Pregnancy After Solid Organ Transplantation: A Guide for Obstetric Management

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Successful pregnancy outcomes are possible among all solid organ transplant recipients. Patients should be fully counseled regarding the potential adverse fetal outcomes, including prematurity and low birth weight. Transplant recipients are at an increased risk for both maternal and neonatal complications and should be seen by a high-risk obstetrician in conjunction with their transplant teams. Ideally, preconception counseling begins during the pretransplantation evaluation process. Initiating contraception early after transplantation is ideal, and long-acting reversible methods such as intrauterine devices and subdermal implants may be preferred. Pregnancy should be avoided for at least 1 year after transplantation to limit the potential risks of early pregnancy that may adversely affect both allograft function and fetal well-being. Hypertension, diabetes, and infection should be monitored and treated to minimize fetal risks during pregnancy. Maintenance of current immunosuppression is usually recommended, with the exception of mycophenolic acid products, which (when possible) should be discontinued before conception and replaced with an alternative medication. Throughout pregnancy, immunosuppression must be maintained at appropriate dosing to avoid graft rejection. During labor and delivery, cesarean delivery should be performed for obstetric reasons only. A multidisciplinary team should manage pregnant transplant recipients before, during, and following pregnancy. Breastfeeding and long-term in utero exposure to immunosuppressants for offspring of transplant recipients continue to require further investigation but have been encouraged by recent reports. Continued reporting of post-transplantation pregnancy outcomes to the National Transplantation Pregnancy Registry is highly encouraged.

[Rev Obstet Gynecol. *2013;6(3/4):116-125 doi:10.3909/riog0230*]

KEY WORDS

Contraception • Counseling • High-risk obstetrics • Immunosuppression • Pregnancy after transplantation

In 2011, 25,787 recipients received a solid organ transplant in the United States, including transplantation of the kidney, liver, pancreas, small bowel, heart, and lung.[1] Among these recipients, 9662 were women and 3505 were women of childbearing age (18-49 years). Additionally, 765 recipients were girls (≤ 17 years) who may become pregnant later in life.[1] Year after year, this trend is consistent; approximately 37% to 38% of transplant recipients are women and approximately 14% of transplant recipients are women in their childbearing years.[1]

Obstetric considerations are therefore a pertinent part of the pretransplantation counseling process. For many women, the underlying disease may compromise fertility, and one of the benefits of transplantation is its restorative effect on ovulation and fertility. The first successful pregnancy after transplantation occurred in 1958 and was reported in 1963 by Murray and colleagues.[2] In the subsequent six decades, there has been steady progress in ensuring that successful pregnancies and live births are increasingly possible among this unique obstetric cohort. Pregnancy after transplantation is increasingly common. Additionally, children with organ transplants are living longer, and are able to reach childbearing age and become pregnant. Over the years, through both registry information and single center reports, there has been an accumulation of data and knowledge on how to best manage these high-risk pregnancies.

Much of our understanding of this population stems from recent data that have been collected by the National Transplantation Pregnancy Registry (NTPR). The NTPR was established in 1991 to evaluate pregnancy outcomes in transplant recipients in North America. It contains outcome data on both transplant recipients who have had post-transplantation pregnancies and transplant recipients who have fathered pregnancies. Data include follow-up of both parents and offspring to investigate long-term health implications of post-transplantation pregnancy for the recipient or graft, as well as any sequelae for the offspring. To date, it is the largest and longest continuously running post-transplantation pregnancy registry, with records of more than 1500 solid organ transplant recipients and over 2400 pregnancies as of January 2012.

In the NTPR database, kidney and liver transplant recipients comprise the majority of pregnancy outcomes. NTPR data (for North America) represent one-third of the data on post-transplant pregnancies that are available internationally. Recently there were two systematic reviews and meta-analyses that quantified the various maternal complications, neonatal outcomes, and graft outcomes in both kidney and liver transplant recipients.[3,4] The review of kidney transplant recipients investigated 4706 pregnancies in 3570 recipients and the second review on liver transplant recipients analyzed 450 pregnancies in 306 recipients. Both reviews had similar conclusions: pregnancies in kidney and liver transplant recipients had a high rate of live births compared with the general US population. However, there were complications reported for both mother and neonate for post-transplantation pregnancies. Thus, post-transplantation recipients who become pregnant require appropriate management and counseling efforts from both the transplant and obstetric teams.

