secondary deposits in that organ. In one case I was able to remove as much as half a pound of the liver with success.

Cancer of the Lip.

Even if the pre-cancerous stage has passed, a free removal of the disease at an early stage and while it is still local enables a very good prognosis to be given.

Mr. Butlin's analysis of 114 cases of epithelioma of the lip from the Gottingen clinic showed that 53 per cent. of cases were alive and well or had died of other diseases more than three years after removal, and of these twelve had lived for at least twelve years and one for eighteen years after operation.

Dr. Lo's analysis of the returns of the Tübingen Hospital for 1843 to 1885 and found that the cures averaged 51 per cent., but in the years from 1885 to 1898 they had increased to 66 per cent.

Mr. Marmaduke Sheild has told me of one patient from whom he removed an epithelioma of the lip with submental glands twenty years ago. The patient died last year at the age of 81, without recurrence.

Cancer of the Penis.

In epithelioma of the penis amputation yields a cure in one-third of the cases operated on.

Mr. Butlin gives cases under his own observation living and well from six to ten years later, and of some collected cases well for nearly twenty years.

Mr. Sheild has told me of 4 cases of his well after nine, seven, six and a half, and three years respectively, and I can point to one case well after fifteen years and to others at lesser periods.

Cancer of the Uterus.

Much may be done to prevent this dread disease by careful surgical treatment, and that without risk. Even when the pre-cancerous stage is passed, if women could be educated to the fact that were they to seek advice earlier, and, in fact, whenever an abnormal sanguineous discharge appears, apart from a menstrual period, in a very large percentage of cases the cancer would be recognized in its incipient condition when the disease is local, and removal could be carried out and cure effected.

In order to prove these statements I wrote to the medical attendants of all the private patients on whom I had operated, and was very much gratified to find many not only living but in robust health, from whom I had removed cancer of the uterus by complete or partial hysterectomy years ago. I made an attempt to get the statistics of my hospital patients, but found it absolutely impracticable, as nearly all the letters were returned on account of change of address, so that the statistics are limited to private patients; and as these cases were nearly all seen at an early stage of the disease, and the growth was examined microscopically after removal, I think they form a valuable addition to the statistics of uterine cancer, for every case can be verified.

They are 27 in number—12 total hysterectomies without a death, of which

1 is alive and well 8½ years after operation.

1 " " 7 " " "

1 " " 6 " " "

2 are " 5 " " "

2 are " 3 " " "

1 is " 1½ " " "

From 4 no answers were received.

14 very free supravaginal amputations of the cervix without a death, of which

1 is alive and well 11½ years after operation.

1 " " 10½ " " "

1 " " 10 " " "

1 " " 9 " " "

1 " " 6 " " "

1 lived for 5 years and died of heart disease without recurrence of cancer.

From 2 no answer was received.

1 lived 4 years, and recurrence took place.

5 lived 1 year or less, and recurrence took place.

Mr. Jessett has been so good as to furnish me with his statistics.

He has performed hysterectomy 180 times with 10 deaths, but of the last 73 cases only 1 died. Of the first series of 107 cases, very many being hospital cases were lost sight of, but 5 are living and well, 11, 10, 9, 9, and 8 years respectively. Of the last series of 73 cases, 12 are known to be well from 2 to 5 years after operation.

Professor Olshausen's experience in vaginal hysterectomy extends to 303 cases; up to 1903 he had performed 671 operations, with a mortality of 6 per cent.; since 1903 he had done 137 operations, with a mortality of 4.4 per cent. As to the ultimate issue, 70 per cent. lived for 2 years without recurrence and 38 per cent. had had no recurrence after 5 years. The extensive operation involving the removal of the pelvic glands results in a high mortality, and it has not yet been shown that a greater number of cases have been radically cured than by the vaginal opera-

tion. When once the glands have become infected a radical operation, Olshausen thinks, is impracticable.

Professor Wertheimer, who performs an extensive operation; only operates on a small proportion of the patients he sees, and his ultimate results are consequently very good—9 out of 14 patients free from disease at the end of 4 years.

Professor Zweifel, of Leipzig, of 153 operations for uterine cancer since January 1st, 1897, had 35.6 per cent. of the cases well and free from recurrence after 5 years.

These facts prove beyond a doubt that cancer of the uterus is a curable disease if diagnosed and removed in its earlier stages. It seems to be most desirable that some crusade against the neglect of the well-known early symptoms of uterine cancer should be undertaken, and that women should be warned how important it is for them to consult their medical attendants at an early stage, when, in case of doubt, a small piece of tissue can easily be removed and examined microscopically.

