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AFFECTIONS OF THE KIDNEY IN RELATION TO PREGNANCY.*

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CHANGES IN THE KIDNEYS DURING PREGNANCY.

For many years there has been much discussion as to the alterations occurring in the kidneys during pregnancy, and, at the present time, there is considerable difference of opinion as to the nature of these changes, their frequency, causation and significance. The literature of the subject is abundant in speculative inquiries, while records of trustworthy facts derived from careful and systematic observation are scanty. Indeed, though theories have multiplied, it is doubtful whether we are very much wiser than we were fifty years ago, for the latest and most favored views, originating among French workers, are only an elaborated expression of the opinion published by Virchow in 1848.

This authority then pointed out that, of all the organs in the female organism, the most frequent functional or structural alterations due to pregnancy were found in the kidneys. He regarded the cause mainly as connected with altered metabolism, changes being induced not only in the kidneys, but in the liver, spleen and other parts. In association with these alterations, he pointed out the frequency of albuminuria.

In view of the time limits which the present occasion demands it is impossible to do more than present a summary of the main lines of investigation along which workers have moved in their efforts to throw light on a difficult subject.

That the kidney becomes somewhat hypertrophied as a result of pregnancy all are agreed, though the nature of the enlargement and range of variations are not at all definitely known. The quantity of urine is increased and it is of a lower specific gravity.

Sugar is found in a considerable number of cases of pregnancy, and more frequently after delivery, but this is only milk-sugar absorbed from the breasts, not true glucose. The latter is no more frequent in pregnancy than in the non-pregnant state.

Peptones are occasionally found in pregnancy; by many being thought to indicate death of the fetus, though there is no proof whatever of this. They are very frequent after the first three or four days of the puerperium, when they are derived from the involuting uterus.

With regard to occurrence of albumin in the urine and its significance, there is an amazing difference of opinion. Its frequency has been variously estimated by different workers.

The following statistics are given by different German authorities: Meyer, in 76 parturient women found albumin in 40.78 per cent.; Litzmann, in 100 parturient women found albumin in 43.7 per cent.; Löhlein, also in 100 parturient women found albumin in 37 per cent.; Flaischen, in 537 parturient women found albumin in 16.9 per cent., and Winckel, in 367 parturient women found albumin in 19.4 per cent.

These percentages are noticeably higher than those given by leading French obstetricians. Thus, Pinard states that out of 1249 parturient women in the Baudelocque Clinic in 1890, only 73 cases of albuminuria—5 per cent.—occurred: of these slightly less than 3 per cent. were associated with pregnancy, the rest with labor.

So far as may be gathered from more recent observations, it may be stated that serum-albuminuria occurs in about 2 per cent. of all pregnant women who are healthy at the beginning of pregnancy. The process of labor causes albuminuria in a still larger percentage of cases. Aufrecht found it was produced in 18 out of 32 women examined; Ingersley in 50 out of 153 cases of labor. It is most frequent in women during the first pregnancy, especially in those who are no longer young or in those who are very young. Of all cases it is belived to be most associated with the presence of more than one fetus *in utero*. It occurs mainly in advanced pregnancy, only rarely in the early months.

What is the significance and explanation of this albuminuria of pregnancy? Is it, as some hold, a physiologic process of no importance, or is it to be regarded as many authorities consider it, as the result of pathologic changes induced in the cortical portions of the kidneys? In favor of the former view may be adduced the cases of healthy men and non-pregnant women in whom a temporary albuminuria may be caused by various factors, e. g., changes in temperature, food, exercise, etc. The investigations of the late Grainger Stewart undoubtedly appear to justify the view that there may be an albuminuria, which is to be regarded as a physiologic peculiarity and not the indication of a pathologic process. *A priori*, then, it must be conceded that a like explanation may suffice for some cases of the albuminuria in pregnancy.