This review serves as a management guide, based on the literature and consensus summaries, for obstetricians and gynecologists to provide comprehensive prenatal, perinatal, and postnatal care for solid organ transplant recipients. The primary goal is to outline key points of consideration for obstetricians to address in transplant recipients.

Contraception After Transplantation

A woman of childbearing age who receives a transplant is typically advised to avoid pregnancy for at least 1 year after transplantation, based on data that show an increased risk of potential graft dysfunction, rejection, or loss, and increased risk of prematurity for neonates.[5-7] One of the anticipated benefits from solid organ transplantation is the restoration of fertility[8,9]; as a result, women can still be at risk for unplanned pregnancy. Ovulatory cycles may begin as soon as 1 month after transplantation.[8,9] Thus, prior to transplantation, gynecologists and transplant professionals should counsel women transplant recipients on potential methods of contraception to avoid unplanned pregnancy. Although sterilization is also an option, it may not be the desired contraceptive choice for recipients who are considering future childbearing.

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The World Health Organization issued a Medical Eligibility Criteria guide for contraceptive use to

evaluate the risks and benefits of contraception among women with medical conditions.[10] In 2010, the Centers for Disease Control and Prevention (CDC) stated that a woman who received a transplant in the past 2 years was at an increased health risk for an unintended pregnancy.[11] For women with uncomplicated solid organ transplants, all forms of contraceptive were classified as Category 2, meaning that the advantages for using the method generally outweigh the theoretical or proven risks. On the contrary, in women with a complicated solid organ transplant that involves higher risk of graft failure, rejection, or vasculopathy, estrogen-containing methods of contraception are considered Category 4, or as having an unacceptable health risk if the method is used. Intrauterine devices are considered Category 3, meaning that the theoretic or proven risks may outweigh the advantages of using the method in recipients with a complicated solid organ transplant. These statements are based mostly on expert opinion due to the paucity of data in this area.

When working with a recipient to determine an appropriate form of contraception, it is important to consider the (1) type of transplanted organ, (2) hormonal (estrogenic) levels of the contraceptive, (3) potential interactions of the contraceptive with immunosuppressive agents, and (4) underlying medical conditions of the patient. For example, combined hormonal methods (estrogen + progestin) are contraindicated in women with cardiac allograft vasculopathy or active liver disease. In addition, combined oral contraceptives are relatively contraindicated in women with hypertension, age $>$ 35 years, and smokers (especially in combination). They may also increase the blood levels of immunosuppressants such as corticosteroids, cyclosporine, tacrolimus, and sirolimus. Thus, blood levels of immunosuppressants must be monitored to ensure safety. Liver dysfunction can also interfere with estrogen metabolism that may adversely alter the efficacy of combined oral contraceptives. Gastrointestinal disturbances can also reduce proper absorption of estrogen and alter efficacy of hormonal therapy.

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Perhaps the best contraceptive option for the transplant population is long-acting reversible contraception; more specifically, intrauterine devices (IUDs). The IUDs have negligible drug interaction, are highly efficacious, are reversible, and have minimal risk to the recipient. Furthermore, recent studies have shown that they are safe to use in immunocompetent and immunocompromised patients.[12-14] Table 1 displays the array of contraceptive options available for transplant recipients, along with advantages and disadvantages of each, and their CDC criteria for safety.[11]

Preconception Counseling

Although preconception counseling is ideally introduced before transplantation, it should continue through the post-transplantation process. Preconception counseling should be offered to both the transplant recipient and his or her partner. Obstetricians should work with their patients to determine the ideal timing of conception and pregnancy. The original disease should be considered, as well as the potential risk of recurrence. The original disease may be associated with its own pregnancy-related morbidities and patients should be counseled appropriately. For example, poorly controlled diabetes is associated with an increase in birth defects and pregnant women with diabetes are at increased risk of thromboembolic phenomena.[15] Contraception can be discontinued when it is determined that pregnancy would be relatively safe for the mother, her graft, and fetal development.

