in consequence of which they offered a large superficial area to the blood current and to the injurious substances circulating therein.

Professor Sir T. GRAINGER STEWART said it was necessary to select certain points for remarks, inasmuch as they were so numerous, and he should desire to speak rather of the clinical than of the purely pathological aspects of the subject. He remembered that apart from such local conditions of Bell's paralysis, as regards one great group of cases of the kind, namely, the alcoholic, he was indebted for his first definite acquaintance with the subject to the writings of the President of the Section, Dr. Wilks. He went on to refer to the clinical features of the first series of cases which he published about fourteen years ago—motor paralysis, loss of sensibility, and trophic changes, beginning at the fingers and toes and spreading upwards. He had three such cases in his clinic about the same time. Two gradually recovered, one took pneumonia and died, and *post-mortem* examination revealed definite changes in the nerves of the affected parts with no lesion of the cord or brain. He then spoke briefly of a series of points which had influenced him, namely (1) The remarkable tendency to recovery when the disease does not involve nerves of vital organs. (2) That this condition at once indicated the explanation of the temporary paralyses which occur in the early stages of locomotor ataxia. (3) That further experience had proved that not infrequently vital nerves were affected, and that death resulted. He gave some details of illustrative cases. (4) The strange way in which one found in some cases particular groups of fibres in an individual nerve, sometimes in a strand, as in optic neuritis, sometimes affecting the motor fibres, sometimes the sensory fibres alone; and, further, he thought that his experience justified what Dr. Sharkey had suggested, namely, that the vasomotor and trophic fibres are occasionally selected. (5) He begged to offer his testimony as to the great variety of toxins which might induce these changes, alcohol and diphtheria, influenza, and others. (6) That he had found remarkably good results from the subcutaneous use of strychnine after the first acuteness of the case was once passed.

Professor D. J. HAMILTON took up the question whether the term "neuritis" is really applicable to the disease in question. There existed until lately, and even yet the matter was not quite cleared up, much dubiety as to what affections of the central and peripheral nervous systems are and what are not inflammatory. Some years since the speaker had made some experimental observations on the spinal cord with the object of eliciting what the changes are which occur in the organ when it is inflamed artificially. These changes were found to be twofold, namely, those affecting the blood vessels and interstitial tissue, and those having their seat in the nerve cells and tubes. Those affecting the former were found to be identical with what are found in inflamed vascular parts elsewhere. The reaction of the nerve tubes, however, were quite peculiar and consisted chiefly in a contraction, moniliform swelling, and final segmentation of the axis cylinders. Fatty alterations were in abeyance. Similar lesions occur in syphilitic inflammations of the brain in man. In peripheral neuritis, however, it often happens that the interstitial tissue of the nerve remains unaltered while the nerve fibres are extensively degenerated. The degeneration, moreover, is not alike with that seen in myelitis or neuritis artificially induced. There is much greater evidence of disintegration of the nerve fibres followed soon afterwards by fatty degeneration. The conclusion which the speaker had arrived at was that widespread peripheral neuritis so-called is in most cases not inflammatory, but in reality a degeneration due to the action of a poison. The action of this poison is probably like that of phosphorus upon other tissues. In reply to remarks made by Drs. Saundby and Sharkey, he maintained that any reactive phenomena noticed in the interstitial tissue of the nerve might quite possibly be secondary to those found in the nerve fibres. Cases occurred over and over again, as in that recorded by Sir T. Grainger Stewart, where the nerves were profoundly degenerated without the slightest reaction in the surroundings. On the other hand, every one knew that secondary degenerations of the spinal cord from trophic causes were often followed by thickening of the neuroglia.

Dr. ELIZA WALKER DUNBAR (Bristol) said the widespread

influence of the toxin of influenza had brought the question of neuritis and pathology of the nervous system generally before every medical practitioner. She had been struck by the absence in peripheral neuritis of the signs of swelling, which they had learned to associate with inflammation, and, in some cases, by the fugitive nature of the symptoms. The toxin of influenza, for instance, might call forth in the course of half an hour in the same individual an intense hunger due to excitation of some of the nerves of the stomach, giving way to severe pain in the extremities, going on to producing restlessness due to irritation of the nerves of the muscles and passing deafness and blindness. She believed that in very many cases of so-called peripheral neuritis the pathological change was a chemical one.