PALLIATIVE OPERATIONS.

[Mr. Mayo Robson then spoke of the value of palliative operations, especially in cancer of the stomach and intestines, not only to prolong life, but to prolong it in greater comfort, and in concluding his lecture he said:]

My purpose will have been served if I have been able, in however small a degree, to convince those who have the chance of seeing patients in the early stages of their illness, that in many cases cancer can be prevented by treatment in the pre-cancerous stage; that even when cancer has developed, if it be seen early and thoroughly removed it is frequently a curable disease; and lastly, that even in the later stages much may be done by surgical treatment to give real relief.

Is it too much to hope that some of the views I have enunciated may filter through the profession to the public, and serve to convince them that until a true prophylactic for cancer is discovered, they will be consulting their own interests best by seeking medical advice earlier, since to trifle with their ailments in the early stages is to lose the favourable moment and ultimately to hear the verdict—alas, too often pronounced—too late!

REFERENCES.

¹ Medical News, April 16th, 1904. ² Thèse de Paris, 1882. ³ Lancet, May 20th, 1903. ⁴ BRITISH MEDICAL JOURNAL, June 13th, 1903, p. 1362.

The Horace Dobell Lecture

ON THE

LIFE-HISTORY OF SAPROPHYTIC AND PARASITIC BACTERIA AND THEIR MUTUAL RELATION.

Delivered before the Royal College of Physicians of London on
November 22nd, 1904.

By E. KLEIN, M.D., F.R.S.,

Lecturer on Advanced Bacteriology at St. Bartholomew's Hospital.

[ABSTRACT.]

[AFTER acknowledging the honour conferred on him by his selection to deliver the first Horace Dobell Lecture, Dr. KLEIN said:]

The subject I have to deal with will best be considered under the following three heads: (1) Morphological; (2) Chemical; (3) Physiological.

MORPHOLOGICAL.

What are bacteria? Since v. Naegeli's—and particularly F. Cohn's—fundamental researches into the morphology and development of bacteria, these micro-organisms are considered as a special order amongst fungi, being spherical, oval, or cylindrical cells without a nucleus, enclosed in a sheath, devoid of chlorophyll, and multiplying by first enlarging and then dividing by simple fission, hence their name "schizomycetes." Amongst the bacterial species some have been shown in which the individual cells are capable of concluding their life cycle by forming in their interior spores of a permanent character, which spores, after the total disappearance of the remainder of the cell, become free, and are capable of preserving for long periods their germinating power, and consequently of starting new generations, notwithstanding various inimical influences of locality, temperature, etc., surrounding them.

A considerable number of observations have, however, been

recorded since Cohn's time. In the first place, the question has to be asked whether and to what extent bacteria are comparable to vegetable cells? That some bacteria, like the constituent elements of the higher fungi and of higher plants, are possessed of a cellulose membrane, is a fact which admits of no doubt; a simple micro-chemical (iodine) test proves this. Another point of similarity to the cells of the higher fungi is this—namely, that, as in the constituent elements (both young and old) of the higher fungi, vacuoles or drops of fluid appear in the protoplasm also of some species of bacteria in certain phases of their growth, and particularly when growing in media much diluted by water—that is, in which the nutritious elements are scanty and reduced in amount. In these respects a resemblance is noticeable between the cells forming the threads of mycelium of the higher fungi (*saccharomyces* or *oidium*, *aspergillus*, *penicillium*, *mucor*) and the bacterial cells. A further analogy is offered by the cells constituting the threads of streptothricheae, including actinomyces, which as to their morphology and mode of growth may justly be considered as intermediary links between the mycelial threads of the hyphomycetes and those bacteria which are capable of forming threads.

The next point deserving attention is the question of the nucleus. When living bacteria are rapidly dried in very thin films and stained, their protoplasm shows differentiation of at least two substances, one of which, generally situated centrally or nearly so, stains deeper or in a different tint than the peripheral portion. All that can be maintained, however, is that under certain conditions of staining different parts of the cell protoplasm possess different chemical affinities to the dye—affinities which in some instances seem to indicate the presence of "granules" differing from ordinary protoplasm (metachromatism).

We must conclude, however, that at present no data are at hand which would justify our ascribing to bacteria a nucleus, that is, that definitely shaped and definitely placed well-defined central substance which in the cells of higher plants and of animals plays the part of division centre. If further proof were needed it is found in studying bacteria during division. Here no appearances can be observed which would denote a division of the alleged nucleus. In this respect, then, the bacterial cell compares with and belongs to the same group as the cell constituting the hyphomycetes and streptothricheae, and is not comparable with the cells of higher plants.

