These all appeared suddenly, practically in the state we now see them.

If Weismann's theory be true, we shall have to modify our opinions of the rate at which evolution of species has occurred. Darwin taught that animals and plants have a tendency to vary from the parental type, and that by natural selection the advantageous varieties are preserved and those less fitted for the environment are destroyed, and that new species have resulted from the gradual and slow accumulation of minute variations. They have evolved, as it were, on an inclined plane by a sort of continuous process.

A more recent theory, associated especially with the name of De Vries, is that variation has not been continuous, but discontinuous, not along an inclined plane, but by steps, that new forms, completely and sharply separated from the parent species, have frequently if not generally come into existence. "The new species is all at once there" without transitional forms. This is known as "the mutation theory."

According to De Vries there are two kinds of variation:

1. "Fluctuating variation," such as we are familiar with in all animals and plants. These cannot overstep the bounds of the species, and cannot therefore give rise to new species or any new constant character, for they are always indefinite.

2. "Mutation" is a perfectly definite change, which may or may not be as marked as a fluctuating variation, but it is constant, and tends to be repeated in succeeding generations. It produces new species, and is of germinal origin.

The product of fluctuating variations, being of somatic origin, can only be kept at the highest point of development by the most rigid care. If selection ceases for only a few generations, the new form sinks back to the original level, as is well exemplified in the various breeds of pigeons.

According to Darwin's selection theory, only useful characters can survive; according to the mutation theory, useless characters may do so also, and even those that may be hurtful in a small degree, and surely this is in accord with well-known facts.

There are several stumbling-blocks in the way of the theory of natural selection acting on variation as the sole means by which species have originated. I need only mention degeneration and parasitism, dimorphism and trimorphism in plants, exact bilateral and radial symmetry, and especially the extreme perfection of development in certain directions, for instance the hand of man, the development of his vocal organs, his mathematical and philosophical abilities, and keen sense of colour, which seem to go beyond the limit required for the perpetuation of the race or the individual, whereas they are not at all inconsistent with the theory of advance by "mutation." De Vries has proved conclusively that mutations, or "sports" not infrequently occur amongst plants, and give rise to true breeding varieties. If Mendel's law applies to such cases, they are not likely to be swamped by intercrossing with the normal type.

Thus we get a new view of evolution: "Natural selection may explain the survival of the fittest, but it cannot explain the arrival of the fittest" (De Vries).

I submit that the various facts that I have mentioned point out with unmistakable clearness the only way by which hereditary disease can be eliminated. We hear nowadays a great deal about physical deterioration, and a great deal of benefit is expected from education and from improved sanitary conditions; but neither education nor sanitary laws can eradicate hereditary disease except by preventing the marriage of the affected individuals. Just as a purely brachydactylous race might be produced, so it would be equally easy to eradicate this abnormality by preventing the marriage of the abnormal individuals, and there is little doubt that other hereditary defects and diseases can be practically made to disappear by the same means. Unfortunately, modern legislation tends to produce the opposite effect, for everything is done to encourage not only the marriage, but the early marriage, of inferior members of the community, at the same time that the burdens of taxation retard more and more the marriage of the middle classes. Free education, free meals, free clothing, are all very well for a certain class, but they are not remedies, and the net result to this nation will in the long run be detrimental.

HEREDITY

IN

DISEASES OF THE NERVOUS SYSTEM.

INTRODUCTION TO A DISCUSSION ON HEREDITY AT THE ROYAL SOCIETY OF MEDICINE.

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MR. PRESIDENT AND GENTLEMEN.—The scientific study of heredity, which has undergone so wonderful a development since the mists were swept away which for long had hidden Mendel's work, cannot be applied to the diseases of man. The human race is not open to Mendel's essential methods, and its mere complexity of development involves innumerable differences from lower forms of life, the effects of which may be greater than we can well realize. Potential fallacies surround almost every inference that can be drawn. We can seldom look back far at preceding generations, and the future we must leave to those who may follow us. The difficulties of precision and fullness of knowledge are great, and the chance fertilization, from which the flowers of Mendel were guarded by his paper bags, is the rule in the human race, unalterable by us, however we may wish. Hence it seems useless even to apply the hereditary terminology to facts that are in general inconsistent with its grounds. I can only hope to present a few of the more salient facts of heredity in diseases of the nervous system, well known as they are, and I trust that they will be supplemented by others. We are only in the stage of random observation.

