of experimental skill and theoretical insight. Scores of new compounds were carefully characterized in the course of the work, which throws much interesting light not only on the structure of cryptopine and protopine, but on other related alkaloids. It is of course unnecessary to refer to the fact that it is to researches such as these that we owe inspiration and direction, not only in the work of the synthetic preparation of the natural alkaloids of therapeutic value, but in the artificial synthesis of new drugs.

Cushny¹⁹ has lately made some noteworthy observations on the pharmacological antagonism existing between atropine and pilocarpine. These experiments were made on the salivary secretion, and showed that in different dogs a constant amount of atropine was necessary to oppose the action of a constant amount of pilocarpine, and in the same dog the ratio of the two drugs remained the same, irrespective of how the actual amounts injected might vary. It appears, therefore, that the antagonism proceeds according to the laws of mass action rather than those of simple chemical combination in definite proportions. The investigation is an interesting example of the application of physico-chemical methods to the elucidation of the mechanism of the action of drugs.

ANTITOXIC SERUMS.

Reference has already been made to the discovery by H. R. Dean and R. S. Adamson²⁰ that the toxicity of Shiga dysentery vaccines could be enormously reduced by the restricted action of hypochlorites and other oxidizing agents without lowering their immunizing power. This gratifying and rather surprising result has been abundantly confirmed, and points the way to a number of other allied problems of practical importance which might be successfully attacked, especially if an adequate analysis of the chemical reactions concerned should result from further investigation.

One result of the war has naturally been an enormously increased consumption of various antitoxic serums. The concentration of serums by the use of fractional precipitation of the contained proteins by salts such as ammonium sulphate has led to the preparation of high titre serums from which much of the inert material has been removed. In a recent communication from the antitoxin laboratories of the Lister Institute at Elstree, Miss Homer²¹ has described a number of practical improvements in the methods originally developed by Banzhaf and Gibson, which promises to make the method easier to carry out and to give more uniform results.

Theoretical studies by Dale and Hartley²² on the relation of anaphylaxis to different serum proteins offer some practical considerations. They show that each and all of the individual proteins of a serum can act as anaphylactic antigens, and that the ideal to be aimed at in concentrating the curative elements in a specific immune serum is simply the reduction of the ratio of total protein to antitoxic value. For the purpose of reducing serum reactions the elimination of albumin appears to be as important as that of the cuglobulin when, as is usually the case, the pseudoglobulin is the fraction carrying the therapeutic power. Dale and Hartley find that the latent period of sensitiveness to albumin is relatively long compared with the globulins, and this may have a bearing on the successive crops of serum rash which have been recorded as following a single injection of serum.

PROTECTION AGAINST POISONOUS GASES.

In closing, reference must be made to an extremely important branch of biochemical work about which, for obvious reasons, little can be said. The introduction of gas warfare by an unscrupulous and inhuman foe at once led some of the ablest chemical and physiological investigators in the country to devote their energies to devising the best methods of protection against asphyxiating gas and lachrymatory shells. The ingenuity displayed by the enemy in employing every conceivable means of chemical attack has been steadily met by corresponding improvements in methods of protection. These researches, often conducted at considerable personal risk, have presented problems calling for rapid solution, which demanded the highest grade of scientific work, and it is unfortunate that more cannot at present be written of the admirable way in which these problems have been solved. No line of scientific endeavour is more appealing than that of giving

to our own and allied soldiers the best possible protection against this barbaric form of attack, and the success that has been attained must be universally appreciated.

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The Croonian Lectures

ON

ADAPTATION AND DISEASE.

DELIVERED AT THE ROYAL COLLEGE OF PHYSICIANS,
JUNE 14TH, 1917.

By J. G. ADAMI, M.D., F.R.S.,
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LECTURE I.

INTRODUCTORY: THE BASAL PROBLEM OF EVOLUTION.

