muscles in these parts into action. When, for example, the skin of the poisoned leg was pinched, the irritation was transmitted up the sensory nerves, in the direction of the arrows, towards the spinal cord, and reflected by it down the motor nerves of the other limb to the muscles both above and below the knee. But it was only below the knee, in the part protected from the poison, that they responded to the stimulus. As he had previously determined that the contractility of the muscles was not affected by the poison, this experiment seemed to prove that the action of the poison was limited to the peripheral ends of the motor nerves. For the sensory nerves, the spinal cord, and the trunks of the motor nerves above the knee had all been exposed to the action of the poison, and yet they still continued to do their work. Thus, it appears that the fault must lie with the terminations of the motor nerves within the muscles, and with them only.

It often happens that the discovery of some prominent fact throws others into the shade for a while, and it is only after some time that its importance, at first overlooked, begins to be recognised. Thus it was with curare. Its action seemed at first to have been so strictly limited to the motor nerves, by Bernard's experiments, that any slight indication to the contrary would have been passed over without attention. But, after some time, Van Bezold noticed that reflex action ceased before the nerves had completely lost their power over the muscles; and Schiff observed that, when the circulation in a frog was arrested at the knee, a pinch below the ligatured point caused movement, while it had no effect on the poisoned skin of the thigh. Bezold's observation showed that the spinal cord was affected by the poison, and Schiff's, which I have myself repeated and confirmed, shows that the sensory nerves have their conducting power destroyed by curare, but that they are less affected, and after a longer interval, than the motor nerves.

Magendie noticed, in his experiment with the upas, that the symptoms not only came on more slowly, but were less violent, when the poison was introduced into the intestines, than when applied to a wound, and that when they might be controlled by arresting the return of blood from the point of introduction. In Bernard's experiments with curare, he observed that, although invariably poisonous when introduced into a wound or injected directly into the circulation, it apparently did not act at all when taken into the stomach, unless the dose was very large. At first, Bernard imagined that this might be due to the destruction of the poison by the juices of the stomach. Mixing it, however, with gastric juice, he found that its activity remained unimpaired. Another reason then suggested itself, viz., that while absorption was taking place from the stomach, excretion of the poison might occur by the kidneys. If these were to go on *pari passu*, the amount of poison present in the blood at one time would be too small to produce its characteristic effects. This hypothesis he at once tested by extirpating the kidneys of a frog, and thus entirely checking excretion through those organs. When curare was then administered by the stomach, poisoning took place more slowly, but quite as surely, as when it was applied to an open wound. The same result was arrived at independently by Ludimar Hermann, who was unaware of Bernard's researches. In his experiments, he used warm-blooded animals, and tied the renal artery, instead of extirpating the kidneys. These researches enable us to understand how it is that drugs exert a more rapid action when introduced into the empty stomach than when given along with a full meal; why a dose of morphia, injected under the skin, should not only act more quickly, but more powerfully, than the same quantity given by the mouth or by rectum.

[To be continued.]

PADDINGTON.—Dr. James Stevenson commences his report by reminding the vestry that he only took office at Midsummer 1874, and stating that he has adopted the statistical forms of the Society of Medical Officers of Health, which is commendable. He estimates the population at 105,221, and the inhabited houses at 12,746. There were 2,927 births and 1,992 deaths, which would give a birth-rate of 27.8 and a death-rate of 17.6 per 1,000 population, or, including the deaths in hospitals, 18.9; whilst there were only 2.7 deaths from zymotic diseases per 1,000 population. The deaths of children under one year were 14.1 in each 100 births; the deaths of children under five years, 38.4 per cent. of total deaths. These figures certainly indicate a satisfactory condition of the public health. Dr. Stevenson obtained some milk from cows infected with foot-and-mouth disease, and submitted it to Dr. Sanderson, Mr. Wanklyn, and Professor Anderson, neither of whom could detect any difference, either chemically or microscopically, between it and ordinary milk. As, however, it readily took on fermentative action, they came to the conclusion, and especially Mr. Wanklyn, that it was unfit for food.

THE CROONIAN LECTURES

ON

THE DIFFERENCE BETWEEN THE SEXES IN REGARD TO THE ASPECT AND TREATMENT OF DISEASE.

Delivered at the Royal College of Physicians of London.

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LECTURE I.

IN endeavouring to respond to the kind permission with which you have favoured me, to give this year's Croonian Lectures, I thought it might be of some advantage if I brought together the principal points in respect of which the human male and female differed; because, although writers on pathology have noticed very fully the difference between the sexes in the several diseases of which they have treated, yet I have not been able to find any separate monograph of these variations. As many, if not most, of these are well known to you all, I must crave your indulgence if I seem to introduce topics by no means new.

