The Goulstonian Lectures

ON

THE INFLUENCE OF PREGNANCY UPON CERTAIN MEDICAL DISEASES, AND OF CERTAIN MEDICAL DISEASES UPON PREGNANCY.

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LECTURE I.

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INTRODUCTION.

MR. PRESIDENT AND GENTLEMEN,—The title of these lectures perhaps requires a few words of explanation in case it might be at all misleading. The subjects that it is proposed to discuss will not be dealt with from an obstetrical point of view, but purely from their medical or pathological aspect. The gynaecologist and the obstetrician must naturally be interested in the medical diseases which may arise in a pregnant woman, and in some cases the treatment in these circumstances may be gynaecological or obstetrical rather than medical. I have not the ability to deal with gynaecological or obstetrical treatment and shall therefore say nothing about it. On the other hand, the fact that a medical disease arises, or is already present, when a patient has become pregnant by no means necessarily implies that the immediate treatment of the patient should be carried out from a gynaecological or obstetrical standpoint. It is true that there are conditions under which the aid of the obstetric physician may be required to terminate the pregnancy artificially, and it is also true that similar aid will be essential when the pregnancy reaches its natural term, or earlier if any accidental termination to it should arise. There are, however, many conditions in which the pregnancy may be, as it were, an accidental concomitant or complication of the medical disease; there are other conditions in which pregnancy is actually the cause of the medical disease, and many of these cases are of direct interest to the physician.

If in a given case it should be decided that the pregnancy may be allowed to run its natural course, the responsibility for the patient's health would rest with the physician until such time as the pregnancy either reached its term or ceased to be itself normal. It is, therefore, essential that the physician should be fully acquainted with the probable effects both of the pregnancy upon the medical disease from which the patient may be suffering and also of the medical disease upon the pregnancy. Two examples may perhaps assist this explanation. Suppose, for instance, that a pregnant woman contracts typhoid fever. Three questions at once arise—namely, Is the fact that this patient is pregnant likely to make the typhoid fever more severe than it otherwise would be? Is the patient's pregnancy likely to terminate abnormally on account of the typhoid fever? Ought the treatment of this patient to be different in any way from that of other persons suffering from typhoid fever? It is clear that, so far at least as the typhoid fever is concerned, the treatment should be carried out by those most familiar with typhoid fever if it can be shown that the treatment of such cases ought to be upon the same lines as that of non-pregnant persons suffering from the disease. So far as the typhoid fever is concerned the pregnancy may be an accidental concomitant, but it is important to the physician to know what is likely to be the result of the combination.

As my second example, may I take that of a patient who presents herself with that peculiar skin eruption, herpes gestationis? If she were not pregnant she would not have the eruption; but having the eruption the immediate treatment of the patient for her skin trouble is probably best carried out by one who is most familiar with skin diseases, provided it is known that the pregnancy is not likely to run an abnormal course.

It is only from the medical point of view that I am in a No. 4418.

position to discuss the mutual effects of pregnancy and medical diseases; and seeing that there are few medical diseases that cannot either themselves arise during pregnancy or else permit of pregnancy occurring when they are already in existence, it is clear that the whole field cannot be covered in three lectures. I am obliged therefore to restrict the discussion to a few affections which appear to possess particular interest.

In the first place, there are certain medical diseases for which pregnancy appears to be itself directly responsible. One of the most definite of these, comparatively rare no doubt, yet full of interest from a pathological point of view, is

HERPES GESTATIONIS.

This disease is apparently related to pemphigus, to hydroa, to erythema bullosum, and to dermatitis herpetiformis or Dühring's disease. The eruption is variable in the extent to which erythematous patches, pinkish-red papules, and wheals not unlike those of urticaria are present, but to whatever degree these may coexist the distinctive lesion is vesicular or bullous. Sometimes the blebs are comparatively large and widely separated and they are preceded by more or less erythema, in which case the eruption is very similar to that of erythema bullosum. More rarely the bullæ occur before any erythema is obvious and pemphigus is simulated. In other cases again the vesicles are smaller and they may be arranged in groups upon an inflamed base like those of herpes zoster—the herpetiform variety. The cases that I have seen have exhibited a mixed condition, the majority of the vesicles being only moderate in size, with here and there amongst them a few that were large enough to be called bullæ; the smaller vesicles have shown a slight tendency to be grouped together as in herpes, but it is not often that they are confluent or that a single group contains as many vesicles crowded together as is the case in well-marked herpes zoster. The vesicles, whether large or small, have been preceded by an itching erythema which has in the beginning been smooth but which has rapidly become first papular and then vesicular. The eruption itself has been more like that of dermatitis herpetiformis than anything else, the chief clinical distinction between the two being solely the direct relationship of herpes gestationis to pregnancy.

*An illustrative case.*¹—The following is an illustrative case. The patient, 41 years of age, was under the care of Sir Cooper Perry in Guy's Hospital, and was sufficiently ill to require treatment in bed for over a month. Her history was briefly this: She was the only member of her family troubled with the complaint. She had been perfectly well up to, and for some time after, her marriage, when she was 23 years old. She had had seven living children and four miscarriages. The first miscarriage occurred after she had had three living children and it was then that she suffered from her skin trouble for the first time. Since then, though quite free from it between whiles, she had had the eruption with each successive pregnancy, the itching erythema, vesicles, and bullæ recurring constantly upon her hands and arms and sometimes upon her trunk, legs, and feet. She was three months' pregnant at the time of her admission to the hospital; one month previously her ninth attack of herpes gestationis began with pains and irritation on the hands and forearms, rapidly followed by the eruption of discrete water-blisters of moderate size which, owing to scratching, broke down and discharged clear fluid. Each bleb dried up and healed in about a week, leaving a reddish mark which was slow to fade, whilst fresh vesicles kept on appearing daily in the neighbourhood. There was no pyrexia and no marked constitutional disturbance beyond what could be attributed to broken sleep, the result of irritation in the affected areas of skin. The arms and hands had been involved for three weeks before vesicles developed elsewhere, and then without apparent cause a precisely similar eruption came out upon the face and ears, spreading thence to the chest, abdomen, buttocks, lower limbs, and feet. The number of blebs upon the trunk was never so great as that upon the limbs. Flexor and extensor surfaces were equally involved and the parts were not only irritable but also painful. The pains were doubtless due, in part at least, to the sore places being made worse by scratching. Left to themselves the blebs healed without breach of surface and without pyoderma. Some of the vesicles that had been interfered with either bled or became pustular; the latter change

