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Emergency Contraception

SPECIAL FEATURE

By Jeffrey T. Jensen, MD, MPH, Editor

Synopsis: *We now have three options for emergency contraception — the copper IUD, oral ulipristal acetate, and oral levonorgestrel. One of the most important considerations in using emergency contraception is the initiation of ongoing regular contraception. The special feature will discuss the opportunities and considerations for use of these three different methods of postcoital contraception.*

With several options available for emergency contraception (EC), a number of considerations exist for patients and providers. In most practice settings, the health care provider is taken out of the conversation due to the availability of over-the-counter (OTC) products. Overall, having OTC options is a good public health policy. However, since the counseling available from pharmacists will vary widely throughout the country and since there are prescription-only options that offer unique advantages, it is important to be informed about the latest developments. The best time to talk to your patients about EC may be prior to its need. In particular, those women using barrier methods, those with a history of prior contraceptive failure, and those who have infrequent sex deserve a short conversation about the state of the art of EC during routine health check-ups.

Oral levonorgestrel (LNG), a progestin, is now available to all women in the United States without a prescription. It has been well established that a single dose of 1.5 mg LNG is as effective as two 0.75

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mg doses taken 12 hours apart.[1,2] LNG works by blocking the luteinizing hormone (LH) surge. If the LH surge has initiated, ovulation will proceed normally, and there is no convincing evidence of any pregnancy disruption effect with LNG.[3] Although the science is clear on this, it has not reduced the level of public misinformation, and concerns about a post-fertilization effect remain an important barrier to the OTC availability of EC.[4] Biologically, pregnancy does not occur until after implantation so abortion cannot occur before this event. Although some individuals have moral objections to any method that might allow fertilization of the oocyte and disrupt implantation, this is not abortion. Some may argue this is just semantics, but I do not think anyone would suggest that an embryo in the freezer of an IVF clinic is the same as a 6-week intrauterine gestation. Family planning methods that allow fertilization but prevent implantation are more correctly termed contragestives (contra-gestation). Since LNG does not have contragestive properties, it needs to be taken as soon after unprotected intercourse as possible to prevent ovulation. Since sperm can remain viable for up to 5 days after ejaculation, the use of LNG EC is done to prevent ovulation during this window. LNG EC is generally recommended for use only within 72 hours of unprotected sex; the product is most effective if taken as soon as possible and efficacy declines as time progresses.[5]

Ulipristal acetate (UPA) is a selective progesterone receptor modulator. It is available by prescription only. A single dose of 30 mg of UPA will prevent follicle rupture in the 5 days following treatment, even when administered at the initiation of the LH surge.[6] Although the available evidence suggests that UPA still relies on suppression of ovulation as the mechanism of action, the drug provides a longer window of activity then LNG. UPA is FDA-approved and marketed for use up to 5 days after unprotected sex, while LNG is recommended for up to 3 days only. Since 5 days covers the window of time that sperm would be viable, it should effectively prevent ovulation throughout the fertile period. Clinical trial results back up these mechanistic details. A large, randomized clinical trial and meta-analysis concluded that UPA was more effective than LNG, preventing more than two-thirds of expected pregnancies compared with 50% for LNG.[5] This is an important message that should be communicated to our patients. Another important consideration with UPA is that ovulation is not always prevented or disrupted. It may be just delayed. Follicle rupture typically occurs about 6 days after use of UPA.[7] This brings up another important counseling point. EC is not designed to provide regular contraception. Condoms should always be recommended for 7 days, and a regular method of contraception should be started (see below). For both methods of oral EC, the biggest risk of pregnancy occurs with repeated acts of unprotected intercourse in the same cycle.

Recent data have highlighted a number of other important considerations, and these all deserve clear counseling. First, obesity impacts results with LNG. There is convincing evidence that efficacy of LNG is greatly reduced in women weighing > 75 kg, and it appears to be not effective in women weighing > 80 kg.[8,9] In contrast, there is no strong evidence of a weight effect with UPA. Although further studies are needed to clarify the upper boundary of this relationship for both drugs, the available data at this point strongly suggest that women weighing ≥ 75 kg should only be offered UPA. Clearly, the fact that LNG is available OTC while UPA is by prescription complicates this recommendation; this is another reason advanced counseling is important.

