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IN THIS ISSUE

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Neonatology Today (NT) is a monthly newsletter for Neonatologists and Perinatologists that provides timely news and information regarding the care of newborns and the diagnosis and treatment of premature and/or sick infants.

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Neonatal Neurology
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35th Annual Conference- Miami Neonatology 2011 and One Day Workshop, "Advances in Respiratory Care"
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Patent Ductus Arteriosus Stenting – Problems, Complications and Technical Consideration

By Mazeni Alwi, MD

Advances in surgical techniques and postoperative care have significantly changed the management of cyanotic congenital heart disease. The trend is towards definitive repair in early infancy as far as possible, obviating the need for palliative surgery as first stage treatment in many conditions. This is best illustrated by the way non-duct-dependent Tetralogy of Fallot (TOF) is managed in the modern era, where total correction is often performed during mid to late infancy, such that palliative modified Blalock-Taussig Shunt (BTS) is rarely performed except in the very small symptomatic patients. However, the BTS, as a bridge towards definitive repair still forms an important part in the management of the more complex cyanotic heart disease, particularly for those in whom the pulmonary blood flow is duct-dependent. This applies to diverse lesions, from TOF to hearts with single ventricle physiology where pulmonary atresia is the unifying thread. Because these are duct-dependent lesions, BTS in the modern era is almost exclusively performed in the neonatal period. Compared to BTS performed later in childhood, those performed in the neonatal period are not unexpectedly associated with high morbidity. The early complications include early shunt failure due to acute thrombosis, overshunting with heart failure features, chylothorax, pleural effusions and diaphragmatic paralysis. There is especially increased mortality in patients with pulmonary atresia with intact ventricular septum (PA-IVS) with the added feature of major coronary sinusoids. Because the shunted-branch pulmonary arteries are often small, no bigger than 4 mm in most cases, the late complications of pulmonary artery distortion or stenosis is of concern, especially those destined for the Fontan track. Because of these issues related to neonatal shunts, there have been a number of novel attempts to maintain ductal patency for a longer term as an alternative form of palliation in these duct-dependent lesions. Formalin infiltration of the patent ductus arteriosus (PDA) at thoracotomy was one of the earliest suggestions but this is almost just as invasive as conventional shunt. Oral Prostaglandin has also been advocated but the frequency at which it has to be administered makes this impractical whilst there was also concern about its efficacy. With

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advances in transcatheter balloon dilatation techniques in the neonates, simple balloons or balloon heated with laser or radiofrequency has been suggested, but again the problem of efficacy or consistency of results arose.[1]

The real prospect of transcatheter manipulation of the ductus arteriosus to reliably maintain its patency became possible when balloon expanded coronary stents came into wide clinical use as an extension of PTCA in the management of CAD. In an experimental study involving newborn lambs, Coe et al successfully implanted stainless steel stents without encountering major complications, achieving continued ductal patency for up to 3 months when they were sacrificed.[2] However, transferring PDA stenting from the animal laboratory to clinical practice has met with several major problems.

The early report of PDA stenting in duct-dependent cyanotic heart disease by Gibbs highlighted these difficulties and potential complications of this procedure in neonates. Obviously small patient size and, therefore, small vessels, cardiac chambers and thin walls are susceptible to damage and perforation with manipulation of stiff catheters and guide wires. Moreover, the stent and balloon during that era required a 5F or 6F sheath for delivery, making the transfemoral arterial route not possible.[3] But more than just patient size, the PDA in cyanotic duct-dependent lesion are often longer, more tortuous and arise more proximally from the aorta. This is especially so in TOF with pulmonary atresia (PA) where the PDA may arise very proximally from the underside of the arch, giving the appearance of a vertical duct. This poses a major technical problem when stenting is attempted via the femoral arterial route due to the difficulty of engaging the ductal ampulla and getting a stable wire position for tracking of balloon and stent. For these two reasons, PDA stenting in these duct-dependent neonates were performed via axillary artery cut-down in the earlier reports.

The additional difficulties that were encountered in this early experience were the inability to enter the duct, ductal spasm and incomplete stenting of the full length of the duct, hence requiring repeat procedures. It is hardly surprising that after 6 years with 7 successful procedures out of 11 patients with duct-dependent pulmonary circulation (most probably not all consecutive patients were recruited) with 2 failures and 2 deaths due to ductal spasm, apart from poor duration of palliation due to endothelial proliferation, the authors concluded that ductal stenting in this group of patients cannot be recommended.[4]

However, Schneider et al reported a more encouraging outcome of PDA stenting in neonates with duct dependent pulmonary circulation performed within the similar period.[5] The authors divided the patients into two groups, the first (8/21) were those with critical pulmonary stenosis (PS) or pulmonary atresia intact ventricular septum (PAIVS) who primarily underwent transcatheter relief of right ventricular outflow obstruction, but later required additional source of pulmonary blood flow due to mainly small right ventricular size/poor right ventricular compliance. In this group, PDA stenting was performed transvenously via the newly opened pulmonary valve. The other group (13/21) was comprised of patients with pulmonary atresia in the setting of TOF, tricuspid atresia and transposition of great artery (TGA), ventricular septal defect (VSD). In this second group PDA stenting was performed by the transarterial route. The access was via axillary artery cut-down in the majority of cases.

Similarly, Gewillig et al also reported encouraging results of PDA stenting in patients who required additional source of pulmonary blood flow after relief of right ventricular outflow tract obstruction in critical PS or PAIVS.[6] Clearly, in this group of patients, PDA stenting by the transvenous route is a fairly straightforward procedure once the pulmonary valve is opened.

The current generation of coronary stents, delivery catheters and wires have better flexibility and lower profile, allowing them to overcomesome of the earlier problems of PDA stenting. Newer features such as heparin coating and drug elution may be helpful in extending the duration of palliation. It is perhaps timely to examine the problems and technical difficulties and suggest technical improvement of PDA stenting in the other group – pulmonary atresia in the setting of TOF, tricuspid atresia, TGA, VSD and univentricular hearts where access to the PDA is only via the aorta given the limitations to vascular access via the femoral arterial route due to small vessel size and the peculiar morphology of the ductus which in these lesions tend to be long, tortuous and arise proximally. In the past, this has been achieved by axillary artery cut-down to engage the ductal ampulla and secure good wire position for stent delivery and deployment. However, most cardiologists today find axillary artery cut-down too invasive and perhaps a major deterrent to attempts at PDA stenting. Can this be performed via the femoral artery?