I CAN well imagine that in these critical days, had you honoured a civilian Fellow of the College with the invitation to deliver the Croonian Lectures, he would have found it difficult to offer to you material which he, and which you, regarded as reaching the standard attained by the long series of his predecessors. There is no Fellow of this College who does not find the war and its issues so all-pervading as to exclude full and uninterrupted consideration of other topics. Still less can one who has donned khaki and been given an administrative post do justice to the opportunity most graciously afforded to me. He could, it might be urged, select some branch of military medicine as his topic, but to do this while the war is in progress is to sacrifice perspective and afford an incomplete presentation. Administrative duties in the office have debarred me from sustained personal observation and research in the clinic or the laboratory. The time is not yet ripe to attack the vast mass of material bearing upon the incidence of disease in the army already collected by the Medical Research Committee at the British Museum. It will, in the first place, demand long months before that material is sorted and ready for statistical and other studies; in the second place, the policy of publication of studies of this nature during the continuance of the war may well be called in question; and, lastly, it has to be confessed that, taken as a whole, the material collected at the British Museum, while far in advance of any collected in any previous war, is nevertheless of value only for comparison with the statistics gathered in these previous wars. The nomenclature of disease employed—an abbreviation of that established and authorized by this College—is in many respects not sufficiently precise for a thorough analysis. There are, for example, many forms of acute nephritis and of valvular disease of the heart. The official nomenclature does not encourage any precise distinction between the various forms. My colleague, Captain G. Campbell, C.A.M.C., has afforded me evidence that gonorrhoeal endocarditis is more frequent in the army than in civil life; but the material collected—the index cards, medical case sheets, etc.—in itself gives no indication of this increase. In short, so far as I can see, the only way in which the material now being collected can be rendered valuable from a scientific point of view, is for specialists both here and overseas to make an intensive study of groups of individual

cases, sufficiently large to permit them to apply the results obtained to the sum total of the cases belonging to those groups which have been recorded.

This being so, I have almost inevitably been led to choose for these lectures the consideration of a subject which is as far as possible removed from war and its concerns, and to afford you not present studies, but a summing up of the work and conclusions reached gradually in the years that preceded the war. Taking this course, I must of necessity refer to and repeat data and deductions which I have employed in earlier writings. If, taking this course, I from time to time evince a less suave and a more militant spirit than that to which these walls have been accustomed, I must beg you to be lenient and to attribute my declension from grace to the environment of the last two years. For in so doing I must of necessity take up the cudgels on behalf of medical workers as against the upholders of what is to be regarded as the dominant biological teaching of our time. Indeed I have selected this subject of adaptation and disease, not merely because of its importance to us as physicians, but also because of its broader biological significance. The time is ripe, and more than ripe, for attention to be directed to the bearing of the investigations of the bacteriologist on the one hand, and of the student of immunity on the other, upon what are some of the most important problems of general biology. For some little time I have been impressed by the fact that the latter-day investigations in medical science are of the very highest significance to the general biologist, and that, with singularly rare exceptions, the professional biologist—be he zoologist or botanist—is superbly indifferent to them and to their bearing upon the basal problems of heredity and variation, and this notwithstanding the fact that investigations into heredity and variation are, and must always be, his greatest concern.

For this indifference or neglect there are, or may be, several extenuating circumstances. We ourselves are largely to blame in that we are more concerned with the bearing of our results upon our own medical work than with their wider biological significance. This wider significance, if it is referred to at all, finds incidental note. The titles of our articles, that is, are not such as attract the attention of the biologist, nor do we publish in the journals to which he is addicted. The *Journal of Pathology and Bacteriology*, the journals of *Experimental Medicine*, of *Hygiene*, of *Infectious Diseases*, of *Medical Research*, are as unknown territory to him as the *Quarterly Journal of Microscopical Science* or the *Proceedings of the Linnean Society* are to us. We would sooner think of writing a letter to the *Times* than to that academic go-between of men of science, *Nature*.

And then, again, just as in the old unhappy far-off days a Bart's man disbelieved that any good surgery could come out of Thomas's or George's, and the Thomas's or George's surgeon returned the compliment, just as the British medical man disbelieved such articles as appeared in the American medical journals, or, to come nearer to our own times, just as the Germans of late years, with rare exceptions, regarded themselves as the sole recipients of pathological truth, treating British and French pathologists in general as very Nazarenes, so, it has to be confessed, there is a tendency for the academic biologist to be indifferent to, if not actually to resent and throw discredit upon, the work of those who, not belonging to his particular class, are therefore to be regarded as of the nature of outsiders. This is not a revelation of the spirit of pure science, but a comforting demonstration that men of science are after all pure human beings. Underlying this spirit is a natural and in many respects wise caution in accepting the observations of workers with whose quality and standing the individual is unfamiliar. But this hesitancy may be carried too far.

