Pregnancy in women with underlying renal disease

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- There are two questions that need to be addressed when a woman with underlying kidney disease becomes pregnant:

- What is the effect of **pregnancy on the kidney disease**?
- What is the effect of the **kidney disease on pregnancy?**

- Even mild CKD is associated with a higher risk of adverse maternal and fetal outcomes, including worsening of maternal kidney function, proteinuria, and hypertension, as well as preterm birth and fetal growth restriction.

Preconception counseling —

- Contraceptive methods to avoid unintended pregnancy.
- Pregnancy outcomes (both maternal and fetal) in the setting of CKD.
- Maternal risks, including both potential obstetric complications and risks to the kidneys.
- Management of medications before, during, and after pregnancy.
- Timing of conception

- For women who desire the most effective contraception or durable contraception, we discuss long-acting reversible contraceptives (LARCs), including
- the copper intrauterine device (IUD), levonorgestrel-releasing IUDs, and the etonogestrel implant

- **Depot** medroxyprogesterone acetate **(DMPA)**

- **Progestin-only pills (POPs)**
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- **Combined estrogen-progestin contraceptives** –

Baseline evaluation

- discontinue and/or substitute medications that have been identified to be potentially teratogenic or fetotoxic [eg, angiotensin-converting enzyme (ACE) inhibitors])
- Vaccinations
- Blood pressure
- ●Serum creatinine, bicarbonate, and electrolytes
- ●Liver function tests.
- ●Complete blood count
- ●Urinalysis and spot urine protein-to-creatinine ratio from a first or second morning void (and, if proteinuria is present, a 24-hour urine collection for protein) .
- ●Fasting plasma glucose and glycated hemoglobin (A1C) in patients with pregestational diabetes mellitus.
- Assessment of disease activity in patients with SLE

- In patients with undiagnosed CKD, some clinicians obtain a renal ultrasound to rule out structural, congenital, or cystic kidney diseases in the patient.

Management of medications

- **ACE inhibitors and ARBs —**
- **Diuretics —**
- **Immunosuppressive agents —**
- **Monitoring for pregnancy —**
- **Diagnosis of pregnancy —**

• Anatomic changes

- Kidney size increases by about 1-1.5 cm, primarily in the collecting system.
- Dilatation of the ureters and pelvis occurs and is presumed to be secondary to the smooth muscle–relaxing effect of progesterone.
- These changes may persist for up to 12 weeks post-partum.

- Glomerular filtration rate (GFR) increases immediately after conception to about 50% above baseline in the second trimester and then falls about 20% in the last trimester, resulting in significant hyperfiltration.

- Renal plasma flow also increases significantly in early pregnancy, causing the filtration fraction to fall in mid-pregnancy.
- As a result the normal serum creatinine level falls, so any value above 0.8 mg/dl should be considered abnormal.

- Similarly the value for blood urea nitrogen (BUN) falls.

- Blood volume increases by 20%, and sodium retention of up to 900 mEq occurs.
- Although edema may therefore be benign in pregnancy.
- The osmotic threshold for arginine vasopressin resets downward, leading to lower serum sodium values.
- The higher GFR increases urate clearance, lowering serum uric acid values, and the filter load of glucose increases, which may result in renal glycosuria.

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- Although up to 300 mg per day of proteinuria can be normal in pregnancy

- it is important to distinguish between changes in clinical manifestations and possible alterations in the long-term course of the disease.
- As an example, the degree of proteinuria increases in about one-half of cases and hypertension develops or worsens in about one-quarter of cases ;
- severe hypertension can occur, potentially leading to maternal injury, premature delivery, or poor fetal outcome .

- **Marked worsening of edema** also can be seen in women with the nephrotic syndrome.
- These changes generally resolve after delivery.

- **Effect on renal function** —
- Renal function may **decline** as a result of pregnancy among patients with renal disease, determined in part by the severity of **underlying renal disease:**

- Pregnancy is associated with **a permanent decline** in renal function in between 0 and 10 percent of women when the glomerular filtration rate is initially normal or only mildly reduced (plasma creatinine concentration less than 1.5 mg/dL or 132 µmol/L) .
- Other patients may experience a **transient** decline in renal function during pregnancy.

