OBSERVATION AND EXPERIMENT AND THEIR USE IN THE MEDICAL SCIENCES.

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THE METHODS OF SCIENCE IN GENERAL.

THE accumulation of verifiable knowledge, which is the object of science, depends fundamentally on the discovery of invariable sequences of events in the complex and apparently random phenomena of our experience. The obvious method of doing this is that of observation. We study the natural succession of events as they pass before us and observe those resemblances and recurrences which betray an underlying relation. The power of the method has been increased by refinement and elaboration until it can scarcely be recognized in this simple statement of it. Instruments such as the telescope, the microscope, the spectroscope, have increased its range and its precision; completeness and exactitude of record have increased its trustworthiness; and mathematics has given it the power of detecting relations among recorded facts too complex or too obscure to be within range of direct contemplation. But refinement of method, however far it may be carried, can never surmount the limitation by which observation in its very nature is restricted. This limitation is the circumstance that the observer must wait upon the natural occurrence of the phenomena he wishes to study. The phenomena may be too infrequent for their significant recurrence to come within the span of human life, they may be too complex, and too closely mixed with irrelevant events for the invariable sequences they possess to be detected.

Science has found a means of escape from the limitations of the method of observation in the method of experiment. Partial as the solution of the problem must be admitted to be it has proved of the highest value—of such value, indeed, that its own limitations tend sometimes to be a little overlooked. It will therefore perhaps be useful to examine more closely the relations of the two methods.

The method of experiment seeks to free the man of science from the arbitrary natural distribution of the phenomena he wishes to study. It seeks to give him the required phenomena at command and unmixed with irrelevant events which may modify the essential facts and confuse the study of them. Experiment, then, isolates the event to be studied from the common order of nature, and causes it to occur in circumstances as far as possible simplified and subject to specification.

Applicability of Experiment.

Certain sciences have not merely benefited by experiment, but have been created by it. This is true of physics and of chemistry, and is so nearly true of physiology as scarcely to need discussion. In all these sciences experience has proved that the laboratory "event" is as good as the natural "event," and that the simplification needed for experimental precision is not necessarily accompanied by distortion of the phenomena concerned. On the whole perhaps it is surprising that physiology has been able successfully to isolate for study so many of the phenomena of living organisms, but of the fact there can be no doubt.

Regarded as subjects for experiment certain sciences stand at the opposite extreme to the position occupied by chemistry and physics. Such are astronomy, geology, meteorology. In the material of their sciences the scale of time and space and the forces concerned are so large that it is usually impossible to produce in the laboratory conditions approaching those of the natural event. These sciences therefore must be, and apparently must continue to be, primarily observational. This is, however, by no means to deny that they can and do have useful relations

with experimental methods, though these relations may be less direct than in other sciences. In geology we may, for example, study in the laboratory some of the elements in the process of metamorphism, though we can command no more than an almost negligible fraction of the time and the force that have gone to the formation of metamorphic rocks in nature. In meteorology, again, we may study the differences of electric potential that are produced by the breaking up of falling water drops, but we must remain almost infinitely far from the scale and magnitude of a natural thunderstorm. In astronomy, a science of whose debt to experimental work there can also be no question, the impossibility of reproducing in the laboratory the conditions of the natural event is still more apparent.

Thus in geology, meteorology, and astronomy experiment occupies the position of the small scale model and is therefore subject in its degree to the defects of the argument from analogy. These sciences must in fact be described as sciences of observation and *collateral* experiment, and have very plain methodical differences from the sciences of *direct* experiment such as physics and chemistry.

Experiment in the Biological Sciences.

Physiology has been included here among the sciences of direct experiment, and there can be no doubt of the thoroughness and success with which it has established itself there. It has been hinted, however, that the case of physiology is to some extent different from that of the other sciences of direct experiment, and its brilliant evolution has had to overcome difficulties special to it. The living organism has a certain, perhaps indefinable, but not the less substantial unity, and it is this unit and not its constituent parts or processes that has been the material acted on by evolutionary forces. A physiological process may therefore be expected to lose something of its full natural character when it is isolated from the complete animal for purposes of experimental study. This consideration does in fact express one of the limitations of experimental physiology, and one that is apt to become increasingly manifest in the most advanced branches of the subject. On the whole, however, it is highly remarkable with what success the physiologist has been able to defy this limitation and to detach bodily processes into circumstances of such simplification, or such complete specification, as to make study fruitful without unduly distorting their natural character. Such classical simplifications as the nerve muscle preparation, the isolated heart, the spinal animal, have been justified beyond all question by the substantial additions to knowledge that have been made through them. These preparations cannot, however, fail to remind us sharply of the difference in the status of experiment in physiology and in physics and chemistry. The essence of a scientific experiment is the specification of its conditions. Now the normal medium of any bodily organ or process is the intact living animal, and its normal activity is closely compounded with that of the whole organism. In drawing conclusions from the behaviour of a physiological preparation it is necessary, therefore, to specify how far it has been modified by being isolated. The difficulty of doing this with fullness and precision is not inconsiderable—even the necessity for it is not always closely attended to—and does undoubtedly counterbalance to some extent the advantages of simplification that the experimental method possesses. When this lack of specification is least surmountable we can see in physiology a tendency to become a science of collateral rather than of direct experiment.