Although it is tempting to conclude that UPA is a better emergency contraceptive under all circumstances, there are a number of other considerations. Many women are advised to use EC after missing one or two doses of a regular combined oral contraceptive pill. Although EC should be used if the pills are missed at the end of the hormone-free interval, the role of EC after missing one or two pills during the active pill weeks is not clear. There is no evidence that the use of EC in this circumstance is superior to simply following the recommendation of doubling up on the missed pills. However, if EC is to be used in this situation, LNG would be a better recommendation. Adding a high dose of a progestin will not interfere with ongoing contraceptive action of a combined or progestin-only product. Although we have no clear published data, pharmacologic considerations would support that use of a

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Questions & Comments
Contact **Leslie Coplin**, Executive Editor, at leslie.coplin@ahcmedia.com.

Table 1. Guidance for EC Counseling

	Ulipristal acetate	Levonorgestrel	Copper IUD
Dose/route	30 mg/oral	1.5 mg/oral	Intrauterine
Accessibility	Prescription only	Over-the-counter	Requires clinic visit
Optimal timing	Up to 5 days after UPI	Up to 3 days after UPI	Up to 5 days after UPI
Pregnancy risk reduction	67%	50%	98%
Mechanism of action	Contraceptive	Contraceptive	Contragestive
Impact of obesity	No evidence of reduced efficacy up to 80 kg	Good evidence for reduced efficacy >75 kg, no efficacy > 80 kg	No evidence of reduced efficacy with obesity. No mechanistic concerns. Placement may be more difficult

Table 2. Guidelines for Initiation of Ongoing Contraception

	Ulipristal acetate	Levonorgestrel	Copper IUD
Condoms	Use for 7 days	Use for 7 days	Not needed
Combined hormonal methods	Wait at least 3 days	May initiate immediately	
Implant	Wait at least 3 days	May initiate immediately	
DMPA	Wait at least 3 days	May initiate immediately	
LNGIUS	May initiate immediately	May initiate immediately	
Copper IUD	May initiate immediately*	May initiate immediately*	

* UPA and LNG provide no additional benefit for EC over copper IUD alone.

regular contraceptive containing a progestin may interfere with the emergency contraceptive mechanism of UPA, a progestin-receptor antagonist. Furthermore, UPA may interfere with the ongoing contraceptive mechanisms of the progestin.

As mentioned previously, repeated acts of unprotected intercourse in the cycle of EC use provide the biggest risk of unintended pregnancy. Use of condoms and initiation of regular contraception are important and will not be stressed in a pharmacy-only visit. Clinicians need to consider mechanism of action when advising women on starting regular contraception after using EC. Many clinics have been advocating a "quickstart" approach for initiation of regular contraception; starting the pill on the same day of or the day following the EC pill. In my opinion, our enthusiasm for starting a regular method should not compromise our best approach to providing EC. No evidence-based recommendations exist, so it makes sense to consider the biologic plausibility of interaction between progestins and progesterone receptor antagonists as outlined above. With LNG EC, there is no important interference and regular contraception with any method can be initiated without delay. For UPA, the possibility of interference exists, and it is prudent to wait 3 days before starting a combined hormonal method, a progestin-only pill, or inserting a contraceptive implant. Quickstart of the LNG intrauterine system should not present a problem, as the mechanism of action is predominantly local and the low circulating LNG levels are not likely to interfere with UPA activity. Although depot medroxyprogesterone acetate (DMPA) theoretically will interfere with UPA action, the very high dose of this method quite likely provides an emergency contraceptive benefit of its own similar to LNG. Prior to 72 hours, or in non-obese women, use of UPA will not likely offer any additional benefit from DMPA given on the same day. However, if a woman presents 4-5 days following unprotected intercourse or weighs > 75 kg, it would make most sense to use UPA and then administer DMPA 3 days later.

Starting regular contraception will be the most important consideration for most women presenting for emergency contraception. Since the rules for starting a combined hormonal method are different for UPA and LNG, office staff and pharmacists need to be educated. In the study by Turok et al,[10] there was no reduction in immediate pregnancies when women were randomized to a copper IUD or LNG. However, pregnancy within 6 months was significantly reduced among copper IUD users. This provides strong evidence that ongoing contraception is the most important consideration. Women presenting to a family planning clinic should be offered the copper IUD as a first-line emergency contraceptive treatment. There is solid evidence that supports that the copper IUD is the most effective option and the only option that provides ongoing contraception.[11] However, unlike UPA and LNG, the copper IUD does appear to have a contragestive effect. It is important to communicate this as a unique property of the copper IUD and not a general characteristic of EC.