Since I ventured to select this subject, I feel more than ever diffident, because one of your Fellows and late Censor has said, in a recent address, that he almost envied me this opportunity. One difficulty has specially presented itself to me, namely, the limitation of my remarks to disease; because the physiological differences are so interwoven, as indeed it is in all clinical pathology, with disease. But specially this is shown in women, who are so prone to functional disturbances, because the border between the maximum of natural function and disease is ill-defined. To enter into the physiological aspect would be to lead me too far, and would introduce subjects which scarcely come under the consideration of so august a body of gentlemen, except in their social functions. I will, therefore, endeavour to keep as closely as possible to the clinical aspect of the variations of disease.

The divergencies, although rather of degree than of essence, present some very salient appearances, valuable for reflection; for the obscure condition of the one may receive light by the more prominent state of the other sex. Thus, as Dr. Barnes has recently pointed out, the condition of pregnancy affords a series of ready-made experiments, throwing light both on physiology and pathology. And it must be borne in mind that woman differs from man in having given to her an organ intimately connected with the sympathetic system, almost entirely supplied by ganglionic nerves, subject to great changes of form, size, and structure; capable of being seen, handled, and treated with an ease denied to any similar organ, at least in extent. Only in rare cases has the stomach been so immediately under examination; the bladder rather more frequently so; but then there is in it but little variation of form and growth. It is, then, by taking advantage of the opportunity of observing the effect of the greater changes in the uterus, and its various sympathies, that we gain some insight into the minor changes in other parts supplied in like manner.

It is not my intention to discuss the differences of sexual organs, excepting so far as their form, shape, and actions tend to disease more in one than in another. But, first of all, it will be well to consider some points connected with the differentiation of the sexes, which, as we all know, occur very early—from the third to the fifth day of fetal life. It has been the habit of many to consider that the two sexes remain very much the same in the condition of the general body and mind, till near the change of puberty; but a little consideration of various facts will show that the difference, although not so manifest, takes place *ab initio*, and that, whatever the first impetus may be which produces that change, it gradually progresses till it culminates in the mature man and woman. It would be difficult to say whether the man or the woman may be considered as most typical of the human race. The general opinion of mankind has been that the man is the standard; but Darwin, as far as I gather from his remarks, looks upon the man as having diverged from and advanced upon the woman. Referring to the secondary sexual characters, he says (*Origin of Man*, vol. ii, page 321): "This fact indicates that, so far as these (size and height), it is the male which is chiefly modified, since the races diverged from their common and primeval source." However, in regard to hairiness, he considers it is the woman that has diverged from the more hairy progenitor. Again, with regard to mental powers, he considers the

woman, as a rule, inferior; the result of the transmission "to the male at mature life of those qualities required, in his male ancestors, in the struggle for life and keen competition with other males". And again: "It is generally admitted that, with women, the powers of intuition, of rapid perception, and perhaps imitation, are more strongly marked than in man; but at least these faculties are characteristic of the lower races, and therefore of a past and lower state of civilisation."

We know nothing of the initial force which causes the differentiation of the sexes; but we can watch the progress of development almost from the first. I do not wish to detain you long on the development of the sexual differences in the fœtus; but some interesting points have recently been added by Waldeyer to those already made out. It is this: that in both sexes, about the second or third day, there is a "sexual eminence", extending the whole length of the Wolffian body, covered by cylindrical cells, some of which are conspicuous on account of their size. In the male, these remain for a time, and shortly disappear; while in the female, on the contrary, they remain, enlarge, and gradually the larger cells apparently sink into the interior, by the exuberant growth of the underlying mesoblast rising up between them. These depressions are seen with the large-sized epithelium-cells at the bottom, while the sides are lined by the cylindrical epithelium. After a time, the walls of the depression close in, and thus is formed the Graafian follicle; the large cells being the future ova, and hence called the primordial ovum. Thus, it will be seen that both sexes begin with ovaries. Now, the testis springs from a different spot, though not far from the ovary. Hence, though we have been accustomed to consider the ovary and testis to be homologous, they cannot be, supposing the observations just mentioned are correct.

Both the male and female have been long known to be supplied by two filaments called ducts of Müller, one on each side, which in the male dwindle and become useless, but in the female remain, forming the oviduct or Fallopian tube; and, uniting below, become fused into a single tube—the future uterus. It is curious to observe that in birds, where the left ovary generally disappears, the corresponding Müller's duct also dwindles.