If I speak with a little feeling, it is because I still cannot forget the reception accorded by zoological confrères to the most original, and at the same time most sound physiologist of his period, a Fellow of this College, my old teacher and friend Walter Gaskell, when he was led by his studies upon the functions of the nervous system—studies which have so profoundly influenced modern medicine—to trace its development, and doing this, after long years of close study of its comparative morphology, to reach conclusions regarding the origin of the vertebrata

which were not in harmony with the doctrines of descent then currently accepted. So far as I, an outsider, could determine, each link in the chain of Gaskell's reasoning was supported by appeal to observed facts, and by microscopical studies of singular interest; so far as I, a pathologist, could test his conclusions, I found that incidentally they explained, as no other or earlier work had explained, the inter-relationship between the sympathetic system and the endocrine system, between the pituitary, thyroid, adrenals, and genital organs. Nor, so far as I can weigh evidence, can I find that any essential link in the chain has been shown to be out of place. Yet the attitude of the morphologists as a body was that of the Levite of the parable; his brother physiologists could not take up the cudgels on his behalf; it was for the morphologists to test and declare the value of the morphological evidence upon which his conclusions were based, and the morphologists in general declined to notice it, but, as though they regarded it as presumptuous for him, a physiologist, to enter their territory, they passed by on the other side. And the years followed the years, and Gaskell died feeling sore that the most sustained piece of work of his life had been side-tracked by those whom it should most have interested.

Do not misunderstand me, and think that I am making a specific attack upon zoologists and botanists. As I have pointed out, we of the medical profession are tarred with the same brush. All I would urge is that just as those of us who are most interested in the advance of medical science accept gladly the results and the discoveries of workers in all branches of science, applying them to the elucidation and treatment of disease, so, in return, when investigators into the problems of medicine make notable advances, these be accepted willingly and utilized by the workers in other branches. It is not a matter of what we owe to those other branches in the first place; that is freely admitted. The renaissance of medicine in our generation is due to the labours of men like Ferdinand Kolm the botanist, Pasteur the physical chemist, and Metchnikoff the zoologist, but if the dwarf perched on the shoulders of the giant^{*} sees further and sees more than does the giant, it is not well to neglect his observations on the ground that he is a dwarf.

THE NATURE OF VARIATION.

The supreme biological problem of our times has been that of the ways and means of evolution. The fact of evolution all thinking minds accept. But as to how evolution has been, and is being, brought about is a very different matter. There is still as much debate as there was in the year following the publication of the *Origin of Species*. Upon consideration, it will be seen that the fight truly centres upon the cause or causes of variation—whether the tendency to vary is something inherent in living matter, numerous variations being produced through this inherent tendency of which those that are best fitted for their environment alone survive and are perpetuated, or whether variation is primarily and essentially brought about by the influence of forces acting from without upon a relatively labile living matter—whether, that is, variability is primarily inherent, proceeding from within, or primarily acquired, proceeding from without.

This, I would emphasize, is the basal problem of evolution, but oddly enough it has been largely neglected, the fight through all the years waging around what after all is a secondary problem—that, namely, as to whether properties acquired by the parent are capable of being transmitted to and reproduced in the offspring. Long years prior to Darwin, you will remember, Lamarck propounded that they were, as did Erasmus Darwin and Lord Monboddo; Darwin wanted to believe that this was possible, but could obtain no clear evidence, and brought in finally a verdict of "non proven." Herbert Spencer made this transmission one of his principles of biology, but Weismann violently opposed the doctrine, carrying with him the bulk of latter-day biologists, until to-day Bateson, replete with his studies upon Mendelian properties, reaches the antipodal suggestion that when a new property manifests itself in any

^{*} As might be expected, this metaphor was not original with the author of the *Anatomy of Melancholy*. I find that Firmin-Didot (Alde Manuce, Paris, 1875, p. 343) cites Haureau (*Histoire de la Philosophie Scholastique*, Paris, 1872) as deriving it, according to Johannes Sarisberienensis (*Metaphysics*, vol. iii, cap. 4), from Bernard of Chartres in the twelfth century.

individual of any species it is not new, not due to addition, but to subtraction and loss of properties already possessed; there is nothing new under the sun, and in his opinion evolution—like a squid—progresses backwards; what appears to be a new property is on the contrary *primaeval*, is the epiphany of a property possessed by the forerunners of the species which all along has lain latent, present but unable to manifest itself in consequence of the coexistence of inhibitory factors.

