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The candidate

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CONTENTS

INTRODUCTION

Pregnancy is a major event in the life of women, this event could be a happy one. Unfortunately this happiness is usually clouded by many troubles which render pregnancy a heavy burden and a source of pain and weakness.

Urological troubles are responsible for a major part of these ones; hence the importance of our work. Our aim is to review the literature about this subject "Urinary Tract Problems During Pregnancy" to study it in detail and to shed light upon the practical applications of these hard and fast scientific data,aiming at last to lessen the sufferings of our female patients,making pregnancy safe and painless experience and also and above all to save the urinary system from permanent damage which may persist even after the termination of pregnancy.

Urinary tract infection comes on the top of the list of this kind of troubles, actually this subject, in particular, received a major concern in the essay.

Also this study included the subject of urinary lithiasis which, during pregnancy,constitute a major diagnostic and therapeutic challenge.

Hypertension is a serious event during pregnancy due to its obvious relation to toxemia of pregnancy,again this study is handled in detail.

Renal failure is not uncommonly encountered during pregnancy on diverse conditions, dealing with this serious situation is dealt with in this study.

Finally we ended our study by the situation of pregnancy in transplant patients, which is a rare finding but a very curious situation indeed

CHAPTER [I]

UROLOGICAL CHANGES DURING PREGNACY.

Anatomical changes.

physiological changes.

A- ANATOMIC CHANGES

The anatomic relationship of the genital and urinary tracts is intimate because of their common embryologic origin. Thus, conditions affecting one system often exert an influence on the other.Pregnancy,which is the most common genital tract condition in the female,is associated with substantial morphologic change in the urinary tract.Various parts of the urinary tract are affected.

1- KIDNEY:

Renal length increases approximately 1cm during normal pregnancy . It is thought that this does not represent true hypertrophy but it is the result of increased renal vascular and interstial volume. No histologic changes have been identified in renal biopsies (Waltzer, W.C: 1981) (Cietak and Newton 1985 a,b).

2-RENAL PLVIS AND URETER:

A- Pyelo ureteral dilatation :

It represents the most striking morphologic effect of pregnancy on the urinary tract .First recognized in autopsy studies performed more than 200 years ago,the effect has been confirmed repeatedly by roentgenographic and sonographic techniques.the term physiologic hydronephrosis and hydroureter of pregnancy has been applied widely,emphasizing both the frequency of the changes and their apparent normalcy.

Characters:

a-Onset and course:

Studies using intravenous urography usually have indicated that pyeloureteral dilatation appears abruptly at approximately 20weeks' gestation and both the incidence and severity remain essentially constant from 20 weeks until term (Schulman and Herlinger,1975) Relatively rapid postpartum resolution is the rule, with most of the changes returning toward normal within 48 hours of delivery ,although several weeks may be required for complete resolution (Harrow et al.,1964).

More recent studies using ultrasonic measurement of the kidney and renal pelvis have suggested a pattern of onset and progression somewhat different from that based on earlier radiographic studies.

Fried(1979) investigated a large number of asymptomatic gravidas at various stages of gestation;he observated an onset during the first trimester in a substantial proportion and a tendency toward increasing severity with progressing gestation.

b- Site :

The change typically involves the renal pelvis and upper two thirds of the ureter (i.e.,above the brim of the bony pelvis),whereas the pelvic ureter is involved rarely if at all (Schulman and Herlinger,1975).

c-Side:

A major characteristic of pyeloureteral dilatation is the preponderance of rightsided involvement *Schulman and Herlinger (1975)* examined intravenous urograms of 200 patients in the last half of pregnancy and noted the right side to be fuller than the left in 85.7% compared with only 10% in whom the left side was fuller.Additional observations on the side of involvement are summarized in table (1).

(TABLE 1)

		Normal	Mild	Moderate	Severe
First trimester	(N=18)	39%	61%	0	0
Second trimester	(N=90)	31%	49%	20%	0
Third trimester	(N=110)	30%	45%	22%	3%

(Data from ultrasound observations by Fried A.M. Hydronephrosis of pregnancy; Ultrasonographic study and classification of asymptomatic women.Am.J. Obstet.Gynecol.135;1066,1979)

More than three fourths of patients were judged to have definite dilation on the right, an incidence twice that on the left. The average degree of right-sided dilatation estimated on an arbitrary scale was more than twice that on the left, and the proportion of subjects with severe changes exhibited a fourfold preponderance of right over left.None of the subjects in this study, strictly speaking, had normal pregnancies since all had some clinical indication for intravenous urography.However, the most common reason for investigation was ntepartum bleeding, a condition not likely to be associated with inherent urinary tract defects, whereas patients known to have previous or subsequent urinary tract disease were excluded. therefore, the data can be accepted as representative of a normal population.

