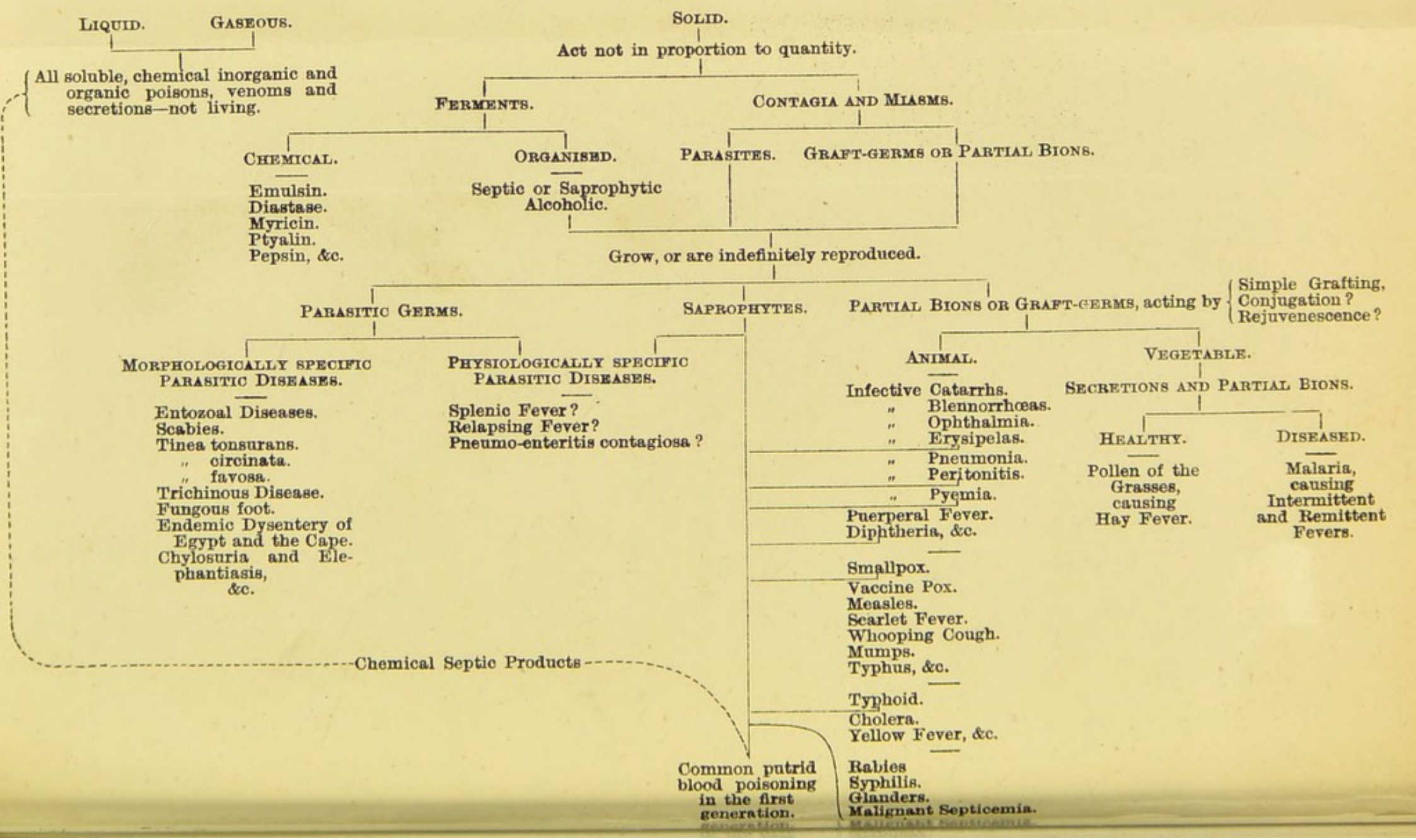
The germ theories of infectious diseases / by John Drysdale.

NATURE OF INFECTIOUS MIASMS.



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THE GERM THEORIES

OF

INFECTIOUS DISEASES.

BY

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ON THE GERM THEORIES OF INFECTIOUS DISEASES.

THE "pestilence that walketh in darkness" has from the earliest times affected so profoundly not only the happiness of families, but the wealth of nations, and even the course of civilisation, that it may be deemed a fit subject to be brought before a non-medical Society. I hope that the bearing of such inflictions on human affairs may be also considered of a sufficiently general nature to allow its being taken as the topic of the Opening Address of the Session.

When we consider the awful mortality of the great epidemics recorded in history — the Black Death of the fourteenth century having, for example, swept off one-quarter of the population of the old world in four years — and the almost total impotence of medicine for direct cure, we may indeed consider this a question more for statesmen and governing bodies than for physicians. Nevertheless, it is necessary that the efforts of the former should be guided by such knowledge of the nature and causes of these diseases as the science of the day can afford. Nor is such knowledge less to be desired for the people in general in order to counteract the baneful effects of ignorance and prejudice. It is a fact that, from the time of Thucydides down to the outbreak of the cholera in our own day, in all severe epidemics a false suspicion has prevailed that the wells or provisions were poisoned by supposed public enemies. To this groundless suspicion thousands of lives have been sacrificed, and it was the cause of the fearful persecution of the Jews in the fourteenth century. The simple knowledge of the fact of the universal prevalence of this suspicion, and, still more, the knowledge which medical science can now give with

certainty that no such poisons exist, ought to go far to prevent such aggravations of natural calamities for the future. And let not people fondly imagine that the days of national epidemics are over. On the contrary, there has been a constant succession of greater and lesser epidemics since the beginning of history, and the immunity of any generation from the greater plagues may be merely an interruption of the course liable to terminate any year by a fresh outbreak of some old or a quite new plague. For instance, the memory of the Sweating Sickness of 1485 was obliterated by the Plague of London, in 1499, but the former returned again unaltered in 1506; and again a third, fourth, and fifth time during the first half of the sixteenth century. Diphtheria has also reappeared again and again after being forgotten in intermediate generations, as also many varieties of spotted and typhous fevers and numerous other diseases. The subject is thus one of universal and abiding interest and concern to us all, so, without further preface, I will proceed to consider the light that may be thrown on these mysterious scourges of humanity by the so-called germ theories of which so much has been heard of late.

§ 1. Let us restrict our attention to those diseases the material exciting causes of which are termed, generically, miasms. Following a recent writer,* diseases arising from miasms may be divided into the miasmatic simple, the contagious, and those which partake of both characters, and hence called miasmatic-contagious. 1st. The contagious diseases arise from a contagious miasm or *contagium*, or specific excitant of disease, which is reproduced in the organism suffering from the specific disease. Under this head come smallpox, measles, scarlet fever, typhus, plague, glanders, &c. 2nd. Under the term miasmatic are comprehended malarious diseases, viz., the intermittent and

* Liebermeister, in *Ziemssen* I., p. 25.

remittent marsh fevers. Here the poison develops itself externally to the body, and is not reproduced therein so as to affect other men from thence, nor is it excreted thence to propagate itself in any other way. 3rd. The miasmatic-contagious comprehend cholera, typhoid, dysentery, and probably some others; here the disease is not readily, if at all, transmissible from person to person; nevertheless, these diseases never originate spontaneously or from purely malarious influences, but always after some person affected with them has been in the neighbourhood; so it is supposed the secretions from infected persons undergo development in favourable media out of the body. In other words, the reproduction of the miasm is partially performed out of the body.

§ 2. What is the intimate nature of this miasm or infectious matter? In the first place, as regards its physical state, it has been determined with respect to the vaccine and some other animal poisons, and is almost certain with the rest, that the specific power does not reside in anything which is gaseous, or liquid, or capable of solution, or diffusible from the medium in which it is contained. * Thus when we hear of sewage or paludal liquids or gases spoken of as the exciting causes of infectious diseases, it is to be understood that the true specific matter is a solid merely suspended in the liquid or gas. This at once cuts off a large number of both inorganic and organic substances from the category of possible causes of the specific disease. [See diagram]. Next

*Dr. Lionel Beale first attributed the infective properties of vaccine and other contagious diseases exclusively to solid matter, and this was experimentally demonstrated afterwards, first by Chauveau and then by Dr. B. Sanderson, by the method of diffusion. Filtration was ineffectual for separating the extremely minute particles in which the contagion resides, from the matrix fluid. Chauveau found the same principle to apply to variola, pleuro-pneumonia, glanders, and sheep-pox. The experiments with the vaccine matter have been recently repeated with greater care and detail by Drs. Braidwood and Vacher, of Birkenhead, who have proved that the liquid diffused out from vaccine matter is totally devoid of infective power.

is the distinguishing mark that they act independently of the quantity introduced into the body. This again cuts off all inorganic and organic stimuli and natural secretions not already disqualified by their liquid or gaseous nature, and leaves only the ferments and the contagia.

§ 3. Now, there are two distinct kinds of ferments, both of which may be said to display the last character, viz., the chemical ferments which catalytically excite an indefinite amount of change in other bodies without being themselves decomposed in the process; and the organised ferments which produce changes in virtue of their vital activity and growth as living organisms. The application of the same word, fermentation, to these different processes is one cause of the confusion in which the so-called germ-theory is involved, and which can only be avoided by keeping in mind the cardinal distinction between them, which is, that the chemical ferments, besides being soluble, and acting almost instantaneously at a very wide range of temperature, are *not reproduced* during their activity, whereas the organised ferments are reproduced therein.

§ 4. Now, although all living matter is particulate, and all contagia may be assumed to be particulate, and nothing reproduces itself except living matter, yet it does not follow that contagia must necessarily be living. For it may be that certain non-living morbid secretions may simply be capable of exciting in other persons a similar morbid secretion as specific stimuli not containing in their own nature, as living matter, the explanation of their reproduction. This would be simply to state the facts of contagion in the sense of its being a non-parasitic pathological phenomenon without any attempt at explanation. But, especially considering the minimal dose, there are good grounds now for looking for the explanation in the hypothesis of the living nature of the contagion itself. Granting, therefore, the possibility of this,

we are now by the above process of exclusion restricted to three known substances:—1st, parasites, already known as such; 2nd, the organised ferments; 3rd, portions of altered protoplasm, or living matter capable of transplantation and subsequent growth in the bodies of other persons; here called partial bions or graft-germs. Now, as the organised ferments are independent animal and vegetable beings, with their proper life history and mode of reproduction, they would necessarily come into the category of parasites if capable of running their course within the higher animals. The exciting causes of infectious disease is thus narrowed into two categories, viz., Parasitic-germs and Graft-germs.* [See diagram]. An immense step is thus made in unveiling

* It will clear up the subject amazingly if we set aside the questions of fermentation and spontaneous generation from all connection with infectious diseases. The superficial resemblance between the specific fevers and the process of fermentation is false and misleading, and it is unfortunate that the name of Zymotic should be sanctioned by authority as applied to those diseases. The true chemical ferments are recognised as agents which break up, with or without combination with oxygen, dead chemical matters by a purely chemical or non-vital process. There is no proof or probability that any chemical agent acts or could act thus on the living tissues or blood in the production of disease. And the sole analogy between the action of a contagious miasm and a chemical ferment is the circumstance of their both acting in minimal dose. From very different causes however; the organised ferment reproduces itself, and is thus multiplied indefinitely, while the chemical ferment simply acts over and over again without addition of new particles, and hence the analogy with a contagious miasm quite fails. There is a fallacy in the common mode of comparing the action of a chemical ferment to disease. For example, it is said, a single drop of septicemic blood introduced into the blood of a healthy animal acts like a ferment which, without being itself consumed, alters the whole blood and kills the animal. Again, a drop of the blood of this last animal (containing thus a mere fraction of the original drop) may alter the whole blood of a second animal and kill it. And so on indefinitely, always because an indefinite quantity of blood can be split up catalytically by the ferment, in however small a dose, seeing that it is not consumed in the process. This mode of statement involves several assumptions, and is contrary to the facts. For the natural ferments require a certain degree of concentration, and will not convert an unlimited quantity, and are slowly consumed or absorbed in the process, thus requiring renewal by secretion. If the second

the mystery which has hitherto enveloped the mode of propagation of infectious diseases. For such germs being exceedingly minute, in fact, ultra-microscopic, it is easy to see how they can be spread abroad unsuspected in every variety of vehicle, and their power of survival, as well as their liability to destruction, corresponds accurately to what is known in these respects of the fomites of contagia. Their conveyance by solids and liquids presents no difficulties, but until lately it was not possible to trace them in the air, and, accordingly, numerous telluric and imponderable influences were imagined as the cause of the origin and spread of infectious diseases. But it has been demonstrated by the admirable experiments of Tyndall that all ordinary air contains ultra-microscopic

a nd succeeding generations of the poisoning were really caused by fractions of the original drop, the disease would be gradually slower and less virulent in its progress, whereas the exact contrary is the case. Besides, the known chemical ferments can hardly be called poisons, and even if injected into the blood would not be injurious except in far greater quantity than the contagia require; and therefore the law of minimal doses does not apply, while any injurious effect they may thus have is no doubt solely that of noxious foreign matters, of which any considerable quantity of any kind is injurious thus introduced. There is no proof whatever that they act as ferments when thus hurtful, and to assume that the contagia are chemical ferments of an unknown nature which may so act on the non-living part of the blood, is simply a gratuitous hypothesis. Thus, while failing to account for the cardinal phenomenon of multiplication of the contagion, the chemical ferment theory fails equally to account for the immediate operation of animal poisons.