- **In summary, an elevated plasma creatinine concentration (above 1.5 mg/dL or 132 µmol/L) and hypertension are the major risk factors for permanent exacerbation of underlying renal disease.**

- It has been proposed that the **type of disease** also may be important as **accelerated progression** may be more likely in :
- **membranoproliferative glomerulonephritis, focal segmental glomerulosclerosis, and reflux nephropathy.**

- **women with autosomal dominant polycystic kidney disease who are hypertensive have a high risk for fetal and maternal complications**

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- Women with vesicoureteral **reflux may be at increased risk for urinary tract infection.**

- Systemic lupus erythematosus

- In women with systemic lupus erythematosus (SLE), the best outcomes occur in those who have had stable, inactive lupus for 6 months or longer before conception.
- **Lupus nephritis in pregnancy usually presents as proteinuria, hypertension, and falling GFR, making the distinction from preeclampsia very difficult.**
- However, **low complement levels may be helpful in distinguishing between women with preeclampsia and patients with active lupus nephritis.**

- All pregnant patients with SLE should be screened for anti-SSA (Ro) antibodies, due to the risk of congenital heart block.

- Treatment is problematic, because cyclophosphamide and mycophenolate mofetil, agents used in lupus therapy, are potentially teratogenic in early pregnancy.

- Diabetes mellitus

- Women with pre-clinical or mild diabetic nephropathy with only microalbuminuria or minimal proteinuria and well preserved glomerular filtration rate, and normal or only minimally elevated blood pressure may have transient increases in proteinuria and blood pressure.

- These women do not have significant progression of their renal failure, but in women with moderate diabetic nephropathy and lower creatinine clearances prior to conception renal function may significantly worsen during and after pregnancy without complete recovery.

- **Kidney biopsy during pregnancy** —
- Although there are few indications for kidney biopsy during pregnancy, this procedure can be performed safely by **experienced operators in women with well-controlled blood pressure and normal coagulation indices** .
- It has been suggested that a biopsy may be performed if there is a **sudden unexplained deterioration in renal function or markedly symptomatic nephrotic syndrome occurring before 32 weeks gestation.**

- **Biopsy after week 32 is not recommended**.

EFFECT OF KIDNEY DISEASE ON PREGNANCY

Pregnancy in mild to moderate CKD —

- CKD is associated with higher rates of adverse maternal outcomes.-
- **more likely to develop gestational hypertension, preeclampsia, eclampsia, or to die .**

- **Preeclampsia may be more difficult** to diagnose in women with CKD who already have **hypertension and proteinuria**.
- Fetal outcomes are also worse in women with CKD

MANAGEMENT DURING PREGNANCY

- **Maternal and fetal monitoring** — Pregnant women with CKD should be monitored jointly by a nephrologist and by a maternal-fetal medicine specialist.
- ●**Maternal – For obstetric care, we see patients at least monthly during the early first trimester, every two weeks by the second trimester, and weekly by the third trimester. Some patients require even closer follow-up throughout pregnancy.**
- The following assessments should be performed at least once per trimester and more often as clinically indicated:
- •Blood pressure (in addition to daily monitoring at home) •Serum creatinine, bicarbonate, and electrolytes
- •Fasting blood glucose in patients with diabetes mellitus
- •Complete blood count and differential
- •Liver function tests
- •Urinalysis (and a urine culture if the dipstick reveals white blood cells or nitrates) and spot urine protein-to-creatinine ratio or urine albumin-to-creatinine ratio

- In addition, in patients without a history of pregestational diabetes, we perform oral glucose tolerance testing to screen for gestational diabetes at 24 to 28 weeks of gestation or sooner in patients with risk factors, such as those receiving glucocorticoids and/or calcineurin inhibitors.

