CHAPTER VIII

HEREDITY AND DISEASE

"Naturam expellas furca, tamen usque recurbet."—HORACE.

§ 1. *Health and Disease*

What is Disease?—The distinction between health and disease is relative to an ideal—the maximum efficiency and well-being of the organism under given conditions; and pathology, the science of deranged function or disturbed metabolism—deranged or disturbed in comparison with what we call "normal"—is, strictly speaking, part of physiology, the science of all vital activity. What we call "normal" in one animal—*e.g.* a bird's mode of excretion—is called "diseased" in another; what is normal at one

period of life—*e.g.* the breaking down of tissue in a chrysalid—may be a disease at another period; what is normal in one part of the body—*e.g.* proliferation of cells—may be a morbid growth in another region. Disease is a relative concept and does not admit of strict definition.

Our point here is indeed a familiar one, for the tritest of quotations remind us of the kinship between genius and madness, or of the resemblance between the lunatic, the lover, and the poet. As a matter of fact, Ziegler remarks, genius, talent, and mental derangement do sometimes occur in one family. The useful glutinous threads of mucus with which the male stickleback fastens together his nest of seaweed are remarkable renal secretions which, if we did not know their utility, would almost certainly be regarded as the symptoms of a kidney disease. Whether we take the changes in the adult salmon when fasting in freshwater, or the dissolution of the blowfly's maggot as it passes into the pupa state, or the condition of the tadpole as it loses its tail and becomes a miniature frog, or the necrosis at the base of a stag's antlers before they fall off, we have to deal with processes which, though now normal occurrences in the cases cited, would in other cases spell disease.

A great authority puts the point tersely: "Disease is a state of a living organism, a balance of function more unstable than that which we call 'health'; its causes may be imported, or the system may 'rock' from some implicit defect, but the disease itself is a perturbation which contains no elements essentially different from those of health, but elements presented in a different and less useful order" (T. Clifford Allbutt, *System of Medicine*, 1896, vol. i. p. xxxii).

Optimism of Pathology.—It does not seem possible to find any criterion which will serve in all cases to differentiate a new variation making for increased efficiency from another which makes for disease. Experience lends security to the judgment of the physician or the breeder in a large number of

cases, but it is probable, as Virchow has maintained, that some new beginnings which are now—looking backward—regarded as normal steps in progressive evolution would at the outset have been claimed by the pathologist as hints of fresh disease. Leaving microbic and acquired diseases out of account, we may safely say that various processes of hypertrophy and atrophy which are associated with disease in a well-finished organism like man are, as it were, recrudescences of important steps in past evolution. The persistence of germinal activity in a patch of cells may give rise to a tumour, but is it not, as it were, an echo of the power that lower animals have of regenerating lost parts? So it may be that some of the cerebral variations which we call for convenience "nervous diseases" are attempts at progress.

Diseases due to Innate Predispositions and to Acquired Modifications.—From the biologist's point of view diseases are of two sorts: (1) they are abnormal or deranged processes, which have their roots in germinal peculiarities or defects (*variations*, to start with), which express themselves in the body to a greater or less degree according to the conditions of nurture; or (2) they are abnormal or deranged processes which have been directly induced in the body by acquired *modifications*—*i.e.* as the results of unnatural surroundings or habits, including the intrusion of parasites. Often, moreover, an inborn predisposition to some deranged function may be exaggerated by extrinsic stimuli, as in the case of gout,* or when a phthisical tendency is aggravated by the intrusion and multiplication of the tubercle bacillus. That is to say, deranged processes which are primarily due to germinal variation often afford opportunity for equally serious disturbances which must be referred to exogenous modifications. A rheumatic tendency may be fatally aggravated by inappropriate nutrition.

* It is now suggested, however, that gout is due to the toxic effect of some germ or germs.

Disease more Frequent in Man than in Animals.—Diseases occur among wild animals, but, so far as we can judge, they are very rare. They are certainly rare when compared with the frequent diseases of mankind. Why is this? One reason, probably, is that natural selection has a grip on wild life that man has refused to allow it to have over him. Elimination is keener and the wild race is healthier. Animals born diseased are killed off before they can reproduce. To parasites they adjust themselves, or become immune. Another reason is that wild animals live "more natural" lives, and that the stimuli provoking disease are therefore fewer. A third reason, perhaps, is that man is relatively younger than most wild races, and, therefore, with more idiosyncrasies. Fourthly, it seems that where epidemics occur among wild animals, they are almost invariably due to human interference. (See Ray Lankester's *Kingdom of Man*, 1907, p. 32.)

It should also be recognised that man has created around himself a social heritage which often evolves quickly, hurrying and pressing its creator, who cannot always keep pace with it. This is a frequent condition of mental disorder. More generally, we may venture to say that many human diseases, especially of a nervous sort, seem in part due to the fact that the germ-plasm is not varying quickly enough to keep pace with the changes in environment—physical, biological, psychical, and social. We try to adjust ourselves to these by a panoply of modifications, and this business of adjustment is a strain that provokes disease.

As the physiological and the pathological are really but two aspects of the general problem of vital activity, it is mainly for practical reasons that we have ventured to devote a special chapter to the facts of inheritance in connection with disease. Apart from practical interests, it will be seen that, though the available facts in regard to disease do not lead us to any novel considerations which are not illustrated in normal cases,

they throw some useful side-lights on the general problems of heredity.

§ 2. *Misunderstandings in regard to the "Inheritance" of Disease*

As with the transmissibility of acquired characters, so with the transmissibility of the ills our flesh is heir to, we have to face a number of current misunderstandings, which in many cases obscure the real facts. The long series of transmissible diseased conditions which Prosper Lucas, for instance, gave in 1847, will not pass muster to-day. It includes many cases which are outside the rubric of inheritance altogether. A more critical study, particularly of recent years, has led physicians as well as biologists to define a number of distinctions between real and apparent inheritance. Thus, to take a simple instance, it seems a confusion of thought to speak of the inheritance of any microbic disease.

1. **Reappearance not equivalent to Inheritance.**—The reappearance of a diseased condition in successive generations does not prove that it has been transmitted, or even that it is transmissible. The Alpine plants which Nägeli brought to the botanical garden at Munich were much modified in their new environment, and their descendants were similarly modified. The unusual characters reappeared generation after generation, but experiment showed that the reappearance was not due to inheritance, but was due to the re-impression of similar modifications on each successive crop. So it is with many diseased states which reappear generation after generation, not because they have been transmitted, but because of the persistence of the unhealthy stimuli in function or in environment which originally evoked them. Collier's lung is a modificational result; it reappears in generations of colliers, but there is no warrant for regarding it as heritable.

2. **Pre-natal Infection is not Inheritance.**—Even when a child is born with symptoms or definite expressions of a disease which one or both of its parents exhibited, it does not follow that the disease was part of the inheritance. If the disease is microbic, it is never in the strict sense inherited. It may be acquired by infection through the mother during the fœtal period. This may be illustrated by the rather rare occurrence of congenital tuberculosis and by some cases of congenital syphilis. No one who thinks clearly can maintain that these diseases are in the strict sense heritable.

The unborn offspring may be directly inoculated *in utero* with the germs of certain contagious diseases affecting the mother, and this in spite of the fact that the placenta is a wonderfully perfect filter. "Diseases of the contagious type seem to differ in the facility with which they are transmitted by this means. Thus, in the case of anthrax and tuberculosis, the infection of the fœtus through the mother occurs only very rarely, while we know that in that of syphilis the liability is extreme" (Hamilton, 1900, p. 290). It is said that a fœtus *in utero* may take small-pox from the mother; but this is contagion, not inheritance. Syphilitic symptoms may appear in the new-born—microbes from the father or from the mother have passed into the child; but this is contagion, not inheritance. Some say this is an academic distinction without a difference, but to fail to make the distinction means confusion of thought.

3. **Inheritance of a Predisposition to a Disease is not Inheritance of the Disease.**—In many cases it seems possible and useful to draw a distinction between the inheritance of a definite disease and the inheritance of a constitutional predisposition towards it. Thus, since tuberculosis is a bacterial disease, since relatively few children are born tuberculous, and since the disease attacks very unequally those who are equally exposed to the same external conditions of infection, it seems probable that what is really inherited is a constitutional peculiarity (arising originally as a germinal variation), which expresses

itself, for instance, in " vulnerability of the protective epithelia," —in fact, in a deteriorated power of resistance to the tubercle bacillus.

In the same way, to take a case provisionally non-bacterial, it seems probable that gout is not, as such, transmissible, but that what is inherited is a constitutional peculiarity (arising originally as a germinal variation), which expresses itself in an altered mode of eliminating nitrogenous waste—a constitutional vice which may be exacerbated by excess of food and alcohol.

4. **Acquired and Innate Abnormal Conditions should be distinguished.**—Closely similar abnormal states of the body may arise in two different ways, and their heritability will differ with the mode of origin. If the abnormal condition is inborn in the strict sense—*i.e.* if it is the expression of a constitutional peculiarity arising originally as a germinal variation—the probability of transmission is often great. But if the abnormal condition has been induced adventitiously by external influences (including food, drink, poisons, etc.), then the probability of transmission is slight. The distinction is a real one, but it is not always readily drawn in actual practice.

Thus the difficulty of distinguishing inborn deafness from exogenous or adventitious deafness—the result, for instance, of various infectious diseases,—may, perhaps, explain a curious peculiarity in E. A. Fay's statistics (3,078 marriages, 6,782 children). The percentage of deaf children in families where both parents were deaf was 8·458, while in families where only one parent was deaf the percentage was *larger*—namely, 9·856. There seems something wrong here, and the explanation may be that there are two quite different phenomena slumped under the title deafness—viz. innate or idiopathic deafness, and acquired or exogenous deafness.

As the case appears instructive, let us pursue it further. Where both parents were believed to be congenitally deaf the percentage of deaf children was 25·931 ; where one parent was deaf congenitally and the other adventitiously, it was 6·538 ; where both parents were adventitiously deaf, it was only 2·326. Where one parent was congenitally deaf and the other normal, 11·932 per cent. of the

children were deaf; where one parent was adventitiously deaf and the other normal, the percentage was 2·244. In short, there is no evidence that adventitious deafness is heritable at all.

It may be noted further that Fay's statistics show that deafness among the relatives of the parents increases very markedly the likelihood of there being deaf children; and they also seem to show that consanguineous marriages greatly increase the probability of the inheritance of deafness, or of constitutional conditions, *e.g.* lymphoid exaggeration, such as naturally lead to deafness. This is what would be expected from the fact that an individual inheritance is a mosaic of ancestral contributions.

The position we venture to maintain is expressed in the following sentences:—"As inherited (on the part of the offspring) or transmitted (on the part of the parents), Biology includes only those characters or their physical bases which were contained in the germ-plasm of the parental sex-cells" (Martius, 1905, p. 11). Similarly, Virchow says: "What operates on the germ after the fusion of the sex-nuclei, modifying the embryo, or even inducing an actual deviation in the development, cannot be spoken of as inherited. It belongs to the category of early acquired deviations, which are therefore frequently congenital." This pronouncement is the more remarkable since Virchow believed in the inheritance of acquired characters.

Is the Distinction between Innate Disease and Acquired Disease Practicable?—It is true that the distinction between an "innate" predisposition to a disease and an acquired disease "looks better on paper than by the bedside." This is simply an instance of what we continually find, that the "abstract" theoretical concepts of science are not always readily applicable to the intricacies and subtleties of nature. And yet the distinction is quite legitimate and thoroughly sound and useful in the present state of our knowledge. We cannot object to the utility of abstracting an "organism" from its "environment," although we know that a living

creature is inseparable from surroundings of some sort ; and we must not object to the distinction between *innate* (or idiopathic) diseases and *acquired* diseases because we know that the innate disease must have an evocative environmental stimulus, and that an *acquired* disease necessarily involves *some* organismal susceptibility.