Scientific Method in Human Biology.

The distribution of method in the sciences not concerned with the life of man is relatively simple, because all the larger deciding factors are entirely beyond human influence or control. With the sciences of human life,* the

* The interrelation of physiology and pathology is so close that from the point of view of method they may be usefully regarded as continuous and inseparable. The apparent necessity for the medical student to complete his knowledge of the normal before beginning his study of the abnormal is probably as fallacious as it is practically wasteful and inconvenient.

situation is complicated by the prejudice and the ethical limitations to which direct experiment in man is subject. The effect of these circumstances has been to make the study of the processes of the human body in health and disease dependent chiefly on observation in man combined with experiment in animals. Experiment in animals has had great success in solving the problems of human biology, and has provided one of the most complete proofs of the value of experimental science and of the general similarity of the fundamental vital processes in all animals. At the same time, however, it must be recognized that these experiments have in the strict sense and in relation to man collateral rather than direct validity.

THE APPLICATION OF ANIMAL EXPERIMENT TO MAN.

The success of animal experiment in human physiology and pathology has been so great and continuous that there has never been any serious call for its collateral quality to be dwelt upon. With the increase of knowledge, however, and the need for a finer and finer penetration into the processes of health and disease, the usefulness of a closer critical examination of the actual state of affairs will probably become manifest. To those whose work in human biology lies in the observational study of man rather than in animal experimentation the value of such an examination tends constantly to present itself. The gap between man and any other animal is large even when judged on the crude basis of manifest structure. When the relation of man to animals is regarded from the functional point of view the gap is seen to be larger and much more significant. It may be useful to specify some of the biological anomalies in the situation of man which cannot be safely ignored in applying experimental results obtained in animals.

The Upright Posture.—The simplest case in which the conditions common to most other animals have been drastically rearranged in man is the upright posture. The essential mechanics of the skeleton and of the circulation were established, and as it were tried out, in quadrupedal forms through an enormously long space of time. Upon this well-proved arrangement, and it would seem rather suddenly and without a fundamental mechanical reorganization, was imposed a posture which threw on the old scheme fresh strains that have tried it to within reach of the actual margin of safety. The results of this late and so to say hurried revision of the structural plan show themselves far and wide in the pathological field. It is not unreasonable to see these strains as important factors in the so-called static deformities, and in the excessive liability of the lower limbs to diseases of the bones and joints and to circulatory disorders on both the arterial and venous sides. Echoes of the same disturbing element are perhaps to be found in abdominal pathology, and even in the peculiarities of the cerebral circulation. In general, however, it is perhaps in relation to the special qualities of the circulation as a whole in man that the upright posture should arouse the most caution in applying the results of animal experiment.

Longevity.—The fact that in man survival to an age long past that of reproduction is a common event makes his general biological position in some ways unique. Morbid states that show themselves on the whole only when reproductive activity is normally waning or at an end can have no selective elimination acting against them; they can thus flourish untouched by what is probably the strongest of all checks upon diseases that normally have their range in or before the active period of sexual life. It seems reasonable to suppose that an essential factor in the inveteracy of cancer and its excessive frequency in man is its existence in what we may call a biological backwater, where it has no effects of selection to contend with. The difference in frequency of sarcoma and carcinoma might perhaps plausibly be accounted for in the same way. In applying the results of animal experiment to pathological conditions in man it seems likely that this peculiar feature in the situation of the latter may be a cause of difficulty, and perhaps of wrong conclusions.

The Effects of Unrestricted Food Supply.—It is well recognized that normally, and in a general way, the inclination for food is directly related to emptiness of the

stomach rather than to the nutritional needs of the animal concerned. The usefulness of this arrangement is obvious: if the impulse to seek food were felt only when the body was in need of it to carry on its functions, there would be a risk that the animal would already have lost the energy necessary for the search. The normal animal eats, then, because the stomach is calling for food, not because the body is calling for nourishment, and the physiological situation is satisfactory as long as the food is of low nutritive value, as in the herbivora, or has to be worked hard for, as with the carnivora. Civilized man has broken through the natural safeguards of the process by obtaining a food supply unlimited both in nutritive value and in amount, but he still regulates his eating by the demands of his stomach rather than by the needs of his body. The result is that by the time middle-age is reached the absence of some degree of adiposity is statistically abnormal, and may well give rise to a suspicion of disease. Here again we find a gross functional discrepancy between man and animals which may well have a confusing effect in the application of experimental results.

