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ORIGINAL ARTICLES.

LITHIASIS IN PREGNANCY.

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When honored by an invitation to contribute a paper to the proceedings of the Obstetrical Section of the American Medical Association, I was anxious to select a topic which, while possessing some novelty and belonging to the wider domain of General Medicine, might be useful and pertinent to the subjects within the province of this department.

It is some years since first I observed the frequent manifestations of certain symptoms during pregnancy, and their subsequent persistence, that could be explained most satisfactorily by ascribing them to the influence of the lithic acid diathesis. Additional observation and reflection having satisfied me that the association was more than coincidental, I have concluded to submit my speculations to the consideration of this Section. That many observers have noticed the association of lithiasis with pregnancy is beyond question, but I am not aware of any attempt to present the facts and inferences in continuity. It is not so evident, either, that the profession generally has recognized the affiliation or the tendency which the phenomena of gestation have to develop this dyscrasia. My intention is to review the characteristics of lithiasis, their analogous manifestations in pregnancy with the physiological processes in the last-mentioned which favor their development, and thus I shall endeavor to establish a definite relation between the two conditions.

For the sake of continuity I will briefly recapitulate a few generally recognized principles concerning lithiasis. It is a diathesis associated with the presence of an excess of lithic, or uric acid in the system, and made manifest by very varied phenomena, affecting almost every structure and function. Uric acid is derived from the proteid tissues and from the albuminous or nitrogenous foods. The manner of the formation of uric acid is a subject as yet involved in much obscurity, but it is generally conceded that, when it exceeds the normal quantity, marked disturbance of the structure or the functions of one or more important organs is the result. Primarily or second-

arily the liver, stomach, kidneys, nervous system, lungs, and the blood are severally or collectively involved, although in many instances no departure from the normal condition can be detected in some one or more of these factors. Lithiasis is intimately associated with those important excrementitious substances, urea and the urates, which result from and, other things being equal, represent in constant proportions the constructive and the destructive cell-changes of the system. The intermediate link between the presence of uric acid and the manifestations of lithiasis is the deposition of the former in the affected tissues or of the salts produced by its combination with some of the inorganic elements, notably that with sodium. The resulting disturbance of the functions or the nutrition of the invaded organs produces the symptoms of the diathesis, and verily their name is legion.

The specific gravity and the alkalinity of the blood is diminished and the excrementitious matters, especially the uric acid and the urates, are increased in quantity, the alkalinity of the blood is less than normal and the fibrin is increased. The objective symptoms of anæmia also are frequently present and, naturally, they are associated with a reduction of the red corpuscles. The results of these abnormal conditions of the blood are very numerous, eczema, pruritus, phlebitis, neuralgia, myalgia, œdema and dropsy being prominent among the many. In the vascular system the arterial tension is increased and cardiac hypertrophy, simple or complicated, is a frequent consequence. Palpitation, irregularity of action, syncope and other diseased cardiac conditions are often present.

It is reasonable to suppose that respiration is involved in an important manner, as uric acid is the result of arrested oxidation of the nitrogenous elements which otherwise are convertible into the easily eliminated urea. The most frequent examples of disturbance of the respiration are dyspnoea, irritable cough and hiccough.

The connection between lithiasis and the digestive system is close, and its manifestations are marked and frequent. Without dwelling upon the causal influence of gastric acidity and imperfect digestion, we must notice their frequency in lithiasis. The various actions and secretions are deranged, producing morbid appetite, gastralgia acid and other eructations, nausea, vomiting, irritative diarrhoea or constipation, tympanites, hæmorrhoids, and several other symptoms.

The liver suffers more from functional than from structural derangement, although inflammatory changes are not infrequent. We must not forget that one of the best sustained theories of lithiasis attributes this morbid condition to the functional disturbance of this organ, and we also witness biliousness, jaundice, and hepatitis. That the spleen is involved in lithiasis is indicated by the constant presence within it of a large quantity of uric acid.

The relation between lithiasis and the kidneys is universally recognized, although in some rare instances no structural changes can be detected. As a rule, however, some of the varied phenomena of inflammation, from hyperæmia to cirrhosis, degeneration or a deposition of the solid constituents of the urine can be demonstrated, and the character of that fluid is greatly and variously modified. The phenomena associated with the urinary organs are too numerous to be detailed, but in definite relation with lithiasis are abnormal polyuria and diabetes, suppression and retention of urine, irritable bladder and cystitis.

