Renal and urinary tract physiology in normal pregnancy

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Literature review current through: Jun 2017. | **This topic last updated:** Jan 12, 2016.

INTRODUCTION — Normal pregnancy is characterized by profound changes in almost every organ system in order to accommodate the demands of the fetoplacental unit. This topic will review changes in the lower urinary tract and kidney.

URINARY TRACT CHANGES — Pregnancy affects both the kidney and the remainder of the urinary tract.

Increased renal size — Both kidneys increase in size by 1 to 1.5 cm during pregnancy [1]. Kidney volume increases by up to 30 percent, primarily due to an increase in renal vascular and interstitial volume. There are no histological changes or changes in number of nephrons, but the glomerular filtration rate is also increased (see 'Increase in GFR' below).

The renal pelvises and caliceal systems may be dilated as a result of progesterone effects and mechanical compression of the ureters at the pelvic brim (see 'Ureters' below).

Ureters — Dilatation of the ureters and renal pelvis (hydroureter and hydronephrosis) is more prominent on the right than the left and is seen in up to 80 percent of pregnant women [2]. These changes can be visualized on ultrasound examination by the second trimester, and may not resolve until 6 to 12 weeks postpartum.

The dilated collecting system can hold 200 to 300 mL of urine. The resulting urinary stasis can serve as a reservoir for bacteria, which may contribute to the increased risk of pyelonephritis in pregnancy. (See "Urinary tract infections and asymptomatic bacteriuria in pregnancy".)

Hydroureter and hydronephrosis in pregnancy have been attributed to hormonal effects, external compression, and intrinsic changes in the ureteral wall [3]. The following factors may contribute:

- High concentrations of progesterone reduce ureteral tone, peristalsis, and contraction pressure.
- More prominent involvement of the right ureter may be due to dextrorotation of the uterus by the sigmoid colon, kinking of the ureter as it crosses the right iliac artery, and/or proximity to the right ovarian vein.
- The vessels in the suspensory ligament of the ovary enlarge and may compress the ureter at the brim of the bony pelvis.
- Uterine enlargement may cause the ureters to become elongated, tortuous, and displaced laterally as pregnancy advances. In rare cases, compression of the ureters causes pain and true urinary obstruction, which resolves with placing the mother on her side, insertion of stents, and/or delivery [4]. (See "Acute kidney injury (acute renal failure) in pregnancy", section on 'Urinary tract obstruction'.)
- Hypertrophy of Waldeyer's sheath (the connective tissue that surrounds the ureters within the true pelvis) may prevent hormone-induced dilatation below the pelvic brim [5].

Pathologic obstruction (ie, by nephrolithiasis or stricture) will also lead to ureteral dilatation. It frequently results in flank pain, and can often be distinguished from physiologic hydronephrosis by radiographically or

sonographically visualizing the cause of the obstruction. (See "Nephrolithiasis during pregnancy".)

Bladder — The bladder mucosa is edematous and hyperemic in pregnancy. Although progesterone-induced bladder wall relaxation may lead to increased capacity, the enlarging uterus displaces the bladder superiorly and anteriorly, and flattens it, which can decrease capacity. Studies of bladder capacity during pregnancy have yielded conflicting results.

Vesicoureteral reflux — Bladder flaccidity may cause incompetence of the vesicoureteral valve. This change, combined with increased intravesical and decreased intraureteral pressure, appears to result in intermittent vesicoureteral reflux [6,7].

URINARY SYMPTOMS — Urinary frequency, nocturia, dysuria, urgency, and stress incontinence are common during pregnancy [8].

Frequency and nocturia — Urinary frequency (voiding >7 times per day) and nocturia (voiding ≥2 times at night) are among the most common pregnancy-related complaints, affecting 80 to 95 percent of women at some point during gestation [9-11]. Frequency appears to be multifactorial which is in part due to changes in bladder function and in part to a small increase in urine output (see 'Polyuria and diabetes insipidus' below) [9,12]. Urinary frequency typically begins in the first trimester; thus, mechanical compression of the bladder by the enlarged uterus is not likely to be the primary cause.

Nocturia is common and increases with advancing gestation. In a survey of 256 pregnant women, 86 percent reported nocturia by the third trimester, with 20 percent of women indicating they voided three or more times nightly [13]. The major cause of nocturia appears to be that pregnant women excrete larger amounts of sodium and water during the night than nonpregnant women [14]. In the latter stages of pregnancy, this may be partially attributable to nocturnal mobilization of dependent edema in the lateral position.

