

2

Preconceptional counseling

Rahat Khan and Hassan Shehata

INTRODUCTION

Preconceptional counseling is different from antenatal care and should not be confused with it. In particular, it is more important than antenatal care, as 30% of pregnant women begin traditional antenatal care in the second trimester and after the period of maximal organogenesis (between 3 and 10 weeks' gestation)¹. Preconception care refers to interventions that aim to identify and modify biomedical, behavioral and social risks to women's health or pregnancy outcome through prevention and management.

To date, the evidence as to the best means for delivering preconception care is limited. The Preconception Care Work Group of the Centers for Disease Control USA recommends that preconception care should be an essential part of primary and preventive care, which involves good communication and liaison between the primary and secondary care providers²⁻⁴.

Preconceptional evaluation and counseling:

- Begin with attitudes and practices that value pregnant women, children and families, and respect the diversity of people's lives and experiences
- Incorporate informed choice, thus encouraging women and men to understand health issues that may affect conception and pregnancy
- Encourage women and their partners to prepare actively for pregnancy, enabling them to be as healthy as possible

- Attempt to identify the risks of pregnancy for the mother and her fetus, educate about these risks, and institute proper interventions including referral to specialists before conception.

Depending on their personal choice, women can go to any of the following health care providers for preconceptional counseling:

- Local doctor (general practitioner or family physician)
- Private obstetricians and gynecologists, specialists and obstetric physicians.
- Maternity hospital clinic, preconception health clinics or organizations
- Family planning, community health center or women's health nurse.

Health care providers can dispense preconceptional care and counseling during any encounter involving contraception, infertility, pregnancy testing, evaluation for sexually transmitted disease or vaginal infection, or periodic health examination, especially if the woman has pre-existing medical problems.

FACTORS ADVERSELY INFLUENCING PRECONCEPTION CARE

- *Unplanned pregnancy* In one US study, 40% of the mothers surveyed within 3–6 months after delivery reported that their pregnancy was unplanned; of these,

two-thirds had one or more indications for preconceptional counseling (smoking and drinking within 3 months of pregnancy, low body mass index (BMI) or late booking)⁵.

- *Financial issues* A number of women with low income may have difficulties with child care and transportation, or may be reluctant to seek pre-pregnancy counseling. In the USA, on the other hand, preconceptional counseling often is not fully reimbursed by third-party payers. It is for this reason that it was proposed that it be included in a variety of otherwise routine encounters (see above).
- *Inadequate training of health care providers* All women's health care providers should be trained to provide adequate assessment of risk factors in pregnancy and offer appropriate recommendations for interventions.
- *Lack of co-ordination between primary and secondary care providers* As lack of co-ordination can represent an important barrier to optimum pre-pregnancy care, health care systems should develop policies for timely referrals to specialists and timely appointments.
- *Risk factors for adverse outcome* These include advancing maternal age, genetic history, infertility, fetal aneuploidy, gestational diabetes, pre-eclampsia and prior stillbirth, among others.
- *Lack of knowledge and education about health and pregnancy* Basic patient education should be an integral part of all women's health care provider systems, as numerous women have multiple risk factors and are unaware of the adverse pregnancy outcome associated with them.

COMPONENTS OF PRECONCEPTIONAL COUNSELING

The three integral components of pre-pregnancy counseling are:

- Identification of risk factors related to pregnancy
- Patient education regarding pregnancy risks, management options and reproductive alternatives
- Initiation of interventions, when possible, to provide optimum pregnancy outcome.

Risk identification

Thorough history taking is the key to risk assessment in any woman planning a pregnancy. This can be accomplished at the primary or specialist care level after referral.

Physical examination

A preconceptional health check does not necessarily involve a 'hands-on' physical check; rather, it focuses on obtaining information and discussing health issues to help the woman and her partner make informed decisions. A routine periodic health examination is all that is needed, documenting maternal BMI, assessment of breasts, thyroid, heart, skin, cervical smear and, if indicated, screening for *Chlamydia* and gonorrhoea. As dental caries and other oral diseases are common and may be associated with preterm delivery, inspection of the oral cavity should be included in any examination protocol, thus, prompting referral to a dentist when appropriate.

Laboratory assessment and screening

The choice of laboratory tests depends upon the general guidelines recommended for all

pregnant women and the individual's personal medical history.

Routine laboratory testing includes:

- Rubella and varicella titer, the latter being particularly important in women with a negative history of varicella
- Screening for hepatitis B, syphilis and HIV in all antenatal pregnant women
- Complete blood count with red cell indices (mean corpuscular volume (MCV) less than 80 may indicate hemoglobinopathy).