On the other hand, the so-called organised ferments perfectly meet the cardinal point of reproduction; but even supposing they are proved to be the cause of contagious diseases, how far can this operation be compared to their effects on dead organic matter known as fermentation and putrefaction? In these processes it is obvious the fermentive and putrefactive organisms may act in two ways:—1st. They may secrete a chemical ferment which may do all the work chemically; or, 2nd, they may, as a vital process, consume the fermentable substance as other living creatures do pabulum, and the products, viz., alcohol, carbonic acid, ammonia, succinic acid, &c., may simply correspond to the urea carbonic acid, water, &c., given off by the higher animals. Now, it is proved that yeast does secrete such a chemical ferment, and it is highly probable that the bacteria do so also, and it may be accepted that the living ferments operate in both these

organic matter; and further, by the method of subsidence in these experiments these matters are proved to be particulate and ponderable, and to contain among them living germs of a great variety of septic and alcoholic ferment-organisms and monads, differing according to the locality of the air tested. Thus a perfect cloud of noxious living matters may be wafted hither and thither in air, apparently quite pure and transparent. While we accept the fact that organic matters are contained in all air, however apparently pure, and what is also the fact that among these organic matters a great variety of protozoal germs are included, it does not follow that there are no other organic and even organised matters which may play the part of contagia. Nevertheless, as we are all liable

ways, although it is not settled yet to what extent each contributes to the final result. It is, however, by far the most probable that the chemical effect of a secretion is quite subordinate in the result as a whole, and is confined to altering the dead matter so as to be more suitable for pabulum; that, for example, a secretion from the bacteria acts on the nitrogenous matter somewhat as the gastric juice does on the food of higher animals. The bacteria, in fact, having no intestinal cavity, live as it were in their own gastric juice, and therefore require a certain stillness or stagnation in the liquid medium in order to thrive. The great bulk of the action of ferment and putrefactive organisms is thus simply that of devouring dead organic matter. How, then, do they act on the living body? Assuredly not by the chemical ferment, for that can only break up definite dead chemical compounds, and not the living matter itself; while the chemical ferment and the other products of bacterial life must act on the living matter as more or less noxious stimuli, and thus produce *disease* long before they could exert any notable changes on the non-living portions of living bodies as chemical agents. Hence the signs of action of saprophytes in the living body, except quite locally, are not signs of putrefaction, but signs of disease. The chemical products of the putrefactive organism thus acting as noxious stimuli are decomposed or eliminated long before they can act as purely catalytic ferments. On the other hand, the living organisms themselves, yeast and bacteria, cannot devour living matter—no pabulum is living—they must first kill it, and then devour. That is to say, unless they are themselves first killed and devoured by the living bioplasts, which is the case in health with respect to the large majority of such organisms introduced (or their germs) into the larger animals and plants. (See § 12. Vital resistance.) There are some exceptions in which the juices of the host and its living matter are either favourable to or tolerate the sub-

to be more impressed with what we see than by what we don't see, and as bacteria are readily demonstrated in a test tube with proper pabulum, while it is impossible so to exhibit, say the smallpox, in a like way, and as some contagious specific diseases are certainly attended with the growth of microphytes in the blood and other parts, it has been concluded somewhat hastily that the growth and development of these germs as parasites is the cause of specific diseases in general. In recent times the chief patrons of this theory, following Pasteur and the distinguished botanist, F. Cohn, of Breslau, have been natural historians and physicists, while in the medical profession, which is naturally more familiar with the clinical facts of disease, its adherents have hitherto been

ordinate organism. In such case the latter lives, and is called a parasite, and when, in certain circumstances, saprophytes survive in the higher animals, it must be as parasites; and, like them, they may produce disease by competing with the host for pabulum, by mechanical obstruction, by irritation, and by the formation of noxious products, all of which cause disease, but which together do not constitute what is known as fermentation and putrefaction of dead matters, although the mere life of the saprophyte is the same. The question of spontaneous generation is also here an idle one in these diseases. For they would still act as parasites whether sprung from dead matter or heterogenetically descended from the bioplasts of the host. And if they came into being *de novo* in the diseased body-fluids, it is beyond all credibility that they should always assume the exact form of those organisms whose access from without is so easy to account for. (§ 11.) In Dr. Bastian's paper, in the *Journal of the Linnæan Society*, for October, 1877, and May, 1878, he sums up against the germ-theory as it is presented by Dr. Wm. Roberts, and substantially is in accordance with Dr. Beale. The discrepancies still remaining between them could be reconciled, I think, by the additions here made by me to Dr. Beale's theory, if the questions of fermentation and spontaneous generation were put aside. But Dr. Bastian unfortunately still continues to mix them up with the pathology of infectious diseases, and thereby much weakens the influence of his deservedly great authority as a pathologist against the exclusively parasitic theories of Pasteur and Cohn. It is quite allowable to contend for the hypothesis of spontaneous generation as a thesis in general biology, although the majority may be as yet unconvinced by him; yet what good purpose can it serve to bring it into our subject, when he admits the origin of contagious diseases *de novo* by what is substantially the same as Beale's degradation of protoplasm into disease-germs, or what are here called partial bions?

in the minority. But recently the distinguished clinical pathologist, Dr. W. Roberts, of Manchester, in his admirable Address on this subject before the British Medical Association, in 1877, has pronounced in favour of the parasitic-germ theory. And the foremost of our experimental pathologists, Dr. Burdon Sanderson, speaks, although with much hesitation, also in its favour. In the attempt to unravel the complexities in which the parasitic-germ theory of infectious diseases is involved, let us shortly trace its history, for it is by no means quite new, as some imagine. The doctrine of *contagium animatum*, which was even then old, was revived in the last century by Kircher, it was partially sanctioned by Linnæus, and early in this century was supported by more specific facts brought forward by Schönlein, Langenbeck, Sir Henry Holland, and others. But the most complete statement was given first by Henle, in 1840, and again in his *Rationelle Pathologie*, in 1853. Since then little has been added to the theoretical aspect of the question, although an enormous addition has been made to the known facts. The fundamental points of the theory are shortly these. We may safely hold that a parasite is the cause of all those symptoms which are brought on by the introduction of the parasite and disappear with the removal of it. Thus parasitic diseases may be called contagious, if the parasite is transferred from one person to another, and the parasite itself may with propriety be called the contagium. Now, as Henle says, it certainly sounds ridiculous, with our usual ideas of the nature of miasms, to speak of an eight-footed or a two-inch long contagium; but, on the other hand, is it not a mere play upon words to say of the itch that it is not contagious, since it is discovered to depend upon the transference of the *Acarus scabiei?* So it is quite legitimate to say that, if in any recognised contagious diseases we find the exciting cause to reside in a parasite, we have explained the contagious process in such diseases.

And if the same holds good in all, we must allow that the parasitic theory explains contagious diseases in general. All depends upon the facts. The simple statement that a particular disease is coincident with the presence of foreign organisms, or even of a particular parasite, covers many fallacious inferences, for their presence may be secondary or accidental. The subject must therefore be followed out in detail.

§ 5. First take as the starting-point the entozoa, commonly called worms, the old-established typical parasites. Here, if the symptoms displayed by the host are to be called a disease at all, it is one certainly dependent on the presence of living beings, not produced spontaneously, nor by heterogenetic descent from the host, but which are distinct animals with, for the most part, a known life-history. The symptoms do not at all resemble those of the specific infectious diseases, and seem to depend on simple irritation and the abstraction of nutriment. But there are here already some analogies between the two, for the relationship between the parasite and the host is very close. Not only almost each species, animal and vegetable, has its proper parasite, but even different varieties or races of the same species have different and exclusive parasites, just as the specific diseases are confined to one or few species. Also, there is an indirect contagiousness, in that one stage of the life cycle of the entozoa is passed in a different host, just as in the miasmatic-contagious diseases morbid matter must pass out of the body of the patient and undergo some change outside before it can infect another person. They also resemble the infectious diseases in having a specific habitat; for of the entozoa some inhabit the stomach, some the liver, others again the large intestines, the kidneys, &c., just as smallpox attacks the skin, scarlet fever the throat, &c.

§ 6. We now pass to those affections which have been

long known as contagious and infectious diseases, and which have been more recently discovered to depend on the presence of parasites. Of these scabies, or the itch, was proved about fifty years ago to depend on the presence of the *Acarus scabiei*, or itch mite. Then, about thirty years ago, the various forms of ring-worm were traced to the presence of one or more species of fungi, from the transplantation of which, or the spores, the propagation of the disease depends. Within the last twenty years the list of epidemic and contagious diseases traced to animal and vegetable parasites has increased rapidly, and, if we include those of the lower animals and of plants, is now very large. It is sufficient to name as examples the potatoe disease as depending on the *Peronospera infestans;* the opium-blight, on the *P-arborescens;* the ergot of rye, on the *claviceps purpurea;* the grape vine disease, and a host of others among plants on well-described parasites; the fungoid diseases of silk-worms and other insects. What more immediately interests us is the tracing of internal diseases in the human species to the presence of parasites, as shown, for example, in the remarkable history of the discovery of the *Trichina spiralis*, or flesh-worm. The existence of this worm has been recognised for some years, but its connection with specific states of disease was hardly suspected till the simultaneous occurrence of a number of fatal cases of an unknown disease was traced to its agency. In 1863, in a small town in Prussia, occurred one of the most striking instances. After a public banquet about one hundred persons were struck down with disease, which proved fatal in a large number. The symptoms were great lassitude and depression of body and mind, complete loss of appetite, sleeplessness, then fever closely resembling some of the specific fevers such as typhoid; then excruciating pains in the muscles, especially of the extremities, and contraction of the knees and elbows, which could not be

extended for extreme pain; œdema of the eyelids and legs, difficulty of moving the tongue, profuse clammy perspirations, inflammation of the lungs, exhaustion, unconsciousness, and death. After death numberless living trichinæ were found in all the striated muscles, including those of the heart, some straight and some coiled, in all different stages of development. The parasite is bisexual, producing its young alive in the mucus of the intestines, in which it lives and moves freely; from thence the immature forms bore their way into the muscles, wherein they become encapsuled for a longer or shorter time, but may resume their activity and go through their complete stages and propagate again in the intestines. The whole process may be gone through in three to four weeks. The discovery of this horrible parasitic disease produced a profound sensation in all civilised countries, and it became evident that it could be nothing new, but an explanation was merely given of various anomalous epidemic and solitary cases of disease hitherto set down as typhoid or unknown forms of fever. It afforded, also, a good example of the ultimate tendency of the reduction of disease to parasitic exciting causes, viz., that for the protection of society against such diseases we must rely on police regulations for destruction of the sources, rather than on medicine, for in this case the latter was powerless to find a remedy. And in all such cases where the whole tissues or the blood are pervaded by innumerable microscopic organisms, it is hardly to be expected that we shall find substances which shall be poisons to these low creatures and at the same time harmless to the infinitely higher organisation of the host.

Another parasitic disease may be noticed derived from the vegetable kingdom, viz., the "fungous-foot" or "madura-foot" of India.

In this disease the spores of a mucedinous fungus penetrate the skin of the naked feet of the natives through small

accidental cracks or abrasions. These being capable, like true parasites, of living in the healthy fluids and tissues, grow rapidly and, with the tremendous molecular force of growing organisms, bore their way even into the bones, causing destruction of them and of the soft parts, with suppuration and wasting fever, so that death is only averted by amputation of the limb. Specimens of this fungus sent home to Mr. Berkeley were cultivated by him, and identified with the genus *Chionyphe*, and named by him, after the discoverer of the disease, *Chionyphe Carteri*. We have here, therefore, an example of a true parasitic disease, and one of peculiar interest, as it has been supposed to throw light on the nature of hospital gangrene, which is the scourge of military hospitals. Another disease traced to a parasite, this time animal, is the endemic dysentery of Egypt, which has been found to depend on the presence of a fluke-like worm, called the *Bilharzii hæmatobium*. Finally, we may note the more recent discovery of Dr. Lewis, of Calcutta, that the disease of the kidney, called Chyluria, and certain forms of Elephantiasis (a kind of leprosy), depend upon the presence of the *Filaria sanguinis*, a parasite which inhabits the blood-vessels. And here we may notice the still more recent discovery of Dr. Manson, of China, as throwing light on the mode of communication of infectious diseases, viz., that these worms are actually conveyed to men or animals by mosquitoes, which suck up the small worm with the blood of their victims, and thus transfer them to other living creatures.*

§ 7. The above are certainly proofs of the dependence of certain diseases, hitherto ranked among the miasmatic and contagious, on the presence of parasitic animal and vegetable organisms. So far, therefore, such a class of diseases exists.

* It is possible that we have here an explanation of the destructive power of the Tsetse fly, for it may be the intermediate host of some similar blood-parasite; or it may be the carrier of some infective poison. It is highly improbable that any mere poison or venom should exist so powerful as to cause the death of a large animal in such small dose.

But in all these cases the parasites are tolerably large and well-defined morphologically specific organisms; and the diseases themselves are comparatively rare, and differ so considerably from the common specific and infectious diseases, that it is only by somewhat straining the definition that they can be brought within the class. Are there examples among the true specific forms, such as measles, scarlet-fever, typhus, smallpox, &c., in which the universal presence of a special parasitic organism can be shown? The answer can now be given *primâ facie* in the affirmative in respect to two human diseases, viz., the splenic fever or anthrax, or malignant pustule of cattle and men; and the relapsing fever of men.

The anthrax, or malignant pustule, is a disease of extreme virulence and fatality both in cattle and in men, and is extremely contagious, so that a drop of the blood of an infected animal falling upon any uncovered part of the skin, even if unbroken, will produce the characteristic boil, followed by speedy infection of the whole blood. The course of the disease is extremely rapid, proving fatal in a few hours in some cases, and in most within a day or two; the symptoms being general disturbance, shivers, followed by febrile heat, debility, muscular twitches; then convulsions, hæmorrhages, and total collapse, with coldness and inability to move, difficult breathing, and death. In this fearful disease bacterial organisms were discovered in the blood by Davaine, about twenty-five years ago, and they were seen at different intervals since. Still their presence for long was not looked upon as an essential feature in the disease, and even in 1866 no mention is made of them in Aitkin's text-book of Medicine. Within the last eight or ten years, however, proofs have been gradually accumulating of the causal connection of this bacterium with the disease, and the observations of Dr. Koch, in 1876, are generally considered to amount to

positive demonstration. The facts are, that the blood is always found to contain an abundance of rod-bacteria, supposed by Davaine originally to constitute a distinct species, and, therefore, named *Bacteridia*, but which are pronounced by F. Cohn not to be distinguished morphologically from the *Bacillus subtilis* of the butyric fermentation, and, therefore, called by him *Bacillus anthracis*. The mode of action of the contagium is peculiar; the actual contact of the blood or exudations of a diseased animal infects another with certainty, but "animals placed in the closest proximity to the diseased ones, and placed in the most favourable circumstances for infection through the air, are not infected." (B. Sanderson.) The infective power of the blood is transitory, and is lost on the appearance of ordinary putrefaction, and it cannot be kept for more than a week generally, or at most five weeks, without losing its activity. Nevertheless, it is a fact that the contagion can exist in a persistent form, and lurk about stables and sheds for months, and even years, and can be transported across the Atlantic in hair and wool, thus infecting by air-borne dust. The blood, while capable of infecting, always contains the above bacilli, but when filtered through porcelain is no longer poisonous. The explanation of these facts is given by the experiments of Dr. Koch, since confirmed by those of Dr. Ewart, of University College, London.* It was found that the bacilli, at the height of the disease, are still growing and immature, and if such blood is quickly dried in small portions, or undergoes ordinary putrefaction, the bacilli perish, and with them the power of infection. But if a drop of the fresh blood, with living

* *Lecture on the Germ Theory*, by Dr. Burden Sanderson, 1878. Dr. Ewart has since published his results in the *Quarterly Microscopical Journal*, April, 1878. He finds that the rods are not motionless, as stated by Davaine. The formation of spores requires a moist state and a temperature between 28 and 33 C; and that it took place as well after death and out of the body. A heat of 37 C prevents the germination of the bacilli.

bacilli, is placed in serum at the temperature of the body, the bacilli soon begin to grow enormously in length, become studded with bright oval dots, and finally break up, leaving those dots, which are in reality spores, possessed of immense powers of resistance, and capable of germination after drying and passing through numberless vicissitudes. The same formation of spores may take place in larger masses of spleen or blood slowly dried. Thus are explained the fugitive and the persistent forms of the contagium—the one depending on the living bacillus, and the other on the spores. The reason why the infective power of the living blood is speedily lost is that the bacilli are propagated therein solely by fissiparous generation; and it is only in the blood of the dead animal, or in suitable dead nutriment, that the formation of spores takes place. Koch then proved by observation that these spores reproduce the rod-bacilli. Next, by experiment, he showed that these bacilli from cultivated spores had the same pathogenic activity as the fresh bacilli from the living animal; for by inoculation with the spores death was produced by splenic fever, with its usual abundance of the bacilli. He also noticed that in a specimen which most of the spores had fallen to the bottom, while few remained floating in the liquid, inoculation with the bottom fluid, thus richer in spores, produced death within twenty-four hours, while that with the surface fluid only in three or four days. The inoculation with the cultivated spores is no doubt the crucial test, for inoculation with blood containing bacilli does not prove that the contagium resides in the bacilli; it might reside in some other poisonous matter introduced at the same time; whereas the cultivated spores may be presumed to be free from other non-parasitic contagious poison. I am bound, however, to say that, on careful perusal of the details of the experiments, it appears to me the possibility of that was not excluded. To show that the cause of death in these inoculations was not

from ordinary septicemia from putrid matter, Koch inoculated several mice with minimal doses of putrid blood, putrid serum, and crystalline lens, all free from bacilli. Only two out of twelve died, and in these the blood was free from bacilli. And further to test the specificity of the *Bacillus anthracis*, animals were inoculated with a putrid crystalline lens in which had spontaneously grown a kind of spore-forming bacillus not distinguishable from the *B. anthracis*, but neither it nor its spores could produce splenic fever; nor did the spores of a bacillus cultivated in hay infusion by Professor Cohn. These facts, he thinks, complete the proof of the physiological specificity of the *B. anthracis* as the cause of the disease. Unless I must add, as above said, no other poison accompanied the bacilli or spores, although even in that case the persistence of the poison is hard to account for if it did not reside in the spores. For matter containing these spores could be dried into dust, again wetted, and dried repeatedly, kept in putrefying liquid for a week, and, according to Pasteur, exposed to boiling heat, without losing its infective power. This, however, is contradicted by Ewart, who found that the spores do not resist boiling heat, nor oxygen at twelve atmospheres. It is difficult to suppose that amorphous protoplasmic particles like graft-germs could stand such an ordeal. Until, therefore, new facts come to light, showing an equal power of survival by graft-germs, we must for the present place the splenic fever in the category of parasitic diseases. Some of the above facts are still disputed, but it would take too long to go into details.

