ARTICLE II.—*The Action of Fungi in the Production of Disease.* By TILBURY FOX, M.D. Lond.

SINCE the publication of my work on Vegetable Parasitic Diseases of the Skin, my attention has been assiduously devoted to the acquirement of new facts; and as the action of fungi in the production of disease calls loudly for examination, but is shunned by almost every observer, I trust I may be doing some service in stating the results of my own further observations and experiments. Vegetable parasitism is a subject whose study demands a great deal of patience, and the sacrifice of a good amount of time; it also necessitates a cautious regard to facts of a botanical and chemical nature, but holds out the promise of important results; it includes not merely the direct action of fungi upon man, but the as yet but little explored field of the intertransference of diseases of men, plants, and animals; that of ergotism or the influence of foods infested by minute vegetable organisms; the possible fact of the conveyance of poisons from person to person by the fungus elements, and the actual aiding of special poison production. The novelties in these and other similar matters are not of greater extent than their importance. Indeed, it is a conviction in the minds of many who have thought much upon the subject, that a not far distant time will see some of the greatest generalizations that medicine has as yet seen in connexion to this and kindred subjects.

Those who have carefully watched the matter during the past years are now confident that the time has arrived when a very fair and correct sketch may be given of this question, about which laudable but too ample differences have obtained; and, indeed, that many of the knotty points which have been made subjects of hot debate and contest, may receive a rational explanation acceptable to all. I would ask that the remarks about to be made may be regarded as constituting an appendix, as it were, to my original work.

There are three chief lines of investigation which especially deserve research, and these may be represented by the three following queries:—

1. Are the so-called parasites vegetable or not in nature?
2. What is the limit of variation in each kind of fungus? Are not most of the forms usually considered distinct, but varieties of a very *few*, perhaps *one*, species?
3. If vegetable, are fungi "accidentals" in disease, or do they necessarily directly or indirectly cause any special morbid changes; if so, of what nature are these?

To settle such questions as these requires considerable observation, and that not in a limited area: analogical evidence, derived from a search amongst facts, presented by the phenomena and behaviour of the healthy and diseased states and doings of plants and animals,

is most valuable and most *corrective* in its application. This I have endeavoured to procure.

With regard to the first point, the *vegetable* or *non-vegetable* nature of parasites. It is admitted on all sides, with scarcely one single exception, that the fungi met with browsing upon and within our surface are really of vegetable nature, that the germs are derived from the exterior, and that there is no such thing as some have indeed imagined, viz., a conversion of the elementary particles of the animal structures by a process of degeneration into those of vegetable nature, may I say a heresy that would uproot every sound principle of physiology, an ultra-polymorphism which denies *in toto* the existence of any law of limitation, the interdependence of life, and whose fair application legitimately carried to its fullest extent would arrive at a *reductio absurdam* the most amusing. There are most satisfactory reasons for rejecting the acceptance of such an hypothesis.

Firstly, The growth and independent life of the cell structures (fungi) when removed from the presence and influence of all living animal structures. I have over and over again made the elements of these cryptogams to vegetate freely in preparations put up for the purpose, and it has become a familiar experiment with me, although the failures—as one might expect—are in the great majority.

Secondly, The peculiar action of reagents, and especially liquor potassæ. As far as I know there is no animal structure that resists the action of this reagent in the same way that spores, sporules, and mycelia do; they remain practically unchanged, and do not swell up and become indistinct as is the case with the other structures. Iodine, again, detects the presence of the primordial utricle. Other behaviours might be mentioned, but I pass to—

Thirdly, The fact, of the presence of *identical* parasitic forms in the hard structures of animals, and indeed vegetables, where no (epithelial) cell structures of animal nature exist from whence the vegetable elements could spring. In bivalves, in corals, foraminifera, and a host of others, as shown by Müller, Claripede, Rose, Kölliker, and many more. The examples in the vegetable kingdom need not be detailed.

Fourthly, The want of transitional forms. Authorities rested the hypothesis of the "granular degeneration" mainly upon the supposed evidence of transitional forms. One writes, "We maintain that we have seen the cells of the rete mucosum passing through these stages of growth which have converted their nuclei into granules, the so-called sporules; we maintain that the granular condition is the normal fœtal structure of the young epidermal cell, and that the morbid condition in question is an arrest of development of these cells at their fœtal stage, and the cause of their consequent modification of destiny, no longer to rise through those higher stages of animalization which culminate in the production of

horn, but doomed in their crude condition to the lowest functions which belong to immature organic matter, viz., proliferation." I deny the existence of any transitional forms. It is easy to confound normal nuclei and sporules, but the arguments already made use of, and, especially the use of liquor potassæ, determine the difference. I believe it to be a very common mistake to confound nuclei and sporules. There is no further similarity, for directly the tubed phase (mycelial) commences all similarity goes at once. But in this particular point we will call to aid argument the—

Fifth, That the fungus elements are first visible at the upper part of the hair follicle, and migrate from above downwards towards the papilla and root; in other words, there is *a priori* evidence that the germs of the parasite are derived *ab externo*, and this is proved to be a fact by clinical observation. If the so-called fungus is a granular degeneration, such degeneration must commence where the nuclei are formed, and abundant in the early developmental stages, viz., at the formative point or papilla. Such is not the case. The earliest trace of spore, sporule, or mycelium is subepidermic and located just at the upper part of the follicle; from thence the parasite may be traced downwards to the bottom, whence it finds its way to the interior of the hair; and the effects of treatment tell the same tale. Remove or destroy every vestige of parasite, in the early stage particularly, and the disease is stopped. To affirm that this could alter such a thing as "granular degeneration" is not conceivable. Pluck out a diseased hair; if no spore is left behind, the hair is healthily formed at once. Besides there is no confirmation in the character of concomitants. The cells at the root of the hair are healthily formed; until the spores increase largely or specially invade the papilla there are no transitions. You have healthy structures in contrast with the fungus elements, until the formative apparatus is attacked. The mere plucking out of a hair could not alter the whole character of the nutrition as to bring back a disease (granular degeneration) abruptly into a state of health. The cause of the cell alteration is clearly not in the cell formation primarily, but due to some superadded influence which from without acts upon the cell nutrition.