That I may not be thought to exaggerate or misstate let me quote in the first place from his address on heredity delivered to the International Medical Congress here in London in 1913:

Perverse as such a suggestion may appear, I do not think we should close our minds to the possibility that these dominants arise by a process of loss of some inhibitory factor. . . . Let me call your attention also to the inference which this suggestion would have on the conception of evolution. We might extend the same reasoning to all cases of genetic evolution, and thus conceive all alike as due to loss of elements present in the original complex.

That clearly this was not a passing fancy is shown by the address delivered by him at Melbourne in the summer of 1914 as President of the British Association for the Advancement of Science.

We are even more sceptical (said Professor Bateson) as to the validity of an appeal to changes in the conditions of life as direct causes of modification, upon which, latterly at all events, Darwin laid much emphasis. . . . Abandoning the attempt to show that positive features can be added to the original stock, we have further to confess that we cannot often actually prove variation by loss of factors to be a real phenomenon.

Nevertheless this must be so, and he quoted the case of the "Coral King" *Primula*, given off from the "Crimson King," concluding that here "The salmon (pigment) must have been concealed as a recessive from the first origin of the variety," and continued:

Variation both by loss of factors and fractionation of factors is a genuine phenomenon of contemporary nature. If we have to dispense, as seems likely, with any addition from without, we must begin seriously to consider whether the course of evolution can at all seriously be represented as an unpacking of an original complex which contains within itself the whole range of diversity which living things present.

And further:

At first it may seem rank absurdity to suppose that the primordial form or forms of protoplasm could have contained complexity enough to produce the divers types of life. But is it easier to imagine that these powers could have been conveyed by extrinsic additions? Of what nature could these additions be? Additions of material cannot surely be in question. . . .

And he winds up:

In spite of seeming perversity, therefore, we have to admit that there is no evolutionary change which in the present state of our knowledge we can positively declare to be not due to loss.

Now, Professor Bateson is scarce a believer in the multiple origin of animal and plant forms; we know, indeed, that years ago he traced man and all vertebrate forms from the invertebrates through an out-of-the-way animal, *Balanoglossus*; and incidentally, in his Melbourne address, he mentions this solution of the problem only to reject it. Wherefore, pushed to its logical conclusion, the Batesonian doctrine means this: that the primal unit, or units, of protoplasm, from which all living animal and plant forms have descended, possessed within it in a latent form the "Anlagen"—or, not to be beholden to our enemies, the originals—of every organ and distinctive portion of an organ or part, even down to the conformation and coloration of individual hairs and scales, and feathers and leaves, and petals and stamens, of all the manifold forms of life subsequently derived therefrom; that which was to outward seeming the most simple form of life was verily in constitution the most marvellously complex; and that, actually, what we regard as the higher forms of life are the lower, owing their development not to progressive accretions of properties, but to the reverse; so that "reversion," instead of being a degenerative manifestation, a loss of properties acquired by the species, is on the contrary a recovery of higher and completer powers. Did ever any exercise of mediaeval scholasticism lead to more perverse conclusion?

The truth seems to be that Professor Bateson and the Mendelians, so far as regards the problems of evolution, are working in a cul-de-sac. Valuable and fascinating as