The small vessel size is largely overcome with lower profile designs of coronary stents and delivery catheters today which can be delivered via 4F sheath. For this, 4F long sheaths are available by special order (Cook Inc.). The other problem with the transfemoral arterial route is the difficulty of engaging and securing a stable wire position due the proximal origin of the ductus which are often long and tortuous especially in patients with TOF-PA.

This is largely overcome by using a pig-tail catheter with its tip cut off such that it forms the general shape of an "inverted U" (Figure 1). The curve may be refined to suit the origin ("verticalness") of the ductus. In tricuspid atresia and PAIVS, the ductal origin may not be as proximal and the ampulla may thus be engaged easily with a Judkins® catheter. In a small number of cases of TOF–PA, the PDA arises very proximally, such that it is almost impossible to engage the ductal ampulla, allowing only a short length of guide wire to be passed into the pulmonary artery which is certainly insufficient for tracking of balloon and stent. Instead of axillary artery cut-down, the transvenous approach may be used. A 5F Judkins® guiding catheter may be passed from the femoral vein to the right atrium, right ventricle and the aorta via the VSD (Figure 2). Once the tip is engaged in the ductal ampulla, a stable guide wire position is easier to achieve. The extra support choice PT wire (Boston Scientific Inc.) is most useful because it has a short floppy hydrophilic tip which enables crossing of long, tortuous and tight ductus yet has a relatively stiff body, such that once firmly anchored in a branch pulmonary artery, it straightens the ductus arteriosus and provides

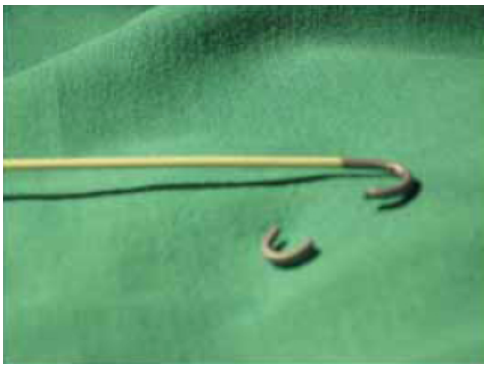

Figure 1. Cut pigtail for engagement of ducts with proximal origin

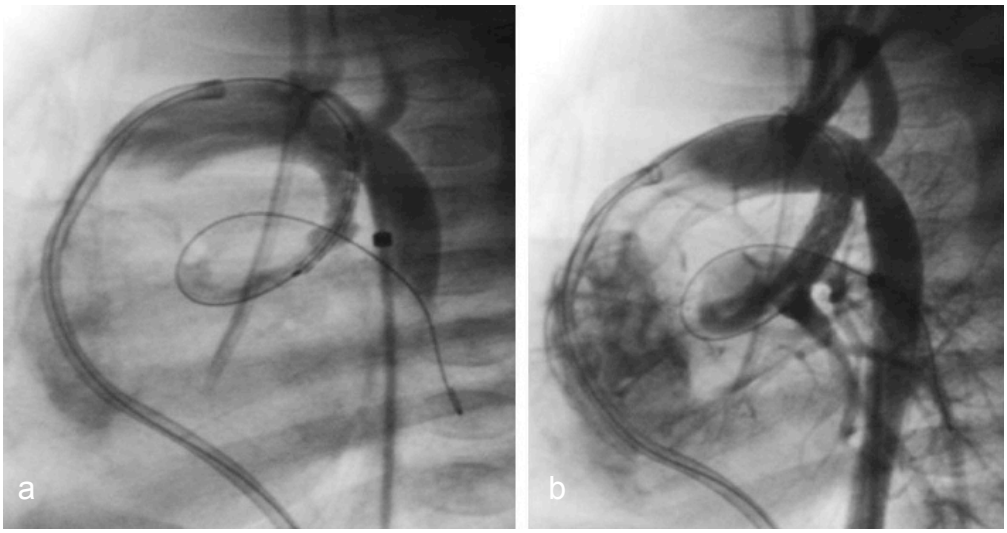

Figure 2. Tetralogy of Fallot with pulmonary atresia, proximal origin of PDA. Stent implantation by transvenous route through the VSD. Balloon and stent across the PDA (a). Stent fully expanded (b).

stability for tracking of stent and balloon catheter (Figure 3).

Stent Length and Size

Extrapolating the experience of Blalock-Taussig shunts, we use mainly 4.0mm, and to a lesser degree, 4.5mm diameter stents. Neointimal proliferation and in-stent stenosis develop fairly quickly such that it is wise to plan the second stage operation (Glenn shunt or Rastelli type operation) within 6 – 12 months of PDA stenting, although in a small number of patients good palliation can be achieved beyond 2 years.

Choosing the stent length is more exacting. As a principle, the entire ductus should be stented, otherwise the unstented segment will rapidly constrict and compromise pulmonary blood flow. The exception to this are ducts that arise for the subclavian artery which tend to be very long and have an acute take-off. Length measurement is best taken once the ductus is straightened by having an extra support coronary wire across it, usually using the lateral projection or the 4 chamber view. Stent lengths are chosen to allow 10% shortening with full expansion.

Branch Pulmonary Artery Stenosis

The PDA in cyanotic heart disease, apart for its proximal origin, length and tortuosity may be associated with branch pulmonary artery stenosis. In our experience this is especially frequent in TOF– pulmonary atresia, but much less in PAVIS and tricuspid atresia. This is thought to be due to the extension of ductal tissue into the medium of pulmonary arterial wall, leading to "pulmonary coarctation" when the ductus constricts (Figure 4). We have noted that PDA stenting tends to accelerate pre-existing branch pulmonary artery stenosis, which may require a "salvage" BT shunt on the affected vessel.[7] It is thus important to exclude proximal branch pulmonary stenosis (especially left pulmonary artery) and we consider its presence a contraindication for PDA stenting, especially those destined for the Fontan tract. The 4 chamber view is generally helpful in opening up the pulmonary bifurcation and unmask branch pulmonary artery stenosis at the site of ductal insertion.