Thus, we have in both sexes ovaries and their ducts; these in the male becoming obliterated, while the testis is added at a slightly later period, joining and making use of the Wolffian body and its duct; while, on the contrary, the Wolffian body becomes effete in the female. Thus, we seem to have an explanation sufficiently satisfactory for those curious anomalies where, in the same animal, a testis is found on one side and an ovary on the other.

Bureau, in his work *Maladies des Ovaires*, mentions the names of Hunter, Rudolph, Verdier, and others, as having met with instances.

A point of interest arises here: how far the general differences in the sexes—I mean the secondary sexual characters—are dependent on these changes in the sexual organs; or how far they are only part of the mutation, the common result of a primary force extending to the whole body. Is woman (to quote Van Helmont) a woman because of the womb, or does the uterus exist because belonging to the woman? And before this can be answered, we require solution to another question, very difficult to answer: How are the tissues first formed, or what relation do the nervous structures bear to the parts they supply?

Perhaps the following remarks may help us. Recent microscopical investigations have shown that the nerves enter more intimately into the tissues than had before been supposed; that the ultimate fibres, for instance, of the nerves supplying the muscles enter a branch into each fibre; that the epithelium of the mucous membranes, instead of being an inert effete layer of cells without sensation, is closely associated with and pervaded by expanded terminations of the nerves, in such a manner that it is difficult to separate them. For instance, Longet, in his *Traité de Physiologie*, 1869, tom. iii, page 893, says to this effect: "The nerves are not produced as prolongations from the cord into the various tissues, nor do they extend from the various tissues to the cord; but they are developed in each tissue by a separation of histological elements, from the cells of which the parts are originally constituted, which at first appear to be identical in their morphological characters." This being the case, it leads one to ask the question: whether we should not consider the elementary tissues to which the nerves go rather the exponents of the qualities of the nerves, than look upon the nerves as simply conductors from and to the tissues.

This idea will not seem so very improbable when we consider that, in the early forms of animal life, the nervous element and sarcoid are intimately mixed; and that, as we ascend the scale, the nerve-cords keep up an intimate connection between them, though separate. And thus, may we not look upon the genital organs, as well as the other parts of the body, as intimately associated with the nervous system, so intimately that we may look upon the one as the counterpart of the other? If this be so, then any change which takes place in one will to

an equal degree influence the other; the nervous elements and the organs are correlated. Therefore, we may argue that it is neither from the ovaries, uterus, nor testes alone, nor from the nervous system alone, that the influence springs which makes the difference between man and woman; but rather this distinction is a consequence of an influence acting before the appearance of either. In support of this view, we may point to those cases of total absence of ovaries, uterus, and vagina, where the rest of the body and habit is essentially feminine in character.

There is, of course, no doubt that the sexual organs react in their influence on the nervous centres, and *vice versa*; and also, this impression extends to those parts in sympathy with them, and thus, in due course, the whole economy is swayed. Let us now trace the effects of this differentiation through the various stages of life, so far as concerns the relative liability of each sex to disease.

These effects are shown in many ways, even during intra-uterine existence, exercising important influence on the welfare of the fœtus.

Now, as to the relative frequency of errors of development, there is a marked difference in the sexes.

With regard to the heart, Geoffroy St. Hilaire, in his work *Anomalies de l'Organisation*, endorses the fact pointed out by Schüller, Nasse, and Meckel, that cyanosis is much more frequent in the male. Most of these cases result from deficiencies of development, either before or immediately after birth. And this fact coincides very much with the relative frequency of occurrence of congenital deformities, resulting from defect of development in other parts. This is well shown in the following table, for which I am indebted to my colleague Mr. Bryant, being taken from his note-book.

	No. of Cases	Male.	Female.	
1. Spina Bifida	30	13	17	
2. Ectopia Vesicæ	20	14	2	(doubtful)
3. Epi-padias, or Hypospadias	26	22	2	2 (?)
4. Hare-lip	64	44	20	
5. Hare-lip, with Cleft Palate*	21	17	4	
6. Malformation of Bowel	8	2	6	
7. Malformation of Extremities (not including Talipes)	46	27	19	
8. Malformed Ears	4	3	1	

It is curious to note that, whilst in deficiencies of the anterior median line males far exceed, in deficiencies in the posterior females rather preponderate. Altogether, it appears that the male is peculiarly exposed to deficiencies of development; although one would have been prepared for the opposite result, if we consider the male a development upward from the female. I mean that one would have expected a more vigorous action in the male than in the female, more at least than enough to carry it further than the female in actions common to both; though one might have not been surprised if there had been any arrest in the male genitals, as in some forms of hermaphrodites.