The American Society of Transplantation (AST) consensus summary recommends that pregnancy is allowable if there has been (1) no rejection within the past year, (2) there is adequate and stable graft function (in kidney recipients creatinine $<$ 1.5 mg/dL, no or minimal proteinuria $<$ 500 mg/24 h), (3) no acute infections that may impact fetal growth and well-being, and (4) maintenance immunosuppression is at stable dosing.[16] With regard to infections, it is particularly important to monitor cytomegalovirus infection, which can reactivate in transplant recipients and can cause fetal malformations if left untreated.[15] In addition, both the NTPR and the AST consensus groups advise recipients to wait at least 1 year after transplantation for graft function stabilization and reduction of immunosuppressant medication dosage to maintenance levels before conceiving. In the meta-analyses reported by Deshpande and colleagues,[3,4] investigators noted that delaying pregnancy for 1 year after transplantation was associated with better maternal and neonatal outcomes and decreased incidence of obstetric complications.

TABLE 1

Contraception Management in Transplant Recipients

Method	Advantages	Disadvantages	CDC Category (Uncomplicated)	CDC Category (Complicated)
Copper-T IUD	Most effective, long acting, reversible	Heavy menses	2	Initiation: 2 Continuation: 3
Progestin IUD	Most effective, long acting, reversible, decreased anemia	Irregular bleeding	2	Initiation: 2 Continuation: 3
Depot medroxyprogesterone acetate	Highly effective, decreased anemia	Decrease in BMD, irregular bleeding, possible cholestatic effect	2	2
Progestin implant	Most effective, long acting, no BMD decrease	Irregular bleeding	2	2
COC	Menstrual regulation, decreased anemia	Contraindicated in those with uncontrolled hypertension, active liver disease, and personal history of myocardial infarction, stroke, or DVT; first-pass liver metabolism; gastrointestinal disturbance may decrease absorption	2	4
Contraceptive patch	First-pass liver metabolism avoided	Higher circulating levels of estrogen; contraindicated in those with uncontrolled hypertension, active liver disease, and personal history of myocardial infarction, stroke, or DVT	2	4
Vaginal ring	First-pass liver metabolism avoided, lower circulating estrogen	Contraindicated in those with uncontrolled hypertension, active liver disease, and personal history of myocardial infarction, stroke, or DVT	2	4
Progestin-only pill		Less effective than COC; first-pass liver metabolism	2	2
Condoms	No drug interactions, protects from sexually transmitted diseases	Less effective	1	1
Cervical cap/ diaphragm	No drug interactions	Less effective	1	1
Emergency contraception	Effective after sexual intercourse	Not effective as ongoing method	1	1

CDC Categories of medical eligibility criteria for contraceptive use: 1: a condition for which there is no restriction for use of the contraceptive method; 2: a condition for which the advantages of using the method generally outweigh the theoretical or proven risks; 3: a condition for which the theoretical or proven risks usually outweigh the advantages of using the method; 4: a condition that represents an unacceptable health risk if the method is used.
BMD, bone mineral density; CDC, Centers for Disease Control and Prevention; COC, combined oral contraceptive; DVT, deep vein thrombosis; IUD, intrauterine device; Data from Centers for Disease Control and Prevention.[11]

Immunosuppression Modification and Management

When planning a pregnancy, recipients should discuss with their transplant teams their immunosuppressive regimens and potential benefits and risks to the allograft and the fetus, and whether there are potential changes prior to conception.

Most immunosuppressive medications are considered relatively safe as they have not been shown to cause either an increase in the incidence of or a pattern of birth defects. These relatively safe medications include prednisone, azathioprine, the calcineurin inhibitors, cyclosporine, and tacrolimus.[17] There are extensive data on azathioprine and pregnancy; at therapeutic doses, transient neonatal leukopenia is common, but there is no increase in the risk of birth defects.