The Effects of Personality.—The living animal is a functional unit dependent on the close correlation and harmonious working of its parts. There is no reason to suppose that there is any less essential need for harmony among its mental activities and between them and its bodily activities than there is for harmony in the bodily sphere itself. In animals other than man disharmonies within the mind or between mind and body, though they sometimes give hints of their presence, are generally inconspicuous. The relatively enormous development of mental activities in man has enlarged correspondingly the region in which a lack of harmonious working may arise. Disharmonious mental states, such as those due to the clash of individual and social needs, are notoriously apt to interfere with bodily function to a degree and with a duration and constancy that may simulate organic disease and perhaps initiate it. It is a fact unfortunately beyond contest that, though the interaction of mind and body presents problems to the importance of which lip-service has been abundantly paid, these problems have never received thorough realistic and scientific treatment. The explanation of this deficiency may be in the consideration with which we are here specially concerned, that this is a region in which the functional gap between man and other animals is at its widest and most profound.

THE FUNCTION OF OBSERVATION IN HUMAN BIOLOGY.

We have pointed to some of the corrections which may have to be applied to animal experiment before its significance for man can be established. There is, however, another limitation of the range of collateral experiment in human biology. This is in regard to investigations in which access to the subjective side of experience is indispensable. The relation between cerebral states and states of consciousness in the normal and abnormal, and the physiology and pathology of pain, present problems of this class. All these considerations taken together, while they can, of course, in no way depreciate the inestimable gifts human biology has got, and will probably continue to get, from collateral experiment, yet do suggest that for the finest and deepest insight into the most characteristic phenomena of man's life it will be necessary to use, with all its inherent restrictions, the method of direct experiment in man himself.

Our knowledge of normal physiology in man, such as it is, is almost wholly due to the experimental method. In the study of disease, on the other hand, while the experimental method has been very valuable, and promises to be increasingly so, it is to be noted that the method of observation has behind it a long and honourable history; but it cannot be denied that for a considerable time essential progress in our knowledge of disease has come less and less from the time-honoured method of observation and more and more from experiment. Moreover, with all its opportunities, observation has at its best been able to disclose but little of the fundamental processes of disease, of the exact meaning of morbid phenomena, or of the precise mechanism lying behind symptoms; whereas experiment has a remarkable series of successes of these very kinds already to its credit. In view of such considerations as these it may well be asked

whether the time has not come when it should be recognized, with all the practical consequences that would follow, that observation can no longer be regarded as able to effect serious advances in medicine.

The method of experiment studies phenomena under the simplified and specified conditions of the laboratory; the method of observation studies phenomena as they are presented in the random order of natural events. The first tends to yield clear results capable of analysis by further experimentation; the second tends to yield broader, vaguer conclusions, and its power of penetration by analysis is usually limited. The first requires patience, caution, ingenuity; the second, insight, great familiarity with its material, and what we may call the intuition of reality—that is to say, the power to choose among equally plausible hypotheses the one that best fits the general behaviour of the material in question. In a very broad way it may be said that successful observation depends more directly on a special mental aptitude than does successful experiment.

The chief limitation in practice on the value of even the best kind of observation is the difficulty in proving its conclusions and therefore of making them available to the general body of science. We have said that successful observation is dependent on special aptitude, and it is notorious that ten experiences will yield a great deal more to one man than a hundred of the same kind to another. This, of course, means that there must usually be a large intuitional element in the conclusions of the able observer, who is apt to be impatient of the drudgery of scientific proof, correspondingly careless in attempting it, and therefore little apt to advance substantially the scientific structure of his subject. The evolution of medicine, which has been so largely dependent on it, illustrates in a peculiarly pointed way the disadvantages to which purely observational inquiry is subject. The method failed to penetrate the nature of infective processes on the one hand, and on the other it ascribed, and indeed still ascribes, a wholly undue importance to insignificant climatic conditions as direct causes of disease. It has held the key to the pathology of vitamin deficiency, to endocrine disorders, to the relation of malaria and mosquito, but has lacked the power decisively to enter into and exploit these new provinces. It has had for the most part to leave unelucidated the events that connect the processes of disease with the symptoms they produce, so that even to-day, for example, pain, which is by far the commonest of all symptoms, is the bugbear of diagnosis and treatment.