The formation in certain species of bacilli of spores, conspicuous by their shape, chemical reaction, and position within the cell protoplasm, and by their high resistance to inimical influences, is a subject which, since Cohn's researches, has received a great deal of attention. Of several points in relation to spores which as yet have not received sufficient attention two stand out prominently: (1) What is the exact and intimate mode of their formation? and (2) what are the conditions necessary for their formation?

When studying carefully the formation of spores in some species, the following observations can readily be verified: while certain individual bacilli of a given species enlarge, becoming thicker and more transparent, in which the spore formation is completed in the recognized manner, there are other bacilli of the same species and sometimes even in the same preparation in which the initial glistening globule, which in others continues to grow till it reaches the size of the adult spore, remains small and does not grow up into the oval spore. These globules do not stain in the exact manner of spores, and in some bacilli are double, nor can they be confounded with vacuoles, because they are solid bodies reacting in the manner of fat globules or of some substance similar to fat, and behaving more or less like acid-fast substance, such as furnish the tubercle bacilli with their power to withstand nitric acid. *B. anthracis*, which has been carried through many generations in the laboratory in artificial culture and in which formation of adult full-sized spores has become sparse, shows the above appearances very strikingly. By continued transference in artificial media the formation in many sporogenous species, particularly of the pathogenic kind, of adult spores becomes more and more inhibited, so that after many generations the spore formation altogether ceases and the microbe may become asporogenous.

In other species the enlargement and greater transparency of the cell protoplasm is observed; but instead of a spore being formed in the enlargement a central condensation of the substance takes place in it, which stains somewhat differently and more deeply than the rest of the latter. It may even assume the fatty, glistening aspect; but here the

process ceases—no further growth and enlargement of this body occurs; it does not stain after the exact manner of spores, being less liable to retain the first stain and being less acid-fast; moreover, it is devoid of the power to germinate and to give origin to a new bacillus.

These observations justify us in concluding that we are dealing here with an "abortive spore formation"—that is, an arrest of the process. It falls short of the development of the essential part of the spore in so far as of the constituents of a real spore only the fatty matter has been formed, but not the true living substance capable of subsequent germination, which process is, after all, the essence of the nature of a spore. It is this power of germination in the true sense used by botanists which must be considered as the determining factor in what is and what is not a true spore; and we shall see that an organism merely capable of preserving its vitality under adverse circumstances does not justify us in considering it as a spore.

It had been at first assumed that spore formation in the sporogenous bacilli depends in a given culture on the consumption of the nutritive substances below a certain point—that is to say, when, owing to the continued growth and multiplication of the bacilli in a given amount of nutritive material, this latter is becoming exhausted, the bacilli close their life-cycle and form their permanent seeds or spores. But this explanation is not borne out by observation, for spore formation not only happens in the central part of the colony, which one might perhaps suspect of being the part where exhaustion of nutritive material is making itself first felt, but it can be observed quite unmistakably at the margin of a colony. At present we are driven to the conclusion that bacilli, having reached maturity, conclude their cycle by spore formation, and in this respect differ essentially from non-sporogenous bacteria in which the whole life is of a more uniform nature, consisting in growth and simple division, lasting as long as the conditions of growth are favourable for it.

I would claim for those species of bacilli which are capable of forming spores a separate position amongst the bacteria, as separate as, amongst the mycelial fungi, the sporogenous species, like *mucor*, *aspergillus*, or *penicillium*, are from the tribe of *oidium*.

Whether in the sporogenous bacilli something of an interaction of sexual elements, as sometimes occurs amongst the mucorinæ or of elements of a different nature is required for the establishing and creating the spore, is a subject well worthy of further attention. The fact already quoted of deficient progress, or rather want of further progress, observed in the "abortive spore formation" is not incompatible with such a view.

Amongst the species of bacteria in which spore formation has not been observed, there is one group which seems to stand out prominently, because, owing to its high resistance to inimical influences—drying and heat—it is credited with the possession of spores—namely, the group of acid-fast bacilli, notably the *bacillus tuberculosis*. The most careful microscopic examination of the tubercle bacilli of sputum or of other tuberculous deposits or of artificial cultures fails to show spores such as occur in the real sporogenous bacilli. The unstained spaces between the stained granules—at first thought to be unstained spores—have long been recognized as spaces free of chromatic substance.

But the high resistance of tubercle bacilli being a fact, it is feasible to explain it by ascribing it to the waxy substance, that is, the part of the bacilli which furnishes it with the acid-fast character. As a matter of fact the fatty (waxy) envelope of the real spore (of sporogenous microbes) is, according to many accounts, the cause of the high resistance of the spores, and further, spores of some bacillary species treated in the same way for acid-fast condition as the tubercle bacilli, show the same or similar staining characters as the latter, but it will hardly be said that all acid-fast parts of the tubercle bacillus—and as a matter of fact the whole of it is acid-fast—is spore.