Numerous nervous phenomena appear in lithiasis which may be collectively attributed to the development of increased irritability and malnutrition. Psychological, sensational, spasmodic and trophic phenomena are constantly witnessed and appear to stand convertibly as cause and effect with the disease. Manifestations of these nervous perturbations are frequently witnessed in the form of convulsions, cramps, myalgia, neuralgia, hysteria and mental aberration.

The changes produced by lithiasis in the skeletal structure and those of the connective tissue series generally, are characteristic. The bones suffer by the formation of nodes, laminae and exostoses, the ligaments and fasciæ by the deposition of the urates and the consequent inflammation, contraction and rigidity. The synovial membranes are affected with inflammation, adhesions and induration.

The influences which predispose to lithiasis are many, and it would appear that a marked departure, either idiopathic or acquired, from the normal standard of the function of any important organ determines its development. It is also significant that the influence of a single manifestation of lithiasis is liable to be followed by serious and far-reaching consequences, indicating the establishment of the diathesis.

If we now turn our attention to the phenomena of pregnancy, we cannot fail to observe a remarkable coincidence between the diseases as well as the pathology of that condition and of lithiasis. All those features to which I have alluded when reviewing lithiasis are frequently seen in pregnancy. The structural changes which are present in the former are of common occurrence, and the physiological conditions of gestation are favorable to its development. In the etiology of the two classes of diseases the parallel is sustained, as in both we have the same hæmic influences, the same irritable or "explosive" state of the nervous system, and the same renal and digestive disturbances. In pregnancy we find additional and potent factors in the increased metabolic energy, and the mechanical conditions which, if present in a lithæmic individual, would most prob-

ably contribute to the development of the disease. Those morbid conditions which are ascribed with the greatest confidence in pregnancy to the mechanical factors, as venous dilatation, œdema of the lower limbs and the genitals, hæmorrhoids, retention and irritable bladder, are frequently seen also in gouty males and non-pregnant females.

The condition of the maternal blood in gestation is in keeping with the physiological relation which exists between the mother and the development of the fœtus. The cell changes of the composite animal are increased proportionately with the growth of the fœtus and the containing uterus. The fœtal organs, with the exception of the heart and liver, are practically inert, and the double duty is imposed on the corresponding maternal organs. The medium through which these additional functions are performed is the maternal blood, and consequently the quantity of the nutritive and the excretory substances conveyed by that fluid is necessarily increased and, owing to the greater constructive and metabolic energy exerted during the process of development, increased most probably in more than in the ratio of the dimensions of the utero-fœtal mass to the mother. The chief nutritive and excretory matters circulating in the blood are nitrogenous and inorganic, and consequently are most conducive to the development of lithæmia, as well as of puerperal septicæmia, eclampsia, peritonitis and thrombosis. The alkalinity of the blood which is so essential to the solution of the lithic acid compounds is diminished. Owing to the reduction of the number of the red corpuscles, together with the constant absorption of the nutritive materials by the exacting fœtus, hydræmia frequently exists. The consequent tenuity should be additionally favorable to the deposition of the uric acid and the urates. The increased quantity of fibrine which has been observed during gestation may afford a clue to some cases of cardiac disease, as well as to the not unusual occurrence of embolism and thrombosis. It may be permissible to speculate upon the possibility of those conditions, which the fœtal fluids would naturally share with the maternal blood, affording a clue to the etiology of some of those obscure cases of intra-uterine deformities and disease, as well as of congenital cardiac lesions and adherent placenta, depending upon plastic and inflammatory changes of the serous and enveloping membranes of the fœtus.

In the vascular system the most constant results of pregnancy are the increase of the arterial tension and of the cardiac action. The cause of these conditions in the earlier months of gestation is rather obscure, but as pregnancy advances it becomes very obvious. The increased quantity of fluid which the heart must propel, the augmented functional activity of the kidneys and the other maternal organs, the additional resistance which is offered by the utero-placental circulation, which may be largely due to the osmotic process in the placental circulation during the interchange of the maternal with the fœtal blood, all contribute to throw more labor upon the heart. This organ is stimulated to greater rapidity of action in the entire 24 hours by the profuse cell