What, then, is the distinction ? It is the old distinction between a variation and a modification. An innate disease presupposes some germinal variation to start with, some germinal peculiarity to continue with. It is there, whether it finds expression or not. If it does not find any appropriate nurture, it will not express itself in development, but neither will the normal process of thinking find expression without the appropriate liberating stimuli. If an indispensable process, the structural rudiment of which is a component part of the normal inheritance, finds no nurture, the organism of course dies. If a dispensable process, such as an innate disease—the structural rudiment of which is also part of the inheritance—finds no nurture, the organism may of course survive if otherwise normal ; but the rudiment of the disease may simply lie latent, and may be expressed in the next generation. Eventually, whether it finds expression or not, it may die away altogether, just as useful variations seem sometimes to disappear. This might be called the *racial* cure of disease.

An *acquired* disease is exogenous, not endogenous, in origin. It arises, apart from any particular innate predisposition, as the direct result of inappropriate nurture (in the widest sense) ; of unnatural function, over-function, or lack of function ; and of intruding parasites—*e.g.* bacteria.

But there are two complications—(1) An acquired disease may operate in an organism which has an innate bias to disease —*e.g.* when a tubercle bacillus infects a phthisical constitution. (2) A diseased condition may be the result of premature or local arrests of development, or of excess of development, or of

disturbance of the time-relations of the developing organism: and this may be due (*a*) to an intrinsic weakness or disproportion in some components of the complex mosaic of inheritance, in which case it is likely to be transmitted; or (*b*) to some disturbance of the nutritive and other conditions during ante-natal life, in which case it is not likely to be transmitted.

To sum up in the words of a well-known pathologist, "the term 'acquired' should be applied only to what arises in the individual life-time—from the period of development onwards—under the influence of external conditions; and never to what arises, as we say, spontaneously—that is, from rudiments already present in the germ" (Ernst Ziegler, 1886, p. 13).

All discussion about "congenital," "pregenital," and "postgenital" heredity or inheritance is writing on the sand—mere verbiage and confusion of thought. The inheritance is the organisation of the fertilised ovum—nothing less, nothing more. That the developing offspring may be infected or poisoned at an earlier or later stage, before birth or after birth, has nothing to do with inheritance. The word "congenital" is properly used to denote what is manifested by the offspring at birth; the "congenital" character may be hereditary—*i.e.* due to the parental germ-cells—or it may have been acquired in ante-natal life. But the word is also used by many to imply an innate constitutional character which is part of the inheritance in contrast to a character which has been adventitiously acquired. Therefore, as far as possible (without undue purism or pedantry), the word should be dropped altogether.

§ 3. *Are Acquired Diseases transmissible?*

It seems certain that diseased conditions may arise from germinal variations appropriately stimulated, as in gout, rheumatism,* obesity, and insanity; it seems equally certain that diseased conditions may be induced from without by peculiarities

* Even if gout and rheumatism (in its acute form) be complicated by the presence of specific microbes, we may regard the microbe as the appropriate stimulus to an idiopathic predisposition.

of function and environment, including, of course, food and drink. Without there being any observable hereditary predisposition, a man may acquire cirrhosis of the liver, neurasthenia, cardiac hypertrophy, and so on through a long list. That a man may be invaded by microbes without being in any way peculiarly susceptible to them, or that he may be poisoned in a score of ways without there being any constitutional weakness to blame, seems certain. But are such acquired diseases in any sense transmissible? It seems to us that the answer should be in the negative, but the general reasons for this answer must be sought in the previous chapter—that dealing with the transmissibility of acquired characters in general.

No one can suppose that microbic diseases acquired by the parent can be transmitted to the offspring, though there may be ante-natal infection, and though the offspring may be prejudiced by the fact that the parents had the disease. If the maternal constitution is seriously affected, it is probable enough that the child may be born weakly, or imperfectly developed, or even poisoned. In other words, the embryo is disadvantageously modified by deficient or abnormal ante-natal nurture. If the parental constitution is seriously affected it is possible that the germ-cells may be likewise affected. This is most likely in the case of the ova with their relatively larger cytoplasm or formative cell-substance. In other words, there may be a transmission of secondary effects of microbic disease. The same will apply to any case where it can be definitely said that the parental body is saturated with poisons or toxins. But to admit this is very different from admitting that a specific modification of the parent's body can be transmitted to the offspring. Yet some who should know better persist in calling this "a distinction without a difference."

Leprosy.—In a leprosy district the children of lepers may exhibit the disease, but this may mean nothing more than that they were exposed to the endemic conditions, whatever they may

be, which cause the disease, or that they caught the contagion, if the disease is contagious, as many believe. "It is quite certain," Mr. Jonathan Hutchinson says, "that the children of lepers, born out of leper districts—in England or the United States, for example—never inherit it."

Gout.—Because gout sometimes sets in after a particular course of diet, some have attempted to regard it as an acquired character, just as Herbert Spencer regarded short-sightedness and a liability to consumption as acquired characters. But there is no warrant for such interpretations. In all three cases we have to do with innate germinal qualities which find various degrees of expression according to the conditions of nurture. There is no reason to believe that the expressions of goutiness in a father can specifically affect the germ-cells in such a fashion that the son *thereby* becomes gouty. Moreover, in many cases the son who becomes gouty was born before his father became gouty. What, then, is meant by the "heritability of gout"? The cases of gout "running in a family" are too numerous to allow us to take refuge in the suggestion that a germinal variation which was expressed as goutiness in the father occurs *de novo* in the offspring. All that can be said at present is that the *predisposition* to gout is an inborn character, which, like any other, may be transmitted. Even if gout turns out to be definitely microbic, the general argument will not be seriously affected.

Albuminuria.—There seems to be such a thing as constitutional albuminuria, and a predisposition to it seems to be heritable. This means that a defect or peculiarity in the filtering apparatus of the kidney arises as a germinal variation, and is handed on from generation to generation. Under conditions which may mean nothing to normal subjects, the inborn peculiarity may find expression in the active disease of albuminuria. As in the case of gout, a constitutional tendency to albuminuria is very transmissible, but the disease must not be called "acquired" simply because particular external conditions of life seem to supply the liberating stimuli which lead to its expression. Where the albuminuria is transitory

and of modificational origin, where it is really an acquired condition, there is no warrant for believing that it is transmissible.

OTHER CASES.—It proves nothing to cite instances of myopia appearing in adolescence and reappearing in the early life of the offspring; of neuroses manifested after an accidental shock in the parent, but patent from the first in the child; of rupture manifesting itself in the parent after an abnormal strain, and occurring without apparently adequate cause in the next generation,—and so on. It is always possible, and indeed reasonable, to answer that we have in such cases to deal with an inherited germinal predisposition.

Cardiac hypertrophy due to over-work is in a sense a diseased condition, though from a wider point of view it may be said that the organism is here, as always, doing its best in the way of adaptive response to novel conditions. But is there any warrant for supposing that cardiac hypertrophy in a father will induce cardiac hypertrophy or even a tendency to it in his son? "Of course, the constitution that made the father liable to hypertrophy would also make the child liable, but this is inheritance of a constitutional (non-acquired) character—a thing no one disputes" (Dr. Leslie Mackenzie, *Scot. Med. Surg. Journ.* vi., 1900, p. 324).

Those who accept the concept of a germ-plasm of unimaginable intricacy, persistent with remarkable dynamic inertia from generation to generation, changing and yet stable, oscillating in parts and yet on the whole "breeding true," will not lightly assume that modifications in the body can bring about a specific change of structure in the germ-plasm. It is *possible* that profound bodily changes, such as some acquired diseases effect, may shake the kaleidoscope and provoke a change to a new position of organic equilibrium; but it does not seem likely. On the other hand, important bodily modifications, *e.g.* serious derangements due to infectious diseases, may effect a change in the vigour (functioning-power, growing-power, developing-power, resisting-power) of particular elements in the inheritance. And this admission is probably enough to cover all the well-authenticated cases of inborn changes in the offspring of parents who had acquired serious diseases.

Nervous Diseases.—In regard to so-called "acquired nervous diseases," I venture to quote again from my colleague, Dr. D. J. Hamilton (1900, p. 299): "Have we crucial evidence to show that a mental disease may be excited through external agencies, as, for instance, by the abuse of alcohol in a person free from any ancestral taint, and that this disease so excited can be transmitted through several generations? My own impression is that we have not. . . . So far as I am personally informed, I feel that, in mental derangement, and in excess of perhaps any other form of disease, we have to do with an inherited peculiarity or variation—a variation which may have occurred in a far-back ancestor and lain dormant for many generations, but which inevitably manifests itself under conditions of unusual external stimulation, and which is in no respect bound up etiologically with or necessitated by this stimulus. The substratum which underlies the mental peculiarity is allied to that underlying the predisposition to tuberculosis or gout, and, probably, is referable to a fault in metabolism excited, it may be, by an inherent bias towards degeneration in the nerve-cells of the brain, and this is eminently hereditary."

The general verdict of those experts who admit the validity of the distinction between endogenous germinal variations and exogenous somatic modifications may be thus summed up: (1) externally induced nervous disorders (apart from the results of wounds and wholesale poisoning of the system) are extremely rare in persons free from ancestral taint; (2) hereditary transmission in such cases is quite unproved, if we discount cases where the whole system of the parent (including the germ-cells) is poisoned by alcohol, opium, or the like.

In short, whenever a disease has been acquired, when there is no specific predisposition towards it, when it is in biological terminology *modificational*, it seems unlikely that there will be any *specific hereditary effect* on the offspring. The most that can be admitted is that very virulent *acquired* disease may in

a general way poison or weaken the germ-cells along with the whole body, or that in the case of a mammalian mother the fœtus may be poisoned or weakened through the placental circulation.

It must be noted, however, that many medical authorities do not in the least agree with the position which we have stated. Thus Mr. Jonathan Hutchinson says: "Without venturing to do more than mention the Weismann logomachy, which has recently disturbed the creeds of some biologists, I will take permission to avow my belief that with the sperm and germ supplied by parents there may pass to the offspring tendencies to the reproduction of all that these parents had acquired up to the date of the sexual congress. By the term 'acquired' is meant all that has been received by modification of vital processes, not what has been imposed or taken away by external violence." We must refer to the chapter on the transmissibility of acquired characters for our answer to this opinion.

Experimental Evidence.—It is sometimes said that the famous experiments of Brown-Séquard showed conclusively that artificially induced "guinea-pig epilepsy" is transmissible. But a scrutiny of the case, such as we have given in the previous chapter, leaves us reluctant to base an argument on Brown-Séquard's results.

The only other cases which seem relevant are those which have to do with artificially induced immunity. By injections of serum and the like—the details do not concern us—it is possible to render an organism immune, *e.g.* to diphtheria. Are the offspring thereby rendered hereditarily immune? No case is known where the offspring of an immunised father showed any "anti-bodies" in the blood or any hint of immunity. There is no convincing evidence of transmission of immunity from the male parent.

It is known, however, that the offspring of an artificially immunised mammalian mother (guinea-pig, rabbit, etc.) may exhibit immunity. But this probably means that the "anti-bodies," agglutinins, precipitins, or whatever they may be called, passed viâ the placenta from the maternal to the fœtal blood. ***But this has nothing to do with inheritance.***

§ 4. *Can a Disease be transmitted?*

This is not a gratuitous question. Perhaps it is best answered in the negative!

"A disease," says Prof. Martius (1905, p. 14), "is not an entity nor a character, but a *process*—an abnormal process injurious to the organism, which is set a-going by a *causa externa* and runs its course in some part of the body." The process is not transmitted, but the potentiality of it is involved in some peculiarity in the organisation of the germ-plasm. "In the sense in which the word 'inherited' is used by biology, *there are no inherited diseases.*" They may be a-going before the offspring is born, but they are not as such inherited.