During the last ten years or so, a good deal of attention has been directed by morphologists to the appearance of branched forms amongst some species of bacilli, and to the clubbed ends of the branches. It requires no stretch of imagination to conclude that these species of bacilli, which under ordinary conditions of growth are made up of non-branched, rod-shaped or cylindrical bacilli, under other conditions are capable of reverting to and of assuming forms of an atavistic type, a reversion not unknown among plants and animals. If this be the correct interpretation, it would lead

us to suppose that these bacillary species have at one time of their evolution been, not what we now consider them to be, namely, typical species of bacilli, but something akin to the saccharomyces form of blastomycetes—that is to say, they were originally derived from a parent stem of the nature of an oidium or saccharomyces.

There are, in support of this view, two further points. Taking, for instance, certain species of micrococci, it is not at all difficult to meet in perfectly active and recent cultures individuals which are four and more times as big as the typical cells of the species; they look like single giant cocci. Then we find such giant cocci in which a division into two or four big cocci is more or less indicated, and lastly giants in which the division into two or four is complete. We have, then, in these giants the growth of a coccus to great size without division, in which division has been greatly delayed while enlargement continues, whereby the coccus reaches the size of a torula or blastomycetes. In cultures of some strains of streptococcus one meets in older cultures on solid media with appearances which markedly resemble not fission forms such as are generally typical for cocci, but forms which suggest gemmation—namely, a typical coccus of the normal size from which projects a very small coccus. Another point leading to a similar interpretation is observed on some strains of *B. anthracis*, in which forms resemble strikingly the forms seen in saccharomyces or oidium albicans, with torula forms, spindle forms, and threads or mycelial forms.

From the facts I think we are justified in drawing the conclusion that the same phylogenetic relation exists between cocci and bacilli as between the true torulae and saccharomyces or oidium; and, further, that the bacilli themselves are the counterpart of those blastomycetes which belong to the group of saccharomyces or oidium; this would lead us to the further conclusion that, just as saccharomyces or oidium is phylogenetically considered an offshoot of the primary and true torula, so, also, the bacteria—both cocci and bacilli—are, as shown by their conditional relapse into atavistic forms, phylogenetic offshoots of blastomycetes. If this view be the correct interpretation of the phenomena enumerated, we should have to start with the true torula as being situated at the parent trunk, bacteria commencing with cocci, as representing one kind of branch, oidium another, and sporogenous hyphomycetes as the farther phylogenetic diversion of the latter. Amongst the bacteria, the typical cocci, like staphylococci, would be the primary forms, next would come streptococci and coccobacilli, and last the true bacilli. And amongst the bacilli, those species which are capable of forming true spores would represent a phylogenetic advance on other bacterial species, just as hyphomycetes, which are capable of forming spores like penicillium, mucor, or aspergillus, are phylogenetically a higher branch than saccharomyces or oidium and streptothrichae.

CHEMICAL.

I mentioned at the commencement that bacteria in morphological respects are comparable to plants. But many years ago it was pointed out by the late Sir Edward Frankland that bacteria, unlike plants, and more like animal cells, break down higher and complex organic bodies into simpler compounds, and there can be no question that this universally holds good for bacteria—namely, that either by oxidation or reduction they are engaged during their life in dissociating more complex into less complex matter. But it has nevertheless to be remembered that some, at any rate, are capable of building up higher compounds (their own protoplasm) from simpler combinations.

It is outside the scope of the subject of this lecture to discuss the manifold chemical processes with which many species of bacteria are connected, and I must confine myself to a few points bearing directly on the evolution and differentiation of bacteria.

Intracellular Phlogogenic Poison.

Certain species of bacteria—apart from the question of capability or non-capability to set up specific disease in the human and animal system—possess in their cell bodies a phlogogenic poison, which, judged by the result of peritoneal injection into the guinea-pig, causes acute inflammation (peritonitis) with fatal result; this result being uniform for all active species must be due to a poison common to them all; it is a poison lodged in the cell substance itself, and in most instances is readily obtained by simple emulsion. This result is produced equally with the living as with the previously killed emulsion. In this action there is nothing of

the nature of a specific disease, and as a matter of fact it is observed in some species of bacteria which have no action of an infectious nature on the animal body. Taking, for instance, two microbic species like *B. typhosus* and the common *B. coli*, the former being the cause of a specific disease, the latter not, it will be found that both possess the same kind of intracellular phlogogenic poison, causing the same kind of acute fatal peritonitis.