The *variation* of fungi is a subject of intense interest at the present time. Observations crowd in upon us every day tending to overthrow the distinctions of species in most of the ordinary groups of cryptogams. The researches of Tulasne and De Bary especially have contributed to the establishment of the doctrine of polymorphism, which implies that one fungus may pass through a cycle of development, and in its different stages gave rise to many very different forms originally regarded as distinct species. Now, it is impossible to go into this matter very widely; and I therefore shall only adduce a few of the more striking examples of these forms of fungi which do not infest the human body, especially for the purpose of illustration. A striking example is afforded by the cases of uredinous plants. Mr

Berkeley experimented with "bunt" (Tilletio). He made the spores germinate; when they did so, they put out a species of stem or process, upon the which a second generation of thread-like spores was produced; these after a while joined together by transverse processes, in fact conjugated. The result was the production of a third generation, in turn giving rise to a fourth order. Bunt exhibits these four different kinds of fructification. Tulasne has also shown that the coniomycetous fungi have modes of reproduction by conidia, by stylosphores, by spermatia (pycnidia), and asci. The pyrenomycetes have been shown to possess no less than six different kinds of form. De Bary's late researches into the history of Puccinia graminis (Neue Untersuchungen über Uredineen, insbesondere die Entwickelung der Puccinia Graminis, von A. De Bary, reprinted from Proceedings of the Berlin Academy, 1865; see also Ann. des Sc. Nat. xx. p. 1) have also shown that certain species of puccinia and uromyces exhibit five different sorts of reproductive organs: *spores*, teleutospores, as they are called, giving rise to a *promycelium*, upon which sporidia appear; these germinate and give rise to *æcidia* with spermagonia; the spores of the æcidium germinate, and, entering the stomata by small processes, give rise to a filamentous mycelium, upon which is produced the fifth form of the plant, viz., *uredo;* the uredo in turn produces teleutospores. This is the cycle observed, De Bary thinks, in all uredinous fungi. It occurs upon the same, or is spread over different plants. De Bary has shown also that the notion of the old relation of barberry rust and puccinia is quite a fact. It is quite certain that uredo, uromyces, puccinia, and æcidium are forms of the same fungus.

In reference to human parasites, I have already pointed out the various relations which exist between them. Torula is the fungus around which all the others group themselves; and I must refer to my work for details, the novel matters, concern puccinia, sarcina, and aspergillus more particularly. I am now fully convinced that no true puccinia occurs in the human subject. I have seen over and over again the appearance that I believe has been mistaken for true puccinia, but have never seen anything like the spores of the puccinia. I have found the same fungus which I figured in my work several times; recently in a case of the cast of the mucous membrane of the ear, sent me for examination by Mr Toynbee. The appearances had an exact resemblance to those figured by Dr Purser in the Dublin Quarterly Journal for November 1865, where the nail fungus is described as representing appearances identical with those of aspergillus, achorion, and puccinia. I conclude that the so-called puccinia is nothing more or less than a clavate termination of the mycelium of an oidium, or, what is the same thing, is penicillium. I am also quite sure that the leptomitus is nothing more or less than the basal condition of the oidial mycelium.

In the Botanische Zeitung, No. 2, for this year, will be found some very interesting observations upon the aspergillus. Sarcina

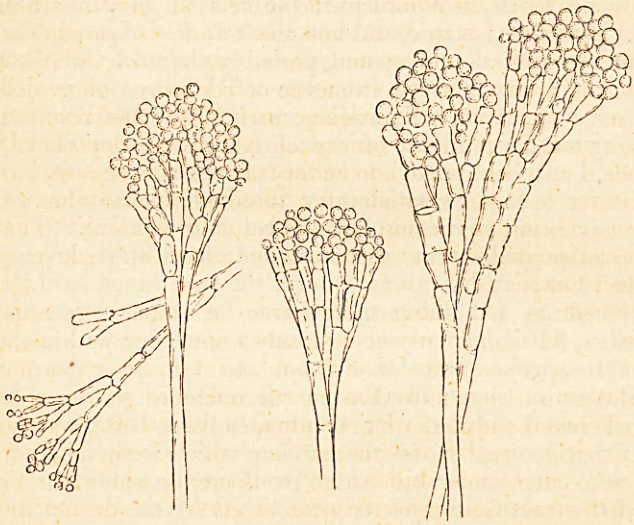
has always claimed my particular attention. It was in 1857 that I noticed a quaternate arrangement of spores, probably developed from the trichophyton, in a case of tinea tonsurans. In 1860 I produced the same by germinating the microsporon mentagrophytes; and in July 1860 began some experiments with penicillium, which gave me the same result, and indicated the relation of penicillium and sarcina. Sarcina, I stated, did not result from fissiparous division, but from a conjunction of spores, probably the nuclei of the torula cells, in their turn derived from the aerial spores of penicillium. Endogenous formation of nuclei occurring "as the result of the mixture or mutual influence of endochromes." From what I have seen since, I still believe such to be the true state of the case, but have never been able to get a satisfactory germination of sarcina, so as to produce any result that could be regarded as conclusive. The fructification of penicillium occurs in connexion with the development of sarcina, but it is difficult to connect the two things as stages. I am indebted to Dr Brinton, however, for some very important information, but it has only come to my knowledge within the last month. It appears that Dr Brinton and I were experimenting about the same time, and that he succeeded in getting a decided result, whereas I did not. Dr Brinton, in June 1860, watched the changes that took place in the sarcinæ which were taken from a patient who came under his care. Dr Brinton assures me that he obtained the fructification of the penicillium by the development of the sarcina, and that he was enabled to watch the intermediate changes. The sarcinæ became indistinct, endogenous formation of cells would appear to have taken place, and so far our experiments agree.

Further, the sarcinæ sprout, develop a mycelium, and from this mycelium the penicillium fruit is produced. The figures given are those kindly placed at my disposal by Dr Brinton, and were taken from the microscopic objects at the time of observations in June 1860.

It is important to notice that the fact of the endogenous growth of cells inside the sarcinal masses militates strongly against the theory of fissiparous division. I think it will be found that there is some peculiarity of nitrogenized matter which conduces to the development of the sarcina. It would appear, however, that the latter is, under certain circumstances, able to produce penicillium; and one thing necessary to such a result is the production of endogenous cells. This mode of increase is seen in torula, conjoined to sprouting. In the stomach, fungi are subjected to the influence of both fluid and air. Growth in fluid conduces to endogenous growth, and the influence especially of the external air to the production of shoots or mycelial threads.

