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SOME THOUGHTS ON THE EVOLUTION AND AFFINITY OF DISEASE.

By F. Le Gros Clark, F.R.S.

The theory of Evolution, as it is now generally understood and accepted in its application to normal development, demands a similar recognition in the study of pathology; for it requires no argument to prove that the various indigenous diseases of civilised life are not coeval with man's creation, and that the farther he recedes from a savage state the more complex do the ailments become to which he is obnoxious. The study of pathology in this aspect is not, as it appears to me, one of mere speculative interest, but of possible practical value, the measure of which it would be rash to limit until the field of inquiry it offers has been fairly cultivated in all its details. A more watchful observation of the development of disease, and of nature's methods of relief, and a more loyal reliance on her ability to cure, have already borne rich fruit in the substitution of a rational for the empirical treatment of disease; and a tardy recognition of the laws of hygiene has tended in the same direction, by denying the necessary conditions of environment for its evolution. It is, therefore, by patient observance of the progressive steps by which various pathological changes are developed, and the retrogressive steps by which a healthy condition is restored, that we may hope to frustrate or modify the former, and to facilitate the latter; possibly in time even to banish many diseases which are now prevalent.

The investigation to which I refer may be expressed in the following propositions:—(1) That there are affinities between diseases, which though remote may be traced; (2) that the divergence from a simple type, and the resulting variety in disease, are due to evolution; (3) that such evolution is influenced or determined by environment, heredity, or accidental or acquired idiosyncrasies; (4) that the principle of reversion to original type is a valuable guide in the treatment of disease.

No doubt much that may be written on this subject is purely speculative or hypothetical: but the region of speculation is

that also of opinion; and the same objection may be urged against evolution generally; and time and opportunity alone can show how far such speculation may be justified: for this subject is not one which can be brought to the test of direct experiment. Yet the present state of our knowledge has prepared the ground, and supplied much of the material which constitutes a foundation on which to raise a superstructure of reasonable probability.

During my student life I became interested in the subject of this paper, by having my attention directed to the evolution of syphilis by Mr Travers, whose articled pupil I then was. This eminent surgeon and philosophic thinker was an advocate of the unity of the venereal poison, and of its original derivation from an inflamed mucous membrane. I naturally adopted this view; and the experience of my professional life has confirmed the impressions thus early received. I will state briefly the line of argument pursued in illustration of pathological evolution, as exemplified by the venereal disease;[1] and then offer a few remarks on the affinity of disease and evolution in pathology generally.

The first proposition is, that the existence of an inflamed mucous membrane is capable of exciting a similar condition in a healthy mucous surface with which it is placed in contact; as demonstrated by instances of inflammatory leucorrhœa causing suppurative ophthalmia in new-born infants; and even purulent discharge from the male urethra. There is, no doubt, more susceptibility to such infection in some persons than in others, as is exemplified in the communication of gonorrhœa; and this receptiveness, whatever it may be due to, is a potent factor in the development of this, as of other diseases. The next stage is the production of a sore; and this, as I apprehend few will question, may result from the simple application and retention of gonorrhœal matter from the vagina on an excoriation or cutaneous crevice of the glans penis or prepuce. The secretion from the ulcer consequent on this lesion may, when absorbed, infect the system, producing mild secondary symptoms, mani-

[1] This branch of the subject has been more fully treated in a paper published in the *British Medical Journal* of April 24; and some passages in it, relevant to the present paper, have been transferred to these pages.

fested chiefly in the throat and on the skin, but sometimes affecting the joints.

The more virulent form of primary sore—the excavated ulcer with hardened circumference—Mr Travers regarded as a constitutional sore, the product of a system already impregnated with poison: or, to use his own words, "a gonorrhœal sore in a fresh subject produces, by absorption, constitutional symptoms of the first order (those referred to above); and communicates a similar sore, having the same tendency to propagate the first order of symptoms. But a gonorrhœal sore, occurring in a person already the subject of the first order of symptoms, becomes a constitutional sore, and secretes a matter capable of producing the second order of symptoms (those from hard chancre) in the individual."[1] Of course Mr Travers meant that this is the way in which a chancre was originally caused, and may still be produced; and here, no doubt, individual susceptibility greatly influences the result. Probably also the maximum intensity of the poison is not reached until it has passed, under favourable circumstances, both personal and antecedent, through several individuals. The impressions I acquired thus early have been confirmed by subsequent observation and experience, and may be formulated thus, viz., that there are superficial sores—mere ulcerated excoriations, which heal without constitutional treatment, and have no after consequences: that there are other superficial sores which appear after a varying period of incubation, and, though possesing none of the special characteristics of chancre, namely, induration, and exedent ulceration, yet may entail mild secondary symptoms: and there is a third class, the genuine chancre, with a longer period of incubation, and entailing, more certainly, severer and more complicated secondary symptoms, which are far less amenable to treatment. Between the last two or constitutional varieties of the disease no hard and fast line can be drawn; the gradations between the extremes being many, and determined by circumstances both personal and extraneous, in which the susceptibility of the recipient, as well as the quality of the virus, plays an important part.