Regarding the view that a morbid process in the cortices of the kidneys is the essential cause the following facts may be stated: In very many cases of albuminuria other signs of renal diseases may be present. Thus edema may be frequently met with. Winckel's statistics may be noted: In 1874, in 319 pregnant women edema occurred in 20 per cent; in 1876, in 1058 pregnant and parturient women it occurred in 4.35 per cent.; in 1877, in 1091 pregnant and parturient women it occurred in 6.96 per cent., and in 1878, in 1050 pregnant and parturient women it occurred in 5.52 per cent. Leyden is of the opinion that anasarca is much more common than albuminuria and that when they co-exist the edema has appeared first. Then, again, there is

* Read before the Chicago Medical Society.

often a deficiency in the quantity of urine passed and in the total solids excreted. But most important of all is the occurrence in the urine of various formed elements, viz.: casts and blood-corpuscles. Fischer, who has given much attention to this subject points out that these are mostly found in the last weeks of pregnancy, when they often show progressive increase. Hyaline casts are frequent, while granular and epithelial ones and broken-down epithelium may also occur. Red blood-corpuscles and leucocytes may be passed continuously or at intervals.

Now, as to the relationship between the above findings of physical examination on the living subject and those obtained by post-mortem investigation it is impossible to speak with absolute certainty. The great majority of such patients do not die and, comparatively, only a small number of post-mortem studies have been made. There can, however, be no doubt that sufficient work has been done to establish the probability that renal cortical lesions generally occur, though with a considerable range of variation.

The most frequent changes found are as follows: The kidneys are enlarged and less firm than normal; the cortices are swollen, anemic and of pale gray color; cloudy swelling and granular changes are found in the cells of the tubules and, often, fatty degeneration. In a small number of cases it is certain that the kidneys may not recover from this condition after labor, but may pass into a permanent, true parenchymatous nephritis. In the majority of instances, however, there is every reason to believe that they may be restored to their normal condition in a short time. Olshausen has described an interesting case in which the urine contained abundant albumin, casts and blood-corpuscles at the time of labor, eclamptic phenomena being also present. The patient died five days after delivery and at the post-mortem examination no changes whatever were found in the kidneys.

Of extreme interest is the consideration of the etiology of the albuminuria and renal changes above described. The subject is an extremely difficult one and has been the occasion of much speculation and much polemical writing. Only a brief reference to the most important views is here possible.

Compression of the ureters.—Halbertsma of Utrecht, from his studies of eclampsia, believes that increased intra-abdominal pressure due to the pregnant uterus, may by interference with the functions of the ureters, lead to alterations in the renal structure. He thinks that the special tendency to these alterations in primiparæ, hydramnios, multiple gestation, contracted pelvis —in all of which the pressure is increased—strengthens his view. Ries, holding somewhat similar views, believes that in some cases compression of the ureters by the presenting part of the fetus is the most important factor. These views have not been accepted by most authorities. Halbertsma's statement that dilatation of the ureters is frequent in such cases has not been corroborated. Olshausen found dilatation only seven times in 37 post-mortems.

For my own part, I believe that too little attention has been given to the opinions of Halbertsma and Ries.

While it is true that the anatomic relationships of the ureters are such that they are generally protected from the pressure of the pregnant uterus or its contents at any special point, the possibility of an abnormal pressure over a considerable extent of the ureters in certain cases can not be denied. Though the projecting vertebral bodies are the main safeguard from pressure on the ureters, they can not entirely protect it. My frozen sections and casts of pregnant women show that the enlarged uterus moulds itself accurately along the spine and on each side of it. At the brim this moulding is particularly well shown. In conditions of tense abdominal wall, such as is found in young or old primiparæ, or of abnormally large uterus, as in hydramnios or multiple pregnancy, it is very evident that the general pressure on the ureters must be increased. In the late weeks of pregnancy, as is well known, the fetal head lies in the pelvic cavity in primiparæ, and, if the pelvis be justo-minor or funnel-shaped in type, or the head be abnormally ossified or enlarged, the ureters can scarcely escape being unduly compressed against the pelvic wall. Even though in these various conditions there may not be a local interference with the flow through the ureters, there may be produced a paresis of their walls, as Halbertsma first suggested, leading to a marked weakening of their peristaltic action.