Dr. GOODHART wished to ask the question, What is inflammation in nervous tissue? Is it necessarily represented by similar changes in other organs? May it not be special, and therefore may it not be quite possible that the changes in the myelium and that such degeneration may in reality be inflammation? He made this remark in opposition to his own feelings and from the drift of opinion in the discussion. From the clinical side he had certainly come to the conclusion that many cases could not be neuritis in any ordinary sense; the positive course they run, and other facts seemed to him to make it clear that the disease in many cases is of the nature of a toxic degeneration, and although it is always a dangerous line of argument to draw conclusions upon pathological change from the action of medicine, yet he could not but see it in this way, and in support of Sir Grainger Stewart's contention that the action of strychnine injected subcutaneously is of very great value, he felt quite as strongly as regards the value of strychnine administered in this way, and he thought that its sometimes rapid action in the betterment of the patient tended to show that the change was a mere nervous hebetude or degeneration; and it is probable that the action of strychnine does also tend to confirm the observations referred to by Dr. Mott and supported by Dr. Ormerod, that in many cases the nerve cells suffered either alone or in conjunction with the nerve fibre.

Dr. SAUNDBY had arrived in the meeting too late to hear much of the debate, and would not have spoken but for the proposition of Professor Hamilton that these conditions are not inflammatory. Speaking from his own experience, he had seen not only the segmental neuritis described by Professor Hamilton as present in artificially inflamed nerves, but also interstitial neuritis, and observers in every civilised country have abundantly attested their occurrence in these cases. Secondly, the tenderness over the nerve trunks affords clinical support to the theory of the presence of inflammation.

NOTES ON THE INFLUENCE OF HEREDITY IN DISEASE.¹

By WILLIAM SEDGWICK, M.R.C.S.

It seems to have been very generally admitted by those who have directed special attention to the subject, that much progress has been made of late years in the study of the laws on which both hereditary transmission and hereditary development depend; for, on referring to the well-known work by the late Mr. Darwin on the *Origin of Species*, which was published in 1859, we find it stated that "the laws governing inheritance are quite unknown." Although this statement was to some extent qualified by subsequent remarks, yet it was not till after an interval of some years, during which our knowledge of the subject had been greatly increased by a more complete investigation of the family history in cases of heredity, that he was enabled to state in his subsequent work on the *Variation of Animals and Plants under Domestication*, which appeared in 1868, that finally, "though much remains obscure with respect to inheritance, we may look at the following (five) laws as fairly well established." It is not, however, proposed on the present occasion to do more than offer some remarks on the influence of three of

¹ Read in the Section of Medicine at the Annual Meeting of the British Medical Association held in London, July-August, 1895.

these five laws, namely, limitation by age, limitation by sex, and atavism—which, as Darwin has very justly remarked, “depends on transmission and development being distinct powers.” It may be allowable for me to add that among the various contributions which have helped to establish these laws are a series of papers by myself, which were published in the late *British and Foreign Medico-Chirurgical Review* for April and July, 1861; April and July, 1863; October, 1866; and April and October, 1867; for these papers have been cited and acknowledged by Darwin in his last-named work, which contains the important and long-promised evidence on which his theory of the origin of species was based.

With respect to the limitation of hereditary disease, by age as well as by sex, it may be observed that there are not only certain diseases, but also certain classes of disease, in which the effect produced by such influence has been more or less strongly marked. As regards more especially the influence of age, it has been noted that when cataract or amaurosis occurs as an hereditary affection its recurrence is often limited to about one and the same period of life. This has been well shown in Dr. Tatham Thompson's² case, in which cataract was developed for four generations, when the members of the family affected were from 3 to 5 years of age; and in Mr. Berry's³ case, in which the same disease recurred in successive members of five generations at about the age of from 6 to 7 years. There are also many other groups of diseases affecting, for example, the nervous system, the heart, the lungs, and other structures in which there has been often observed a corresponding limitation, either as regards the period of life at which the disease is most apt to reappear in other members of the family, or the age at which it is destined to terminate in death. It is to some extent reassuring to find that when this influence of age on hereditary disease thus affects not only its development, but also its duration, as is not infrequently the case, we are to a great extent justified in expressing a more hopeful opinion respecting the probable prolongation of life than it would otherwise be allowable for us to do. Some attention has been directed to this subject of what may be termed “outgrowing the disease,” in one of my papers On the Influence of Age in Hereditary Disease, which was published in October, 1867. In cases, for example, of phthisis it has been observed that the disease is not only very liable to occur in some families at the same early age, but that it may also admit of being warded off if suitable precautions have been taken in good time to guard against its occurrence. Among cases of this description which have come under my own observation is that of a gentleman belonging to a family in which phthisis had been hereditary for three, if not more, generations, and in which the disease had affected chiefly the male members of the family when they were between the ages of 23 and 26 years. Shortly before this patient had attained the age of 19, there was a suspicious breakdown in his health, with frequent cough, and excessive night sweats, in consequence of which it was thought advisable to send him to Australia, where, for an uninterrupted period of twenty-eight years, he led an outdoor life at a large farm. He not only remained there altogether free from symptoms which could be in any way connected with the chest, but he ultimately became fairly strong and well. Such an occurrence as this of outgrowing an hereditary tendency to phthisis by effecting a complete and an early change in the surrounding conditions of life has not infrequently been observed; but there are also cases in which, apart from any such anticipated changes as those referred to in connection with the last-mentioned disease, patients have outlived an inherited disease of grave character, after it has been fully developed, as occurred in the following two cases of hereditary hæmorrhage, which may be usefully selected for the purpose of illustrating this subject. In the first of these two cases, which occurred in the practice of Dr. Charles Elam,⁴ we are informed that “a gentleman had severe hæmoptysis at 21, which continued some years. It ceased, and he lived until 70 years of age. His son was similarly affected at the same age, and is living still, near 70. The family of the latter have each one, as they ap-