Among live births with cyclosporine exposure reported to the NTPR, the birth defect incidence was 4.9% (19/391), not different from the incidence of 3% to 5% in the general US population. In another NTPR study the incidence of birth defects was 4.2% (3/72) in newborns exposed to tacrolimus. In contrast, with mycophenolic acid (MPA) products, animal studies have demonstrated developmental toxicities, malformations, and increased fetal death. The NTPR has reported that MPA exposure is associated with an increased incidence of spontaneous abortions and an increase in the rate of birth defects (to approximately 24%), and a pattern of structural abnormalities in the fetus.[18,19] Whenever possible, based on the potential rejection risk, patients should be switched from MPA to another agent before attempting conception.

There are limited pregnancy outcome data regarding exposure to sirolimus during pregnancy.[20] According to the package insert, animal studies have not demonstrated teratogenicity; however, decreased fetal weight and delayed skeletal ossification have been reported. An increased incidence of birth defects has not been noted to date. It is important to counsel recipients on the importance of adhering to their prescribed immunosuppressive regimens. Lowering doses or stopping immunosuppression could lead to graft rejection, which could lead to graft loss. The primary goal is to monitor the recipient closely and measure immunosuppressant levels for appropriate drugs through the recipient's pregnancy to assess transplant organ function and the absence of rejection, which can be difficult to manage during pregnancy. Each trimester presents different concerns: for example, morning sickness and drug absorption in the first trimester compared with increased fetal metabolism of medications requiring increased maternal dosing in the third trimester.

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Pregnancy Complications

Solid organ transplant recipients often have comorbidities, such as hypertension and diabetes, which add additional risk to a pregnancy. NTPR publications and reviews have sought to summarize and quantify these risks of pregnancy complications in both generalizable and subgroup-specific manners. Tables 2 and 3 summarize the various incidences of maternal complications stratified by solid organ type. These tables provide information for counseling recipients when discussing pregnancy outcomes, obstetric complications, and neonatal outcomes. However, it is important to note that these data do not take into account the original disease or condition of the recipient, the functional status of the transplanted organ, or the immunosuppressive history (induction medications, maintenance medications past and present). There is a 54.2% incidence of hypertension in kidney transplant recipients and a 27.2% incidence among liver transplant recipients[3,4]; hypertension is an independent risk factor for pregnancy complications.[15] Hypertension before or during should be treated with medications appropriate for pregnancy, because angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are contraindicated during pregnancy.[15]

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Transplant recipients who are women may also have pre-existing diabetes, or develop gestational diabetes. Reported incidences of gestational diabetes among kidney and liver transplant recipients are 8.0% and 5.1%, respectively.[3,4]

TABLE 2

National Transplantation Pregnancy Registry Maternal and Neonatal Outcome Data According to Transplanted Organ Type

	Kidney (%)	Liver (%)	Kidney/ Pancreas (%)	Heart (%)	Lung (%)
Maternal Complications					
Hypertension	53-64	17-40	41-95	28-51	52
Preeclampsia	30-32	20-24	22-32	10-25	5
Diabetes	5-12	2-13	0-5	0-4	26
Rejection	1-2	2-11	0-14	3-21	16
Graft loss within 2 y	6-9	2-8	10-17	0-4	14
Pregnancy Outcomes					
Spontaneous abortion	12-25	15-20	8-31	19-44	27
Live birth	71-77	72-82	64-79	48-70	58
Prematurity (< 37 wk)	52-53	30-48	65-84	8-54	63
Mean gestational age (wk)	35.3-35.9	36-37.3	33.7-34.8	36.1-37.8	33.9
Cesarean delivery	43-57	29-45	61-69	30-57	32

Range of incidence due to subset analysis for different immunosuppressants.
Data from Armenti VT et al.[17]