Moreover, there are some species which, though capable of causing highly virulent infectious disease, are not possessed of the phlogogenic poison. To this category belong *B. anthracis*, *B. diphtheriae*, and the bacillus of swine erysipelas.

It has been found in recent years that while certain pathogenic bacteria readily elaborate specific toxins in certain culture media, others do not do so. Thus, whilst the presence of the specific toxin of anthrax when grown in certain media (blood serum, fibrin), of tetanus in formate and glucose broth, of diphtheria in ordinary broth, is demonstrable in the medium, it is not present in the broth cultures of *B. typhosus* or *vibrio cholerae*. This holds good in a conspicuous degree with the tubercle bacillus, which, as Koch has shown by his different forms of tuberculinum, have stored in their substance several kinds of specific toxins. It is suggested that in the first class of cases the toxin is ectotoxin, that is, outside the bacterial cell—for example, tetanus, diphtheria—whereas in the second the specific toxin is inside, that is, stored up within the bacterial cell: endotoxin—for example, *B. typhosus*, *vibrio cholerae*, bacillus tuberculosis. If this view be the correct one, we should have three different groups of bacteria as regards their behaviour in artificial culture media, namely: (1) such as neither within nor without the bacterial cell produce any specific toxin, that is to say, toxin for the animal body—such are the non-pathogenic, non-specific bacteria; and (2) bacteria which possess the power to produce (secrete?) a specific toxin in the culture media (ectotoxin) or to include (store up) in their substance the specific toxin (endotoxin)—such are the true or specifically pathogenic bacteria, that is, those connected with specific diseases; (3) bacteria, some connected with infectious disease, others not, which possess an intracellular poison of a general phlogogenic character, that is, a poison which is not specific, but which is capable of causing on intraperitoneal injection in all instances the same acute peritonitis.

Putrid Decomposition.

There is one group of bacteria which, from a certain point of view, requires separate treatment; these are the species which cause putrefaction in the narrower sense—namely, decomposition of albumen with evolution of ammonia and sulphuretted hydrogen, and with the simultaneous production of those poisonous alkaloidal bodies known as ptomaines. They are capable of producing poisonous alkaloids, which, injected into animals—rodent as also carnivorous—in sufficient doses directly into the vascular system or subcutaneously cause acute severe gastro-enteritis, rise of temperature, vomiting, diarrhoea, with haemorrhage into the duodenum and rectum, suppression of urine, collapse, and death. These are the poisonous actions which were known already to Bergmann, Panum, and Billroth as “putrid intoxications.” Some of these “putrefactive bacteria” do not multiply in the normal tissues and are harmless when injected by themselves, although others, like some varieties of proteus vulgaris, are capable of growing and multiplying in the subcutaneous tissue of rodents—and probably also in wounds of human beings—of causing the production of ptomaines *in situ* and by absorption of these a fatal intoxication (fatal sapraemia).

PHYSIOLOGICAL.

Saprophytes.

It is agreed on all sides that certain species of bacteria do not under any circumstances cause any pathological effect when introduced into the animal body; when planted into the living tissues they rapidly degenerate and disappear. Bacteria of this kind thrive and grow well in dead tissues, and under the most varied conditions in outside nature are readily capable of keeping up their existence. Such species are distinctly pure saprophytes. But it must be understood that they are not necessarily connected, as their name would indicate, with any definite process of decomposition, such as putrefaction, as above explained. And it is in this sense, namely, being capable of growing and multiplying in outside (dead) nature, in natural or artificial media, that the terms “saprophyte” and “saprophytic” are generally understood, although their exact chemical and physiological rôle is not sufficiently known. The group of pure saprophytes, such,

namely, which cannot grow and multiply in the living body, comprise a very large number of species found in water, soil, air, in dead organic matter of the most varied kind, and they include various species of cocci, streptococci, bacilli—motile and non-motile—vibrios and spirilla.

Parasites.

Then there are species of bacteria which possess this essential character, that they are eminently capable of thriving and growing in the living body and setting up by their substance, or by their chemical products (namely, by their specific toxins), each after its kind, a particular specific infectious disease; this is the case with *B. anthracis*, *B. of symptomatic charbon*, tubercle, haemorrhagic septicaemias of various kinds, tetanus, diphtheria, vibrio cholerae, bacillus typhosus, bacillus pestis, and a host of bacterial species causing other infectious diseases.