In regard to the general group of congenital and developmental diseases of children, we find, in the Statistical Report of Dr. Farr, the deaths, for instance, in 1866, of 7,027 males and 5,311 females up to one year old; and up to the end of the second year, 1,067 males and 941 females. In 1868, the deaths under one year were 6,797 males and 5,395 females; whilst in the second year, there were 994 males and 910 females; thus showing a marked difference between the male and female.

There is also a greater tendency to cerebro-spinal disease in the male before birth. M. Duval shows that, out of 145 cases of congenital talipes, 97 were males and 48 females.

How far the difference in the rapidity of circulation, which has been pointed out by Frankenhäuser, has to do with the variation, it is impossible to say; but there seems no doubt that the male pulse beats, on the average, at 124 per minute, while in the female it is 144, according to Frankenhäuser, though stated at less by other observers. This fact has been put forth as a means of diagnosing the sex before birth.

This difference is less noticeable at birth, and the rapidity of the pulse in the two sexes remains nearly the same till the seventh year, when again gradually the pulsations of the female increase in frequency, till in adult life they exceed the male by from 6 to 14 beats.

Let us now pass on to the consideration of circumstances which remarkably influence the existence of the fœtus at birth. It is a well-ascertained fact, universally sustained and very regularly so, that more males are born than females, in the proportion of 105.8 males to 100 females. But this excess of life on the part of males is reduced in the

* Almost all the cases of double hare-lip are met with in males.

following manner. The male infant is well-known to be larger than the female at full term; so that, on the average, the male is ten ounces heavier than the female, while the length is half-an-inch greater. This, perhaps, would not be of so great importance had not the cranium of the male been more completely ossified than that of the female; so that this, coupled with an increase of circumference, on an average half-an-inch, renders its delivery through a narrow pelvis more difficult than the female's, because of its being less capable of being moulded to a shape easy for passing. In consequence of this, the birth of a male child is more difficult and dangerous to the mother. Sir James Simpson considered the difference in the sexes of great importance; for he calculated that, between the years 1834 and 1837, in Great Britain, from 46 to 47 per 1,000 male infants lost their lives at birth, owing to the excess of size; and three to four thousand mothers also, from the same cause. This may be overrated, because the calculations were made from the statistics of lying-in hospitals, where a considerable number of difficult cases were admitted in labour for operation; and thus the foetal death-rate would be increased above the general average. Still, doubtless, after labour, although the child may be born alive, the effects of the difficulty are felt for some time, and many deaths take place in consequence, in a diminishing ratio, for one, two, or even three or four years.

Dr. Langdon Down has recently, in a paper read before the Obstetrical Society, shown that, according to his notes, there is a marked preponderance in the number of male over female idiots, in the proportion of 2.1 to .9; or rather more than twice as many. He has also noticed that infantile convulsions have occurred among males who have become idiots much more frequently than among females. Dr. Langdon Down attributes these calamities to the increased length and difficulty at the birth of the male by reason of its enlarged cranium, whereby pressure on the circulation produces a kind of asphyxia. He found that first-born children were more frequently afflicted than others; and, as prolonged and difficult labour generally attended the birth of a first child, he considered it probably the result of the pressure.

Exceedingly interesting tables are given by Dr. Collins, of the Rotunda Lying-in Hospital, Dublin, as to the relative death-rate of the sexes shortly after delivery. I will not detain you on this point, but I cannot refrain from quoting the first three lines, which show that, within half-an-hour after birth, 16 males died against 1 female; within the first hour, 19 males died against 2 females; within the first six hours, 29 males died against 7 females. There can be no doubt, therefore, that the male runs a greater risk in its nativity than the female; and this risk is caused by the more protracted and laborious labour which its larger and harder head necessitates. The more firm ossification of the male head, though doubtless a protection to the brain, is more obstructive to delivery than that of the female; and this tells upon the male, more especially in cases where the mother's pelvis is somewhat reduced in size, either generally or partially.

From these considerations, therefore, it would appear that the death of the male in birth and shortly afterwards is not so much the result of direct pressure on the brain, but rather the ill result is owing to obstruction to the circulation in the uterus, placenta, and funis, causing effusion of blood in various organs, and provoking inspiratory movements, which cause an invasion of the larynx and bronchi by the fluids in the passages; in other words, chronic or sudden asphyxia. This being the case, a further deduction is capable of being made; namely, that the longer the labour, if the pains are forcible, the greater the risk to the child, *ceteris paribus*; and, indeed, the truth of this inference is clearly supported by examination of the facts, which need not here be detailed, as they can be found in all modern works on obstetrics. The full recognition of this leads one at once to make a practical rule, viz., that, if the head of the child in labour be detained in the parturient canal after this is fairly opened and the uterus in full action, then the abstraction of the child by art is the more likely to save its life, the earlier assistance is given; and not only to save its life at the time, but to save it from the evils which continue their force after birth. No doubt it is difficult precisely to lay down rules as to the time when assistance should be given; this is not the place to discuss this question; opinions vary, but all modern practitioners, I think, accept the rule given above as a guide in practice, which, indeed, has redeemed modern obstetrics from the old opprobrium of "meddlesome midwifery".