The earlier critics of this worker pointed out that the pressure theory could not explain the cases in which renal disturbances developed in the puerperium. My recent studies of the puerperal woman by means of frozen sections supply a very evident explanation. I have shown that the post-partum uterus in its retracted and contracted condition fills the greater part of the normal pelvic cavity to such an extent as to form a ball plug compressing all extrauterine tissues firmly against the pelvic wall, interfering considerably with the circulation of blood through them. The ureters share in this compression. This condition of affairs lasts for three or four days, during which period renal disturbances mostly occur. The postpartum uterus varies somewhat in size and, therefore, if it be rather larger than normal or if the pelvis be justo-minor or funnel-shape in type, greater compression is produced. Ries, Halbertsma and others have shown that pelvic inflammatory exudates may cause compression of the ureters, and consequent renal disturbance in the puerperium. It is interesting to note, in this connection, that large fibroid and ovarian tumors, especially the former, are not infrequently associated with changes in the urine, kidneys and ureters similar to those found in pregnancy; and in some cases the renal function may be completely destroyed.

Finally, it is interesting to note certain experiments on animals: Aufrecht ligated a ureter in a dog and killed the animal three days later. The corresponding kidney was much swollen, its pelvis along with the upper part of the ureter distended. The cortical tubules of the kidney were damaged, being somewhat dilated, and containing abundant hyaline—fibrinous—casts, their epithelium showing granular and fatty changes.

Apart from compression of the ureters it may be that the kidneys themselves are so affected by certain degrees of increased intra-abdominal pressure as to undergo degeneration; or, it may be, that in the same manner the renal circulation is interfered with. Compression of the renal arteries or interference with the flow of blood in the veins is sufficient to induce albuminuria and degeneration in the kidneys if continued long enough.

Influence of the Products of Metabolism.—Virchow, in 1848, stated that disturbances in the kidneys during pregnancy were mainly due to the influence of altered body metabolism, and he pointed out the frequency with which the renal changes are accompanied by corresponding conditions in the liver. During the past fifty years different theories have been advanced to explain the nature of the alterations induced by the metabolic processes in pregnancy. At the present time the majority of

authors hold to this theory in a general way, though there is very great divergence of opinion as to its actual application.

In pregnancy the increase in maternal metabolic activity is evident. This means a greater quantity of excrementitious matter to be eliminated. As the ovum develops fetal metabolism becomes a more and more important factor. Fetal waste products almost entirely enter the maternal blood by transmission through the walls of the villi from the fetal circulation. An extra burden is therefore thrown upon the maternal kidneys, and if they can not respond to the increased demand on their activity, they are apt to suffer. The waste products may exert a direct poisonous action on the cells of the tubules, or, indirectly, through their influence on the arteries in the kidneys, constricting them and thereby interfering with the nutrition of the tubules. The changes are believed to be similar to those found in such conditions as ptomain poisoning and acute yellow atrophy where the destruction of the kidney tissue may be very rapid.

The influence of the skin, lungs, liver and intestines aids in getting rid of the waste products of metabolism, and it is evident that interference with their functions will throw greater burdens on the kidneys. It is in pregnancy especially that these functions are apt to be interfered with. In most civilized countries a large number of pregnant women have a prejudice against cleansing the skin of the body. The production of albuminuria in a healthy dog by varnishing its skin is a well-known experiment. Then the tendency to irregularity in the digestive tract and to constipation in pregnant women is a very common one. Clinically, it is very easy to prove, in the albuminuria of pregnancy, that promotion of free action of skin or bowels, or of both combined may lead rapidly to a diminution in the quantity of albumin in the urine.