¹ See also C. A. Douglas Bryan, THE LANCET, June 4th, 1904, p. 1570, and numerous papers in the journals of dermatology.

was always consequent upon inoculation by scratching. There was no involvement of mucous membranes, though there are doubtless cases in which the buccal mucosa and the colon may be affected, as has been observed in some instances of erythema bullosum. Under treatment by the yellow oxide of mercury ointment externally and by Fowler's solution of arsenic internally, together with rest in bed, light diet, and laxatives, there was some abatement in the skin trouble after about three weeks, but even during the continuance of the treatment a severe relapse ensued whilst the patient was still in the hospital. The trouble, waxing and waning in this way, persisted until the child was born, living, at term, and then, as on eight former occasions, the herpes gestationis rapidly got well by itself.

This case is fairly typical, and there are but few points to add before passing on to consider the pathology of the condition. It is not only possible for a patient like the above to have no trouble during the first pregnancies and then to develop the disease in later ones, but it is also possible that having had the skin disease in one pregnancy she may escape it at the next and yet develop it again in a later one. The time of onset is usually of the accelerating type, that is to say, in successive pregnancies it is likely that the date at which the herpes gestationis will reappear is a little earlier each time. It is, moreover, probable that the attacks will tend to become severer rather than the reverse. A few cases exhibit severe constitutional disturbance, with pyrexia and loss of appetite. It is, moreover, a curious fact that whereas the majority of the patients develop the trouble during pregnancy and lose it during the puerperium or soon after, it occasionally happens, as in another case under the care of Sir Cooper Perry, that the eruption first appears after labour, lasts a variable number of weeks or months, and then goes away spontaneously not to reappear until just after another child has been born.²

Pigmentation.—Another point that may be of interest perhaps is the increased pigmentation of the skin that is apt to be left after each attack. The pigmentation may be generalised all over the body in much the same way as it is in severe cases of Addison's disease. Usually, however, it is most marked in those parts of the skin in which the eruption itself has been worst. It is well known that uterine disorders are apt to cause pigmentation—the uterine chloasma—but this is, as a rule, much more marked upon the face, especially upon the forehead and around the eyes, than it is elsewhere. There is little or no evidence that the pigmentation which follows herpes gestationis is in any way allied to uterine chloasma; indeed, there is seldom any obvious uterine derangement in the patients who suffer from it. The chief causes of the pigmentation are probably, first, the constant scratching or rubbing that the irritation in the affected parts gives rise to, just as it does in psoriasis, where pigmentation also becomes well marked as time goes on; and secondly, the arsenic which is administered in most of the cases. The darkening of the skin is so great in some patients that they look as if they might be of coloured extraction. There is apparently no record as to whether or not the pigmentation ever occurs upon the buccal mucosa as well as upon the skin, but between the attacks of herpes gestationis it would sometimes not be difficult to mistake the general appearance for that of Addison's disease if the history of the skin trouble were concealed.

Pathology.—The direct relationship of the disease to pregnancy is very remarkable. It seems to be the only point distinguishing it from dermatitis herpetiformis. I should like in this connexion to say a few words about eosinophilia.

Eosinophilia.—It is often stated in a general way that eosinophilia occurs in a large number of skin diseases. To test this I have made differential leucocyte counts in a number of all kinds of eruptions, and in the great majority of the commoner varieties there is no eosinophilia at all.³ If it be granted that nothing less than 5 per cent. of coarsely granular eosinophile cells in the blood can be termed eosinophilia, it is quite exceptional for cases of eczema, psoriasis, and the like to exhibit it. The reverse is true of the bullous dermatoses, however. There are, of course, a good many cases of pemphigus in which no eosinophilia is found at a single examination, and the percentage of coarsely granular eosinophile corpuscles varies not only in different individuals

suffering from the same disease but also in the same individuals at different times. Nevertheless, in patients suffering from pemphigus or from dermatitis herpetiformis, eosinophilia is the rule rather than the exception, as Bettmann, Darier, and others have pointed out. The degree of eosinophilia in the blood is moderate rather than great, the coarsely granular eosinophile corpuscles numbering something between 5 per cent. and 15 per cent. of all the leucocytes in typical cases.

It is worthy of note that the eosinophilia is not in the blood alone, but that the eosinophile corpuscles are also present in the inter-epithelial lymphatic spaces, where they may be seen in the microscopical sections of the skin; and, further, that in the fluid of the blebs themselves there are leucocytes, of which over 70 per cent. may be of the eosinophile variety. It is recorded as a curious fact that, although the fluid in the natural blebs contains so large a preponderance of eosinophile cells, there is no such preponderance of these corpuscles in the fluid of an artificial blister made upon the patient's skin, by cantharides for example.

Herpes gestationis agrees with the other bullous dermatoses in exhibiting eosinophilia. The differential leucocyte count in the case mentioned above was as follows: Small lymphocytes, 11 per cent.; large hyaline lymphocytes, 4 per cent.; polymorphonuclear cells, 71 per cent.; and coarsely granular eosinophile cells, 14 per cent. The significance of the eosinophilia is obscure. There are, of course, three main groups of conditions in which eosinophilia occurs. These are: First, those parasitic affections in which there is constitutional disturbance, notably in patients suffering from ankylostomum duodenale, trichina spiralis, filaria sanguinis hominis, bilharzia hæmatobia, hydatids, and sometimes with tæniæ and scabies, but not with the milder parasitic affections such as those of trichocephalus dispar, oxyuris vermicularis, ascariis lumbricoides, or tinea tonsurans and allied trichophytic affections. Secondly, true spasmodic asthma, in which eosinophilia is found during the attacks but not between them. Thirdly, certain skin diseases, chiefly the bullous dermatoses, as mentioned above. It is difficult to say why eosinophilia should be a prominent feature in these three groups of conditions and not in a great many other affections. It is thought that a poison of some kind is at the bottom of it in the parasitic diseases; that a toxin can produce a local eosinophilia was shown in the Johns Hopkins Hospital where the vascular spaces around appendicular abscesses were demonstrated to be full of eosinophile corpuscles although there was no excess of eosinophile cells in the general circulation. True asthma, however, is usually regarded as primarily a nervous phenomenon, and it is not at all clear why it should be associated with eosinophilia. It may be that there is an unknown poison which starts the neuro-muscular spasm in the bronchioles; otherwise it would seem that eosinophilia may have a nervous as well as a toxic origin.