Constitutional tendencies, whether they be such as may

[1] *Observations on the Pathology of Venereal Affections*, by Benjamin Travers, F.R.S., p. 29.

be termed accidental, or such as are inherited or acquired, are very influential in modifying the characteristics of disease. This is exemplified in various circumstances and in many ways: and there is nothing extravagant in the supposition that a simple inflammatory product may be thereby converted into a specialised form of disease; and again, that this specialised form should, in course of time, assume a specific type,—more permanent in character because it has reached its maximum development in that particular direction. In such evolution time is an essential ingredient; as are likewise the character of the infecting matter and the susceptibility of the recipient; both of which are materially governed by inherited or acquired diathesis. This is exemplified in the circumstance that two individuals, deriving syphilis from the same source, are not necessarily affected to the same degree, or even in the same way.

The study of ordinary septic inflammation from decomposing or diseased animal matter affords an analagous illustration; the susceptibility of the recipient greatly influences the result. Here likewise there is a period of incubation (if it may be so termed) before the zymotic action commences. In these instances the interval is short compared with that in the case of most specific poisons, perhaps because the affinity between the poison and the circulating fluids is closer in those which are non-specific. But the period of incubation in what are termed specific diseases is not such as to admit of their being classified under one general law. It is true that some of the exanthemata are approximately regular as regards the interval between exposure to infection and the manifestation of the disease; but they differ in this respect from one another. Yet in others, and probably also in syphilis, there seems to be a direct ratio between the virulence of the poison, as manifested by its effects, and the length of time it abides in the system before it is developed. Certainly a chancroid, or soft sore, has a shorter period of incubation than a chancre; and it is a question worthy of further investigation, whether there is not a more or less regular association between the length of incubation and the subsequent severity of the constitutional affection. That the interval between innoculation with syphilis and the development of the disease varies very much in different instances is unquestion-

able; and the simplest, and, as I believe, the true explanation of the conflicting evidence on this point is afforded by the admission that there are many grades of the disease; the mildest of which is developed after a short interval, whilst the severer forms are more delayed; the intensity bearing a direct relation to the length of incubation. This suggestion is not inconsistent with the germ theory of disease; inasmuch as we know that time is an essential condition of the multiplication of germs, and possibly also of the augmentation of their virulence, and of that of ptomaines; whereas the relative susceptibility of the recipients would explain the early surrender in some instances, and the more protracted resistance in others, to the influence of the poison. Is it not a rule, subject to exceptions, that the severer the attack in most infectious maladies, the greater the security, after cure, from a second invasion of the same disease? I believe it to be so in syphilis, as in the exanthemata; probably also in carbuncle.

Of the influence exercised by constitutional proneness to disease we have no lack of proof. In some instances this proclivity is exhibited in relation to special diseases, such as catarrh, gout, pneumonia, or bronchitis: in others it may be elicited by parasitic organisms whose spores are present in the atmosphere, awaiting a suitable soil in which to germinate; their activity being suspended until some impairment of vitality or other propitious conditions in their chance habitat favour their multiplication, or, it may be their assumption of a specific character. As regards non-specific poison, its introduction from an extraneous source is not essential to the production of a septic condition: it may be home-bred;—a fact which illustrates, in a remarkable way, how importantly the intrinsic condition of a patient, whether natural or acquired, governs the consequence of exposure to any exciting cause of mischief. Hospital surgeons are familiar with the class of patients amongst whom they may expect this pathogenic tendency. The discharge from a festering wound not only diffuses its poison throughout the system of the sufferer, but is qualified to impart its fatal virulence to others, when it is brought into contact with any trivial breach of surface.

When a specific disease is imported by innoculation, its

subsequent localisation, after perhaps a protracted period, at the original seat of lesion, is not the less remarkable because it is a recognised fact of every day occurrence. What happens in the interval—frequently long—between infection and development? Is the local activity the manifestation of reaction, or is the constitution unimplicated until after the localised poison is matured? I am not aware that these questions have been satisfactorily answered. The early destruction of chancre has been advocated by some surgeons, but with doubtful efficacy. There seems to be a generally received opinion that, in some of the exanthemata, there is a prevailing association between the period of incubation on the one hand, and the duration of infection and the character of the sequelæ on the other, *i.e.*, where the incubation is protracted, the infecting property of the poison is not long retained, and the converse: again, that a short incubation is often succeeded by relapses and more or less persistent sequelæ; whereas a long incubation, followed by a well-developed illness, is a security against the after-consequences which are noticeable in the other case. My own experience does not enable me to confirm these views; but assuming their correctness I apprehend the explanation may be, that there is a limit to the duration of the virulence of the germs in the same nidus; and that their infecting power is in great measure exhausted by protracted residence, before development, in an uncongenial soil. But where the predisposition is pronounced, the resistence is brief: yet the germ-poison may continue to exert its influence, entailing sequences which are absent, when the conditions are reversed. That the presence of such predisposition is a material element under the circumstances is demonstrated, not only by experience and observation, but also by experiment on the lower animals, with different doses of the same poison: for, though the fatality of a germ-poison depends, apparently, as a rule, on the quantity introduced into the circulation, it has been observed that the operation of the dose is far from uniform,—a small dose producing severe or fatal consequences in one case, and causing little or no disturbance in another; as in Koch's experiment with septicæmic poison in a house-mouse and in a field-mouse: and this result can be due only to some peculiarity in the recipient. The

action of many medicines, notably of mercury, in various individuals and in different animals, also supports this conclusion. Probably cholera exemplifies the influence of predisposition to the disease more palpably than other epidemics: and the causes productive of the receptiveness are various, and many of them acquired or dependent on race, as exemplified by the sweating sickness in Ireland in the 15th century, to which the English alone succumbed. It was not unreasonable to anticipate, as experiment suggests, that the incubation period is governed, other considerations apart, by the dose of the poison; *i.e.*, the larger the dose the shorter the interval, and the converse. But here again predisposition must not be lost sight of; nor must it be ignored that the germs themselves are not uniformly virulent; both which circumstances materially qualify any conclusions drawn from observations on the relations between the incubatory stage and the quantity of poison introduced.[1]