With regard to the influence of the fetal waste products it has been noted in cases of albuminuria that death of the fetus may lead to a rapid diminution or disappearance of the albuminuria, and this is believed to be due to the cessation in the transmission of the waste products from the fetus to the maternal blood. There is much speculation as to the nature of the waste products which exert the destructive influence. Various subjects are mentioned, e. g., leucomains and ptomains formed in the bowel and reabsorbed when the bowel action is faulty; also creatin, creatinin, inorganic salts of potash, various alkaloidal products of digestion, etc.

The extent to which the kidneys may be affected depends, therefore, on a variety of factors. In the majority of cases in which they are affected, no permanent damage results nor do serious complications arise. In a certain number of cases serious renal diseases may be induced, and in a considerable number of cases where the disproportion between circulating poisonous waste products and rectal excretory action becomes too great, the serious phenomena known as eclampsia supervene, the woman's life being greatly endangered.

As might be expected, a number of workers have advanced the view that the main factor in producing the toxemia of pregnancy is microbial infection. Some have found germs in the blood, some in the kidneys, others in the placenta. In some cases cultures injected into animals produced general toxemia and changes in the kidneys resembling those found in the altered kidney of pregnancy. Other workers have obtained negative results.

While it is impossible, at the present time, to postulate any well-ascertained results regarding the relationship of micro-organisms to the toxemia of pregnancy, in view of such experiments as those of Doléris and Poney, Blanc, Favre, Gerdes and others, and in the light of Adami's recent work on subinfection, it can not be denied that in some cases of pregnancy-toxemia, the important agent may be some form of microbe, and that in their effort to destroy and remove the organisms, the kidneys may be so affected as to undergo the pathologic changes to which I have already referred, with consequent accompanying alterations in the urinary secretion.

Finally, after reviewing the most important theories advanced by those who have worked in this difficult sphere, it must be admitted that much is to be said in favor of each. Indeed, it is highly probable that something of the truth is contained in all of them, that in most cases no single factor is causal, but rather a combination of various factors, these varying greatly in different instances. The most important of these is undoubtedly the toxic element. Only from such a standpoint is it possible to group into an intelligible synthesis the heterogeneous clinical phenomena and physical changes found in the abnormal condition of pregnancy under consideration.

Nephritis.—Where true nephritis exists before or begins in pregnancy, the disease, as a rule, is a more serious matter than in the non-pregnant state and the prognosis is unfavorable. In the case of chronic nephritis, an acute exacerbation is usually induced. The patient may die from kidney failure, and uremia is very apt to occur. Only in a small percentage of cases are the phenomena of eclampsia noted, as has been pointed out by Fehling and Leyfert.

As regards the influence on the course of pregnancy the tendency to premature emptying of the uterus is to be particularly noted. According to P. Müller it occurs in more than 40 per cent. of cases. It is attributed to various causes, viz.: hemorrhages into the placenta, causing infarcts and destruction of portions of the chorionic villi, or separation of the placenta. The fetus may die as a result of the accumulation of toxic material in the system, and this is an important cause of the premature expulsion. The fetal mortality is very high. Hofmeier noted that the fetus died in twenty out of twenty-three cases of nephritis. Braun has estimated the mortality at 80 per cent.

Treatment.—The treatment of a pregnant woman with symptoms pointing to disturbed renal functions is to be carried out on the lines followed in the non-pregnant state. The strictest watchfulness on the part of the physician is necessary. With regard to the question of allowing the pregnancy to continue, it is difficult to decide. There are, however, certain indications which point imperatively to the induction of premature delivery, in the interests of the mother, viz.: visual disturbances, and continued headache, pulmonary or other marked edema, marked cardiac disturbance, frequent nose-bleedings, continued increase in the casts and albumin in the urine, uremia. In a number of cases the woman may respond to treatment so satisfactorily as to go to full term and be delivered of a healthy child.