Such bacterial species are true parasites, inasmuch as they are capable of thriving in and on the living tissues, each in its particular kind and with its own particular effect. Many of the parasitic bacteria are, however, also capable of thriving in outside nature in dead organic matter, although it is noticed that some do so with little difficulty—anthrax, diphtheria, cholera, *B. pestis*—whereas others are more restricted both as regards the nature of the media in which they are capable of growing (*gonococcus*, *B. influenzae*), as also the temperature at which they can grow (*pneumococcus*, *B. tuberculosis*). With Naegeli we may distinguish the parasites which can and generally do grow also in outside nature as ectogenic, from those parasites which, capable only of growing in the animal body and in order to maintain their parasitism have to be always transferred directly from animal to animal, may be designated as endogenic. While we know of a large number of species of ectogenic parasitic bacteria, bacteriology has so far, perhaps with the exception of the bacillus leprae, not demonstrated bacterial species which can be considered as purely endogenic, that is, purely parasitic in the above restricted sense. There are several infectious diseases, clinically and pathologically well defined, in which of an ectogenic existence of the causal parasite nothing is known, such, for instance, as variola, vaccinia and syphilis, horse-sickness, cattle plague and some others; in these diseases the causal parasite, as far as at present known, is a pure parasite, that is, it does not appear capable of growing and multiplying outside the animal body, but of what nature, whether bacterial or otherwise, is not known. Leaving out the *B. leprae* as doubtful, we are therefore not in a position to say whether there exist any bacterial species of the nature of pure parasites. As regards some of those undetermined microbes we have to admit that our present microscope is not capable of revealing them to the eye (being so infinitesimal as to be capable of passing through a Pasteur filter—for example, the virus of foot and mouth disease, of horse-sickness and others); and we have further to admit that there is no evidence at present forthcoming which would show that they are capable of leading an existence apart from the animal body.

So far, therefore, as our present actual knowledge goes, all the known parasitic bacterial species (with the exception of the leprosy bacilli) can, under one condition or another, lead an existence separate from the animal body—that is, are all ectogenic; in other words, can thrive also saprophytically. Whether under these conditions of saprophytic existence they retain or lose their parasitic—that is, disease-producing—power after a smaller or greater number of transferences, as many do, and as some do in a very short time (*B. influenzae*, *pneumococcus*, and others), does not alter their fundamental nature.

Beyond the fact just stated, that certain species of parasitic bacteria lose their virulence, and ultimately altogether their pathogenicity, when leading for prolonged periods the life of saprophytes, there is in most instances nothing definitely known as to this being constantly associated with alteration of their morphological and cultural characters. For some species, at any rate, such a change is disproved.

But while during this decrease in virulence the parasitic bacteria become more or less like true saprophytes, it does not follow that a true saprophyte may become changed into a parasite. There is at present no proof of such a change—nay, the reverse has been demonstrated. All that has been proved is that a parasite which, owing to continued life in artificial media, has become harmless, like a pure saprophyte can in some instances—as, for instance, by repeated passages

through the animal body—resume the life of a parasite, though there are instances when this seems difficult or altogether impossible, the microbe having permanently lost its capability to live in the animal body (some types of bacillus of plague—the pneumococcus, streptococcus of erysipelas), but it has yet to be proved that a true saprophyte can change into the parasite of a specific disease.

This phenomenon of increase of virulence is well established in the case of many species. Thus the pneumococcus passed from rabbit to rabbit decidedly increases in virulence. This fact might furnish an explanation of a phenomenon known to epidemiologists, of an epidemic starting with a few mild cases which sometimes rapidly, sometimes slowly, give rise to widespread and virulent outbreaks.

Conditional Parasites.

Besides true saprophytes and the true parasites there exists a group of bacterial species which require special consideration. While the saprophytes we have been dealing with hitherto are endowed with the power of causing specific infectious disease, growing and multiplying within the infected body, and by their specific toxins causing the particular infectious disorder, there are a number of species of bacteria which under ordinary conditions are not endowed with such a power, and generally lead a true saprophytic life. Take the common *B. coli* of Escherich, which is found in enormous numbers in the contents of the large intestine. The contents of the large intestine are practically dead matter, and these microbes present in very large numbers do not cause any diseased state while the conditions remain normal, but under abnormal conditions of one sort or another in one or other organ of the body may become endowed with the power of invading those organs, and of causing localized pathological changes, which, speaking generally, are of the nature of inflammatory processes, sometimes with severe results of necrosis.

One of the first experiments in this respect was performed by Wyssokowitch, who showed that while certain species of staphylococcus injected into the circulating blood of an animal (rabbit) are perfectly harmless, they become endowed with distinct pathogenicity if introduced into the vascular system of the same animal species, in which in one or the other organ lesions have been previously produced.