If we say that the effect of a small dose is to diminish or annul any existing susceptibility to a disease, it is simply enunciating, in a familiar way, the doctrine of protection which is now receiving so much attention, and which appears to promise such valuable results. But how this protection is achieved remains a mystery. It must be sought in an explanation of what constitutes the predisposition to a disease; and this may consist in the presence of some material element necessary to the zymotic action, which, when exhausted by a feeble appeal or by the instrumentality of some nearly allied poison, is not reproduced. The fermentation being completed, the addition of more ferment has no power to regenerate the action. I may mention, in connection with this subject, the statement made on the authority of the British Bee-keepers' Association, that the occasional stings to which bee-keepers are exposed need not be guarded against, as they will cause less and less trouble until neither swelling nor irritation will follow. A practical bee-keeper has assured me that he can verify this statement from his own experience. I am informed, on the best authority, that there are no recorded facts tending to show that any similar immunity is conferred on the subjects of snake-poisoning, if they have the good fortune

[1] Mr Walton Cheyne's Observations (*British Medical Journal* for July 31) may be consulted with advantage on these points.

to survive the injury: but my informant adds that he is not aware that the subject has been investigated;—probably for the valid reason that the paucity of material has prevented it.

There cannot be any reasonable doubt that the absence of susceptibility to a second attack implies some remarkable change in the condition of the individual subjected to infection; a change which converts a fertile into a sterile soil. The barren result of exposure is not due to any impairment of inherent virulence in the specific germs: the same opportunity of infecting the system exists as in the virgin soil; but the conditions necessary for their incubation are absent, or their reproductiveness is extinguished. This assumption seems to be suggestive of a concert of conditions, as essential to the activity of infection: in other words, that the parasites are not, *per se*, actively infectious, but require some corresponding or adjusted state of the recipient to excite their specific activity or to stimulate their reproductiveness: this not being present, they remain innocuous, or do not multiply. Variations in the state of the atmosphere, independently of its thermometric and hygrometric conditions, may exercise more influence in the development or hindrance of infection than science has yet discovered;—an influence which may operate either on the infecting agent or on the recipient. Ozone, whether in excess or deficiency, probably acts thus; as I believe its redundance does in encouraging the spread of influenza. The cloud of carbon suspended over coal-burning cities affords, by its antiseptic property, some compensation for its otherwise polluting qualities. Notwithstanding the large share of consideration which electricity has obtained as a therapeutic remedy, it may be doubted whether this primitive and all-pervading force has received the attention to which it is entitled as an organising agent, and in the production or control of disease. Many persons are sensibly affected by varying electric conditions of the atmosphere; and this in an exaggerated degree in sickness or enfeebled health. I have not been able to satisfy myself of its influence—beneficial or otherwise—in the healing of wounds; but I would invite those who still have the opportunities at their command, to renew experiments of this class; and also to ascertain whether the employment of electricity may not have

some effect in the early stages of diseases dependent on the presence of germs, or even in checking the development of malignant growths. More light may be thrown on the management of infection by the further study of those agents which arrest fermentation, such as terebene and borax, or otherwise neutralise its effects: for, it should be remembered that there is a close relation between fermentation and putrefaction; and that in both fermentation and infection the activity of germ-life is much easier to prevent than to control when once established. Some of these agents are, apparently, germicides; but in other instances this explanation is unsatisfactory. The desideratum of course is to render the poison inert without injury to the patient. It is said that the infecting organisms disappear under the administration of appropriate medicines, as when quinine is given in ague. If such be the case, and as the neutralising influence of antiseptics over different organisms appears to vary, we may not unreasonably look in this direction, for an extension of our acquaintance with specifics.

The discussion of immunity after infection naturally suggests the consideration of another class of maladies, such as catarrh, gout, eczema, &c., which manifest a proneness to recurrence. In many instances this tendency is inherited; in some it seems due to the enfeebled power of resistance to an exciting cause, induced by a former attack: special sympathy with other disordered organs will occasionally explain this persistent and intractable phenomenon; and in other cases we must thankfully accept Dr Creighton's interpretation, in his classical work on "*Unconscious Memory in Disease.*" Whether literally or figuratively construed, no other form of words would so appropriately express some physiological as well as pathological facts; such, for example, as the surviving impression in the pregnant female of a previous impregnation, as manifested in her offspring; or the recrudescence of the intermittent type in sickness, long after the ague and its exciting cause have been banished. For an analogous fact I am indebted to Sir John Kirk, who tells me that it is very common for the residents of Zanzibar, who leave the shore in health, to have a sharp attack of remittent fever shortly after putting to sea; thus changing a hot malarious air for a purer and cooler atmosphere. Probably

the change of temperature may fan this dormant something in the system into active life, and thus reproduce the fever from which they had suffered at some previous time. This prolonged latency seems peculiarly associated with malaria, for which quinine is the specific remedy, acting either as an alterative in breaking the habit, or, as some suppose, by restraining the activity of a still present poison in the blood. Whatever the explanatory theory adopted, experience teaches us that general deterioration of health commonly betrays some existing weakness in the constitution, which leaves the sufferer a prey to his particular scourge, without any directly exciting cause; and this infirmity may be either inherited or acquired.

