Diagnosis and Management of Kidney Failure in the Neonate

In the neonate, kidney failure is most frequently due to congenital malformations of the urinary tract. These conditions are among the most common congenital abnormalities. Fortunately, most are innocuous and clinically insignificant. Malformations of one kidney (even absence of one kidney), where its mate is normal, are not associated with risk to the pregnancy or the fetus. As kidney transplantation has demonstrated, a single healthy kidney can provide its owner with a completely normal life.

Although the urinary tract begins its embryological development at 6-8 weeks after conception, only after the 18-20th week of gestation can prenatal ultrasonography adequately image the kidneys, ureters (only if dilated) and bladder. As pregnancy progresses, fetal urine is the main component of amniotic fluid. Malformations of both kidneys significant enough to reduce fetal urine production can result in oligohydramnios. This condition of insufficient amniotic fluid can impair lung development, such that mechanical ventilation support is needed after birth.

Continued from Kidney

Sometimes, prenatal ultrasonography fails to detect serious congenital malformation of both kidneys and the diagnosis is made after birth. Common presentations of such conditions include less than normal urine production, flank or abdominal mass(es), weak urinary stream, and laboratory evidence of impaired kidney function. Whether or not there has been a prenatal diagnosis, postnatal ultrasonography and a radio contrast voiding cystourethrogram (VCUG) are the imaging tools required to make a specific anatomic diagnosis. Some examples are posterior urethral valves, bilateral renal dysplasia (often associated with vesicoureteral reflux) and Prune Belly Syndrome.

In addition to obstructive malformations of the urinary tract, autosomal recessive polycystic kidney disease can be detected by prenatal ultrasonography. This is a genetic condition (both parents must be carriers of the gene, but are unaffected by the disease) that affects both kidneys equally. The pregnancy can be complicated by oligohydramnios. The kidneys can be very enlarged, hypertension is common, and impaired kidney function can be present at birth.

Another situation that can result in kidney failure is the neonate who is born with normal kidneys, but develops sepsis, shock, hemorrhage, severe dehydration, major vessel blood clot or some other catastrophe. Typically, urine production declines and both fluids and electrolytes must be restricted. After several days, urine production resumes and kidney function recovers, often without permanent sequelae.

While the management of the neonate with urinary tract malformation may involve pediatric urology to improve urine drainage surgically, the medical management of kidney failure, regardless of its cause, depends upon the degree of functional impairment. If it is mild, the amount of urine produced is typically normal and no specific interventions are necessary with respect to diet or medications. The more severe the degree of kidney failure, the more likely that there will be predictable complications which will require therapy. Specifically, as the kidneys are responsible for excreting the acid that accumulates from metabolism, acidosis may require alkali treatment. Failure of the kidneys to produce sufficient erythropoetin (a hormone that stimulates the bone marrow to make new red blood cells) results in anemia, which may require regular injections of erythropoietin to treat this condition. The kidneys also help regulate blood concentrations of calcium and phosphorous, required for normal bone metabolism. This too can be successfully treated with medication. Hypertension, if present, requires and responds to drug therapy.

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Overall, the management of the complications of kidney failure, although complex, is quite successful. For those neonates whose kidney failure cannot be adequately managed by these treatments, particularly those whose urine production is absent or minimal, dialysis therapy is indicated. Hemodialysis, a blood cleansing procedure, which requires an extracorporeal circuit, is a high-risk procedure in neonates. Alternatively, peritoneal dialysis is much less so, yet effective in removing unwanted solutes and Neonates and infants with significant kidney failure frequently feed poorly and growth is sub optimal. They may benefit from continuous nasogastric tube feeding and/or injections of growth hormone.