are their observations for the establishment and amplification of the law discovered by Gregor Mendel, of cross-breeding of members of a species, that law only deals with the interplay of allelomorphs, that is, with the combinations and permutations of what, for simplicity sake, may be termed positive and negative unit properties possessed by the species; it only establishes the extent of the variation possible *within the boundary of the species*, and granting the existence of a definite number of allelomorphs, the number of possible strains obtainable within the limits of the species. But here it stops—save that of late workers have recognized the possibilities of fractionation of allelomorphs, and so of increase in the number of permutations and combinations. Accepting Mendelian data, I fail to see how any amount of interplay between properties already possessed by the species will result in the production of individuals which are outside the species. At most we produce different strains of that species which, by cross-fertilization with other strains, produce individuals reverting to the usual type or types. If you invest in a kaleidoscope at a toy shop, if the mirrors are set at an angle of 60 degrees, no amount of rotation will produce other than a six-sided pattern, or increase the number of colours in the pieces comprising the pattern; only from without can new elements of other colour be added, thereby producing patterns of a new order; only from without can the angle of the two mirrors be altered so as to produce, say, a twelve-sided pattern. The interplay of allelomorphs is not evolution, nor is it capable of throwing light upon the progressive development of new species. When Professor Bateson, from the vantage ground of his studies of the last fifteen years or so, begins to lay down the law regarding evolution, I cannot but help being reminded of *Bombus*, the bumble-bee—I would not say "*in vacuo bombinans*," for that was said of a zoological monstrosity, and Professor Bateson is no Chimera, but, blundering out of the fields and hedgerows into a greenhouse, and bumping its head noisily again and again against the glass because of its incapacity to drive into that head the fact that transparency and penetrability are not necessarily associated phenomena.

Nor is he alone. It so happens that some eighteen months ago, at the request of a Fellow of this College, I found myself drawn into a lively discussion with the Nestor of British biologists. I had not sought the fight, but, once in, confess that I enjoyed the opportunity of measuring my lance against so doughty a knight. The discussion arose over a statement by the Fellow in question that the biologists of to-day had much to learn by turning their attention to the results being gained in medical laboratories. And, sure enough, after protesting with not a little vigour that the boot was on the other foot—that we medical men in our ignorance of biological progress were rediscovering and regarding as our own what had been gained by zoologists and botanists a generation or so previously—Sir Ray Lankester proceeded to justify absolutely my friend's original contention by urging that one fallacy in all Lamarckian doctrine^{*} is that adopted by Herbert Spencer—namely, what he called "direct adaptation." There is really, he laid down, no such thing. The supposed mysterious, and as it were miraculous, property of direct adaptation is always due to survival by selection of organisms which varied in many directions—the production of corneous epithelium, of increased hairiness, etc., being favourable variations which hence have become inherent in tissues of all animals.

Here, then, we see the two foremost British biologists of our day, the one in doubt whether change in environment can be a direct cause of modification, and filled with these

^{*} I confess that I do not like being dubbed a Lamarckian, and that because, as commonly accepted, Lamarckianism is supposed to deal purely with the direct acquirement of alteration in structure through use and environment, and Herbert Spencer, by using the term "direct adaptation," is largely responsible for this vulgar error. The phenomena with which we pathologists deal present modification of structure merely as a secondary change; our phenomena underlie structural alteration. But in justice to Lamarck it deserves note that he expressly lays down "whatever the environment may do, it does not work any direct modification in the shape and organization of animals. But great alterations in the environment of animals lead to great alterations in their needs, and these alterations in their needs necessarily lead to others in their activities. Now, if the needs become permanent, the animals then adopt new habits which last as long as the needs that evoked them," and it is the new habits, he points out, which induce the structural alteration. (I quote from Hugh Elliot's excellent translation of the *Philosophie Zoologique*—Lamarck, *Zoological Philosophy*, Macmillan, 1914, Chap. 7.) Granting this, I hold that the physico-chemical explanation which will be put forward in the course of these lectures is something more precise and more limited in its scope than the vague "habits" of Lamarck.

doubts, accepting as a postulate that positive features cannot be added to the original stock, whereby he is led to an utterly perverse hypothesis; the other equally denying that there can be external influences of such a nature that specific variation—that is, variation in particular directions—may be induced, and taking the stand that variation is multitudinous, the favourable variation alone having the opportunity to be propagated and reproduced.

Now, if there be one fact that is constantly being impressed upon the student of immunity and the worker in pathogenic bacteriology, it is that "direct adaptation"—that is, specific modification in response to a specific alteration in environment within limits which will presently be laid down—is one of the basal phenomena of living matter. Our studies make it impossible for us to be blind to the fact that environment is capable of exerting a profound influence upon living beings, bringing about modifications of function and even of structure in particular directions. But evidently our experience and the diverse observations upon which that experience is based are unknown to the academic biologists. It is for this reason that it has seemed to me a useful task here, under the shade of Harvey, to bring together and marshal in order the data bearing upon this matter as they present themselves to us.