To summarize, the copper IUD represents the best option for most women seeking EC. The disadvantages of

the pelvic examination and procedure are far outweighed by efficacy and provision of ongoing contraception. The real-world considerations of clinic access, cost, convenience, and patient preference will likely favor an oral method. Given this, UPA is a clear winner as it has a longer window of activity and higher efficacy. This is particularly important for obese women, as there is no evidence that LNG has any activity in women weighing > 80 kg. Unfortunately, UPA is not available OTC, so obese women should receive counseling and possibly advance prescription for UPA during clinic encounters. One exception to the general preference for UPA is EC use to back up incorrect use of regular hormonal contraception. In most cases, LNG would be preferred to avoid interaction between a progesterone receptor antagonist and agonist. Quickstart initiation of regular hormonal contraception can be offered with LNG EC, but should be delayed for at least 3 days and no more than 7 days after use of UPA. ■

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Should You Advise Your Patients to Eat Peanuts During Pregnancy?

ABSTRACT & COMMENTARY

By Rebecca H. Allen, MD, MPH

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Dr. Allen reports no financial relationships relevant to this field of study.

Synopsis: *In this study, women without allergies who consumed peanuts or tree nuts five times or more per month around the time of pregnancy compared to less than one time per month had reduced odds of having children with peanut or tree nut allergies.*

Source: Frazier AL, et al. Prospective study of peripregnancy consumption of peanuts or tree nuts by mothers and the risk of peanut or tree nut allergy in their offspring. *JAMA Pediatrics* Published online December 23, 2013. [Epub ahead of print.]

This is a nested case-control study using two large national prospective cohort studies — the Nurses' Health Study II (NHSII) and the Growing Up Today Study 2 (GUTS2), which involved offspring of the participants of NHSII. Children in the GUTS2 study were born between January 1, 1990 and December 31, 1994. In 2009, to identify children with food allergies, a questionnaire was sent to the mother of every child in the GUTS2 cohort (n = 10,907). The children themselves had already reported on whether or not they had a food allergy in a 2006 GUTS2 questionnaire. The investigators reconciled answers to these two questionnaires and identified cases of allergy to peanut or tree nuts (P/TN). The cases were then divided into seven levels of confirmation, ranging from likely to possible based on review of available medical record information. The mothers had previously reported their diet on the 1991 and 1995 NHSII questionnaires, and the authors selected the questionnaire closest to the birthday of each child to determine maternal peanut intake. Investigators estimated that 45% of the food questionnaires were answered when the mother would have been pregnant with the child and 76% were within 1 year of the pregnancy.

After exclusions for missing data, the authors identified 8205 children (75% of the GUTS2 cohort) with 140 cases of P/TN allergy. The majority (> 95%) of the NHSII and GUTS2 sample was white, and 2% of the mothers

reported a nut allergy. Women with the highest consumption of P/TN in their peripregnancy diet were more likely to introduce P/TN into their child's diet at a younger age (< 2 years old). In multivariable analysis controlling for maternal age, maternal history of non-nut allergy, maternal allergic rhinitis, eczema, asthma, and season at child's birth, the odds of having a child with P/TN allergy among mothers without a P/TN allergy themselves who had the highest consumption peripregnancy (≥ 5 servings/week) was reduced (odds ratio [OR], 0.31; 95% confidence interval [CI], 0.13-0.75). Interestingly, among mothers with a P/TN allergy themselves, the association was in the opposite direction, although not statistically significant (OR, 2.62; 95% CI, 0.74-9.27).

■ COMMENTARY

The incidence of peanut allergy has increased markedly in the United States from 0.4% in 1997 to 1.4% in 2010.[1] This should come as no surprise to anyone who has children in the daycare or school setting, where peanuts are often banned. Peanut and tree nut allergy frequently occur together and 80-90% of cases occurring in childhood persist into adulthood. Since the majority of the IgE-mediated reactions occur during the child's first known exposure, the theory is that the child was exposed previously either in utero or through other unrecognized environmental or diet exposures. For many years, women have been advised to avoid giving their children peanuts in the first 3 years of life. In addition, some experts advised avoiding peanuts during pregnancy and lactation. These guidelines were then changed when little evidence was found to support them.[2] In essence, a number of prospective studies had shown that maternal consumption of peanuts during pregnancy and lactation had no effect on subsequent development of P/TN allergy.[3]