- **Fetal** –
- Obstetrical follow-up in this high-risk population typically includes a first-trimester screen in conjunction with an ultrasound assessment of nuchal translucency or a maternal serum screen in the second trimester to assess for chromosomal abnormalities including Down syndrome.
- As a serum human chorionic gonadotropin (hCG) is one component of both the first-trimester combined test and the second-trimester quadruple test, false-positive tests can occur in women with advanced CKD.
- As such, assessment of cell-free fetal DNA or more invasive testing including chorionic villous sampling or an amniocentesis may be necessary.

- A detailed ultrasound to assess fetal anatomy is typically performed between 18 to 20 weeks. We do a placental scan to assess placental morphology and Doppler flow at approximately 22 weeks.
- After 26 weeks, fetal growth is assessed as often as biweekly with weekly biophysical profiles if indicated.

- **Nutrition —** Attention to nutritional considerations and proper weight gain are essential for a successful pregnancy . Evaluation and follow-up by a dietician familiar with the requirements of pregnancy and CKD may be helpful.

- Our approach for nondialysis CKD patients is the same as for pregnant women without CKD.
- We generally do not limit dietary phosphate, although we provide dietary counseling to limit non-nutritive sources of phosphate if the patient develops mild hyperphosphatemia.

- **Prevention of preeclampsia —**
- Patients with CKD are considered to be at high risk for preeclampsia.
- Low-dose aspirin therapy has been shown to decrease the risk of preeclampsia in women at moderate to high risk of the disease.
- However, the safety of low-dose aspirin in the general high-risk obstetric population has been well documented.

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- Increasing levels of soluble fms-like tyrosine kinase-1 (sFlt1), a circulating antiangiogenic factor, can antagonize the angiogenic and vasodilatory effects of vascular endothelial and placental growth factors, as markers that may predict the development of preeclampsia and differentiate preeclampsia from other causes of hypertension and proteinuria.

- **Mode of delivery —**
- **Vaginal delivery** is the preferred mode of delivery if there are no obstetric contraindications.
- In most women, elective delivery is indicated if labor has not occurred by the estimated date of confinement.
- Even for low-risk women, there is little benefit in allowing the pregnancy to extend beyond this date, and maternal and/or perinatal risk may increase .
- We suggest scheduling delivery at **39 to 40 weeks of gestation**.
- Cesarean delivery is performed for standard obstetric indications.

- **Preterm intervention —**

- Preterm delivery may be necessary in the presence of severe preeclampsia, fetal growth restriction, or nonreassuring fetal testing (eg, fetal distress).
- The indications for delivery in the setting of severe preeclampsia, fetal growth restriction, or fetal distress are usually the same as for the general population.

- **Use of magnesium sulfate —**

- Many women get magnesium sulfate before delivery, either to **prevent seizures in preeclampsia or to reduce the risk of cerebral palsy** before preterm birth of an infant <32 weeks.

- Women with reduced glomerular filtration rate (GFR) will have an exaggerated rise in serum magnesium and may develop magnesium toxicity at the usual doses of administration; therefore extreme caution is advised when treating women with reduced GFR (<30 mL/min).

- The approach to dosing of magnesium varies among clinicians.
- In all cases, serum magnesium levels should be followed and the patient monitored clinically for evidence of toxicity.

- we use, is a loading dose of 6 g of a 10 percent solution intravenously over 15 to 20 minutes followed by 2 g/hour as a continuous infusion.
- An alternative regimen is 5 g of a 50 percent solution intramuscularly into each buttock (total of 10 g) followed by 5 g intramuscularly every four hours .
- A therapeutic range of 4.8 to 8.4 mg/dL
- Clinical assessment for magnesium toxicity should be performed every one to two hours.
- The maintenance dose is only given when a patellar reflex is present (loss of reflexes is the first manifestation of symptomatic hypermagnesemia), respirations exceed 12 breaths/minute, and urine output exceeds 100 mL over four hours.