As the authority quoted says, the objector will doubtless at once bring forward the case of hæmophilia, which is markedly heritable. But hæmophilia is not a disease. Does not the subject get along fairly well until he receives a wound? There may be some weakness in the walls of his blood-vessels which makes them peculiarly vulnerable, there may be some obscure peculiarity in his blood which prevents it coagulating, so that bleeding even from a slight wound may be very persistent. But there is no disease, if we mean by disease an abnormal *process*. What is inherited is a peculiarity of the vascular system; or perhaps we should put it negatively, and say that some part of the normal inheritance (some "determinant," in Weismann's phrase) is absent in those who show hæmophilia.

Some inborn peculiarity of the nervous system, originating as a germinal variation, may under appropriate conditions of stimulus or lack of stimulus manifest itself as a disease, such as some forms of paralysis. Some inborn peculiarity of the muscular system, originating as a germinal variation, may under appropriate conditions of stimulus or lack of stimulus manifest itself as a disease—such as progressive muscular atrophy. Similarly, some inborn peculiarity of the alimentary

tract—a variation not in itself a disease (*e.g.* simple gastric achylia)—may in appropriate conditions give rise to disease. Similarly, phthisis is not as such inherited; what is inherited is a predisposition to caseous degeneration of tissue and allied pathological processes.

Thus, though it may appear pedantic, and though it will probably be misunderstood, we are inclined from the biological standpoint to agree with the authority quoted above, that "*there are no inherited diseases.*"

§ 5. *Predispositions to Disease*

Up to this point we have argued that mere reappearance of a disease does not imply that it is inherited; that infection or poisoning before birth is quite different from inheritance; that microbic diseases should never be spoken of as heritable; that there is no warrant for believing in the transmissibility of acquired diseases; and that, if disease means a *process*, the inheritance of predispositions to disease is a more accurate phrase than the inheritance of disease.

But is not this inherited "predisposition" something "mystical," suggestive of the "horologity" of clocks?

It may be mysterious, but it is not "mystical." We may not be able to picture it or define it, but it is like any other germinal potentiality, except that it happens to be prejudicial to the organism. It implies something out of gear in the protoplasmic machinery.

Physically considered, life depends on an ordered sequence of constructive and disruptive chemical processes, and the organism is from the outset predisposed, let us say "geared," to perform these in a certain routine. But the gearings are from the beginning very delicately adjusted: a slight initial difference may mean a life-long friction; a slight germinal bias may determine the trend of the whole life.

Among the pathological predispositions of major importance

in human life we may mention those which result in abnormal nervous processes, in rheumatism with its many forms, in gout, in obesity, in tendency to stone or gravel, in asthma, and so on. The reappearance of these diseases in varying degrees is certain, but what is really transmitted is the original germinal irregularity of gearing. No one can explain what this irregularity precisely is, but it is a common experience, baffling to the physician, that if it is adroitly checked in its outcrop in one direction it may manifest itself in another. He may cure the disease, but he cannot reconstitute his patient. Hydra-headed, the predisposition will show itself in polymorphic guise.

Some men are immune to certain diseases—*e.g.* to scarlet fever; all men are immune to fowl-cholera and many other animal diseases. This immunity is mysterious, but it is not "mystical." Of recent years we have begun to understand it, to *measure* it. *And "predisposition" is the other side of immunity.*

It is probable that some "predispositions" are much more definite than others. Thus, hæmophilia may be due to a retrogressive variation comparable to albinism; some particular item in the normal inheritance has been suppressed or kept latent. But the predisposition to tuberculosis is probably much less definite, and due to a more general disturbance of the "protoplasmic gearing," which finds multiple expressions both structural and functional.

The predisposition to gout is well known to be hereditary. It is probably what may be called a general constitutional predisposition, involving a derangement of the normal metabolism. For while it perhaps finds its primary expression in peculiarities of the digestive and excretory organs, it may affect practically every tissue in the body. Its expression may be accelerated by luxurious living and laziness, but, given the predisposition, it may manifest itself in those who live very carefully and take plenty of exercise. That is the peculiar hardship of it!

It may seem unsatisfactory to refer the origin of constitutional diseases, such as insanity and obesity, to a germinal predisposition—*i.e.* to the *terra ignota* of the fertilised egg-cell. But no other course is at present open. We are only doing in regard to diseases what we must do in regard to all variations. The little that can be safely said of their causes has already been said in Chapter III. Variability is one of the fundamental properties of the living organism, and the germ-cells are potential organisms. In their relation to the body which is their mortal vehicle, and in their own history, there is ample opportunity for variations to arise, and among these variations we must rank predispositions to disease. In short, such predispositions form part of the puzzle of individuality.

If we take a peculiarity like colour-blindness we know practically nothing in regard to its origin. It is not known to be associated with any structural defect of the eye; it is certainly not acquired; it arises in a certain percentage of the population, usually in males; it is a good example of a germinal variation which is exceedingly heritable. In the same way, passing to disease, we cannot tell what a predisposition to diabetes insipidus precisely means; we know it in its expressions in the body, but its origin is as obscure as that of colour-blindness; it is a germinal variation which is exceedingly heritable.

To illustrate the matter further, we may point out that the inheritance of physiological "idiosyncrasies" which do not express themselves as diseases is well established. Thus, the inability to digest the proteids of eggs and milk may be a heritable "family idiosyncrasy." It seems quite analogous to those idiosyncrasies which under appropriate conditions manifest themselves as diseases. A tendency to excessive "freckling" seems to be hereditary; it implies an inborn imperfection in the skin; under appropriate stimulation it may express itself as Kaposi's disease. Scores of similar cases are well known,

and they seem to throw a useful light on what is usually called "the inheritance of disease."

Inherited and Independent Variations.—It is hardly necessary to point out that the occurrence of a particular predisposition—whether it be to gout, to diabetes, or only to "freckling"—may be interpreted either as the outcome of an inherited germinal variation, or as an independent fresh variation similar to one which occurred in ancestors, just as the occurrence of great musical or mathematical talent may be interpreted either as inherited peculiarity or as fresh variation. The facts seem to show that certain variations have great staying-power throughout generations, and also that nature often repeats herself. Each case must be interpreted in terms of what is known of the lineage.

Inheritance of Secondary Effects of Disease.—In many cases it seems legitimate, perhaps necessary, to suppose that a disease in a parent may have a secondary effect on the germinal material, and may prompt germinal variations which find expression during the development of the offspring as diseases.

In some forms of rheumatism there is what may be called a poisoning—an auto-intoxication—of the living body with its own waste-products—*e.g.* urates; in some forms of bacterial disease, as the popular phrase "blood-poisoning" suggests, the same result is brought about by the waste-products or by-products of the intruding microbes; and it seems certain that an equally thorough poisoning may be brought about by the intemperate use of alcohol, ether, opium, etc. Even water-drinkers may be in certain areas the victims of lead-poisoning, for which they cannot reproach themselves. Experts may differ as to the most accurate way of expressing the facts, but it is certain that a man may thoroughly poison himself, for a time at least, with alcohol, opium, tobacco, or the like. Organ after organ may be injuriously affected; the blood, the urine, even the sweat will tell the tale, as it were in protest; and even

on *a priori* grounds we should expect the reproductive organs —apart as they are in some ways from the everyday life—to be affected by the widespread disturbance of nutritive metabolism.

Weismann has suggested that the oscillations of nutrition in the body prompt variations in the germ-plasm. Diseases may cause profound changes in the nutritive stream, and those particularly constant forms of whirlpool which we call the germ-cells, which repeat themselves and propagate themselves, generation after generation, age after age, may as the results of bodily disease exhibit variations. Stable as the germ-plasm must be supposed to be, we cannot conceive of it as an unrelated entity. We believe that this interpretation covers many of the cases which are called "inheritance of disease."

It must also be remembered that while the chromatin of the nucleus is almost certainly the real vehicle of the hereditary qualities, the germ-cells also include some extra-nuclear cytoplasm which may be affected in a general way by somatic changes. The ovum, in particular, has a relatively large mass of cytoplasm—its general cell-substance—which is the preliminary building-material of the embryo. It is cutting it too fine to say that what affects the cytoplasm of the egg is not part of the inheritance, since that is really hidden in the penetralia of the nucleus. The egg-cell is a unity, an individuality, a miniature organism, and anything in it (except, of course, another living creature—namely, a microbe) is at any rate a close annexe of the hereditary vehicle in the nucleus.

It is experimentally certain that germ-cells are markedly susceptible to toxins of various kinds, such as alcohol, nicotin, and hydrocyanic acid, and that abnormal developments result. Therefore, since many diseases produce toxins in the body, these may affect the germ-cells prejudicially, and thus there may be an inheritance of the secondary effects of disease.

What comes practically to the same thing for the *individual*

offspring, though it is theoretically different, may result if the toxins in the maternal body affect not the ova, but the developing embryo. They may saturate through the placenta and disturb the normal course of development. This would be *an ante-natal modification*, and we should not expect its consequences to extend beyond the immediate offspring, unless the same detrimental conditions persisted in subsequent generations.

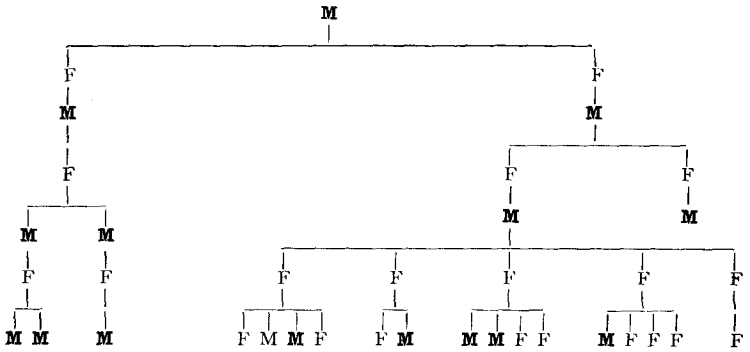
Illustrations.—"Assume that the last egg of a fowl dying from tuberculosis is fertile. Weismann would admit—every one would—that the chick is likely not to be full-grown and robust. It will fail of 'nutrition,' of a full capacity for regeneration, and of normal resistiveness to environment (terms which require fuller consideration). It would appear, then, that this chick has an idiopathic [say, innate] susceptibility to all and sundry, or at least to several, diseases. It is mere slackness to call that heredity in disease. It is equally apt to be variation; the chick turning out to be epileptic, or deformed, or liable to cholera. That is all that Weismann contends for. The disease has not bred itself" (Dr. George Wilson, *Scot. Med. Surg. Journ.* vi. 1900, p. 321).

Martius puts this problem. Two brothers have the same medium predisposition to tuberculosis; both take measles. During convalescence one (A) becomes definitely tuberculous as the result of exposure; the other (B) has his predisposition increased but resists tubercle-infection. Both marry normal wives and have children. Now, will the children of A have a worse inheritance than the children of B? There seems no reason to answer in the affirmative, unless it can be shown that the toxins, etc., engendered by the progress of the disease so saturate through the whole system that the germ-cells also are specifically affected and thus have their predisposition exaggerated. This seems very improbable. But it is possible that when a disease goes far the germ-cells may be in a general way prejudicially affected. And if they are rendered in a general way less vigorous, there is some likelihood that the disorganisation of the germinal machinery may go further.

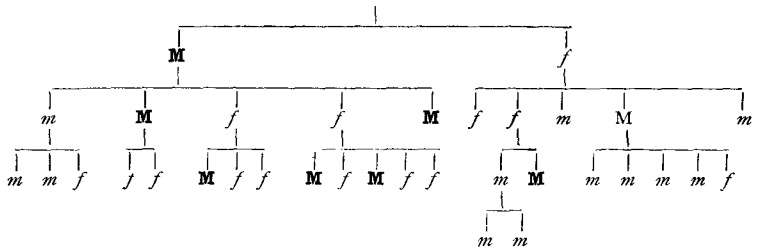
It is interesting to inquire whether, in cured cases of phthisis and the like, the protective substances naturally produced, *e.g.* the 'tulase' of Behring, might not even *lessen* the heritable predisposition of the ovum towards the disease in question.