Another disease which may be placed in the same category is the relapsing fever. This is a contagious epidemic which has been recognised as distinct from typhus and other fevers for above thirty years, and since 1872 it is known to be universally attended with the presence of a spirillum in the blood, named, from its discoverer, the

*Spirillum Obermeieri.** The evidence for the parasitic nature of this disease is similar, although far from being so complete, as that for the splenic fever, so I need not enter into it, but at once allow it to be placed, provisionally † at least, in the same category.

§ 8. We must here pause to point out that in admitting the last category a great leap has been made into the region of hypothesis. In the previous list the parasitic organism was an easily demonstrable morphologically distinct animal or vegetable, and therefore it was comparatively easy to connect it with the disease in the relation of cause and effect, whereas now the most we can do by simple observation is to determine the constant presence of a particular species, or even genus, in the disease, but which can and does exist in other circumstances without being accompanied with the disease. We are therefore compelled to resort to the hypothesis that, although the same in appearance and life history, the parasitic disease-causing-bacterium constitutes a variety physiologically distinct, in that it can secrete a noxious

* This bacterium is, however, not morphologically distinguishable from the *Spirochæte plicatilis*, which is often found in stagnant water, and even in the tartar of the teeth of healthy people. Spirilla are also found in the stomachs of healthy oxen (Cohn), and I may add, from my own observation, that the germs of a spirillum are found abundantly in the Liverpool water, and are swallowed in myriads every day, while relapsing fever is unknown here at present.

† Provisionally; for it is quite possible that when our knowledge of this disease is complete it may turn out that the parasite is merely a subordinate complication. It appears that spirilla were found in the recent famine fever of India; and it is probable they occurred in the famine fever of Ireland, in 1847. Either some internal cause altered the blood so that the common *spirochæta* of stagnant water and of the tartar of the teeth could live and multiply in it; or the cause of the famine coincidently acted on the *spirochæta* so as to produce the evolution of a specific variety, which entered the people and produced the fever. Is this last really probable? Some light may be thrown upon this by a fact observed by Mr. Dallinger and myself in our researches into the life-history of the bacteria, not yet concluded. Wishing to observe the *Spirillum volutans* separate from the

poison, or at any rate live and grow in the healthy body. This may be so, but it is obvious that we must have other proofs except the bare fact of disease accompanying their presence, for the cause may reside in some other poison while the bacteria are a merely subordinate complication. The strongest arguments for purely physiological specificity are derived from analogy, and were first given by Pasteur and F. Cohn, whose statements may be shortly summed up as follows :—The lactic and the acetous fermentations are chemically different processes, as also the ammoniacal urinary, and the mucous wine fermentation, and yet the organisms which produce these respectively cannot be distinguished by the microscope. The bacterial germs which produce the red, yellow, orange, and blue pigments, cannot be distinguished, yet on sowing them out the distinct colour appears. This obtains among the different genera of bacteria, and we may therefore admit purely physiological species as good species; or at least varieties or races which are persistent and breed true like morphological species. As, in fact, we see in plants,

numerous putrefactive organisms in the matrix-maceration, we tried it in Cohn's nutritive fluid and several other clear media, but in vain; it died speedily in them all, and we were for a time quite baffled. However, recollecting that it was a variety of spirillum which flourished in the blood in relapsing fever, we tried fresh (sheep's) blood serum, and found that it answered perfectly, and we could watch the lineal descendants of a few spirilla for many generations in the moist chamber, under the microscope. It is easy to imagine that a small diminution of healthy vital resistance (§ 12), induced by a non-parasitic cause of fever, might allow the spirilla germs in the drinking-water or the tartar to multiply in the blood, while it might not so act with regard to other saprophytes; for Billroth noticed that the commonest putrefactive organism, viz, *Bacterium termo*, does not thrive well in blood. But it is very difficult to imagine that the evolution of a particular specific variety of spirillum fit to breed in the blood should happen just at that particular time. Dr. Roberts (§ 8) compares the origin of specific bacteria to the "sporting" of plants; but sports occur only once in many thousand generations; famines cannot certainly be called common; that they should coincide must be a rare event, but that they should always occur together as a mere coincidence passes credibility.

especially cultivated ones; for of two trees, otherwise indistinguishable, one will bear sweet and the other bitter almonds —the latter being poisonous. In fact, if the parasitic theory of disease be true, this would by analogy furnish an explanation of the origin of infectious diseases; for the sweet and bitter almond, and many kinds of variety in fruits and vegetables, are produced by variation in and descent from common stocks. As an example of such variation, or "sporting," Dr. Wm. Roberts cites from Darwin the origin of nectarines:—"A peach tree, after producing thousands and thousands of peach-buds, will, as a rare event and at rare intervals, produce a bud and branch which ever after bear only nectarines; and conversely, a nectarine, at long intervals and as a rare event, will produce a branch which bears only peaches ever after." Again, in the different sorts of yeast, the formation of races by artificial selection is demonstrated by Rees. Also, just as summer rye is worthless for winter seed, although both races are descended from a common stock, so the upper yeast is useless for Bavarian beer, and almost every kind of wine or beer has its own barm. On these and similar grounds from analogy, F. Cohn constitutes a special group of physiologically specific bacteria, called the pathogenic bacteria. All of these, except two, belong to the globe, or sphero-bacteria, and already distinct names are given to those supposed to belong to the different infectious diseases, such as the micro-sphæra vaccinæ, the micrococcus diphthericus, the micrococcus septicus, &c. The same principle is extended to erysipelas, smallpox, scarlatina, cattle plague, glanders, measles, and even tuberculosis, all of which are supposed to have their physiologically specific micrococcus or sphæro-bacterium not distinguishable from ordinary saprophytes; the only exceptions being the two above diseases, splenic and relapsing fever, which depend on rod-bacteria. Oddly enough these two happen

to be the only ones in which anything like proof of the causal connection with the diseases can be admitted to exist. All the rest, without going into detailed discussion which would be too extensive, I may say at once are as yet entirely destitute of proof and altogether hypothetical. In none of them, except the two already named, has the uniform presence of any single species been demonstrated, far less has the disease been traced to the various organisms which have at different times been found in them. To unravel the complications of the relation of the bacteria and micrococci found in various infective diseases to the disease itself, let us keep in view the different categories in which such organisms can be placed in relation to the disease.

§ 9. These categories are three:—1st, true parasites which live and thrive on healthy animals and plants, and possess special organs to enable them to prey on the juices of the host (suckers: *haustoria*), and which cannot continue to live without the host; 2nd, fungi which thrive on dead organic substances, and can therefore be cultivated on artificial nutriment out of the host; but they are able also to thrive on healthy living animals and plants, and thus excite disease, and in plants consume and destroy them; 3rd, fungi which usually are saprophytes, living on dead organic matter, and unable to attack healthy uninjured tissues, but they can grow and multiply in parts or organisms whose vital powers are lowered by injury or disease (§ 11); in plants, for example, the ordinary moulds will take root and grow on any injured part, especially on fruit, and become injurious parasites. It is evident that the existence of the last category strikes a blow at the doctrine of specific organisms as the sufficient cause of corresponding infectious diseases. The presence of bacteria or other fungi in disease may thus depend on two causes, either, 1st, an alteration in the specific

vital properties of the bacteria enabling them to live and thrive in the healthy body as parasites, and thus produce diseases corresponding to the specific character of the parasites; or, 2nd, an alteration in the tissues and fluids of the body itself, which enables ordinary bacteria, or micrococci, to live and grow therein. In this last case, their presence is merely secondary and a complication, although it may add greatly to the gravity of the original disease.

§ 10. It may well, therefore, be that the discovery of micrococci, even constantly in particular infectious diseases, by no means proves the causation of that disease by specific parasitic germs. Each disease must be studied by itself, and if there is another cause of infection, such as graft-germs, to be treated of presently (§ 17), we have simply to determine whether it is to be arranged under the parasitic or the graft division; and I venture to predict that many diseases that are somewhat hastily assumed to belong to the parasitic division, from the presence of micrococci, will be met by the third category of the foregoing paragraph and transferred to the graft division. Even some diseases we have admitted into the parasitic division, in the second category of § 9, have their specificity determined as much by the specific vitality of the parts on which they take root as by the character of the fungus itself. For example, in the different forms of ringworm, *Favus*, *Herpes tonsurans*, and *Pityriasis versicolor*, a specific fungus was originally given to each, called respectively *Achorion*, *Trichophyton tonsurans*, and *Microsporon furfur*. More recently, however, the question has arisen whether they do not all depend on one fungus, and this has been answered in the affirmative by the celebrated dermatologist, Hebra, who considers that to be the *Penicillium glaucum*. But since then Grawitz, by more careful separation, and culture, and experiment, determines it to be the *Oidium lactis*. Why this should produce differ-

ent diseases depends on the specific difference of the subjects on which they fall, as to age and other predisposing causes. The fungus has an irritating quality, which produces herpetic inflammation, and thus fluid exudations, which favour its further growth. This is confirmed by the facts that parasiticides applied locally can cure the disease, but they are greatly aided by internal medicines, which control the concomitant inflammation. The transference of the fungus after cultivation, it is alleged, gives the disease, therefore we must admit it among the parasitic diseases. Not so those in which the bacteria or micrococci belong to the third category above. (§ 9.) As examples, we may notice aphthæ, diphtheria, smallpox, and erysipelas. In all these micrococci and mould-fungi are invariably found, and their presence adds greatly to the severity of the disease, or gives it actual fatality. Here, also, may be arranged all those diseases in which micrococci or bacteria are not regularly found at some stage of the disease, but in which they may occur at the closing, or so-called putrid stage of disease, and profoundly affect the blood. Even in the rapid death which is produced by over-driving of perfectly healthy cattle, living bacteria are found in the blood. In the aphthæ or thrush the same method of cultivation and experiment has been applied by Dr. Grawitz, and he found that among numerous bacterial and mould-fungi, more or less present, the only invariable form is a species of torula, which can produce the alcoholic fermentation, and appears identical with the *Mycoderma vini*, or common mould pellicle, which infests fruits and vegetable juices. He now attempted to produce the disease with this, but all attempts with healthy animals failed, even if given in milk to young cats and dogs for weeks. But if given to quite young animals, from three to eight days' old, which had not been fed with mother's milk, and whose health was obviously deteriorated, then it

produced disease and death, with aphthæ on the tongue, fauces, and even the larynx. The same principle applies to diphtheria, erysipelas, smallpox, and other infectious diseases, in which the micrococci are incapable of alone producing the specific disease, or indeed disease at all in moderate dose, but after the true specific cause has begun to operate they supervene and aggravate the evil. In simple erysipelas, for example, a zone of micrococci borders the spreading inflammation of the skin. These seem not to be virulent, and to act only mechanically. Their presence most probably depends on the fibrinous effusion which marks that stage of the disease, forming a good nidus for the growth of the micrococci, for in the subsequent stage of the disease they are destroyed and absorbed. In certain cases of smallpox and diphtheria the lining membrane of the heart is invaded by vegetations of the same sort, which produce death by choking up the capillary vessels, not only in the heart, but also of the liver, kidneys, and lungs.

§ 11. *Ubiquity of fungus germs.*—Whence, then, are these organisms derived if they do not pass into the infected body as the causal agent of the disease ? The answer is simple. The germs of them are ubiquitous. This applies to all the three natural groups of the lower fungi, viz., (Naegeli) the mould-fungi, the sprouting or yeast-fungi, and the fissiparous fungi or bacteria. The evidence of this may be shortly summed up as follows:—All the air we breathe and live in contains organic matter, which includes spores of more or fewer of the above fungi. In pure country air the quantity of organic matter amounts to one grain in 200,000 cubic inches, and in the less pure air of towns to one grain in 8,000 to 10,000 cubic inches. (Angus Smith.) The whole of this quantity of organic matter does not consist of spores or germs, but such is the incredible minuteness of these (each of which has been calculated by Naegeli to weigh

the thirty thousand millionth of a milligram) that exposure to the air is sufficient to produce the so-called spontaneous fermentation and putrefaction of organic matters, and the growth in them of some of the known fungi, in a longer or shorter time, according to the degree of contamination of the air. Again, the first portions of water collected in a shower of rain contain more fungus-germs than subsequent portions, and the air becomes purer from them after rain. All water, from whatever source, which has once touched the ground, contains abundance of the above germs. Consequently all animals and vegetables on the face of the earth are continually receiving abundance of fungus-germs in the water essential to their existence. Thus, in the air we breathe, in all that we eat and drink, and touch, and lie on, we are continually exposed to the reception of germs. Accordingly, bacteria, and various fungi and germs, have been detected on all parts of the surface, and of the mucous passages open to the air and in the organs communicating with the mucous membrane. They are found in myriads on the tongue and in the tartar of the teeth, in the nose and throat, and all through the alimentary canal, into which countless myriads are continually poured with our food and drink. Even developed bacteria have been found in the liver and spleen, and in the blood of healthy animals in certain cases; but the germs or spores are diffused through the interstices of the tissues, where, under favourable circumstances, they may come to maturity, as bacteria are sometimes found in abscesses shut off from the air. They are found also in the perspiration of the axilla, the face, and other parts; also in the fluid of blisters raised artificially. Nay even, they are found in seeds and ova; the pink mould has been found in the middle of a nut, and the *Dactylium soyerium* in an unbroken egg. The cells of plants produce fungi, which fructify within them. In short, we may take it as established that the whole of the

higher organisms are interpenetrated perpetually with the germs of the lower fungi, and these may even develop in small numbers without much disturbance of health.