If kidney function is less than 1/3 normal, the natural course of kidney failure is one of progressive deterioration, with a time course measured in years. When kidney function reaches less than 10% of normal, renal replacement therapy (either initiation of dialysis or kidney transplantation) is required to sustain life. However, transplantation is a clearly superior form of renal replacement therapy. Parents are typically very willing to be a kidney donor and are a ready source of this "gift of life" for their child. If necessary, an adult kidney from a living donor can be surgically implanted when a body weight of more than 8 kg is reached. The functional life of a parent to child kidney transplant is now being measured in decades.

The diagnosis of kidney failure in the neonate is frequently straightforward, based upon the results of the pre and postnatal history, physical examination, imaging studies and laboratory tests. However, the management of these infants presents a formidable challenge to the skills of the neonatology medical, nursing and sub-specialty staff. Despite the labor-intensive nature of treatment, most infants and their families have a good quality of life.

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Inhaled Nitric Oxide and the Premature Infant

Inhaled nitric oxide is a selective pulmonary vasodilator that was recently approved by the US Food and Drug Administration for use in term and near-term infants with respiratory failure caused by persistent pulmonary hypertension of the newborn. Its use for the premature infant is currently under investigation. It is often necessary to use high oxygen concentrations in the treatment of pulmonary hypertension. Inhaled nitric oxide in the presence of hyperoxia may generate a number of reactive molecules, including peroxyxenites, which may intensify acute lung injury. Potential consequences of this injury may be the progression to chronic lung disease.

One of the studies being done in our laboratory looks at the effect of nitric oxide on cultured human lung cells that are exposed to hyperoxia (high concentrations of oxygen). We wanted to determine whether nitric oxide would cause the cells to undergo apoptosis. Apoptosis is a process whereby developmental or environmental stimuli activate a genetic program to implement a specific series of events that culminate in the death and efficient disposal of the cell.

Preliminary results show that high doses of and prolonged exposures to nitric oxide resulted in apoptosis, whether the lung cells were in hyperoxic conditions or not. This may imply that prolonged and high dose exposures to nitric oxide may promote the progression to chronic lung disease.

In contrast, the WMC NICU is currently involved in a multicenter trial to determine whether treatment with inhaled nitric oxide will allow the premature infants at risk for developing chronic lung disease of infancy to tolerate lower oxygen concentrations and lower ventilator settings. Because inhaled nitric oxide has been shown to improve blood flow into the lungs, its use may lead to better ventilation-perfusion matching in the lungs and consequently a decreased need for higher oxygen concentrations and higher ventilator pressure support. If this were the case, then the premature lung may be given a chance to heal and the risk for developing chronic lung disease may be decreased or prevented.

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Sound Shore Medical Center in the News

Sound Shore Medical Center of Westchester was in the national spotlight when The Discovery Health Channel aired a segment on Gestational Diabetes featuring Dr. Patricia A. Devine, Chief of Maternal/Fetal Medicine and Evert Owens, RN, CDE, Director of the SSMC Diabetes Education Center. The segment aired three times during June.

June also saw “20/20” back at SSMC to do a story on videotaping the birth of children by families. Many staff members on the Maternity floor were featured.

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Current Management of Ovarian Cysts in Pregnancy

With the increased use of diagnostic ultrasound during early pregnancy, ovarian cysts are more frequently detected. While it is frequent to encounter an ovarian cyst during pregnancy, only 2 to 5 percent of these are malignant ovarian tumors. The incidence is approximately 1 in 18,000 to 1 in 47,000 pregnancies.

Three major types of ovarian neoplasm’s, epithelial, germ cell, and sex cord stromal, may occur during pregnancy. Germ cell tumors are the most common and account for 45 percent; 37.5 percent are epithelial tumors, 10 percent are sex cord stromal tumors, and 7.5 percent are categorized as miscellaneous. The majority of epithelial ovarian tumors complicating pregnancy are of low grade (grade 1 or low malignant potential) or early stage, not uncommonly both low grade and stage I.