TABLE 3

Maternal and Neonatal Complications in Kidney and Liver Transplant Recipients

	Liver (N = 450)	Kidney (N = 4002)
Pregnancy Outcome		
Live birth (%)	76.9 (72.7-80.7)	73.5 (72.1-74.9)
Miscarriage (%)	15.6 (12.3-19.2)	14.0 (12.9-15.1)
Termination (%)	6.2 (4.2-8.9)	9.5 (8.6-10.4)
Stillbirth (%)	0.9 (0.2-2.3)	2.5 (2.0-3.0)
Ectopic pregnancy (%)	0.4 (0.1-1.6)	0.6 (0.4-0.9)
Obstetric Complication	**Liver**	**Kidney**
Hypertension (%)	27.2 (22.9-31.9)	54.2 (52.0-56.4)
Preeclampsia (%)	21.9 (17.7-26.4)	27.0 (25.2-28.9)
Gestational diabetes (%)	5.1 (3.0-8.0)	8.0 (6.7-9.4)
Delivery Outcome	**Liver**	**Kidney**
Cesarean delivery (%)	44.6 (39.2-50.1)	56.9 (54.9-58.9)
Preterm birth (%; < 37 wk)	39.4 (33.1-46.0)	45.6 (43.7-47.5)
Gestational age (wk)	36.5	35.6
Birth weight (g)	2677	2420

N = the number of reported pregnancies for which data were available.
Data from Deshpande NA et al.[3,4]

Pregestational diabetes is associated with congenital anomalies and both pregestational and gestational diabetes are associated with growth restriction or macrosomia, as well as fetal demise. Glycemic control in early pregnancy is important in order to minimize potential harm to the fetus.

Potential adverse neonatal outcomes including low birth weight and prematurity should be considered. Table 2 shows the incidence of prematurity (< 37 weeks of gestation) by transplanted organ. Early ultrasonography should be performed to determine an accurate gestational age and serial ultrasonography every 4 weeks beginning at 24 to 26 weeks of gestation should be maintained to evaluate fetal growth.[12] Monitoring for fetal well-being after 32 weeks is prudent and if desired, patients should meet with a member of the neonatology team prior to the delivery to become familiar with neonatal

care. The incidence of cesarean delivery among kidney and liver transplant recipients is 56.9% and 44.6%, respectively.[3,4]

Nutritional Considerations

Many immunosuppressive medications, such as corticosteroids, tacrolimus, and cyclosporine, are associated with common metabolic and nutritional side effects.[21] For example, corticosteroid therapy may often cause increased appetite, leading to weight gain. As such, maternal nutrition should be appropriately monitored and modified during pregnancy to meet metabolic demand. Carbohydrates should represent 45% to 65% of total caloric intake, with the goal of maximizing intake of complex carbohydrates and limiting intake of simple carbohydrates. Glucose homeostasis may be altered by immunosuppressants, so serum glucose levels should be appropriately monitored with early glucose screening or daily glucose monitoring if the woman has known glucose intolerance. The aim should be to maintain a fasting plasma glucose of ≤ 90 mg/dL and a postprandial plasma glucose of ≤ 120 mg/dL. Fat should represent 20% to 35% of caloric intake during pregnancy and trans fat intake should be minimized. Protein consumption should be slightly increased to 1 g/kg/d to meet increased protein needs during pregnancy. An increase in fiber consumption coupled with adequate fluid intake is recommended to reduce the side effects of decreased gastrointestinal motility and gastrointestinal discomfort as associated with pregnancy. Folate supplementation is recommended to prevent neural tube defects in the fetus.[21] Potassium levels should be monitored, as some transplant medications may cause hyperkalemia as a side effect. Finally, transplant recipients are at an increased risk of developing osteopenia, osteoporosis, and fractures.[15] A simple regimen of 1000 mg/d of calcium and 0.25 µg/d of vitamin D can decrease bone loss and improve the risk of adverse outcomes.

Postpartum Management and Breastfeeding

Postpartum monitoring of the transplant recipient is essential. Immunosuppressive drug levels should be monitored, as blood levels will vary due to changing gastrointestinal function and absorption, loss of effects of fetal liver metabolism, reconstitution of the maternal immune system, the potential for postpartum depression,[15] and medication nonadherence. It is essential to continue monitoring organ function for potential graft rejection in light of the above and the mother's focus on the child's health, potentially distracting her from her own health issues. Breastfeeding by transplant recipient mothers remains a controversial issue requiring further investigation, although recent reports have been supportive. The NTPR has reports from 98 recipients who have breastfed their 126 children while taking a variety of immunosuppressive agents and regimens. There were no specific problems reported in the children related to breastfeeding. It is advisable to check the infant's blood level of the maternal medications for which levels are available—a measurable level in the infant may be a substantial reason to discontinue breastfeeding.[22] Continued study in this area is warranted.[12,17,22-25] When appropriate, recipients should be reinitiated on contraception after delivery. If childbearing is complete, more permanent options should also be discussed.