Urgency and incontinence — Several studies have described an increase in urgency and urinary incontinence during pregnancy [12,15,16], which may be due to uterine pressure on the bladder, hormonal effects on the suspensory ligaments of the urethra, and/or altered neuromuscular function of the urethral striated sphincter [8,12,17,18]. Treatment includes pelvic floor muscle training. (See "Treatment of urinary incontinence in women", section on 'Pelvic floor muscle exercises (Kegel exercises)'.)

Urinary incontinence during pregnancy is associated with an increased risk of persistent incontinence six months postpartum. Pregnancy- and delivery-related urinary incontinence is reviewed elsewhere. (See "Urinary incontinence and pelvic organ prolapse associated with pregnancy and childbirth".)

Postpartum changes — The bladder and urethra inevitably experience some trauma during labor and delivery. The traumatic changes include mucosal congestion and submucosal hemorrhage, which are most evident at the trigone [19].

Bladder sensitivity/sensation is also decreased from trauma. As a result, detrusor atony, increased postvoid residual urine, bladder overdistention, and urinary retention are frequently encountered in women in the first few days after delivery. These symptoms are typically mild, transient, and completely reversible.

RENAL HEMODYNAMICS — Normal pregnancy is characterized by widespread vasodilation, with increased arterial compliance and decreased systemic vascular resistance (figure 1). These global hemodynamic changes are accompanied by increases in renal perfusion and glomerular filtration rate (table 1). In late gestation, assumption of the left lateral position is associated with increases in glomerular filtration rate and sodium excretion [20].

Humoral factors that contribute to volume regulation during pregnancy and cardiovascular and hemodynamic changes related to pregnancy are discussed separately. (See "Maternal endocrine and metabolic adaptation to pregnancy" and "Maternal cardiovascular and hemodynamic adaptations to pregnancy".)

Several authors have published normal reference ranges for laboratory results in pregnant women, which vary slightly [21-23]. The following table represents one example (table 2).

Increase in GFR — Glomerular filtration rate (GFR) rises markedly during pregnancy, primarily due to elevations in cardiac output and renal blood flow. Studies in both rodents and humans suggest that the increase in GFR results from enhanced glomerular plasma flow, rather than increased intraglomerular capillary pressure.

The increase in GFR is observed within one month of conception and peaks at approximately 40 to 50 percent above baseline levels by the early second trimester and then declines slightly toward term [24]. Renal blood flow increases by 80 percent above nonpregnant levels.

The physiologic increase in GFR during pregnancy results in a decrease in serum creatinine concentration, which falls by an average of 0.4 mg/dL (35 micromol/L) to a normal range of 0.4 to 0.8 mg/dL (35 to 70 micromol/L). Thus, a serum creatinine of 1.0 mg/dL (88 micromol/L), while normal in a non-pregnant individual, reflects renal impairment in a pregnant woman. Blood urea nitrogen (BUN) levels fall to approximately 8 to 10 mg/dL (2.9 to 3.9 mmol/L) for the same reason.

Mechanisms — The mechanisms for decreased vascular resistance and increased renal plasma flow during pregnancy are not fully understood. Reduced vascular responsiveness to vasopressors such as angiotensin 2, norepinephrine, and vasopressin is well-documented [25]. Nitric oxide synthesis increases during normal pregnancy and may contribute to the systemic and renal vasodilation and the fall in blood pressure [26,27].

The ovarian hormone and vasodilator relaxin appears to be a key upstream mediator of enhanced nitric oxide signaling in pregnancy. Relaxin is a peptide hormone in the insulin family; it is normally produced in the corpus luteum, and in pregnancy is secreted in large amounts by the placenta and decidua in response to human chorionic gonadotropin (hCG) [28]. Relaxin increases endothelin and nitric oxide production in the renal circulation, leading to generalized renal vasodilation, decreased renal afferent and efferent arteriolar resistance, and a subsequent increase in renal blood flow and GFR.

Chronic administration of relaxin to conscious male and castrated female rats mimics the renal hemodynamic changes of pregnancy (20 to 40 percent increase in GFR and renal plasma flow); these changes can be abolished by the administration of a nitric oxide synthase inhibitor [29]. In pregnant rats, increases in GFR and renal plasma flow can also be abolished by the administration of antirelaxin antibodies or by oophorectomy [30].

Relaxin has systemic hemodynamic effects which may be beneficial in human disease, particularly heart failure. (See "Investigational and emerging therapies for heart failure".)