THE METHOD OF ATTACK.

There are two ways by which problems of this nature are *a priori* most likely to be solved, namely, by experiments upon the very simplest and, again, upon the most complex forms of life. I see that Dr. Bayliss as a physiologist casts doubts upon the value of the former as compared with the latter, pointing out that their very simplicity is in the majority of cases a disadvantage, and quoting Claude Bernard to the effect that the lower (unicellular) forms of life possess all the essential properties which exist in the (multicellular) forms higher in the scale, but possess them in a confused state, distributed as it were throughout the organism. The one organic cell fulfils a variety of purposes which in the higher organisms are relegated to distinct groups of cells. While freely admitting this contention as regards the study of function, it has to be pointed out that for problems of adaptation and heredity the unicellular organisms possess the supreme advantages of rapid reproduction, coupled in the very lowest forms (according to our present knowledge, or want of knowledge) with a complete absence of the disturbing influence of sex and conjugation. There is, that is, a greater likelihood of obtaining results, and the experiment becomes simpler where we can in the course of a few hours subject 100 generations to a particular alteration of environment, than when weeks, months, or years elapse before one new generation shows itself. In the latter case, to obtain results, either the alteration of environment must be made intensive to a degree that is likely to interfere with various vital functions, or, exhibited in a less intensive form, must act over unduly long periods. I know that certain biologists are unwilling to regard the products of asexual binary division of the bacteria, or the torulae of yeast, the results of budding, as true generations, and deny the right to regard the individual bacillus as an individual. One very distinguished biologist went so far as to declare to me that a long cultivation of a bacterial growth is "one continuous individual"—in other words, that not merely do all the millions of bacilli in a single colony, say of the *Bacillus tuberculosis*, constitute one individual, but that one individual *Bacillus tuberculosis* is spread all over the habitable world, and that tuberculosis and not the tubercle bacillus is the entity. This is an impossible position; it formulates that the "divisa" are "indivisum." The very idea of individual connotes independent existence, or if we take a wide survey and include forms like the compound myxomycetes, hydrozoa and polyzoa—potentially independent existence. When a bacillus grows and divides, and each half floats away, there is no longer one individual; and whether, as among the bacteria, the division is binary, or, as in man, one of the many billions of cells that constitute the body undergoes a similar binary division, and one of the products floats away and becomes fertilized, in both cases we deal with the development of a new generation. By the same process of reasoning, basing ourselves upon the doctrine of the continuity of the germ plasm, we might

with equal logic declare that all living beings constitute one continuous individual!

And as regards the advantage in researches upon the bacteria of being freed from the perturbing factor of sex, let me interject that, starting with Weismann and his doctrine of amphimixis, but more particularly during the last fifteen years under the influence of the Mendelians with their studies upon cross-breeding, we have been inclined to lay far too much stress upon the part played by sexual conjugation in the production of variation. In nature, in general, the tendency, if not the function, of sexual conjugation is to preserve the mean, not to induce the extreme, to perpetuate the species rather than favour the variety; sexual conjugation only preserves and intensifies a variation when circumstances favour the segregation of individuals of the two sexes each possessing the variation, or, I would add, when those circumstances actually lead to the appearance of the variation in more than one individual in a particular locality. Even if a property be dominant, with indiscriminate mating, and without segregation, such new property is apt to show itself in fewer and fewer individuals in successive generations. In simpler language, turn a highly-bred mastiff or terrier or beagle loose in a canine population, and his descendants descend to plain yellow dog. It follows, therefore, that on the whole we are more likely to obtain results where this levelling action of conjugation is wanting.

I propose, therefore, in the following lectures to take up first the evidence of adaptation as affecting the pathogenic bacteria, next of adaptation as it affects man and the higher animals, and lastly, to discuss the application of the data brought forward to our conception of disease and disease processes on the one hand, of the evolutionary process on the other.

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LECTURE II.

ADAPTATION IN MICROBES AND THE EVOLUTION OF THE INFECTIONS.