Among diseases of the nervous system are commonly included many that are not of it but merely in it, and this can scarcely be justified. Tumours of the brain and spinal cord are allied to morbid growths in general, for the most part. Yet many of them have a special relation to nervous tissue, such as gliomata, composed of the special interstitial elements of the nerve centres. Endotheliomata, growing from the lining tissue of the cavities and surface of the brain and spinal cord, we do not know how to class, whether with the centres in which they are found or with growths of the same character elsewhere. But all such affections are so rare that they have not yet justified any suggestion of heredity. This is also true of another condition in which heredity might reasonably be expected—the defect in the coarser formation of the spinal cord which leads to the cavities, and undeveloped embryonic tissue adjacent, of syringomyelia. It is often found after death when there have been no symptoms to suggest it. When the causal arrest of development has occurred earlier and involved the enclosing structures, it constitutes a state often conspicuous in infancy—*spina bifida*. Heredity in these affections may be thought likely, but no ground for it has been, I think, discerned, and may not be until every member of the family can be scrutinized after death. Insular sclerosis is another affection in which heredity might be expected, according to one view of its nature, but no facts have suggested it.

Sudden cerebral seizures—apoplexy and the like—depend upon causes that take their heredity far away from the brain in which the lesion occurs. Yet the frequency in which heredity is active is most notable. In some families many members suffer earlier in life than the malady is really common. But we must look to the vessels, and the cause of their degeneration, for the mechanism by which the disease is produced and through which heredity acts.

Toxic states, various in nature and origin, chemical and microbial, are potent causes of disease, but the range of heredity in their occurrence is small. The so-called "inherited syphilis" has, of course, nothing to do with heredity. I do not know of any observations on the children of those who suffer from "inherited syphilis," and their life histories. The question is important, and possibly some Fellows may be able to furnish facts. Any influence heredity may have on the liability to suffer from bacterial maladies affecting the nervous system may perhaps be suggested by the discussion on the similar facts regarding tubercle. The part it may play in the secondary production of chemical agents through an

action on somatic processes is an important problem. It is presented by the paralysis that sometimes follows diphtheria. The experience of our fever hospitals may furnish evidence for or against any family tendency to suffer from it. I think the tendency is not directly proportioned to the severity of the primary disease. There must be very many instances of several members of a family suffering from diphtheria, and it is most important that the records should be so kept as to facilitate the discovery of the disease in another generation of the same family. Such search will be necessary in the case of many diseases, and a special form of index may be needed. Nothing can be achieved unless it is begun.

It would be wearisome even to enumerate the maladies from which we cannot hope to obtain knowledge, but I may mention one class of disease on which we may hope for some facts. Though they are not primarily of the nervous system they often affect it gravely. There are those that consist of deranged chemical processes in the vital laboratory of the human frame, giving rise to endogenous toxins. We see it in the nerve disturbance which occurs in diabetes, probably due to other material incidental to that by which the excess of sugar is produced, whether or not it is the same as that which often causes death. The heredity of diabetes is familiar, but its thorough study is a difficult task. A child not seldom suffers before a parent. The endogenous poisons of what we call gout are certainly many, and some also occur with other constitutional states. Both kinds may cause symmetrical symptoms in the extremities, but of their cause we know nothing. It cannot be doubted that the processes of the body are largely influenced by heredity.

The cases of disease of the nervous system in which the influence of heredity is marked seem to fall into certain classes. One of these consists of the early abiotrophies. I proposed this term some years ago as a convenient designation for the cases in which certain systems of structure, in the nervous or muscular system or elsewhere, have an essential defect of vital endurance in consequence of which their life slowly fails. A marked example is presented by the hair follicles of the scalp, in consequence of which early and extensive baldness occurs in father and son (a convenient subject for the study of heredity). It is seen in the nervous system, as in hereditary optic atrophy, in which the onset is sometimes excited by some extraneous cause, inadequate alone to cause the enduring effect. Hereditary ataxy or Friedreich's disease is another, and so are the various myopathies. By "early" I mean those abiotrophies which begin before the development which coincides with growth is over, and often not many years after birth.