This kind of parasitism differs in an essential respect from that of the true or specific parasites—namely, in this that, unlike the latter, they are not known to produce specific toxins, and do not cause what are commonly considered specific infectious diseases. While ordinarily they behave like true saprophytes, and are not endowed with the power of multiplying in the living tissues and of causing pathogenic action, under abnormal conditions they may assume the life of parasites, and for this reason it may be appropriate to designate this group as “conditional parasites.”

Also from another point of view this group is interesting, for it indicates that species exist which might form a link between true saprophytes and true parasites or specifically pathogenic bacteria. In fact, some bacteriologists assume that with some species this is actually the case; for example, some assume that between the harmless saprophytic pseudodiphtheria or Hofmann's bacilli and the true diphtheria bacilli there exist all gradations. Similarly some observers claim a genetic relation to exist between some *B. coli* and the *B. typhosus*, while others have no difficulty in recognizing a relationship between certain pseudo-varieties and the true parasitic species of other microbes. The experimental proof for these assertions is as yet wanting.

The streptococcus pyogenes is causally connected with some forms of acute as also chronic phlegmons and of abscesses. Of recent years Fraenkel and others, amongst them Koch, have pointed out that what was formerly considered as the specific streptococcus of erysipelas (of Fehleisen), capable of producing the clinically and pathologically well-defined acute febrile exanthem, erysipelas, is no other than the streptococcus pyogenes, that is to say, one and the same species, which under one condition is the cause of simple phlegmon or simple abscess, is capable, under another condition, of causing a different and specific disease, that is, erysipelas.

We may conclude (a) that the demarcation between true saprophytes and true parasites is, owing to the existence of the group of intermediary or conditional parasites, not defined; (b) moreover, that there is evidence to show that an ordinary saprophyte under altered conditions can produce pathogenic effect, thriving in the tissues of an animal; and (c) that a

microbe under one condition an ordinary saprophyte, can raise itself not only to parasitic life, causing pathogenic action, but further to a parasitic action which is as specific as that of *B. anthracis* or *B. influenzae*, as, for instance, is the case with the streptococcus pyogenes, the pneumococcus, and possibly certain species of diphtheroid bacilli. If this be the correct interpretation of the above observations, we could not oppose the view that at a very early history in the evolution of bacteria the first branches were of the nature of "pure saprophytes," that gradually another branch became evolved out of the former, leading to the evolution of what we designated as "conditional parasites," and that to these latter the final and highest branch, the "specific parasites," owe their origin. We may further in this hypothesis find the explanation why many of the specific parasites so readily revert to the stage of conditional parasitism—loss of virulence and loss of specific pathogenicity—ultimately altogether losing the power of maintaining a parasitic life and of causing disease; and, finally, that conditional parasites may return to the state of pure saprophytes, as is the case with some varieties of staphylococcus aureus and albus, *B. coli* and streptococci.

There appears nothing improbable in the view that if the bacteria causing specific infectious disease, that is, the distinctly parasitic bacteria, were prevented from transmitting their species through, and maintaining their existence in, the animal body, that is to say, if they were reduced to a saprophytic mode of existence only, they would ultimately lose their power of parasitism altogether, and in consequence their power for further mischief, and specific diseases caused by them at present would spontaneously disappear in the future. We see an indication, at any rate, for this consummation in what actually occurs in those specific diseases which are imported into a country which is not endemic for the particular disease, for example, plague, cholera.

Symbiosis.

From a number of direct experiments made during the last ten or twelve years, it appears that a definite interaction between certain bacteria can be demonstrated. I am not referring to the fact that pathogenic bacteria distributed in water gradually diminish, and after many days and weeks (in proportion to their initial numbers), ultimately disappear, which is due, not to a destructive action on them by the saprophytic water bacteria themselves, but to entirely other causes, chief amongst them inanition, the pathogenic bacteria requiring for their maintenance highly specialized organic nutritive materials absent in the water or present only in insufficient amount.

Wherever saprophytic bacteria endowed with the power of rapid multiplication find the conditions suitable for their growth and multiplication, they naturally crowd out, as it were, the more specialized and more slowly-growing pathogenic bacteria, though the medium offers to the latter otherwise suitable conditions. It is a question of a "survival of the fittest in the struggle for existence." To the same cause are to be ascribed the well-known adverse effects which putrefaction and decomposition exert on pathogenic bacteria. The comparatively rapid disappearance of non-sporing pathogenic bacteria from the dead body, due to the rapid growth of putrefactive bacteria and their chemical products, has been established experimentally.