For the increased risks to the mother by exhaustion, internal bruising, by inertia of the uterus tending to floodings, and septicæmia after labour, I must refer you to the treatise of Sir James Simpson quoted above, entitled "Sex of Child as a Cause of Difficulty and Danger in Human Parturition", in his *Selected Obstetric Works*, 1871.

The influence which the additional difficulty and length of labour produce on the child, and for how long it was felt by it, it is impossible to gauge exactly, because we cannot deny that the male brain

from earliest age is more prone to active disease than the female. The human male, from earliest history, has had to employ its mental faculties to a much greater degree than the female; and hence, doubtless, that tendency (so well pointed out by Darwin) for each sex to transmit its acquired peculiarities has had an influence in this matter; and this activity, we shall admit, tends to disease and disturbance in a higher degree than if a less activity were present.

Before leaving this subject, I mean the effects of pressure at birth, I must recall to your recollection a paper by Dr. Little, in which he has discussed how far the asphyxia consequent on difficult labour had to do with the production of mental impairment, hemiplegia, and spastic rigidity observed in children in their early years. Of course, at so late a period of life, with so many causes of disturbance existing, notably dentition and imperfect nutrition, it would be difficult to say how far Dr. Little's opinion is correct, wholly or in part.

But there is one more circumstance which cannot be overlooked when we seek for explanation why the severer affections of the brain are more frequent and dangerous in the male child than in the female, and this particularly up to nearly the end of the second year. I have mentioned already that at birth the skull of the male head is in a more advanced state of ossification than the female. This is so noticeable that, before the child is born, one is able to pronounce rightly in eight or even nine out of ten cases whether it be male or female.

The protection the more solid skull offers to the male brain during birth exempts this latter from the disturbance and sometimes injury to which the brain of the female is exposed in consequence of the mobility of the skull; though, as before shown, it may increase its risks by asphyxia.

These observations tend rather to oppose the opinion of some, who put against the forceps-pressure all those evils which afflict the brain of the child; whereas it is generally in the more ossified skull, and therefore less yielding, that we employ them, consequently more in males than in females.

But, when irritation and hyperæmia of the encephalon occur after birth, as specially during dentition, this solidity tends to increase the effects of pressure from within as compared with the more yielding and mobile skull of the female; for probably all have noticed that where the sutures and fontanelles are late in closing, the effects of dentition are not so severe, whether in male or female. At the same time, we must not forget that to which I have just now alluded; the easily moulded skull of the female gives some risk to its owner, in that the brain is subjected to greater pressure, and sometimes severe disturbance to its shape; while, the sutures being more capable of overlapping, the edges are apt to penetrate the longitudinal sinus, and thus cause effusion of blood, or internal cephalhæmatoma, as I have occasionally noticed.

[To be continued.]

A CASE OF EXOPHTHALMIC GOÏTRE, WITH NEW PHENOMENA.*

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CASES of exophthalmic goitre, although always of great interest, both on account of the remarkable phenomena which attend them and the obscurity which still rests on their pathology, are not so seldom seen as to merit any extraordinary attention from a Society like this. Nor should I have solicited the attention of the members of the Clinical Society to the case I am about to show them, were it not that, besides the ordinary phenomena commonly noticed in cases of a like kind, certain others have been developed in the course of this one, which, I believe, have not hitherto been observed, or, at any rate, placed on record. And I take it to be the duty of every clinical observer, whenever he meets with unrecorded phenomena, in cases the precise pathology of which still remains doubtful, to take the earliest opportunity of bringing them to the notice of such a Society as this, where they can be examined and discussed, and their precise relation to the pathological state which has given rise to them, can be either suggested or determined.

The patient in question, who is thirty-five years of age, married, and with four children, first came under my observation on the 6th of May last, when she complained chiefly of palpitation and pain in the left side; she had had a cough for six weeks, and suffered also from shortness of breath; she was losing flesh, had no appetite, vomited frequently, and had a tendency to diarrhoea after every meal, or if she

* Read before the Clinical Society of London, March 9th, 1877.