Estimation of GFR — Management of women with preeclampsia or preexisting kidney disease in pregnancy requires an understanding of whether the GFR (and therefore, disease severity) is changing or stable; knowledge of the absolute value of the GFR is not usually needed. Changes in GFR are best identified by monitoring changes in the serum creatinine concentration. A rising serum creatinine concentration implies a reduction in GFR, a falling level indicates improvement, and a stable value usually reflects stable function. (See "Assessment of kidney function".)

Among pregnant women with a normal serum creatinine at baseline, the creatinine may remain within the normal range despite a significantly reduced GFR. A small rise in serum creatinine usually reflects a marked reduction in renal function. For example, in a physiologic study, women with preeclampsia had a 40 percent reduction in GFR as compared with control pregnant women (89 versus 149 mL/min/1.73m2 BSA), but their serum creatinine levels remained within the normal range (0.89 mg/dL in preeclamptic versus 0.60 mg/dL in control pregnancies) [31]. Hence, careful attention to small fluctuations in serum creatinine is required to detect renal injury in pregnancy.

Assessment of renal function with a 24-hour urine collection for creatinine clearance is cumbersome for the patient, and is of limited accuracy in pregnancy [32]. Overcollection and undercollection of 24-hour urine samples appear to be more common in pregnancy than in nonpregnant women [32]. This may be due, in part, to urinary stasis from dilatation of the lower urinary tract in pregnancy; several hundred milliliters of urine can be trapped in the dilated ureters, resulting in a significant lapse between urine formation and urine collection. Estimates of GFR based on the Modification of Diet in Renal Disease (MDRD) equation are also inaccurate during pregnancy. Studies in early and late normal pregnancy and in pregnancies complicated by renal disease or preeclampsia show that MDRD substantially underestimates GFR as measured by inulin clearance during pregnancy and cannot be recommended for use in clinical practice [33,34]. Similarly, the CKD-EPI estimation formula significantly underestimates GFR in pregnant women [35]. (See "Assessment of kidney function", section on 'Limitations of using creatinine clearance' and "Assessment of kidney function", section on 'Estimation equations'.)

OTHER CHANGES

Mild hyponatremia — The plasma osmolality in normal pregnancy falls to a new set point of about 270 mosmol/kg, with a proportional decrease in plasma sodium concentration that is 4 to 5 meq/L below nonpregnancy levels [36]. The physiological responses to changes in osmolality above or below the new set point (ie, thirst and release of antidiuretic hormone [ADH] from the pituitary) are intact.

The reduced set point for plasma osmolality has been attributed to pregnancy-related vasodilation and resultant arterial underfilling, which stimulates ADH release and thirst. However, intrathoracic blood volume expansion using head out of water immersion does not correct hypoosmolality in pregnant women.

There is evidence that hyponatremia of pregnancy is mediated by hormonal factors. The fall in the plasma sodium concentration during pregnancy correlates closely with increased production of hCG [37,38]. Furthermore, the administration of hCG to normal women during the luteal phase of the menstrual cycle can induce a similar resetting of the thresholds for ADH release and thirst [37,39]. Rather than acting directly, hCG appears to produce these changes via the release of relaxin [29]. As an example, hyponatremia in pregnant rats can be corrected by the administration of antirelaxin antibodies or by oophorectomy [30]. As noted above, relaxin also plays an important role in the increased glomerular filtration rate in pregnancy (see 'Mechanisms' above).

Attempts to correct the physiologic hyponatremia of pregnancy are both unnecessary (the change is mild and asymptomatic) and ineffective. Resetting of the osmostat means that the plasma sodium concentration will be maintained at the new level despite variations in water or sodium intake.

The plasma sodium concentration spontaneously rises to prepregnancy levels within one to two months after delivery [36,38].

Increased protein excretion — Urinary protein excretion rises in normal pregnancy from the nonpregnant level of about 100 mg/day to about 180 to 200 mg/day in the third trimester. This may result in a positive dipstick result when a concentrated urine sample is examined. (See "Proteinuria in pregnancy: Evaluation and management".)

Urine protein excretion is even higher in uncomplicated twin pregnancy, which can lead to diagnostic confusion, because values greater than 300 mg/day are considered abnormal by the American College of Obstetricians and Gynecologists. In a prospective study of 50 twin pregnancies, 15 of 35 women (43 percent) who never developed hypertension had urine protein excretion of at least 300 mg/day at 30 weeks of gestation [40]. If confirmed in a larger study, these findings suggest that the definition of pathologic proteinuria in singleton pregnancies should not be applied to twin pregnancies.