Pathogenic micro-organisms have been carefully studied by many able pathologists, but their history is still very incomplete, and the conflicting results of observation show that there yet remains much to be learned respecting them. Attempts to classify them seem to be foiled by the transformation of some, and by the probable conversion of simple and innocuous forms into poisonous fungi. Their habitat or that of their spores or germs is the atmosphere, water or the earth, as well as living or dead organic matter. In organic structure they do not differ: the same form is found in many different diseases; and some organisms, resembling each other, have varied physiological actions; in this respect resembling the cells of early embryonic life. Some thrive under conditions which are fatal to others. The healthy living tissue seems to be competent to disqualify, and probably kill, some pathogenic organisms, which grow and multiply where the health is impaired or in a decomposing nidus. These circumstances seem to lend support to the surmise already hazarded, that micro-organisms may acquire their virulent attributes, and are simply carriers of infection,—a privilege which probably does not appertain to them exclusively; that their poisonous property is due to a combination of favouring conditions, by which their morphological as well as their infecting characteristics are varied: that they undergo a process of evolution in both respects; but having acquired their special properties, they retain them, and are competent to impart them, and to generate other organisms possessing the same attributes, unless new conditions arise by the instrumentality of which they are again rendered innocuous.

Why is it that certain germ and other animal poisons act by direct absorption into the circulation, but are harmless when swallowed; whereas others, as in cholera and diseases of which milk has been shown to be the vehicle, the poison seems to act through the medium of the alimentary canal? It is probable, however, that this contrast is rather apparent than real; and that the poison mixes with the blood in either case before it becomes operative, though the excreta may be charged with the poisonous organisms. That certain animal poisons should be neutralised in the secretions of the stomach is intelligible; but it is not so plain why others should escape. Possibly those germs which are generated on a mucous surface survive in their natural habitat, where others which are strangers would perish. Most vegetable poisons seem to act indifferently, either by direct or indirect admission into the circulation.

The analogy of parasitic life in animals and vegetables is not without interest and instruction. Various plants are infested by the different kinds, though they very much resemble each other. These parasites are probably influenced, in their effects or activity, by extraneous causes, such as variations in temperature, moisture, character of soil, and other surroundings, especially by overcrowding; as well as by intrinsic conditions, providing means of resistance or the reverse, to the invasion of disease; deteriorated vitality rendering a plant more liable to the attack of parasites. Yeast manifests different forms of organism, under varying cultivation in different media; and such also, I am told, is the case with white mould. Mr Bennett informs me that some species of parasitic fungus have "a remarkable heteromorphy, accompanied by alternations of generations. For example, the mildew of wheat (*Puccinia graminis*) and the rust of the barberry (*Accidium berberidis*) are different stages in the development of the same species: neither reproduces itself, and each reproduces the other. There are many other instances of this heteromorphy, mostly belonging to the family of *Uredineæ*." Over-feeding as well as deficient nutriment makes plants sickly, and more subject to the incursion of parasites. The higher forms of vegetable life, especially when subjected to cultivation, are similarly susceptible. Plants are influenced by heredity, after being changed by cultivation, and have a tend-

ency, when neglected, to return, like Darwin's pigeons, to their original type: and diseases, due to malformation or deficient vitality, may be transmitted to the next generation. There is no satisfactory proof that germs are introduced into the circulation of plants by absorption through the ordinary channels, though it is not improbable such might be the case if the germs could maintain their vitality in the soil. These parasitic diseases appear to extend by contiguity; but there are not any ascertained facts suggestive of an intercommunication of their germs between plants and animals; unless, indeed, the intermittent and remittent types of fever, due to malaria, should be shown to depend on such transfer.

Parasitic organisms infest especially the haunts of man. In mid-ocean or on the summits of lofty mountains they can find no home: but where human life abounds germs increase, *pari passu*, with the population and the usual concomitants of aggregation, viz., impaired vital resistance, and the presence of conditions which favour the generation of micro-organisms. It is needless to enlarge on this subject, which is familiar, beyond referring to some of the more prevalent agencies by which, directly or indirectly, the evolution and extension of disease is favoured in thickly populated countries. The most direct cause, besides the presence of disease, is the impurity of the air and water: but the indirect agents are still more potent, by rendering the recipients of the poison more susceptible. The craving for stimulants, over-feeding and under-feeding, sedentary life; the strain of competition for a living; working against time, and mental emotion; these and other special causes co-operate to the prejudice of those who are subjected to them. They serve to modify organisation and to disturb the physiological equilibrium which constitutes health: and, it need not be added, they are intensified by inheritance. The observed fact that infectious diseases are peculiarly fatal when introduced amongst an aboriginal population does not invalidate these remarks. In vegetation seeds thrive in a virgin soil; and fermentation is expedited where the necessary elements for its activity are abundantly present.