§ 12. *Vital Resistance.*—On the other hand, in the healthy body an equally constant process of elimination and destruction of these germs is perpetually going on. In the air passages the ciliated epithelium is always engaged in expelling spores, as well as other foreign matters, with the surplus mucus. And the mucous corpuscles here and in the other mucous membranes decompose and destroy them. Also the blood, and the healthy juices and secretions, are unfavourable media for their development, while the bioplasts in the blood and of the tissues destroy and consume them ; so that spores are ordinarily not to be detected in the blood and healthy tissues. But only let the vital changes of the living matter slacken ever so little, then the germs escape destruction and accumulate in the interstices of the tissues, and are ready, on further progress of disease, to enter upon growth and development. Of all this, abundance of proof is now extant as the result of experiments which cannot be here adduced in detail. It has been found that injections of putrid fluids full of bacteria can be made into the blood of healthy animals in moderate quantity, with the result of producing only slight febrile disturbance, which is soon recovered from. Here the noxious chemical putrefactive products are in too small quantity to kill or greatly depress the vital powers, and the bacteria and germs are destroyed and consumed or eliminated. The law of quantity here holds good (§ 2); but let a certain moderate quantity of this putrid injection be exceeded, then the animal succumbs to septic poisoning and growth of bacteria. In other experiments, certain spores of the mould-fungi were found to be partly eliminated by the kidneys, and partly dissolved and destroyed in the blood, apparently by the

agency of the living white corpuscles. On the other hand, the effect of disease in lowering vital resistance is demonstrated by the experiment of Chauveau, who injected into the blood of rams, before the operation of bistournage, a quantity of putrid fluid, containing bacteria, too small to kill the animal; then, when the bacteria and germs were well distributed through the blood, the subcutaneous rupture of tissue, in which the operation consists, was performed. The part being then cut off from its supply of blood, has its power of vital resistance so far lowered that growth of bacteria, putrefaction, and septicemic infection takes place. In the healthy animal the operation is harmless, and the part cut off from the circulation gradually passes into fatty degeneration and atrophy; likewise, the injection of the same amount of putrid matter, without the operation, is harmless, but both together are fatal. By the expression vital resistance is meant merely the necessary incidental result of healthy living action, not any specific property or power, such as the imaginary *vis medicatrix naturæ*.

§ 13. We thus see that although fungi may be capable of producing disease primarily, yet the mere fact of their presence in any given disease is no proof that they are directly the cause of it, as there are other ways of accounting for their presence. Doubtless all germs are not present everywhere at the same time, so it may be difficult to account for the invariable presence of one particular form of bacteria in one disease by merely chance spores. But it is already a weak point in the proof of parasitic-germ theory that you can never inoculate with the specific bacterium, say *bacillus* or *spirillum*, without at the same time introducing some of the diseased secretion, or graft-germs, which might be the true contagium; so also, if the latter is the true cause, you can never escape inoculating the particular bacterium along with it which is best adapted to thrive in the disease

secondarily. We have seen that the hypothesis of physiologically specific bacteria was put forth to account for the pathogenic power of bacteria not visibly different from the chance bacteria. Naegeli * also, while objecting to the idea of truly different species, either for disease or the fermentations, owing to the enormous time required for variation of species, adopts the theory of variation in the secretion, which, he thinks, may be brought about in a much shorter time; and thus may be accounted for the changes of epidemic diseases, and the rapid gain of virulence of septicemic disease. But it seems to me that we have no ground to assume that the varieties of yeast and pathogenic bacteria can be evolved with anything like the required rapidity. And, besides, it is not a mere variation in their secretions which must characterise the pathogenic bacteria, but it is the adaptation of the bacterium as a parasite, *i.e.*, its constitution must be so changed that it can live and breed and grow from the most minimal dose in the healthy body, which faculty the ordinary bacteria do not possess. Now, it is generally held that parasites are degradations by variation and natural selection from independent species, but that this process, like all change of species, is only effected in the course of years or centuries. This is quite contrary to what takes place in diseases, where, in a few days, or even hours, ordinary chance bacteria are found living and breeding in the living body, on account of a change in the body and not in the bacterium.

After all, Naegeli, an adherent of the parasitic-germ theory and the physiological variation of the pathogenic bacteria, finds the theory insufficient to explain the specific nature of the infectious diseases, and is obliged to suppose, in addition, that the bacteria absorb and become charged with a morbid secretion from the diseased host; in fact, that they are also carriers

* *Die niedern Pilze*, von C. v. Naegeli, München, 1877.

of an infective or diseased stuff; or, at least, that to produce the full disease some such stuff should be transferred at the same time, whether on or in the bacteria. An analogy for the process is, he thinks, as others have done before him, given by the growth of galls on plants, viz., along with the ovum is deposited by the insect some acrid matter, which excites inflammatory and exuberant growth possessed of less vital resistance than the healthy tissue, and on which, therefore, the ovum can be nourished. Now, no doubt this corresponds to a certain extent with what happens in some of the truly parasitic diseases, *e.g.*, the ringworm; but it opens the door to another cause of the specificity of infectious diseases, viz., morbid secretions, and even graft-germs, which may be the efficient cause, while the bacteria are merely a secondary complication. Indeed, it is particularly noticed by Darwin, that the great variety and fixed character of the different species of galls indicate the morbid specific power of the poison of the insect which produces them respectively. The admission of such a specific poison in the infectious diseases, besides the parasitic germ, vitiates the decisive character of all mere inoculation experiments, and throws us back upon the clinical history of these diseases to determine how far the different theories harmonise with the well-known facts.

§ 14. The following are a few of the cardinal facts of smallpox, which may be taken as the type of the specific contagious fevers:—

1st. A latent or incubative stage, exactly limited to twelve days.

2nd. Almost perfect health during, and abrupt termination of, the latent stage, and invasion of the initiatory fever.

3rd. Immunity from a second attack.

4th. The inoculated disease is very much milder than the natural, but protects as completely.

5th. The latent stage much shorter in the inoculated disease, lasting only seven days.

6th. Vaccination still milder and its latent stage shorter, while it protects as well.

7th. Several vaccine pocks protect more completely than one.

§ 15. The first point is the absence of illness during and the abrupt termination of the latent stage. It is difficult to see how this can be reconciled with the parasitic theory, for the only mode, as yet known, of propagation of the bacteria, on which the disease is supposed to depend, is the fissiparous, or that by division into two. This produces a progression on the whole gradual, although more rapid at the later than the earlier stages; and from the time the number is sufficient to produce any perceptible effect at all the symptoms should increase gradually. It is therefore impossible to understand how in smallpox there should be no symptoms at all for twelve days, and then that the disease should suddenly burst forth in its full violence. Again, no matter how much or how little of the contagium be introduced in the inoculated disease, the length of the latent stage is the same; this also is against the theory of the multiplication of parasites, for the greater number should multiply faster and shorten the latent stage, as was indeed found by Koch in respect to splenic fever. (§ 7, p. 16.) It has been attempted to explain the latent stage by supposing that the parasite was in a different cycle of its life history when introduced, and the instance is given by Henle of the muscardine—a true parasitic disease of silkworms—in which it makes a difference whether the ripe or unripe filaments were used for inoculation; in the latter case the disease broke out much sooner, for the unripe filaments continue to grow at once, while the spores require time for their development. But this only serves to make the contrast between

the specific contagious diseases and the parasitic disease the more glaring, for the disease which had a shorter latent stage was not milder, but, on the contrary, more rapidly fatal than the natural cases, whereas the characteristic fact about the smallpox is that the inoculated disease not only has a five days' shorter latent stage, but it is out of all proportion milder, so as to be counted among the trivial diseases. Again, notwithstanding the mildness of the inoculated disease, it protects as completely. This immunity from a second attack, after the natural as well as the inoculated disease, is itself wholly inexplicable by the parasitic theory. As is also the fact that another similar poison, viz., the vaccine, can protect as well as the smallpox poison itself, as are also a number of the details of the process, especially the fact that several vaccine pocks protect more completely than one; for with a parasite capable of reproduction to infinity, what could it matter a few dozen more or fewer parasites? The immunity from a second attack is, in fact, acknowledged to be inexplicable on the parasitic theory by the best pathologists among those who are inclined to favour it; and the attempts to explain it by less able men only make the difficulty more palpable. As, for instance, when it is supposed that the body of the host contains in health some pabulum suitable for the parasite, and where this is exhausted, not only the parasite stops breeding, but the patient is never again able to nourish the same parasite. This would be a remarkable kind of pabulum, for the loss of it does no harm to the patient, nor does the loss of a dozen other kinds of pabulum which he keeps on hand for the other specific diseases. As far as we know of bacteria, they are also not so very particular, and parasites mostly go on devouring the substance of the host till death. So, why the specific diseases, if they are parasitic, should ever stop, as they do, and that in a curiously definite and fixed way, is

another difficulty, and it would be a wonder that any man or beast should survive were infectious diseases dependent solely on parasitic fungi with such tremendous powers of diffusion, reproduction and destruction, capable of fastening on and multiplying in the healthy body. It is unnecessary to pursue this part of the subject further, so we may conclude that it is impossible to reconcile the clinical facts with any theory, such as the parasitic, which places the cause of them solely in the changes occurring in something foreign to and independent of the diseased body; but that they involve the essential co-operation of the organism itself as the chief, or, at least, an integral part of the process. So we must now turn to the alternative theory, viz., that of tracing the exciting cause to morbid secretions thrown off by the diseased body, coupled with the additional theory that these may contain or consist of particles of living matter.

§ 16. *Morbid Secretions.*—By secretions are meant exclusively those compounds which are formed by purely vital processes. In the vast variety of the products of vegetable life we have abundance of examples of the power of vegetable secretions to act as stimuli on living beings, from the mildest condiments, perfumes, and medicines, up to the most rapid and virulent poisons. In the animal kingdom we have secretions, such as mucus, saliva, pepsin, bile, milk, &c., which fulfil most important functions for the health of the animal itself, while others are weapons of offence or defence, by their power as poisons, in all degrees, from that of the gnat to the rattlesnake. All secretions are liable to be perverted or diseased by a great variety of causes, some even mental, and which act with extreme rapidity, and, in consequence, irritate and excite disease in the individual itself. And as most diseases are attended with the discharge or throwing off of vitiated secretions, it is natural to anticipate that these should produce disease in others. Accordingly,

pathologists have generally admitted diseased secretions as the probable cause of contagious and miasmatic diseases. In Fletcher's *Pathology* it is laid down more particularly that the exciting cause of all contagious diseases consists of diseased secretions thrown off by animals affected with the same disease; while miasms, or malarious poisons, consist in diseased secretions thrown off by vegetables in a state of disease. This last distinction has not yet received the attention it deserves. To illustrate further the theory of diseased secretions, a person with a contagious disease may be looked upon as throwing off a secretion which, in virtue of its vitiation, is noxious to others, just as a venomous serpent secretes a poison in health; and the analogy is closer when we notice that many contagia are thrown off by secreting organs; *e.g.*, the virus of rabies by the salivary glands, scarlet fever by the glands of the throat and skin, measles by the mucous glands of the nose and air passages, typhoid by those of the intestines, &c. But the word secretion must not be limited to glandular products, for it may apply also to all products of perverted nutrition, such as pus, and sanies, and exudations from diseased tissues, or from the blood itself. Thus, if we include the last, viz., all kinds of detachable products of morbid nutrition among secretions, we can perceive that "diseased secretions" form a wide enough category to include the exciting causes of infectious and contagious diseases. And if we state, simply as an ultimate fact, that some have the power of causing a secretion of matter like themselves [contagia] which others have not [venoms], we probably say all that is certainly known, while renouncing the attempt to explain the remarkable difference between the two. Nevertheless, pathologists cannot rest satisfied without hypothetical attempts at explanation, among which, those tracing it to chemical changes in the secretions, independent of the purely vital

action concerned in their formation, are unworthy of attention, and for the most part unintelligible ; while of those tracing it to the presence of living matter, the parasitic category has been already judged.

§ 17. There remains now the hypothesis of Dr. Lionel Beale, the discoverer of the Protoplasmic theory of life, who lays it down that the miasms and contagia are not only formed from the protoplasm, or living matter, of the sick person, like all other secretions, but they consist of actual portions of protoplasm, or living matter, which, being transferred to a new body, continue to live and grow therein, thus causing the phenomena of contagion and infection. They are thus living portions of the diseased body engrafted on a healthy body, and the name of graft-germs may therefore with propriety be applied to them. The word is the more appropriate since it was the one originally given to the operation of inoculation, as is reported in the celebrated *Letters* of Lady Mary Wortley Montague, whose words are :— "The smallpox, so fatal and so general amongst us, is here [Turkey] entirely harmless, by the invention of *grafting*, which is the term they give it." The revival of this word, to designate transplantable disease-particles, is due to Dr. James Ross, in his very clever book, *The Graft Theory of Disease*. He proposes to call the contagium particles simply "grafts," but I think it will be more convenient to use the expression graft-germs. Dr. Beale, who is the discoverer of the theory, calls them simply "disease-germs ;" the word germ being here quite proper and intelligible, for, as he says, "any living particle growing or capable of growth may be termed a germ." To trace this theory to its root, we must remember that all diseased processes ought to be traceable to modifications of healthy ones, or, at least, to a strong analogy with them. Now, on the protoplasmic theory, all secretions, as well indeed as all formations of tissue, are the result of the

transformation, and, in fact, for the most part, the death of protoplasm—the one only living matter. The great majority of the secretions which in health subserve the purposes of the life of the body as a whole, are not living, nor do they contain any particles of living matter; *e.g.*, the gastric and pancreatic juices, the bile, the perspiration, the tears, milk, &c. But there are some others which naturally contain particles of living matter or bioplasm, capable of living for a certain space of time after separation from their point of origin. Of these the most notable are the spermatic and the mucous secretions. We are therefore justified in including the detachment of living matter among the functions of secretion, which last term may thus cover every variety of pus or similar matter thrown off by a truly vital process, although morbid, whether by the glands, the tissues, or the protoplasm contained in the blood itself. In health, the soft viscid transparent fluid we call mucus, is a dead product of the transformation of the protoplasm of the mucous membrane. The fixed protoplasm is not only being continually consumed in the formation of the soft fluid, but portions of it are thrown off living, and survive for a time embedded in the mucilaginous fluid. These are the mucous corpuscles, and they can be seen, with a power magnifying 700 diameters, exhibiting movements like an amœba. During this time they continue to perform their function, being transformed into the mucous fluid, and gradually wasting away. Now, under certain conditions, including over-stimulation and the excessive supply of nutriment, the growth and sub-division of the bioplasts becomes more rapid, while the elaboration of the proper fluid is less perfect; and, "in some cases of inflammation of the mucous membrane, all the viscid matter secreted upon the surface appears to consist of bioplasts, ordinarily termed *pus corpuscles;* while, on the other hand, the proportion of formed material, which was abundant in

ordinary mucus, is exceedingly small. The bioplasm has multiplied so fast that there has not been time for the production even of the soft mucus." * This is the key to the whole theory. All living beings are made up of a vast number of living units or plastids, in groups, each of which has its specific developmental power, inherited from the embryo, and continually being transmitted to their descendents while the conditions of health endure, as long as age permits. Any disturbing cause, such as excessive stimulation, or stimulation of a morbid quality, or altered supply of nutriment, may hurry on vital action and check developmental power from reaching its healthy standard, and the subsequent bioplasm is thus germinally degraded. Germinal degradation is, however, compatible with, and often attended with, increased powers of growth, and altogether an assimilation to lower orders of living creatures, whereby a greater viability in a separate form and other qualitative distinctions are acquired.

Now, although the protoplasm of all tissues and parts is specifically distinct, and, owing to that distinction, in one case produces nerve, in another muscle, in a third bone, in a fourth epithelium, and so on, yet they all, under certain conditions in which their growth is hurried on too fast, give rise to "a common form of germinal matter or bioplasm differing in properties and powers from them all. This is the form of bioplasm known as *pus*, which may go on multiplying for any length of time, producing successive generations of pus-bioplasts, which exhibit remarkable vital properties, although they cannot form tissue, nor produce tissue-forming bioplasts of any kind whatever." (p. 114.) Pus is thus the product of irritation of the protoplasm of all tissue, and not derived from the white corpuscles of the blood alone, as has been more recently upheld by Cohnheim.

* *Disease Germs*, by Dr. Lionel Beale, F.R.S. 2nd Edition, p. 101.