The increase in proteinuria that occurs during late pregnancy in women with preexisting proteinuria is more exaggerated than would be expected from the increased GFR alone.

Chronic respiratory alkalosis — Minute ventilation rises in early pregnancy and continues to increase until term, leading to a modest fall in the pCO2 (to 27 to 32 mmHg) and mild respiratory alkalosis. These changes are due to direct stimulation of the central respiratory centers by progesterone [41]. The increase in minute ventilation allows maintenance of a high-normal pO2 despite the 20 to 33 percent increase in oxygen consumption in pregnancy. (See "Physiologic respiratory changes and dyspnea during pregnancy", section on 'Respiratory changes'.)

Hypouricemia — Serum uric acid declines in early pregnancy because of the rise in GFR, reaching a nadir of 2.0 to 3.0 mg/dL (119 to 178 micromol/L) by 22 to 24 weeks [42]. Thereafter, the uric acid level begins to rise, reaching nonpregnant levels by term. The late gestational rise in uric acid is attributed to increased renal tubular absorption of urate.

Decrease in serum anion gap — For reasons that are not well understood, there appears to be a small reduction in serum anion gap in pregnant women. This was shown in a cross-sectional study of 119 normal pregnant women (6 in the first trimester, 47 in the second trimester, 59 in the third trimester, and 13 postpartum) [43]. The serum anion gap was modestly but significantly lower in pregnancy than postpartum (8.5 versus 10.7).

Impaired tubular function — Pregnancy is associated with reductions in fractional reabsorption of glucose, amino acids, and beta microglobulin, which results in higher rates of urinary excretion. Thus, pregnant patients may exhibit glucosuria and aminoaciduria in the absence of hyperglycemia or renal disease.

POLYURIA AND DIABETES INSIPIDUS — Although urinary frequency due to changes in lower urinary tract function is common in pregnancy, true polyuria, defined as urine output exceeding 3 L/day, is not physiologic. Transient diabetes insipidus of pregnancy is a rare, but important cause of pathologic polyuria, often accompanied by hypernatremia in settings where water intake is restricted. This disorder is related to increased metabolism of antidiuretic hormone (ADH, also called vasopressin).

Transient DI of pregnancy — Antidiuretic hormone (ADH) increases renal water reabsorption and decreases urine output. This effect is mediated by activation of the V2 receptor in the renal collecting tubules, resulting in enhanced renal water reabsorption and the formation of concentrated urine. Between the eighth week and mid pregnancy, the metabolic clearance of ADH increases four- to six-fold because of an increase in vasopressinase (also known as oxytocinase), which is produced by the placenta. Enzyme activity continues to increase, peaking in the third trimester, remaining high during labor and delivery, and then falling to undetectable levels two to four weeks postpartum. In most pregnant women, plasma concentrations of ADH remain in the normal range, despite increased metabolic clearance, because of a compensatory increase in ADH production by the pituitary gland. As a result, most women do not become polyuric.

A small number of pregnant women, however, develop transient DI, which is underdiagnosed because polyuria is often considered normal during pregnancy [38,44-50]. The possibility of this disorder should be considered in women with intense polydipsia and polyuria in the third trimester. The diagnosis is supported by the findings of a high-normal plasma sodium (the plasma sodium concentration in normal pregnancy typically is approximately 5 meq/L lower than in nonpregnant women [39]) in combination with an inappropriately low urine osmolality (ie, below that of plasma) [44-46]. Hypernatremia can occur if water intake is restricted, as in the peripartum period [46,48,51]. If unrecognized and untreated, hypernatremia can result in serious neurologic consequences in both the mother and fetus [51]. Oligohydramnios has also been reported [51].

Transient DI of pregnancy is thought to be due to increased pregnancy-related vasopressinase levels or activity. Women with multiple gestations, because of a larger placental volume, have higher circulating levels of vasopressinase and thus are more likely to experience polyuria. DI caused by increased vasopressinase activity resolves postpartum and does not usually recur in subsequent pregnancies.

Women with preeclampsia, HELLP syndrome, and acute fatty liver of pregnancy are also at increased risk for transient DI of pregnancy. The mechanism in these cases is decreased degradation of vasopressinase due to hepatic dysfunction [49,52].