(Abstract.)

In his second lecture Colonel Adami asked whether it was not absurd to think that the infectious diseases now known to us had afflicted man from his first appearance on the planet. But if this were so, how had they originated?

After a rapid review of the present-day infections that were known to the Greeks and the Hebrews, and of the results of the late Sir Armand Ruffer's palaeopathological studies upon Egyptian mummies, the evidence of caries, osteo-arthritis, etc., in tertiary fossils, the matter of the antiquity of the bacteria was touched upon—Van Tieghem and Renault's findings in the coal measures, Drew's demonstration that chalk formations are due to the activity of the *B. calvus*, Garwood's similar observation of the part played by marine algae in the deposition of dolomite and oolitic formations, and Walcott's discovery of Cyanophyceae, forms closely allied to the bacteria, and of possible micrococci, in the Algonkian, the oldest of all known sedimentary and stratified rocks.

But if bacteria had been present from the beginning, this did not mean that the specific infections had been in existence for the same period. Zymotic phenomena must run parallel with geological. Examples were given of species which had remained unchanged over vast periods of geological time—for example, Lingula, the pearly Nautilus, Anaspides, Ceratolus, Limulus, and yet the vast majority of the fossils known to us were the remains of species which had developed and passed away.

So he considered it must be with infections. The reason why we could not recognize the descriptions of epidemics given by classical authors was not necessarily that they were fools and incapable of noting characteristic symptoms; more probably they described conditions no longer existing. It was known that in more recent times infections had come and gone. The trit test example was the sudor anglicus, or "sweating sickness." Many had made their appearance in comparatively recent times—for example, diphtheria, cholera, syphilis. In the course of the great war two new diseases had made their appearance—"trench fever" and "trench shin." But here a second principle might have to be considered: certain of these might have been present for an indefinite

period endemic in a particular locality, and then, with the opening up of trade routes, have spread rapidly. Admitting this, the conclusions reached by a study of the geographical distribution of animals and plants must also be admitted—that is, that where a species (such as the rabbit or sparrow), when introduced into another continent, showed an immediate spread, the fact that it was not there before was an indication that it had arisen at a period subsequent to the separation of the one continent from the other. Whichever side was taken in the syphilis controversy, it had to be confessed that this disease was non-existent in early Egypt, or in the Rome of the time of Galen.

How, then, was the evolution of an infection to be pictured?

If every infection was due to the diffusion through the body of the toxins of one or other particular species of micro-organism, it deserved to be noted that pathogenic microbes did not form an order by themselves, but, on the contrary, were singularly diverse in their affiliations. With scarce an exception every genus of micro-organism had its representatives among the pathogenic microbes, or, conversely, every pathogenic microbe had closely related forms differing from it in little beyond the fact that the one was virulent, growing in or upon the tissues, the other non-virulent.

Next, these closely allied species were found suggestively either growing in the cavities and on the mucous surfaces of the body, or in the water and foodstuffs taken up by the individual. This state of affairs in itself strongly indicated that at some period or other pathogenic microbes had originated from those saprophytic on the body surfaces, or existing in the foodstuffs. This natural deduction had been opposed notably by the German school of bacteriologists, with the late Robert Koch at their head, who stood out for fixity of bacterial species.

It had to be admitted that on studying the bacteria two apparently opposite and contradictory facts were to be made out: on the one hand, they were extraordinarily conservative; not only was it the case that, given the same foodstuffs and the same general environment, their characters remained unaltered, but also within certain limits, if their environment were changed, they retained their old characters with some obstinacy. On the other hand, there were certain changes of environment which led to certain and definite changes in the properties of bacteria, and, acknowledging this, it was necessary next to study the orders of variation which might be exhibited by them. These orders were usually given as three—fluctuations, mutations, and impressed variations or modifications. Of these, the first, best indicated by the varying heights of members of the same family, did not specially concern the discussion.