The eosinophilia of skin diseases has been so little studied that it does not seem to be known whether the blood contains the excess of eosinophile cells before the eruption comes out or whether the bullæ always precede the eosinophilia. If the former were the case, then both the eosinophilia and the vesicles would probably have a common cause, whether that were nervous or toxic. The general opinion is, however, that the eosinophilia is the result of the skin lesion, due perhaps to the absorption of something from the skin in a way that would be comparable to the eosinophilia of ankylostomiasis, where there is supposed to be absorption of some toxin from the bowel. This raises the question of the pathology of the bullous dermatoses in general and of herpes gestationis in particular. It seems fairly clear that their causes arise within the body and that the lesions are not due to agents acting directly upon the skin from without. Bacteriological investigations have proved negative, the only micro-organisms that have been cultivated from the blebs being such as are readily explained as derived from accidental contamination from the skin.

Histology.—The actual process by which the vesicle or bulla develops seems to be as follows. There is a local dilatation of the papillary and sub-papillary blood-vessels, and an almost simultaneous increase in the quantity of lymph in the spaces around the prickle-cells of the epidermis. The local erythema is caused by the vascular dilatation and the itching is doubtless due to the tension put upon the cutaneous nerve endings by the sudden increase in the quantity of pericellular lymph. There is no proliferation of the cells themselves, such as occurs in eczema, though

² For a case recurring at menstrual periods, see Douglas Bryan, loc. cit.

³ Herbert French: Eosinophilia in Skin Diseases, Guy's Hospital Reports, 1903.

leucocytes may accumulate in the part by diapedesis. The pericellular lymph goes on increasing in quantity until the protoplasmic bridges between the prickle-cells are mechanically torn asunder; larger and larger numbers of dilated intercellular spaces in this way become united into a single cavity and a vesicle results. If the lymphatic dilatation is spread uniformly over a comparatively wide area, a single large bulla is formed; if within the same area the dilatation is irregularly distributed with several maximum points, a group of smaller vesicles is produced; if the original area of vascular dilatation is small, a single vesicle, too small to be termed a bulla, results. The size of the bleb is therefore to some extent an accident. The depth at which the vesicles form is also more or less accidental; in some cases the fluid accumulates quite close beneath the stratum corneum; in others, so deeply that only the papillary layer separates it from the corium. The transitional layer is the level at which the lymph is able to separate the cells with greatest ease, so that it is here that the vesicle or bulla originates most commonly. The surrounding prickle-cells swell up, become more or less spherical, and assume an appearance which led Professor Unna to term them "balloon cells." Notwithstanding their altered appearance, they still retain their nuclei and their vitality for a long while, though many of them ultimately become more and more swollen and homogeneous, and finally break up.

*Allied conditions.*⁴—It would not, I think, be surprising if the degree of lymph accumulation between the prickle-cells sometimes stopped short of vesicle formation. Local patches of erythema, accompanied by much itching and even pain, would then be the only features of the disease, and, as Sir Cooper Perry has pointed out to me, there are not a few cases in which women during each successive pregnancy suffer from skin trouble of this kind. The characters of the lesion are then such as lead to a diagnosis of pruritus or urticaria, as the case may be. The relationship between urticaria and vesicular or bullous eruptions is well seen in young children. Infants have so tender a skin that ordinary urticaria in them not infrequently ends in the production of vesicles. Some of the cases of pruritus or urticaria of pregnancy are very probably examples of abortive or incomplete herpes gestationis. It would be very interesting to know whether or not there is eosinophilia in these patients too, but I have not yet been able to make any investigations upon this point.

The changes described above suggest that the trouble arises from there being something the matter within the vessels themselves. It would seem that the trouble is either primarily nervous or else that there is some poison circulating within the vessels at the time. The generally accepted view appears to be that the disease is primarily nervous, in which case it would be analogous to herpes zoster, or more correctly perhaps with factitious urticaria, or with angeioneurotic oedema. On the other hand, by analogy with the urticaria which sometimes follows the ingestion of certain foods, or with the vesicular or pustular eruptions that may follow the administration of certain drugs, such as the bromide or the iodide of potassium, it is at least quite as likely that there is a toxic agent or poison concerned in herpes gestationis. If the disease were purely the result of an angeioneurosis it would seem surprising that the eruption should so often be restricted entirely to the times of pregnancy. It is true that cases have been recorded in which the attacks came on apart from, as well as during, pregnancy, but this is distinctly unusual, and such cases would be termed true dermatitis herpetiformis rather than the distinct variety we are now speaking of. Pregnancy seems to be an essential cause of the latter. The patients are not necessarily of nervous disposition; the lady whose case has been given above was a most sensible woman; there was no history of nervous disorder in her family, nor of nervous shock nor of anything of that kind in herself. Moreover, one cannot trace any hereditary tendency to the disease, such as is well known in cases of angeioneurotic oedema. It is not at present possible to bring forward any conclusive arguments, however, one way or the other as to whether herpes gestationis is primarily nervous or primarily toxic in origin. No toxin is known, but this does not prove that none is present. It is even possible that no abnormal substance is present in these cases at all, but that the

patients are unduly susceptible to some compound which is a normal metabolic product of the pregnant state. The idiosyncrasy of some persons in regard to strawberries might be used as a comparison. Most people can partake of this fruit in moderation with impunity, but a few cannot eat a single strawberry without suffering acutely from urticaria.