The muscles are not usually considered part of the nervous system, although they present a close relation to it in intimate structure and function. We may take the most typical form of pseudo-hypertrophic paralysis as a convenient instance of the heredity of the abiotrophies. The muscular fibres begin to waste during the first seven years of life, but the bulk of many of the muscles is actually increased by interstitial overgrowth of fibrous tissue and fat; certain muscles are small, and some may seem absent from the first. This disease is always congenital, but heredity is maternal only; it never comes from the father. The tendency to it is thus germinal, a potential defect of development in part of the ovum, that part which will become the muscles. But it is not usually present in all the ova; some sons escape. The female children seldom suffer in this typical form, but they inherit the tendency, or some of them do, and their sons may suffer. In the ova from which the daughters develop, the potentiality of the disease is not in the elements that develop into the muscles, but only in that portion of the protoplasm which will become the germinal tissue for the muscles of their children. The same facts are true of other early abiotrophies—of hereditary optic nerve atrophy, etc.—and sometimes they also are limited to males, and are only transmitted by females.

If the tendency is thus fixed in the germ tissue, and differently fixed according to the resulting sex, does not the fact make it probable that the sex is also predetermined? Many have held this view, and it is not easy to see how otherwise the facts of these diseases can be explained.

The disposition to the disease seems seldom to be present in every ovum. Sometimes it apparently is in every male ovum. Every son has died, as in the well-known family described in the Fifties by Dr. Meryon; but of that, one daughter has failed to transmit the disease; another daughter has had two sons and three daughters—both the sons have died from it, all the daughters are free. In an instance which came under my notice long ago, four sons died, but the fifth escaped, and his sons of course are free, but the only daughter, herself free, has her only two sons, both affected.

We have many similar instances of the disease in two generations. We have known it just long enough—sixty years—to find it in a second generation, but it is curious how seldom we are able to trace the typical disease in preceding generations, although we are not often able to exclude it owing to our lack of knowledge. But I have met with it in the two sons of a lady (the third and sixth of seven sons), whose lineage and that of the mother of Meryon's cases, can be obtained from the Peerage. This lineage presents a remarkable fact. Both were descended from a certain duchess who was married in 1774, and in the case of each the descent is solely in the female line. The mother of Meryon's cases I will call Lady A. and the other Lady B. Lady A. was the grand-daughter of the said duchess; Lady B. is the great-great-grand-daughter. There were sons in both lines, but from their ages at death in Lady A.'s family, there can have been no case of the disease. In Lady B.'s there is only one that suggests its possibility. A son of her maternal grandmother died at 18, but some other cause is intrinsically more probable. We must, I think, regard it as of definite, though unknown, significance that both these maternal producers of the disease had a single ancestor, and, considering the relation of the disease to sex, their descent by the female line cannot be regarded as an accident. I can offer no suggestion of its meaning. But it is remarkable how free from the disease the ancestors of those who produce it generally seem to be. We may note that isolated cases are more frequent than groups, although the groups comprehend a majority of the actual cases. When females suffer, males sometimes escape.

Only once have I known the disease to occur in the offspring of first cousins. There resulted four cases of albinism, one of whom had also pseudo-hypertrophic disease. Neither malady had occurred before. But there had been previous instances of less close intermarriage during the preceding six generations, and, considering the relation of the disease to the ovum, it can hardly be ascribed to the consanguinity of the actual parents.