It is important, in exemplifying the subject of Evolution in

relation to Pathology, to have a clear view of the distinction between a disease and the symptoms by which it is characterised. It is true this is an elementary lesson; yet we are so much in the habit of treating the symptoms that we are apt to regard them as the disease, and thereby much confusion is engendered; and points of contrast are thus rendered more prominent, in many instances, than is justified by their actual divergence from a common type of morbid action. Another point of equal importance to be borne in mind is, that the pathological changes which constitute the symptoms or signs of a disease are, for the most part, eliminative in their nature, and, as such, essentially curative in their purpose, though not infrequently injurious or destructive in their misdirection or excess. This general proposition is, doubtless, modified by various circumstances which influence the operation of evolution: yet the principle survives, and its prevalence cannot fail to be recognised and appreciated by all who look below the surface.

The first manifestation of the presence of any active disease, whatever the exciting cause, is almost invariably the functional disturbance of some one or more of the organs,—chiefly those of assimilation, secretion and elimination;—the nerve centres, and through them the vascular system, taking cognisance of such disturbance, and reacting in the production of various phenomena, tending or designed to restore the lost equilibrium. Accidental lesions arouse a similar attention directed to the same result. The progress and issue of these contending forces —the disease and nature's remedial effort—are governed by various circumstances, inherent and extraneous; and any special outcome dependent thereon may be perpetuated by inheritance or exaggerated by being translated into a congenial soil, whereby specialised or specific forms of disease are gradually developed.

Assuming the validity of the germ theory, so far as it is applicable to disease—for heredity is scarcely admissible in this category[1]—it may be regarded as an open question, for the

[1] It is said that tubercle bacilli have been found in the testis and prostate of the phthisical. But their presence there, as in other organs of tuberculous subjects, is not surprising, and cannot be accepted as a plausible reason for assuming that their germs are transferred to the impregnated ovum. Even if so transferred, do they remain inert and unprolific during the long minority of their host, and then spring into active life? The hereditary communication of specific infection by pathogenic organisms is an improbable conjecture.

reasons already advanced, whether the parasitic organisms are not innocuous in their primitive state, and derive their virulence from residence in the nidus of disease or in the fluids of a diseased body (*e.g.*, the filaria in elephantiasis, of which the mosquito is credited as being the purveyor); a property which they retain and are competent to propagate, but of which they may be deprived by gradual culture, and thus restored to their pristine harmlessness. Innocuous germs, scarcely distinguishable from those possessing virulent properties, may be seen in the blood, as well as in water and other ingesta. The virulence, therefore, of parasitic organisms cannot be regarded necessarily as an original property; and it may be acquired by their transmission through successive soils, favourable to its cultivation and development in some special direction, with an environment calculated to promote the same end. And there is nothing improbable in the supposition that this order may be reversed; that *naturally*, when all the circumstances are propitious, the virulent property of these organisms may diminish in their translation, until they again become innocuous, as demonstrated artificially by Pasteur; thus exemplifying the principle of reversion to original type. In other words, as already remarked, the susceptibility or otherwise of the recipient of infection materially helps to decide the tendency in either direction; and there is no doubt that the soil varies greatly in this respect, and that the virulence of the poison may be attenuated or aggravated thereby. Both the animal and vegetable kingdoms supply us with analogous instances of evolution under cultivation, and of subsequent reversion under neglect. What effect artificial culture has on the properties of poisonous plants I have been unable to learn.

The analogy between biological and pathological evolution is manifested at an early period. The protoplasmic germ possesses attributes, in virtue of which it grows by absorption, multiplies by gemmation or fission, and evinces the varied potentialities derived from its parentage and its environment, which qualify it to become itself an organ with special functions. Such, too, appears to be the history of the pathological germ, whatever that may be. Many inflammatory affections which are simple acquire, under favouring conditions, a specialised character,

which may be transmitted, as virus, to a healthy system; and may display the same property as protoplasmic germs, of multiplication in the living tissues, without the agency of any specific contagium from without; but due to a combination of circumstances which are dependent on inherent, acquired, or inherited proneness to some particular form of inflammation or type of disease.

Inflammation.—It will be interesting and instructive to examine further how far the phenomena of inflammation exemplify the foregoing remarks. It is difficult to define concisely, and at the same time satisfactorily, what is meant by inflammation; for many considerations are involved, and the conditions change at each quickly succeeding stage. Primarily it is augmented local arterial action, accompanied by capillary hyperæmia, dependent apparently on some change in the vital relations between the blood and its containing vessels. This state is usually induced by a topical lesion, or may be consequent on some less direct provocation: but whatever the exciting cause, the local phenomena are, probably in all instances, essentially due to reflex action, originating in the seat of disturbance, and reflected from the vaso-motor nerve-centres, to the degree of activity of which, therefore, all the resulting local changes are attributable. The extension of this disturbance, by sympathy, to the system generally is a secondary condition, and constitutes symptomatic fever. This abnormal state of the blood-vessels must, moreover, be viewed generally, but in some instances only remotely traceable, as beneficent in intention, though sometimes, as already remarked, mischievous in its direction or in its immoderate activity. It may be thought fanciful to adduce inflammation as an epitomised illustration of pathological evolution: yet such it is. The different stages an inflamed area passes through are so many steps which are influenced by various collateral circumstances, until they reach their climax. The reconstruction of disintegrated texture is another exemplification: and where the morbid action stops short of necrosis we may, in like manner, note the retrogessive steps by which a restoration of the normal equilibrium is established: and herein we have an elementary lesson of reversion to original type or pre-existing physiological health. In like

manner chemistry reasserts its sway over dead organic matter; and by retrograde steps, from fermentation to decomposition and disintegration, the product of vital evolution is resolved into its primitive elements; which are then prepared to share in building up a new organisation, under the constructive and energising direction of some fresh vital germ. Thus, whether the progressive evolution of these pathological changes in inflammation result in a wreck, more or less complete, of the affected area, or the pre-existing normal condition, by retrogressive steps, be re-established, each process may be watched; *e.g.*, in surface inflammation by the eye, or in pneumonia by the ear. This careful observation of nature's proceedings in both directions has established more accurate views of disease, as well as its more rational treatment, by discountenancing meddlesome interference at variance with nature's indications.