The right-sided preponderance of urinary stasis and pyelocalyceal dilation has been confirmed and characterized by longitudinal sonographic studies by *Cietak and Newton (1985 a, 1985 b)*, whose findings are summarized in Table(2).

TABLE (2) QULITATIVE CHANGES WITH PREGNANCY (RIGHT KIDNEY/LEFT KIDNEY)

	No Change (%)	Stasis(%)	Hydronephrosis (%)	Hydronephrosis with Clubbing(%)
Weeks				
12	75/86	25/14	—	---
16	51/77	46/23	3/0	---
20	11/43	74/57	14/0	---
24	6/44	47/44	41/9	6/3
29	3/24	30/61	33/12	33/3
32	3/17	40/63	17/13	40/7
36	3/18	33/64	15/12	49/6
Postpartum				
2 Days	12/24	52/73	15/0	21/3
6 Weeks	31/53	69/47	—	—
12 Weeks	25/75	46/54	---	---

(Adapted with permission from Cietak and Newton, 1985.)

Although evidence of stasis was observed in some subjects as early as 12 weeks, actual hydronephrosis did not appear until after 20 weeks and was four to five times more frequent on the right than on the left.

The explanation for the right-sided preponderance of pyeloureteral dilatation, although uncertain, has been attributed to dextrorotation of the uterus or a cushioning effect of the sigmoid colon on the left.

Significance:

Upper urinary tract dilatation has several functional and clinical effects. *Bergstrom (1975)* used isotopic renography in patients in late pregnancy with entirely or predominantly right-sided hydronephrosis and hydroureter and found a nearly fivefold increase in time to peak excretion on the right compared with on the left. However, in the majority of cases, the ratio of pyelographic dead space on one side to that on the other was at least as much as the ratio of calculated excretion rates, indicating that any renographic delay is due to a reservoir effect of the dilated urinary tract rather than to a reduction in urinary flow on the affected side. Thus, urinary stasis does not appear to be a necessary concomitant condition. from a clinical point of view, the increased incidence of urinary tract infection during pregnancy often has been ascribed to pyeloureteral dilatation. However, attempts to relate the incidence and severity of upper urinary tract changes to symptomatic or asymptomatic infection have been unsuccessful *(Schulman and Herlinger, 1975)*.

Symptomatic hydronephrosis in the absence of infection has been reported to respond to ureteral catheterization *(Nielsen and Rasmussen ,1988)*.A very rare complication is acute renal failure due to bilateral ureteral obstruction *(Rasmussen and Nielsen, 1988)*.

Etiology:

The etiology of gestational pyeloureterectasis has been the subject of considerable controversy. two basic causes-endocrine and mechanical-have been proposed as primary etiologic agents, and each has its advocates.*Fainstat (1963)* reviewed the literature and concluded that the primary cause was hormonal in nature, with partial and intermittent ureteral obstruction probably contributing "in an important secondary role." In reaching this conclusion, Fainstat drew heavily on in vitro studies demonstrating diminished ureteral tone and contractility with addition of progesterone and gonadotropin as well as on animal experiments indicating ureteral dilation with various endocrine manipulations. Because of the common embryologic origin of the uterus and urinary collecting system from the urogenital ridge and the well-known ability of progesterone to inhibit uterine motility, he suggested that progesterone and perhaps gonadotropin were primary factors. He also speculated that estrogen might be involved by virtue of its growth-promoting and interstitial fluid-retaining properties,although this hormone tends to stimulate smooth muscle contractility.

Prostaglandins also have been suggested as a mechanism for producing dilatation of the upper urinary tract. prostaglandin E has been demonstrated to inhibit ureteral contractility in animals (Boyarsky et al.,1966).

A review by *Rasmussen and Nielsen (1988)* noted a number of factors arguing against a cause that was primarily endocranial (and therefore in favor of mechanical factors); the abrupt onset at midgestation, the sharp limitation to the portion of the ureter above the pelvic brim, the right-sided preponderance, and the customarily prompt resolution with delivery. these authors concluded "that it is extremely probable that the pregnant uterus compresses the ureters, and thus is the only cause of physiological hydronephrosis during pregnancy."

Studies of intraureteral pressure relationships have indicated that advancing pregnancy is accompanied by progressive increases in contractile pressure and tonus (but not in contraction frequency) in the upper ureter, whereas these same parameters remain low in the pelvic ureter *(Sali and Rubi,1967)*. Furthermore, when a pregnant subject lies on one side, the intraureteral tone of the opposite ureter decreases while that of the same ureter remains high *(Rubi and Sali, 1968)*.