§ 6. *Particular Cases*

Colour-blindness.—Horner, cited by Klebs, gives an interesting family history, showing the hereditary persistence of Daltonism or colour-blindness. The black letters indicate the affected subjects:



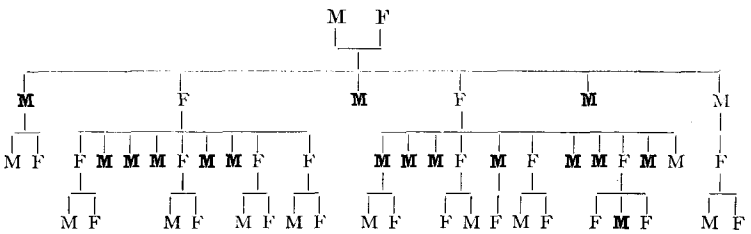
The following pedigree of a family containing colour-blind members was worked out by Dr. Rivers, among the Todas, an Indian hill tribe. It illustrates the " Knight's move " descent, as it may be called. The colour-blindness is exhibited in male members of the pedigree, but the females, though unaffected themselves, may transmit it to their male offspring.



Short-sightedness.—It is generally admitted that short-sightedness is due to an inborn peculiarity in the structure of the eye, occurring in various degrees. In itself it can hardly

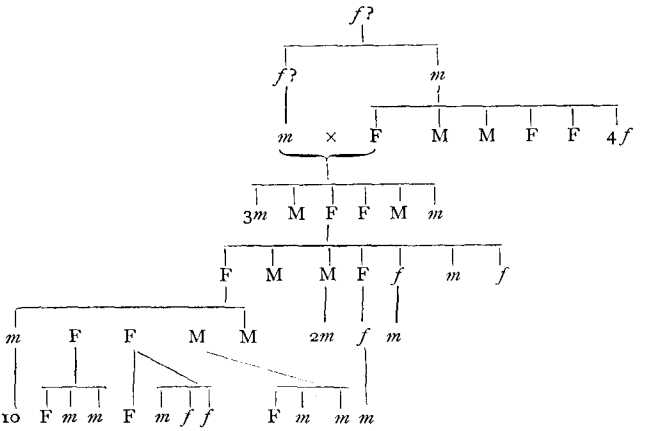
be called a disease in the strict sense, and conditions of life are conceivable in which it might even be advantageous. The innate peculiarity may become exaggerated and complicated when the eyes are forced to function in a way to which they are ill adapted, and acquired "myopic" modifications may be superadded to what was there by inheritance. Sometimes these may even lead to an actually diseased condition. But though the innate peculiarity may be exaggerated and complicated by the addition of acquired modifications, there is no evidence that these can be transmitted. What is transmitted is a structural peculiarity which began as a germinal variation, and that this is very liable to be transmitted one does not require to go to Germany to see. It is said that short-sightedness occurs, though rarely, among wild races.

Bleeding.—A hæmorrhagic tendency or liability to bleeding is well known to be heritable, but it rarely finds expression except in males. A case given by Klebs and cited by Sir William Turner (1889) is instructive in showing how the tendency, though transmitted through daughters (and therefore part of their inheritance), finds expression only in the males, and in illustrating first a *diffusion*, and then a *waning* of the peculiarity. The black letters indicate the affected subjects or "bleeders."

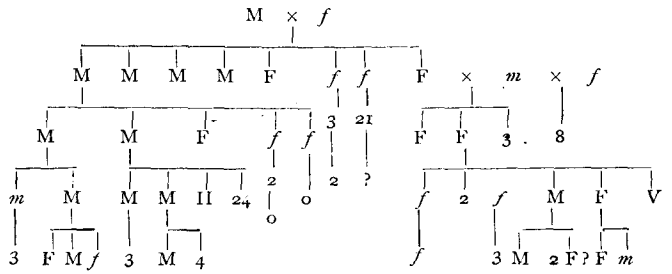


Cataract.—Mr. Bateson cites the following pedigrees of congenital cataract from Nettleship. The female at the top of the first pedigree came of an affected family, but was probably normal. Her son is said to have been certainly without cataract.

As Mr. Bateson points out, such descent of the condition through the unaffected is exceptional. The capitals indicate affected persons.



The second pedigree is also very interesting. The capital letters M and F and the Roman numerals indicate affected persons; the small letters and the small numbers indicate unaffected persons; the circles indicate unaffected persons undetermined.



Alcoholism.—There is practical unanimity among physicians that the abuse of alcohol is prejudicial to the race as well as to the individual, but there is considerable difference of opinion as to the theoretical interpretation of the observed facts. As the

subject has been very frequently discussed, we shall restrict ourselves to a brief survey.

(1) It is certain that the habit of using large quantities of alcohol is prejudicial to health, "poisons the system," and becomes a pathogenic factor. What constitutes abuse varies, of course, with the individual and his conditions of life. There seems to be little utility in labelling alcohol a "poison," though it is a poison in large doses. Arsenic is a poison to man, yet Gautier seems to prove that the presence of minute quantities of arsenic in various organs of the body is a condition of health. Both as regards arsenic and alcohol, it is the amount and the frequency of the doses that tell.

(2) It is certain that abuse of alcohol is prejudicial to the race by lessening in more ways than one the nutritive capacity of mothers. Thus, to refer to one aspect only, the conclusion of Prof. G. von Bunge's investigation of over 2,000 families is that the increasing incapacity of mothers to nurse their children is referable to chronic alcoholic poisoning continued for generations (*Die zunehmende Unfähigkeit der Frauen, ihre Kinder zu stillen*, 5th edition, Munich, 1907).

(3) It is also certain that the alcoholic habit is prejudicial to the race, not merely through custom and tradition, not merely by affecting maternity, but directly through inheritance. There are so many cases of unhealthy, insane, and criminal persons among the offspring of drunkards, that all possibility of coincidence is excluded. There is a causal connection. The disastrous results may be manifested as nervous disorders varying from hyper-excitability to dementia; or as debility and lack of developmental vigour, expressed, for instance, in infantilism, want of control, and imbecility; or as structural abnormalities, especially of the head and brain. The results are so varied that they suggest that what is inherited is general rather than specific; the offspring of alcoholic parents are not necessarily predisposed in any one particular direction, except

that the nervous system is naturally most liable to be affected; they may be epileptic, paralytic, idiotic, insane, or sterile. The variety of result is great, but it is never on the right side.

Dismal statistics on the subject are only too abundant, but a few cases must suffice. In ten families of marked alcoholic habit, Dr. Thomson of Alva (1858) found nineteen dipsomaniacs alive, eighteen deaths in consequence of the habit, ten insane, and three epileptics. In one family history the intemperate father died from a burn while drunk; his two sons and a nephew died in delirium tremens; another nephew, four grandsons, and three granddaughters were alcoholists. Out of eighty-three epileptic children at the Salpêtrière in Paris, sixty had drunken parents (cited by Debierre, p. 27).

(4) In interpreting the dismal statistics it is a mistake to attribute the whole result to the hereditary influence of alcoholist parents. It is necessary to make allowances for cases in which the offspring "have been in the vineyard too." They may be affected through the mother before and after birth by becoming early accustomed to doses of alcohol, and obviously by suggestion and imitation, and also by the persistence of the superorganic conditions which "drove the parents to drink." The resultants of these factors may augment the inherited bias or the inherited germinal defect. Where there has been no direct inheritance the nurture-results may simulate the results of transmission.

The Ostiak forces vodka down his child's throat, and the same happens nearer home. "Whisky-babies" occur in Merrie England. But the mischief may begin further back; even before birth the mother may poison her child.

Féré and others have described the disturbing effects which followed injections of small quantities of alcohol into the developing egg of the fowl. Mairet, quoted by Debierre, found that the offspring of an artificially intoxicated bitch by a sound dog showed "alcoholic degeneration" and soon died.

(5) Just as upbringing in an environment of intemperance may bring about results which simulate direct inheritance, so it should, we think, be frankly and responsibly recognised that there is an occupational factor in the persistence of excessive alcoholic habits. From certain occupations—dreary, unwholesome, underpaid, and what not—relief is sought in alcoholic stimulants. As long as these conditions persist they are likely to prompt successive generations to similar expedients, and this must be borne in mind when we try to estimate how much of so-called alcoholic degeneration is strictly speaking due to inheritance.

(6) It is necessary to recognise that what may be inherited is not the result of alcoholism, but rather the disposition which led the parent to become alcoholic—*e.g.* lack of control power. This is clearly illustrated in cases where the parent did not acquire the alcoholic habit until after he had ceased having children. Thus a great authority observes, "It was not the craving for alcohol that was inherited, but a general psychopathic constitution in which the alcoholic stimulus is an undue stimulus, and the mental control deficient" (T. S. Clouston).

(7) It is not to be expected that the particular modifications which the parent acquired through abuse of alcohol will be transmitted as such to his offspring. There is no secure evidence of this. The father may acquire cirrhosis of the liver, the child may be epileptic. There seems to be no authentic instance of anything like transmission of cirrhosis of the liver from a drunken father to his son. That a drunken son may also acquire cirrhosis proves nothing.

(8) The predisposition which facilitated the hyper-alcoholic habit in the parent is transmitted. There may be intra-uterine intoxication of the unborn child if the mother is a drunkard. The tradition in favour of the abuse of alcohol may persist. The conditions of nurture may also tend to induce the alcoholic habit in the offspring; but *there is more.* Much evidence points

to the conclusion that the germ-cells may (in cases of extreme alcoholism) be prejudicially affected along with the body of the victim. As it is often only the father who is alcoholic, it follows that the poisoning influence, whether of the alcohol itself or of by-products resulting from the nutritive disturbances which its abuse provokes, may affect the germ-cells as such. What exactly the effect is we do not know, but in some measure the germ-cells are probably weakened, or poisoned, or deranged. "This direct deterioration of the germ is a pathogenic factor of the first rank" (Martius, 1905, p. 23). For if the germ-cells are affected the offspring will also be affected.

Nervous Diseases.—That the nervous system is particularly liable to disease is well known, and various reasons have been assigned for this. (1) Nervous organs are of all organs the most intricate in their complexity, and nerve-cells are the most highly differentiated cells. But a high degree of complexity involves greater instability, greater liability to accident. A free-wheel bicycle with two or three grades of gearing is a finer mechanism than, let us say, the old-fashioned high bicycle, where even the complexity of a chain was avoided; but there is in the increased excellence the inevitable disadvantage of a greater range of possibility "for something going wrong." (2) Nervous organs have a very limited power of regeneration after injury. There is no increase in the number of our nerve-cells after we are born, and reports of cases of regeneration of nerve-cells after injury are few and far between as regards backboned animals. (3) Characters of recent origin tend to be more unstable than those of ancient date, and the differentiation of man's brain is relatively recent compared with that of his food-canal. Prof. Adami (1901, p. 1319) refers to the discovery made by James Ross of Manchester that "when there is progressive atrophy of the cells in the cortex of the brain, the first motor-cells to show signs of that atrophy are those governing the muscles which differentiate man from other

animals—namely, the opponens muscles of the hand." (4) Hamilton suggests, *inter alia* (1900, p. 298), that the "germ-track followed in the ontogeny of the nerve-cells is very short, far shorter than in the case of many other cells throughout the body, and hence a state of maturity is reached at a comparatively early period, with an inclination to premature decay." (5) It may also be noted that, especially as regards his nervous system, the so-called civilised man takes liberties of unnatural function and unnatural environment, which often tax the plasticity of protoplasm beyond the limits of endurance, marvellously wide as these are, and allow inborn weaknesses to find dire expression. For these and other reasons, then, the nervous system of man is peculiarly liable to disease.