The essential feature of the observational method is the recognition of groups of events of which the items are significantly related to one another. The simplest case in the detection of such significant relations is when the suspected series recur in the same order often enough to be easily noticeable. The study of disturbed function in the human body when it has passed beyond its most elementary stages does not, however, provide many sequences that by their invariable recurrence and unmistakable identity show that their items are interrelated. The total body of phenomena accompanying disturbance of function is very large and very variable, so that the significant series which is being looked for may present itself in a different disguise of detail at each reappearance. The simple method of establishing the significance of a group of phenomena by the dry statistical record of its invariable recurrence in given circumstances is thus not widely applicable in medicine, and the method of observation has not usually obtained its more considerable advances in this way. More often the observer has to be content with a limited number of recurrences of the group of phenomena, and relies upon his close familiarity with and "feeling" for his material to confirm the relation he suspects between items of the group. This ability to detect significant relations among apparently unrelated phenomena by a kind of direct examination is the distinguishing gift of the able observer.

Observational inquiry then in such a field, for example, as clinical medicine may give results that are questionable on the one hand because too much value has been given to conclusions essentially based on intuition, and on the other hand because the possibilities of exact observation and record have been exaggerated. We are all familiar with instances of large and imposing masses of records vitiated

at their very base by the preconceptions of their compilers or by the impossibility of precise record, and with instances of the hieratic pronouncement that rises superior to the need of proof. Neither of these misuses of the method, however, can justify us in ignoring what has been done by it for medicine in the past or in concluding that the period of its usefulness is at an end.

Before inquiring what function the method of observation may yet be able to serve it is well to bring to mind how little the medical sciences can afford to dispense with any means of inquiry that is not demonstrably and wholly sterile. The success of the experimental method has been so great that it has become almost a fixed convention for any general comment on the course of science to deal almost wholly with the triumphs that have been attained by this method and but little with the tasks that have proved too hard for it. This not unamiable weakness is perhaps partly to be explained and excused, at any rate as far as this country is concerned, by the constant hostile pressure against animal experiment and the consequent supposed need to justify it in season and out of season. If, however, we free ourselves, as we may well do for a moment in so technical a discussion as this, from propagandist optimism we shall very easily see that in the interests of science itself we should spare some attention from the triumphs that light up the past, for the needs that darken the future. The progress of science, when regarded with a due realism, is seen always to have been sporadic, to have been subject to lapses of inspiration, to have gone forward in one part of the field at the apparent expense of slackening effort in another. No better illustration of this irregularity in the line of progress could be found than in the fact that after over half a century of experimental pathology the four great scourges of man in temperate climates—influenza, the common cold, cancer, and rheumatism—remain pathological problems so largely unsolved. In the face of a fact like this it is plain that medicine cannot afford to leave unused any implement, however imperfect—especially, perhaps, one to which a definite function otherwise unfilled can be assigned.

In trying to define the field in which observation seems to have its characteristic use it is of advantage to get a clear idea of what actually are the chief defects and limitations inherent in the method. Two of these are of such predominant importance that they need only be mentioned: first, the limitation of the extent to which observation can be used in following a problem through stage after stage of elucidation until a fundamental solution is found; and secondly, the readiness with which the method lends itself to faulty or even wholly fallacious conclusions. It may be thought that neither of these defects needs discussion, but perhaps the second has implications which are not always fully realized and which may repay some examination.

Observation and the "post hoc" Fallacy.

The characteristic defect of the observational method as commonly used in medicine is its liability to the *post hoc, propter hoc* fallacy. The only means we possess of establishing a causal relation between events is to observe their invariable occurrence in association. The clinical observer cannot bring about at will the recurrence of events he wishes to study or strip them of irrelevant circumstances as can the experimenter. Moreover, his observations are necessarily made under the pressure of the fact that the events he looks for are not primarily material for science but primarily somebody's symptoms and the signals of somebody's need for help. This urgency in the very air of all clinical work does undoubtedly tend towards the finding of significant relations in sequences of events which longer and more thorough observation would have shown to be unrelated. The well-equipped clinician must possess the qualities of the artist, the man of science, and the humanist, but he must exercise them only in so far as they subserve the getting well of the individual patient. It is a hard doctrine but none the less true that this essential function of the doctor—the care of the given patient—may involve the forgoing of exactly scientific diagnosis, of the artistic perfecting of an operation, or even of the interests of society at large.