Complications

Spasm of the patent ductus arteriosus in our experience is surprisingly rare, even in those that are very restrictive. A major, but fortunately rare complication is acute thrombosis

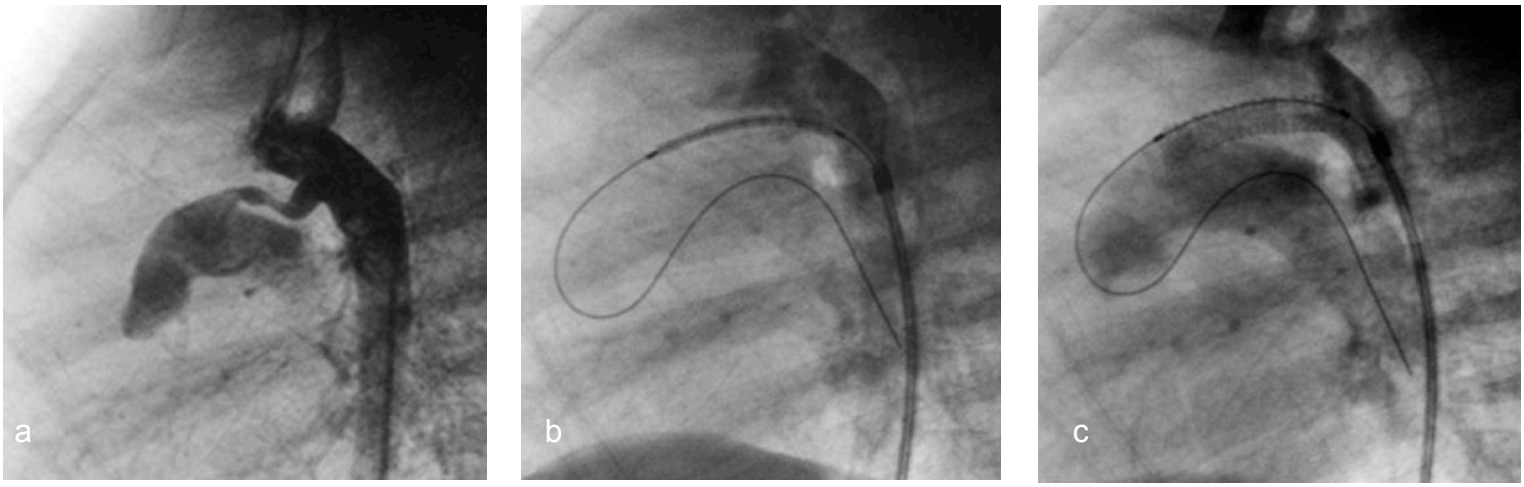

Figure 3. PDA stenting by transfemoral arterial route. Curved PDA (a). Straightens with guide wire (b). Post stent expansion (c).

where thrombus rapidly fills up a stent within minutes of expansion. This manifests as rapid deterioration in oxygen saturation after an initial excellent improvement. In such a situation, thrombolytic therapy is recommended and should be administered to prepare the patient for BT shunt. Inadvertent dislodgement of stent can be minimized by ensuring stable wire anchoring before stent deployment. Transvenous stenting of TOF-pulmonary atresia with proximal origin of the PDA may cause complete heart block as the stiff coronary guiding catheter presses on the rim of the VSD where the AV node runs.

Conclusion

PDA stenting is an attractive alternative to surgical shunt in patients with duct-dependent pulmonary blood flow where there is no continuity between the right ventricle and pulmonary artery. Small femoral artery and the peculiar morphology of the PDA in these lesions present unique difficulties to percutaneous PDA stenting. With the present generation of low profile and more flexible stent and delivery systems, this procedure can be accomplished by the transfemoral arterial route with techniques described above. Occasionally, the transvenous route via the VSD may be required in TOF – PA with very proximal origin of the PDA. Special attention needs to be paid to pre-existing branch PA stenosis at the ductal insertion site which we consider as contraindication to PDA stenting, especially in patients destined for the Fontan track.

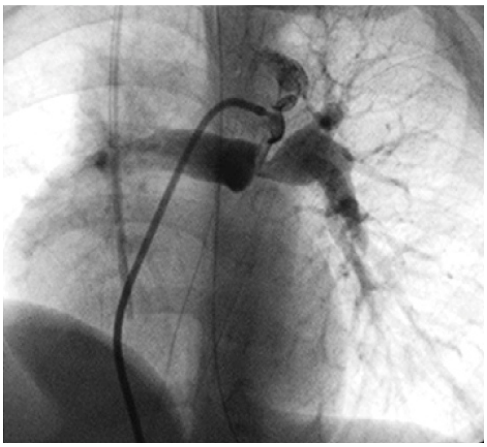

Figure 4. Branch LPA stenosis at the side of ductal insertion in Tetralogy of Fallot with pulmonary atresia.

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Figures 2 and 4. Mazeni Alwi, KK Choo, Haifa Abdul Latiff, Geetha Kandavello, Hasri Samion, MD Mulyadi. Initial results and medium-term follow-up of stent implantation of patent ductus arteriosus in duct-dependent pulmonary circulation. J Am Coll Cardiol 2004; 44: 438 – 445. (c) 2004 Reprinted with permission from The American College of Cardiology Foundation.

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In Utero Catheter Intervention for Congenital Heart Disease

By Audrey C. Marshall, MD and Wayne A. Tworetzky, MD

Advances in diagnostic imaging and surgical technique have allowed most congenital heart disease to be anatomically repaired, even in infancy. However, until recently, the possibility of prevention of congenital heart disease seemed remote. Widespread use of sonographic obstetrical screening, in combination with improved acquisition and interpretation of fetal echocardiograms, now allows us to diagnose many cardiac anomalies by midgestation, and also to observe their prenatal progression. Not unexpectedly, the capacity for early diagnosis has generated considerable interest in prenatal therapeutic intervention.