proached that period of life, been affected in the same way, or one equivalent. These symptoms, which in other persons would have borne the very gravest significance, were seen by the light of the family history to be only transitory and comparatively unimportant phenomena, and were as such explained to the parents, to their great consolation.” In the second case, which occurred in the practice of the late Dr. Babington,⁵ epistaxis was observed to be hereditary for five generations, and it invariably occurred at an early age in such members of the family as suffered from it, of whom the majority were females; and it was noted that all of those females who were liable from a very early period to this affection ceased to suffer from it as soon as they had borne children.

There has been, especially of late years, much attention directed to the greatly increased influence of atavism, which was the subject of my paper at the Worcester meeting of the British Medical Association in August, 1882; and it was moreover in connection with this influence that the late Mr. Darwin remarked “that a being should be born resembling in certain characters an ancestor removed by two, or three, and in some cases by hundreds or even thousands of generations, is assuredly a wonderful fact. In these cases the child is commonly said to inherit such characters directly from its grandparent, or more remote ancestor. But this view is hardly conceivable. If however we suppose that every character is derived exclusively from the father or mother, but that many characters lie latent or dormant, in both parents, during a long succession of generations, the foregoing facts are intelligible.”⁶ In further illustration of this subject a case has been recorded by Darwin,⁷ in which a family peculiarity, affecting the muscles of the scalp, was derived from a common ancestor who could be traced to eight generations back. In his preface to this case he informs us that “some few persons have the power of contracting the superficial muscles of their scalp, and these muscles are in a variable and partially rudimentary condition. M. A. de Candolle,” he adds, “has communicated to me a curious instance of the long continued persistence or inheritance of this power, as well as of its unusual development. He knows a family in which one member, the present head of a family could, when a youth, pitch several heavy books from his head by the movement of the scalp alone; and he won wagers by performing this feat. This family became divided eight generations ago into two branches, so that the head of the above mentioned branch is cousin in the seventh degree to the head of the other branch. This distant cousin resides in another part of France, and on being asked whether he possessed the same faculty, immediately exhibited his power. This case offers a good illustration how persistently an absolutely useless faculty can be transmitted.” Although there is necessarily some doubt with respect to the extent to which members of intermediate generations were or were not affected, yet in the absence of any well-kept family record it may be assumed that the extended limits of atavism in this case were remote and well defined.

The extent of this influence has been well illustrated in a case recorded by Dr. Allan Jamieson⁸ in a paper on Cleft Palate and Incisor Teeth, as “an instance of heredity,” which was read before the Medico-Chirurgical Society of Edinburgh on April 7th, 1880. In this paper Dr. Jamieson states that “among the children and grandchildren of four brothers cleft palate occurs in two, while others present peculiar anomalies in their permanent upper incisor teeth.” In the son (K. M.) of the first brother there was harelip of the right side and fissure of the hard palate extending through the uvula and soft palate, and no trace of a right lateral incisor tooth. In the son (D. M.) of a second brother there was simply an oval aperture in the velum palati. In the son (C. M.) of a third, as well as the son (R. M.) of a fourth brother, the defect was limited to congenital absence of both lateral incisor teeth; and there was the same defect in a grandson (D. M.) of the last-mentioned brother. As not infrequently happens, there was in this, as in some other hereditary cases, a progressive diminution in the amount of con-

² *Lancet*, December 21st, 1880, pp. 1282-3.

³ *Ophthalmic Review*, vol. vii. 1388, pp. 1-6.

⁴ *A Physician's Problems: Natural Heritage*, 1869, p. 28.

⁵ *Lancet*, April 23rd, 1865, pp. 362-3.