Plants manifest changes in the repair of lesion, in many respects analogous to reparative inflammation in animals. If a metallic point be thrust into living wood, Mr Shattock informs me that the local injury produces proliferation by subdivision of cells around the foreign body. The accurate detachment of the frost-bitten portion of a leaf is suggestive of the similar process in partial gangrene, entailing spontaneous separation of a necrosed part: indeed, the fall of the leaf in autumn is no less a vital act; for the withered foliage still clings to the dead limb long after the living branches are denuded.

The differing tendency of inflammation in various tissues illustrates the agency of a natural and salutary influence, by which its development is modified: and many innate peculiarities of temperament, and still more so of habits, decide the direction and issue of an inflammatory attack. Again, an inherited proclivity, some defect in the assimilation of the ingesta, or some faulty organic chemistry determines the localisation of the attack, and imparts to it a special character. In this way some morbid growths may be accounted for, as "in many cases tumours and simple inflammatory overgrowths are structurally identical."

Morbid Growths.—Tumours possess one common affinity, in the circumstance that their tissue development is due to local depraved cell-growth; and although there are many well-

defined characteristics which distinguish them, there is nothing to forbid the supposition that these are consequent on a gradually widening divergence, under favouring conditions, from the typical origin to which, according to Virchow, they may all be traced, in the normal tissues of the organism, in some stage of its development. Moreover, the characteristic of malignancy is one of degree; for a sharp line of separation between the innocent and malignant cannot be drawn, as "but few if any proliferating growths are wholly free from liability to assume malignant properties." Tumours, in the proper sense of the term, *i.e.*, morbid proliferating growths or neoplasms, are spoken of, by one of our most trustworthy pathologists, as having "a very close affinity with simple hypertrophy or hyperplasia on the one hand, and with mere inflammatory growth on the other."[1] Both malignant growths and tubercle may be cited as pathological conditions which are communicable, by translation, to other parts of the system, and, possibly, to other individuals: yet it can scarcely be denied that they may exist without inheritance or other assignable explanation of their presence; certainly they have the properties of development and extension; but at present we know nothing respecting their apparently spontaneous beginning, except that special conditions of environment favour the production and subsequent evolution of tubercle; and that local irritation may, in some instances, determine the position of cancer. It is said that both these diseases may be inherited. This may be; but that cancer is usually so is doubtful: and I am disposed to think that sufficient weight is not assigned to the constant association between parent and child, apart from heredity, as the means by which both cancer and tubercle may be communicated from one to the other. But beyond these sources of contamination their *quasi* sporadic origin and elective localisation are problems, the solution of which must be sought in the endeavour to unravel the complex elements, past and present, which, in the aggregate, and in their fortuitous and favourable combination, constitute the latent morbid condition that awaits an appropriate stimulus to be converted into active disease. In normal evolution a similar

[1] Dr Bristowe (*Theory and Practice of Medicine*), to whom I am indebted for this and the preceding quotations.

association of what we should term accidental circumstances favours the production of new and unexpected forms, which may be perpetuated by inheritance, or be modified and varied by manifesting fresh attributes and new affinities.

Fevers.—However speculation regarding the origin of the so-called fevers may differ, there is a general consensus of opinion that each is due to a specific poison, which produces recognised and well-defined indications of its presence in the system. It may be added that their associated effects, *i.e.*, the signs and symptoms, are an expression of the effort made by nature to eliminate the poison; and that the attendant pyrexia denotes the participation, by sympathy, of the various organs in the disturbance, and especially that of the vascular and nervous systems. Whatever the poison may be, the contagia have the property of multiplication in the affected body, and of infecting, by transmigration, the bodies with which they are brought into contact. Possibly the period of incubation may simply represent the interval required for that self-multiplication to attain the expansion necessary for the outward manifestation of the disease, the intensity of which might, therefore, be dependent on the protraction of that period: but this would necessarily be partly governed by the quantity of poison imbibed, and by other circumstances already noticed.

Notwithstanding the marked contrasts in many of the features of these fevers, there are certain points of resemblance, indicating broadly some affinity between them. The general disturbance which the presence of the poison occasions is similar in all, varying in degree according to circumstances, in which the dose, the length of incubation, and the favourable nature of the soil for cultivation are jointly potential. The principal organs by which elimination is attempted are the skin and mucous membranes, which are likewise the chief communicants and recipients of the contagia. There are also more special affinities, as between the different forms of pock, between measles and roseola, possibly between scarlatina and diphtheria, and between the latter disease and membranous croup. Opinions appear to be divided as to the presence of a specific contagium in *Typhus* and *Typhoid*. The former seems to be more influenced by, if not absolutely dependent on, surrounding conditions associated with a crowded population, such as defective

ventilation, food, and cleanliness. The condition of the recipient is, therefore, another important element in the development of this disease. Whether the contagia, if poisoned germs, are simply latent and awaiting the opportunity which a favourable soil and surroundings would afford, or whether innocuous germs receive their poison from these surroundings, seems to be of little importance: probably both theories are correct in this as in some other instances. In typhoid a high temperature appears to be specially favourable to the development of the poison; and the intestinal discharge from which it is derived seems to "contain some specific, but at the time innocuous, organised substance," which afterwards, under decomposition, becomes virulent. This is an interesting fact, as illustrating the generation of a virulent germ, or, more probably, of the conversion of an innocent organism into one of a specific type, in decomposing animal matter; resembling in this respect non-specific poison generated in the same way;—an important step in tracing these specific poisons to their source.