It is therefore obvious that the influences against the making of scientific observations by those in the actual practice of medicine are very strong; and it is not surprising that the experimenter is apt to find the clinician on the one hand prolific of unsound conclusions and on the other timid and sceptical in applying the results attained in the laboratory by experiment. No better illustration could be found of the characteristic weakness of clinical methods than the extent to which the ascription of disease to trivial climatic discomforts is still accepted or at least tolerated. Colds and phenomena of the order of draughts and wet feet—alleged causes of colds—are sufficiently common to afford ample opportunities for the discovery of insignificant sequences. This fact, together with the psychological influences tending to associate healthy with comfortable conditions, has produced a veritable folklore pathology of colds and chills which true scientific observation would speedily explode, and which presents clinical medicine in one of its least edifying aspects. There are, however, probably even deeper roots of the inveteracy of the *post hoc* fallacy in medicine. If two events A and B occur repeatedly in the same order, experience teaches us to regard them as having the relation of cause and effect—that is to say, of being so related that whenever A appears it will be followed by B, and wherever B is observed it will be found to have been preceded by A. To establish this relation with any great degree of probability the observed recurrences of A and B in that order must be numerous, must be without exception, and the identity of A and B in each observation must be clear. In clinical observation these requirements cannot usually be satisfied with unambiguous severity; the able observer, therefore, while constantly trying to satisfy them as far as the case permits, will depend more or less on the insight and sense of reality that his familiarity with his material and his natural aptitude have given him.

It is notorious that a conviction of the existence of a causal relationship between two events—a very different thing from the objective proof of such a relationship—is far from being dependent on such deliberate and cautious procedures. In everyday affairs, and to a certain extent in the general run of clinical work, the number of accepted causal relationships far exceeds the number of demonstrated and even of probable cases. It seems likely, then, that there is some strong natural tendency which inclines us to ascribe causal relations to events accidentally and arbitrarily occurring near one another. That we have such a tendency is at least suggested by the work of Pavlov on conditioned reflexes. The essential facts of this work are familiar and need not be recalled in detail. In a dog, in which a salivary fistula has been established so that the flow of saliva can be measured, the presentation of food is followed at once by a profuse secretion. Some arbitrarily chosen stimulus such as the sounding of a metronome is now made to precede immediately the offer of food. After this sequence has been repeated a few times it is found that the auditory stimulus causes a similar salivary flow without any presentation of food. The cerebral cortex has been taught by a very short experience to accept the metronome sound as a precursor of food. In mental terms the sound has become a "cause" of food, and an intelligent dog might classify metronomes in the group of things to be hunted like rats and rabbits. The facts especially to be noted for our purpose here are, first, the readiness with which the link of apparent causation has been formed, secondly, the arbitrariness of the sequence, metronomes having no relation with food in the general objective world, and thirdly, the fact that the relation can be fixed only by adding it to a relation already established—namely, a natural reflex—in this case the visual-salivary reflex.

Enough has been said earlier in this paper to enjoin caution in applying the results of experiments in animals to man. Caution must, moreover, be especially stringent in seeking light on mental problems from cerebral phenomena. Nevertheless, it is clear enough that there is a remarkably close analogy between the aptitude for the formation of conditioned reflexes on the one hand and on the other hand the tendency too readily to ascribe

the causal relation to small and unrelated sequences of events; and we may at least suspect that the subjective sense of causation we so easily derive from a few random coincidences is connected with the proved capacity of the brain to pick up arbitrary and as it were "irrational" reflexes. The conditioned reflex then is perhaps the simplest case of the *post hoc* fallacy. When we thus see reason to suspect that our tendency to impute causal relations unjustifiably may be the expression of a characteristic cerebral function we need not be surprised that this fallacy is so common and so difficult to avoid.

We are now in a position to review shortly the disadvantages of the observational method in the study of medical problems as we see it in actual use. These disadvantages fall into three groups.

1. The method as an instrument of inquiry is of limited range. In the systematic attack on a given problem carried on stage by stage until a solution is reached it is notably weak compared with the experimental method to which, in this function, it must always and of necessity remain grossly inferior.

2. The method is known as a matter of experience to be especially open to the *post hoc* fallacy. Though this may not be fundamental and essential as is the limitation noted above we have seen that there may be an organic predisposition underlying it.

3. In clinical medicine the difficulties of securing objective proof by exact observation of identically recurrent events are very great. This tends to make the observer rely on intuition rather than on established conclusions and to make him impatient of the labour of proving or disproving the truth of opinions arrived at by intuition. The result is that the current clinical medicine of any given period is apt to be loaded with "authoritative" opinions often contradictory of one another, many of which are actually capable of, but have never been submitted to, definite proof or disproof.

Limitations of the Experimental Method.

Experiment is observation made in specifiable and controllable circumstances and it seeks to eliminate that dependence on the personal judgement, the tact, the intuition of the observer which is the weakness of the observational method. If we imagine a problem to be attacked and solved independently by experiment and by observation, the solution by the latter method, in addition to having taken longer and being less exact, will generally have demanded a more arduous and intricate intellectual exercise than the solution by the former.