⁶ *The Variation of Animals and Plants under Domestication*, 2nd edition, revised. Fourth thousand. Vol. ii, 1875, p. 25.

⁷ *The Descent of Man*, vol. i, 1871, p. 20.

⁸ *Edinburgh Medical Journal*, vol. xxvi, August, 1880, pp. 117-120.

genital deformity. But what is in some respects still more important, there was evidence to show that the morbid inheritance had probably been transmitted, in a more or less latent condition, from an exceptionally remote source. This paper, which seems to have escaped the notice of Mr. Clement Lucas,⁹ when he published his remarks on The Congenital Absence of an Upper Lateral Incisor Tooth as a Forerunner of Harelip and Cleft Palate, and which "he did not think had hitherto been described" may not only be usefully considered in connection with it, but it may, moreover, serve to negative, at least, to some extent, a suggestion made as far back as 1862, by Dr. Horace Dobell,¹⁰ that in his case of malformation of the hands, which was hereditary for five generations, "the defect once lost has apparently been lost for ever"; for it was ascertained in the case recorded by Dr. Jamieson that there was an entry in the parish register, September 16th, 1699, respecting the baptism of an infant child of T. M., *alias* "Gresech," which is the Gaelic expression, or nickname, for a person suffering from harelip; and that this child had belonged to the same clan, and had the same name as the ancestors in the above group in Dr. Jamieson's case.

The great divergence of opinion which has prevailed respecting the tendency of certain hereditary diseases to increase or diminish in succeeding generations may to some extent be due to the fact that atavism occasionally varies in the extent of its influence, as is very remarkably shown in many cases of hæmophilia, of colour blindness, and of other diseases, among which insanity, syphilis, and gout occupy a more or less prominent position; for, with respect to the last two diseases, there is, as Mr. Hutchinson¹¹ has well pointed out, an important distinction to be made between them, for whilst "in syphilis the taint is transitory, and the parent is gradually getting rid of it, in gout it is permanent, and becomes intensified with advancing years." Moreover, as regards the family history of gout, he has very justly remarked that "we may correctly refer not a few cases of this disease to remote inheritance, in which no corroborative history is obtained"; and he has cited a case in which three brothers, who had all lived temperately, became in middle life "the subjects of severe paroxysmal attacks of joint disease, closely resembling true gout, but eventually taking the form of rheumatic arthritis." There was no family history of either affection, but Mr. Hutchinson informs us that he had no hesitation in referring to the case as one of remote inheritance. There is in consequence much need of caution when discussing the extended influence of atavism in these as well as in other cases of hereditary disease; for although the prolonged disappearance of a disease which has been subject to hereditary influence may lead some observers to suspect that it has disappeared for ever, yet it would be very difficult, if not impossible, for us to assign any strict limits to the range of its influence, especially when the disease, as is usually the case, has been transmitted almost, but not altogether, in the latent condition through successive generations of females, as occurred in the following case of deaf-mutism, for which we are indebted to Dr. McCall Anderson.¹² In this case, which presents a good illustration of prolonged latency in transmission, and which, in addition, is useful from its having been associated on one occasion with direct descent, it was observed that in no fewer than seven out of the eight groups of deaf mutes, who all occupied the same level of descent, there was no instance of a deaf mute intervening between the common ancestor and seventeen of his great-great-grandchildren. There was, however, an eighteenth great-great-grandchild of the male sex, who was not only a deaf mute, but who derived the morbid inheritance from a deaf-mute mother.

Among other cases of a corresponding kind which might be cited are those in which more especially both hæmophilia and colour blindness have been traced back to a remote source. This has been well illustrated in some carefully observed cases on record, in which there has been prolonged, but latent, transmission of the disease through the female

line for many successive generations. In like manner there are other diseases of less frequent occurrence in which the extended influence of atavism has also been well displayed; as, for example, in polydipsia or diuresis, in ichthyosis with some other affections of the skin, and also in many forms of disease in which more especially the nervous system has been involved; whilst there are many cases of congenital deformities, affecting chiefly the fingers and toes, in which there has been latent transmission of the defect through many successive generations. In the interesting series of cases, 17, 17a, 18, 18a, 19, and 19a, observed by Dr. Gibson,¹³ of Argyllshire, the fact that all of them occurred in the same county and were observed by the same medical man, and that all of them, moreover, presented essentially the same peculiarity of digital increase, having reference to additional thumbs and additional great toes,¹⁴ shows that the defect was due to hereditary influence, and that the disposition to skip over generations is, in these as in many other cases, a very common event. For in case 18a, in which the individual referred to was the only member of a family of four children who presented the defect, the morbid inheritance was transmitted in the latent condition and in the direct female line from a common ancestor five generations back.