The exudation of white corpuscles from the inflamed capillaries in inflammation was discovered by Beale in 1863, together with their transformation into pus-corpuscles, but it was then shown by him that this was only one of the sources of pus. The transformation of the to be detached mucus-corpuscles into a degraded but more viable and rapidly growing form of protoplasm, viz., pus, is the first step; and the degradation of the protoplasm of the fixed tissues and of the blood into the same, is the second step in our comprehension of the *contagia* or germinally degraded bioplasts. It has been long known that pus was liable to be of an acrid and irritating nature, and it appears now that this depends on its containing actually living bioplasts, and on the character and degree of germinal degradation of their vital powers. For the pus-corpuscles, as usually figured in books, are dead, as are also the majority of those contained in abscesses in the living body. But many can be found living, especially those formed by the degradation of the protoplasm of mucus and epithelium cells, and these form the first links in the chain of degrees of viability, and differentiation of the disease-germs. The living pus-corpuscle has no cell-wall, but is a formless mass, in continual movement, pushing out protrusions, which become detached, and form new corpuscles. In inflammation of the mucous membrane of the bladder, Dr. Beale has seen them living and moving forty-eight hours after separation from the body, and I can confirm the fact from my own observation. Dr. Beale also states that these same corpuscles can be kept alive in water to which a little serum or albumen has been added. From what we thus know of the viability of pus, which is comparatively so little removed from health, we can easily imagine how the further degraded and differentiated bioplasts of the specific fevers may have sufficient viability to allow the preservation in moist or liquid media, and even the partial

desiccation and transportation through air characteristic of miasms and viruses. It may be said that these last differ so much from pus in appearance, that we cannot reason from any analogy between them. But it is not so; the difference between the appearance of common pus and the clear vaccine virus, for example, is no doubt great, but that depends on the accidental ingredients in which the active part common to both is suspended. (§ 2.) "It is impossible to distinguish many pus-corpuscles from lymph-corpuscles, white blood corpuscles, and many other masses of germinal matter; indeed, if we examine the developing brain of an embryo at an early period, it will be found that this important structure consists of nothing more than a number of spherical cells, which could not, by any means we are yet acquainted with, be distinguished from many forms of pus-corpuscles."* In fact, the bioplasts constituting disease-germs simply share in the common characteristics of all protoplasm, viz., that all kinds are, to outward appearance, exactly alike, from that of the simplest vegetable up to that of the brain of man, although in vital properties they differ so enormously. This is no hypothesis, but a simple fact, and is therefore in favour of the graft-germ theory against the parasitic theory, for the impossibility of finding morphologically specific organisms in the specific fevers, drives its advocates to the hypothesis of physiological specificity of common micrococci. In the graft theory no specific outward distinction is expected or required for the abundant bioplast formations which are met with in the specific fevers, and many of which have been erroneously described as micrococci.

§ 18. Together with the mucous and epithelial cells of the mucous membrane and glands, the bioplasm of the blood itself forms the chief source of the degraded bioplasts which constitute disease-germs. Not only does the blood contain

* Beale, *Disease Germs*, p. 130.

the visible white corpuscles, but an infinity of smaller particles of living matter, and these, as well as the more palpable white corpuscles, become degraded, and thus the source of the disease-germs of contagious and specific fevers.

In all fevers, even when arising from simple non-specific causes, such as catarrhal and inflammatory fevers, this bioplasm of the blood is increased in quantity, and to a certain extent, no doubt, altered in quality, so we can easily imagine it to degenerate, as mucus-bioplasm does, into pus, and thus become the contagious matter of the specific fevers, or, at least, of those in which the blood is specially involved. Now, we are reminded by Dr. Beale that the living matter of the epithelial cells and of the blood possesses remarkable formative powers, which survive even in the adult, and, in particular, the blood bioplasts, when exuded, may develop into analogues of some of the lower tissue-cells, and thus take part in regeneration of tissue and healing of wounds. This is attributed to their being descended from the protoplasm of the germinal area at a period of development before that of most of the fixed tissues, and they therefore inherit some of that more general formative power which enables some animals lower in the scale to regenerate lost complete parts. It is to be noted also that it is just this class of living matter which furnishes the basis for all infective diseases.

It is therefore hardly necessary to go beyond blood and epithelial bioplasts in considering degeneration or degradation of living matter as the cause of infective matter. And with protoplasm of such formative powers, we can easily imagine that degradation may take place from mere alteration in the external essentials of life, viz., pabulum, conditions, and stimuli; also when protoplasm, so degraded, has become more viable, it may be mutually transplanted, not only between one individual and another of the same species, but also between others widely different in the

biological scale, even to those of the vegetable kingdom. On this point, as on many others, Dr. Beale has been anticipated by Fletcher, in whose *General Pathology* (1842) we read :—"Vegetables secrete like animals, and are liable by disease to have their secretions vitiated. Now, diseased animal secretions produce contagious diseases; analogy would therefore lead us to suppose that those miasms from which infectious diseases arise, such as those of marshes, are in like manner secretions from diseased vegetables." This position was supported by the facts known at the time, and now Dr. Beale adds from the facts now known, including his own discoveries, "it is not improbable that the germinal matter of some of the lower, simpler plants and animals, when exposed to altered conditions, may give rise to morbid forms, bearing a relation to their normal healthy, living, germinal matter, similar to that which pus bears to the germinal matter of healthy tissues. It may be that the matter of the malarial poison may thus result, in which case it must be regarded as a morbid bioplasm of some low organism—not as a *species* of any kind whatever—but as a deteriorated form of living matter, freely multiplying, but incapable of returning to its primitive healthy state. (p. 117.)

It is unnecessary to adduce, in support of this, the now admitted fundamental identity of life in plants and animals, and, in particular, the facts more recently made known by Charles and Francis Darwin, but I may quote a striking illustration, given by Dr. Beale himself, of the analogy of the living juices in the two kingdoms:—"If the clear transparent material which moves round the cells of the *Vallisneria* and other plants be carefully examined under very high powers, magnifying upwards of 2,000 diameters, it will be discovered that this is not a simple fluid, like water, containing the nucleus and chlorophyl. But the apparent fluid has suspended in it an infinite number of particles of

living matter, like those of which the amœba, white blood-corpuscles, and other forms of living matter consist." He then goes on to state that it is to the vital movements of these particles that the circulation in the cell is due, and that these particles in the vegetable cell bear the same relation to the nucleus as the similar fine protoplasmic particles do to the white corpuscles of the animal blood, while the red corpuscles correspond to the chlorophyl particles.* Having thus, as a basis, the existence of certain kinds of protoplasm of a lower order of individuality forming an essential part of higher organisms in which degradation and the capacity for a certain amount of independent viability and growth, we next enquire for experimental proofs that such really happens. It is impossible here to go into details, but it may be simply said that abundant proof has been furnished by the experiments of B. Sanderson, Lewis and Cunningham, Onimus, Vulpian, Clementi and Thin, and others, of the following points :—

If you introduce into the peritoneum any common irritant, such as solution of ammonia, boiled so as to sterilise it from bacterial germs, an inflammation of moderate intensity is set up. If now a very small portion of the exudation fluid of this first generation, as it were, be injected into a second animal, we have a much more intense inflammation set up. From this second generation a third and fourth, and further, may be derived, each increasing in virulence and intensity, till death is produced in a few hours by the introduction of a fraction of a drop. If, however, the matter of the first inflammation be boiled, it has no such poisonous effects ; the poison also is non-dialysable—in these two points agreeing with the theory of degraded living matter. It is true that, although no bacteria are introduced at first, they are found in the subsequent increasingly poisonous

* Beale, *Disease Germs*, p. 139.

inflammation-fluids, derived, no doubt, from the ubiquitous germs (§ 11), and brought to maturity by the diminished vital resistance (§ 12) of the diseased state. But they are not the cause of the virulence of the disease, for a similar amount injected without the inflammation-poison would be innocuous.

It has likewise been found that the matter of inflammation of the cornea, produced by a non-specific cause, *e.g.*, mechanical injury, becomes contagious. (Eberth.) Perhaps the most striking development of an organic poison by successive inoculation is that discovered by Davaine, and confirmed by many experimentors. Here the case is generally complicated by the introduction of bacteria at first, and it would require too much space to go into the whole question, so I merely note the undisputed facts which bear on our present subject. These are the rapid increase of virulence with each generation of inoculation and the dosage. At first a considerable quantity of putrid blood* requires to be injected into the circulation in order to produce death by simple putrid poisoning. But by successive inoculations from the blood of this first animal, the virulence of the poison increases so much and so rapidly, that, in a few generations, the tenth, the hundredth, thousandth, millionth, and finally, it is said, even the trillionth† of a drop is sufficient to produce death. No chemical poison, or even venom, approaches in the remotest degree in deadliness equal to this. Nor does the effect of self-reproducing ordinary septic bacteria bear any comparison with it, for a palpable quantity is required to produce any evil effect.

* Even putrid albuminous matter, boiled in alcohol, thus destroying all bacteria, will produce the first generation of septic blood-poisoning (B. Sanderson); also dialysed putrid products. The poison is here evidently chemical, but Onimus found that the virus of true septicemic blood, *i.e.*, subsequent generations, is non-dialysable.

† This has been doubted, and attributed to some experimental error. Clementi and Thin, however, confirm the principle up to beyond the hundred millionth.

We may therefore consider it established that by the operation of non-specific causes a contagious phlogogenic (or inflammation-producing) virus can be developed *de novo* in living beings.

§ 19. We have thus a solid basis of fact and experiment on which to rest an explanation of the origin of virulent and contagious diseases by perversion of the living processes within the body itself. In this way may be easily conceived to arise infective blennorrhœa, ophthalmia, erysipelas, pyemia, and puerperal fever. The conditions of the origin of this last, indeed, form in crowded communities and in lying-in hospitals an involuntary experiment on a large scale, in inoculating successive generations of increasingly degraded blood, mucus and pus-bioplasts, till they acquire the fatal virulence of that dreaded disease. In the above class of diseases the graft-germ theory fits far better than the parasitic-germ, for the existence of purulent and other degraded living particles cast off from the diseased body is undoubted, and the analogy of transfusion of blood and transplantation and grafting of skin, periosteum, and other tissues, shows there can be no difficulty in their being also transplanted and growing in other individuals, thus constituting contagion. While the *rapidity* of the process of alteration and degradation is quite what we should expect as disease, whereas it is quite contrary to what we know of the production of new species, or even varieties of independent organisms, such as parasites. With respect to the origin of the specific fevers, which never arise spontaneously now, the two theories are equally at fault as regards positive knowledge. But, as in all febrile states, arising from common causes, the white corpuscles of the blood and the bioplasts of the capillaries are always in a state of over-action and rapid development, they are thus in a state bordering on the degree of degradation which would make them contagious particles, and it is not difficult to suppose that in certain

circumstances of famine, over-crowding, and other noxious influences, they may have become fully developed and differentiated into the specifically distinct graft-germs now known.*

* Although neither chemical agencies, organic or inorganic, nor septic organisms, constitute the external factor in the proximate cause of the specific diseases when formed, yet all these may play an important part indirectly in the causation of the degradation of the living plastids, which become the starting-point of a contagious disease, not necessarily like the direct effects of the noxious chemical agent, but always henceforth retaining its own specific character. Hence popular opinion is to a certain extent justified which attributes the origin of epidemics to noxious influences arising from the great convulsions of nature, such as earthquakes, volcanic eruptions, floods and droughts, and from the permanent evils of dirt and bad drainage. For example, hay-fever, as proved by Dr. Blackley, of Manchester, is caused by the irritation of the pollen of the grasses acting on certain predisposed individuals, and is, of course, not contagious. But it would not be difficult to imagine that were a number of such patients kept in close proximity, the mucus-corpuscles thrown off in the cough, and inoculated and re-inoculated through the air from patient to patient, might become degraded into pus, and finally into infective catarrh-germs. It is possible the influenza epidemics may have so arisen: first, a catarrh caused by chemical, probably plant, emanations, and then continued by an animal poison formed in the system. Probably epidemics of yellow fever arise in a similar manner, for, although apparently depending on malaria, yet it never arises except in pretty closely-settled communities of men, whereas the intermittent fevers are the direct effect of the malarious germs on solitary individuals exposed to them. Yellow fever, therefore, depends probably on an animal poison developed in the system, owing to the noxious action of chemical agencies, probably drawn from plants. This applies equally to the so-called diblastic theory of this and typhoid, cholera and the miasmatic-contagious diseases, which assumes the existence of two poisons, *i.e.*, a ground-poison and a body-poison which, by their co-operation, produce the disease. The addition of the graft-germ theory gives us, in fact, increased scope for explanation of the labyrinth of apparently contradictory facts to which the parasitic theory alone fails to give us the clue. The rôle of bacteria in the causation of pyemia is, no doubt, of the same indirect character. In all wounds, and in injuries with unbroken skin, if sufficiently extensive, there is a certain amount of traumatic fever present, and in this state the bioplasts of the blood and injured tissue are already degraded and multiplying too rapidly, and a small additional noxious influence will further degrade them into infective graft-germs; while, at the same time, the vital resistance, described at § 12, is lowered. The presence of any notable amount of bacteria, and the consequent putrefaction of non-living matters in the wound, is such

On the other hand, no plausible conjecture ever has been put forward for the origin of specific parasites. Thus we may take it as proved, by experiment and observation, that altered living matters, here called graft-germs, do exist, and are capable of explaining the phenomena of contagion equally, as respects viability with the parasitic germs, except on one point. The exception is the power of growth and multiplication in indifferent media out of the body. Supposing we allow it is sufficiently proved that graft-germs can retain

an influence, and a most powerful one; when, therefore, this occurs in ill-tended wounds, infective pus or graft-germs form, which, either at once or after passing from one patient to another, acquire the virulence of the hospital pyemic infective poison. But the growth of bacteria, and the noxious influence of the chemical poison secreted by them (sepsin.), is not the only cause of pyemia, hence "the antiseptic method" hardly designates correctly Professor Lister's admirable and successful mode of treating wounds. It is generally admitted now that the total exclusion of bacteria is not necessary, nor is it attained by the spray during operation, and the impervious dressings after. Bacteria have been found in the best dressed and quite healthy wounds; and Billroth and Ehrlich found no difference in the putrefaction of blood drawn directly from an artery and sealed-up under spray, and that without such protection; the spray did not either keep off nor destroy the bacterial germs. Besides, if mere bacteria acted as a pyemic poison as self-reproducing, and in minimal dose, like the poison of rabies, syphilis, and smallpox, nobody could survive the smallest cut or abrasion, and vaccination and subcutaneous injection would be certain death. It was proved experimentally by Dr. Roberts (*British Medical Address*, 1877, p. 25) that the ordinary dose of morphia solution for subcutaneous injection, caused speedy putrefaction in sterilized beef infusion, just like any other septic germ inoculation. So it seems generally agreed that good surgery with the open method, where that is practicable, is quite as successful as the Listerian method, except in hospitals. And for the same reason, viz., that the bacteria are kept from multiplying *in quantity sufficient* to produce fever and inflammation, leading to degradation of the bioplasts and formation of graft-germs, and thus *originating* the infective poison. The true explanation of the action of the carbolic acid or other antiseptics is, I believe, that given by Dr. Beale, viz., that, besides, of course, preventing the growth of bacteria, they stop the formation of pus, and with it the further degradation of the bioplasts into more virulent infective graft-germs. It is, in fact, an abortive process. The question is different where this poison has been fully developed, and clings to the surroundings of an hospital patient. Here the most fastidious

their vitality in moist and dry media as long as the contagia are known to do, and allowing that pus-corpuscles can grow and multiply in milk, serum, &c., as shown by Dr. Beale, yet we require more experimental evidence that they can be propagated in that way to the extent that the bacteria can be. For example, in Dr. Klein's * recent experiments on the organism found in the pneumo-enteritis contagiosa of pigs, it was found that a needle-point of the virus kept in a closed cell with a drop of pure aqueous humor for twenty-four hours, multiplied and grew. From this successive generations were cultivated, each time with only a small fraction of the drop. From these generations, up to the eighth, successful and fatal inoculations of animals were made. The author concludes, from these experiments, that the contagium resides in a different variety of the *Bacillus subtilis* from that which causes the splenic fever, and that this disease belongs to the category of physiologically specific parasitic diseases. Unless, therefore, it can be shown that graft-germs can be propagated to the extent above noted, out of the body, and might, therefore, have been the real contagium present at the same time as the bacilli, it is

precautions of the Listerian method cannot be called exaggerated, for we have to deal with a true morbid poison, which acts in minimal dose. And it is exactly here, in old, ill-constructed hospitals, that the greatest triumphs of the method have been won. The process is here, if perfect exclusion fails, almost purely abortive (like, in fact, the cautery to the bite of a rabid dog), and little, if at all, antiseptic, unless the theory be true that the poison consists of physiologically specific bacteria. Against this is the fatal objection that the specific poison may arise *de novo* in single isolated cases—thus, in far too short a time for the evolution of a new species of bacterium. The conclusion of Billroth is substantially that of Beale, that the specific poison is formed in the system, and does not reside in bacteria. But he calls it (*Coccobacteria Septica*, p. 166) a "phlogogenic ferment," or "phlogistic zymoid." No doubt the diseased part may secrete many noxious matters, and some may be ferments, but the specific poison cannot be a ferment, for, as said (§ 4), no chemical ferment reproduces itself, nor does it cause a living body to secrete more of it.