The pregnancy itself is not interfered with by the skin disease provided that suitable treatment is adopted to prevent pyoderma and to enable the patient to get a sufficiency of sleep. The children are born living and healthy, and it seems that the offspring of a mother who has been subject to the complaint are not particularly liable to any of the bullous dermatoses, nor are the females more liable than others to herpes gestationis. It is, however, very difficult to obtain direct evidence on this point, because few physicians see any large number of the cases and fewer still are likely to pay particular attention to the point in question.

This may, perhaps, be a good opportunity for mentioning a subject which Dr. Lauriston E. Shaw has spoken to me about sometimes—namely, that of the necessity for collective investigations being made upon special clinical and pathological points of this kind. There are many questions which, owing to the smallness of the number of cases that any individual is likely to see, can only be elucidated by collective inquiry. The Clinical Society, the Royal Medical and Chirurgical Society, and other similar bodies have from time to time instituted inquiries of the kind, but for the most part the data have been collected *after* the cases have been seen—from ward reports, post mortem records, and so forth. The very points upon which one wishes information are often not referred to at all in these, simply because the student or other person who wrote the report had not the knowledge or the interest to make a note about it. There are many conditions in which those who, having made a study of the cases up to a certain point, and having come across difficulties upon which they can nowhere find fuller information, could advise others as to special points to be upon the watch for and to pay particular attention to in *future* cases as they come under observation. The selection of the questions that might seem suitable for collective investigation in this way must necessarily lie with those who already know much. Dr. Mahomed when he was alive initiated a system of the kind but it died with him. The anatomists have a list of points upon which collective investigation is required, and in the dissecting room at Oxford there was a book in which were entered certain features of the anatomy of the vermiform appendix in each cadaver that was dissected, in order that by the accumulation of these and of a similar series of records from various other dissecting rooms certain debated points as to this particular part of anatomy might finally be settled. Some similar scheme might be possible as an assistance in settling debated points in medicine a few at a time. It would require a central authority for the selection of the points to be investigated, and the collaboration of all physicians at all hospitals would need to be sought. The central authority would doubtless be a permanent committee of physicians, and if the scheme were feasible at all the selection of such a committee for the direction of collective inquiry into obscure or debatable points in medicine and pathology would best, perhaps, be made under the auspices of either the Association of Physicians of Great Britain and Ireland or else of the Royal Society of Medicine of London. If Dr. Shaw's suggestion commends itself to others it should not be a difficult matter for a beginning to be made.

One might be asked, for example, whether an unmarried lady who had suffered from severe dermatitis herpetiformis previously to marriage would be likely to have still worse attacks of this disease should she marry and become pregnant. There are, so far as can be ascertained, no statistics to help one to answer such a query, important though it might be in some particular case. The general impression that is left upon one's mind after seeing a few cases and reading of as many more as one can find is that dermatitis herpetiformis and herpes gestationis, though in many respects so similar to one another, are yet sufficiently different to warrant the statement that pregnancy is by no means likely to bring on an attack of the former, though almost certain to cause a repetition of the latter. Again, one might be asked whether a patient who has suffered from dermatitis herpetiformis before marriage or from herpes gestationis after marriage would be likely to transmit the tendency to either disease to her children. As has been mentioned, one's general impression is that there is no

⁴ See also H. Radcliffe Crocker, Lettsomian lectures upon the Conditions which Modify the Characters of Inflammations of the Skin and their Influence on Treatment, Lecture II, THE LANCET, March 7th, 1903, p. 643.

likelihood whatever of such transmission, but it would be much more satisfactory if there were clear facts to base such an opinion upon, and such facts could best be accumulated by a collective inquiry.

OTHER SKIN DISEASES IN RELATION TO PREGNANCY.— IMPETIGO HERPETIFORMIS.

It has been suggested above that the pruritus, erythema, abnormal pigmentation, and urticaria which may develop during pregnancy may be regarded as minor manifestations of that which, in its full development, is herpes gestationis. There is another skin lesion known as impetigo herpetiformis which may perhaps be regarded as coming at the opposite extreme of the same series; that is to say, it seems to be a virulent degree of herpes gestationis, dangerous to life. Fortunately, the disease is very rare and a short account of it will suffice. According to Dr. J. F. Payne⁵ the majority of the cases have been met with on the continent and all but two of them have been in pregnant women. The eruption is not vesicular but pustular, groups of small pustules upon a red swollen base from half an inch to one inch in diameter appearing first in the groins, arm-pits, and mammary regions, and thence spreading until the whole of the body may be covered. The pustules dry up with the formation of scabby crusts, fresh pustules appear in the adjacent skin, and so on, the process extending in a circinate manner. No ulceration results but there is severe constitutional disturbance. The patient has continuous fever of the remittent type and with each new crop of the eruption there may be an exacerbation of the pyrexia with occasional rigors. Vomiting and delirium are usual and the patient nearly always dies within a few months. Parturition does not prevent the fatal termination. Cases of recovery from one attack have been recorded in which a succeeding pregnancy led to a return of the impetigo herpetiformis with fatal result.

The post-mortem examinations have shown no evidence of pyæmic or septicæmic infection. The general opinion appears to be that both the skin trouble and the constitutional disturbances are the result of an internal toxæmia, and it seems reasonable to suppose that a similar toxæmia rather than a primarily nervous cause is at the root of the whole series of lesions that have been mentioned, from apparently simple pruritus at the one end of the chain to herpes gestationis and to impetigo herpetiformis at the other.

There are only two other skin diseases upon which pregnancy seems to exert any definite influence. These are eczema and psoriasis, and it is only upon the latter that the effect of pregnancy is at all marked.

ECZEMA AND PREGNANCY.

Eczema is so very erratic in its behaviour that it is always very difficult to attribute any exacerbation in it to any particular cause. It is true that certain women, who never suffer from eczema otherwise, may develop a skin eruption which is apparently an eczema during pregnancy. The skin lesion may be papular or it may be vesicular—eczema papulosum or eczema madidans as the case may be; but when it occurs only during pregnancy and not between whiles it may be suggested that it is really allied to the urticaria and to the herpes gestationis that we have been discussing rather than to true eczema. The matter could be decided by microscopical examination of sections of the skin to determine whether there was epithelial cell proliferation, as in eczema, or none, as in herpes gestationis, but no histological work appears to have been done upon this particular point and I have had no opportunity of doing any myself. When, on the other hand, a lady is subject to undoubted attacks of eczema apart from pregnancy, it by no means follows that the skin trouble will become worse during the pregnant state; if any general rule can be laid down it would be that the patient's eczema will very likely be mitigated rather than made worse during pregnancy.