- **Renal insufficiency** — Magnesium sulfate is excreted by the kidneys.
- Women with renal insufficiency should receive a standard loading dose since their volume of distribution is not altered, but a reduced maintenance dose.
- We suggest 1 g/hour if the serum creatinine is >1.1 and <2.5 mg/dL (110 to 221 micromol/L) and no maintenance dose if the serum creatinine is ≥2.5 mg/dL (221 micromol/L) or magnesium toxicity is suspected.
- For patients with mild renal failure (serum creatinine 1.0 to 1.5 mg/dL or oliguria (less than 30 mL urine output per hour for more than 4 hours), ACOG suggests a loading dose of 4 to 6 g followed by a maintenance dose of 1 g/hour

- **Management of CKD during pregnancy**
- **Hypertension —**
- We generally try to maintain blood pressure between 120/70 and 149/90 mmHg.
- Medications with an acceptable safety profile in pregnancy include nifedipine (and most calcium channel blockers), labetalol, and methyldopa.
- Diuretics may be necessary in women with hypertension associated with edema and reduced GFR.

- **Metabolic bone disease —**
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- The alterations in calcium, phosphate, vitamin D, and parathyroid hormone (PTH) during pregnancy that have been observed in normal pregnancy have not been assessed in pregnant women with CKD.
- Most women with near-normal GFR will not require any specific treatment for CKD-MBD during pregnancy.
- Those with more advanced CKD can be managed similarly to their management prior to conception, with the understanding that pregnancy-related hormonal changes, as well as renal hemodynamic adjustments, may alter levels of calcium, phosphorus, vitamin D, and PTH.
- **Thus for women on treatment, we recommend that calcium, phosphorus, 25-hydroxyvitamin D, and PTH levels be monitored at least once each trimester.**

- If phosphate binders are required, then calcium carbonate is preferred as there are limited pregnancy data on other phosphate binders (ie, sevelamer, lanthanum carbonate, calcium acetate).
- Severe hyperphosphatemia is not common during pregnancy, even among patients with advanced CKD.
- Mild hyperphosphatemia is usually effectively treated with dietary counseling that limits the intake of non-nutritive sources of phosphate.
- Phosphate binders may reduce the absorption of fat-soluble vitamins and folic acid.
- Calcitriol may be used before and during pregnancy, and the indications are similar for the nonpregnant CKD patient.
- We generally do not use cinacalcet during pregnancy, because there are limited data regarding safety.

- **Anemia —**
- Pregnant women often require higher doses of ESAs to maintain an adequate red cell mass since the physiologic changes and demands of pregnancy may result in worsening of anemia.
- The target hemoglobin concentration is the same as for nonpregnant CKD patients.
- We suggest giving ESAs to nondialysis CKD patients who have a **hemoglobin <10 g/dL, provided that the transferrin saturation (TSAT) is >25 percent and ferritin >200 ng/mL.**
- We suggest targeting hemoglobin levels between 10 and 11.5 g/dL using the lowest possible ESA dose.
- **ESAs do not cross the placenta because of their large molecular weight.**

- We give oral and intravenous (IV) iron preparations as necessary to maintain adequate iron stores. When providing IV iron, we use iron sucrose rather than other formulations, which are less well studied in pregnancy. Preparations other than iron sucrose may contain benzol alcohol, which can pass into breast milk.

- **Indications to initiate hemodialysis —**
- If the estimated **GFR (eGFR) declines below 20 mL/min/1.73 m^2 or the blood urea nitrogen (BUN) increases >50 to 60 mg/dL** (18 to 21 mmol/L), we consider the elective initiation of dialysis.

- The rationale for starting dialysis at a relatively high eGFR is that untreated CKD of this severity is associated with very poor pregnancy outcomes, including **polyhydramnios, preterm delivery, and poor fetal growth.**

- The indications for initiation of dialysis (eg, signs and symptoms of uremia; persistent volume overload; refractory acidosis, hyperkalemia, or hyperphosphatemia) are the same for pregnant CKD patients as for the nonpregnant CKD population.