* *Quarterly Microscopical Journal*, April, 1878.

difficult to resist the conclusion that the latter was the true cause.

There is nothing *a priori* unreasonable in the supposition that bacilli should produce splenic fever or pneumo-enteritis just as the *Bilharzii Hæmatobium* is the cause of Egyptian dysentery; and I do not think Dr. Beale is justified in refusing to admit the physiologically specific parasitic as a possible category of contagious diseases, although I do not think it yet quite settled whether the three diseases admitted into it in the diagram belong to it, * although, as said, the

* The experimental proofs tracing special contagia to particular parasitic saprophytes, even the cultivation experiments, although strong, have been trusted to too much, as there are still several sources of fallacy which have not yet been obviated. For instance, Dr. Klein believes that, by his cultivation experiments, he has proved that the specific virulence of the pneumo-enteritis contagion lies in the bacilli rather than in the bacterium termo, both of which he reports as present, and he seems to assume there was nothing else present in which it could lie, notwithstanding the evidence of Lewis and Cunningham, and many others, that there exists an animal poison in peritonitis not bacterial at all. From my experience with putrefactive fluids, I should say the difficulties are much understated and not at all met by Dr. Klein. In transferring a drop of infective peritoneal secretion to the microscope stage we should see, with a comparatively low power, not only *B. termo* and *Bacillus subtilis*, but a number of other globe and chaplet bacteria, and varieties of rod and screw bacteria, besides granular matter and masses of germinal matter capable of growing and multiplying. With higher powers we should, in addition, see multitudes of finer globe-bacteria and amorphous particles of germinal matter, and we have reason to believe, beyond these again, exist bacterial germs and germinal particles totally invisible to our present microscopes. Dr. Klein admits the difficulty of separating the *B. subtilis* from the *B. termo*, and says nothing at all about the rest. From my experience, it is impossible, without further processes than he describes, to separate the different objects above named, and therefore I have no doubt that in his final cultivation, wherein he supposes he had nothing but *B. subtilis*, that he had also abundance of *B. termo* and globe-bacteria, besides germinal matter, here called graft-germs, in addition to other bacterial organisms of which no account is taken. I hold, therefore, that until he has excluded the possible action of the termo and globe-bacteria, he has not proved the virus to reside in the bacillus; nor till he has excluded the graft-germs, to reside in a parasitic organism at all. How this is to be done it is difficult to divine, for both are non-dialysable, and both are killed pretty nearly by the same

mode of development of the contagium out of the body is in favour of the supposition for them, as well as possibly typhoid and cholera, if an organism peculiar to them should hereafter be discovered. On the other hand, the impossibility of propagating smallpox, vaccine, and other contagia out of the body, tells more for the graft theory, although it is not decisive against the parasitic, for many parasites cannot thrive without their proper nidus.

§ 20. Here we strike upon the much-vexed question, "What is an individual?" If these bioplasts, or masses of degraded living matter, can not only be transplanted and live, and propagate themselves by fission in the solids and fluids of higher living beings, but can do so even out of the body altogether in indifferent pabulum, how do they differ from the independent species we call parasites?

On this subject I think we cannot do better than follow Häckel, according to whom absolute individuality does not exist in animate nature, but only relative; and that the whole of organic nature may be arranged into different orders or categories of relative individuals. Of these orders he makes six, and among them man and kindred organised beings occupy the fifth order, viz., Prosopa or Persons. A person or prosopon is not a single homogeneous vital unity, but is built up of a number, harmoniously arranged, of all the previous orders of individuality, and during the embryonal stage passes through all these lower orders in the course of its development. The first or fundamental order of which all the rest are constructed consists of cells, more or less

things. So let no one think the question is so easily settled. At the same time, although pus-corpuscles multiply in indifferent media, yet, as above said, more evidence is wanted that naked protoplasmic particles, like graft-germs, can survive the treatment which bacillus spores can. But is it not possible that extremely minute graft-germs may be shut up in bacillus spores? They are small enough; and some fungus spores are known to be shut up in ova.

complete, or protoplasam-masses, called by Häckel plastids, of which, specifically differentiated and combined, tissues and organs, symmetrical parts, and prolongations constituting the different orders are formed, and these together make up individuals of the fifth order or Persons. When these are connected by a common circulation and nervous system with unity of consciousness, and descended from a single ovum, as the offspring of two parents, the result is one which we have no difficulty in recognising as an individual, and to which we indeed apply the term of individual proper, and from which we take our ideas of individuality, and endeavour to apply them to organic nature as a whole, though with but indifferent success. For, not to speak of the absence of a nervous system and of consciousness in plants, the plastids of our different tissues and organs still retain their specific kind of vitality, and form, in fact, subordinate individualities in each person. Now, the greater the perfection of an organism the more are the separate individualities subordinated to the whole, and thus incapable of maintaining a separate existence. Consequently, in the mammals it is only in the order of plastids, and the lowest type of these, that we can expect to find a power of separate life for a time after detachment from the organism as a whole. For to each morphological or anatomical order of individuality corresponds a functional or physiological individuality, which enables it to sustain its existence independently, and manifest its vital activity. To the physiological individual Häckel applies the convenient term of *Bion*. Besides the *actual bion*, or mature physiological individual, and the *virtual bion*, or immature form, there exists a third form of bion, in which it can maintain its existence as an apparent independent bion for a longer or shorter period after separation from the complete physiological individual, without, however, being able to develop itself into an actual bion. This is termed a *partial bion*. The partial

bions, belonging to man and kindred animals, are chiefly the white blood and the lymph-corpuscles, the mucus-corpuscles, and the epithelial cells, and more particularly the spermatozoa, which, in fact, do not begin to perform their proper physiological functions until they are detached from the actual bion. There exists, therefore, already a biological category into which the degraded bioplasts or graft-germs naturally fall. They are, in fact, *partial bions*, produced either by degradation or disease of the healthy partial bions, or by the conversion of the fixed plastids into partial bions by degradation or disease. *

* Häckel distinguishes six orders of individuality, each of which is represented both by an anatomical or morphological individuality, and by a physiological individuality. His definitions of these are as follows:—"A morphological individual, or form-individual, or organic form-unity, means, as a general expression, that particular form-phenomenon which forms a self-contained and formally continuously connected whole; a whole from whose constituent parts none can be taken away or asunder without destruction of the essence and character of the whole form. A form-individual is, therefore, a simple connected magnitude in space, which, at the moment of judgment, we must regard as an unchangeable figure."

"A physiological individual, or functional-individual, or vital-unity, is that particular form-phenomenon which is capable of maintaining its own existence quite independently for a longer or shorter period; an existence which expresses itself, in all cases, in the activity of the most general organic function, in that of self-preservation. The functional-individual is, therefore, a simple connected magnitude in space, which is observed to live as such for a longer or shorter time, *i.e.*, that can nourish itself, and which, at the moment of judgment, is to be looked upon as variable. Very often the same may, in addition, propagate itself, and perform other vital functions. For shortness, let us once for all give to the physiological individual the name of *Bion*."

Both the anatomical and the physiological individualities occur in nature under six different categories, or *orders of individuals*, as follows:—

I. Plastids (cells and cytodes, or elementary-organisms).

II. Organs (cell-stocks or fusions, simple or homo-plastic organs, composite or hetero-plastic organs, organ-systems, and organ-apparatus).

III. Antimers (counterparts or homo-typical parts, rays of the radiata, halves of the bilateral symmetrical animals, &c.).

IV. Metamers (prolongations or homo-dynamic parts, "internodes" of the phanerogams, "segments," rings, or zonites of the articulata and vertebrata).

§ 21. A clear distinction being now made between parasites and detached living particles of higher organisms, let us see how far the theory of graft-germs, or partial bions, fills up, and how far it shares, the defects of the parasitic germ theory. Partial bions are particulate, living and propagating rapidly by subdivision and growth, thus sharing equally with parasitic germs in the power of explaining the chief property of contagia. Besides, they are actual portions of a diseased body, and are formed by degradation or disease of it, and thus can subsist in a great variety of shades of

V. Persons or prosopa (shoots of plants and cœlenterata, &c., "individuals," in the strictest sense, in the higher animals).

VI. Cormi (stocks or colonies, trees, shrubs, &c., composite plants, salpa-chains, and polyp-stocks).

All these orders are represented throughout animate nature, on the one hand, as independent beings, and on the other, as built up into each other, the lower into the higher, to form the compound orders of individuality, of which all above the first consist, and each of the higher contains all of those orders below it.

The first order, or plastids, is represented as independent organisms, which never rise higher by most of the protista and many algæ, such as amœba, actinophrys, the so-called unicellular organs, including even the gigantic caulerpa, bryopsis, &c. Within the higher orders the plastids form, of course, the basis of all the parts of which they are built, and are represented by the protoplasm-masses, or bioplasts, or cells, to which alone the protoplasmic theory of life restricts the possession of vitality.

Order II. is represented by many independent species of protista, algæ, and cœlenterata.

Order III. The antimer-state is hardly represented in nature as independent, excepting the larva-state.

Order IV. The metamer-state is largely represented in nature by most of the mollusca and many worms and algæ.

In the higher orders, "the organ, in its purely morphological sense, is a complex of two or more united plastids. The antimer or homo-typical part is a complex of two or more united organs. The metamer or homodynamic part is a complex of two or more united antimers."

Order V., or persons, is a "complex of two or more united metamers." It is represented by the majority of the higher animals, but by few plants as independent beings. On the other hand, the majority of plants and cœlenterata reach the stage of persons, but cannot exist so independently, so they form Order VI., viz., the stock or cormus, which is a complex of two or more united persons.

difference, and originate *de novo*; they consist of amorphous protoplasm, which may have every variety of power while apparently identical in physical aspect; their specific power is developed with rapidity. In all these respects the graft-germs have the advantage of the parasitic germs in explaining the phenomena of infectious diseases. But beyond that, as long as they are merely transplanted and increase solely by the subdivision of the actual particles originally conveying the infection, then they must share the defects of the parasitic theory.

It is stated by Dr. Beale, as his deliberate conclusion, "that the millions of contagious particles produced in the

The physiological individuality which corresponds to the above six orders may itself consist of three different kinds, so there are thus eighteen possible organic vital unities to be considered. The three kinds are :—

I. "The *actual bion*, or physiological individual in the strictest sense, is each completely developed organic individual which has reached the highest degree of morphological individuality which belongs to it, as mature full-grown representative of the species. For example, the actual bion in the phanerogams is a morphological individual of the 6th, in the vertebrates of the 5th, in the majority of mollusca of the 4th, in the spongiæ of the 3rd, in the volvocinæ of the 2nd, and in the unicellular algæ of the 1st order.

II. "The *virtual bion*, or potential physiological individual, is each undeveloped organic individual, so long as it has not yet reached the highest degree of morphological individuality which belongs to it as a mature full-grown representative of the species, and to which it can develop."

III. "The *partial bion*, or apparent physiological individual, is each part of an organic individual which has the capacity, after detachment from the potential or actual bion, of surviving a longer or shorter time, and continuing its existence as an apparently independent bion, without, however, being able ever to develop into an actual bion."

The partial bions generally perish after a time, during which, however, they may have exercised a determinate function (*e.g.*, reproduction); as, for example, is the case with the hectocotylus of the cephalopods (an organ), with the proglottis of the cestodes (a metamer), with the male flowering shoot of the vallisneria (a person)." The white blood corpuscles of animals, and the cells of the spongiæ and other amœba-like plastids, often continue to move after separation from the organisms to which they belonged. And, according to Recklinghausen, even the blood-cells of the

organism in an eminently contagious disease, are all the direct descendants of the very few, or perhaps even single particle, first introduced."* He positively rejects the idea that the morbid action and the multiplication of the disease-germ are the consequence of the peculiar influence of the disease-germ on the healthy living matter. Hence, the graft-germ theory, as far as interpreted by Beale, is open to all the objections to the parasitic germ theory given at § 15, and which need not be recapitulated. And, in addition, all diseases caused by disease-germs ought to be contagious, whereas the whole large class of the purely miasmatic are not. (§ 24.) Further, although excessive action of the common stimuli and pabulum may easily be conceived to hurry on vital activity so as to cause degradation of the bioplasts into pus, yet mere growth by self-division in different media can hardly explain the rapid gain of specific virulence by successive inoculations, without some other influence such as spoken of at § 23, p. 62. I conclude, therefore, that although it explains the first batch of animal graft-germ diseases on the diagram much better than the parasitic-germ theory, yet it quite fails in the specific fevers which follow next. Besides, can we really imagine that in diseases that are known to have existed for centuries, such as smallpox, all the countless millions of graft-germs are derived from mere subdivision

higher animals can, under favourable circumstances, not only survive out of the body, but even multiply and go through determinate changes. The ciliary cells, also, of many, especially the lower animals, continue their movements for long after detachment. Many plant-cells, when detached from the parenchyma, can live for long, and even multiply by fission, without being able to develop into actual bions. The pollen grains of the phanerogams possess a high degree of physiological individuality, and most of all the zoosperms of the cryptogams and the animals. The physiological activity of partial bions is even more completely illustrated by those belonging to individualities of higher order, but it is chiefly those of the order of plastids which interest us here.— See Häckel's *Generelle Morphologie*, vol. i., chaps. 8 to 11.