PSORIASIS.

Psoriasis is more definite in its behaviour during and after pregnancy. Before the birth of the child the mother, if she be already subject to psoriasis, will either be very much less troubled with it than before, or else will develop a severe exacerbation. It is not possible to give any certain prognosis as to which of these two things will occur, but more patients have their skin disease mitigated than increased whilst they are actually pregnant. On the other hand, the effect of lactation upon psoriasis is almost

invariably bad. The eruption is liable to increase during the puerperium in any case, but if the mother suckles her child she is almost certain to develop a very severe attack of the psoriasis. This, therefore, is one of the conditions under which the mother ought not to suckle her child. Artificial feeding of the infant should be adopted from the beginning and immediate steps be taken to dry the mother's breasts.

THE PYELONEPHRITIS OF PREGNANCY.

Leaving the skin diseases now, we may pass on to the discussion of a condition in which, although the pathology is of quite a different kind, pregnancy again appears to be an important factor in the causation of the trouble. This is the pyelonephritis which of late years has been recognised with increasing frequency in pregnant women. Mr. G. Bellingham Smith has recorded several cases in the *Journal of Obstetrics and Gynecology* (1905) and others in the *Guy's Hospital Reports* (Vol. LX., 1906); upon the continent and in the English journals there have been a good many papers upon the subject during the last few years, such as those of Reblaub, Jeannin and Cathala, Vinay, Cumston, and others. The observations made previously to 1899 were summarised by Cade in *L'Obstrétrique* (Vol. IV., 1899, p. 230).

Illustrative cases.—The following are notes of two cases that have recently been in the medical wards at Guy's Hospital, the one under myself, the other under Dr. A. F. Hertz in the first instance and under Dr. G. Newton Pitt subsequently. These two examples are chosen, not only because they were in the wards almost at the same time but also because they exemplify two very different degrees of the severity of the disease.

CASE 1.—The patient, aged 28 years, had had two children, now aged five and two years respectively; she had had no miscarriage and she was pregnant for the third time when, at the beginning of the fifth month, she was suddenly seized with severe pains round the waist. The suddenness of the onset of the symptoms may be gathered from the fact that she was in her usual health, preparing her husband's midday dinner, when the pain seized her acutely in the loins; she was unable to go on with the dinner preparations; she took to her bed and remained there a fortnight under treatment before she was transferred to the hospital. The pains across the loins persisted all the time, waxing and waning to some extent, but not in such a way as to suggest colic. Vomiting had been frequent, especially after food, and this notwithstanding her diet being milk and soda-water only. In addition to the vomiting there had been severe headaches and upon several occasions rigors. The skin was dry for the first five days but since then there had been copious perspirations.

Upon examination the chief abnormality was in connexion with the right kidney. The abdomen was supple and it moved well with respiration. The kidney could not be palpated, but there was a slight degree of fullness in the right flank, and at a spot just below the right twelfth rib there was acute tenderness on the slightest pressure. The bladder was normal and there was no frequency of micturition. The urine was alkaline, abundant, and of specific gravity 1010; it contained enough albumin to give a marked cloud with the boiling test, and microscopically there were large numbers of pus corpuscles, a few renal cells, and an occasional granular tube cast. A catheter specimen of the urine, examined bacteriologically, gave a pure culture of bacillus coli communis. There had been considerable pyrexia during the fortnight previously to admission. Here is the temperature chart for the first two weeks after admission:—

CHART 1.

Absolute rest in bed and the administration of urotropine were followed by rapid alleviation in the symptoms, and the patient went out in three weeks' time, feeling quite well, though there were still a few pus corpuscles in the urine. It was by her own desire that she went out, and it would certainly be wiser in other similar cases to continue the treatment till term; for within a fortnight she had all her acute symptoms back again and she had to be put back to bed. Fortunately, the severer symptoms of the relapse passed off in a similar way to those of the original attack, but the patient had to be extremely careful for the rest of her time. Her baby was born alive at full term.

⁵ Clifford Allbutt: System of Medicine.

The puerperium was normal, and the patient is now strong and well. Her urine has been quite free from pus and from other abnormal constituents since that time.

The above might be termed an ordinary case of the kind; the following is an instance of a much more severe type.

CASE 2.—The patient, aged 24 years, had been married two years and had had no living child, though nearly a year ago she had a miscarriage at the fourth month, followed by rapid and uninterrupted recovery. She was now five and a half months pregnant. She had been perfectly well until a fortnight previously to admission, when, without apparent cause, she suddenly experienced severe pain in the right loin, which persisted and soon extended round from the loin into the right iliac fossa. She had always been subject to constipation, her bowels being moved only twice a week as a rule, and during the fortnight previously to her admission to hospital enemata had been required upon several occasions. Vomiting had occurred only once. The patient's temperature was 103.6° F., her pulse-rate 124, and her respiration-rate 26 per minute. The uterus extended to just above the umbilicus and, owing to the pregnancy, palpation of the rest of the abdomen was difficult. Tenderness was more marked in the right iliac fossa than elsewhere, and there was also cutaneous hyperæsthesia here. The general impression at first sight was that the patient had appendicitis, but more detailed examination showed that the tenderness extended from the right iliac fossa well back into the right loin and as high as the twelfth right rib. There was only slight rigidity of the muscles over the right iliac fossa. If the condition were appendicular the same symptoms might have been caused if the inflammatory trouble had tracked up behind the ascending colon into the perinephric tissue, but the patient herself was quite clear that the pain had started in the right loin and had thence extended into the right iliac fossa, and not *vice versa* as would most likely have been the case if the trouble had been primarily appendicular. There was no lump to be felt and the right loin was not filled out. The urine was acid, of a specific gravity 1020, and a pale yellow colour. It contained a flocculent deposit of pus, a fair quantity of albumin, and no obvious blood. Microscopically pus cells without crystals abounded in the deposit and there were also many renal cells, both from the pelvis and from the tubules, a few red blood corpuscles, and several tube casts chiefly of the granular variety. The other general systems were natural, except that the vesicular murmur was deficient at the base of the right lung. A diagnosis of pyelonephritis of pregnancy was made.