- **Maternal complications —**
- Significant potential complications specific to pregnant women with CKD include **preeclampsia, gestational diabetes mellitus (GDM), and infection.**
- The diagnosis of preeclampsia is challenging in this patient population because of preexisting proteinuria, reduced GFR, and hypertension.
- Close monitoring for the development of the nonrenal manifestations of preeclampsia include fetal and placental indicators of compromise including poor fetal growth, dropping platelet counts, and increasing liver function tests .

- In addition, women on immunosuppression are at increased risk for infection and should be carefully monitored.
- Bacterial urinary tract infections are common in normal pregnancy, and the development of pyelonephritis has been associated with adverse pregnancy outcomes.

- **POSTPARTUM CARE —**
- Postpartum care is similar among women with and without CKD. There are no contraindications to breastfeeding among CKD patients
- Among patients who have indications (ie, hypertension or significant proteinuria), we resume an angiotensin-converting enzyme (ACE) inhibitor, even if breastfeeding.
- We use either captopril, enalapril, or quinapril, all of which have been shown to be absent in breast milk .
- **We do not use angiotensin receptor blockers (ARBs), as they have not been adequately studied.**
- We continue erythropoiesis-stimulating agents (ESAs) and intravenous (IV) iron as necessary in all patients.
- We monitor serum creatinine levels and spot urine protein-to-creatinine ratio (or albumin-to-creatinine ratio) to reestablish the patient's kidney function and degree of proteinuria postpartum, respectively.
- In patients who are taking calcineurin inhibitors, calcineurin inhibitor levels must be closely monitored for several weeks postpartum and doses should be appropriately adjusted to maintain the desired target levels.

- Dialysis should be initiated when the serum creatinine level is 3.5-5.0 mg/dL or the glomerular filtration rate (GFR) is below 20 ml/min.
- Fetal outcome is improved with longer, more frequent hemodialysis sessions, which usually involves 20 hours of dialysis per week.

- Daily dialysis is more likely to prevent hypotension and significant metabolic shifts.

- Dialysis should aim to keep blood urea nitrogen levels below 50 mg/dL, because controlling uremia may avoid polyhydramnios, control hypertension, and improve the mother's nutritional status.

- Peritoneal dialysis with smaller volumes and frequent exchanges can also be done to achieve these same goals.

Pregnancy in the dialysis patient —

- The diagnosis of pregnancy may be difficult in women with end-stage renal disease, particularly because **serum levels of beta-human chorionic gonadotropin (beta-hCG) may be increased** in the absence of pregnancy.
- Among women suspected of being pregnant who have elevated serum beta-hCG, **ultrasonography** should be performed to verify the presence of a viable fetus and to obtain the approximate gestational age.
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Management of the pregnant dialysis patient

- Intensification of dialysis
- **Blood urea nitrogen should be maintained below 50 mg/dL (17 mmol/L) to avoid polyhydramnios.**
- If hemodialysis is used, intensification of the regimen should be considered, **5 to 7 sessions per week** is likely to provide more optimal control of uremia, and better fecal outcomes.

- The prescription should include bicarbonate buffer, **minimal heparinization and slow-rate ultrafiltration, in order to avoid dialysis hypotension and volume contraction.**
- **If peritoneal dialysis is used, the exchange volumes should be decreased (eg, to 1.5 liters) and the frequency should be increased.**

- Adequate supply of calories and protein
- Protein intake should be **1 g/kg per day plus an additional 20 g/day for fetal growth.**
- Diet should be supplemented with water soluble vitamins and zinc.
- Antihypertensive regimen
- **Diuretics, ACE inhibitors, angiotensin receptor blockers (ARBs) are avoided.**
- **Acceptable antihypertensives include labetalol, Nifedipine XL, methyldopa, and metoprolol.**

- The **diastolic blood pressure should range between 80 and 90 mmHg**.
- Correction of anemia
- **Erythropoietin should be given to maintain a hemoglobin level of at least 10 to 11 g/dL.**
- **Iron and folic acid should be supplemented.**
- **Avoidance of metabolic acidosis**