This economy of experiment in its demands upon certain of the less definable aptitudes of the mind is no doubt a contributory cause of its great success as a method, but probably it has secondary consequences which in the long run and on the large scale are not wholly advantageous. A science which is strictly limited to the experimental method is apt to favour in its workers a tendency to deprecate any great speculative activity and to regard an interest in the free play of ideas for their own sake as evidence of a lack of scientific stability and trustworthiness. Such a distrust of the intellect involves an unsound view of the function of ideas in science. It is a mistake to suppose, as it is so easy to do, that science enjoins upon us the view that any given idea is true or false and there is an end of it; an idea may be neither demonstrably true nor false and yet be useful, interesting, and good exercise. Again, it is poverty rather than fertility of ideas that causes them to be used as a substitute for experiment, to be fought for with prejudice or decried with passion. When ideas are freely current they keep science fresh and living and are in no danger of ceasing to be the nimble and trusty servants of truth. We may perhaps allow ourselves to say that the body of science gets from the steady work of experiment and observation its proteins, its carbohydrates, and—sometimes too profusely—its fats, but that without its due modicum of the vitamin of ideas the whole organism is apt to become stunted and deformed, and above all to lose its resistance to the infection of orthodoxy.

The state of inorganic chemistry in the early nineties of the last century showed some traces of the conditions

which too exclusive a reverence for experiment is apt to bring about. The inspiration of the atomic idea was manifestly dying, yet any whisper that the atom might not be the ultimate unit of reality was apt to be snubbed as speculative and unscientific. Nevertheless this impeccable science could tolerate for many years a discrepancy of the order of 1 per cent. in the results of the different methods of preparing nitrogen, and with all its faith in experiment could ascribe the discrepancy to experimental error. And all the while, behind the meagre veil of this experimental error the inert gases of the air were impatiently awaiting discovery. The agitated scepticism with which the discovery of argon was received, no less than the great growth of which that discovery was the germ, illustrated how much chemistry had for the moment lost the aptitude for new ideas and the elasticity of mind which their currency produces. Physiology, though in a less extreme degree, has illustrated from time to time the periodical languor to which a purely experimental science is subject in the absence of the stimulation of ideas from without. Fortunately, its inevitably close, though perhaps not very highly prized, relation to medicine has repeatedly given it the stimulus necessary for renewed vitality, as, for example, in the case of the idea of cerebral localization and the idea of internal secretion. With such illustrations in mind it may perhaps be admitted that experimental science does not of itself and of necessity produce the most useful attitude towards ideas.

It is sometimes taken as a matter of course that scepticism is the very highest flower of the scientific spirit. The thesis might be admitted to have an aspect of truth if it did not so often cover a mere automatic means of protecting ourselves against the painful irruption of new ideas. If the reader of this paper will ask himself what has been his attitude towards anything in it that may have been new to him, he will probably find that his reaction has been far less to explore what possibilities the unfamiliar idea may have happened to possess, than almost automatically and at first sight to look for arguments against it. And if he were challenged to give the reasons for his matter of course use of this method he would no doubt defend it as essentially scientific.

Even if it is admitted that opposition towards ideas is an attitude of mind not best calculated to extract what value they may contain, we are apt to be told that the true scientific position is that of the famous "suspense of judgement." It cannot, however, be conceded that even this time-honoured phrase represents an attitude quite free of the defensive taint. The truly scientific mind is altogether unafraid of the new, and while having no mercy for ideas which have served their turn or shown their uselessness, it will not grudge to any unfamiliar conception its moment of full and friendly attention, hoping to expand rather than to minimize what small core of usefulness it may happen to contain. It is this capacity in scientific workers for what we may call provisional acceptance that encourages in science the steady flow of ideas and tends to preserve it from those periods of intellectual languor to which, as we have seen, the purely experimental sciences seem in some degree to be prone.

We have shown that observational study is subject to certain defects, especially in its liability to fallacy and its limitations as an exact instrument. But when it is successfully practised it renders necessary the special cultivation of certain qualities of mind—intuition, imagination, the feeling for reality—which are just those which may be expected to provide that flow of ideas that keep the study of a science animated and interesting. It would seem, therefore, that it must be an advantage to an experimental science to have an observational side, the function of which, in addition to its use as an implement of research, would chiefly be to promote the atmosphere of intellectual liveliness which is so important an evidence of health.