Management — Transient DI of pregnancy can be effectively treated with desmopressin (dDAVP, 5 to 20 mcg intranasally or 2 to 5 mcg subcutaneously every 12 to 24 hours) [46]. Desmopressin is a vasopressin analog that is resistant to degradation by vasopressinase [44,49,53]. Arginine vasopressin, the form of ADH secreted by the neurohypophysis, is degraded by the high levels of vasopressinase found in transient DI of pregnancy, and is therefore ineffective. No adverse maternal or fetal effects from desmopressin use during pregnancy have been reported [54]. It should be given at dosages equal to or slightly higher than those used to treat central DI in nonpregnant patients. We suggest restriction of water intake to 1000 mL per day during desmopressin therapy to avoid the development of iatrogenic hyponatremia [46].

In the rare patients who develop hypernatremia, simultaneous water administration (either orally or intravenously) is necessary to correct the total body water deficit. The serum sodium concentration should be closely monitored and the rate of correction limited to no more than 12 meq/L per day to avoid cerebral edema from a rapid fall in serum osmolality. (See "Treatment of hypernatremia", section on 'Step two: Choose a rate of correction'.)

Subclinical central or nephrogenic DI — Some pregnant women with signs and symptoms of DI have central or nephrogenic DI that was subclinical prior to pregnancy [44,49,55]. On careful questioning, they typically describe polyuria and polydipsia prior to pregnancy, with transient worsening of symptoms during pregnancy. In these cases, polyuria tends to recur with every pregnancy. (See "Clinical manifestations and causes of central diabetes insipidus" and "Clinical manifestations and causes of nephrogenic diabetes insipidus" and "Treatment of central diabetes insipidus" and "Treatment of nephrogenic diabetes insipidus".)

Other causes of DI in pregnancy

- Some women develop transient polyuria that is responsive to vasopressin, as well as desmopressin, that recurs in subsequent pregnancies [44]. Limited secretory reserve may play an important role in this setting, as the patient cannot compensate for even a modest increase in ADH catabolism.
- True vasopressin- and desmopressin-resistant nephrogenic DI has been reported in a few women [44,56]. The mechanism is uncertain, but spontaneous resolution occurs after delivery.
- Central DI rarely occurs postpartum in women with severe hemorrhage at delivery and subsequent hypopituitarism [44]. (See "Causes of hypopituitarism".)

SUMMARY AND RECOMMENDATIONS

- Physiologic ureteral dilatation (hydronephrosis and hydroureter) is common during pregnancy, and results from hormonal effects, external compression, and intrinsic changes in the ureteral wall. Kidney size also increases. (See 'Urinary tract changes' above.)
- Urinary frequency and nocturia are among the most common pregnancy-related complaints, but usually require no specific treatment. Urinary incontinence also can occur during pregnancy. (See 'Urinary symptoms' above.)
- Glomerular filtration rate (GFR) and renal blood flow rise markedly during pregnancy, resulting in a physiologic fall in the serum creatinine concentration. A serum creatinine of 1.0 mg/dL in a pregnant woman probably reflects significant renal insufficiency. (See 'Renal hemodynamics' above.)
- In most clinical settings, including preeclampsia and pregnant women with mild renal insufficiency, precise estimation of GFR is not required. Whether the GFR is changing or is stable is best determined by monitoring changes in the serum creatinine concentration. (See 'Estimation of GFR' above.)
- Other physiologic changes occuring in pregnancy include chronic respiratory alkalosis and mild hyponatremia. Fractional absorption of glucose, amino acids, and beta microglobulin are decreased, which can lead to mild glucosuria and aminoaciduria. Protein excretion increases. (See 'Other changes' above.)

- The release of vasopressinases from the placenta results in an approximate four-fold increase rate of ADH catabolism, but ADH levels remain normal because of a concomitant rise in the pituitary production of ADH. Women who have higher than normal vasopressinase levels or decreased vasopressin reserves may develop gestational diabetes insipidus. This disorder can be effectively treated with desmopressin (dDAVP). (See 'Polyuria and diabetes insipidus' above.)