Weaknesses, abnormal peculiarities, and actual diseases of the nervous system are not only very common, but they appear to be peculiarly persistent in family histories. In old days it was often remarked that generation after generation of a particular family might be "possessed of the devil"; and there were families of "sorcerers" and "witches" who turned their hereditary neuroses to account. So now we speak of the neuropathic family.

It is generally admitted that lack of control, morbid idiosyncrasies, subjection to delusions, monomania, hysteria, epilepsy, chorea, locomotor ataxy, extreme passionateness, homicidal and suicidal mania, insanity and imbecility, tend to reappear generation after generation with appalling regularity. It is often said that about one-fourth of those who are confined in lunatic asylums have had some more or less insane not-remote ancestor.

In regard to this very difficult question we wish simply to make three remarks: (1) in many cases what the facts suggest is the inheritance of a general, not a specific, predisposition; (2) on the other hand, there are some instances of apparently very precise and specific inheritance, as if some very definite

"blot on the brain" was transmitted from generation to generation; and (3) that there seems to be little warrant for believing in the transmission of a nervous disorder of exogenous origin.

(1) In most cases the facts seem to suggest that what is inherited and transmitted is a general predisposition to some dislocation or derangement of the nervous system. If such a dislocation or derangement occur in a case where we can exclude the probability of its being due to any infection, intoxication, or lesion of external origin, we must refer it to some initial defect or disturbance in the organisation of the germ. As such, it is likely enough to be transmitted, whether it be hysteria or epilepsy, melancholia or idiocy; but it does not by any means follow that it must be transmitted, or that, if transmitted, it will have in the offspring the form it took in the parent. In fact, the frequency with which the expression changes almost forces us to conclude that what is inherited is something general, not specific. Another reason for this conclusion is to be found in the fact that the nervous disorder is so often associated with some more general constitutional disturbance. Thus the association of hysteria, epilepsy, chorea, etc., with rheumatism is well known. In such cases it is probably more accurate to speak of the inheritance of a constitutional vice, a derangement of metabolism, and to avoid expressions which suggest that there is, to begin with, anything definitely wrong with the cerebral machinery. In the third place, it is instructive to note that the cerebral equipment may work well for years of ordinary life, and yet break down hopelessly in face of some extraordinary excitement or some constitutional crisis (puberty, parturition, menopause, etc.), which again suggests the inheritance of general weakness rather than the inheritance of specific disease.

The fact that predispositions to nervous diseases so often change in particular expression from generation to generation

points to the position which many hold, which is well argued for by Rohde (1895), that what is really inherited is a constitutional peculiarity (*arising originally as a germinal variation*) which may express itself in general neurasthenia, easy exhaustibility, deficient control, etc., *or*—under sufficient provocation—in some specific form of acute neurosis. After a careful survey Rohde concludes that the only nervous disorders which are transmissible are those which have a germinal origin; and another authority, Dr. T. S. Clouston, says, "A neurotic heredity is seen to resolve itself into general morbid tendencies rather than direct proclivities to special diseases." What is inherited is a predisposition, not a disease; and, fortunately, the predisposition may never realise itself.

What we have just said does not imply that persistent nerve-fatigue and neurasthenia in parents may not favour the outcrop of neurosis in the offspring, for the abnormal nervous condition in the parent may, through nutritive disturbances, affect the germ-plasm in a generally deleterious way (as Weismann expressly says), and the development of the nervous system of the unborn child may be affected disadvantageously by the abnormal condition of an over-fatigued mother.

It is exceedingly probable that many neuroses are due to primary defects in the development of some of the nerve-centres or of the cells that compose these. Thus, a weakening in the developmental power of certain rudiments in the inheritance, which might well arise as a germinal variation, and which might by hypothesis be inherited, would account for the recurrence of certain forms of nervous disease generation after generation, *e.g.* for a similar breakdown at adolescence or in senescence.

(2) On the other hand, there are some cases—a small minority—which suggest that a specific predisposition may be heritable. Thus, some of the records of inherited nervous disorders disclose an appalling exactness in their mode of expression, though it is probable that this is due in part to

suggestion. The point may be illustrated with reference to suicidal mania.

Debierre (1897, p. 19) cites a case, reported by Maccabruni, of a suicide's family. Out of seven, three made away with themselves; a fourth, who was assassinated, left a child who committed suicide. But the tragedy of the inheritance of a suicidal tendency is increased by the fact that it may manifest itself in the offspring at precisely the same age and in precisely the same way as it did in the parent.

"A monomaniac in the prime of life, Moreau de Tours reports, was seized with melancholia and drowned himself; his son, in good health, rich, the father of two well-endowed children, drowned himself at the same age." In another case a man who had met with a disappointment tried to drown himself, was rescued, but afterwards accomplished his design. It was found that his father and one of his brothers had committed suicide at the same age and in the same manner.

It should, we think, be borne in mind that the outcrop of a morbid hereditary tendency at the same age—often a critical age—in father, son, and grandson, may not be any more mysterious than that they should begin to shave at the same age. Nor should we exaggerate the tragedy of similar suicides by forgetting that the methods available are not very numerous. Originality is as rare in suicide as in other actions. Thirdly, we should remember the dire influence of suggestion: secret brooding over the nature of the father's death has doubtless in many cases added weight to the hereditary burden.

(3) In regard to the transmissibility of nervous disorders of exogenous origin—*i.e.* traceable to some external shock or wound—it may be enough to quote the deliberate conclusion of an expert pathologist: "I can find no facts which prove that an acquired disorder of the nervous system can be transmitted to the offspring" (E. Ziegler, 1886, p. 30). Where a nervous breakdown followed a shock, a wound, or an illness such as pneumonia,

and reappeared in the offspring, it is probable that there was behind the provocative stimulus an inborn predisposition, and that the latter alone is transmitted. The case of alcoholism has been discussed separately.

Microbic Diseases.—In the strict sense there can be no inheritance of microbic diseases, for a microbe cannot form part of the organisation of the germ-plasm. "No specific infective disease is hereditary, if we use the term 'heredity' in the sense which Darwin and the biologists have given to it. If it appear congenitally it is simply communicated to the fœtus by infection" (A. A. Kanthack, in Allbutt's *System of Medicine*, vol. i. p. 555). Let us take two concrete cases—tuberculosis and syphilis.

Tuberculosis.—As this familiar disease, in its many forms, is always associated with the presence of a specific microbe, the tubercle bacillus, it is not in itself transmissible. What is transmitted is a predisposition making infection easy, a vulnerability of epithelial surfaces, a weakness in the power of resisting and dealing with the invading microbes. As Debierre puts it, "On ne naît pas tuberculeux, on naît tuberculisable."

Theoretically, it matters little when or where infection occurs, but the various possibilities are of practical interest.

(1) It seems very unlikely that the spermatozoon is ever the bearer of the tubercle bacillus. Out of sixteen guinea-pigs inoculated with the sperm of tubercular males, six became tubercular, according to Landouzy and Martin, but many have repeated this experiment with negative results. Landouzy, quoted by Debierre, gives the case of a phthisical officer who married a wife without any hereditary taint in that direction. The five children all died of tubercular disease; but, of course, this may have been due to post-natal infection.

(2) Similarly, it seems very unlikely that the ovum is ever the bearer of the tubercle bacillus.

(3) In a few cases there is direct evidence that the mother may infect her unborn offspring, the bacillus passing through the placenta. In rabbits and guinea-pigs and some other animals this ante-natal infection has been demonstrated; but it is interesting to notice that while tuberculosis is extremely common in cows (sometimes

it is said, in 16 per cent.), the young calf is very rarely tubercular. Leclerc found only five cases out of 400,000. As to man, only about a dozen instances of congenital tuberculosis were admitted by an expert as securely established in 1905, and Dr. R. Schlüter's exceedingly careful scrutiny (1905) of alleged cases of congenital tubercle in human infants led him to the conclusion that for practical purposes the possibility of ante-natal infection might be in this case disregarded. Thus, Prof. D. J. Hamilton writes: "With extremely few exceptions—so few that they may almost be neglected—children are not born tubercular even of tubercular mothers, nor are the young of animals born tubercular under like conditions" (1900, p. 293). Even if the mother have genital tuberculosis, specific contamination of the unborn child seems rare, and there is no proof that genital tuberculosis in the father has any specific effect on his offspring.

(4) In all ordinary cases, then, the infection with tubercle bacillus occurs after birth, and in many cases long after.

The fact that tubercular disease may be a shadow over a family history for generations is doubtless mainly due to an inheritance of what began as a truly germinal or blastogenic variation, which is only a biological way of expressing what the physician means by "a particular predisposition," "a tubercular temperament," "a diathesis," and so on. To discuss what the particular weakness precisely is does not fall within our province; Prof. Hamilton says, "Most likely the particular vulnerability resides in the epithelial protective coverings of the body being too little resistant, too easily stimulated by external agencies, too readily penetrated by the parasite of the disease" (1900, p. 294). "In support of this assertion are to be taken into account certain epithelial manifestations which accompany the tubercular habit—namely, the very dark or very light degree of colour of the hair, the overgrowth of hair in the bushy eyebrows and long eyelashes, and, lastly, the occurrence of a lanugo-like overgrowth in tubercular children along the spine and over the legs. To my mind, these all point to an anomaly of the epithelial type which is peculiar to the tubercular habit of body" (Hamilton, 1900, p. 295).

If it be the case that the tubercle bacillus usually gains access, even to the lungs, mainly by the digestive tract, and almost entirely through the intestine, and may penetrate into the large lymph channels without any apparent lesion, we have still perhaps to do

with epithelial vulnerability, and in any case, which is all that our argument requires, with a general constitutional peculiarity or germinal variation.

For the benefit of those who are not satisfied with referring the hereditary predisposition to a germinal variation (though beyond this vagueness it is hardly safe at present for any biologist to venture), we wish to quote again from Prof. Hamilton's address on "Heredity in Disease," and we are glad to have so clear a judgment from a pathologist so eminent.

"Where has the inherited strain come from? What is its ancestral history? Can it be generated by vicious surroundings? I question whether it can. No doubt, once in the blood, the particular habit may be fostered by every external agent which tends to deteriorate the natural powers of resistance. But will such external agencies tend to produce a particular colour of hair, a certain narrowness of chest, tallness of stature, and other peculiarities which are distinctive of the tubercular constitution? My conviction is that they will not, and that we must go much further back in the history of the human race to get at the explanation of the matter. My own impression is that these features are the lineal descendants of a variation which took place far back in our history, that the variation has occurred irrespective of surroundings or external agencies, and that its influence has been propagated in the descendants ever since. It may be a variation which is common to many races, but one which apparently is intensely hereditary" (1900, pp. 295–6). It should be noted, however, that this way of looking at the facts is not unanimously accepted. Some experts will hardly admit the inheritance of even the tubercular diathesis as a thing more to be remarked than the disposition to typhoid or diphtheria. The tubercle bacillus is very parasitic, and may bide its time for years, slowly producing, even from a single infected gland, all the appearances of the tubercular type. Moreover it should be remembered that (*a*) open-air animals rarely suffer from tuberculosis, but suffer at once when confined; (*b*) that well-to-do, well-nourished people are much less liable than the poor and ill-fed; and (*c*) that phthisis is commonest where overcrowding is greatest, and lessens as hygiene improves.

In any case, the distinction between the inheritance of a predisposition to a disease and the inheritance of the disease is far from being a quibble about words, as some prejudiced writers still declare.

This is evident from the successful results of modern preventive medical practice in regard to consumption.

Statistics showing that in one sanatorium 35 per cent. of the tubercular cases belonged to tubercular families, in another 38 per cent., and so on, are not of great theoretical interest. The reappearance is due, in the first place, to the inheritance of the constitutional predisposition—*i.e.* of a bodily soil very open to the entrance of the weed, very suitable for its culture, very weak in the power of resisting its ravaging growth. The reappearance is due in the second place to the too common persistence of functional and environmental conditions favourable both to infection and to the enfeeblement which means defeat. It is enough to allude to the lack of fresh air and exercise. It is an old story, told in many forms and very true, that one boy of a tubercular family went to sea and alone escaped the doom which befell his brothers and sisters. Nor are cases unknown where a return in imagined security to the old home in the town, and to the sedentary life of a clerk, has resulted in belated but fatal infection. In the third place, we have to bear in mind the likelihood of one member of a family infecting another with the tubercle bacillus.