Suppose we take torula; what would seem to be its changes? If it grow in fluids without much air, the formation of brood cells and the discharge of nuclei, which may enlarge and produce cells like

the originals, or conjoin and give rise to *sarcina*, all depends upon the nature of the fluid medium. If the influence of the air be slight, torula tends to take on the mycelial form, and *leptomitus* is produced, when the filaments reach the air, oidium. If the influence of air be in excess



Penicillium from Sarcina. (About 350 diameters.)

and that of the fluid slight, then penicillium results from the fructification of the nuclei of the torula cells, and the free aerial spores of the penicillium reproduce torula again. Now, suppose the influence of air be brought to bear upon the early stages of these forms, to a certain extent a modification ensues, and thus sarcina may give rise to penicillium it is supposed. Such is an indication of the line of research opened out to inquirers. If I must give my own view, it would be one which regards torula, penicillium, and sarcina as forms of one and the same fungus,—oidium and leptomitus being included in the meaning of torula.

There is also a generally received impression that, in regard to the ordinary cryptogams of the surface, little importance is to be attached to the supposed difference of form, size, and shape, as indicative of distinct species. We have only to glance at the facts of botanical knowledge which have recently been made known, to show us how utterly futile is the attempt to make fructification even a differential test. I have always contended that all the forms of trichophyton and achorion are one and the same in nature, and consider this matter proved. I have now observed in the ordinary ringworm of the surface, the trichophyton assume the features of the aspergillus more than once, or at least answer to the description given

by authorities) of the latter fungus. The other experiments I have made entirely confirm Dr Lowe's observations as to the identity of achorion and aspergillus. The chief reason for refusing to admit the identity of parasitic fungi of man is based upon the difficulty in securing an interchange between the several varieties: this shows a want of knowledge in regard to the subject in hand; each cryptogam holds its own, so to speak, and the inability to produce the one from the other is no just ground, *per se*, for denying their identity. The variety A implies the existence of certain peculiar conditions which you cannot at will produce, and these conditions will not suit the growth of B (a variety of A), nor produce a modified result, such as would make one variety change into the other. This is seen in the uredines very plainly; therefore, the fact that achorion grows as achorion on an herpetic subject, and continues to preserve its own characters, without assuming the aspect of trichophyton, is really to be expected.

But there is something more herein contained that deserves attention. The most recent researches into fermentation clearly teach that *varieties of the same fungus* tend to give rise to different results, well shown by Pasteur in reference to acetic fermentation. When the mycoderm gets into an advanced stage of development, it gives rise by its growth not only to the production of acetic acid but various suffocating compounds which the chemist knows will result from the oxidation of ether and alcohol by platinum black. The application of this principle teaches us the necessity of finding out what is the peculiar state of soil adapted to the trichophyton, the favus, or other forms, just as we should discover the chemical properties of different kinds of fermenting fluids. Take the case of sarcina, there is some very special quality of fluid which is suited to the development of this plant from the penicillium spores; if we could discover this we should get most likely a clue to that diseased condition upon which all the symptoms in connexion with dilatation of the stomach, pyrosis, and sarcinal development depend. The fact of identity, in kind, implies to a certain extent similarity of principle, as regards therapeutical treatment; but it is more important to look upon *varieties* of fungus as indices to so many different conditions of the nutrition of the patient. This is what we entirely neglect. In the British and Foreign Medico-Chirurgical Review, April 1864, a reviewer writes that, "after all, the question is one which concerns the botanist more than the medical man, be the fungi one or many it is the same thing to the practitioner." To admit such a statement as true, is, I believe, to effectually bar out the most important consideration in the whole subject of parasitic diseases. It is contradicted by every fact which has come to light within the most recent period. It will be well, if in the future we attempt to work out the peculiarities of habit, of nutrition, and other concomitants allied particularly with each separate *phase* of fungus. That is to say, pay a little more attention

to the state of the patient, without, however, neglecting the action of the fungus itself, which we shall notice presently.

It may be as well to notice that the earlier the life of the fungus, the more simple is its structure, the more liable is it to change in form, and the more certain is its so-called catalytic action. Botanists express it by asserting that the fungus is most active in its spermatiferous state. This illustrates the importance of attending to the nuclear form of parasites, to which I have always called special attention, but which has been almost disregarded by observers. It is very important in a therapeutical and diagnostic point of view. I would sooner have a hair infiltrated with large spores, than minute sporules; because I recognise in the latter case a potential activity which is absent in the former, a power of growth and reproduction peculiarly active. Many a time have I seen in an apparently healthy hair a little collection of minute sporules, which, as the hair grows, are carried up into the shaft, presently developing and bursting the hair, splitting it up into its separate fibres, and giving rise to bending and fracture.

If I were asked to sum up briefly the result of the most recent minute observation, I would say that the parasitic fungi found upon *the human surface* are varieties which cluster around the penicillium or torula in their sporular state as the type; that in the air the tendency is to the production of the aspergillus form of fructification; that the parasites of the mucous membranes, or entophytes, are more or less forms of oidium, mycelial forms of the sporous state of penicillium; that sarcina is a conjugated form of the latter. Chionypte Carteri, the fungus of the madura foot, being nothing more or less than a higher stage of the oidium, approaching closely the genus mucor. I do not comprehend the distinction of aspergillus, penicillium, and mucor *as seen on the human surface*, having noted all the appearances supposed to be characteristic of each, in the development of the same fungus penicillium taken from the contents of the stomach of a pyrotic patient. Human parasitic crytogams furnish capital exemplification of polymorphism; our duty is plain: to investigate and define the special diseased conditions which are related to and indicated by special phases of fungus.

The mode of entry of the Fungus into the System.—There is no difficulty in accounting for the access of germs to living bodies, for these germs are freely distributed and disseminated in the air. The best illustration of this fact may be noted in the experiments of M. Bazin (Gazette Méd. de Paris, July 30, 1864), which consisted in passing currents of air over the head of a favus patient, and thence over the open mouth of a jar containing ice. The ice cooled the air, causing the deposition of moisture, in the drops of which the achorion sporules were detected. The same thing may be shown by holding a moistened glass slip near the head of a patient, and just rubbing his scalp freely. Of course, actual contact is much more effectual in the implantation of germs. But, without delay, let us suppose that the sporular elements find their way to the

human surface; how get they deeply into the tissues? In various ways probably. Let us take a general sketch. The greater the degree of moisture and heat, the better is the chance of entrée.