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DISCUSSION.[1]

DR. JAMES B. HERRICK said, with reference to the patchy character of the renal changes, that it seems to him that this offers a possible explanation in some cases of so-called functional albuminuria. It is difficult to explain why in certain cases patients have albumin in the urine at a certain hour of the day, after a little exertion, after a particular kind of meal, etc., and yet it is conceivable that in some of these cases only very small areas of the kidney are diseased. These areas are not extensive enough to produce the cardiovascular changes that accompany nephritis.

As to the paper of Dr. Webster, it seems more probable that toxemia has more to do with the production of albuminuria of pregnancy than has pressure, and the facts cited by Dr. Webster lend color to that theory. The carelessness regarding excretion through the skin in pregnancy; the very commonly-met-with constipation; the increased and altered metabolism; the very commonly-met-with digestive disturbances of the stomach and of the intestines, and the fact that the pregnant mother has to eliminate for the child as well as for herself, etc., all lend color to the toxemic theory and make it more attractive than the pressure theory.

Referring to the treatment, Dr. Herrick confessed that the more of these patients he sees, the more it is impressed on him that it is a safer procedure to empty the uterus early. Senator's definition of functional albuminuria was given. On the slightest increase in the albuminuria, in spite of treatment, on the indication of uremic manifestations, whether they be in the form of a persistent headache, amaurosis, nausea and vomiting, or what seems to him a valuable and significant symptom, a severe epigastric pain, even without nausea and vomiting, on the appearance of edema of the face, which can not be ascribed to pressure, he believes it is always a safer plan to empty the uterus. While this may not be in accord with the teachings of obstetricians, yet he has never regretted emptying the uterus early.

Speaking of the paper of Dr. Davis and of the etiology of nephritis, he believes the intestinal tract is frequently at fault. This fits in with the toxemic theory of the origin of many cases of nephritis. The diet depends not so much on the percentage of albumin that may be in the food as on the way in which the alimentary tract handles the food. In other words, the diet should depend more on the condition of the alimentary tract than on the food itself.

Referring to the intermittent administration of milk as a diet in chronic diffuse nephritis, he spoke of an acquired tolerance of the kidneys for certain kinds of food. We have a patient, for instance, with chronic nephritis, who is constantly passing albumin; on feeding him with certain kinds of food the amount of albumin increases. On the other hand, put the patient to bed, give him a very restricted diet—a pure milk diet—for a time, and the amount of albumin begins to diminish. The kidney is having a rest, and after a rest of three or four, or possibly six or eight, weeks the patient tolerates articles of food that he could not before tolerate. He can now be given a mixed diet, with perhaps a liberal amount of meat, and the percentage of albumin will not be increased in a way that it would be formerly.

DR. N. S. DAVIS, JR., in closing, said that his attention had been drawn to the effect of the condition of the alimentary tract in the production of albuminuria and the appearance of tube casts in the urine, because of the frequent finding of either tube casts alone, or albuminuria alone, or the two combined, in all sorts of maladies in the more acute stages. However, this condition is usually transitory. There is not really produced a genuine nephritis in these cases, but simply a moderately disturbed functional activity of the kidney, and yet enough to produce these symptoms. He has seen them repeatedly in connection with digestive disorders, and in connection with simple and chronic bronchitis, as well as other maladies observed in hospital practice. A study of the records of hospital laboratories would reveal the fact that in a large proportion of the patients who enter hospitals traces of albumin, or tube casts, are found, which disappear—at once, and usually permanently—from the urine as soon as the intestinal tract is thoroughly emptied and the patients are placed on a simple diet that is well assimilated and well digested by the stomach and bowels. These facts have impressed on him the relationship of the condition of the alimentary tract and digestion to the production of nephritis. It is not the only cause, but simply one of the causal factors of renal troubles.

[1] The paper by Dr. N. S. Davis, Jr., was printed elsewhere and is abstracted in our Current Medical Literature Department, this week, p. 72.