REFERENCES

1. Bailey RR, Rolleston GL. Kidney length and ureteric dilatation in the puerperium. J Obstet Gynaecol Br Commonw 1971; 78:55.
2. Rasmussen PE, Nielsen FR. Hydronephrosis during pregnancy: a literature survey. Eur J Obstet Gynecol Reprod Biol 1988; 27:249.
3. Beydoun SN. Morphologic changes in the renal tract in pregnancy. Clin Obstet Gynecol 1985; 28:249.
4. Irving SO, Burgess NA. Managing severe loin pain in pregnancy. BJOG 2002; 109:1025.
5. Dure-Smith P. Pregnancy dilatation of the urinary tract. The iliac sign and its significance. Radiology 1970; 96:545.
6. Mattingly RF, Borkowf HI. Clinical implications of ureteral reflux in pregnancy. Clin Obstet Gynecol 1978; 21:863.
7. Heidrick WP, Mattingly RF, Amberg JR. Vesicoureteral reflux in pregnancy. Obstet Gynecol 1967; 29:571.
8. Nel JT, Diedericks A, Joubert G, Arndt K. A prospective clinical and urodynamic study of bladder function during and after pregnancy. Int Urogynecol J Pelvic Floor Dysfunct 2001; 12:21.
9. FRANCIS WJ. Disturbances of bladder function in relation to pregnancy. J Obstet Gynaecol Br Emp 1960; 67:353.
10. Stanton SL, Kerr-Wilson R, Harris VG. The incidence of urological symptoms in normal pregnancy. Br J Obstet Gynaecol 1980; 87:897.
11. van Brummen HJ, Bruinse HW, van der Bom JG, et al. How do the prevalences of urogenital symptoms change during pregnancy? Neurourol Urodyn 2006; 25:135.
12. Thorp JM Jr, Norton PA, Wall LL, et al. Urinary incontinence in pregnancy and the puerperium: a prospective study. Am J Obstet Gynecol 1999; 181:266.
13. Aslan D, Aslan G, Yamazhan M, et al. Voiding symptoms in pregnancy: an assessment with international prostate symptom score. Gynecol Obstet Invest 2003; 55:46.
14. Parboosingh J, Doig A. Renal nyctohemeral excretory patterns of water and solutes in normal human pregnancy. Am J Obstet Gynecol 1973; 116:609.
15. Cutner A, Cardozo LD, Benness CJ. Assessment of urinary symptoms in early pregnancy. Br J Obstet Gynaecol 1991; 98:1283.
16. Wesnes SL, Rortveit G, Bø K, Hunskaar S. Urinary incontinence during pregnancy. Obstet Gynecol 2007; 109:922.
17. Wijma J, Potters AE, de Wolf BT, et al. Anatomical and functional changes in the lower urinary tract following spontaneous vaginal delivery. BJOG 2003; 110:658.
18. Weidner AC, South MM, Sanders DB, Stinnett SS. Change in urethral sphincter neuromuscular function during pregnancy persists after delivery. Am J Obstet Gynecol 2009; 201:529.e1.
19. van Geelen JM, Lemmens WA, Eskes TK, Martin CB Jr. The urethral pressure profile in pregnancy and after delivery in healthy nulliparous women. Am J Obstet Gynecol 1982; 144:636.