This study aimed to clarify the association with peripregnancy consumption of P/TN by mothers and the subsequent development of P/TN allergy or not in their children. This is the first study in humans that showed ingestion of P/TN during pregnancy may actually protect against allergy in the offspring, at least among women without any allergy themselves. The investigators worked diligently to confirm cases of P/TN allergy by reviewing medical records, allergy skin test results, and specific IgE data. At the same time, the data on P/TN consumption were limited by the fact that the questionnaires were not specific to the actual dates of pregnancy. Therefore, the authors are assuming that the mother's eating habits were stable in the peripregnancy time period. To respond to this, the authors compared P/TN consumption during a pregnancy to that same individual's diet when not pregnant and found that 72% of women reported similar intake. Nevertheless, the quality of the data is not the same as a true prospective study where diet is diligently recorded during pregnancy. In fact, I find it questionable that the authors use the word "prospective" in their title. The quality of the data is also dependent on how accurately women filled out the questionnaires regarding their diet. In addition, no data were collected on exclusive breastfeeding rates or duration, which may or may not influence the development of allergies.[2]

The bottom line is that it is difficult to definitively prove causation with observational studies, especially in this realm where there are multiple confounding factors. The pediatric guidance currently states that there is not enough evidence that maternal dietary restrictions during pregnancy play any role in the prevention of atopic disease in infants.[2] Similarly, there is not enough evidence to say that consumption of dietary food allergens in pregnancy will reduce the chance of allergy development to those allergens in the infant. So, if your patient asks you about eating peanuts during pregnancy, I would say there is no good evidence it will cause or prevent a peanut allergy in her child; we just don't have enough information. So, pregnant patients can indulge any peanut butter cravings! ■

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Cancer-reducing Effect of OCPs in BRCA1/BRCA2 Carriers: Do They Work?

ABSTRACT & COMMENTARY

By Robert L. Coleman, MD

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Dr. Coleman reports no financial relationships relevant to this field of study.

Synopsis: *The association between oral contraceptive use and ovarian or breast cancer in BRCA1 or BRCA2 mutation carriers are qualitatively similar to associations reported in the general population. Oral contraceptive pill use is inversely associated with ovarian cancer risk. However, it is also associated with a*

modest, but not statistically significant, increased risk for breast cancer. The analysis was unable to provide conclusive recommendations as to their use as preventive measures given these and other unmeasured risks. However, oral contraceptive pills appear safe for contraception in this population.

Source: Moorman PG, et al. Oral contraceptives and risk of ovarian cancer and breast cancer among high-risk women: A systematic review and meta-analysis. *J Clin Oncol* 2013;31:4188-4198.

Risks for ovarian and breast cancer are substantially elevated in women who carry germline mutations in BRCA1/2. The most effective method of cancer prevention is surgical resection; however, in those who wish to preserve fertility options, non-permanent prevention strategies are desired. Currently, non-invasive screening is unproven even in this high-risk cohort. Oral contraception pills (OCP) have been documented to reduce ovarian cancer risk in the general population and the magnitude of effect is related to the duration of use. The current study was conducted to analyze the known datasets of OCP use in high-risk women (i.e., carriers of BRCA1/2 or with a strong family history) for ovarian and breast cancer risk. The meta-analysis considered 6476 unique citations examining ovarian and breast cancer risk and settled on six addressing ovarian cancer risk and eight addressing breast cancer risk. Among germline mutation carriers combined, the meta-analysis demonstrated an inverse association between OCP use and ovarian cancer (odds ratio [OR], 0.58; 95% confidence interval [CI], 0.46-0.73) and a non-statistically significant association with breast cancer (OR, 1.21; 95% CI, 0.93-1.58). Findings were similar when examining BRCA1 and BRCA2 mutation carriers separately. The data were inadequate to perform a meta-analysis examining duration or timing of use. Additionally, there were four studies examining risk for ovarian cancer and three for breast cancer among women with a family history of ovarian or breast cancer. However, differences between studies precluded combining the data for meta-analyses, and no overall pattern could be discerned. The authors concluded that ever use of OCPs in women carrying a germline mutation in BRCA1 or BRCA2 was similar to that demonstrated in studies of population-risk patients. However, risk/benefit could not be directly addressed precluding a recommendation for their use for prevention of ovarian cancer.