It is not infrequently owing, moreover, to this extended influence of atavism that many cases of diseases and defects, which are habitually liable to occur in certain families, have been observed to be limited to some two, three, or more members of the same generation, and sometimes also of the same sex, without its being possible to trace them to the ancestor by whom they have been introduced. As I have already had occasion to show in some of my previous writings on heredity, there can be little, if any, doubt that such is the real explanation of many of those cases in which, for example, not only brothers, but also male cousins belonging to the same level of descent, suffer from the same morbid peculiarity or disease. But in addition to such cases there are many others in which the transmission has been distinctly associated with not only remote, but also with indirect atavism. In cases, for example, of pseudo-hypertrophic muscular paralysis, with other and closely allied diseases, which occur for the most part in early life, and which may consequently be grouped together as diseases of development, it is not unusual to find that the female conductors of the disease have had collateral relations, usually of the male sex, who have died from it at a comparatively early age, like some of their own male offspring. Dr. Russell,¹⁵ of Birmingham, has recorded a case in which two sons, in a family composed of four sons and five daughters, were thus affected. The mother and the maternal grandmother were both healthy, but two brothers of the mother, and one brother of the maternal grandmother, suffered from the disease. Whilst Dr. Gowers¹⁶ has cited Dr. Heller's well-marked case "in which a son of a woman by one husband and two sons by another were all affected, and the mother's brother was also the subject of the disease." Dr. Gowers¹⁷ has also cited a case, observed by Nicolaysen, in which two half-brothers were thus affected; and a corresponding case of the same kind has been recorded by Dr. W. T. Gairdner.¹⁸ But the disease could not be traced, in either of these two latter cases, to any collateral member of the family affected. But the influence of atavism in these, as in other diseases, has been recognised by many writers on the subject; and especially by Dr. Gowers,¹⁹ who has referred to families in which, as he informs us, "antecedent cases can be traced,

¹³ Cited by Dr. Struthers, the *Edinburgh New Philosophical Journal*, 1863, pp. 93-5.

¹⁴ Although attention has been directed, in some of my previous writings on heredity, to the comparative regularity and order observed in the development of a large number of cases of so-called monstrosities, and especially in those characterised by redundancy of structure, yet it may be useful to direct attention to Mr. Bateson's lately published and important work entitled *Materials for the Study of Variation*, in which this branch of the subject has been very fully illustrated by cases observed, not only in the human subject, but also in many of the lower animals and in plants. In these observations Mr. Bateson has shown that, contrary to the opinions entertained by Darwin, Weismann, and other writers "every fragment (of organic nature), even each of its very aberrations, is replete with order of its own kind and in its due degree" (p. 89).

¹⁵ *Medical Times and Gazette*, May 29th, 1869.

¹⁶ *Pseudo-Hypertrophic Muscular Paralysis*, 1879, p. 24.

¹⁷ *Ibid.*

¹⁸ *BRITISH MEDICAL JOURNAL*, April 29th, 1882, p. 619.

¹⁹ *A Manual of Diseases of the Nervous System*, 2nd Edition, vol. i, 1892 p. 506.

⁹ *BRITISH MEDICAL JOURNAL*, December 3rd, 1887, p. 1212.

¹⁰ A Contribution to the Natural History of Hereditary Transmission, *Med. Chir. Trans.*, vol. xlv, 1863, pp. 25-28.

¹¹ On the Hereditary Transmission of Gout, *Medical Times and Gazette*, May 20th, 1876, pp. 543-5.

¹² *Medical Times and Gazette*, September 5th, 1863 [pp. 247-8].

and these are invariably on the mother's side. The disease is thus transmitted by women who are not themselves its subjects." Even in such an exceptional case as that recorded by Professor Friedreich,²⁰ of Heidelberg, in which two brothers began to be affected with hyperostosis of the entire skeleton, at the respective ages of 18 and 17 years, no previous history of this morbid affection could be obtained. In like manner there are many cases in which, as already mentioned, cousins, either with or without other relations of the same sex, have been affected in the same way and by the same morbid peculiarity or disease. It is now some years since my attention was directed to a case of albinism affecting cousins on the same level of descent, and yet so remotely connected that their common ancestor was five generations back; but no proof could be obtained of its previous occurrence in the family.