But besides the transmission of a constitutional vulnerability, besides the rare occurrence of ante-natal infection, besides the likelihood of household infection, besides the persistence of conditions of life which favour the disease—are there any other factors? There are probably two others. On the one hand, a seriously tubercular mother may be unable adequately to nourish her offspring before and after birth, and the ill-nourished offspring becomes the more readily the prey of disease. On the other hand, it seems likely that the bodily disturbances induced by tubercular disease in the parents may prejudicially affect the vigour of the germ-cells themselves, and thus lead to the production of inferior offspring.

Syphilis.—As this disease appears to be due to a specific microbe, its reappearance in the offspring of syphilitic parents is not strictly a fact of inheritance. The father may infect his offspring without the mother being affected, and it is possible that the microbe may enter the ovum with the spermatozoon. The father may affect his offspring indirectly by first infecting the mother—that is, the microbe may pass through the placenta into the child. In certain cases—*e.g.* when conception occurs soon after the date of the primary disease—the probabilities of the offspring being infected are great,

though there is always some uncertainty. Of twins, one may be infected and the other not. But the chances are so many that a patently syphilitic father will have syphilitic or in some way deteriorated children, that the marriage of a patently syphilitic subject can only be called a crime—the more heinous since the disease in the offspring is often more serious than in the parent. It seems, furthermore, certain in the case of this disease that, apart from the specific ante-natal infection of offspring, the toxins produced by the microbes in the body of the parent or parents may induce general disturbance or debility of constitution in the germ-cells, and thus result in inferior offspring.

§ 7. *Defects, Multiplicities, Malformations, and other Abnormalities*

For convenience, though we are here passing away from disease, we may include in this chapter a few references to the inheritance of abnormalities in the wide sense.

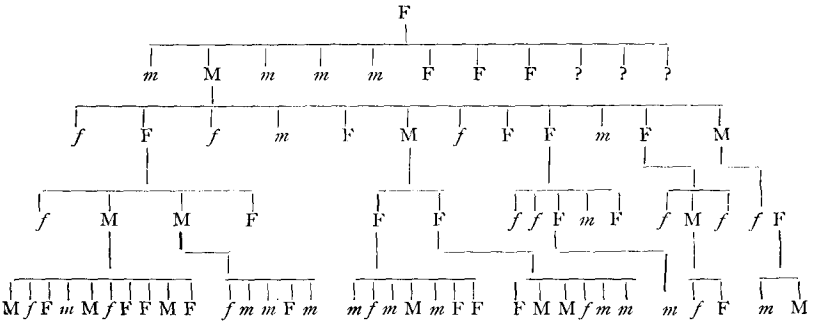
(A) **Defects.**—There are many cases on record where an absence or deficiency of a particular structure has persisted for several generations. Some of these minus variations have been utilised by man as the origin of new domesticated breeds. It is enough to mention hornless cattle—*e.g.* Polled Angus; earless sheep—*e.g.* of Syria and China; tail-less cats—*e.g.* of Japan and the Isle of Man; short-tailed dogs and pigs. Such cases must be distinguished from others quite different in nature, where a part is absent through mechanical constriction during development, and then, of course, no inheritance is to be looked for.

Albinism or absence of pigment is frequently inherited in man.

Sir William Turner gives a rather striking case where a shortening or imperfect growth of the metacarpal bone of the ring-finger of the left hand "was traceable throughout six generations, and perhaps even in a seventh, and was, as a rule, transmitted alternately from the males to the females of the family."

In a family in Pennsylvania described by Farabee many of the

members had all their fingers and toes two-jointed like the thumb and big toe. The normal members had normal children, even in the case of a first-cousin marriage. The abnormal members married normal individuals, and the fourteen families bred in this way contained 33 normals and 36 abnormals—a close approach to equality. The abnormals are indicated by capitals.



Along with defects of parts we may include imperfections due to an arrest of the normal course of development at certain stages, perhaps through inadequacy of nutrition, perhaps because of what we must vaguely call "deficient developmental vigour." Thus, hare-lip is practically the persistence of a normally transient condition, and cleft palate is in the same category. Hutchinson has recorded hare-lip in ten members of a family of twenty. The interest of some of these cases is considerable, since among animals there are not a few examples of what might be called normal arrests. Thus, every one is familiar with the hare-lip of the hare and its relatives, and the persistent external groove which connects each nostril of the skate with the corner of the mouth is even more striking.

Inhibitions or disturbances during ante-natal life are believed to result in various other abnormalities, such as cleft-palate, cervical fistulæ (persistence of traces of visceral clefts), spina bifida, certain peculiarities of the eyes and teeth, and so on.

These abnormalities occasionally recur repeatedly in a family tree, but it seems probable that what is really inherited is a deficiency in "developmental vigour," accentuated by nutritive defects on the part of the mothers during the period of gestation.

(B) **Multiplicities.**—As with defects, so in regard to multiplicities. Polydactylism has been known to recur through six generations of a human family. Bédart records quadruple polydactylism of hands and feet through three generations of a Périgord family (*C. R. Soc. Biol. Paris*, 9th series, vol. iv. 1892,

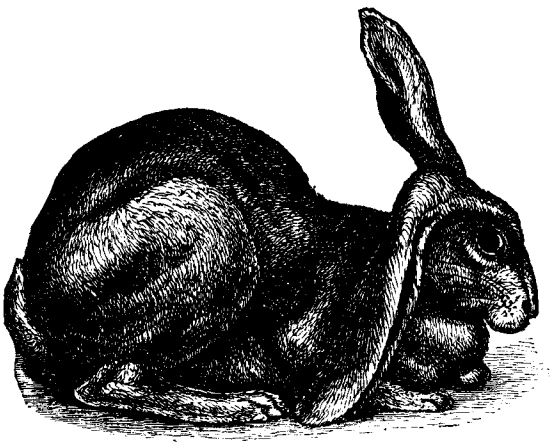


FIG. 28.—Half-lop rabbit, an abnormal variation, which by artificial selection has become a stable breed. (From Darwin.)

p. 367). Lucas cites a case of a Spanish family which included forty instances of polydactylism, and Pliny tells of similarly distinguished families in ancient Rome. Hereditary polydactylism is well known in cats.

(C) **Malformations of Parts.**—There are records showing the hereditary recurrence of abnormalities in dentition, in the eyes, in the hands (*e.g.* webbed fingers), in the feet (*e.g.* club-foot) —indeed, in most parts of the body; but in most cases the likelihood of transmission does not seem to be great.

(D) **Pre-natal Influences resulting in Mutilations, Multiplications, etc.**—Recent embryological experiments have shown incontestably that certain types of monstrosity can be readily induced artificially by subjecting the developing ovum to shakings, alterations of temperature, injections of various stuffs, and so on; and although the experiments relate mainly to birds, amphibians, fishes, and lower animals, there is some evidence that analogous factors may occasionally operate in mammals. Thus, the pressure of amniotic strands may divide the rudiment of a limb into two or may cause a mutilation. All such cases are equivalent to accidents in after-life; they are in no way expressions of the inheritance, and there is no evidence to show that they have any effect upon the inheritance.

"The Hapsburg lower lip or the large nose of Orleans is truly an item in the inheritance, but the occasional absence of an arm (due to a constriction of the rudiment by a strand of the amnion) is an intra-uterine acquisition; it is congenital, but it is not inherited" (Martius, 1905, p. 14).

It has sometimes been remarked that certain families show a hereditary tendency to have wens ("small cystic or encysted tumours") on the head and upper parts of the body. The nature of the growth, its inconstant position, and the time at which it appears (usually about middle age) show that we should not speak of the inheritance of a wen, but rather of the inheritance of some skin-weakness.

§ 8. *Some Provisional Propositions*

1. **Abnormal Peculiarities may find Expression in One Sex only.**—It is an interesting fact that an abnormal element in the inheritance may find expression in the males only or in the females only. If we could understand this we should be nearer understanding what sex really means.

Hæmophilia or a tendency to bleeding is a heritable ab-

normality, partly associated with weakness in the blood-vessels, which do not contract as they should and are apt to break, and partly connected with a lack of coagulating power in the blood. It is usually confined to *males*. But as it passes from a father through a daughter to a grandson, and so on, it must be a latent part of the germinal inheritance of the females, though for some obscure physiological reasons it fails to find expression in them, or has its expression quite disguised. Colour-blindness or Daltonism has been recorded (Horner) through the males only of seven generations. Déjérine cites another case (*fide* Appenzeller) in which all the males in a family history had cataract through four generations. There are other instances of what is sometimes awkwardly called the *unilateral transmission* of abnormal qualities.

Edward Lambert, born in 1717, is said to have been covered with "spines." His six children showed the same peculiarity, which began to be manifest from the sixth to the ninth month after birth. One of his children grew up and handed on the peculiarity to another generation. Indeed, it is said to have persisted for five generations, and in the males only,—*unilateral transmission*. (See *Phil. Trans.* 1755; Prichard, *History of Mankind*, 1851.)

2. **The Expression of Disease-inheritance may change from Generation to Generation.**—"Diseased organisms are apt to breed disease, but not always, though sometimes, their own disease." This cautious statement seems to be well borne out by the facts.

Hannot (*Arch. gén. de Médecine*, 1895) gives the following illustrations. A typical gouty subject, with his joints hampered by accumulations of urates, may beget a son as gouty as himself, or it may be that the son is asthmatic. An alcoholic patient may have an epileptic child. A tubercular mother may have a child with Pott's disease. A man infected with syphilis may have a son afflicted with general paralysis. In regard to the

last case, it may be, as has been recently suggested, that even general paralysis has its associated micro-organism, which finds a suitable soil in syphilised tissues. It is probable, at all events, that syphilis is one of the predisposing causes of general paralysis.

It is easy to add to these illustrations. " An inheritance from a parent who has suffered from psoriasis may possibly be transmitted as ichthyosis, or some form of chronic eczema or lichen " (Hutchinson, 1896, p. 66). A man with tabes may beget a child with epilepsy. An eye defect, such as microphthalmia, may be represented in the offspring by quite a different abnormality. Perhaps the best examples of change of outcrop are furnished by nervous disorders. Convulsions in one generation may be represented by hysteria in the next, or hyperæsthesia by mania, or insanity by epilepsy, and so on.

It may appear for a moment that these illustrations prove too much, suggesting as they do that the inheritance of morbid predispositions is very inconstant. But it must be noted, first, that there are even more abundant instances of diseased predispositions breeding true, and second, that they bear out what has been already emphasised, that in most cases what is inherited is rather an abnormal metabolism than a specific disease.

It is doubtful whether we are warranted in speaking of the " transmutation of disease," for this phrase seems to suggest that a particular kind of process may change in hereditary transport into another particular kind of process. It is probable that some diseased conditions which get different names are fundamentally the same ; it is their expression only that changes in response to the conditions of nurture and environment, just as a plant changes superficially in fresh soil, or just as crystals of the same substance sometimes take different forms in different conditions. It is generally allowed that there are groups of closely related diseases.

But the facts which are cited under the phrase " transmutation

of disease" seem to point to another consideration—that what is inherited is sometimes a very general peculiarity, which finds this or that expression in relation to the conditions of the body, which is a very variable soil, according to the liberating stimuli which are available, such as the diet, climate, and other conditions of life.