■ COMMENTARY

"Oral contraceptive use had no significant effect on ovarian, breast cancer risk in BRCA1/2 carries" was the headline in a recent medical periodical highlighting this specific article. As can be appreciated, the sound bite is misleading, and although it gets one aspect correct (impact on breast cancer), it is stated with the intent to highlight the lack of protection by OCPs for ovarian cancer (false) and breast cancer (false) development in this high-risk group. While the authors clearly demonstrate an inverse protective effect of OCP use and ovarian cancer, the concern was not in protection of breast cancer but rather that OCP use would increase breast cancer risk, particularly in this patient cohort of individuals at substantially higher risk of breast cancer. Previous reports have raised concerns that OCP use may increase breast cancer risk in the general population.[1,2] The authors demonstrated an OR for breast cancer risk of > 1.0, but it was not statistically significant. Overall, this should be reassuring, yet, it was concluded that there was a "non-statistically significant" association of OCP use and the development of breast cancer.

This experience raises two take-home messages: first, headlines and sound bites may be very misleading and should be reproduced with caution; and second, data from observational studies and meta-analyses are hypothesis-generating and should be limited in their scope to these activities. Although randomized controlled trials are the gold standard in assessing effect, such studies involving an intervention like OCPs are impractical. However, properly designed and monitored cohort studies, in this setting, can provide strong estimates of effect. Third, meta-analyses are tricky to perform properly, and heterogeneity in study design, patient cohorts, treatment or intervention used, follow-up, and confounders of the individual trials included in the exercise make it extremely difficult to assess questions of risk.[3] As was appreciated in this current study, the ratio of assessable trials filling the eligibility criteria was about 1:1000 in the reported literature. Finally, we are cautioned to accept even the author's conclusion based on the presented data. In this manuscript, the authors state, "There is insufficient evidence to recommend oral contraceptive use as a chemoprevention strategy in high-risk women, if they otherwise would not be taking them for contraception." At face value this may be true, but the intent was not to diminish the effect seen in their use, but rather to provide a statement regarding the risks of OCP use (which they could not assess due to trial heterogeneity in their sample set) and benefits (which they did evaluate in their sample set).[4] As is often the case, medical practice is governed by imperfect data and we are left to critically interpret the information before us; this should be done with caution. ■

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First Trimester Anatomy

ABSTRACT & COMMENTARY

By John C. Hobbins, MD

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Dr. Hobbins reports no financial relationships relevant to this field of study.

Synopsis: *A meta-analysis of 19 studies involving first trimester screening for fetal anomalies has shown that a majority of major structural abnormalities can be diagnosed between 11 and 14 weeks and that even cardiac abnormalities can be identified with ultrasound with reasonable efficiency.*

Source: Rossi AC, Prefumo F. Accuracy of ultrasonography at 11-14 weeks of gestation for the detection of structural anomalies: A systematic review. *Obstet Gynecol* 2013;122:1160-1167.

As mentioned in previous alerts, standard screening protocols for fetal aneuploidies have been revamped to include, and actually feature, cell-free DNA (cf DNA). Most "combined" screening protocols had been built around first trimester assessment of nuchal translucency (NT). However, for high-risk patients, the emergence of cfDNA has rendered most previous screening combinations superfluous. The original NT is the possible exception — since it remains a useful adjunctive tool for aneuploidies not detected by cfDNA, as well as for many cardiac abnormalities and multiple anomaly syndromes. So, rather than abandon first trimester ultrasound in today's restructured screening protocols, some have expanded the NT exam to include first trimester fetal anatomy surveys.

Two authors from Italy scanned the literature for studies that explore the efficacy of a first trimester anatomy survey to detect major anomalies. Of the more than 1000 articles evaluated, only 19 lived up to their stringent statistical rules of inclusion. Together these studies involved 78,000 patients who had ultrasound examinations between 11 and 14 weeks. The major anomaly rate in this mixed-risk population was 12 per 1000 and the overall detection rate was 54%. The best detection rate involved abnormalities of the fetal neck (92%), abdomen (88%), brain and spine (51%), and fetal heart (48%).

Data involving the fetal heart were particularly interesting. These were the most common abnormalities encountered in the meta-analysis — noted in 418 patients, 201 of which were detected. About half of the heart abnormalities were identified by echocardiogram, while the other half were detected by the complete anatomic survey alone. However, the detection rate was far superior with the concentrated echocardiographic approach than with the standard fetal survey alone (50% vs 13%). Doppler investigation did not increase the detection rate.

Although 89% of the major anomalies were isolated, the detection rates were much higher when multiple anomalies were present (60%) than if isolated (40%). Also, having risk factors (such as maternal age, family history of cardiac or other anomalies, or exposure to potential teratogens) increased the chances of detection (60% vs 50%), but only 18% of the anomalies in the study came from patients in the high-risk category. If one combined transvaginal sonography (TVS) and transabdominal sonography (TAS), the overall detection rate was 62%, with 51% by TAS alone and 34% by TVS (which was a surprise to me).