Certain clinical observations also tend to support mechanical obstruction as a primary feature. Hydronephrosis and hydroureter,although common in gravidas with normally situated kidneys, do not occur in pregnant women with pelvic kidneys *(Johnson et al.,1967)*. Furthermore, complete ureteral obstruction by a greatly overdistended uterus can occur, albeit rarely *(O'Shaughnessy et al., 1980)*

Historically, mechanical theories invoking ureteral compression at the pelvic brim by the growing uterus usually were accepted until about 35 years ago, when endocrine factors began to receive greater emphasis. However, during recent years there appears to have been a swing back toward obstruction as a basic mechanism, and two new theories involving variations on the mechanical them have been proposed. *Dure-Smith (1970)* described a filling defect called the iliac sign on intravenous urography that was thought to represent ureteral compression by the iliac vessels.The right-left difference was explained by the observation that the right ureter tends to cross over the common iliac artery, whereas the left is more likely to lie on the less rigid vein. In addition, the course of the right ureter was said to be more at a right angle to the iliac vessels than is the course of the left ureter.On the basis of autopsy dissections, intravenous urography, and pelvic venography, *Bellina and associates (1970)* described dilatation of the right ovarian vein complex during pregnancy and suggested that this anatomic change causes partial ureteral compression with resultant stasis.However, excision of the ovarian vein in other studies in subhuman primates did not affect the course of ureteral dilatation *(Roberts, 1971)*.

Although neither mechanical nor endocrine factors alone appear adequate to explain all of the observed characteristics of pyeloureteral dilatation during pregnancy, the bulk of the evidence appears to favor partial ureteral compression by some structure (uterus,iliac artery, or ovarian vein) as the primary mechanism, with endocrine effects playing a contributory role.

b-Elongation of the urters :

Ureteral alterations less dramatic than dilatation also accompany pregnancy. The ureters tend to elongate and frequently exhibit increased curvature as a consequence. These curves actually are quite gentle when viewed three-dimensionally, but in the conventional two-dimensional urogram they may appear acutely angulated , leading to their customary (but inaccurate) designation as "kinks."

c-Lateral dislocation of the ureters:

The ureters also may be located more laterally than usual, probably as a result of elongation and displacement by the enlarging uterus . Lateral displacement is observed during the last half of pregnancy in 20% of cases on the left and 8% to 10% of cases on the right *(Schulman and Herlingr, 1975)* The right-left difference presumably reflects the position of the sigmoid colon between the uterus and the left ureter.

3- BLADDER

Because of its intimate anatomic relationship to the cervix and lower uterine segment, the urinary bladder is displaced anteriorly and superiorly as the uterus grows. Thus, as pregnancy progresses, the bladder becomes more of an abdominal and less of a pelvic organ. The base of the bladder also broadens, and with descent of the presenting part as term approaches,the cystoscopic appearance of the trigone changes from that of a concave to that of a convex surface. The bladder participates in the generalized hyperemia of the pelvic organs, and the mucosal surface often exhibits congestion and increased size and tortuosity of its superficial vessels. Some degree of muscular hypertrophy, presumably as a result of estrogenic stimulation, may be noted in histologic sections, but the effect usually is not evident cystoscopically.

Bladder capacity increases during pregnancy, apparently as reflection of the well known atonic effect of progesterone on smooth muscle.However,the extent of the change is unclear. *Mattingly and Borkow (1974)* described a progressive increase during the second and third trimesters to a capacity of 1L or more. *Rubi and Sala (1972)* recorded mean bladder volumes of 756 and 838 mL in nonpregnant and pregnant subjects,respectively,which is a statistically insignificant difference. These latter investigators also reported significantly less increase in bladder pressure with voiding in pregnant than in nonpregnant patients, although pregnancy did not influence resting pressures.

4- URETHRA:

Anatomic changes in the urethra are relatively minor, at least those occurring before parturition. Upward displacement of the bladder results in a tendency to lengthen the urethra. On urethroscopy,the mucosa appears congested and hyperemic cytologically,the transitional epithelium becomes more squamouslike under the influence of high estrogen levels.

Urodynamic studies by *Iosif and col-leagues (1980)* in nulliparous women in normal late pregnancy and again in the puerperium have documented gestational changes in lower urinary tract function.Urethral length, both absolute and functional, increased during late pregnancy.Maximal urethral pressure increased by an average 23 cm H_2O compared with a mean increase in bladder pressure of only 11 cm H_2O, leading to greater urethral closure pressure during pregnancy. These two effects-increased urethral length and elevated urethral closure pressure-both tend to promote continence.