One point of particular interest was that the patient's leucocytes were increased up to 25,000 per cubic millimetre of blood, so that a leucocyte count is apparently of no service in helping to distinguish this disease from appendicular abscess and the like, though it helps in excluding typhoid fever—a condition which the pyrexia might suggest. The temperature chart 2 sufficiently indicates how ill the patient was.

A catheter specimen of the urine, examined bacteriologically, gave a pure culture of bacillus coli communis, and a similar result was obtained upon three subsequent examinations. The vagina and uterus were perfectly healthy and there was no disease of the bladder. The latter was examined with the cystoscope and purulent urine was seen issuing chiefly from the right ureter, but the mucosa of the bladder itself was perfectly normal. There was no dilatation of the vesical orifices of the ureters. The pain in the right loin, with exacerbations accompanied by vomiting, persisted in spite of everything that was done. The pyuria and albuminuria showed no abatement, and a moderate degree of jaundice developed. The patient seemed to be getting steadily worse and at the end of the sixth week she consented to undergo an operation with a view to deciding whether there was anything in the right renal region that could be either removed or drained. Mr. F. J. Steward exposed the kidney and found that it was studded all over with small abscesses. There was no large collection of pus that could be incised and drained, and the patient's condition was so critical—her pulse-rate being over 170—that nephrectomy was out of the question, so the wound was sewn up, a space being left for a gauze drain. The ureter had been felt to be dilated above the bladder, although it had been shown by the cystoscope that the vesical orifice was normal.

The patient steadily improved after the operation, notwithstanding the fact that nothing particular was done. It should be noted that no pus and no urine drained through the lumbar wound for a fortnight after the operation, but that upon the fourteenth day urine came away from it in abundance and continued to do so for some weeks after the patient was convalescent. It is very difficult indeed to say what part the operation itself played in the subsequent recovery, particularly in view of the vaccine treatment that was adopted about the same time. The vaccine was prepared from cultures of bacillus coli communis obtained from the patient's urine. The injections were made at intervals of about a fortnight, as shown upon the temperature chart, and each dose consisted of the products of 500,000,000 bacilli. To judge by the chart the improvement dated from the exploratory operation itself; it was already well marked before urine began to come through the loin, so that actual external drainage of the abscesses in the kidney did not seem to be the deciding factor in the case. The urine continued purulent; indeed, the quantity of pus in the urine was noted as being greater after the operation than it was before it. It is possible that in some way the manipulations which were necessary at the time relieved some pressure that had previously existed upon the right ureter in its pelvic course and that the discharge of urine from the wound in the loin 14 days after the operation was a sign that the obstruction to the ureter had then re-established itself. In any case the patient steadily improved, although pyuria persisted. It was not until the temperature had already been normal for several days that the pregnancy showed any signs of terminating. Without much warning and without difficulty a living premature child was born on the seventy-seventh day of the illness. The puerperium was uneventful. The pus and albumin had both entirely disappeared from the urine within a month of the birth of the child. The wound in the loin had healed up and the patient was soon up and walking about, quite well.

Before passing on to discuss the pathology of the malady in general, stress may perhaps be laid upon three particular points in the above case. The first of these is the dilatation of the ureter that was demonstrated—a dilatation not

CHART 2.

A, Exploration of the kidney. B and D, Eight cubic centimetres of vaccine, 500,000,000. C, Urine began to discharge through the loin; eight cubic centimetres of vaccine, 500,000,000. E, Prematurely delivered of a living child. The temperature on Nov. 25th, 26th, and 27th fluctuated between 97.4° and 100.2° F.; after the 28th it did not rise above 99.0°. The patient began to get up on the 91st day (i.e., on Dec. 8th). She went home well on the 108th day. The temperature remained normal.

beginning at the bladder itself, but just above the bladder about the level of the pelvic brim. The second is the fact that the inflammation is not confined to the pelvis of the kidney in these cases, but extends right up into the cortex, as was demonstrated at the operation. And the third is that notwithstanding the existence of large numbers of small abscesses in a kidney affected by an extreme degree of suppurative pyelonephritis of this kind, uræmia in the ordinary sense need not supervene and the patient may recover completely. No doubt it depends to some extent upon the nature of the organism present whether recovery is likely to occur or not, and in these cases it is always, or nearly always, the bacillus coli communis. This organism, however, is usually accredited with particular virulence when it affects parts outside the alimentary canal; and if the miliary abscesses had not been ocularly demonstrated at the operation it would have been difficult, in view of the subsequent complete recovery, to have believed that such abscesses had actually been present. One wonders whether it is as true as it is usually held to be that multiple abscesses in another organ—namely, the liver in suppurative pylephlebitis—must necessarily be fatal also. In view of these multiple abscesses in the kidney getting well it would seem possible, if not probable, that similar multiple abscesses in the liver may get well too sometimes.

The pathology of the pyelonephritis.—Turning now to the pathology of the pyelonephritis of pregnancy there are certain points that are fairly clear. The cases that have been collected by Mr. Bellingham Smith and others all indicate that previously to the pregnancy there was no renal trouble. It is probable, therefore, that the gravid uterus is a responsible factor in the production of the mischief. It is also clear that the pyelonephritis is not secondary to cystitis, for in practically all the patients the bladder has been healthy, at any rate at the beginning of the disease. Further, it has been demonstrated at the necropsy in some cases, and at operation in others, that there is dilatation of the ureter, beginning about an inch above the bladder. Putting all these facts together it seems almost certain that the sequence of events is: enlargement of the uterus; compression of the ureter against the brim of the true pelvis; consequent difficulty in the ejection of urine secreted by the corresponding kidney; infection of the urine retained in the partially obstructed ureter and renal pelvis; and subsequent spread to the kidney substance itself. The pyelonephritis of pregnancy would thus be comparable in some respects with pyelonephritis due to other causes, such as enlargement of the prostate in man; and just as in the latter case removal of the obstruction tends to cure the renal mischief, so does the birth of the child result in most cases in rapid amelioration and even complete cure of the trouble from which the pregnant woman has suffered.

