greater one still between a modern European physicist and a Chinese physician or a cabalistic mystic. Here the divergence between thought styles is so wide that in comparison, the divergence between the thought styles of the physicist and of the biologist dwindles into nothing. One could actually speak of nuances of style, of varieties in style, and of different styles. But it is not the aim of this book to construct a complete

theory of thought styles. All I want to do is point out a few distinctive properties of the communication of thoughts between collectives.

The greater the difference between two thought styles, the more inhibited will be the communication of ideas. Collectives, if real communication exists between them, will exhibit shared traits independent of the uniqueness of any particular collective. The principles of an alien collective are, if noticed at all, felt to be arbitrary and their possible legitimacy as begging the question. The alien way of thought seems like mysticism. The questions it rejects will often be regarded as the most important ones, its explanations as proving nothing or as missing the point, its problems as often unimportant or meaningless trivialities. Depending upon the relation between the collectives, single facts and concepts are considered either free inventions, which scientists simply ignore like, for instance, "psychic facts" [*spiritistische Tatsachen*]. Less divergent collectives, alternatively, may produce only different interpretations, translations into another dialect of thought, as, for instance, theologians would translate these same psychic facts. Scientists have similarly adopted many individual alchemic facts. So-called commonsense, as the personification of the thought collective of everyday life, has become in this same way a universal benefactor for many specific thought collectives.

Words as such constitute a special medium of intercollective communication. Since all words bear a more or less distinctive coloring conforming to a given thought style, a character which changes during their passage from one collective to the next, they always undergo a certain change in their meaning as they circulate intercollectively. One could compare the meaning of the words "force," "energy," or "experiment" for a physicist, a philologist, or a sportsman; the word "explain" for a philosopher and a chemist, "ray" for an artist and a physicist, or "law" for a jurist and a scientist.

In summary, the intercollective communication of ideas always results in a shift or a change in the currency of thought. Just as the shared mood within a thought collective leads to an enhancement of thought currency, so does the change in mood during the intercollective passage of ideas produce an adjustment in this cash value across the entire range of possibilities, from a minor change in coloration, through an almost complete change of meaning, to the destruction of all sense. Compare the fate of the philosophical term "absolute" in the thought collective of scientists.

In chapter 1 we described the passage of the syphilis concept from one thought community to another. Each passage involved a metamorphosis and a harmonious change of the entire thought style of the new collective arising from the connection with its concepts. This change in thought style, that is, change in readiness for directed perception, offers new possibilities for discovery and creates new facts. This is the most important epistemological significance of the intercollective communication of thoughts.

Something remains to be said about the individual's belonging to several thought communities and acting as a vehicle for the intercollective communication of thought. The stylized uniformity of his thinking as a social phenomenon is far more powerful than the logical construction of his thinking. Logically contradictory elements of individual thought do not even reach the stage of psychological contradiction, because they are separated from each other. Certain connections, for instance, are considered matters of faith and others of knowledge. Neither field influences the other, although logically not even such a separation can be justified. A person participates more often in several very divergent thought collectives than in several closely related ones. There were and still are physicists, for instance, who profess the religious or spiritualist thought style, but few of them have been interested in biology once it became an independent discipline. Many physicians are engaged in historical or aesthetic studies but only a few in natural science. If thought styles are very different, their isolation can be preserved even in one and the same person. But if they are related, such isolation is difficult. The conflict between closely allied thought styles makes their coexistence within the individual impossible and sentences the person involved either to lack of productivity or to the creation of a special style on the borderline of the field. This incompatibility between allied thought styles within an individual has nothing to do with the delineation of the problems toward which such thinking is directed. Very different thought styles are used for one and the same problem more often than are very closely

related ones. It happens more frequently that a physician simultaneously pursues studies of a disease from a clinical-medical or bacteriological viewpoint together with that of the history of civilization, than from a clinical-medical or bacteriological one together with a purely chemical one.

As I select out of an abundance of data these few phenomena concerning the communication of ideas, I am fully aware of the fragmentary nature of my presentation. But they may suffice to demonstrate to science-oriented theoreticians, in particular, that even the simple communication of an item of knowledge can by no means be compared with the translocation of a rigid body in Euclidean space. Communication never occurs without a transformation, and indeed always involves a stylized remodeling, which intracollectively achieves corroboration and which intercollectively yields fundamental alteration. Those who fail to grasp this point will never reach a positive epistemology.[7]

4. Some Characteristics of the Thought Collective of Modern Science

In the previous section we described the general structure of thought collectives—their esoteric and exoteric circles, and the general rules of intra- and intercollective communication of thought. We shall now discuss the special structure of the thought collective of modern science, particularly the effect of both the esoteric circle and the exoteric circle within the framework of science. We shall disregard characteristic features of any specialized thought collective such as that of the physicists or that of the sociologists, because the structure of modern Western science has many common features.

Take the case of a researcher who creatively approaches a problem and is a "specialized expert" informed in the greatest depth—for example, a radium specialist in the science of radioactivity. He constitutes the center of the esoteric circle of this problem. The circle includes, as "general experts," scientists working on related problems—all physicists, for instance. The exoteric circle comprises the more or less "educated amateurs." A contrast between *expert* and *popular* knowledge is hence the first effect of the