- **Prevention of hypocalcemia**
- Oral calcium carbonate should be administered.
- Hypercalcemia should be avoided at the end of hemodialysis treatment.
- Treatment of premature labor
- The use of beta agonists as first-line drug treatment is preferred.
- **Nonsteroidal antiinflammatory drugs are used with great caution and only for a limited duration.**
- Reinforced fetal monitoring as soon as viability is reached

- Although the recommended weight gain in the second and third trimesters is **between 0.3 to 0.5 kg per week**, it is difficult to distinguish excess fluid gained between dialysis sessions from that due to pregnancy associated weight gain.

Pregnancy in the renal transplant recipient —

- **Fertility generally returns** after renal transplantation
- . However, the rates of both pregnancy and successful pregnancy (ie, resulting in a live birth) remain **far lower** than in the general population.

- there is a higher risk of miscarriage, therapeutic abortion, stillbirth, ectopic pregnancy, preterm birth, low birthweight babies, and neonatal death.

- **Pregnancy usually has no important early effect on renal function** in this setting and is limited by the same factors described above in women with any underlying renal disease — **a plasma creatinine concentration above 1.5 mg/dL (132 µmol/L) and hypertension** that cannot be easily controlled

- **a poor pregnancy outcome was predicted by >1 previous kidney transplants, first trimester serum creatinine >1.4 mg/dL (125 µmol/L) and diastolic blood pressure >90 mmHg in the second and third trimesters.**
- **This suggests that pregnancy does not have long-term adverse effects on survival of either the allograft or patient.**

- **Women are usually advised to wait at least one year after living related donor transplantation and two years after deceased transplantation to** avoid complications arising from immunotherapy and rejection.

- In addition, the renal allograft should be functioning well, with a stable serum creatinine level of less than 1.5 mg/dL (132 µmol/L) and urinary protein excretion less than 500 mg/day .

- **Vaginal delivery should not be impaired**, as the pelvic allograft does not obstruct the birth canal in most patients.
- The obstetrician should review operative notes from the transplant procedure to confirm location of the allograft and ureter.
- A renal ultrasound might also aid in precise location. This information should be placed in the prenatal record to guide the surgeon if a Cesarean delivery is performed.
- **Prophylactic antibiotics and careful wound closure are warranted to avoid complications in these immunocompromised patients.**

- Recommended immunosuppression in kidney transplant recipients includes:

- Prednisone – Less than 15 mg per day (mg/d)
- Azathioprine – 2 mg/kg/d or less
- Calcineurin inhibitor–based therapy at appropriate therapeutic levels
- Breast-feeding on cyclosporine is not recommended; tacrolimus may be taken during breast-feeding though monitoring of infant levels is recommended.
- Mycophenolate mofetil and sirolimus should be discontinued for 6 weeks prior to conception
- If necessary, methylprednisolone is the preferred agent for treatment of rejection should it occur during pregnancy

- The following are complication risks in kidney transplant recipients:

- Immunosuppressive agents increase the risk of hypertension during pregnancy
- Preeclampsia occurs in approximately one third of kidney-transplant recipients
- Almost 50% of pregnancies in these women end in preterm delivery due to hypertension
- Blood levels of calcineurin inhibitors need to be frequently monitored due to changes in volumes of distribution of extracellular volume
- There is an increased risk of cytomegalovirus, toxoplasmosis, and herpes infections, which raise concern for the fetus

- Cyclosporine —
- The safety of cyclosporine is not **established in pregnancy. Hypertension** can be induced or exacerbated and some clinicians have suggested that the dose be limited to **2 to 4 mg/kg per day .**
- Cyclosporine does **not appear to be a major teratogen.**

- during pregnancy and higher doses may be required to maintain plasma levels in the therapeutic range .
- There is no consensus regarding whether or not cyclosporine doses should be increased in pregnant women whose levels are subtherapeutic.
- **In women several years post-transplant with stable renal function, our approach is to continue the prepregnancy dose.**