20. Almeida FA, Pavan MV, Rodrigues CI. The haemodynamic, renal excretory and hormonal changes induced by resting in the left lateral position in normal pregnant women during late gestation. BJOG 2009; 116:1749.
21. Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. Obstet Gynecol 2009; 114:1326.
22. Klajnbard A, Szecsi PB, Colov NP, et al. Laboratory reference intervals during pregnancy, delivery and the early postpartum period. Clin Chem Lab Med 2010; 48:237.
23. Larsson A, Palm M, Hansson LO, Axelsson O. Reference values for clinical chemistry tests during normal pregnancy. BJOG 2008; 115:874.
24. Davison JM, Dunlop W. Renal hemodynamics and tubular function normal human pregnancy. Kidney Int 1980; 18:152.
25. Gant NF, Chand S, Whalley PJ, MacDonald PC. The nature of pressor responsiveness to angiotensin II in human pregnancy. Obstet Gynecol 1974; 43:854.
26. Danielson LA, Conrad KP. Acute blockade of nitric oxide synthase inhibits renal vasodilation and hyperfiltration during pregnancy in chronically instrumented conscious rats. J Clin Invest 1995; 96:482.
27. Deng A, Engels K, Baylis C. Impact of nitric oxide deficiency on blood pressure and glomerular hemodynamic adaptations to pregnancy in the rat. Kidney Int 1996; 50:1132.
28. Conrad KP, Jeyabalan A, Danielson LA, et al. Role of relaxin in maternal renal vasodilation of pregnancy. Ann N Y Acad Sci 2005; 1041:147.
29. Danielson LA, Sherwood OD, Conrad KP. Relaxin is a potent renal vasodilator in conscious rats. J Clin Invest 1999; 103:525.
30. Novak J, Danielson LA, Kerchner LJ, et al. Relaxin is essential for renal vasodilation during pregnancy in conscious rats. J Clin Invest 2001; 107:1469.
31. Hladunewich MA, Myers BD, Derby GC, et al. Course of preeclamptic glomerular injury after delivery. Am J Physiol Renal Physiol 2008; 294:F614.
32. Côté AM, Firoz T, Mattman A, et al. The 24-hour urine collection: gold standard or historical practice? Am J Obstet Gynecol 2008; 199:625.e1.
33. Smith MC, Moran P, Ward MK, Davison JM. Assessment of glomerular filtration rate during pregnancy using the MDRD formula. BJOG 2008; 115:109.
34. Alper AB, Yi Y, Webber LS, et al. Estimation of glomerular filtration rate in preeclamptic patients. Am J Perinatol 2007; 24:569.
35. Smith MD, Moran P, Davison JM. EPI-CKD is a poor predictor of GFR in pregnancy. Arch Dis Child Fetal Neonatal Ed 2011; 96.
36. Lindheimer MD, Barron WM, Davison JM. Osmoregulation of thirst and vasopressin release in pregnancy. Am J Physiol 1989; 257:F159.
37. Davison JM, Shiells EA, Philips PR, Lindheimer MD. Serial evaluation of vasopressin release and thirst in human pregnancy. Role of human chorionic gonadotrophin in the osmoregulatory changes of gestation. J Clin Invest 1988; 81:798.
38. Lindheimer MD, Barron WM, Davison JM. Osmotic and volume control of vasopressin release in pregnancy. Am J Kidney Dis 1991; 17:105.
39. Davison JM, Shiells EA, Philips PR, Lindheimer MD. Influence of humoral and volume factors on altered osmoregulation of normal human pregnancy. Am J Physiol 1990; 258:F900.
40. Osmundson SS, Lafayette RA, Bowen RA, et al. Maternal proteinuria in twin compared with singleton pregnancies. Obstet Gynecol 2014; 124:332.
41. Lim VS, Katz AI, Lindheimer MD. Acid-base regulation in pregnancy. Am J Physiol 1976; 231:1764.

42. Lind T, Godfrey KA, Otun H, Philips PR. Changes in serum uric acid concentrations during normal pregnancy. Br J Obstet Gynaecol 1984; 91:128.
43. Akbari A, Wilkes P, Lindheimer M, et al. Reference intervals for anion gap and strong ion difference in pregnancy: a pilot study. Hypertens Pregnancy 2007; 26:111.
44. Dürr JA. Diabetes insipidus in pregnancy. Am J Kidney Dis 1987; 9:276.
45. Durr JA, Hoggard JG, Hunt JM, Schrier RW. Diabetes insipidus in pregnancy associated with abnormally high circulating vasopressinase activity. N Engl J Med 1987; 316:1070.
46. Brewster UC, Hayslett JP. Diabetes insipidus in the third trimester of pregnancy. Obstet Gynecol 2005; 105:1173.
47. Aleksandrov N, Audibert F, Bedard MJ, et al. Gestational diabetes insipidus: a review of an underdiagnosed condition. J Obstet Gynaecol Can 2010; 32:225.
48. Sherer DM, Cutler J, Santoso P, et al. Severe hypernatremia after cesarean delivery secondary to transient diabetes insipidus of pregnancy. Obstet Gynecol 2003; 102:1166.
49. Durr JA, Lindheimer MD. Diagnosis and management of diabetes insipidus during pregnancy. Endocr Pract 1996; 2:353.
50. Katz VL, Bowes WA Jr. Transient diabetes insipidus and preeclampsia. South Med J 1987; 80:524.
51. Hanson RS, Powrie RO, Larson L. Diabetes insipidus in pregnancy: a treatable cause of oligohydramnios. Obstet Gynecol 1997; 89:816.
52. Kennedy S, Hall PM, Seymour AE, Hague WM. Transient diabetes insipidus and acute fatty liver of pregnancy. Br J Obstet Gynaecol 1994; 101:387.
53. Davison JM, Sheills EA, Philips PR, et al. Metabolic clearance of vasopressin and an analogue resistant to vasopressinase in human pregnancy. Am J Physiol 1993; 264:F348.
54. Ray JG. DDAVP use during pregnancy: an analysis of its safety for mother and child. Obstet Gynecol Surv 1998; 53:450.
55. Iwasaki Y, Oiso Y, Kondo K, et al. Aggravation of subclinical diabetes insipidus during pregnancy. N Engl J Med 1991; 324:522.
56. Ford SM Jr, Lumpkin HL 3rd. Transient vasopressin-resistant diabetes insipidus of pregnancy. Obstet Gynecol 1986; 68:726.