It is well known in medicine that a predisposition or diathesis may express itself in half a dozen different ways—being polymorphic, as it is said—though there may be one way or two ways which, being most frequent, may be called "diagnostic" or "distinctive." Thus, the tubercular tendency has several different ways of expressing itself, probably depending mainly on the nature of the nutritive and other environmental influences. The parallel to this in natural conditions is seen when the same kind of animal develops or grows differently in different surroundings.

But if the same disease may find different expression in, let us say, three brothers, it is not surprising that the disease of a parent may take a different, though analogous, form in the offspring, and perhaps a third form in the grandchildren. It may be intensified, or weakened, or directed on new lines, the change depending, so far as we can see, partly on the amphimixis or duality of the inheritance, and partly on the external conditions. Thus, if both parents have a markedly phthisical tendency, the probability is that there will be in the offspring a more pronounced similar predisposition than if one of the parents had belonged to an untainted stock; or, again, apart from amphimixis, a thorough change in habits and surroundings may at least greatly inhibit the phthisical outcrop in the offspring.

There is probably a very simple reason why a hereditary tendency to nervous disease should have different expressions in successive generations, and it is this: that many if not most abnormal neuroses—*e.g.* epilepsy and insanity—emerge during

the period of development, and are due to defects or arrests in the development, ultimately traceable to deficient nutrition of the tissues, or to a lack of vigour in the germinal material to begin with. What is inherited is this general tendency to debility, and it is for the environmental influences to determine the precise lines of least resistance.

3. **Some Predispositions to Disease are much more heritable than others.**—Statistics seem to prove what a general outlook suggests, that some predispositions to disease are much more likely to have hereditary re-expression than others. But the cautious student will bear in mind two saving clauses: (1) that non-expression does not necessarily imply non-inheritance, for a morbid character often skips a generation, or more than one; and (2) that recurrence does not necessarily imply inheritance, for a particular predisposition may crop up *de novo*, or, in other words, the fountain of variation may repeat itself. No one will go the length of supposing that the rheumatic tendency has not originated afresh over and over again, or of tracing the whole burden of rheumatic disease back to man's pre-human ancestry because rheumatism occurs in monkeys. As already noted, acute rheumatism is probably microbic.

A few illustrations of the variable probabilities of transmission must suffice. In one long family history, gout is said to have persisted for four centuries. Out of 523 gouty subjects, 309 had a family taint (about 60 %); out of 156 cases, 140 had a family taint (about 90 %); various sets of cases show percentages varying from 50 to 100. Out of 104 cases of diabetes mellitus, 22 had a family taint (about 20 %). In one long family history, dealing with about 400 members, there were 26 cases of hæmophilia; in another, dealing with 100 members, there were 17 "bleeders."

Out of 901 admissions to an asylum, 477 had insane relatives; out of 321 cases of epilepsy, 105 had a family taint (about 35 %); out of 208 cases of hysteria, 165 had a family taint (about 80 %).

Various specialists on mental disorders have found reason to believe in hereditary transmission in from 25 to 85 per cent. of their patients, the diversity being doubtless in part due to the great variety of nervous diseases.

4. **Many Uncertainties in Inheritance.**—It is seldom possible to say that a predisposition to a disease expressed in a parent *must* be transmitted to the offspring. A predisposition to a disease is rarely a sharp and definite character, such as we are familiar with in "varieties" (of a species), which so frequently breed true. It often means simply a slight disturbance of what we may call the "gearing" of an organism—a slight derangement of the normal sequences of the metabolism. It is an unstable fluctuating variation. It is usually admitted that there are families hereditarily predestined to be gouty or rheumatic, but is any expert on either disease willing to stake his reputation on the prediction that a particular gouty father is sure to have gouty children?

It is not difficult to understand why individual prediction as to the inheritance of predispositions to certain diseases is impossible. An individual inheritance is a mosaic of parental and ancestral contributions. The reduction of these in the process of maturation, the possibilities of fresh permutations and combinations in amphimixis, the variability of the germ-plasm under the influence of nutritive oscillations in the blood-stream, the probable occurrence of some sort of intra-germinal struggle among the hereditary items (all living and self-assertive), the importance of nurture in favouring the expression of one character and hindering that of another—the whole circumstances of the case, in short, are so complex that prediction for individuals is out of the question, no matter how certain we may be as to the average result in 1,000 cases. A predisposition to a disease has to run the gauntlet just like a predisposition to mathematical insight or musical talent. There is just this difference, that predispositions to disease are commoner, that they often occur

in many ancestors of a given child, and that the chances of their being transmitted are therefore greater.

Even when there is reason to believe that an offspring has inherited a predisposition to a particular disease, it does not necessarily follow that this item in the inheritance must be expressed in development.

5. **Predispositions may dwindle away.**—There is, at least, some evidence to show that hereditary tendencies to particular diseases may dwindle until it becomes almost permissible to say that they have been eradicated.

The biological interpretation of this is twofold: (1) that interbreeding with an untainted stock may result in an overpowering of the vicious tendency or in a re-habilitation of the normal; and (2) that in the course of selection the more severely tainted tend to die out, thus leaving the race relatively stronger. The biological caution is that we must not infer from non-reappearance, or from non-expression—*e.g.* in healthier conditions of function and environment—that the evil tendency has ceased to be inherited. Prof. Hamilton says (1900, p. 301), "My firm conviction is that if a vicious line be introduced it may die out, and probably does in most cases die out by interbreeding with a series of pure stocks; but that no reliance can be placed upon its not recurring atavistically, it may be, generations after."

§ 9. *Immunity*

Immunity to a disease may be inborn or acquired. It may be acquired in various ways: by having the disease and surviving it—thus, recovery from smallpox usually confers an immunity which lasts for years; by being inoculated with the modified virus of the disease—thus, vaccination confers immunity from small-pox; by being inoculated with a very minute quantity of the virus; by being inoculated with the metabolic products or toxins of the microbes; by having injections of the blood or

serum of another artificially immunised organism; and even by ingesting the microbes or their products. (See A. A. Kanthack, Allbutt's *System of Medicine*, vol. i., article "Infection.")

It seems that artificial immunity depends on processes within the body which make the tissues able to destroy intruding bacteria and to rob their products of their fatal potency. It seems that specific anti-toxins are formed which immunise the body to specific infection.

An acquired specific immunity may be transferred from a mother to her offspring through the placenta, but this is not in the strict sense inheritance. Ehrlich and others have shown experimentally that rabbits and the like may be born immune if the mother has been artificially rendered immune; and it has been asserted that in mankind the fœtus may become, through the mother, immune to smallpox.

In support of the view that those who are infected with a plague and survive can transmit relative immunity to their offspring, attention is called to the fact that epidemics have their day and cease to be. But this admits of another interpretation—the plague eliminates the most susceptible and leaves the race in this way more resistent. What is transmitted is the inborn power of resistance—which may be enhanced by the selective process, especially if the plague is very severe and lasts a long time. It is to be feared that there is very little evidence of the transmission of *acquired* immunity—to smallpox, for instance!

What is to be made of the alleged fact that two of the commonest infective diseases in Britain—namely, scarlet fever and measles—are much less virulent than they used to be? According to a skilful pathologist, Dr. William Russell, "this is almost certainly to be attributed, not to an attenuation of the virus, or to improved treatment, but to a measure of immunity acquired by a population whose progenitors for generations have passed through the ordeal of these infections."

Of course, this is a very difficult question, in regard to which no one would wish to dogmatise. But one must not too readily assume that the correct interpretation is the hereditary transmission of acquired immunity. (1) It is possible that the micro-organisms concerned are evolving in the direction of attenuated virulence. (2) Much may be due to improved treatment. Thus "measles" may not be really milder, but simply better treated. (3) The result may be in part due to an elimination of the most susceptible, which leaves the race as a whole more resistent. (4) There may be a quite independent widespread variational change in the direction of more resisting power to these two diseases—a germinal variational change quite apart from the ordeal of infection. (5) The power of resistance may be improved by diet; thus measles is often most acute in out-of-work winters, and least acute when the nutritive conditions are good. (6) The severe so-called "types" of certain diseases were probably "mixed infections." Nowadays there is perhaps a greater number of "pure infections." (7) Some of the more virulent germs are probably being stamped out. There is no proof that the germ of the now somewhat rare scarlatina maligna is the same race as that of the common scarlatina simplex. (8) It is possible that the mothers may through the placenta confer their own acquired immunity on their offspring.

Natural immunity is a well-known inborn peculiarity, sometimes racial, sometimes personal, and manifested in various degrees. Negroes are relatively immune to yellow fever and ague; Algerian sheep are relatively immune to anthrax; certain individuals appear to enjoy peculiar immunity in the midst of epidemics.

It is generally believed that racial immunity has been gradually wrought out in the course of natural selection. Germinal variations in the direction of immunity enable their possessors to survive; the survivors transmit their refractory constitution; the

most susceptible are persistently weeded out: and thus, if the infection persists long enough as a common mode of elimination, a race may become relatively immune. No one doubts the heritability of natural immunity, though there is still great uncertainty as to what the mechanism of immunity is.

§ 10. *Note on Chromosomes in Man*

In a very interesting paper, Prof. H. E. Ziegler has illustrated the modern doctrine of the material basis of inheritance with particular reference to man ("Die Chromosomen-Theorie der Vererbung in ihrer Anwendung auf den Menschen." *Archiv. für Rassen- und Gesellschafts-Biologie*, iii., 1906, pp. 797–812).

Let us take two parents, P^1 ♂ and P^1 ♀ ; in each body-cell there are 24 chromosomes, and in each mature germ-cell there are 12 chromosomes. Thus the fertilised ovum has again 24, and in each cell of the offspring (F^1) there are 12 chromosomes of paternal origin (from P^1 ♂) and 12 of maternal origin (from P^1 ♀).

In the mature sperm-cell or egg-cell of the parent (P^1 ♂ or P^1 ♀) there are 12 chromosomes, but it does not necessarily follow that 6 of these must be from a grandfather (P^2 ♂), and 6 from a grandmother (P^2 ♀). Why not? Simply because in the reduction of chromosomes from 24 to 12, which occurs in maturation, it does not necessarily follow that the parental (P^2) contributions are retained in equal number. The total number 12 always results, but it may be made up of 5 from P^2 ♂ and 7 from P^2 ♀, or of 8 from P^2 ♂ and 4 from P^2 ♀, and so on. Suppose the mature sperm-cell had 9 from P^2 ♂ and 3 from P^2 ♀, then, as far as the paternal inheritance goes, we should expect the offspring (F^1) to be very like its grandfather.

The chances are that the grand-paternal and grand-maternal contributions in any mature germ-cell will approximate to equality, but the numerous possibilities enable us to see one reason at least why there is often great diversity in a family.

If we suppose that the chromosomes are all of equal value, there is always a theoretical possibility in a human family of 169 different combinations of the grandparental contributions. It is a well-known fact that certain predispositions to disease may be seen in two or three children in a household and be quite absent from other two or three.

The chromosomes of the four grandparents (P^2) are made up of contributions from eight great-grandparents (P^3), and if the reduction processes were always quite regular, the 24 chromosomes in a fertilised egg-cell should contain in the 12 of paternal origin, 6 grand-paternal and 6 grand-maternal; and either of these groups of six should contain 3 great-grand-paternal and 3 great-grand-maternal contributions. But if the reduction-processes do not exhibit this improbable regularity, we may look for a great variety of possible mosaic arrangements,—as indeed we find. If we accept the chromosome theory, we can readily understand how an innate defect or morbid predisposition in, let us say, a grandfather, may be sifted out of the lineage; and similarly for a virtue!

The business becomes more complicated when we notice that in a number of cases there are differences in the size of the individual chromosomes; it may be that particular characters are bound up with particular chromosomes, and are not represented even by analogous items in others. Thus a particular predisposition to disease in a particular organ may be embodied in a particular chromosome, which might be thus conceivably sifted out of the lineage altogether. In man, however, the chromosomes are approximately of equal size.