First of all, the fungus elements may enter by fissures or natural orifices; for example, in ordinary ringworm the sporules lodge themselves at the opening of the hair follicles, and presently get beneath the epithelial scales. We shall see, directly, how. A great many experiments have been made at different times, upon this point, in the case of plants. De Bary (Die gegenwartig herrschende Kartoffelkrankheit, ihre ursache und ihre Verhutung. Leipsic, 1861), found that, in terminal filaments of potato mould, so-called zoospores were formed, which bud, protrude filaments forming a mycelium which has the power "of penetrating the cellular tissue in twelve hours, and when established there it bursts through the stomata of the leaves." This "boring" operation is quite likely to occur, especially where the structures are diseased; as, for example, the muscardine in silkworm, in diseased mucous surfaces or epithelial changes: here the entrance by continuity is easily accomplished by the growing filament. It has been supposed that mycelium may get within the shaft of the hair in some part of its course, in this way. I do not believe it. If a fungus finds an entrance, it is either through a cut end, a distinct fracture, or, what is usually the case, the soft growing root. A good deal of doubt has been expressed as to whether the spores could find their way into the interior of plants through the stomata. It seems pretty clear that the latter are not sufficiently large for the occurrence. There can be no question, however, that, in a large number of instances, the spores send out little processes, which get into the plant through the stomata. Here the recent experiments of De Bary help us again. They are noticed by Mr Cooke in his admirable popular work on microscopic fungi. This observer took a large number of common garden cress plants, placed their roots in water containing zoospores, and though the former became covered with these latter bodies, yet not a jot of evidence of penetration occurred. De Bary, however, found that if the cotyledons or seed-leaves are watered with fluid containing zoospores, that slender tubes put out by the zoospores enter the stomata, the terminal ends enlarge, branch out, and become the centres from which a ramifying mycelium is produced, which presently shows itself externally. De Bary tested 105 plants in like manner and under similar circumstances, with water free from zoospores, and without the production of any sign of rust in these. De Bary concludes that plants are not infected by spores entering through the roots or leaves, but through the medium of the seed leaves of cotyledons. But it is probable that the fluid contents of the spore cells may be absorbed and give rise to disease. The Rev. Mr Berkeley, several years ago, found that the germs of bunt placed in contact with seeds, infected them, without there being any evidence to show that any spore or mycelial thread had effected an entrance. It

seemed as if the granular fluid contents were taken up by the plant and caused mischief. It is possible that minute threads might have penetrated the seeds nevertheless. There is, however, no difficulty in supposing the granular contents of spores (sporules) capable of reproducing the typical spore. But, in the next place, there cannot be a doubt but that in the human subject the germs of the fungus find their way to the roots of the hairs, and are carried bodily upwards into the shaft in the process of growth, developing as they go, till at last they degenerate and break up the fibrous structure in which they are. By analogy we should quite expect that such a thing is possible, and, indeed, of frequent occurrence in the case of the tender roots of plants; and this is more likely to happen when the contents of the original spore (which is as large as the spongiole cell) happen to be discharged by bursting. Moreover, it is quite clear that the germs of parasites enter at a much earlier period than we are apt to imagine, and lie dormant, brooding mischief till the favourable opportunity arrives. De Bary proved this in the case of the white rust (cystopus) which hybernates as it were in the sub-epidermal structures during the winter, till the spring arrives. In addition, the fungi "make head," so to speak, into structures in virtue of the chemical action which they set up. This is best seen in the hard structures of animals. Carbonic acid is given off at the terminal cells. This dissolves the lime of the shell and allows the parasite to effect an entrance most easily. The experiments of Wittich, quoted by Robin, all tell in the same direction. Panceri has come to the conclusion, however, that in the case of the egg, the minute germs effect an introduction through minute microscopic holes which exist in the shell. *Lastly*, traumatic lesions afford an easy channel for the conveyance of fungi to deep structures. This is what happens in the mycetoma or fungus foot of India.

We have then, as modes of entrance — (1.) That through natural orifices; (2.) That in which the growing force forces the mycelial thread beneath the layers of the superficial tissues; (3.) That in which processes shoot out from the spore and enter by such openings as stomata; (4.) That where the cell contents are absorbed; (5) That in which the spores are carried bodily inwards by growing parts; or (6.) dissolve away the opposing structures by chemical action; or (7) enter by traumatic lesions. In each and every instance the germs of parasites are derived *ab externo* and not generated *spontaneously*.

There are some special circumstances that deserve comment. It has been asserted that microscopic entophytes have been discovered in close cavities utterly cut off from communication with the external air. But these instances are open to grave objection; fungi have been found in the fluid of the ventricles of the brain, which, however, was allowed to stand all night exposed before it was examined. Again, it is asserted that in the kidneys the like has been found. This is

open to exactly the same objection. The case of the egg parasite has been explained away by Panceri; and it has yet to be shown, supposing the urine has ever during life contained fungus elements, that air cannot enter the bladder. The case of germs of vegetable nature in the blood current presents some difficulty; but even here the most considerable caution is needed. We know that fungi spring up with enormous rapidity; and it must be proved that those spores and mycelia are present at the moment of death, nay during life, before we can give credence to any theory which asserts that they have been present and introduced during life, and not by a communication with the external air. It is still a question whether the endosmotic action of the villi may not be able to account for the presence of cryptogams in the blood current. As far as the facts of vegetable parasitism go, we are bound to deny any such occurrence. And, upon analogical grounds, I venture to assert that the entozoa found in muscle, which have lately caused no little sensation, are not vegetable in nature. Should they be proved so, it will entirely alter the whole subject of vegetable parasitism; for we are justified at present in asserting that there is probably no known instance of a growing plant in any situation not in direct or possible communication with the air. I am bound to say that Dr Thudicum believes in the vegetable nature (see Report of Medical Officer of Privy Council for 1865) of the rinderpest entozoa (?).