- Mycophenolate mofetil —

- Adverse effects on fetal development have been reported in laboratory animals with doses of mycophenolate mofetil (MMF) lower than those used in clinical practice.
- MMF is listed as a **category D** drug (positive evidence of risk) for use in pregnancy by the FDA due to increases in **both first trimester pregnancy loss and congenital malformations, including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidneys.**

- Mycophenolate is contraindicated in pregnancy. As a result, females of childbearing potential should have a **negative pregnancy test within one week prior to beginning therapy.**
- Two **reliable forms of contraception** should be used beginning four weeks prior to, during, and for six weeks after therapy.

- **We recommend that kidney transplant recipients who wish to conceive should change from MMF to azathioprine** , if there are no contraindications to the switch**. MMF should be discontinued at least six weeks prior to attempted conception**

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- Sirolimus — Sirolimus (Rapamycin) is contraindicated in pregnancy as animal studies have demonstrated **embryotoxicity and fetotoxicity with increased mortality, reduced fetal weights and delayed ossification**.
- **In general, we recommend that women post-transplant who wish to conceive be switched prior to conception from sirolimus to tacrolimus or cyclosporine .**
- **Upon delivery, it is our practice to switch the mother back to her basal immunosuppression** in view of the potential benefits of the newer agents to prevent late acute rejection and chronic allograft nephropathy.

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- Tacrolimus —
- As with cyclosporine , patients taking tacrolimus require frequent monitoring of renal function and drug levels.
- **During pregnancy, the hepatic cytochrome P450 enzymes may be inhibited, which can lead to increased serum levels of tacrolimus.**

- **The dose may therefore have to be significantly reduced to prevent toxicity (sometimes by as much as 60 percent).**

- **Male fertility after transplantation —**

- Immunosuppressive agents used in renal transplantation may affect male fertility.
- Although numerous reports have indicated that male transplant recipients can successfully father healthy offspring , one report suggests that **sirolimus may cause impaired spermatogenesis and reduce male fertility**

- Evaluation of renal dysfunction —

- The differential diagnosis of renal dysfunction and the evaluation of the **pregnant allograft recipient are similar to that in the nonpregnant transplant patient.**
- Additional concerns include the **causes of renal dysfunction unique to pregnancy** as well as the interplay between pregnancy and the presence of a renal allograft .

- Although women are advised to wait a sufficient period of time after transplantation to become pregnant, **episodes of acute rejection are not uncommon during pregnancy** .
- Obstruction of the transplant ureter by the uterus, although unusual, has been reported.
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- Severe preeclampsia and TTP-HUS (due to pregnancy) may be difficult to distinguish in the pregnant transplant patient, **particularly since they both present with hemolysis and thrombocytopenia.**
- Although **a TTP-HUS-like picture may also be observed in transplant patients with hyperacute rejection or in those administered OKT3 or cyclosporine ,** these clinical settings occur immediately or soon after transplantation and are therefore unlikely to be observed in a pregnant patient.

- OBSTETRICAL MANAGEMENT OF WOMEN WITH UNDERLYING RENAL DISEASE — **Patients with renal disease should be monitored jointly by a nephrologist and by an obstetrician familiar with the effects of renal disease on pregnancy.**

- General principles of management include the following:

- Increased frequency of prenatal visits; these should occur every two weeks until the third trimester and then weekly.
- Early detection and treatment of **asymptomatic bacteriuria**.
- Serial monitoring (at least monthly) of maternal renal function.
- Close monitoring for the development of preeclampsia.
- **Fetal surveillance with ultrasound and fetal heart rate monitoring to assess fetal growth and well-being.**
- **Aggressive treatment of maternal hypertension**.
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- Preterm intervention may be necessary in the presence of **deteriorating renal function, severe preeclampsia, fetal growth restriction, or nonreassuring fetal testing (eg, fetal distress).**

- In most women, elective delivery is indicated if labor has not occurred by the estimated date of confinement.