In such cases as those in which diseases and defects are subject to the usual influence of atavism, and transmission is in consequence restricted to alternate generations of females, and development to alternate generations of males, it may readily be perceived that its suppression on one or two occasions, in the usual line of descent, would lead to great difficulty in tracing the defect to its more or less remote origin. In such a case, for example, as that of colour blindness, which was lately cited by Sir William Turner²¹ in his Newcastle address on Anthropology, it would have been very difficult to have traced this peculiarity to its source if any such extensive suppression had occurred. For whilst the development of the colour blindness in this case was strictly limited to the males in the first, third, fifth, and seventh generations, its transmission was, with equal strictness, limited to the females in the second, fourth, and sixth generations. Seven females in this sixth generation became mothers, and by them the morbid inheritance was conveyed to eight out of their nine sons; whilst their nine daughters, in common with the females of all the preceding generations referred to in this family, remained free from it. But in addition to the many illustrations which have been published of hereditary cases of disease, which have been to a greater or less extent subject to the usual influence of atavism, there are some in which this influence has been occasionally associated with transmission through the male instead of through the female line of descent; and it has sometimes happened, even in those cases which are habitually subject to the influence of atavism, that this has been altogether superseded by direct transmission and direct development of the disease, with decided limitation by sex. There are, moreover, some carefully recorded cases in which diseases and defects of a strictly male character, and which consequently the male sex could alone develop, have been transmitted, in the latent condition, through the female line of descent, to male offspring, in whom they have reappeared.

As regards the first of these two groups of exceptional cases attention may be directed to a case of colour blindness recorded by Professor Horner,²² of Zurich, in which the genealogy extends to eight generations, and which is alleged to be quite certain up to six generations. In this case, which has been recorded for the purpose of illustrating what has sometimes been referred to as "Horner's law" of the transmission of colour blindness, there were two male cousins in the third generation who are said to have derived their colour blindness from their maternal grandfather. From one of these cousins the colour blindness was conveyed through alternate generations of females to male offspring in the fifth and seventh generations, all of whom were colour blind, whilst it has been assumed that the defect was conveyed from the male cousin in the third generation, through a grand-daughter, who married her colour-blind cousin in the third degree, to their only son who was colour blind. At this stage in the descent the usual sequence was therefore interrupted, to be, however, resumed in the succeeding generation; for their colour-blind son had five daughters, who, in common with all the other females referred to in this case, were free from the defect. These daughters, who represented

the seventh generation, married and had seven sons and eight daughters, of whom five sons were colour blind and two sons and eight daughters were free from the defect. The evidence in this case is certainly favourable to the view that the colour blindness in the male representative of the sixth generation was derived not from his colour-blind father but from his maternal great-grandfather, who was also colour blind. If we assume, as we are certainly justified in doing, that the latter is the correct explanation of the case, it would help to support the principle enunciated in Horner's so-called law—that the hereditary transmission of colour blindness is usually effected through the female line. But, whilst it must be admitted that such has been observed to be the rule even before Horner's time in a very large majority of cases of colour blindness, there are, on the other side, not a few cases in which there is direct transmission from parent to offspring; and such transmission may occur through the direct male or the direct female line, either with or without being associated with any latent intermissions. In the following and early observed case, which was published in the *Philosophical Transactions*,²³ a colour-blind man, who had married a woman whose brother was colour blind, had a family consisting of three children—namely, a son and a daughter who were both colour blind, and a daughter who was free from the defect. The colour-blind son had a son and a daughter also free from the defect, and the colour-blind daughter had two sons who were colour blind and a daughter who was exempt. The case is instructive in connection with that recorded by Horner, as it shows that colour blindness may have been derived from the maternal line of descent instead of having been directly transmitted from a colour-blind father to a colour-blind child. The only essential difference to be noted in these two cases is that the influence of consanguinity was present in the one case but not in the other. Apart from such cases as these, there are others of an equally, if not of a more exceptional, character, in which both the transmission and the development of colour blindness, in common with other hereditary diseases and defects, have been more or less independent of the influence of atavism, as occurred in some cases observed by Cohn,²⁴ Magnus,²⁵ and Sir Henry Holland.²⁶ From among other illustrations which might be cited of the direct transmission of colour blindness from father to son is that related by Mr. Adams Frost,²⁷ in which the father was colour blind and six out of seven sons were similarly affected. There were three daughters in this case who were not colour blind, but one of them had a son who was red blind, thus showing that this exceptional transmission in the direct line to six sons in one family was associated on one occasion with the usual latency of transmission in the female line, whilst on the other side it has to be noted that in M. Cunier's²⁸ remarkable and altogether exceptional case of colour blindness which was cited in my paper of April, 1861, this defect of vision occurred in thirteen individuals of the female sex who belonged to five generations of one family, and that it was developed only in the direct line of descent from mother to daughter without the usual occurrence of any latent intermissions. There were five sons in this case, one of whom belonged to the second, one to the third, and three to the fifth generations, who were all free from the defect, although they were directly descended from colour-blind mothers.