I pass to the consideration of the part played by fungi in diseased states. Two theories the most opposite in intention have been held by writers and others, so opposed that really the conclusion is forced upon one that both *must* be wrong and a middle belief correct. Whilst one batch of inquirers affirms that parasites are accidental, another contends that they are the essential cause of those diseased conditions found in "association" with their growth. Ehrenberg, in speaking of organized parasites at a time when the exact nature of many of them was indistinctly recognised, said, "that there is more cause for wonder at the limitation of their effects by the actions of living bodies they inhabit, than at any morbid effects they appear actually to produce." It must first of all be noted that there are certain conditions which are peculiarly favourable to the growth of vegetable parasites. The latter are ubiquitous, capable of resisting the action of heat, cold, and decomposition, have a tremendous and rapid power of increase, and will remain for a very long time in a state of inactivity; yet, notwithstanding all this facility, there are certain states of organisms against which they fail; which will somehow resist their inroad and attacks; and it is now clear that though parasites may for the moment get a temporary hold, yet they will not flourish upon a typically healthy surface. This is a fundamental truism that must be observed in reference to therapeutics. For rusts and mildews prevail in direct ratio to the wetness of the season, or after drought, as in the pea or hop; damp itself is very favourable, and where there is much

drought the vigour and the circulation of plants are diminished very considerably. When plants are very ripe also, there is a less degree of vitality present, in consequence of the cessation in great extent of the circulation and vital connexion between the fruit and the stem. The same thing holds good in every instance where animals, plants, or men are attacked. We may instance the case of muscardine. The experiments of Claude Bernard also showed that frogs kept in captivity got out of order, and aphthous conditions arose. A healthy frog brought near its diseased fellows "set contagion at defiance," but unhealthy frogs were at once attacked by the vegetation flourishing on the aphthous surfaces of others; and the case of favus in man, or scab in sheep, of which an account may be seen in the Gardener's Chronicle for April 24, 1864, as illustrative of the fact under notice.

There is always a certain resistent power about all healthy living beings; and a certain amount of fungus, however it acts, may be present without giving rise to what one can possibly call disease. In young life, of course, one would expect that fungi would obtain a hold more effectually than in old life; and it is very remarkable that the white rust before referred to, according to De Bary's experiments, should effect an entrance into the system of the garden cress, by attacking the young leaves or cotyledons. The young and tender stage becomes an easy prey; and this is exactly what we find in the human subject, the young being most liable to ringworm.

Taking all things into consideration, it is clear that parasitic disease, or—as I have named it generically *tinea*,—cannot be explained by either of the conflicting theories I have referred to, but consists of three distinct components, which must be recognised, if the physician would cure his patient well and quickly.

1. A certain state of soil: in speaking of the polymorphism of fungi, I noticed that each fungus appeared to require each its special kind of pabulum.

2. The access of air, and the presence of heat and moisture,—the conditions necessary to support the life of fungus. And,

3. The introduction from without to and action upon the body of the vegetable germs.

The first and second will be passed over without comment: my remarks are specially intended to define the action of the parasite in the production of diseased states. Now fungi are not "accidental" and unimportant, but act in several distinct ways when once they take hold and grow upon the surface. This is important; if we insist upon some *one modus operandi*, we shall assuredly find our position utterly untenable. They act then (often in more than one way in the same instance be it remembered),—

Firstly, mechanically.—If you simply rub into the surface some of the fungus elements, in many cases you get what we know as irritation. This is seen in the ordinary herpetic ringworm of the

surface, where the mycelial threads range over the skin beneath the epidermis, and lead to erythema, etc. A very remarkable case is recorded by Dr Kennedy of Dublin, in which a quantity of flax powder was inhaled by a lad, who became attacked with measles and peculiarly severe local dyspnœal symptoms, evidently dependant upon the direct mechanical irritation exerted by the fungus elements. In the case of mildew of plants the same thing is seen, the threads of the mycelium grow and force asunder the tender structures near it. Now, it is this mechanical action exerted by the growing force which is at work, especially in ringworm. The fungus finds its way to the sub-epidermal space, from thence to the hair follicle, irritating and interfering mechanically with the growing parts, enters into the hair, and by its increase and development simply splits up the hair shaft, appropriating also its juices, and rendering it all the more brittle, and therefore the more easily destructible. To declare in such a case that the parasite is accidental in any sense of the word is to turn a deaf ear to the plainest voice of facts; but this very action can be isolated. I have performed a good many experiments at different times with diseased hairs out of the body, and occasionally it is possible to get a hair containing spores, which spores will germinate and actually produce the splitting up of the hair, and the other changes that are observed in ringworm. In fact, *to produce the lesion of ringworm out of the body.* In those instances in which the mycelium abounds, the epithelium seems to suffer particularly. On the mucous surfaces there are no such structures as hairs which form a lodgement, so to speak, for the fungi, and hence no marked results are visible. The cells of the tissues are invaded and destroyed, the mycelial phase abounds and ramifies in the secretion, and not in the tissues themselves; but there is the same *capability* of damaging when parasites attack only the internal surfaces. If we would wish for examples of the enormity of the force exerted by a growing fungus we have only to confine some of the more ordinary varieties and see the result. Now, it so happens that no other agent can produce in disease the same kind of action as that exerted by a growing fungus,—such as splits up the hairs in the way in which this is observed in tinea; and it is this state of things which I regard as the pathognomonic lesion of ringworm, viz., the mechanical action of the parasite upon the hair and epithelium, in connexion with other minor changes.

One word as to definition. I use the word tinea as the generic term, and particularize each variety by the terms favosa, tonsurans, sycosis, vesicolor, circinata, etc. The tinea signifying especially the diseased state of the hair and epithelium. Now, take the case of sycosis, which means inflammation of the follicles of the chin and lips. It may not be caused by a parasite; but undoubtedly cases are sometimes caused by a fungus, and these I called tinea sycosis. Again, tinea circinata means the parasitic herpes circinatus, and

tinea decalvans the baldness produced by the fungus (microsporon Audouini), as distinguished from alopecia, non-parasitic baldness, the result of many different causes. The term tinea is very distinctive.