Several fundamental principles underlie the field of fetal intervention. The fetal diagnosis must be certain, and there must be an understanding of how the disease will evolve through the remainder of gestation. The resultant condition at birth must be associated with significant mortality or morbidity. Finally, a procedure must be available that can correct the initial lesion and thereby improve the outcome at birth; this procedure must offer sufficient benefit to the child to justify the risk to both mother and fetus.

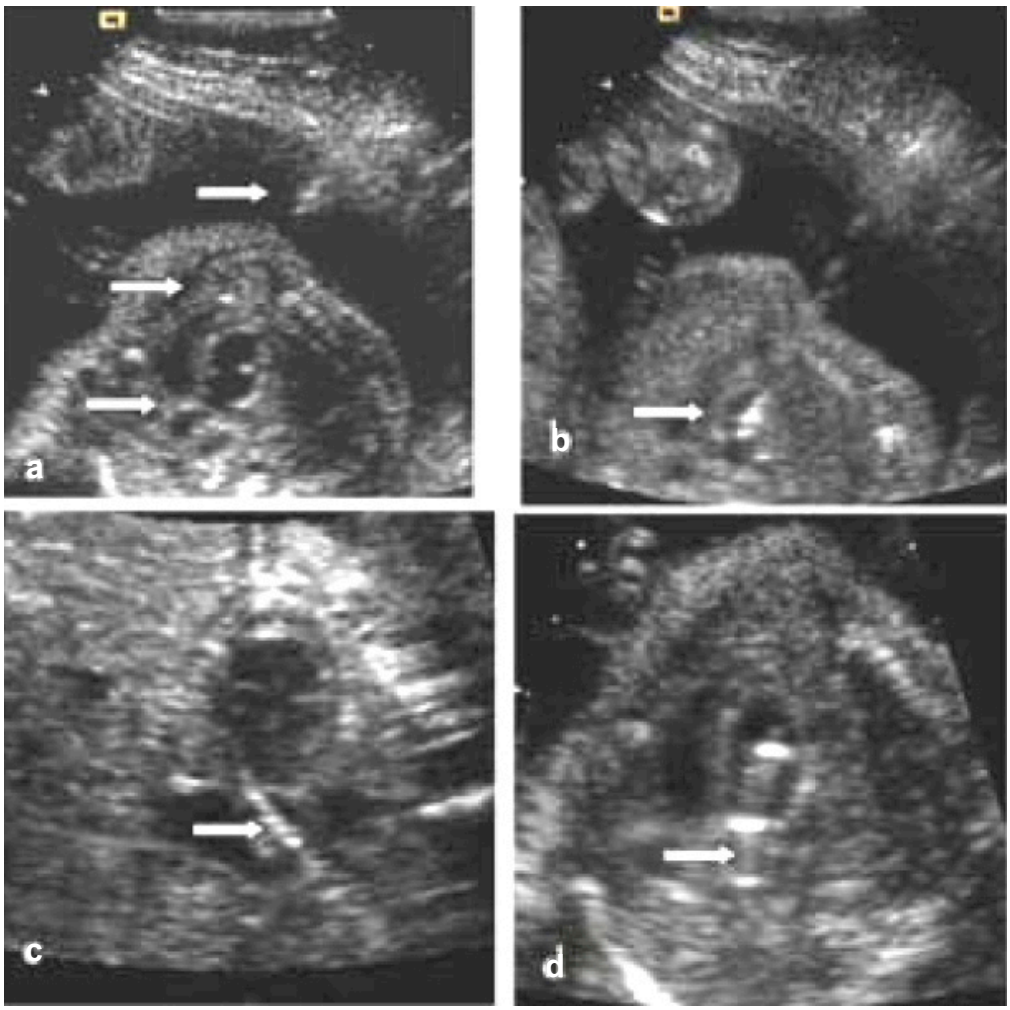

Figure 1. Transabdominal ultrasound imaging of fetal aortic valve dilation. a) The introducer cannula is seen advancing through the myometrium and into the amniotic cavity (first arrow) toward the fetal chest wall (second arrow), with the aortic valve in view (third arrow). b) The needle is advanced into the LV cavity until the tip is in the subaortic region. c) The wire is advanced through the valve and into the ascending aorta. d) The balloon is advanced over the wire and inflated while straddling the valve.

Hypoplastic Left Heart Syndrome (HLHS), though rare, remains the congenital cardiac defect associated with the most deaths in the first year of life. Characterized by a left ventricle (LV) inadequate to support the systemic circulation, the syndrome may result from one of a number of primary left heart lesions. Included among this list of causative primary lesions is valvar aortic stenosis (AS). In fact, fetal echocardiographic observation has demonstrated that AS associated with LV dysfunction, when diagnosed in the second trimester, progresses to HLHS[1]. Thus, critical AS diagnosed in the mid-trimester fetus presents an ideal target lesion for prenatal intervention.

The mechanisms through which AS begets HLHS are poorly understood. It is hypothesized that increased LV afterload and decreased coronary perfusion lead to LV myocardial damage. Initially, this LV injury is manifest as LV dilation and systolic dysfunction. With impaired LV filling, pulmonary venous return is diverted at the atrial level. The resultant decrease in left heart flow leads to growth arrest, and

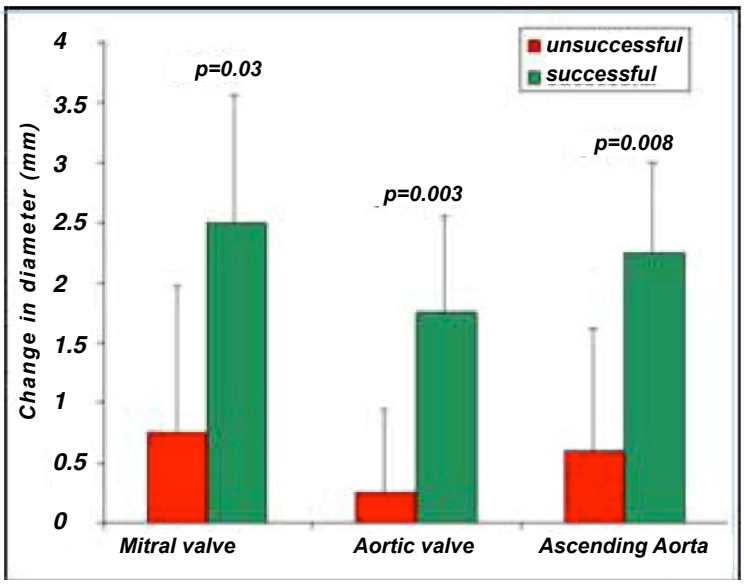

Figure 2. This graph depicts the change in dimension of left heart structures (mitral and aortic valves and ascending aorta) in fetuses that had a technically successful in utero aortic valvuloplasty compared to those with an unsuccessful procedure and those that declined the procedure. Only fetuses with pregnancies carried to near term delivery (>33 weeks gestation) were included. The data reflects the first and last measurements made during gestation.