It is a curious but very definite fact that in nearly every case the right kidney is very much more affected than is the left. In both the patients of whom notes have been given this was so. It is probable that the left kidney does not escape entirely, and indeed there is usually some pain in the left loin as well as in the right, but in the majority of cases the symptoms indicate that the mischief is mainly on the right side. There have been several explanations offered to account for this; perhaps the best is that of Cumston. He states that whilst the pregnant uterus develops its borders come nearer to the ureters, upon which they become pressed. The uterus develops much more to the right than to the left; it also inclines to the right, and besides this it undergoes a rotation on its vertical axis and turns in the direction of its greatest development—that is to say to the right, thus freeing the organs on the left side and exerting a greater compression on those of the right. Be this as it may, the facts that the ureteral obstruction begins at the level of the pelvic brim, that it is in some way due to the pregnant uterus, and that the right ureter is as a rule more obstructed than is the left have been repeatedly demonstrated.

Seeing that partial stenosis of the ureter by the pregnant uterus is generally regarded as the essential predisposing factor to this kind of pyelonephritis, it might very well be suggested upon theoretical grounds that the illness ought to be much more common and much more serious in those who have deformed and particularly contracted pelves and in those who have pelvic tumours, such as uterine fibromyomata or ovarian cysts, in addition to their pregnancy. These complications have existed in a few of the cases and theoretically they should play an important part in the pathology of the condition. Nevertheless, the existence of

pelvic tumours or the like with pregnancy is by no means essential, or even common, as a cause of the pyelonephritis. The cases recorded have almost all had normal pelves and normal pelvic organs. The disease is therefore one which may arise in otherwise healthy women.

In regard to the question of whether a woman is liable to it during her first or a later pregnancy, opinions differ. It seems quite clear that the first few pregnancies may be quite uncomplicated and yet that pyelonephritis may develop during a later one; several observers lay stress upon its occurrence in primiparae, but the truth seems to be that it may arise during any pregnancy and that in the differential diagnosis no stress can be laid upon the fact of the patient being a primipara or otherwise. It is clear that if obstruction to a ureter is an essential factor in the disease, the trouble is not to be expected in the earliest months of pregnancy. This is borne out by the cases themselves. The pyelonephritis may not appear until quite late in the pregnancy, but in the typical cases the mischief begins about the fifth month, as in the two cases described above.

The bacteriology of the pyelonephritis.—The bacteriology of the condition is very constant. In all but a very few of the recorded cases the organism that appears in cultivations from the purulent urine has been the bacillus coli communis. It has nearly always been in pure culture. Mr. Bellingham Smith found it in seven consecutive cases, and in only one case, recorded by Vinay, was the mischief attributable to another micro-organism—namely, a streptococcus.

There is some difficulty in determining the route of infection; this applies, of course, not only to the pyelonephritis of pregnancy but also to the similar suppurative lesions that may ensue when there has been residual urine in the bladder for a long time, even though no catheter or other similar instrument has ever been passed. The three paths by which the micro-organisms might, it may be supposed, reach the kidney are: first, from the bladder, ascending by the ureters; secondly, by the lymphatic vessels; or thirdly, by the blood stream. It must to some extent remain a matter of opinion as to which of these three paths is the more usual in these cases. Personally I agree with Mr. Bellingham Smith in thinking the blood stream the more likely route of infection, his arguments being as follows. Whereas it is true that, as Opitz urges, the female urethra always contains organisms and that the bladder in pregnancy is very liable to cystitis, nevertheless there are two objections to the view that the path of infection in the pyelonephritis of pregnancy is *via* the bladder—one anatomical, the other clinical. The anatomical objection is that the ureter in these cases is dilated, not in its whole extent, but only above the brim of the pelvis; the valve-like opening of the ureter into the bladder, which normally protects the former from infection, is still present and in perfect working order; there is no dilatation of the vesical end of the ureter, such as to cause a free communication between the latter and the bladder, and consequently there is no free path for the ascent of organisms from the bladder into the ureter. The clinical objection is still greater. The chief feature of pyelonephritis in pregnancy is the presence of pus in the urine without any symptom pointing to cystitis. None of the cases under discussion have afforded any evidence of preceding cystitis and cystoscopic examination in the severer of the two cases of which notes have been given showed that the bladder was perfectly healthy. There are no doubt other cases of pyelonephritis secondary to existing cystitis, the symptoms being aggravated by the existence of pregnancy, and in such cases the path of infection would doubtless be from the bladder just as it might be in a non-pregnant person; but in the cases of pyelonephritis under discussion there is no cystitis, pregnancy is an essential factor in the disease, and it seems unlikely that the organisms reach the kidney by ascent from the bladder.

Infection by the lymphatic vessels is very difficult either to prove or to disprove and there is little or nothing that can be stated definitely about it. Infection by the blood stream, on the other hand, is possible, and, if the vesical and lymphatic routes can be excluded, even probable. Experiments have been made on animals in which after artificial stenosis of a ureter purulent nephritis followed injection of bacillus coli communis cultures into the blood stream. Moreover, it has been shown that the healthy kidney sometimes excretes micro-organisms such as tubercle bacilli and typhoid bacilli in patients and animals who are suffering from an apparently local tuberculosis or from apparently uncomplicated typhoid fever. In these cases the micro-organisms have presumably

reached the kidney in the blood stream, and if tubercle and typhoid bacilli can do so it would not be surprising if the bacillus coli communis did so too. The healthy kidney would eliminate the bacillus without itself suffering. The existence of stenosis of the ureter might well cause the urine containing such bacilli to stagnate long enough to allow of infection of the walls of the passages, even without supposing that there was diminished resisting power in the parts owing to the obstructed outflow. The ease with which the bacillus coli communis can reach the blood stream is well known from post-mortem examinations, where cultivations from organs situated far from the bowel nearly always yield this micro-organism in cultures made soon after death. It is held by some that a similar escape of the bacillus coli communis from the bowel into the blood stream can occur during life, particularly when there are abnormalities in the functions of the alimentary canal.