Management of ovarian cysts in pregnancy is controversial. Because of the risks of surgical intervention may favor a conservative approach during pregnancy. Serial sonograms may be used in determining the nature and biologic behavior of the tumor. Surgical intervention of an ovarian cyst during pregnancy was indicated for 3 reasons: (1) danger of torsion, rupture, or hemorrhage, (2) danger of malignancy, and (3) elimination of a possible cause of dystocia. If a patient presents with symptoms consistent with torsion, rupture, or hemorrhage, surgical intervention is needed immediately. Surgical exploration is also recommended for an associated when there is evidence of malignancies such as ascites and metastatic disease such as extra-ovarian masses and omental lesions. Other than lesions that warrant immediate management, it is preferred to delay surgical intervention until the fetus is matured or during the postpartum period. A number of opposing risks require consideration prior to following a conservative approach. The risk of a delay of surgical intervention could permit a malignant ovarian tumor to be undetected and lead to progression of the tumor. However, considering the rarity of advanced-stage poorly differentiated epithelial tumors in this age group, this risk is relatively small. There may be an increased probability that an ovarian neoplasm during pregnancy will undergo torsion or rupture, and surgical intervention for these events is associated with higher fetal loss than an elective procedure. Occasionally, ovarian tumors may be the cause of obstructed labor, this is uncommon. Serial ultrasound evaluations may identify the rare tumor that remains in the pelvis during later trimester of pregnancy.

Recently, laparoscopic management of ovarian cysts during pregnancy has been considered as an alternative procedure. In addition to the generally accepted benefits of laparoscopy with respect to laparotomy, there are some specific advantages in the case

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of pregnant patients. Reduced postoperative pain may minimize fetal exposure to narcotics. Early mobilization may reduce the risk of maternal thromboembolism. In addition, the avoidance of large abdominal incisions reduces the risk of wound problems that could be aggravated by the gravid uterus. Furthermore, the reduction in intraoperative uterine manipulation may reduce the risk of uterine irritability and thus the risks of spontaneous abortion and of preterm labor. Surgical intervention with laparoscopy is usually delayed until the second trimester. One of the critical factors in the laparoscopic approach is the gravid uterus. Laparoscopic surgery for ovarian cysts should be performed between the 12th and 16th weeks of gestation.

When a malignant ovarian tumor is encountered during pregnancy, surgical management is similar to that for the non-pregnant patient. Prior to surgery, a comprehensive discussion with the patient should guide the extent of surgery if metastatic disease, especially a high-grade epithelial lesion, is encountered. If the patient is preterm and the tumor appears confined to one ovary, consideration should be given to performing the staging to cytologic washings, unilateral oophorectomy, and a thorough exploration of the abdomen and pelvis. The potential benefit of more extensive staging, including aortic node sampling, may be offset by higher pregnancy loss or neonatal morbidity. Depending on the gestational age and the patient's desires, limited surgery followed by chemotherapy and additional surgery following delivery must be offered in certain patients.

Preoperative serum tumor markers are of limited value during pregnancy due to the physiologic increases in hCG, alphafetoprotein, and CA 125. Following histologic confirmation of a malignant ovarian tumor, the appropriate serum markers are useful to monitor the course of the management of the disease.

Postoperative adjuvant therapy should follow the treatment guidelines for the non-pregnant patient. Since 1995, the combination of cisplatinum and taxol has become the standard regimen for treatment of ovarian cancers. There is no information available at this time regarding the potential toxic effects of taxol on a developing fetus. Because of the earlier stages of ovarian malignancies that one encounters during pregnancy, these malignancies are usually associated with an optimistic outcome.

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Happy Mother's Day
**GENETICS WEB SITES**

Good resources for clinical genetics

Perinatal Section of AAP News


http://www.ibis-birthdefects.org/start/sites.htm

http://www.nlm.nih.gov./medlineplus/geneticsbirthdefec

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**Congratulations** to Dr. Edmund LaGamma on your election to Alpha Omega Alpha! Honor Medical Society!

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