Secondly, Fungi act by inducing local chemical change.—They absorb oxygen and give out carbonic acid, and, as has been before observed, they hereby secure to themselves the power of penetrating calcareous structures. In addition, a large amount of gas is evolved, as in cases of sarcinal disease. Moreover, they lead to fatty degeneration. If any one will take the trouble to examine carefully some of the old stubs in favus, he will notice a certain amount of fatty changes going on in the cell structures. Remove a hair of this kind loaded with sporules, and get the latter to germinate, and the fatty alteration goes on at a rapid rate, till after a time a large quantity of crystalline fat is produced. Now, this will not happen unless the fungus germinate; but happening, it is worked out in accordance with the views lately put forth by Dr Bence Jones, and was expressed in precise terms in my book on parasitic diseases. It has been remarked by many observers that fat is always present in considerable amount in connexion with the development of fungi. M. Signol believed that fat very much favoured the development of bacteridia. Perhaps the very best exemplification of the association of fatty change with parasitism is that afforded by the case of the madura foot, where the oily matter is so very abundant. The tissues degenerate, and the crystalline fat is so varied and peculiar as to have actually misled observers into the belief that it was a form of fungus. Now, it becomes a question whether fat assists the development of fungi, or whether the latter attract fatty matter, the fungus forming a centre of attraction for crystallization, or the fatty change be the result of cryptogamic growth. I adhere to my original belief, and Dr Carter is of the same opinion, that the fatty change is coincident with and a consequence of the growth of fungi. Nitrogenized and other matter becomes fatty in this way very readily. Of course, under such circumstances the fungi become a centre of attraction for the fat. It is a chemical action entirely, as far as the degeneration is concerned; a process of oxidation which the fungus induces under favourable circumstances in connexion with the performance of its own vital functions.

Thirdly, Fungi act as conveyers of poison.—This is a mode of influence which has been altogether disregarded by observers. If the endogenous pus cell can convey the noxious poison of an acute disease, why may not the elements of a fungus act in a similar capacity? Recent research has shown that all fungi exhibit great transportability. Now, what action have the cells afloat in the air of hospitals during the time of epidemics, such, for instance, as cholera (see Dr Thomson's Observations at St Thomas's in 1854); may they not take the virus of a hospital gangrene from one patient to another, acting the part of a fomes in the very same way, com-

paratively speaking, that man himself does? Suppose we inoculate with fungus elements, it is clear that in some instances symptoms ensue (as in Dr Kennedy's and Salisbury's cases) before the onset of local symptoms. Again, the fungous elements would appear to be most active in their early stage, that is to say, when the poison produced simultaneously with their development is in its freshest and most active condition. Again, respirators in epidemics have been found to be efficacious. And, lastly, direct experiments, upon plants especially, have shown that disease may be produced by the contact of fungus elements, when there is not a particle of evidence to prove that sporules, spores, or mycelial threads have entered the organism of such plants, but where there is the greatest probability that the granular and fluid contents may be the poisonous compound which, when absorbed, gives rise to the subsequent malady. It is not unlikely that in catarrh and influenza especially such a conveying property may be at work. We have the strongest possible amount of analogical evidence in regard to animal life, comprehended in all the details of the "animalcule theory of disease,"—a doctrine that may be pooh-poohed by some, but which must erelong be fairly discussed. One might give a great deal of very interesting matter under this head. Those who are interested in the subject should read Sir Henry Holland's article in his Medical Notes and Reflections, 4th edition, I think, on the Animalcule Theory of Life, and Dr Daubeny's essay in one of the volumes of the Edinburgh Philosophical Journal, some few years back. The occurrence of epidemics, be it noted, moreover, is often associated with the peculiar prevalence of various moulds and mildews,—a source of terror and superstitious horror in bygone time, which gave rise to the idea of a raining of blood. Plutarch refers to such an occurrence in the plague of Rome. Hecker, in his work on the Epidems of the Middle Ages, also associates it with the disasters of 789 and 959. The spots were actually observed on garments, and called lepra vestium; *signacula* was another term. In 1502 and 1503, it again frightened everybody. Agricola was certainly one of the first to give a rational explanation, he attributing it to the appearance of a lichen. The fungi attacked walls, bread, cheese, meat even, and garments, in Venetia, in 1819, and also articles of food, and garments, and all fruits, during the years following to 1829. And is there not something similar observable now-a-days? Have not we had some very remarkable and severe epidemics, and have not fungi been remarkably abundant on vegetation? I will not theorize, but merely just draw attention to the coincidence. The particular action of fungi now under notice will perhaps be better appreciated in connexion with that now to be described.

Fourthly, which looks upon these organisms as developers of poison, and comprehends Dr Richardson's forsaken theory of zymosis,—a doctrine that appears to me most satisfactory. It has been sug-

gested at different times by one and another observer that the fungi themselves induce change *actually in the circulating current* sufficient to account for disease, either by setting up a kind of fermentative action in the blood, giving rise to the production of a specific compound,—a poison, in fact, just in like way to that which happens in ordinary fermentation, or setting up change by catalysis,—a wonderful enigma. Others affirm that no poison is produced in the body itself, but that the fungus helps out its increase when once introduced into the system. For my own part I cannot believe that any very important change could be induced by the growth of fungi in the blood current. The presence of air is so very necessary; and not only mere presence, but such as is implied by a direct communication between the growing vegetation and the external air. Outside the body, or in the cavities which communicate with the air, many very important and frequent changes are induced without a doubt.

Dr Salisbury is a careful observer. He declares, and as far as I know holds to his opinion, that a form of disease, if not identical, at any rate very like measles, results *under certain circumstances* from the inoculation of the fungus of wheat straw. Dr Kennedy has given confirmatory evidence. Does the fungus *per se* produce the result, or is it a conveyer, or is it the producer of the poison outside the body in the musty straw?