changes in the nutritive and excretory organs of the two systems and by the elevation of temperature in the uterine circulation. I may mention incidentally that the abeyance of the phenomenon of the decrease of the beats on the assumption of the sitting or the recumbent posture has been recently proposed as of diagnostic value in cases of obscure pregnancy, which I have verified as early as the second month. The result of the additional strain is conservative hypertrophy of the heart. The form of hypertrophy is a matter of speculation, and whether it is simple or eccentric is a question of interest both to the physiologist and to the physician. Another natural result of this condition is the more forcible action of the heart and an increase of the violence with which the valves and the other mechanical structures perform their functions. This violence is liable to produce local inflammation at the points of areas of valvular impact or contact and at the sites of traction of the chordæ tendinæ. These localities are thus prepared for the deposition or the infiltration of the morbid elements of the blood, with consequent stenosis and valvular insufficiency. The resulting irregularity or roughness of the endocardium also affords a suitable surface for the deposition of the so-called "vegetations" to which the excess of fibrine is peculiarly favorable. These conditions may be independent, or associated with the results of the hypertrophy, which may be followed, like the uterus, by normal involution or the analogous conditions of subinvolution, or that which is rarer, superinvolution, thus producing simple or complicated cardiac hypertrophy or weakness with or without dilatation. Again, if the process of involution be rendered abnormal by the presence of lithiasis or some other disturbing influence, the result may be fatty, calcareous or other cardiac or vascular degeneration. To the last specially mentioned condition the discovery of lacunæ of calcareous matter in the organism of the pregnant female would indicate a special tendency. The heart suffers mechanically also during gestation by the encroachment of the gravid uterus on the thoracic cavity, as is evidenced by the palpitation which is sometimes produced when the pregnant female assumes the recumbent position, and which is rapidly relieved by change of posture.

The influence of gestation upon the respiration is not as distinct as upon the other functions, but although a certain compensatory change occurs in the shape of the thorax by its increased antero-posterior and transverse dimensions, it is obviously disturbed by the growth of the uterus, and the inspiratory and expiratory movements must be diminished. The most marked change in the expired air is due to the increased elimination of the carbonic acid, and probably of the water which is a natural consequence of the respiratory needs of the second organism. The most frequent disturbances of respiration are dyspnoea, hiccough and irritable cough. A particular interest is attached to the fact that physiologists have recently localized the centre which is supposed to preside over the formation of uric acid at a point close to the respiratory centre in the floor of the fourth ventricle. That this has any practical bearing upon

our present investigation is not very evident, but when the principal difference between uric acid and urea is the lesser atomic combination of oxygen with the former, the relative position of the two centres may have some causal relation to the presence of the acid in pregnancy.

The phenomena presented by the chylopoëtic system in pregnancy are so numerous and important that we can only briefly indicate their relation to our subject. In the first instance we find that as gestation advances the pregnant woman generally consumes a greater quantity of food and of a more varied kind, a circumstance which is notorious for its association with the gouty diathesis. She also suffers from functional dyspepsia, cardialgia, eructation and vomiting. The success which so frequently follows the exhibition of anti-lithic remedies in such cases tends to indicate the nature of these disturbances. The intestines furnish us with additional links for our chain of evidence by the occurrence of diarrhœa, often of an irritative character, and of constipation symptoms which are frequent in lithiasis.

The hepatic disturbances are additionally interesting owing to the weight of evidence which has been adduced to convict the liver of being the chief offender in the production of the lithiasis. There is undoubtedly more than a causal relation between pregnancy and hepatic disturbance as is evidenced by the frequency of pigmentation and jaundice, acute yellow atrophy of the liver, a disease which is associated with gestation with significant frequency. This fatal disease, as well as some other hepatic lesions, is additionally interesting in our present speculation owing to its causal relation, which it shares with pronounced lithiasis or gout, to grave nervous depression, emotional disturbance and bad hygienic surroundings.

The mechanical influence which the gravid uterus exerts on the digestive organs is easily recognized with regard to the gastro-intestinal tract, but unless obstructive jaundice is produced in the later months of gestation by the traction of the biliary ducts consequent upon the upward displacement of the liver, it is difficult to recognize it as an important factor. It is hardly possible for the biliary ducts to be compressed in the carefully protected position which they occupy, first, in the transverse fissure of the liver, guarded by the lobulous quadratus and in front of the vena cava, then in the lesser omentum behind the duodenum, and lastly, between the heart pancreas and the second portion of the duodenum. It is more probable that this phenomenon is the result of direct pressure upon the liver, or some coincidental disturbance attributable to the dyscrasia or to an occult reflex nervous influence. So little is known of the spleen and its relativities that we cannot expect to establish a definite connection between it and the diseases of gestation, but in that rare disease, leucocythæmia, we find that a very large proportion of the cases occurring in females are associated with pregnancy.