ultimately, hypoplasia. Consistent with this hypothesis, the echocardiographic hallmarks of critical AS of the fetus include:

1. primary AS as evidenced by thickened valve tissue and a narrowed antegrade flow jet,
2. severe LV dysfunction,
3. echogenicity of the LV myocardium
4. left to right flow at the atrial septum, and
5. retrograde flow in the ascending aorta (Figure 1).

Authors had described a percutaneous fetal aortic valvuloplasty procedure as early as 1991 [2]. Although the work of several groups had resulted in a total of 12 procedures re-ported through the year 2000, the experience yielded limited technical success and a high rate of fetal mortality [3]. The procedure did, however appear to be technically feasible. With the benefits of improved imaging, instruments, and intraoperative obstetrical management, we believed the procedure could be per-formed more safely and with better technical results.

In March 2000, we began to offer fetal aortic valvuloplasty to mothers of fetuses with critical AS at less than 26 weeks gestation, as part of an innovative therapy protocol at the Children's Hospital, Boston, and the Brigham and Women's Hospital. Candidates were required to meet all of the echocardiographic criteria described above, with at least 3 experienced fetal echocardiographers attributing a high likelihood of progression to HLHS. Furthermore, the LV had to be deemed "salvageable," that is, without significant hypoplasia (length within 2 S.D. of normal for gestational age) at the time of diagnosis.

Between March 2000 and March 2004, twenty mothers elected to undergo the procedure. All gave informed consent for the procedure after meeting with pediatric cardiologists, fetal surgeons, perinatologists, and anesthesiologists. The aortic valvuloplasty was performed successfully in 14 cases, giving a technical success rate of 70%.

The procedure is performed with the mother under general anesthesia In many cases, the procedure can be performed percutaneously. When transabdominal fetal positioning fails, a limited laparotomy is performed. Not only does the laparotomy afford greater access for fetal manipulation, but it also allows higher resolution imaging directly on the uterine surface.

Once ideal fetal position is established, the fetus is given intramuscular anesthetic and muscle relaxant. A 19 G needle introduced into the maternal abdomen is guided under ultrasound through the fetal chest wall and into the LV cavity. Once inside the LV, the needle is used as an introducer for a standard PTCA catheter over a wire. The balloon diameter is intended to be ~120% the diameter of the valve annulus. The wire is used to probe for the aortic valve orifice. Once the wire has crossed the valve, the balloon is advanced, and the balloon is inflated straddling the valve (Figure 2). All of the equipment is then withdrawn.

Using this technique, we have not observed maternal complications related either to anesthesia or to the catheterization procedure. A variety of fetal complications have occurred; the most common complications being bradycardia and small pericardial effusions. The fetal bradycardia responds to either intramuscular or intracardiac epinephrine. Effusions often resolve spontaneously, but can also be drained at the conclusion of the procedure. Although we have not seen fetal demise intraoperatively, 3 fetuses were found to have expired within 72 hours of the procedure.

Of 14 fetuses who underwent successful aortic valve dilation between 21 and 29 weeks gestation, 3 were born with 2 ventricle circulations. The

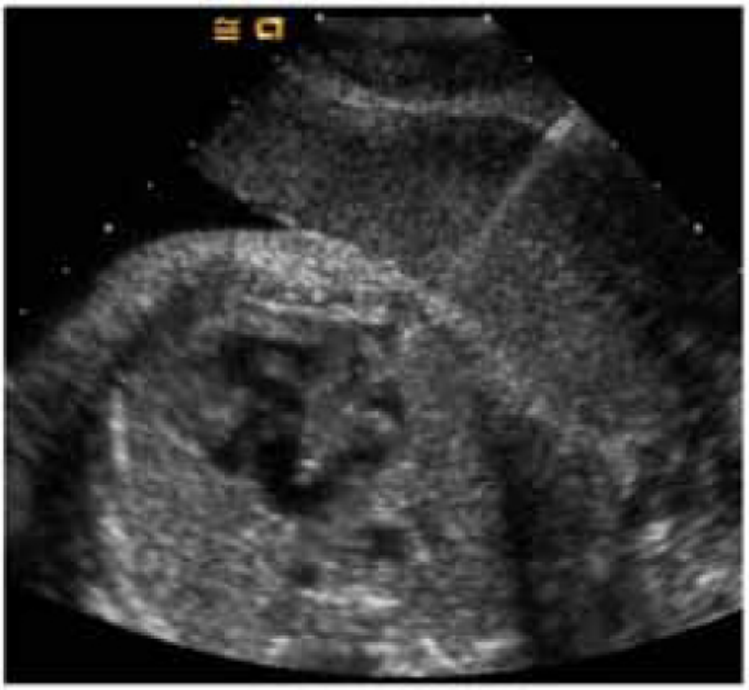

Figure 3. Transabdominal ultrasound imaging of a fetus during puncture through atrial septum. The needle traverses the maternal abdominal wall, the uterine myometrium, the fetal chest wall, and the free wall of the right atrium. Here, the tip of the needle distorts the intact atrial septum, driving it leftward, prior to needle entry into the left atrium.

"Fetal cardiology is emerging as one of the most rapidly growing fields in our specialty. The potential for echocardiographic diagnosis in utero has already favorably impacted care of children with congenital heart disease."

remainder of the live-born fetuses who underwent either successful or unsuccessful aortic valvuloplasty procedures had a diagnosis of HLHS at birth. Although only 3 fetuses did not require a Stage I palliation, technically successful fetal aortic valve dilation was associated with significant growth of left heart structures including the mitral valve, aortic valve, and ascending aorta (Figure 3).[4]

The lack of maternal complications and the possible prevention of HLHS in 3 fetuses have encouraged us to cautiously pursue this intervention. We are in the process of developing a protocol to investigate more closely the impact of successful aortic valve dilation on the growth of left heart structures in utero.