Dr Richardson, quoted by the late Dr Barker of Bedford, records the onset of erysipelatous mischief from a like cause. In France the most serious inflammatory mischiefs of veins and lymphatics have followed wounds inflicted with instruments used to cut off the diseased vine-shoots. Dr Collin, the medical inspector of the waters of the St Honoré, Nievre, records even fatal results. MM. Demartes and Bouché of Vitrany have also investigated this subject, and conclude that the oidium *can* produce such mischief, but they suggest some sort of coincidence between the special development of the oidium and the occurrence in greater frequency of inflammatory disease. It is to be hoped that the French Academy will, now it has taken note of the subject, enter into a full investigation of it. It is true that ill effect does not always follow experiments with the oidium. MM. Speneux and Letellier failed to produce anything beyond a little redness and irritation by inoculating people with the rasping of leaves diseased by the oidium (Pract. Jour. of Med. and Surgery, Nov. 1864); and MM. Leplat and Taillard on the one, and M. Wertheim on the other hand, came to opposite results by injecting fungus elements into veins of dogs and other animals. There can be no questioning that some fungi are more hurtful than others, and much depends upon the concomitant conditions. The arundo donax, the large reed of the south of Europe, is attacked by a black rust, and those who cut the reeds suffer from very violent headaches; and it is affirmed by M. Michel that the spores produce a papular rash on the face, with much

swelling, and a good many serious general symptoms (Yearbook, 1861–2). It would seem that the fungus, *per se*, is not sufficient, but that there is something in addition which is intimately connected with the vitality of the fungus. This would seem to be taught by the case of bacteridia. Whatever they be, no injurious results happen unless the medium itself in which they exist contain some peculiar virulence of its own. Just as in the case of inflammatory attacks caused by oidial inoculation. The power of vegetable organisms to induce transformation, which must of course be accompanied by distinct chemical change, has been well exemplified by an experiment of M. Lemaire, who took some beans, placed them on a moist sponge, and found that bacteridia soon sprang up, before germination, being succeeded by monads and vibriones; and the like happened after the soil used had been heated to a red heat. Now, if a small quantity of phenic acid (which has the property of suspending infusorial development) was added, the germination came to a standstill until the phenic acid evaporated, when it recommenced. M. Pasteur's experiments on acetic fermentation tend to the like result; and M. Trècul's observations lead to the belief that the change induced in solutions by fungi, as in the case of alcoholic fermentation, depends upon the performance of the nutritive act of the vegetable cell. The fact is, the fungus, when growing, necessarily decomposes the medium, and induces chemical change, whilst the result depends upon the composition of the material acted upon. In like manner, it is conceivable that the fungus of wheat straw acts upon the juices of the stem, producing some subtle compound; bacteridia do the same in *sang de rate* and the oidum in the vine disease.

It has been supposed that the poisons of measles, influenza, cholera, nay, asthma, and some other acute diseases, may be produced in the way indicated; but it must be remembered that two or more of the modes of action already noticed may be conjoined; that is to say, a fungus may act mechanically as a conveyer and developer of poison at the same time, and in one case. But not only acute but chronic diseases are produced. I refer to the large class of instances in which vegetable parasites induce slow changes of deleterious nature in articles of diet, giving rise to "ergotism." Bad grain, bad potatoes, bad rice, bad maize, are illustrative. The late Russian epidemic, the Irish fevers, pellagra in Lombardy, gangrene in sheep and beasts, ergotism in horses, have all been regarded as taking origin especially from the play of ergotized foods. In the group of *chronic* maladies the material acted upon by the fungus is a solid. The access of air is not so perfect nor so free; the moisture is considerably less; all of which tends in great measure to account for the difference of the quality of the resultant morbid product. The productiveness of grain so infested is considerably lowered. Sir H. Davy proved this long ago. He found that diseased wheat yielded from 21 to 65 per cent. of nutritious

matter against the 95 per cent. of the healthy grain. It has been suggested at various times that the degeneration of rice by parasitic action gives rise to the formation of products which occasion very severe symptoms of intestinal irritation, resembling dysentery, and that œdema of the leg often follows. And it is not unlikely that the many peculiar ulcerative conditions of the lower extremities are favoured by the quality of food and induced in like manner. The diminution in the productiveness of the silkworm affected by muscardine affords a capital instance of analogical occurrence. The statistics issued by the Chamber of Commerce of Turin show that although formerly about some 650,000 myriagrammes of cocoons were produced in the country, in 1864, there were 525,000, and last year 283,000 only. I have been paying some little attention to the case of mildewed cotton,—hunting after *illustrative* facts,—and I find that the germs of mildew are really present in the cotton in its rough state, as sold in the market before it reaches the manufacturer. It of course is possible that the processes through which it passes in the hands of the latter may destroy all the vitality of the fungi, but this is not certain; but if it really does, still the fact of the presence of mildewed germs in vigour would imply the existence of a certain degree of deterioration in the actual fibre itself, perhaps induced by the bad cultivation or growing of the original plant,—a point of no mean interest to the merchant. It would make the fibre less able to resist the action of the size and other agents used in the manufacture into stuffs.

I have spoken of things going on outside the body, and then introduced to it; but within a recent time, certain facts have come to hand showing that under special conditions, though good food be taken into the stomach, yet, in the digestive tract, changes of objectionable character may be induced by the agency of fungi. I have to quote Dr Salisbury again as my authority. He believes that chronic diarrhœa in the army is caused in this way (see the Report of the Surgeon-general of Ohio, in the Amer. Jour. of Med. Sciences, 1865). Wherever there is a poor amylaceous diet, and there be retention of the food, the torula, almost always present, grows, and in so doing induces fermentative changes, with the evolution of gas,—the production of intestinal irritation and diarrhœa,—the torula vegetating into a myceliated "algoid" mass, which may be observed in the fæces; and it appears that its amount is in direct relation to the severity of the disease; the production of sugar being rapid and detectable in the mucous tissues. The green stools of children are so produced, and Dr Salisbury thinks also that semi-paralytic symptoms ensue. The case of sarcinal disease is on a par entirely; deranged digestion, detention of food, the presence of penicillium, and the evolution of gas with the formation of sarcinæ; vomiting is the result of gastric, as diarrhœa that of intestinal irritation. The stomach in the former, and the intestines in the latter, getting semi-paralyzed, at least losing tone and getting relaxed. In both

cases there is the mechanical action of the fungus and the induction of chemical changes within the body. The case of diseased foods is one of surpassing consequence, and deserves all the attention we can afford to it.