If these considerations are sound they afford good reason to think that our desire to forward the scientific study of medicine and the branches of knowledge on which medicine depends will be best fulfilled not only by promoting the use of experiment wherever possible and by bringing every problem that admits of it to an experimental test, but also by keeping alive the method of

observation in medical studies and doing what we can to give it the benefit of scientific principles of use. In order that observation should have its proper value certain principles we have already indicated must be thoroughly familiar. The true nature of the method must be understood, its special liabilities to fallacy must be known, and its weakness of trusting to intuition when actual proof is possible, overcome. There can be little doubt that it is this last-named characteristic of ordinary clinical practice that inclines the critics of the observational method in medicine to view it with so little charity or hope. In clinical work proof is usually difficult to obtain, often tedious and unencouraging to attempt, and not rarely altogether impossible; at the same time any effort towards it is constantly overshadowed by the urgency to act. It is natural, therefore, for the expert clinician to rely on his intuition and judgement even when actual and final proof is possible, though this preference does constitute a reproach to the method from any scientific point of view. If clinical observation is to renew its prestige and to continue its indispensable function of stimulating the experimental attack on medical problems, it can do so by showing resolution in looking for proof wherever proof is possible, and a scientific standard in its scrutiny of evidence.

CONCLUSION.

In reviewing the principles of method by which the task of the medical sciences is to be carried forward we have seen reason to group the resources available into three classes: first, experiment with animals; secondly, experiment with man; and, thirdly, clinical observation. All of these methods are necessary for sound and continuous progress, but each has its special province, and each has certain limitations which prevent its being wholly independent of the others.

1. *Animal Experiment*, which we have ventured to call collateral experiment, must always be the chief instrument for the solution of fundamental medical problems. It has to be recognized, however, that the functional gap between man and other animals, and especially those commonly available in laboratories, is larger even than the morphological gap. We have pointed out four of the regions in which this discrepancy is largest, and where, therefore, special caution is necessary in applying animal results to man. The need for such caution is, however, fundamental and general, if medicine is to get the fullest benefit from what has been, and still is, its most fruitful resource.

2. *Experiment in man*, or direct experiment, limited in possibilities of application as it necessarily must be, is the one wholly unexceptionable method available for the solution of problems of human health and disease. Though its history is still very short, it has already proved remarkably fruitful. There can be no doubt that one of the chief duties before medicine at present is the exploitation of the method of direct experiment. The natural history of sciences, however, seems to indicate that a diet of pure experimentation in a limited field is not enough for permanent scientific health. If experimental medicine is to progress healthily it must have a full supply of ideas, and must know how to deal with them. Such a purpose can best be served by a close contact with the realities of clinical medicine.

3. *Clinical observation* has given to medicine very long and very honourable service. There is a certain melancholy in recognizing, as we must, that it has never been, except in the hands of an occasional genius, a very effective instrument for penetrating the fundamental secrets of health and disease, and in recognizing that we now possess far more effective instruments for this purpose. To recognize these facts is, however, by no means to acquiesce in the view that clinical observation has no longer important functions to fulfil in progressive medicine. In the first place it is still a valuable method of scientific research. At the same time it must be admitted that the method is, in some respects, far less general and far less simple than that of experiment; that it lends itself to the solution of only a limited class of problems, and that it demands, at any rate for its great strokes, a somewhat special aptitude of mind. Moreover, if it is to make itself less

dependent on special aptitude, a wider interest in the need for, and the means of proving its propositions will be necessary. It is possible that the increasing knowledge of experimental methods may bring this about and stimulate a renewed vigour in purely clinical work. In the second place, as successful clinical observation demands a certain special aptitude, and the unrelenting contemplation of a very large and rich material such as we find at its highest in, for example, a Hughlings Jackson, it should be the source and reservoir of that flow of ideas which alone can maintain the fertility of the whole field of medical science.

To the experimenter immersed in his research, and to the clinician struggling with the load of experience and the needs of his patients, it may seem impractical to concern ourselves with the theory of medical knowledge. On the other hand, it is perhaps the lack of rational doctrine and a general interest in the problems of method that has made medicine the scene of so much disunited and contradictory effort, and helped to put it down from its historical position as the mother and the nurse of science.

INFECTION BY ANAEROBIC STREPTOCOCCI IN PUERPERAL FEVER.

BY

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THERE are many cases of puerperal fever in which we are unable to make a precise bacteriological diagnosis. Blood cultures give no growth and cultures made from the cervix uteri give a mixed growth of several bacterial types. If haemolytic streptococcal colonies occur in any number it is usual to assume that an infection by that organism is responsible for the patient's fever—and probably that assumption is more often right than wrong. When haemolytic streptococci are absent we are left in doubt as to the nature of the infection, and without a laborious, and possibly unfruitful, examination of the patient's blood for evidence of an antibody response to one or other of the uterine microbes, we can get no further. All these cases—and they constitute a considerable proportion of the total puerperal infections—have to be written down as *infections of uncertain origin*.

HISTORICAL.