Ziegler supposes that in man each chromosome has the same value and influence, that each is capable of influencing the whole organism, and that they differ only inasmuch as they are derived from different ancestors, and thus embody diverse hereditary tendencies.

The chromosomes of an individual usually represent eight

families, and it is therefore likely that every one has some chromosomes with a predisposition to some disease, such as phthisis, or gout, or diabetes, or "nerves." A mosaic made up of contributions from eight families can hardly avoid some such taint. But the important point, Prof. Ziegler continues, is this,—what numerical proportion do the tainted chromosomes bear to the untainted? If 3 out of the 24 have a diabetic taint, this will mean much less than if there were 12 tainted. It follows that taint on both sides of the house is particularly dangerous.

Ziegler gives the following illustrative schema.

Father—with marked taint, inherited from his father and mother, as shown by the dark chromosomes—13 out of 24.

○○○ ●●● ●●● ●●○ ○○● ●●● ●○○ ○○○

Three mature sperm-cells showing three different combinations

a. ○●● ●●● ●●● ●○○
b. ○○○ ●●● ●○○ ○○○
c. ○●● ○○○ ○○○ ○○○

Mother—normal, though with a latent taint, inherited from her mother, as shown by the dark chromosomes—4 out of 24.

○○○ ○○○ ○○○ ○○○ ○●● ●●○ ○○○ ○○○

Three mature egg-cells showing three different combinations

d. ○○● ●●● ○○○ ○○○
e. ○●● ○○○ ○○○ ○○○
f. ○○○ ○○○ ○○○ ○○○

It is evident that the child resulting from $a \times d$ would have a badly tainted inheritance, that another resulting from $c \times f$ would have a good inheritance, and that another from $c \times e$ would be in the same position as the mother, and so on.

§ 11. *Practical Considerations*

Pessimism unwarranted.—A consideration of the extent to which predispositions to disease form part and parcel of our

natural inheritance does not promote cheerfulness, yet there can be little doubt that the oppressiveness of the facts is commonly exaggerated—especially by those who do not trouble themselves to think out the business clearly.

A medical authority (quoted by F. Martius, 1905) goes the length of saying, "For the practitioner the concept of heredity is quite useless, and he should not deal with it at all. What is wrought out during the life of the individual can be dealt with. *What is due to the parents is unalterable.*"

This is an extreme expression of the practical pessimism which many feel. We cannot choose our parents; we cannot refuse our legacy. The Ethiopian cannot change his skin, or the leopard his spots.

But this extreme pessimism is unwarranted. The fact is that, if "the inheritance of disease" really occurred to the extent and *in the manner* many medical writers assume with so much conviction, the human race would have been extinct long ago, or in any case we could not now have the broad and strong stream of healthfulness which, in spite of all disease, still surges around us.

Let us look for a little at the more hopeful aspects of the question:

(1) As regards microbic diseases, a *predisposition* to which may be inherited, the progress of hygiene and preventive medicine tends increasingly to diminish the risks of infection or of fatal infection.

(2) There is some reason to believe that, in regard to some microbic diseases, a relative constitutional immunity is in process of evolution.

(3) There is no scientific warrant for believing that acquired diseases—*i.e.* those arising as modifications from without, to which there is no specific predisposition—are as such transmissible. By liberating toxins and the like in the body, or by depressing the general nutrition, acquired diseases *may* pre-

judicially affect the germ-cells, and therefore the offspring. But this is more remediable than specific changes in the germ-plasm. Thus, an authoritative expert writes: "Every diseased condition, which is primarily of exogenous origin, may be combated. *Sublata causa, tollitur effectus.* Intra-uterine infection and direct toxic deterioration of the germ may be preventible and will be increasingly prevented. The struggle against sexual diseases and against exaggerated alcoholism and similar toxic deteriorations is not merely the business of the physician; it is the attainable objective of racial hygiene" (freely translated from Martius, 1905, p. 39). It has been said by another well-known authority that consumption—taken early enough—is one of the most curable of diseases! Prof. E. Ray Lankester is sanguine enough to say that if men would boldly and wholeheartedly enter into possession of their kingdom, "all epidemic disease could be abolished in fifty years."

Our view of the harm done by an ill-considered widespread belief in the transmissibility of modificational or exogenous diseases has been well expressed by one of the keenest workers in the Public Health service: "The nightmare of the specific inheritance of acquired diseases overloads the spontaneity of life, paralyses the will, and hampers the preventive service in its efforts to improve the environment. Weismannism exalts the social inheritances, which, as the great organs of selection, constitute the basis of preventive medicine" (W. Leslie Mackenzie).

(4) In regard to constitutional diseases, it seems on the whole that "the inheritance of predispositions to particular diseases" is a more accurate description of the facts than the common phrase, "the inheritance of disease." There is no doubt that many predispositions to particular constitutional diseases are inherited. What have we to set against this? We must recognise that every item in an inheritance requires an appropriate nurture if it is to be expressed, or expressed fully,

in development. This nurture is to some extent in our hands. Adaptive nurture, individual hygiene, change of habits and habitat, and the like may prevent or inhibit the expression of a predisposition. In short, the organism is extremely plastic—for the better as well as for the worse.

An organism with a predisposition to a constitutional disease —let us say albuminuria, asthma, gout, diabetes, or some nervous disorder—is obviously handicapped, more or less terribly according to the strength of the predisposition. There is a struggle for existence. But in this struggle a most momentous factor is nurture in the widest sense—the conditions of function and environment. If these favour the morbid elements in the inheritance, the organism has to fight a battle with two fronts, which is seldom hopeful. But if well-adapted conditions of life be secured, and secured early, there is always considerable hope that nurture may inhibit the full expression of the undesirable elements in the inherited nature. "He that will to Cupar, maun to Cupar" is a familiar Scotch proverb, but the other side of it is the "plasticity of the organism."

(5) It seems to us that even expert writers have sometimes exaggerated the *necessity* of the persistence of constitutional taints and defects; for as it is well known that a highly advantageous variation may fail to persist, why may not this be equally true of one that is highly disadvantageous? A "retrograde variety"—that is, one which has lost one of the characteristics of the parent species—may arise in our garden and breed true. Why may not something analogous occur in a peculiarly vulnerable stock? Why may not the vulnerability, the disadvantageous predisposition, disappear? Apart from natural selection, sexual selection, and the like, it may be that the subtle process of germinal selection is sometimes able practically to eradicate an abnormal or morbid peculiarity.

(6) Crosses between wheat-plants immune to rust and others susceptible to rust yield hybrids which are all susceptible. But

if these hybrids be inbred, the progeny are partly susceptible and partly immune, and all those that are immune breed true. If it is thus possible among plants " to get a pure thing out of an impure "—it may be that for domestic animals and for man himself the purification of a tainted stock is not a chimera.

(7) As to the diffusion of disease by the intermarriage of badly tainted with relatively healthy families, we have this in our own hands, and we need not whine over it. The basis of preferential mating is not unalterable; in fact, we know that it sways hither and thither from age to age. Possible marriages are every day prohibited or refrained from for the absurdest of reasons; there is no reason why they should not be prohibited or refrained from for the best of reasons—the welfare of our race. For the average man instinctive " falling in love " will probably remain a safer guide than any scientific eugenic counsels, but there is no reason to doubt that eugenic considerations will in the course of time enter subconsciously into the prolegomena of that mysterious process. Moreover, in many matings there is no question of love at all.

By the education of conscience on a scientific basis there is already arising a wholesome prejudice against the marriage and especially the intermarriage of subjects in whom there is a strong hereditary bias to certain diseases—such as epilepsy and diabetes, to take two very different instances. Is it Utopian to hope that this will extend with increasing knowledge, and that the ethical consciousness of the average man will come more and more to include in its varied content " a feeling of responsibility for the healthfulness of succeeding generations " ? It seems more direct in the German phrase—" Verantwortungsgefühl vor der Heiligkeit der kommenden Generationen."

The argument always used against deliberate preferential mating on a eugenic basis is that our ignorance is immense. And this must be frankly admitted. Yet there are some things that we do know. We know that " the manifestly syphilitic

subject who marries before he is thoroughly and definitely cured commits a crime, not only because there is the possibility—indeed, the probability—that he infects his wife, but also because he deliberately [*voraussichtlich*] begets syphilitic children. . . . The Eugenic office of the future, which will have to test applicants for a marriage-licence, not merely juristically or socially, but also biologically and medically, to decide as to their fitness for legitimate reproduction, will have no difficulty in refusing permission to uncured syphilitics and incurable drunkards, and perhaps also to those who are patently tubercular" (freely translated from Martius, 1905, p. 24).

That the best general constitutions should be mated is the first rule of good breeding.

That a markedly good constitution should not be paired with a markedly bad one is a second rule—a disregard of which means wanton wastage.

A third rule is that a person exhibiting a bias towards a specific disease should not marry another with the same bias. A man with a phthisical tendency, if he marries at all, should not marry a woman whose family history is known to show many phthisical subjects.

In other words, every possible care should be taken of a relatively sound stock. The careless tainting of a good stock is a social crime. Every reasonable precaution should be taken to prevent a badly tainted stock from diffusing itself.

(8) Besides the advance of preventive medicine, the spreading enthusiasm for health, the awakening of a eugenic conscience, the suggestions as to "marriage-licences" and other forms of social selection, all making for the greater healthfulness of the human breed, we have, of course, to remember that our race has not got beyond the scope of natural selection, much as we try to evade it.

In the course of natural selection, keenest during the early years of life, the most tainted and the least immune or resistent

tend continually to be " weeded out," and the standard of fitness is thus kept from falling rapidly. When predispositions to specific diseases accumulate (*e.g.* by in-breeding of similars), a non-viable, sometimes a non-reproductive, type arises, and—disappears for ever. Rotten twigs are always falling off the tree of life. There is a continual irrecoverable precipitation of incapables, who thus cease to muddy the stream.

But while this is true, every one is aware that man is so constituted that he cannot submit to Nature's winnowing. For reasons that go to the very foundations of our social framework, we can neither act as Spartan eliminators ourselves nor allow Nature to have her way. That this does not prevent us from being perhaps more cruel than either, is to be gravely feared, but, in any case, the fact is that we consistently try to conserve lives which natural selection would eliminate. This may be for social reasons necessary, but it cannot be regarded with satisfaction unless it is associated with positive selection of the fitter types.

It has often been said that modern hygiene, in tending to eliminate our eliminators—the microbes—is destroying a most valuable selective agency which has helped to make our race what it is. This seems a little like saying that the destruction of venomous snakes in India is eliminating a most valuable selective agency which has helped to evolve the Wisdom of the East.

It is difficult to find justification for the enthusiastic confidence which some seem to have in the value of microbes as eliminators. Which microbe ? Surely not that of plague, which strikes indifferently, and is no more discriminatively selective than an earthquake. Surely not that of typhus, which used to kill weak and strong alike. Surely not that of typhoid, which may strike anyone, and does not confer more than a passing immunity. And so on through a long list.

It would perhaps be a subtler and more convincing line of

argument to say that, throughout the ages, man has been selecting the microbes, lessening their virulence, in a sense taming them—sometimes to death—as his phagocytes were strengthened by more suitable food, or as his " Opsonic Index " improved, again perhaps in relation to food. As the body increases in its power of holding out—and this is demonstrably *modifiable*—it can prolong the contest with intruding microbes with more and more hope of ultimate victory. Typhus used to kill off the Irish by tens of thousands, but it never seemed to leave the generations less susceptible. Now, apart from an occasional prowl, the typhus germ has ceased to be important, and the Irish are all the stronger for its absence.

In any case, whether microbes have been important and valuable selective agents or not, it is a sad confession on the part of the " paragon of animals " if he cannot discover other selective agencies—more discriminating, let us hope—to take the place of disease germs.

At present, we can only indicate that the future of our race depends on *Eugenics* (in some form or other), combined with the simultaneous evolution of *Eutechnics* and *Eutopias*. " Brave words," of course ; but surely not " Utopian " !