The quality and character of the poisons or products of this fermentative act are matters of no little interest. Dr Richardson has lately deserted the zymotic, and given his adhesion to a new theory, which regards the poisons as of an alkaloid character,—basing this position upon the supposed isolation of the pyæmic poison; however, further experiment is needed to establish the truth of the new doctrine. If the poison of so-called zymotic diseases be chemically inorganic, how comes it that nothing of the kind can be obtained by chemical analysis? The diffusion and spread of disease is opposed also to such a view. There is a power of increment about these viruses which is very marvellous and peculiar. There is also a vital principle or act which is very distinct. Another feature worth notice is this, that the effect of the poison does not seem to be, as is the case with mere chemical agents, proportionate to the dose, so to speak, but to the peculiar virulency, which varies as much as the state of the nutrition of the organism acted upon. The viruses certainly, as to their characters, vary considerably, and are not *definite* in the way that we would expect if they were of an alkaloid nature. Independently even of these kinds of influence already noticed, fungi, in the fifth place, would seem to possess inherent noxious qualities in some cases. Just as insects have the power of producing special poisons, so may fungi in a much less degree. The anamita muscaria affords a resinous principle, which chemists isolate. In other cases—for example, the mushroom—there is evidenly an alkaloid, as MM. Sicard and Schoras have shown (Journal de Pharmacie, 1865); but the action of it is different from that of viruses altogether.

Now, I have mentioned five different ways in which fungi may act; and these may be summed up as follow, being divided into those which are direct and indirect. Directly, they may act mechanically, or by inducing local chemical change; indirectly, by bringing about changes in substances out of the body, which are brought to influence the latter; by setting up a kind of fermentative action in part due to the oxidation consequent upon the nutritive changes in the plant, or by giving rise to products having an acute or a chronic action, and whose nature is at present a matter of doubt.

And now I am prepared to meet the hypothesis that parasitic disease has nothing essential to do with the development of parasites. Mr Hunt takes the boldest view in the ranks of the opposition, declaring that the causes of parasitic disease are four, and four only, —uncleanliness, atmospheric impurities, deficient exercise, and contagion. I take my stand upon the mechanical action of fungi, and the induction of fatty changes, and defy any one to shake me the

least from my footing. Mr Hunt states that the above four conditions "poison the blood, producing not only their immediate effects in the form of parasitic skin diseases, but laying the foundation probably of more serious disorders, manifested in after life by the presence of lumbrici, ascarides, tape-worm, pediculi, fungi, hydatids, tubercles, and perhaps cancerous germs, in the various organisms." What does this mean? That these varied mischiefs have not each their proper cause, but arise from one and the same influence. This is surely either subversion of the logical definition of cause—unconditional sequence—which is so tenaciously upheld and received as our only true belief. I grant that the four states lower the nutrition of the system, and make it more fit for parasitic growth; this is only one item of the total. The true state of the case I take to be this. That there is a necessary nidus, which is exalted by some into the position of the supreme disease, to the negation of any and every effect produced by the fungus itself, which finds the soil congenial,—a soil associated with bad living, and bad hygiene of all kinds; the fungus growing acts in the various ways already detailed; in ordinary cutaneous affections, the effect upon the hair and epithelium (mechanical and chemical) being *pathognomonic.* Parasitic disease, then, is a composite affair, consisting of mal-nutrition, a growing parasite, and certain effects of such growth.

There is yet one category of facts that needs a word or two of comment, viz., the comparative pathology or the intertransmission of parasitic (vegetable) maladies. In addition to what I have given in my work, a good deal of information has been accumulating. It is now admitted that the transmission of the common ringworm of the surface from animals to man is very common. I am informed upon good authority that this is of very frequent occurrence in Australia, the milkers of cows especially being largely affected. Professor Gerlach (abstract in Ed. Vet. Rev., vol. ii.) has noticed it in dogs, horses, and oxen, and in man, but the sheep and pig seem to offer exception. Dr Frazer (Dub. Quart. Journ. of Med. Science, May 1865) contributed a paper, "Remarks on a Common Herpetic Epizootic Affection, and on its alleged frequent Transmission to the Human Subject," containing cases. This gentleman quotes Mr Brady, and Mr Whitla, in reference to other instances. Dr Fehr has noticed in Switzerland the transmission from cattle to man. I can confirm by my own experience the truth of these statements. I do not mention any old cases, such as mice, affecting man; but my friend Dr Allchin informs me that he has seen the transmission of mange from a cat to a child.

Now, I might argue just in like manner in regard to the animal parasites. The two classes of cases are mutually illustrative of each other's *modus operandi.* I take the case of scabies. The acarus demands a suitable soil. It has been pretty well shown, in animals especially, that acari will not grow on all surfaces, but only on those whose hygienic condition we have reason to know from the

circumstances that have been at play is not that of health. The limit of variation is by no means made out in the case of the animal parasites. The relations of acari on bodies generally is being canvassed, especially by German writers. The mode of entry has an analogy also. There is the same difference of opinion as to whether the acari are accidentals or *veræ causæ;* but there is plenty of evidence to indicate the iraction as mechanical irritants, and as the possible developers of irritant products. But these points I cannot now enter upon.

The matter of the action of fungi is a large and wide one; already we see enough to show that the studious inquirer will be amply repaid if he tread carefully the somewhat now uncertain path before him, and the promising indications of success are many.

Lastly, one word for critics. I have attempted to put together novel points for those who feel inclined to know what is the exact position of our present knowledge on parasitism; to collect into a "digest" form what is scattered about in the pages of recent medical literature, as an appendix to my parasitic book. I crave indulgence at the hands of my readers, for I have found it very difficult to condense my remarks. An examination of the subject promises, if only in the field of analogical reasoning, the happiest and most usable results, which will certainly help in no little degree to remove from the escutcheon of Medicine the unjust opprobrium that it is an inexact science.

ARTICLE III.—*On the Conjoined Influence of the Nervous System and of Constitutional Tissue-Changes in the Production of Dropsies, and on the various Methods of Treatment applicable thereto.* By THOMAS LAYCOCK, M.D., Professor of the Practice of Medicine and of Clinical Medicine, and Lecturer on Medical Psychology and Mental Diseases in the University of Edinburgh. PART II., in continuation of a preceding Paper.

IN the first part of this communication (p. 775) I restricted myself to a demonstration of the fact that the nervous system exercises an important influence both directly and reflexly in producing and preventing dropsies and dropsical effusions. It is hardly necessary to remark that such influence can only take effect under appropriate conditions; for multitudes of nervous diseases occur without any dropsy supervening. The same point has been already considered in reference to all those causes of dropsies usually alleged, whether humoral, congestive, or hydrostatic, and which are admissibly predisposing causes. It is necessary, then, to the better understanding of dropsies, that an inquiry be made into another element, namely, the state of the affected tissues themselves, as shown by clinical observation, so as to determine what is the true