When I referred to a definite interaction between certain bacteria, I was not referring either to the indirect action which the products, generated in culture media by the growth of one species, are capable of exerting in some instances adversely, in others favourably on the simultaneous or subsequent growth and action of another species, either *in vitro* or *in corpore*, but to a direct influence which one species is capable of effecting on another species simultaneously present—that is, growing symbiotically either in artificial culture or in the animal body. The enhanced influence of streptococcus pyogenes on the virulence of *B. diphtheriae*, as also that of streptococci, proteus vulgaris and other putrefactive microbes on bacillus tuberculosis, may be inferred from the increase in virulence of the two diseases respectively in the noxious presence of the above species. This influence of symbiosis within the animal body of one microbe not necessarily other than saprophyte on a specific parasite, though in some instances shown to be *nil*, is in other instances distinct, in some it is antagonistic, in others enhancing.

From the experimental evidence already gained, it must be obvious that this branch of bacteriology—namely, the study of the effect of symbiosis—offers a fruitful and important field of research, important both in theory and practice. To

mention one consideration only: the greater or lesser susceptibility to infection with a particular specific disease of one person over another is justly considered a complex subject, for it must depend on the mode of contagion, on the virulence of the contagion itself, on the condition of the individual, on the presence or absence of protective substances in—that is, in the vulnerability of the individual—and probably on other at present unknown factors.

Taking a specific instance—for example, the now notorious typhoid oyster banquets at Winchester and at Southampton in November, 1902, investigated by Dr. Bulstrode. A considerable percentage of the consumers of the oysters were taken ill the next day with gastro-enteritis, which obviously was not typhoid, nor could it have been due to the ingested typhoid bacilli. In epidemics of typhoid by infected water such acute illness—namely, transitory gastro-enteritis—is not recorded. The initial acute transitory gastro-enteritis must have been, therefore, due to some cause other than that of *B. typhosus*, which latter, and in a percentage only of these cases, manifested itself in due course—that is, after the usual incubation period of ten to fourteen days. This other cause, producing the acute transitory gastro-enteritis, more abundantly present in the oysters than the *B. typhosus*, is probably to be sought in the simultaneous presence in those oysters of some pathogenic microbes belonging to the group of the *B. enteritidis* of Gaertner. As a matter of fact, in oysters which were taken at a subsequent date but from the same pit from which the above typhoid oysters were derived, I found in a percentage of them distinct evidence of the presence of bacteria belonging to the group of *B. enteritidis* of Gaertner. The ingestion of this microbe, producing the initial transitory gastro-enteritis, may have had an important influence not only in raising the susceptibility *per se* of the affected person towards the typhoid bacillus, but it may have directly been instrumental in enhancing the virulence of this latter. In the animal experiments such an enhancing of the virulence of the typhoid bacillus by the *B. Gaertneri* was directly demonstrated. May not such symbiosis be at least one of the factors contributing to the consummation of infection?

Experimentally it has been proved that the symbiosis of *B. pseudo-tuberculosis* has an enhancing influence on the *B. tuberculosis*, and from a paper by Professor Hueppe, who collected the statistics from various observers, it appears that of persons considered to be free from either general or pulmonary tuberculosis there were, nevertheless, discovered, on the *post-mortem* table, in nearly 40 per cent. tubercle bacilli in the bronchial glands, or in one or the other organ, in slight lesions only discoverable on the *post-mortem* table. Is it not conceivable that the absence in these individuals of the other enhancing microbe is the real cause of this immunity to general tuberculosis? Is it not conceivable that the terms "predisposition to consumption" and "greater vulnerability of the tissues to tuberculosis" may include symbiosis of another microbe, which prepares the ground for, and enhances the activity of, the tubercle bacillus? These are questions which experimental pathology will be able to solve, and which, in the interest of practical medicine and of hygiene, are well worthy to be undertaken.

THE "MICROCOCOCCUS RHEUMATICUS": ITS CULTURAL AND OTHER CHARACTERS.

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IN their communication to the BRITISH MEDICAL JOURNAL, January, 1903, Beaton and Ainley Walker described with considerable detail the microscopical and cultural characters of the organism which they called the "micrococcus rheumaticus." Recently I have had the opportunity of repeating their work. My results, as will be seen, are in the main confirmatory, though there are a few points and conclusions in which we differ.

The organisms with which I worked were of two different strains. One obtained from the synovial membrane of a girl with acute rheumatism and recovered from the vegetations of an endocarditis in a rabbit. The second was from a culture very kindly sent to me by Dr. Paine.

The microscopical and cultural characters of the two were practically identical; the only difference noted being that the