Evidence was brought forward to show that in the bacteria at least what were usually considered as mutations, chance variations, were in truth impressed variations due to specific alterations in environment. Whereas under the ordinary conditions of experiment certain members only of a bacterial colony took on the property of fermenting a foreign or new foodstuff, this condition of experiment could be so altered that all the members of the colony could with absolute precision be made to acquire this new property. The experiment could be so arranged as to demonstrate that there was here no question of chance variation, of the survival of those forms, and those forms alone, which had exhibited variation in a favourable direction, no question, that is, of survival of the fittest, but that there was, within certain limits, direct adaptation in the Spencerian sense, direct equilibration between the organism and its environment. Certain experiments recently conducted by Major F. B. Bowman, C.A.M.C., with the typhoid bacillus, proving this point, were given in detail.

Similarly, if an example were needed of variation by loss of factors, there was the classical experiment of Pasteur and his lieutenants Roux and Chamberland, in which by exposing any culture of the anthrax bacillus over a given period to a high temperature of growth, with absolute precision the power of spore production is lost, and now for years—and hundreds of thousands of generations—grown under ordinary conditions, spore production does not manifest itself.

If this were true of other properties, it must be true regarding virulence. Methods were known by which the virulence and pathogenic properties of bacteria could be

surely exalted or depressed. By passage of a virus through a succession of animals of one species the virulence for animals of that species could be rapidly intensified up to a certain point, while simultaneously by this procedure the virulence in respect to animals of another species could be reduced.

What was more, it was possible to take harmless non-pathogenic bacteria, and with absolute precision, and not by chance variations, convert these into highly pathogenic virulent forms. It was this direct adaptation evidently that explained the origin of the infections, and this demonstration had been given in London by two well-trained and capable observers, Thiele and Embleton, at University College. The process was most ingenious. A perfectly harmless soil bacterium, like the *B. mucoides*, was taken—a form which might be inoculated by the million into a rabbit or guinea-pig without setting up disturbance. First, by the principle introduced by Dallinger thirty years ago and more, this was gradually educated to grow, not at room temperature, but at body heat (Adaptation No. 1). Then use was made of the principle of anaphylaxis—of developing the first stage of immunity, that of greatly increased susceptibility. A small dose of the (dead) bacilli was injected into the tissues of the guinea-pig, and then eight to ten days later a second and larger dose of the living bacilli was given. At this stage the tissues were rendered so susceptible to the specific dissociation products of the particular bacterium that they were incapable of destroying them. Wherefore the bacilli, instead of being destroyed, multiplied, and became accustomed to grow in the tissues (Adaptation No. 2). And here was the point: Simultaneously they gained the property of virulence, of attacking and breaking down the tissues of their host. If now a culture were made from the tissues of this animal, and inoculated into a second guinea-pig, this without any previous anaphylactic stage became infected—the bacteria multiplied and killed it.

There was here, then, the mechanism, or at least a mechanism, whereby a harmless saprophytic microbe might occasionally in nature find the conditions under which it became pathogenic.

But this was clearly the evolution of a new property by direct acquirement—contrary to the hypotheses and dogmas of Professor Bateson and Sir Ray Lankester.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

SOME FRIENDLY CRITICISMS.

WHILE in London lately I noticed that every man with a splinted arm carried the forearm in the position midway between pronation and supination, the palm of the hand lying against the body.

1. This is contrary to the best surgical teaching, which advocates the position of full supination for the forearm. An x-ray screening shows that the radius and ulna are most nearly parallel, and furthest from one another, in the supinated position. Every man with a fractured forearm, once said a leading surgeon, should have it so splinted that he can spit into the palm of his hand. An additional argument in favour of this position is that supposing rotation of the bones of the forearm be lost, by the radius and ulna uniting across the interosseous space, pronation can still be largely accomplished by lifting the arm at the shoulder; whereas a pronated hand cannot be helped by any similar movement.

2. Too little attention is paid in hospitals at the front to the stiffening of joints, often in bad positions, while wounds are healing. Men arrive home with knees flexed, feet extended and wrists dropped quite unnecessarily. This stiffness from disuse and adhesions causes considerable trouble to rectify.

3. Half the effort to secure a perfect antiseptic to replace others arises from the fact that those in use are inefficiently employed. Most syringes are furnished with nozzles which cannot reach to the bottom of many wounds and sinuses, while an irrigator nozzle is commonly shaped like a small carrot, so that the thick end plugs the wound exit and hampers any return flush. It is no wonder surgeons thus equipped slit open all sinuses.