Long-term Outcomes for Transplant Recipients and Their Offspring

There has long been speculation that in utero exposure to immunosuppressive agents may be associated with the development of autoimmune disease, renal insufficiency, and neurocognitive deficits later in life.[26] To date, NTPR reports have not confirmed these concerns. In the 2011 NTPR report, kidney transplant recipients (n = 71) who took cyclosporine (modified) or tacrolimus while pregnant and had a child under the age of 6 at the time were contacted by phone.[17] Participants were asked standardized questions from the Development Assessment of Young Children assessment. The data suggested that the children showed normal cognitive and physical development that appeared comparable with the general population.[17]

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In another NTPR study by Stanley and colleagues,[27] 175 children (mean age 4.4 years) exposed in utero to cyclosporine from 133 renal transplant recipients were surveyed. This survey showed that 16% (n = 29) of children were noted to have delays or need educational support and 1.7% (n = 3) of children had major disabilities. Thus, there was an absence of developmental delay in 84% of offspring of mothers who were renal transplant recipients.

Conclusions

Successful pregnancy outcomes are increasingly possible among the transplant recipient population. A multidisciplinary team should be involved in the monitoring and care

TABLE 4

Summary of Obstetric Management for Pregnancy After Transplantation

After Transplantation

1. Delay conception for at least 1 year with adequate contraception
2. Assess and monitor graft function
3. Maintain immunosuppressive regimen
4. Manage comorbid conditions

Preconception Counseling

1. Discuss the effect of pregnancy on transplant organ function
2. Discuss risks of maternal complications: hypertension, preeclampsia, diabetes, rejection, and graft loss
3. Obtain good control of prepregnancy hypertension and diabetes
4. Discuss risks of neonatal complications: prematurity and low birth weight
5. Modification of immunosuppressive regimen if necessary
6. Test for cytomegalovirus and other potential infections

Early Pregnancy

1. Accurate and early diagnosis and dating of pregnancy
2. Close monitoring of graft function and immunosuppressive drug levels
3. Surveillance for bacterial infection [urine culture and viral infection (cytomegalovirus and herpes simplex virus)]
4. Fetal surveillance for malformation, fetal growth, and well-being
5. Maternal surveillance for hypertension, gestational diabetes, and preeclampsia
6. Anesthesia evaluation/consult for heart/lung transplant patients

Labor and Delivery

1. Aim to deliver at term
2. Perform cesarean delivery only for appropriate obstetric reasons
3. For heart, lung, and heart-lung recipients: continuous cardiac monitoring, judicious use of intravenous fluids, early involvement with anesthesiology

Postpartum

1. Monitor immunosuppressive drug levels and alter doses and regimen as necessary
2. Begin contraception when appropriate
3. The documented benefits of breastfeeding may outweigh the potential risks of infant immunosuppressive exposure
4. Mental health counseling if needed for postpartum depression

Data from Mastrobattista and Gomez-Lobo[15] and Armenti VT et al.[17]

of the transplant recipient before, during, and after pregnancy. We recommend that all transplant recipients be evaluated by a high-risk obstetrician in conjunction with their transplant team. To summarize the key considerations for obstetric management of transplant recipients, we have provided an outline of important steps to be taken after transplantation, including preconception counseling, pregnancy, labor and delivery, and in the postpartum period (Table 4).

Preconception counseling should be introduced as early as practical, preferably during the evaluation process, and reiterated throughout the transplantation process. Contraception should be started following transplantation to limit the risk of unplanned pregnancy. Long-acting reversible contraception, such as IUDs, are the most effective and should be considered. Recipients should delay pregnancy for at least 1 year after transplantation to reduce the potential risk of maternal and neonatal complications.