Cholera may be classed with typhoid in respect of its origin, favouring surroundings, and epidemic character; and they also resemble each other, apparently, in being developed from germs which multiply indefinitely, and ripen into virulence after their discharge from the intestine: but in other respects the two diseases present a striking contrast. Cholera is said to be indigenous in India, and to assume periodically an epidemic character. I am not aware whether it has been satisfactorily shown that this disease does not originate spontaneously. Unquestionably both environment and personal qualification exercise much influence in its development. Not only habits of life but special conditions of health may predispose to an attack, as demonstrated by the importance of careful diet and precautions in case of diarrhœa, during the prevalence of an epidemic. Moreover, isolated cases occur periodically, which differ very little from the true Asiatic type. It seems reasonable, therefore, to suppose that the evolution of cholera, in its virulent and epidemic form, needs certain conditions, under which its contagia or germs become highly poisonous and prolific, but again lose this character as these conditions are gradually withdrawn or artificially controlled. Assuming, then, that

the contagia in typhoid and cholera are, as is most probable, parasitic organisms, the circumstance mentioned, respecting their primitive innocuous character and subsequent virulence, seems to point to the important conclusion that their poisonous nature is an acquired and not a necessary attribute; that they obtain their infecting property from the nidus in which they are bred; and that they may be deprived of this property, as has been demonstrated artificially, by the withdrawal of the conditions which favoured the development of their virulence. It may be added that the symptoms of non-specific septicæmia, according to Burdon Sanderson, very closely resemble those of cholera in their leading characteristics.

The recent and startling announcement that scarlet fever may probably be communicated from the cow is fraught with much interest, not only for its own sake, but on account of the speculations it suggests in reference to the development of other diseases under similar conditions, notably diphtheria and vaccinia. It may be reasonably argued that if milk be a suitable medium wherein the germs of scarlet fever may mature, and may produce this formidable disease when swallowed, why may not vaccinia, in like manner, be regarded as competent to produce variola, after admixture with the milk and cultivation therein? In both cases the udder of the cow is the source of the contagium: and whilst transference, by innoculation, to the human subject may modify its action and change the character of the disease, cultivation in a suitable medium may intensify it. As regards the cow, in neither case does the disease seem to be attended by constitutional disturbance. The two cases *seem* to be parallel.

Erysipelas.—The difference of opinion among pathologists respecting the specific nature of erysipelas is best reconciled by regarding it as a simple inflammatory affection of the skin and subcutaneous areolar tissue, which may assume a specific type, under the influence of local environment and temporary or persistent personal susceptibility. I would even include, in the same category, erythema, where the areolar tissue is excluded from participation; and likewise the more exaggerated class of cases in which deeper textures are involved, and diffused suppuration ensues. Such, at least, is the teaching of one's hospital experience. The constitutional disturbance varies in accord-

ance with the extent and depth of the inflammation; and I should as anxiously remove an operation from the proximity of a case of phlegmonous inflammation as from one of idiopathic erysipelas. Is not the latter form sometimes climacteric and eliminative, as some other forms of inflammation and carbuncle occasionally appear to be? Pneumonia may be included in this category, occurring sometimes without any other assignable cause, and, if cured, leaving no ill effects behind.

Rheumatism and Gout.—However opinions may differ respecting the affinity between these two diseases, there certainly is, in their history, development, and characteristics, much that is common to both. Soil and atmospheric influence are extraneous predisposing causes, which seem competent to induce rheumatism without any special predisposition on the part of the patient; so that some localities are almost as notorious for this complaint as others are for ague. Yet there is no doubt that intrinsic susceptibility, which is generally acquired or fostered by incautious excesses in diet, co-operates in promoting the development of the disease. The alliance between rheumatism and gout has found expression in the conjunction of the two words: and although rheumatic gout may not be a strictly pathological compound, it indicates the fact that there is, practically, no defined line of separation between the two diseases. The special characteristics of gout do not appear to be dependent on environment: some predisposition to its development no doubt exists in most cases; and in some this inherited proclivity, handed down perhaps through two or three generations, assumes an intensity which is almost uncontrollable. But it may be acquired, *de novo*, by introduction into the system of the elements on which it thrives, provided there coexist that faulty organic chemistry which liberates those elements to work their will. To deny, so far as practicable, these necessary conditions, and to put the vital laboratory in working order, seem to be the rational indications for treatment: but it may require the self-denial of two or three generations to obliterate this morbid inheritance, and to secure a reversion to the original type of health. The elective and eliminative characteristics of gout, and its apparent affinity with the neuroses, are interesting features in its history.