Interventions

Preconceptional interventions are directed at educating the patient, providing optimum therapy for medical disorders and, when appropriate, referral for specialized care.

Age-related risk

Women should be clearly informed that advanced maternal age is associated with an increased risk of conditions such as infertility, fetal aneuploidy, stillbirth, gestational diabetes and pre-eclampsia, among others.

The risk of fetal chromosomal anomalies, in particular Down's syndrome, increases sharply with increasing maternal age. The estimated risk of having a baby with trisomy 21, 18 and 13 is 6 per 1000 live births at age 35 years, 15 at age 40 years and 54 at age 45 years. There is also an increased risk of miscarriage, twins, fibroids, hypertension, gestational diabetes, labor problems and perinatal mortality, although it is equally true that most pregnancies in older women who do not have underlying diseases are uneventful.

Couples should be told that the probability of conception is highly dependent on maternal and, to a lesser extent, paternal age and they should take this into account in family and career planning.

Medical conditions

Data from clinical trials demonstrating improved outcome with preconceptional intervention exists for many chronic conditions, including diabetes mellitus, autoimmune conditions, hypertension, renal disease, thyroid disease and cardiac problems^{6,10-12}. It is important to clarify the following points in history on the record:

- All medical and surgical conditions for which a woman has been treated, as it is useful for discussing the effect of pregnancy on these conditions and the effect of such disorders on pregnancy
- Contact details for present and past specialist care providers.

Pre-existing diabetes mellitus (see Chapters 5 and 32)

- For women with pre-existing diabetes, pre-pregnancy tight glycemic control is associated with enhanced pregnancy outcome; pre-pregnancy counseling provides an opportunity for assessment of diabetic retinopathy, nephropathy and neuropathy. Poor control of diabetes increases the risk of major fetal congenital abnormalities and miscarriage⁶.
- Referral should be made to a specialist who cares for patients with diabetes (if contact has not been previously established) and, if available, to a diabetic preconceptional counseling clinic.
- The safety of oral hypoglycemic agents is now well established, and patients should be informed that outcomes are improved in women taking oral agents and comparable to those of insulin.
- Women should receive preconceptional folic acid (5 mg/day) up to 3 months into pregnancy as well as in the months preceding conception^{26,27}.

Chronic hypertension (see Chapter 12)

- The goal should be to control blood pressure prior to conception for any woman on angiotensin converting enzyme (ACE) inhibitors; the health care practitioner should be satisfied with control, and effective contraception is advisable.
- All women with hypertension should be referred to a specialist for advice on drug manipulation and to organize shared care monitoring.
- ACE inhibitors should be avoided during pregnancy (fetal growth restriction, oligohydramnios, renal failure in fetus). Methyldopa or labetalol are the drugs of choice in pregnancy.

Asthma (see Chapter 4)

- Patients should be advised to use their peak flow meters regularly.
- Women with repeated asthmatic attacks or severe disease should be referred to a specialist in asthma therapy and not managed by the local doctor.
- If necessary, the use of steroids (inhaled and systemic) in pregnancy is generally safe.

Thyroid disease (see Chapter 6)

- Severe and untreated thyrotoxicosis should prompt referral to an endocrinologist during the preconceptional period, as this condition can lead to anovulation, miscarriage, growth restriction and pre-term delivery⁷. Patients with elevated thyroid stimulating antibodies who become pregnant have the risk of neonatal/fetal thyrotoxicosis.
- There is insufficient evidence to recommend for or against routine screening of thyroid function and antibodies in women planning a pregnancy⁸.

- In known hypothyroidism, thyroid function tests (TFTs) permit evaluation of adequacy of treatment and, if needed, support referral to specialist care.
- In newly diagnosed hypothyroidism, specialist advice should be sought about the levothyroxine starting dose and the woman should be referred for specialist management.

Cardiac problems (see Chapter 3)

- Women with a history of cardiac problems should be referred to a cardiologist for baseline cardiac assessments and discussion of potential pregnancy risks.
- Adequate diagnosis and functional assessment of the severity are necessary to predict maternal and fetal risks.
- Women advised against pregnancy should be given appropriate contraception.

Epilepsy (see Chapter 11)

- Women should be referred to a neurologist for a thorough discussion of the risk of anticonvulsant medications, adjustment of drug regimen and close monitoring during pregnancy.
- Polytherapy should be avoided to minimize the teratogenic effects of anticonvulsants.
- Preconceptional folic acid (5 mg/day) is advised for women on anticonvulsants^{28,29}.
- Prescription of an oral contraceptive pill with 50 µg of ethinylestradiol should be considered.