Other forms of myopathy have been traced through several generations. The facial form of Déjerine and Landouzy has been traced through five generations. This form often does not begin early; its progress may go on through life, and males may transmit it. The first series of Déjerine and Landouzy, just mentioned, bears a distant but interesting resemblance to Mendel's facts. A man and woman married, the woman being atrophic. They had one daughter, who was normal, and married a quite healthy man and bore three daughters, all affected. One of these married a healthy man and had two children—a girl healthy, and a son in whom the atrophy only showed itself at 26 and did not become general until 50. He married a healthy woman and had nine children, six sons and three daughters. A son and a daughter died in childhood; of the remaining seven, four were atrophic—two sons and two daughters. If we regard the normal state as dominant, the atrophy as recessive, the absence of the latter in the second generation, recurrence in the third, and equality in the fourth and fifth are noteworthy features—almost Mendelian.

I have dwelt on these muscular maladies because they present features that are well-defined, and because most, if not all, the early nerve abiotrophies agree with them in origin, even in their maternal heredity.

A second class may include the hereditary maladies which begin later in life, after the period of growth is over. They often present persistent disturbance of function and are commonly hereditary, but from either side. In the so-called heredo-ataxy of Marie, the symptoms begin about 30, and are usually fatal in about twenty years. It has been found to depend on atrophy of the cerebellum, associated with certain tracts of the spinal cord, at least,

in one case, in which three generations were affected. Huntingdon's chorea begins usually in the senile period of life, but its heredity is well-marked, and so is that of the peculiar rigidity called Thompson's disease, a lifelong peculiarity of action of the motor nerve structures, also called myotonia congenita.

I must pass some interesting diseases—paralysis agitans, tremors, Graves's disease, etc.—in which heredity can be traced seldom, but sometimes remarkably. I think it is probable that we shall hereafter find that special forms of heredity are associated with other characters in a manner that will make it an aid in distinguishing maladies now classed together, but for this we must wait.

A third class of diseases in which heredity is operative consists of the so-called functional affections. Some of them vary extremely in degree, and baffle attempts to group them so as to discover their relation to heredity. Such are hysteria and the defective nerve strength, which may manifest itself in varied ways, and which we are all drawn, sometimes against our better judgement, to designate "neurasthenia." Other functional disorders, such as chorea and neuralgia, have relations too complex for the clear discernment of heredity, and migraine, defined as it is, is connected with quite different constitutional states than disease of the nervous system. Two forms of functional disease have been much studied in relation to heredity—epilepsy and insanity.

Some cases of epilepsy are outside our subject. Those that result solely from organic lesions of the brain, from disease, or trauma, or difficult birth, are not concerned with heredity. The question of acquisition is here important. I confess I have always acted on the belief that the tendency to convulsions in such acquired cases, without other evidence of disposition, may be regarded as not transmissible. I have never hesitated, on this ground, to permit the marriage of a sufferer, and I have not had any evidence to show that I was wrong in doing so, however early in life the damage arose. I do not question the guinea-pigs of Brown-Séquard, but I do question an inference from guinea-pigs to men. But such cases of "organic epilepsy" are rare. They constitute so small a proportion of the cases as to have little influence in statistics of heredity. The difficulties in ascertaining the facts of family histories are vast. Among hospital patients genuine ignorance often hinders. A woman brought her son for epilepsy and denied that any of his relations had had fits. As soon as she had left the room she returned with two of his brothers suffering from them. It had not occurred to her that a brother is a relation. In patients seen in private, the stigma supposed to attach to some diseases leads to concealment, which produces actual ignorance in another generation. A middle-aged lady with an epileptic nephew denied any neurotic antecedents, and was indignant when I told her that three great-aunts had been in asylums. But it was so.

In my own inquiries into the heredity of epilepsy I have limited myself to these two maladies, epilepsy and insanity. I find that in the cases seen in private there is a family history of one or both in 47 per cent., in antecedents and present or past collaterals. The difficulties I have just mentioned justify the assumption that at least 50 per cent., and probably more, really present a family tendency. Among hospital patients the number is not more than 35 per cent., so great a difference does ignorance apparently make. In the facts presented the percentage was taken from 2,400 cases, of which 600 were seen in private. The proportions are much less than have been ascertained by others who have included a larger number of diseases. It may be well to confine myself to the cases in which a parent suffered. Jeremy Taylor tells us, in one of his sermons, that "an epileptic son doth often come from an epileptic father."