While critical AS is currently the most common diagnosis referred for fetal cardiac intervention, indications will likely expand as additional procedures become available and practiced. One additional disease that has been proposed as a target for fetal therapy is pulmonary atresia with intact ventricular septum. Perforation and dilation of the pulmonary valve can be performed using a technique similar to that used for aortic valve procedures. The difficulty in offering intervention to this group of fetuses lies in the clinical spectrum of the disease, and our inability to predict the postnatal morbidity based on prenatal appearance. Although it seems likely that pulmonary atresia can be treated prenatally, we first need to be able to identify those fetuses who would have the poorest postnatal outcomes, and would therefore have the most to gain from fetal intervention.

In fact, the emergence of a second indication for fetal intervention has, in our center, been driven primarily by the identification of a uniquely high risk set of neonates. Infants born with HLHS and an intact atrial septum have a failing circulation until left atrial (LA) decompression can be achieved. These infants have markedly elevated mortality rates, compared to others with HLHS. We hypothesized that a prenatal procedure to create an atrial septal defect would aid in postnatal stabilization and thereby improve neonatal outcomes. By decompressing the LA in utero, one might attenuate secondary tissue/organ damage occurring in the lung, and might favorably impact longer term survival.

We have performed 7 of these procedures; 6 of 7 have been technically successful. As with the aortic valve procedure, we have not experienced any maternal complications. Furthermore, we have been able to access the atrial septum in all cases without the use of a laparotomy. Due to the technique and equipment used, the newly created atrial defects are small, but appear to persist through gestation.[5] Although we have not yet demonstrated clinical effect, we expect that the introduction of equipment and techniques dedicated to this procedure will improve our ability to make large defects in the atrial septum, and will ultimately lead to clinical benefit.

Fetal cardiology is emerging as one of the most rapidly growing fields in our specialty. The potential for echocardiographic diagnosis in utero has already favorably impacted care of children with congenital heart disease. A therapeutic arm has been added to the field with regard to management of fetal arrhythmias. Now we are developing the means of modifying structural disease in utero. It is our hope that with the continuing collaborative efforts of fetal imagers, obstetricians, fetal surgeons, and interventionalists, we can add prevention to the management of some forms of congenital heart disease.

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Global Neonatology Today Monthly Column-
How the Various Countries Spend Their Commitment to Global Strategy for Women & Children's Health

By Dharmapuri Vidyasagar, MD, FAAP, FCCM

As previously discussed in this column before, every year, 358,000 women in the developing world between the ages of 15-49 die of pregnancy and childbirth-related complications. Every year, 2.6 million children are stillborn, and a further 8.1 million die before their fifth birthday, including 3.3 million babies in the first month of life.

On May 19th sixteen countries announced new commitments to dramatically reduce maternal, newborn and child mortality as part of the *Global Strategy for Women's and Children's Health*. The commitments build on the momentum of recent months, and prove that saving the lives of the most vulnerable can attract support at the "highest levels," says Ban Ki-moon, the United Nations Secretary-General, who is leading the *Every Woman Every Child* campaign to accelerate progress on Millennium Development Goals 4 (child mortality) and 5 (maternal health). The countries making these commitments are: Burundi, Chad, the Central African Republic, Comoros, Guinea, Kyrgyzstan, the Lao People's Democratic Republic, Madagascar, Mongolia, Myanmar, Papua New Guinea, Sao Tome and Principe, Senegal, Tajikistan, Togo, and Viet Nam.

"Political and financial support for action on women and children's health is reaching new and encouraging heights." writes the Secretary-General Moon in a May 20th press release. Adds D, Babatunde Osotimehin, the Executive Director of *United Nations Population Fund (UNFPA)*. "The commitments by countries today demonstrate that we are on the verge of a tipping point." Countries in different regions and situations are stepping forward as the Global Strategy catches fire."

Nine of the 16 committing countries committing represent the African continent. These commitments come, in addition to the 18 made in September 2010 by the African States, bringing the total of African countries having committed to better the health of women and children to 27. The commitments, made with the support of *UNAIDS, UNFPA UNICEF, The World Bank* and *WHO* (collectively known as the H4+ agencies), focus on measures proven effective in preventing deaths, such as: increased contraceptive use, attended childbirth, improved access to emergency obstetric care, prevention of mother to child transmission of HIV, and childhood immunizations.

"'The Global Strategy is an unprecedented opportunity to help the women and children who need it most. The commitments made by member states, donors and other partners are an impressive signal that we collectively take responsibility to achieve the health-related Millennium Development Goals and save more women's and children's lives," says World Health Organization Director-General Dr. Margaret Chan.

"Focusing on the women and children in greatest need is not only the right thing to do, it moves us faster and most cost-effectively towards meeting the health Millennium Development Goals," says Anthony Lake, *UNICEF* Executive Director. "By choosing to redouble their efforts on maternal and child health, these 16 nations are not only saving lives, they are making an investment in their future."

These commitments to the *Global Strategy* follow a Declaration by Heads of States at the 2010 July Summit of the African Union to strengthen efforts to improve maternal, newborn and child health and a March 2011 Resolution by African Ministers of Finance and Budget to improve health investment and strengthen their dialogue with health counterparts.

Release of New Recommendations

As part of the Global Strategy, new recommendations were also released back in May by the Commission for Information and Accountability for Women's and Children's Health, including a recommendation to ensure that future commitments are spent as most needed.

"The Global Strategy has created a rallying point for all countries to be part of a global conversation about women and children," says Dr. Julio Frenk, Chair of the Board of the *Partnership for Maternal, Newborn and Child Health (PMNCH)*, and Dean of the Harvard School of Public Health.