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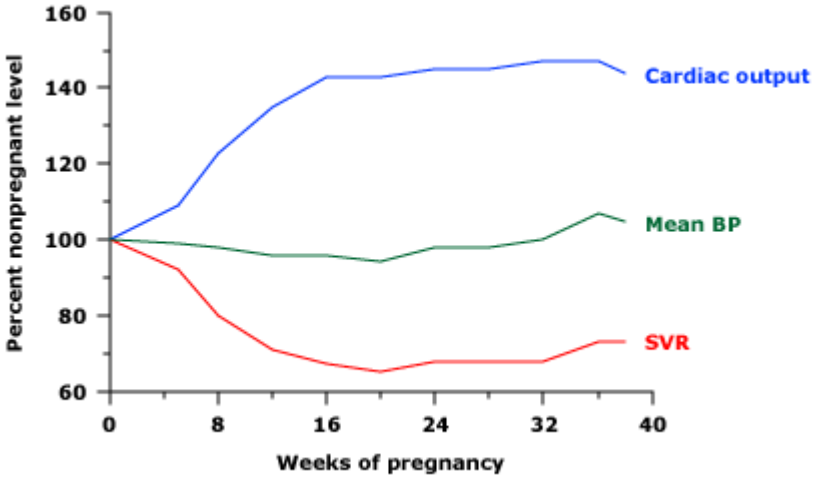
GRAPHICS

Hemodynamic changes in normal pregnancy



Normal pregnancy is characterized by an increase in cardiac output, a reduction in systemic vascular resistance, and minimal change in mean blood pressure. These changes are associated with a 10- to 15-beat/minute increase in heart rate.

BP: blood pressure; SVR: systemic vascular resistance.

Graphic 54685 Version 6.0

Hemodynamic and renal changes during normal pregnancy

Systemic hemodynamics
Increase in cardiac output
Fall in vascular resistance and blood pressure
Blood volume expansion
Renal function and electrolyte balance
Increase in glomerular filtration rate
Chronic respiratory alkalosis
Hyponatremia due to resetting of osmostat
Increased ADH metabolism and polyuria in selected women

Graphic 66445 Version 1.0

Normal reference range of renal function tests in pregnant women

Test	Normal (reference) range		
	First trimester	Second trimester	Third trimester
Sodium (mEq/L)	133 to 148	129 to 148	130 to 148
Potassium (mEq/L)	3.6 to 5.0	3.3 to 5.0	3.3 to 5.1
Chloride (mEq/L)	101 to 105	97 to 109	97 to 109
BUN (mg/dL)	7 to 12	3 to 13	3 to 11
Creatinine (mg/dL)	0.4 to 0.7	0.4 to 0.8	0.4 to 0.9
Calcium (mg/dL)	8.8 to 10.6	8.2 to 9.0	8.2 to 9.7
Magnesium (mg/dL)	1.6 to 2.2	1.5 to 2.2	1.5 to 2.2
Phosphate (mg/dL)	3.1 to 4.6	2.5 to 4.6	2.8 to 4.6
Uric acid (mg/dL)	2.0 to 4.2	2.4 to 4.9	3.1 to 6.3
Albumin (g/dL)	3.1 to 5.1	2.6 to 4.5	2.3 to 4.2
24 hour protein excretion (mg)	19 to 141	47 to 186	46 to 185

Data from: Abbassi-Ghanavati M, Greer LG. Reference Table of Normal Laboratory Values in Uncomplicated Pregnancies. In: Cunningham FG, Leveno KJ, Bloom S, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics, 23rd Edition. New York: McGraw-Hill, 2010.

Graphic 89016 Version 2.0

Contributor Disclosures

Ravi I Thadhani, MD, MPH Nothing to disclose **Sharon E Maynard, MD** Patent Holder: Beth Israel Deaconess Medical Center [Angiogenic biomarkers for preeclamspia (Elecsys Preeclampsia sFlt-1 & PlGF)]. **Richard J Glassock, MD, MACP** Speaker's Bureau: Genentech [Vasculitis (Rituximab)]. Consultant/Advisory Boards: Bristol-Myers-Squibb [Lupus nephritis, FSGS (Abatacept)]; ChemoCentryx [Vasculitis, diabetes (Acocapan)]; Retrophin [FSGS(Sparsentan)]. Equity Ownership/Stock Options: Reata (Bardoxolone). **Richard H Sterns, MD** Nothing to disclose **Kristen Eckler, MD, FACOG** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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