Corresponding observations have been made with reference to many other diseases and defects, as was well shown in some cases recorded by Mr. Christopher Heath,²⁹ Mr. Lingard,³⁰ Mr. Darwin,³¹ and also by other well-known observers. Sir William Broadbent³² has remarked in his Harveian Lectures on Prognosis in Heart Disease that "in no class of cases is it more necessary to inquire into the family history than in diseases of the heart," and only a few years have passed since special attention was directed to a remarkable instance of this family predisposition in the direct male line which was

²³ Vol. lxxviii, 1779, p. p. 611-3.

²⁴ Cited by Dr. B. Joy Jeffries, *Colour Blindness*, 1879, p. 62.

²⁵ *Ibid.*

²⁶ *Op. cit.*, 3rd edition, 1855, pp. 31-2.

²⁷ BRITISH MEDICAL JOURNAL, April 23rd, 1881, p. 645.

²⁸ *Annales d'Oculistique*, 15 Juin, 1839, pp. 417-18.

²⁹ BRITISH MEDICAL JOURNAL, January 11th, 1868, p. 25.

³⁰ *Lancet*, April 19th, 1884, p. 703.

³¹ Inheritance, *Nature*, July 21st, 1881, p. 257.

³² BRITISH MEDICAL JOURNAL, January 19th, 1884, p. 141.

²⁰ *Medical Times and Gazette*, June 13th, 1868, pp. 651-2, from *Virchow's Archiv*, April 8th, B. xlviii, p. 85.

²¹ Report of the Fifty-ninth meeting of the British Association for the Advancement of Science, September, 1889, p. 763.

²² Cited by Dr. B. Joy Jeffries, *Colour Blindness*, 1879, 58.

presented by the well-known Arnold family; for "the father of Dr. Arnold, of Rugby, Dr. Arnold himself, and now two of his sons have all succumbed to chronic heart disease."³³

As regards the second group of cases, which are of a still more exceptional character, it may be observed that structural peculiarities and diseases of distinctively male organs, and which consequently females would be altogether unable to develop, have been transmitted by them in the latent condition to some of their male offspring, in whom they have reappeared. It has, for example, been observed that hydrocele, phimosis, hypospadias, and other morbid affections of distinctively male structures, can be transmitted through the female line of descent to male offspring, through the influence either of direct or of indirect atavism. Sir Henry Holland³⁴ has, for example, recorded a case of hydrocele which came under his own observation, and in which the males of three out of four generations in one family were affected; the omission depending on a female being the third in the series, and in whose son the complaint reappeared. In like manner phimosis has been not infrequently transmitted by women to some of their male offspring, as occurred in a case recorded by Dr. J. W. Ogle,³⁵ in which operations for its relief had been performed on a father and his son, and on the son of a second and also of a third brother of the father. The three brothers in this case had two sisters, one of whom transmitted it to two sons, and the other sister to one son. And Mr. Prescott Hewett³⁶ has mentioned that he has often had occasion to operate for this malformation (phimosis) in a family in which it "existed in the father and several of his sons and their children, as also in several sons of some of the married sisters;" but he has added that "the defect was worse in the sons of the brothers than of the daughters." As regards hypospadias, which has been and is often met with as an hereditary defect, Meckel³⁷ has recorded a case in which a woman, born of a family which presented many examples of hypospadias, gave birth to two boys affected with this congenital malformation. Heuremann³⁸ has in like manner recorded the case of a family in which the females had for several generations given birth to males who were all affected with hypospadias.

The following example of the heredity of this condition has been lately published by Dr. E. Lesser,³⁹ in which a hypospadian transmitted the defect through a daughter to four hypospadiac grandsons; and through a son, who was unaffected, to another group of four hypospadiac grandsons. Whilst a sister of their hypospadiac grandfather transmitted the defect through her son, who was unaffected, to three hypospadiac grandsons, who must have derived their inheritance from a still more remote source. Another and a more remarkable illustration of the transmission of this defect, through the female line of descent, has been observed and recorded by Mr. Lingard,⁴⁰ in which a hypospadian, whose father and paternal grandfather were similarly malformed, married and had three hypospadiac sons, from whom descended, in the direct male line, seven hypospadiac grandsons and two hypospadiac great-grandsons, and one great-grandson not malformed. The widow of the man from whom these three generations of hypospadians were descended married again, after an interval of eighteen months; and in this instance the second husband was not only free from the defect, but there was no history of it in his family. By this second marriage she had four hypospadiac sons and four hypospadiac grandsons; whilst there were seven grandsons and three great-grandsons who were not malformed. Mr. Lingard informs us that "it has been impossible to trace the history through the females of these six generations; but," he adds, "it may fairly be presumed that one or more of them transmitted the hereditary peculiarity to some of their male offspring." The case, however, is chiefly interesting as an