Analyzing Global Strategy Commitments of the 16 Countries

Burundi: Burundi commits to: increase the allocation to its health sector from 8% in 2011 to 15% in 2015, with a focus on women and children's health; increase the number of midwives from 39 in 2010 to 250, and the number of training schools for midwives from 1 in 2011 to 4 in 2015; increase the percentage of births attended by a skilled birth attendant from 60% in 2010 to 85% in 2015. Burundi also commits to increase contraception prevalence from 18.9% in 2010 to 30%; *Preventing Mother to Child Transmission of HIV (PMTCT)* service coverage from 15% in 2010 to 85% with a focus on integration with reproductive health; and reduce percentage of underweight children under-five from 29% to 21% by 2015.

Chad: Chad commits to increase health sector spending to 15%; provide free emergency care for women and children; provide free HIV testing and Anti-retroviral drugs (ARVs); allocate of US$10 million per year for implementation of the national roadmap for accelerating reduction in maternal, newborn and child (MNC) mortality; strengthen human resources for health by training 40 midwives a year for the next 4 years, including creating a school of midwifery, and constructing a national referral hospital for women and children with 250 beds; and deploying health workers at health centres to ensure delivery of a minimum package of services. Chad also commits to pass a national human resources for health policy; increase contraception prevalence to 15%; ensure 50% of the births are assisted by a skilled birth attendant; and increase coverage of PMTCT from 7% to 80%, and pediatric HIV coverage from 9% to 80%.

Central African Republic (CAR): Central African Republic commits to increase health sector spending from 9.7% to 15%, with 30% of the health budget focused on women and children's health; ensure emergency obstetric care and prevention of PMTCT in at least 50% of health facilities; and ensure the number of births assisted by skilled personnel increase from 44% to 85% by 2015. CAR will also create at least 500 village centers for family planning to contribute towards a target of increase contraception prevalence from 8.6% to 15%; increase vaccination coverage to 90%; and ensure integration of childhood illnesses including pediatric HIV/AIDS in 75% of the health facilities.

Comoros: Comoros commits to increase health sector spending to 14% of budget by 2014; ensure universal coverage for PMTCT by 2015; reduce underweight children from 25% to 10%; increase contraception prevalence

rate from 13% to 20%; and the births that take place in health facilities from 75% to 85%. Comoros will also accelerate the implementation existing national policies including the national plan for reproductive health commodity security, the strategic plan for human resources for health, and the roadmap for accelerating reduction of maternal and neonatal mortality.

Guinea: Guinea commits to establish a budget line for reproductive health commodities; ensure access to free prenatal and obstetric care, both basic and emergency; ensure provision of newborn care in 2 national hospitals, 7 regional hospitals, 26 district hospitals, and 5 municipality medical centres; and introduce curriculum on integrated prevention and care of newborn and childhood illnesses in health training institutes. Guinea also commits to secure 10 life-saving essential medications in at least 36 facilities providing basic obstetric care and 9 structures with comprehensive obstetric care by 2012; ensure at least three contraception methods in all the 406 centres of health in the public sector by December 2012; and include PMTCT in 150 health facilities.

Kyrgyzstan: Kyrgyzstan commits to ensure that 100 % of the population of reproductive age have choice and access to modern contraception with at least 3 modern methods of family planning; 100% free medical care for pregnant women and children under the age of five; ensure at least 80% of births take place at a health facilities and 90% of health facilities have access to centralized water supply system. Kyrgyzstan will ensure that 95% of health facilities with antenatal services provide both HIV testing and PMTCT; 35% family medicine centers provide the standard package of youth-friendly health services; and that70% of children receive evidence-based services within integrated management of childhood illness.

The Lao People's Democratic Republic: The Lao People's Democratic Republic commits to provide free deliveries in order to ensure access to the most vulnerable; produce 1500 new midwives by 2015 by upgrading existing staff and training and recruiting new staff; and increase immunization from 67% to 90% by 2015. Lao PDR will also increase the proportion of couples with access to modern contraception and the proportion of births attended by a skilled attendant.

Madagascar: By 2015, Madagascar commits to increase health spending to at least 12%; ensure universal coverage for emergency obstetric care in all public health facilities; increase births assisted by skilled attendants from 44% to 75%; and double from 35% the percentage of births in health facilities. Madagascar will also address teenage pregnancy by making 50% of primary health care facilities youth-friendly; reduce from 19% to 9.5% the unmet need of contraception by strengthening commodity security; increase tetanus vaccination for pregnant women from 57% to 80%; and institute maternal death audits.

Mongolia: Mongolia commits to implement a policy on increasing salaries of obstetricians, gynecologists and pediatricians by 50%; increase financial allocation to national immunization program; improve provision of micronutrients to children under 5; ensure reproductive health commodity security; and increase the number of health facilities for women and children, including the construction of a new Women's and Children's Health Centre in Ulaanbaatar.

Myanmar: Myanmar commits to ensure 80% ante-natal care coverage; 80% of births attended by a skilled attendant; 70% access to emergency obstetric care; and 80% coverage for PMTCT as well as its integration with (Maternal, newborn and child health) MCH. Myanmar will also ensure universal coverage for the expanded immunization; increase the proportion of newborn who receive essential newborn care at least two times within first week of life by 80%; increase contraception prevalence to 50%; reduce unmet need for contraception to under 10%; improve ratio of midwife to population from 1/5000 to 1/4000; and develop a new human resources for health plan for 2012-2015.

Papua New Guinea (PNG): PNG commits to improve midwifery education and register 500 new midwives by 2015; increase number of obstetricians from 17 in 2011 to 40 in 2020; improve access to drugs and equipment necessary for maternal newborn and child health; introduce maternal health audits in all districts; and develop comprehensive plans to improve existing health services in all four regions of the country by 2015.

Senegal: Senegal commits to increasing its national health spending from 10% of the budget currently to 15% by 2015. It also proposes to increase the budget allocated to MNCH by 50% by 2015. The country commits to improving coordination of MNCH initiatives by creating a national Directorate for MNCH, reinstating the national committee in charge of the implementation of the multisectoral roadmap for the reduction of maternal and child mortality and to accelerate the dissemination and implementation of national strategies targeting a reduction of maternal mortality. Through these efforts the government hopes to offer a full range of high impact MNCH interventions in 90% of health centers, increase the proportion of assisted deliveries from 51% to 80% by increasing recruitment of state midwives and nurses and increasing contraceptive prevalence rate from 10% to 45%, among others.