A fetus exposed in utero to MPA appears to have an increased risk of miscarriage and a fourfold increase in birth defects (24% vs 4%). Before conception, when possible and based on the potential rejection risk, women planning pregnancy should be switched from MPA to an alternative agent. During pregnancy, immunosuppression should be closely monitored and appropriate dosing maintained to avoid graft rejection. If there is suspicion of graft dysfunction during pregnancy, appropriate investigation is warranted; biopsy should be performed if necessary. Throughout pregnancy, there should be appropriate monitoring and management of maternal nutrition and fetal growth.

During pregnancy, obstetricians and the multidisciplinary team should be attentive to monitoring potential maternal complications such as hypertension, gestational diabetes, and preeclampsia. Cesarean delivery should be performed for obstetric reasons only, and avoided if possible. Transplant recipients should be fully counseled regarding risks of premature delivery and low birth weight newborns.

It is important to note that we have made great progress in collecting and analyzing data on post-transplant pregnancies; most of the currently available information stems from case series, registries, and literature reviews. These data may be biased because of incomplete or selective sampling. Ideally, prospective studies involving maternal and neonatal outcomes

after transplantation should be performed. Continued studies are needed to assess the long-term health outcomes in transplant recipients and their offspring. Overall, pregnancy after transplantation is possible for all solid organ transplant recipients and continued reporting to the NTPR and through publication is encouraged. ■

Neha A. Deshpande, BA, Veronica Gomez-Lobo, MD, and Michael J. Moritz, MD, report no conflicts of interest and have received no financial support for the research. Vincent T. Armenti, MD, PhD, has received grant support from Novartis (New York, NY), Pfizer (New York, NY), Astellas Pharma US (Northbrook, IL), and Bristol Myers Squibb (New York, NY). The National Transplantation Pregnancy Registry has received grants from Novartis, Astellas Pharma US, Genentech (South San Francisco, CA), Pfizer, Teva Pharmaceuticals (Petah Tikva, Israel), Sandoz Pharmaceuticals (Princeton, NJ), and Bristol-Myers Squibb.

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MAIN POINTS

- Successful pregnancy outcomes are possible among all solid organ transplant recipients. Transplant recipients are at an increased risk for both maternal and neonatal complications and should be seen by a high-risk obstetrician in conjunction with their transplant teams.
- A woman of childbearing age who receives a transplant is typically advised to avoid pregnancy for at least 1 year after transplantation, based on data that show an increased risk of potential graft dysfunction, rejection or loss, and increased risk of prematurity for neonates. Perhaps the best contraceptive option for the transplant population is long-acting reversible contraception, more specifically, intrauterine devices. Contraception can be discontinued when it is determined that pregnancy would be relatively safe for the mother, her graft, and fetal development.
- Most immunosuppressive medications are considered relatively safe as they have not been shown to cause either an increase in the incidence of or a pattern of birth defects. These relatively safe medications include prednisone, azathioprine, the calcineurin inhibitors, cyclosporine, and tacrolimus. There are extensive data on azathioprine and pregnancy; at therapeutic doses, transient neonatal leukopenia is common, but there is no increase in the risk of birth defects. Among live births with cyclosporine exposure reported to the National Transplantation Pregnancy Registry (NTPR), the birth defect incidence was 4.9%, not different from the incidence of 3% to 5% in the general US population.
- Breastfeeding by transplant recipient mothers remains a controversial issue requiring further investigation, although recent reports have been supportive of the practice. The NTPR has reports from 98 recipients who have breastfed their 126 children while taking a variety of immunosuppressive agents and regimens. There were no specific problems reported in the children related to breastfeeding. It is advisable to check the infant's blood level of the maternal medications for which levels are available—a measurable level in the infant may be a substantial reason to discontinue breastfeeding.
- There has long been speculation that in utero exposure to immunosuppressive agents may be associated with the development of autoimmune disease, renal insufficiency, and neurocognitive deficits later in life. To date, NTPR reports have not confirmed these concerns.

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