The influence of gestation upon the urinary organs is very marked owing to their anatomical association as well as to the important duties which they perform as the chief emunctories of the system. The quan-

tity of urine is notably increased and the total amount of the excreted solids is greater than in the non-pregnant state. The changes which take place in the kidneys vary from slight and transient hyperæmia to the acute and chronic parenchymatous nephritis of pregnancy. Almost all the pathological changes to which the kidneys are liable are associated with gestation, but those which are most frequently present are such as are usually found in lithiasis. It has not been demonstrated that renal hypertrophy accompanies normal gestation, but from analogy with the conservative changes which take place in the abiding organ when one kidney has been extirpated, or destroyed by disease, we would expect to find compensatory enlargement owing to the greatly increased functional labor of these organs. We are familiar with the idea that renal disease is easily induced in those individuals upon whom nature has bestowed organs which are barely adequate to their ordinary necessities. When any unusual strain is put upon them by exposure, disease, rapid increase of weight, or overwork, the mediocre organs fail, and we have another example of the close relation which exists between weakness and irritability or disease. That such a strain is considerable in pregnancy is very obvious, arterial tension is increased, the amount of solids and fluid passing through the organs is greater, of the total vital force they experience a diminished influence and the disastrous results are only too frequent. It is very probable that the so-called puerperal diseases of the kidneys originate during gestation, and that the evil effects have only culminated when the additional strain of parturition is imposed upon the diseased and incapable organs.

The theory of the mechanical influence of the gravid uterus by its pressure on the renal veins has been ably refuted by more than one observer, with whom, upon anatomical grounds, I entirely agree, but I consider it more than probable that the ureters are subjected to such interference in the lower portion of the abdominal cavity where they lie on the psoas muscles or in the cavity of the pelvis in close contact with the cervix uteri, and where every modification of position and dimension must produce mechanical effect. The results following the ligation of the ureters in the inferior animals, which produces grave structural changes in the kidneys and the copious accumulation of the urates and uric acid in the blood and the tissues generally, clearly indicate the consequences of any mechanical obstruction. This is most liable to occur in the later months of pregnancy or during parturition, and it may explain the appearance of eclampsia and other acute disorders, especially in difficult or tedious labors. The remarkable absence of the elevation of the general temperature during the greatly increased metabolic activity of pregnancy, and notwithstanding the fact that the uterine temperature is higher than that of the system, may have some connection with the great depression of vital heat observed after ligation of the ureter.

The nervous system is peculiarly prone to abnormal manifestations during pregnancy. The influence of this system over all other organs of the body and their reciprocal effects are too well known to require

more than a cursory notice. Morbid conditions of the blood exercise a marked effect upon the nervous phenomena owing to the consequent mal-nutrition of the delicate nervous structures, and this may account for the frequency of nervous perturbation during gestation. These nervous lesions which appear to have an etiological relation to this condition have already been mentioned in connection with lithiasis, but it is difficult to determine the proportion of causality to be attributed to the one and the other of those indissolubly associated or reciprocal factors. The frequency of insomnia is interesting and may constitute a clue to the investigation of the purely nervous group of symptoms. In the vomiting of pregnancy the closest investigation frequently fails to discover any cause other than a nervous influence, the nature and relations of which I have already discussed at some length in a paper entitled, "Causality in Disease," which appeared in the *Boston Medical Journal*, of April 15, 1886.

I shall briefly refer to the conditions of the muscular and skeletal structures which we witness in pregnancy. That condition which is termed mollities ossium, which is closely associated with child-bearing, is peculiarly interesting as evidencing the powerful influence of the nutritive demands made by the fœtus on the maternal system. In this disease the inorganic elements being supplied in deficient quantity by the digestive system of the mother, are absorbed from her bones and carried by the blood to the placental circulation. The presence of rheumatoid and other arthritic lesions are notably frequent during the child-bearing period and their occurrence after gestation is often observed. The relation between these diseases and lithiasis is generally recognized and affords additional testimony in favor of the nexus which I am endeavoring to demonstrate. The frequency of muscular rheumatism and spasm, or cramp, is also notable, and their association with lithiasis is well established.

As in the *résumé* of lithiasis I wish to recall the persistent effects upon the system caused by the occurrence of a single pregnancy which manifesting themselves by various lesions not to be ascribed to any other other influence and indicating the permanent adoption by the constitution of a morbid action which must be regarded as being closely related to lithiasis. In endeavoring to establish a parallel if not an identity between the constitutional tendency produced by lithiasis and pregnancy, I have indicated that both originate in a grave disturbance of nutrition, they present a similar modification of the blood; the pathological changes bear a close resemblance; the prominent functional disturbances are broadly identical; the numerous sequelæ are similar; and lastly, after one or more visitations the constitution is prone to adopt the induced condition as a diathesis.