Sao Tome and Principe: Sao Tome and Principe commits to increase the percentage of the general budget for health from 10% to 15% in 2012; increase the ratio of births attended by a qualified health personnel from 87.5% to 95%; reduce the percentage of inadequate family planning service delivery from 37% to 15%; increase the geographic coverage of PMTCT services from 23% to 95%; increase the percentage of pregnant women receiving ARVs from prenatal centres from 29% to 95%; and increase the prevalence of contraception from 33.7% to 50%.

Tajikistan: Tajikistan commits to ensure that by 2015, 85% of midwives are trained in provision of emergency obstetric care; at least 85% of maternity facilities apply the clinical protocols approved by the ministry of health; youth friendly health services are expanded from pilot to nationwide implementation; and 50% of the needs of women of reproductive age in modern contraceptives are covered from the budget. Tajikistan will also develop an accreditation policy for maternity institutions and ensure that 90% of maternity hospitals are certified.

Togo: Togo commits to ensure 95% coverage of vaccination for children under 5, and to implement the Campaign on Accelerated Reduction of Maternal Mortality in Africa (CARMMA).

Viet Nam: Viet Nam commits to increase rate of pregnant women with access to PMTCT services from 20% to 50%; increase the rate of people with disabilities who have access to RHC services from 20% to 50%; increase rate of pregnant women receiving antenatal care (at least three visits during 3 trimesters) from 80% to 85%; increase the rate of couples who receive pre-marital counseling and health checks from 20% to 50%; and increase the rate of women giving birth with trained health workers from 96% to 98%.

"The Clock is Ticking!"

NT

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Screening Very Preterm Infants for Autism at 18 Months Often Inaccurate

Extremely premature infants who screen positive for Autism Spectrum Disorder (ASD) at 18 months of age may not actually have autism. Rather, they may fail screening tests due to an unrelated cognitive or language delay, according to research presented, May 1st, at the Pediatric Academic Societies (PAS) annual meeting in Denver.

The American Academy of Pediatrics (AAP) recommends that pediatricians screen all children for ASD at 18-24 months of age, and that those who fail the screening test should be referred for a formal assessment. Based on the AAP guidelines, many neonatal intensive care unit follow-up clinics that monitor former extremely preterm infants have instituted this screening protocol. However, it is not known how accurate early screening is in identifying ASD in this high-risk population.

Researchers, led by Bonnie E. Stephens, MD, FAAP, Assistant Professor of Pediatrics at Brown University's Alpert School of Medicine and neonatologist/developmental and behavioral pediatrician at Women & Infants Hospital of Rhode Island, suspected that many preterm infants who screen positive for ASD at 18 months do not have ASD, but are failing these screens due to a cognitive or language delay, both of which are common in extremely preterm infants at 18 months.

To test their hypothesis, the investigators screened infants born at their hospital before 28 weeks' gestation with three measures, one of which was designed specifically for use in high-risk populations such as preterm infants. They sought to determine the rate of false-positive screens for ASD at 18 and 30 months of age and to explore the relationship between a positive screen and cognitive and language delay.

A total of 152 infants were screened for ASD at 18 months (age corrected for prematurity), and 116 infants were screened at 30 months corrected age.

Results showed that 18% screened positive for ASD at 18 months, while 10% screened positive at 30 months. Only 3% of infants had positive results on all three screens at either point in time, and all of the infants who screened positive for ASD on all three screening tests at 30 months were later diagnosed with ASD.

In addition, a positive screen at 18 or 30 months was associated with cognitive and language delay.

"While these findings have important implications, further work is needed," Dr. Stephens said. "To determine which of these infants actually have ASD, a study that includes a formal diagnostic assessment on all children with a failed screen is needed."

Dr. Stephens and her colleagues are seeking funding to support a multicenter study of more than 500 preterm children. "This will allow us to determine the true rate of ASD in this population, the rate of false-positive screens at 18 and 30 months, the optimal time to screen, and the optimal ASD screening tool for the extremely preterm population."

Chemical in Plastic Linked to Wheezing in Childhood

If a pregnant woman is exposed to bisphenol A (BPA), especially during the first trimester, her child may be at higher risk of wheezing early in life, according to a study presented at the May Pediatric Academic Societies (PAS) annual meeting in Denver.

BPA is a chemical that has been used for more than 40 years in the manufacture of many hard plastic food containers and the lining of metal food and beverage cans. Trace amounts of BPA can be found in some foods packaged in these containers, and the chemical is detectable in over 90% of the US population.

The National Toxicology Program of the National Institutes of Health has some concern that exposure to BPA might affect the brain, behavior and prostate gland in fetuses, infants and children. In addition, exposure to BPA in the perinatal period has been associated with asthma in mice, but studies in humans are lacking.

In this study of 367 pairs of mothers and infants, researchers examined the relationship between prenatal exposure to BPA and wheeze in childhood. BPA levels were measured in the urine of the pregnant women at 16 and 26 weeks' gestation as well as when they delivered their babies. In addition, every six months for three years, parents were asked whether their child wheezed.

Results showed that 99% of children in the study were born to mothers who had detectable BPA in their urine at some point during pregnancy. The amount of BPA detected in a mother's urine was related to wheezing only in the youngest group of children. At 6 months of age, infants whose mothers had high levels of BPA during pregnancy were twice as likely to wheeze as babies whose mothers had low levels of BPA. However, no differences in wheezing rates were found by 3 years of age.

Researchers also found that high BPA levels detected in women at 16 weeks' gestation were associated with wheeze in their offspring, but high levels at 26 weeks' gestation and birth were not.

"Consumers need more information about the chemicals in the products they purchase so they can make informed decisions," said Adam J. Spanier, MD, PhD, MPH, FAAP, lead author of the study and Assistant Professor of Pediatrics and Public Health Sciences at Penn State College of Medicine. "Additional research is needed in this area to determine if changes should be made in public policy to reduce exposure to this chemical."

Until more information is available, Dr. Spanier concluded, women of child-bearing age should consider avoiding products made with BPA.

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