Influenza.—Whatever may be the contagium of influenza there can be no doubt that its epidemic character is due to some unknown cause, and that it is communicable from one to another. But it would be a bold assertion to say that there is any strict line of demarcation between this epidemic form of catarrh and common catarrh. In all their essential characteristics they are identical, and glide one into the other. Some persons are specially susceptible of both; and atmospheric influences often render common catarrh in a measure epidemic; its communicability, moreover, is as recognised as that of influenza. Certainly the striking epidemic character of the latter, and the severity of the attack, involving, as it often does the mucous membrane of the sinuses in, and in communication with, the nostrils, would seem to point to some special atmospheric cause,—not improbably, as conjectured, an excess of ozone. In some instances the suddenness of the attack is suggestive of immersion in a poisonous current of air. Hay fever exemplifies the influence of special susceptibility, whatever may be the exciting cause of this allied affection. Probably catarrh is sometimes eliminative.

The study of disease on the lines indicated is not only consistent with the theory of biological evolution, but is also supported by pathological observation. In both cases the chief factor, heredity, is modified by environment and intrinsic circumstances; and in both a tendency is manifested to assume more complex characteristics, or, under favouring circumstances, to obey the principle of reversion to original type. Further, divergence from a simple type does not imply the absence of early affinity, or even of identity of origin: and these remarks apply to the vegetable as well as to the animal kingdom. As in biology complex forms are the offspring, through many intervening grades, of one common parentage of simple type; so, in pathology, under analogous circumstances favourable to such evolution, or it may be degeneration, a simple deviation from a normal state of health may issue ultimately in the development of specific disease; and the variety of phases or combinations through which each

has passed renders it difficult to trace its derivation and lineage in either case.

Thus it is likewise with man's moral nature, and the psychologist may find satisfaction in tracing, on parallel lines to the foregoing, the evolution of moral deformity and disease, in such wise as would leave but little to the imagination to render the analogy complete. The disposition to special forms of degeneration or active disease is, unhappily, prevalent in mind as well as body; and heredity asserts in each its sway, by repeating original abnormality and acquired vice. Contagia in various forms infect the moral atmosphere, and multiply abundantly with civilisation and in a crowded population. Some are subtle and slow in their operation; others, in a receptive nature, where the will to resist is feeble, defy control and are rapidly destructive. The distempered cell-growth in the moral man manifests the same affinity with its healthy type, as the morbid growth of the material man holds to the normal tissues of his organism in some stages of its development: in each case the association constitutes the connecting link between health and disease. Some virtuous impulses, if uncontrolled or misdirected, are prone to expand into vicious habits: and envy, hatred, and malice may have small beginnings; but, if nurtured in the rank and congenial soil of selfishness, they ripen into a moral cancer, which poisons the life that nourishes it. The inlets of evil are many, and thoughtless and foolhardy exposure to contamination is fraught with equal risk in both cases. The craving for mental and emotional stimulants may be classed, in its effects, with the importunity of the sensual appetites, the morbid indulgence in each case entailing an enfeebled power of resistance and a dissipated habit, which need only time and opportunity, with freedom from restraint, to issue in hopeless degeneracy or disease. On education and training, as on medicine and hygiene, we rely for the means by which to correct these morbid tendencies in either case, and to fortify the moral as well as the physical nature against the many and insidious inroads of disease: but when that has established its hold, the enforced sacrifice of the offending member, alike literally and figuratively, is often the only remedy whereby life can be saved. "*Nemo repente turpissimus*" is an implied recognition of the

law of evolution in our moral nature, in the same sense as we concede that our diseases are the culminating product of evolutionary steps. The aim, alike of the moralist and of the physician, is to fortify the constitution, and to neutralise the activity of the poison germs, by withholding the conditions essential for their development and multiplication; and thus to arrest and reverse the downward tendency, and to restore to man a larger share of his pristine vigour and purity.

Many things in biological evolution are obscure, and many facts are, with our present knowledge, too stubborn to conform to its law, or to be brought within the range of its assumed principles. Yet, that law is not rejected, those principles are not ignored. So likewise the details, by which the law of evolution as governing pathological action may be exemplified, will require time and patience to develop; together with a recognition of, and some faith in, the principle of "reversion to original type" in the study and treatment of disease.

P.S.—Since this paper was written I have had the opportunity, through the courtesy of Dr Creighton, of perusing his valuable monograph, read before the British Medical Association in 1883, on the "Autonomous Life of Specific Infections;" and am gratified to find that my views are so much in unison with his. Dr Creighton's observations on the history of yellow and jail fevers, and on the remarkable immunity of the black race from the worst effects of the former, have an especial interest in relation to the subject of this paper. I am tempted to repeat a quotation from Sir Thomas Watson, which this address contains, as it anticipates so precisely some of the views I have ventured to express. When speaking of the contagiousness of Egyptian ophthalmia Sir Thomas observes:—"There is nothing absurd nor unlikely in the supposition that diseases may arise from some other source, and then become capable of spreading by contagion. . . . . My own creed on this matter is this: that the disease may and often does arise independently of contagion, from the agency of ordinary causes of inflammation; and that, having so originated, it acquires contagious properties, which develop themselves only under circumstances that favour the propagation of most of the contagious complaints." A

similar opinion is expressed on the same subject by Mr Travers in the treatise already quoted. In speaking of this suppurative form of ophthalmia, so fatal to our soldiers in Egypt, he remarks that he entertained no doubt that the disease originated in gonorrhœa "exasperated by local causes, and especially by its facile and extensive communication through so large an assemblage of men, under the favouring circumstances of predisposition and excitement."