This raises the question of whether the pyelonephritis of pregnancy can occur when there has been no abnormality in the intestinal functions, or whether, in addition to pregnancy and partial stenosis of the ureter, some error of the bowels, particularly constipation, is essential to its production. This is a very difficult matter to decide. It is very certain that a great many pregnant women may suffer from constipation without any other deleterious effects. Nevertheless, granted that a patient were on the verge of developing pyelonephritis, the existence of severe constipation might very possibly cause a certain number of colon bacilli to enter the blood stream and thus prove to be the final or determining factor in the illness. This seems to have been the case, for example, in connexion with the second patient described above; always very constive, she was suffering so much from constipation just before the pyelonephritis set in that she could only get her bowels to act by the use of repeated enemata.

The effect of the pyelonephritis upon the pregnancy.—A number of questions arise, to each of which the physician may be required to give an answer if he can. Amongst these are the following: To what extent does the pyelonephritis interfere with the course of the pregnancy? Is it likely that the child will be born dead? Seeing that pregnancy is a fundamental factor in the pyelonephritis, ought obstetrical measures for the termination of the pregnancy to be advised? Is the time of labour one of special danger? Is the patient particularly liable to uræmic symptoms? Is there any relationship between pyelonephritis and puerperal eclampsia? Is the condition likely to be completely cured after labour, or is a residuum of kidney inflammation to be expected? Is the patient very liable to have a recurrence of the pyelonephritis in a succeeding pregnancy?

It is only by a collective inquiry, in which mild as well as severe cases are included, that conclusive answers can be given to these questions. Under present conditions it is dangerous to base opinions upon published cases only, because those which are thought worthy of being published are often not the ordinary cases but rather those which present points of special interest. On the other hand, an individual can scarcely hope to meet with a very large number of cases himself, so that until records of consecutive and unselected cases can by some means be gathered together it is only possible to base one's opinion either upon recorded, and therefore selected, cases or else upon the few cases that one has oneself watched.

It would seem that, diagnosed early and treated by confinement to bed with antipyretic remedies, the condition usually tends towards resolution, notwithstanding continuance of the pregnancy. Moreover, in the majority of what may be called cases of ordinary severity the pregnancy is not particularly apt to come to an end prematurely. The children do not show any special liability to die in utero and the mother is not subject to uræmic convulsions at the time of labour. No doubt there are individual cases in which the illness is so severe that it might be wise to advise relief to the ureteral obstruction by the use of obstetric measures for emptying the uterus. The kind of case in which this might be the best course to follow would probably be one in which the renal mischief had set in with severity during the earlier months of the pregnancy and had then persisted for a month or more without abatement in the symptoms, notwithstanding all the medicinal treatment available. Such cases as these are distinctly the exception, however. The majority of the patients require the adoption of no obstetrical measures for the time being. Treatment upon purely medical lines, by

absolute rest in bed, light nourishing diet, laxative, and such drugs as are known to benefit pyuria, begun early and carefully followed, will usually relieve the patient of her untoward symptoms comparatively soon—that is to say, within three weeks or a month. The pyuria will often persist for a month or six weeks after the patient herself feels quite well, and unless considerable care is observed a relapse is apt to occur before the pregnancy reaches term. Repeated microscopical examination of the urine is therefore essential, and medical supervision is required as long as any pus is present. Eclampsia is not to be expected and the patients nearly always get perfectly well of their pyuria after the child has been born.

It would not be at all surprising if similar pyelonephritis were to recur in succeeding pregnancies, and cases are on record where this has actually been the case. This is not the invariable rule, however. If the pyuria is completely cured after one pregnancy, and care is subsequently taken to insure that there is neither constipation nor diarrhoea such as might predispose to invasion of the body by the bacillus coli communis from the intestines, it is quite possible for a succeeding pregnancy to pass by without any symptom of pyelonephritis at all.

In conclusion of this lecture, stress may well be laid upon the fact that the pyelonephritis of pregnancy may easily be mistaken for something else. The milder cases may be regarded as simple pain in the back, as lumbago, as influenza, and so forth; severer cases may be thought to have pneumonia, pleurisy, or the like; the most severe cases may be diagnosed as appendicitis or as some other intra-abdominal condition. The main symptoms of the disease are backache and pyrexia, with or without headache, vomiting, or rigors, and unless the urine is carefully examined for pus corpuscles the real cause of the trouble might readily be overlooked.

A Lecture

ON

THE SPECIAL PSYCHOLOGY OF WOMEN.

Delivered at the Institute of Hygiene on March 10th, 1908,

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LADIES AND GENTLEMEN,—By psychology we mean the mental processes in their subjective and objective ramifications, what they appear to be, or should be, to the individual, and what they are, or should be, to the external world—to society in all its gradations. To speak on this subject presupposes that one has, at least to some extent, such a share in the form of mental action as will justify the audacity of criticising what can only partially be experienced. This would be easy enough in the uni-sexual mind, but women are women and men are men, and though there are points of resemblance, both in bodily and mental structure and function, there are yet such profound differences that the one must always be a puzzle to the other. We may be able to say what women ought to do, but that we find them acting and talking very differently merely proves that we have not correctly estimated the factors upon which their motives have been formed, and since a complete fusion of intellects is not possible the psychology of women must always remain a paradox to men. It is a different form of mind that we are asked to appreciate, and it is no more possible for the mere man to predict what the mere woman will of necessity do than it is for the timid person to understand the *audace* of a lion-tamer or for the rat-catcher to flee at the presence of a mouse. And yet this dis-association of mind in the two sexes is not a complete one; there are many common features. There are men of whom it may be said that there is much of the woman in them and there are what are called masculine women who seem to be composed largely of the attributes of the male mind. We shall see that much depends upon education and environment and that except in one particular direction there is in reality little difference between the two classes of mind—that one