B-PHYSIOLOGICAL CHANGES

Pregnancy causes alteration in homeostasis in virtually all systems, particularly the cardiovascular and respiratory systems, and in water and electrolyte control. The kidney plays a significant role in these homeostatic changes as a simple excretory organ as well as the organ responsible for coordination of homeostasis in the intact organism. Ideally, the changes in renal function in pregnancy should accommodate the needs of both mother and fetus through improved control of maternal excretion and recovery to provide the proper environment for the fetus and more accurate regulation than that normally achieved in the nonpregnant woman. Many of the physiologic variations of pregnancy, however, appear to conflict with the needs of the fetus and the mother; the recent development of non invasive methods of investigation of the cardiovascular and renal systems has provided a better understanding of the effects of the normal physiologic changes that occur during pregnancy.

1- GENERAL HEMODYNAMIC CHANGES:

Renal function is affected by changes in other systems, particularly by those that occur in hemodynamic control.

A) Blood Volume

Plasma and red cell volumes increase markedly early in pregnancy, but the increases are disproportionate.Plasma volume increases more than blood volume, obtaining its maximum of 40% between the 26th and 36th weeks. Red cell volume increases progressively throughout pregnancy, but only by 25% *(Chesley 1974)*.

B) Cardiac Output

Cardiac output increases in the first trimester and reaches a maximum of 30 to 50% between 24 and 28 weeks.Most of this increase in cardiac output is established by the end of the first trimester. The measurement of maximal cardiac output in prenancy depends on maternal posture.In the supine position,cardiac output is highest between 20 and 24 weeks;in the sitting and lateral recumbent positions,it is maximal between 28 and 32 weeks *(Ueland et al 1969)*.the increase in cardiac output is due to an increase in stroke volume resulting from the fall in total peripheral resistance.The mechanism for the change in resistance is not known,but it is not a result of increased uterine blood flow or metabolic demands imposed by the fetus *(Metcalfe 1974)*. Peripheral vasodilation is often clinically evident as palmar erythema and spider telangiectasias. As pregnancy continues, heart rate increases and the stroke volume decreases simultaneously to nonpregnant values (*Metcalfe 1974*).

C) Blood Pressure:

Mean blood pressure decreases early in pregnancy and. by the second trimester, diastolic levels are 10-15 mmHg lower than before the patient became pregnant *(MacGillivray et al 1969)*. Blood pressure then increases slowly, approaching prepregnancy value shortly before delivery since cardiac output rises quickly in the first trimester (reaching values that are 40 per cent greater than those before pregnancy) and remains relatively constant thereafter, the decline in blood pressure must be due to a marked decrease in peripheral vascular resistance. This is greatest in the uterine vasculature, which eventually develops into a large, low resistance shunt.However,other organ systems, especially the kidneys and skin, participate in the generalized vasodilation which is characteristic of normal pregnancy. The rise of blood pressure toward nonpregnant levels after the second trimester suggests that increasing vasoconstrictor tone is a feature of late normal pregnancy *(Gant et al 1980)* and if the clinician is not aware of this pattern of change diagnostic errors may ensue.

2- RENAL HEMODYNAMIC CHANGES:

A) Renal Blood Flow:

There is a marked increase in effective renal plasma flow (ERPF) during pregnancy. The pattern of the increase,however, is not completely understood because of the difficulty in obtaining precise measurements. The increased urinary dead space because of dilatation of the pelvis calyces and ureters (discussed before). Also, posture exerts an effect on renal hemodynamics. In the lateral recumbent position, gravidas have a higher renal plasma flow compared to results obtained in the supine,sitting,or upright positions.Renal plasma flow gradually rises during the first half of pregnancy, and in mid pregnancy is 60 % to 80 % greater than in the nonpregnant state. in the third trimester, it is approximately 50% greater than preconception values. *(Davison 1980)*.

B) Glomerular Filtration Rate:

Glomerular filtration rate (GFR) rises in pregnancy. It reaches a peak of 40-50 % higher than nonpregnant values between 9 and 11 weeks ,and is sustained until at least the 36th week. A relative paucity of published data exists after the 36th week. However, those data that exist do not indicate a significant decrease in GFR *(Davison 1980)*. In pregnancy, expressing GFR in terms of "permeter squared body surface area"is not appropriate,and its measurement is subject to the same errors as described above for renal plasma flow.

It should be noted that these changes occur before significant expansion of the maternal plasma volume, but at about the time of systemic arteriolar vasodilatation. They cannot be reproduced in experimental virgin animals by injections of progesterone or prolactin and the mechanisms of increased GFR and RBF in pregnancy remain unclear.

Elegant micropuncture studies in rats have demonstrated equal affer-