■ COMMENTARY

In the past, most screening strategies had been directed toward detecting aneuploidies and, in particular, trisomy 21, simply because of its association with advanced maternal age. However, the rate of aneuploidy in the overall population is small potatoes compared with the rate of major structural abnormalities, which complicate about 2% of all pregnancies. By switching the thrust of today's investigation to the fetal anatomy, not only will most anomalies be detected, but also most of the aneuploidies — which tend to be associated with structural abnormalities.

The major problem with screening for anomalies between 11 and 14 weeks is the inability to identify some anomalies that take time to develop. For example, agenesis of the corpus callosum and some causes of ventriculomegaly, along with abnormalities involving the posterior fossa, do not become apparent until after 20 weeks. Also, in many cases the small size of the fetal organs makes imaging difficult, especially if using TAS in obese patients.

In the interest of cost-effectiveness, it is often recommended that fetal surveys be postponed until the second trimester. However, this recommendation would only be appropriate if we were limited to one ultrasound examination per pregnancy. If the emphasis were more on efficiency and convenience, screening for anomalies would not be limited to an "either or" choice. In fact, few would argue against first trimester surveys being done in high-risk patients, but, as demonstrated in this study, only 18%

percent of the anomalies in the total population came from patients with high-risk factors.

A major reason to move any screening protocol into the first trimester is to meet our patients' requests for earlier information that will either allay their anxieties or, if an anomaly is found, can initiate further testing to allow them to weigh their options at that time. Unfortunately, just because patients want this does not necessarily mean that in a, now, cost-conscious health care atmosphere, this initiative will fly with third-party payers.

The effectiveness of a first trimester anatomy search was well demonstrated in this study, but what about the cost? This could be based in part on the effort generated to accomplish this task. With this in mind, we initiated a small pilot study to determine how often in the first trimester we could clear the anatomy using the standard American Institute of Ultrasound in Medicine (AIUM) protocol (drafted originally for second and third trimester exams), and we tabulated the time required to do this. In the first 116 patients studied, we were able to clear every required portion of the fetal anatomy more than 90% of the time, with the exception of the kidneys (36%). The heart, however, requires special mention. With color Doppler we could obtain adequate four chamber views in 80% of the cases, crossing of the great vessels 54% of the time, and adequate three vessel views in 64% of cases. The average time required to accomplish the whole survey was 22 minutes, which included discussion of the findings along the way and performing the NT and nasal bone examinations according to Nuchal Translucency Quality Review guidelines.

Without data, it would be hard to argue that the first trimester scan should *replace* the second trimester anatomy survey, but it *seems* short sighted, even from a cost perspective, to limit ultrasound in a low-risk population to one per patient.

The take home messages from this meta-analysis are:

1. More than half of fetal major anomalies can be identified between 11 and 14 weeks.

2. The detection rates are even better if one suspects an anomaly — e.g., another anomaly has been noted, high-risk factors are present, or when a targeted examination, like an echocardiogram, is undertaken.

3. A combined approach of TVS and TAS was somewhat more effective than either approach alone. ■

CME Instructions

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CME Questions

1. **After emergency contraception, the best timing for initiation of a combined oral contraceptive pill would be:**
   a. the same day with the LNG EC pill, but 3 days later if UPA was used.
   b. the same day with both the LNG and UPA pills.
   c. 3 days after either the LNG or UPA pill.
   d. only after a normal menstrual period and a negative pregnancy test.

2. **Women should avoid eating peanuts during pregnancy and lactation to prevent the development of a peanut allergy in their children.**
   a. True
   b. False

3. **Which of the following is true regarding the study of oral contraceptive pill use and cancer risk?**
   a. It is best described as a cohort study of BRCA1/2 women.
   b. The patient population did not include patients with a strong family history of ovarian or breast cancer.
   c. The association of OCP use and breast cancer was linear, but not statistically significant.
   d. The statistic used to assess association was relative risk.
   e. The association of OCP use and ovarian cancer risk was stronger in BRCA1 mutation carriers than in BRCA2 mutation carriers.

4. **A combined approach using transabdominal sonography and transvaginal sonography was the most effective in detecting fetal anomalies.**
   a. True
   b. False

In Future Issues:

Continuous Use of a Non-androgenic OCP Improves Endometriosis Pain and Endometrioma Reoccurrence