The suggestion that anaerobic streptococci may play an important part in puerperal infections is not a new one, although it has received hardly any attention in this country. In 1899 Menge and Krönig recovered these organisms from the peritoneum in cases of suppurative peritonitis, and claimed that they ought to be regarded as definitely pathogenic for man. Krönig (1895) had previously demonstrated that similar streptococci were often present in the vagina of pregnant women. They were first cultivated from the blood in puerperal fever in 1910 by H. Schottmüller, whose papers make an important contribution to our knowledge of the clinical aspects of this disease. He applied the name *Streptococcus putridus* (later *putrificus*) to this organism on account of the fetid gas produced by it in cultures when blood was present. Veillon had (1893), however, previously named it *Micrococcus foetidus*. In Schottmüller's series of 50 cases he obtained a pure culture of *Streptococcus putridus* from the blood in 5, and in one case a mixed culture of *putridus* and *haemolyticus*. In the same series of 50 cases a pure culture of haemolytic streptococci was obtained from only two cases. Uterine cultures showed these two types to be present in an equal number of cases—namely, fifteen.

The further experience of twenty years has served to strengthen Schottmüller's belief that these anaerobic streptococci are at least as important as the haemolytic variety in the causation of puerperal post-partum infections. An analysis of his findings in 231 fatal cases published in 1923 showed that the haemolytic streptococcus was obtained in pure culture from the blood of 42 patients,

and *Streptococcus putridus* from 41. In 11 other cases blood culture gave a mixed growth of anaerobic streptococci with other species. Peritonitis occurred in 89 of the patients, haemolytic streptococci being obtained in pure culture from the pus twenty-eight times, *Streptococcus putridus* thirty-one times. *Streptococcus putridus* grew in mixed culture from the pus of 7 other cases. The clinical conditions most frequently associated with infections by *Streptococcus putridus* were subacute and chronic thrombophlebitis affecting the parametrial venous plexuses, and salpingitis. Abscess formation was a common sequel.

Reviewing the whole subject of puerperal infection in 1928 Schottmüller states that the haemolytic streptococci account for scarcely one-third of all his fatal cases. He still recognizes only a single type (*putridus*) of anaerobic streptococci. His view as to the importance of the anaerobic types is not shared by all his German colleagues, but recently Sommer, in an analysis of 261 cases of generalized infection occurring in Berlin (186 of them post abortum and 58 post partum), has brought some support to it. Sommer's observations led him to conclude that staphylococcus is by far the most common cause of the generalized infections following abortion (71 cases out of 186) and that haemolytic streptococci and *Streptococcus putridus* (in that order) are responsible for most of the post-partum septicaemias.

Schwarz and Dieckmann (1927) have also reported an investigation carried out by them in Washington. Combined aerobic and anaerobic blood cultures were made in a series of 68 puerperal fever cases occurring during a period of two years. In 11 cases a pure growth of strictly anaerobic streptococci was obtained, and in 6 cases a growth of "aerobic organisms" (types not specified). Ten patients died, of whom five had a generalized infection by anaerobic streptococci. In 35 cases cultures from the uterus gave a growth of these cocci.

Schwarz and Dieckmann do not suggest that they encountered an epidemic of infection due to these anaerobic streptococci, and their conclusions are in general agreement with those of Schottmüller. They did not attempt the differentiation of the strains isolated from their cases, but (unlike Schottmüller) they did not regard them as a homogeneous group all conforming to the *putridus* type. They call particular attention to one type which was cultivated in nine blood cultures (? from nine different patients)—a small Gram-negative coccobacillus which produced black discoloration of blood agar. It is not quite clear whether they included this organism among their anaerobic streptococci.

Two facts, then, stand out from the investigations of the past—namely, (1) that in Germany and in America strictly anaerobic streptococci have been isolated from the blood of a number of cases of puerperal fever, particularly those of the thrombo-phlebitic type; and (2) that similar organisms are frequently present (estimates vary between 5 and 20 per cent.) in the vagina during pregnancy (Krönig, Natwig, and others).

Beyond these facts we have learned very little. The description of strains by Veillon (1893), Krönig (1895), Natwig (1905), Schottmüller, Lewkowicz (1901), Sternberg (1900), Graf and Witneben (1907), and particularly the laborious investigation of Prévot (1924), seem to show that there is a large group of these anaerobic streptococci, and that their final differentiation is likely to prove a matter of considerable difficulty. Prévot has suggested a preliminary differentiation into three main classes: (a) those which produce fetid and other gases in culture; (b) those which do not—mostly very small cocci; (c) those which are only "anaerobes of predilection"—that is, they can be educated, more or less, to aerobic growth. This differentiation Prévot found to be justified by serological tests. A few of the strains examined by him were pathogenic for laboratory animals and a few produced a feeble exotoxin. No specific treatment of the infections by these organisms has yet been forthcoming.

AUTHOR'S OWN EXPERIENCE.

During the years 1923-28 I made bacteriological investigations of a large number of cases (about 240) of severe, and moderately severe, puerperal fever. From 55 to 65