Of the total cases in which inheritance was paternal the father himself suffered in 40 per cent., when maternal the mother suffered in only 36 per cent. When epilepsy itself occurred in a parent, it was the father who was epileptic in 49 per cent. of the cases, the mother in 51. The cases with insanity in a parent are only one-third the number with parental epilepsy. Of the cases with parental insanity the father was insane in 37 per cent., the mother in 63. One effect of heredity is to increase the female cases. Where it was absent the excess of males amounted to 4 per cent., but in cases with heredity the same excess

was presented by females. This is partly due to the fact that inheritance is more frequently from the mother's side, by 13 per cent., and that then females are in excess by 18 per cent.

The influence of heredity is sometimes strikingly emphasized by the number of sufferers in a family. In one instance six brothers suffered, their mother, two of her sisters, and both her parents. In another, five sisters, five of their children, the mother, her brother's son and her own mother.

Such facts might be multiplied almost indefinitely regarding many diseases. But we are told we are working on an entirely wrong method. Diem states that he has found neuropathic heredity in nearly 70 per cent. of healthy persons. If he has included every conceivable malady that involves the nervous system it is quite credible, but of no significance. It has been urged that the essential facts for every member of each generation must be recorded to make observations of value.

But I may not take up your time longer, for there are here to-day those from whom we may learn, who have given up their ability and time to the scientific study of heredity. I hope that they will tell us how we may make our future observations of more service.

TWO CASES OF UTERINE FIBROIDS SHOWING PERITHELIOMATOUS CHANGES: LONG IMMUNITY FROM RECURRENCE AFTER OPERATION.*

BY

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[Abstract.]

THE following are the details of the cases:

CASE I.—*Cystic Uterine Fibroid of large size in a 5-para aged 49: Infection of a loculus after tapping: Fibroma of ovary: Supravaginal hysterectomy—removal of the fibromatous ovary: Opposite Fallopian tube and ovary not removed: Uterine tumour malignant (perithelioma) according to microscopic appearances: Convalescence protracted through infection, probably from the tapped loculus: Speedy recurrence expected, yet patient living and very corpulent four and a half years after operation.*

E. J., aged 49, was admitted into Mr. Doran's wards in the Samaritan Free Hospital in November, 1903. The abdomen had been enlarging for seven years. She had been tapped five weeks before admission, and over a pint of rosy fluid had come away without much diminution in the size of the tumour. The periods had recently been irregular. The patient had been married for thirty years, and had borne five children, the last confinement occurring eighteen years before admission.

On admission the patient looked fairly healthy, thin yet hardly cachectic. Both legs were slightly oedematous. The abdomen was greatly distended, the measurements on November 5th being: Girth at umbilical level, 55½ in.; ensiform cartilage to umbilicus, 16½ in.; umbilicus to symphysis pubis, 7½ in.; right anterior superior iliac spine to umbilicus, 11½ in.; left ditto to umbilicus, 9½ in. The integuments of the abdominal wall were neither glossy nor oedematous, and there were no enlarged inguino-femoral glands. There was universal dullness, excepting high up in the epigastrium, and fluctuation at every point, not transmissible from flank to flank nor from the upper to the lower limits of the tumour. There was a scar below the umbilicus, the result of the recent tapping, and the parietes were much less tense at that point than higher up, as the above measurements showed. This fact suggested loculi. The uterus could be plainly defined, bulky and anteverted by the tumour, no part of which came down below the brim of the pelvis.

Operation.

On December 1st, 1903, Mr. Doran removed the tumour. When the peritoneal cavity was opened a very vascular cyst wall was exposed. The omentum was strongly adherent, with its vessels greatly dilated. An artery and vein were ligatured, the remaining vessels were clamped, and the omentum detached and tied in segments. Four inches of the transverse colon, including the splenic flexure, were firmly adherent to the cyst wall, a thin layer of which was detached, leaving it on the bowel, which was then set free. The under surface of the transverse mesocolon adhered firmly to the upper part of the tumour, and was torn in two places, but the lacerations were longitudinal and did not involve any of the big vessels. Several

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