* *Disease Germs*, p. 191.

of the single particle, or few particles, which were first differentiated? It is contrary to experience that fissiparous generation should continue perpetually in independent species, but some other mode of generation must intervene at intervals. Much more is it against the nature of partial bions, which are the true physiological analogues of the disease germs. Their duration is always temporary, and although it is stated by Darwin that the male reproductive element is "enabled to keep alive for four or five years within the spermatheca of a female insect," yet that is an extreme case, and the most we can expect from partial bions is that they should have a power of survival equal to what is known of the contagia. There can be little doubt, therefore, that the partial bions of contagion take a new origin from co-operation with the previously healthy blood or tissue-protoplasm of each subject of the disease.*

§ 22. The partial bions of the specific fevers thus fall into the category of *specific stimuli, i.e.*, they excite in the healthy parts an altered vital action, which constitutes the disease. They are, therefore, only one factor in the process which results, among other things, in the secretion of matter of the same nature as themselves. By their action as specific stimuli may be explained some of the phenomena not so well, if at all, explicable by either the parasitic or the simple graft-germs, such as the different intensity of the same morbid poison on different individuals, the elective affinity of organs or tissues, the immunity from second attack, and partly the relations of the latent stage; for all positive agents act as stimuli on the living matter—not only as functional excitants, but as modificators of nutrition—each in its own specific

* This was substantially the opinion of Jenner in respect to smallpox, and it has been confirmed by the best observers since, whose opinions are summed up by Dr. Braidwood, who says we must "acknowledge that the variolic virus generated by an animal is not the same as that which was introduced into it." (*Morphology of Vaccine Lymph*, 1874.)

way, and for which the living matter has a corresponding specific irritability or susceptibility. This specific irritability is proper to each organ and tissue; hence the elective affinity of all medicines and poisons each to its proper seat. The degree of specific irritability differs in all individuals; hence the different degree of intensity of action of the same poison on different individuals. All irritability is liable to exhaustion by excess of action of stimuli; and most varieties of specific irritability may be diminished or lost, at least for a time, by the action of their corresponding stimuli, while the power of reacting with other stimuli remains. Thus is explained the influence of use and wont, whereby many things at first highly pleasurable or painful become by repetition blunted in their operation, and finally indifferent. By these principles is explained the law of immunity from a second attack of the specific fevers, which is quite unintelligible on the parasitic and simple graft-germ theories. Only the morbid poison has a much more complete effect in that direction than the ordinary chemical poisons; still this is merely an exaggeration of what pertains to the action of all stimuli. In favour of this being a question of stimulation, and not altogether belonging to the more mysterious quasi-sexual function of the partial bions, to be alluded to presently (§ 23), may be noticed, that not only does vaccine matter, which is a modified smallpox partial bion, protect against the latter, but Belladonna, which is merely a chemical stimulus, protects, though temporarily, against certain types of scarlet fever to which its action is the pathological *simile*. Likewise, a latent stage is found in the action of nearly all poisons, and even medicines, and some light is thrown on the mysterious connection between the length of the latent stage and the severity of specific diseases by the general principles of the action of stimuli. For it is laid down as a law deduced from observation by Fletcher, that,

ceteris paribus, the severity of the disease is in proportion to the length of the latent stage. This is supported by the action of ordinary stimuli. "If a pinch of snuff be received into the nostrils, the excitement which it occasions is short, the collapse and increased secretion are slight and soon over; but if a similar pinch of asarum be received, the excitement lasts for some hours, during which we are not conscious of any effect, but the collapse and increased secretion which follow are proportionally severe and of long duration; and it is a remark very frequently made with respect to common catarrh, that the sooner it displays itself after the exposure to its exciting cause, the less violent it is and the sooner it is over. * Of course the *ceteris paribus* must be rigidly kept in mind, otherwise the exceptions may easily appear more numerous than the rule. The author is less happy in the alleged cause of the shortening of the latent stage by inoculation of small-pox matter, when he says, "that in its concentrated state it produces so strong a contraction of the capillary arteries as is incompatible with a long continuance, and the subsequent relaxation in which the disease consists is in proportion to this continuance." (p. 136.) Too much stress is here laid upon the mere capillary constriction and dilatation which doubtless make up one factor in all inflammatory and febrile diseases; but, nevertheless, in a specific qualitative change in the living matter which in a certain time exhausts the susceptibility to the specific stimulus producing that change, it must be of consequence to the result to shorten that time wherein the morbid influence acts. As a matter of fact, however, we do not know whether the concentration of the virus has the effect above assumed, nor how it spreads from the focus of infection. On this subject Dr. James Ross has some ingenious suppositions which deserve attention,

* *Elements of General Pathology*, p. 83. MacLauchlan, Edinburgh, 1842.

although they are as yet only hypothetical.* In favour of Fletcher's law, though not of his explanation, is the fact that when inoculation succeeded in propagating scarlet fever, the latent stage was not shorter, and the disease not milder.

§ 23. Still, the action of the partial bions of the specific fevers as specific stimuli does not explain the reproduction of secretions like themselves as the outcome of their operation, although this is obvious and intelligible with both the parasitic and the simple graft-germs. Hitherto we have had a solid bases of facts to rest on; there are parasitic germs, and there are partial bions, which may act, some as graft-germs and others as specific stimuli, and we have legitimate grounds on which may be discussed the propriety of arranging particular diseases in one or other of these categories; but now we must enter on hypothetical ground, and trust to inference and analogy for further elucidation of the subject. So much must be said not to prejudice what has gone before.

As a rule, the material stimuli consist of non-living chemical substances; and, during their operation, they become incorporated with the living matter, exalting or modifying its vital activity, while they themselves are decomposed, or enter into new combinations and are eliminated. On the other hand, foreign living matter coming into contact with that of any organised being is generally destroyed and decomposed, being consumed as pabulum, or acting as a dead stimulus. But there is a conspicuous exception in one of the partial bions to analogy with the physiological action of which we trace the nature of disease-germs, viz., the genital element, whose function it is to blend with other living matter, without being destroyed in the process, but, on the contrary, to form with it a new modified living being, which shall run a fresh life-cycle. We may imagine that the cause of death of all individuals is the gradual loss of the germinal

* *Graft Theory*, p. 128.

faculty, which may consist in a certain energy of position of the ultimate elements of the complex living matter, during its self-renewal by interaction with the environment which constitutes life. None of the external conditions, including pabulum and non-living stimuli, can apparently restore the energy of position proper to youth, hence decay and death of all living beings. But the interaction of two somewhat different kinds of protoplasm upon each other can do this, as we see in the process of reproduction. Hence the incomparable power of living matter above all dead stimuli and conditions as modificators of the germinal faculty; and could we only find this in disease-germs it would explain both their tremendous power and their reproduction.

Such is the theory of the quasi-sexual operation of disease-germs. The first intimation of this, in my recollection at present, is by Trousseau and Pidoux, where they compare the taking of a contagious disease to *conception*, and the idea has been more or less frequently present to pathologists since. It is alluded to by Dr. Beale in these terms, while, however, he rejects it for the alternative given at § 21 :—"It might be maintained that the contagious material actually passing into certain portions of the living germinal matter of the organism excited in these new actions, and caused them to divide and subdivide very actively, and communicated to them the same properties which the original particle possessed, somewhat in the manner in which the wonderful powers existing in connexion with the germinal matter of the spermatozoa are communicated to that of the ovum, and affect, to some extent, every one of the multitudes of living particles resulting from its division." * Since Dr. Beale's alternative is so inadequate and unsatisfactory, it may be well to reconsider the one he rejects. In the first place, as we are dealing here exclusively with plastids of the first or

* *Disease Germs*, p. 188.

lowest order of individuality (§ 20), we have not to look for visible distinction of sexes. In independent individuals of this order, for the most part, either no sexual differentiation is found, or both sperm and germ-cells belong to the same individual. Nevertheless, we cannot say that any species can persist without sexual generation occurring in some part of the cycle of their life-history. According to Häckel's definition, "the criterium of sexual generation is the material union of two different generative substances," and this is equally fulfilled by the process of conjugation proper to the lower orders of animate beings, whether the sexual elements are preceptibly differentiated or not. Asexual generation is represented in external nature by fission or fissiparous generation and by spore-formation. Of the former there are two kinds, viz., simple division into two parts of equal age, and budding, in which a portion grows out, and is then detached, forming a product of different age. These processes are known to occur in partial bions, as we see in pus-corpuscles, which are the simplest type of disease-germs; hence, no doubt, Dr. Beale is so far justified in limiting his theory of disease-germs to those whose mode of propagation is proved, and to extend it further carries us into the region of hypothesis. Still, hardly any hypothesis could appear more marvellous and improbable—were we not familiar with them—than the phenomena of infection still unexplained by him. Asexual spore-formation has not been proved to occur with partial bions, otherwise that might account for some of the facts of long survival and dormancy of miasms. It is in the various forms of conjugation that we must hope to find analogies with the process of infection. In conjugation, a more or less complete blending of the protoplasm of two individuals, which apparently do not sexually differ, takes place. The result of this is the formation of what are usually called spores [zygospores], but which De Bary and

Häckel consider to be impregnated ova, because they are preceded by the essential condition of sexual generation, viz., the union of two separate portions of living matter. It is immaterial that the genital elements are not differentiated, but diffused through the whole protoplasmic mass. Häckel thinks it a probable supposition that some such separation of the different elements has already taken place in each plastid, and that conjugation is thus in reality a mutual impregnation of two hermaphrodite individuals of the first order—a phenomenon which is the rule in hermaphrodites of higher orders, such as snails.

The form of conjugation characterised by complete blending of the two plastids into one, followed by its total breaking up into spores, as occurs in gregarinæ, and rhizopoda and some infusoria, can hardly be represented in the process of infection, except possibly in those gland-cells which are destroyed in the disease, as is the case with many tonsillary glands in scarlet fever, and certain mucus-glands of the intestine in typhoid. This destruction of glands is used by Dr. Maclagan*—a partizan of the parasitic theory—to explain the immunity from second attack, inasmuch as these parts form the special nidus of the parasite, and when destroyed, it can find nowhere to lodge in a second time. This theory goes only a small way towards explanation of the immunity; but, as far as it goes, the conjugation of partial bions fits better than the lodging of parasites.

In the incomplete form of conjugation there is merely adherence at some point, and partial blending of the protoplasm of the two plastids, while the individuality of each remains more or less complete. This occurs in Desmids, Zygnemaceæ, and some infusoria. Rejuvenescence is another process in which change without destruction of the cell-contents takes place. This, till lately, has been limited to a

* *The Germ Theory*, by Dr. T. Maclagan. London, 1876.

change in the cell-contents of the Œdogonium and some other low plants, whereby they are converted into swarm-spores; but Bütschli has recently extended the significance of the phenomenon. It is supposed that in rejuvenescence of single cells a differentiation takes place in the contents of the single cell, and the different parts blend, and hence a new departure in reproduction is taken.* Conjugation of two separate cells as a prelude to rejuvenescence is, Bütschli† thinks, seen more plainly in the bacillariaceæ, but it is not followed by coalescence of the two cells, and formation of a zygospore or a sporangium, as in ordinary conjugation. On the contrary, the cells become larger and more vigorous, and a rejuvenescence has taken place. Bütschli, in fact, considers the conjugation of these and several species of infusoria, up to the rank of paramecia, to be a prelude to rejuvenescence, and a fresh departure of merely fissiparous generation, without the formation of any true sexual products. As a matter of fact, I believe it will be shown that he is wrong in respect to the paramecia in which the formation of spores after conjugation does occur. But that conjugation, as a quasi-sexual process, is followed by increased reproductive vigour, without destruction of the cells, *i.e.*, rejuvenescence, is probably to be accepted as a natural process. We have thus in external nature, in conjugation and rejuvenescence, a parallel to the process of infection, which may thus be looked on as the quasi-sexual stage, which is interpolated in the life-history of all species, as it occurs in disease-partial-bions. The rejuvenescence will probably tell more on the floating partial bion than on the fixed plastids, with which a kind of hybrid is formed and cast off; but it may also tell on the fixed plastids, modifying them so as to produce the immunity,

* Archer. *Nature*, 13th June, 1878.

† *Studien über die ersten Entwicklungsvorgänge der Eizelle, die Zelltheilung und die Conjugation der Infusorien.* Von O. Bütschli. Frankfurt, 1876.

and possibly other changes, not necessarily for evil. For the powerful stimulus of living matter may restore the germinal faculty if weakened or degraded. It has been noticed that in cases which recover from the specific fevers (if not prevented by sequelæ, in the form of local inflammations, etc.), an unwonted vigour of health sets in, and specific tendencies to disease are overcome; *e.g.*, the tuberculous diathesis is said, at times, to be extinguished after typhoid fever. I have read also of a case in which the susceptibility to smallpox was regained after typhoid fever. These facts gives us a hint of the possible use of the morbid poisons as therapeutic agents.

As before said, we have no actual proof that partial bions can be reproduced in any way except by fissiparous generation; but the above mode of reproduction, if applicable to them, might suffice to explain the cardinal facts of the specific fevers. The last word of science is not spoken; other modes of generation in external animate nature may be discovered, and partial bions may be shown to be capable of the above or other modes of reproduction. In the meantime, we may conclude that all action of living matter, as a stimulus, has a strong analogy with the quasi-sexual processes. In this we may probably find the explanation of the remarkable increase of virulence by the successive inoculations of diseased partial bions, described at § 18. The union of these with the similar, but somewhat different, fixed plastids, may be compared to the effect of intercrossing in fully sexually-developed species; and an increase of vigour takes place till a certain acme for each specific disease-germ is reached.

§ 24. In transplantation of plastids combined into tissues and organs, forming the second order of individuality (§ 20), as when a piece of skin is grafted, it becomes attached to and nourished by the new person, and is now as much a

piece of his skin as it was of the old person's; it does not affect the neighbourhood except by contiguity and nerve-attachments. So also in transfusion of blood, no doubt the partial bions of the first order, the living corpuscles, simply continue the same function in the new person as they performed in the old, and no disturbance arises where their quality is nearly identical. But when a slight alteration has taken place by disease, even the healthy plastids may act as living stimuli. This is probably what takes place in that modification of skin-grafting for the cure of ulcers, wherein they are sprinkled with the mere scrapings of healthy cuticle, containing small particles of still living epidermic protoplasm, or with the fluid of a blister containing such. The latter, no doubt, blends, while remaining still living, with the protoplasm of the open sore, and exerts a quasi-sexual stimulation, which restores their full germinal power to the weakened plastids of the ulcer, and enables them to form healthy skin. A similar effect, beyond mere transplantation, is seen in grafting among plants; and the affection of the stock by the scion after grafting attracted the attention of Mr. Darwin—whose genius has given the impulse to a new departure here, as it has in almost every branch of biology—and induced him to compare such affection to an inoculated disease in the case of animals. This probably attracted the attention of Dr. Ross, and became the exciting cause of his book on the Graft Theory of Disease, in which he has collected a number of facts which support the theory of quasi-sexual stimulation rather than of simple grafting. A few of the most striking may be quoted. Mr. Darwin's words are as follows:—"It is certain that when trees with variegated leaves are grafted or budded on a common stock, the latter sometimes produces buds bearing variegated leaves; but this may perhaps be looked at as a case of inoculated disease." And again, "It is notorious that when the variegated jessamine is budded on

the common kind, the stock sometimes produces buds bearing variegated leaves. Mr. Rivers, on the authority of a trustworthy friend, states that sound buds of a golden variegated ash which were inserted into common ashes, all died except one; but the ash stocks were affected, and produced, both above and below the points of insertion of the plates of bark, bearing the dead buds, shoots which bore variegated leaves. Mr. Brown, of Perth, observed, many years ago, in a Highland glen, an ash tree with yellow leaves, and buds taken from this tree were inserted into common ashes, which, in consequence, were affected, and produced the blotched Breadalbane ash." *