illustration of the curious and important influence of a previous marriage on the succeeding offspring, through the agency of what has been termed "indirect atavism," and to which special attention was directed in one of my previous papers on heredity in July, 1863. It may, moreover, help to overcome some of the objections which have been urged against the influence of a previous marriage on the subsequent offspring by a second, or even by a third husband; for with reference to this subject it has lately been suggested by Dr. Douglas Lithgow⁴¹ that "although facts are forthcoming as to such an influence affecting the lower and even the higher animals, yet so far as man is concerned the instances of this are very few, if they occur at all."

From these and from other cases which have been or which may be cited, it is evident that although there is a very great and sometimes even a preponderating influence of the male sex on development, yet as regards health as well as disease, transmission is more commonly and more readily effected through the female rather than the male line of descent, and this preference for the one sex rather than the other has been popularly recognised from a comparatively early date, as is well shown by the following use of the term "mother wit" in Spenser's satirical fable entitled *Mother Hubbard's Tale of the Ape and Fox*, which was published somewhat more than three centuries ago (1591):

But the false Fox most kindly plaid his part;
For whatsoever mother-wit or arte
Could worke, he put in prooffe.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

EXTREME CIRRHOSIS OF LIVER IN A BOY.

J. D., born in August, 1881, first suffered from troublesome diarrhoea at Christmas, 1893, followed by jaundice in March, 1894, by great ascites, hæmatemesis and melæna in May, 1895, and death in February, 1896. During the sixteen months prior to his death he suffered constantly from diarrhoea and jaundice; the skin and conjunctivæ being always obviously yellow, though varying in degree from time to time; the urine usually loaded with urates and bile pigment; and the motions varying in colour between pale drab and putty, though sometimes white, and occasionally natural. He frequently suffered also from slight gastric catarrh. On three or four different occasions he had marked ascites, so that his girth was increased by 3 inches and more; fluctuation was quite distinct, and the navel protruded to the size of a grape, all of which symptoms nearly or quite disappeared each time after a few weeks' rest in bed. The gums were usually swollen and inclined to bleed; and on one occasion (nine months before death) there was hæmatemesis to the extent of over a quart, with melæna to a less alarming degree, and at about the same time both anasarca of and petechial hæmorrhages on the lower limbs. There was no albuminuria, no heart or lung trouble, and no pruritus throughout. These symptoms, with marked reduction of liver dulness and retraction of the liver out of reach, left little room for doubt about the diagnosis. No medicinal treatment had any perceptible effect, the chief administrations being full doses of corrosive sublimate, with and without full doses of iodide of potassium, extending over some months, and a variety of tonics. The hygienic conditions were throughout quite satisfactory, and the diet nutritious and non-stimulating.

At the necropsy, made a few hours after death, two or three pints of bile-stained ascitic fluid were found; the liver was not more than one-third of its natural size, profusely hobnailed, the hobnails being mostly pea-sized, a few bean-sized; the left lobe was very small; the gall bladder small, collapsed, and empty; the liver was very tough, and on section seemed mostly made up of yellowish pea-sized islands of fibrous-looking tissue. The spleen was nearly twice its natural size, soft and pulpy. The peritoneum was healthy, and through it the cæcum and colon were seen to be much inflamed, while the small intestine remained apparently healthy. The kidneys seemed normal.

⁴¹ *Heredity: a Study, with Special Reference to Disease*, 1889, p. 28.

³³ BRITISH MEDICAL JOURNAL, April 21st, 1888, p. 867.

³⁴ *Op. cit.*, p. 31.

³⁵ On Hereditary Transmission of Structural Peculiarities, *Brit. and For. Med. Chir. Review*, vol. xlix, 1872, p. 510, note.

³⁶ *Ibid.*

³⁷ *Handbuch der pathologischen Anatomie*, tom. i, p. 20.

³⁸ Cited by Sir J. Y. Simpson, *Cyclop. Anat. and Phys.*, Art. Hermaphrodite, p. 375.

³⁹ On Hereditary Hypospadias, *London Medical Record*, vol. ii, 1889, p. 519; from *Virchow's Archiv*, Band cxvi, Heft 3, S. 537.

⁴⁰ The Hereditary Transmission of Hypospadias and its Transmission by Indirect Atavism, *Lancet*, April 19th, 1884, p. 703.