Similar facts related by Dr. Masters are still more striking, for he states, on the authority of Mr. Rivers, that "an unhealthy or feeble stock has been restored to health by the imposition of a healthy graft." And again, "Cases have been observed where, from the stock *below* the graft, fruits and flowers of the same appearance as those borne on the scion have made their appearance. This has been observed in the case of the pear grafted on the mountain ash, and in other cases." And again, "The effect produced even by a temporary contact with the variegated bud, is confirmed by a case that fell under our own observation. A year or two since a beautiful *Abutilon*, with leaves mottled with yellow, was introduced into our gardens. It was very desirable that this should be propagated as largely and speedily as possible. Propagation by means of cuttings was easy enough, but naturally the plants were small, and took a considerable time to grow bigger. Grafting was therefore had recourse to. The scions of the variegated *Abutilon Thomsoni* were grafted on to green-leaved stocks of other *Abutilons*. This was done by many nurserymen on the continent as in this country, and it was soon found that the grafted plants were apt to produce

* *Animals and Plants under Domestication.*

variegated leaves from the stock; in other words, that the peculiar qualities of the scion were manifested throughout the entire organism. To show that the variegation was really due to the influence of the scion, we may mention a curious fact communicated to us by M. Van Houtte, the well-known nurseryman of Ghent. Like his compeer, he had plenty of illustrations of the fact that a variegated scion of this particular *Abutilon* will communicate its properties to the stock on which it may be grafted, but he further ascertained that if by some accident the graft were separated from the stock, the leaves subsequently produced from the latter were wholly green, as before the grafting, and even the variegated leaves originally produced lost their mottled character."* These facts have a wider bearing than may at first appear, for they lead us to perceive that the migration of partial bions, not only occasionally but permanently, may be one of the means of bringing about the unity of the individual of the higher and compound orders of individuality (§ 20), such as Persons. The somewhat overburdened nervous system cannot here be taken into account. Indeed, in animals we can no more expect the nerves to convey material specific properties than we could expect telegraph wires to carry goods as well as messages. Here, at least, we can only suppose that particles of the living matter of the scion are carried in the juices of the plant through the whole plant, and act as living stimuli on those parts, and on those only possessing a corresponding irritability or susceptibility, thus producing a marked alteration on the germinal faculty, but one which is apparently not permanent, as there is a tendency to revert to the original type unless the stimulus is kept up. This seems to be almost parallel to the influence of the development of the sexual organs at puberty in producing the change of voice, the growth of the beard, and a

* *Popular Science Review*, April, 1871. Quoted by Dr. Ross, pp. 42–43.

certain masculine character of the whole habit of body, which are all apt to fade away after castration. The sympathy by which these phenomena are made interdependent is generally attributed to stimulation conveyed by the nerves directly or reflexly to the secondarily altered organs or parts. But it is quite possible that they may be in great part owing to the continued action of partial bions which are thrown off by the testicles, and act as stimuli to the germinal faculty of the parts susceptible of this special influence. The same principle may probably be extended to many other evidences of the constitutional unity of character of nutrition in each person, who is yet made up of such a number of separate parts, each with its inherent specific vitality. For the influence of the separate parts on each other's nutrition can hardly be more palpable than the above examples in plants which have no nerves. The same principle extended to disease has probably even a wider scope, and we may thus comprehend the nature of certain so-called constitutional diseases which seem to be transferable from one part to another, and we may understand better some forms of metastasis and the nature of the evil effects of suppressed discharges. For although the reflex actions of the nerves of organic sympathy are really the cause, and suffice to explain the greater part of sympathetic morbid actions, still there are some not reached, more especially gouty metastasis and the evils of suppressed secretions. For, in spite of the efforts of dogmatic pathologists, the vulgar still retain the fear of "driving in the disease," inherited from the times of the old humoral pathology, and this fear is shared in by many thoughtful practitioners. Although, of course, on the protoplasmic theory, it is impossible that the liquid blood can be alive, and therefore absurd to speak of it as diseased, yet we must not look on it as a source of disease only as altered pabulum or the vehicle of noxious chemical stimuli, but as

containing particles of living matter which have most important functions in health, while similar particles in a diseased state may act as noxious living stimuli on the healthy plastids of distant parts, and thus convey specific diseases. This idea has recently received an important application in the theory of secondary cancer put forth by Dr. Creighton, and received with favour in the medical world.* The theory is that the secondary cancerous tumor is not caused by the transplantation of complete cancerous cells from the primary tumor, which take root in a different organ and grow there, but that it is produced by the transformation of the previously healthy cells of the organ—say the liver—by the operation of an extraneous influence, "which is to be compared to a spermatic influence produced in some unknown manner by the parent tumor." Thus the quasi-sexual operation of partial bions, or portions of living matter thrown off by healthy or diseased living tissues and organs, may have an extensive application within the body itself, and it is only natural to extend the same principle to the action of one body on another in explanation of the nature of contagious diseases.

I conclude, therefore, that an assumption of a conjugational or quasi-sexual power in the partial bions constituting the exciting cause of the specific infectious diseases would remove the objections applying to both the parasitic and the simple graft-germ theories, which tell especially in the fevers of the smallpox group. I propose, therefore, to add the term conjugation-germ to those already in use. (§ 17.)

To go into the detailed application of these principles to the infectious diseases in general is impossible, as my space is nearly exhausted. A few words only on their applicability to the clinical facts of the smallpox group, which demand that the multiplication of the poison shall depend on the co-operation of the organism, and not on the self-multiplica-

* *Privy Council Health Reports*, 1874.

tion of a foreign organism merely sojourning within it. At the time of infection of smallpox we may imagine the conjugation-germs absorbed and diffused in extremely minute subdivision through the whole blood, whence they are speedily removed and blended with the fixed plastids specifically adapted to combine with them, for the blood, as a rule, does not convey the disease. In the latent stage, some unknown change, in addition to that which happens with all stimuli, is taking place, like the early stage of conception, which gives rise to few symptoms. Some, however, can be detected; for instance, wounds will not heal at that time. At the period of invasion the sudden and enormous reproduction of the specific partial bions from the infected fixed plastids begins, thus causing the initiatory fever. But the reproduction of the specific partial bions is not the proximate cause of the whole febrile symptoms; for the irritation of that process causes a large amount of the febrile disturbances which are common to all kinds of fever, including those arising from non-specific causes. We have the irregular distribution of blood from irritation of the vaso-motor centres (which though attracting most attention is less important), and, above all, the increase of the bioplasts of the blood and capillaries, which is the essential proximate cause of the febrile and inflammatory states. This is recognised by Dr. Beale, who points out that not all the abundant masses of germinal matter and bioplasts found in infective ophthalmia are the descendents of the infecting graft-germs, but many or most are simply the super-abundant formation of non-specific bioplasts, which is the essence of inflammation and fever. This is important, as the non-specific part of the disease greatly complicates and aggravates the total result, and may be what determines the fatal event in particular cases. Besides therefore the varying susceptibility to the specific poison, we have the same variety

towards common exciting causes, for no two people suffer alike in degree from the common causes of disease, such as cold or other perversions of the ordinary conditions of health. Hence a double cause exists for the varying intensity of the total disease in different persons; and hence also the existence of a margin of possible success in treatment, even although we may not possess a specific antidote for the specific poison. Another subordinate complication of some specific diseases is the presence of saprophytic parasites, which may contribute largely to the severity of the total disease. Their relation to the specific cause has been already dealt with. (§§ 10, 11, 12, 13.) In some specific diseases we are probably concerned only with graft-germs propagating asexually; in others, especially those both inoculable and infective through the air, both kinds of germs must be taken into account. It is not yet clear how the conjugation-germs spread through the system from the point of inoculation, but certainly they are diffused everywhere before the specific secreting vesicle is complete. Bryce's test shows that the system is affected enough to influence the course of a second vaccination in a new place, before the original vesicle is fully developed. Therefore, the full development of the latter is not the cause of the affection of the system. It is quite possible, also, that the morbid poison in the form of graft-germs may be inoculated and grow asexually in the spot for a time, even when the system is protected—thus showing the difference between graft-germ and conjugation-germ-action. This probably takes place often in revaccination, for the percentage of cases in which a vesicle is formed exceeds those of liability to a second attack of smallpox. Vaccinators do not like to use that matter, but its specific efficacy has not been disproved. It is said that the old inoculators of smallpox sometimes kept up a supply of matter on their own arms.*

* *Germinal Matter and the Contact Theory*, by Dr. Morris, p. 67.

Similar principles apply no doubt to all the animal poisons which have a constitutional as well as a local action. Also the vegetable morbid poisons constituting Malaria must act as conjugation-germs, and the result of their union with the fixed or the blood plastids is no doubt an infertile hybrid, probably from the too great dissimilarity of the parent organisms. Hence the non-contagious nature of these diseases.

But it is impossible to pursue the subject further here, and I must be content to have given the above outline of an addition to Beale's graft-germ theory, and leave it to some future opportunity to follow out in detail the analogies of grafting, hybridization, need of intercrossing, etc., to the intricate processes involved in the infectious diseases.*

§ 25. In conclusion, let us pass again for a few minutes from matters of technical detail to the bearing of the principles here set forth on the general welfare of society, as affected by the fearful scourge of infectious diseases. The tendency of the foregoing has been to restore these diseases to the domain of medicine proper, in opposition to the parasitic hypothesis, fashionable for the moment, which would, as it were, consign them to a department of natural history. Were it so, there would be little hope of their extinction or mitigation by the medical art. On the other hand, if they are diseases bred within us from altered conditions of health, our prospects are better, though not unreservedly so. As long as infectious diseases, such as the catarrh and erysipelas group, arise from the operation of mere common non-specific causes, if by any chance they were swept clean out of the land, they would infallibly re-

* In fact, the subject forms part of a work on "The Stimuli," with which I have been engaged for some years. I may also say that since the printing of this paper was finished I have found that Dr. James Ross had already noticed the analogy between disease-germs and the partial bions of Häckel, which is satisfactory as a corroboration of the views independently given here.

appear, so long as poverty, dirt, overcrowding, famine, war, vice, etc., afflict the human race.

And with respect to the diseases of the class which now never arise except from infection, and whose origin is hidden in the night of time, although we may circumscribe the area of their operation by such means, yet we can never hope that good food, virtue, drainage, and ventilation will extinguish them altogether as long as man is a social animal. That hope lies in the medical art, and, strangely enough, in the use of the very morbid poisons themselves whose tremendous power for evil has just occupied our attention. We have already two examples of the marvellous perfection as medicinal agents of these incomparably powerful specifics; and as it is contrary to the continuity of nature that there should be exceptions to any laws, these instances cannot stand alone. Our hope for the future must therefore be, by diligent experiment and research, to extend the same principle to all the fixed infectious diseases. The two examples alluded to are, one of protection against disease by the wonderfully perfect operation of vaccination; the other of cure, viz., of Pannus, by inoculation with the virus of purulent ophthalmia. Of the former it is needless to speak, as its merits are universally acknowledged; but the latter is little known out of the medical profession, so it may be described more in detail.

The word Pannus, which means literally a cloth, is applied to an opacity and thickening of the cornea like a cloth, producing blindness. It is characterised by a superficial vascular opacity of the cornea, due to the formation of a layer of new-formed cells beneath the epithelium, and in the superficial layer of the cornea, which becomes thickened and its surface rough and irregular. It is attended with great injection of the blood-vessels and sensitiveness of the conjunctiva and globe of the eye in general, flow of tears, intolerance of light, and more or less complete blindness. It

often remains as the consequence of the Egyptian or infective purulent ophthalmia, and is a fertile source of disablement of soldiers. It also arises from granular ophthalmia from whatever cause. When fully developed its cure is almost hopeless, all ordinary topical and internal medicines producing, at best, temporary relief, or none at all.

In 1812, Jaeger, of Vienna, discovered that inoculation with the matter of purulent ophthalmia, by exciting a fresh attack of that disease, had the effect of dispelling the pannus and restoring vision. As usual, we may unfortunately say in medicine, this was at first scouted and rejected by the profession, and Jaeger himself was discouraged, and ceased to employ the method till 1827, when Dr. Piringer * adopted and carried it out systematically with such success that, in 1841, of the one hundred and forty-five cases operated on by him and by Jaeger, one hundred and thirty-eight were cured. Since then it has been adopted into medicine generally, and is used especially with success in Belgium and England. The marvellous completeness of the cure by this operation strikes one with astonishment, and shows us that we are dealing with an agency far more powerful than ordinary medicines. One of the earliest cases in this country came under my observation. It was that of a young woman of twenty-one, who had been affected with granular ophthalmia and pannus since childhood; she was unable to count the fingers of a hand held up, had never learned to read, and was led about with bowed head, unable to bear the light, and the eyes running with a thin acrid discharge. A minute drop of matter from the eyes of an infant with purulent ophthalmia was, at my request, put into her eye by Dr. Dudgeon, now of London. In a few weeks the result was reported by him as follows:—"Instead of walking in the open air with her head bent forwards and her eyes scarcely open, she now walks

* *Die Blennorrhœ am Menschenauge.*

erect, and does not experience the slightest inconvenience from the brightest sunshine. She can see the minutest needlework, and is no longer dependent on the care and attention of others." * This is the rule: the eye is simply touched with the infective matter, and the disease allowed to run its course without the slightest medicinal interference, and with the above result. There is no fear of relapse, which constantly occurs after all other means of amendment.

In accordance with what is seen with smallpox, the inoculated disease is here milder than the purulent ophthalmia caught naturally, and the latent stage is shorter. (§ 22.) We find it also stated by Mr. Soelberg Wells,† "The matter from an eye suffering from inoculation is stronger than that from an infant [from which it is taken], as its activity appears to be increased by the inoculation." This agrees with what has been said at § § 18, 23. In accordance with the principles set forth in the foregoing pages, the *rationale* of the cure by this method is as follows:—The plastids of the conjunctiva and cornea are in a state of germinal degradation, with so great a loss of formative power that they cannot produce the compact, transparent, healthy form of these tissues. Then the infective partial bions inoculated, unite with them, exciting a temporary increase of similar protoplasmic matter and profuse non-living secretion. When this subsides, the effect of the stimulus to the fixed plastids is seen in rejuvenescence, or regeneration of their full germinal faculty and formation of healthy tissue anew. (§ 23.) The result of this operation does indeed strike the observer as in reality a renewal of youth, or a new birth of the part. The tendency of the plastids in a state of germinal degradation, or, in fact, variation, to revert to their original state,

* See *London and Edinburgh Monthly Journal of Medical Science*, May, 1844.

† *Treatise on Diseases of the Eye.* 2nd Ed., p. 67.

which is the cause of spontaneous as well as all other cures, seems to be here wanting, even to the extent that ordinary medicinal stimuli specifically adapted fail to rouse it, and the more powerful stimulus of living matter (§ 23, p. 58) seems to be required. Here also in the cure we have an analogy with the influence of the scion on the stock in grafting, mentioned at § 24, p. 64.

With these splendid examples before us, one of the chief aims of medicine should now be to turn these fearful engines of power into agents of protection against, and cure of, the very evils produced by their uncontrolled natural operation. Or, in the words wherein the intuitions of the poet anticipate the reasoning of science,

> "Take thou some new infection to thy eye,
> And the rank poison of the old will die."

The path is already marked out for us. There is no chemical poison whose violence may not be effectually tamed by simple dilution, while its specific quality remains unchanged. That resource, of course, fails us with a poison which is reproduced by its very operation; but a similar result can be attained by passing it through the system of some other animal. For it is now established that the vaccine virus is nothing but the smallpox virus modified by passing through the cow. By the light of this knowledge, and guided by Fletcher's law of the relation of the latent stage to the severity of the disease (§ 22), let experimental research be pursued with unwearied perseverance, until the causes are found why those two examples of prevention and cure have so long stood alone, and success is attained in extending their number. Happy they who, with intellectual ability, have the leisure and the opportunity to devote themselves to experimental research directed towards this object. For some among them is, assuredly, reserved a place in the temple of Fame, beside the name of Jenner, as benefactors of the human race!