Chronic renal disease (see Chapter 8)

- Blood pressure and baseline renal function tests should be performed; any woman with renal disease planning a pregnancy should be referred to a specialist.

- Women should be informed that the outcome of pregnancy and any adverse effects on underlying renal disease are influenced by the presence and degree of renal impairment, hypertension (10% risk of fetal loss if pre-existing) and proteinuria.
- Renal disease during pregnancy is associated with risk of prematurity, growth restriction and deterioration in maternal renal function.
- Women with renal transplants should be asked to avoid pregnancy for a minimum of 2 years until renal function is optimized on a reduced amount of immunosuppressants.
- Women on warfarin planning a pregnancy should be referred to a specialist for advice. Warfarin is teratogenic and stopping or switching over to low molecular weight heparin, before the 6th week of pregnancy may minimize this risk.
- Inherited or acquired thrombophilia may also be responsible for recurrent fetal loss, pre-eclampsia and fetal growth retardation.

Hemoglobinopathies

Autoimmune disorders (see Chapter 7)

- All women with sickle cell syndrome or thalassemias should be referred to a specialist/hematologist. Partners should be screened appropriately and advice sought if the trait is identified.
- Hemoglobin electrophoresis detects beta thalassemias, but alpha thalassemias can only be confirmed by globin chain synthesis. Ethnic minorities should be screened for particular traits (Asians and Cypriots for beta thalassemia; Africans, Afro-Caribbeans, Afro-Americans and Asians for sickle cell).
- Most autoimmune conditions improve in pregnancy, except systemic lupus erythematosus.
- Referral should be made to an obstetric physician, as preconceptional counseling involves knowledge of anti-Ro/La, lupus anticoagulant, renal and blood pressure status.
- Maternal medications may need to be changed because of potential risks to the fetus.
- Pregnancy outcome is improved if pregnancy occurs in remission period; the increased risks of pre-eclampsia, miscarriage, fetal death and growth restriction are related to the presence of anticardiolipin antibodies or lupus anticoagulant, lupus nephritis and hypertension.

Review of medications

(see Chapters 22 and 23)

It is important to minimize exposure to all non-essential drugs, including self-medication with over-the-counter drugs.

Dietary evaluation (see Chapter 22)

Venous thromboembolism (see Chapter 9)

- Specialist advice should be sought for women who have a past history of deep venous thrombosis (DVT) or pulmonary embolism (PE), or with an abnormal thrombophilia screen.
- Vegetarians are at risk of various nutritional deficiencies and may benefit from nutritionist referral.
- Asian women are at risk of vitamin D deficiency and may benefit from a specific supplement.

- Eating habits should be reviewed, and women should be asked to avoid cat and sheep litter; uncooked meat, fish and eggs; and unpasteurized milk and soft cheese because of dangers of toxoplasmosis and listeriosis.
- Undiagnosed or untreated celiac disease in both men and women may cause subfertility, which resolves after adoption of a gluten-free diet.
- Megavitamins, non-essential dietary supplements and herbal preparations should be discontinued, as their risk to the fetus has not been evaluated. Multivitamins containing more than 5000IU of vitamin A should be avoided.
- Women with phenylketonuria are at a high risk of having a baby with mental retardation and should be placed on a special diet to reduce levels prior to conception.
- All women planning a pregnancy should be on 400 µg/day of folic acid at least 3 months prior to conception to reduce the incidence of neural tube defects, such as spina bifida, by 72%.
- Maternal obesity (BMI more than 30 kg/m²) is associated with infertility, reduced *in vitro* fertilization (IVF) success rates, miscarriage and several pregnancy complications, such as gestational diabetes, pre-eclampsia, stillbirth, congenital anomalies in the fetus and postpartum complications.
- The overall health benefits of achieving a normal BMI pre-pregnancy are well described. Obesity-related hormonal changes appear to adversely affect sperm parameters and can cause erectile dysfunction.
- Obese women should be referred to a weight management clinic and dietician; women with polycystic ovaries should be referred to a gynecologist.

Body mass index (see Chapter 30)

- Approximately, 60% of American women are overweight and 33% are obese. Women who are underweight or overweight are at risk of subfertility and may need referral to a pre-pregnancy weight management clinic and dietician. Problems with obesity and low weight are not confined to the American population, and obesity is almost as prevalent in the UK and in parts of Europe. In the UK, the prevalence of obesity among women of reproductive age is expected to rise from 24.2% in 2005 to 28.3% in 2015³⁰.
- Past obstetric and gynecological history is important for identifying factors that may contribute to infertility or pregnancy complications in the future.
- History of irregular menstrual cycles, abnormal cervical smear, ectopic pregnancy, pelvic surgery or uterine fibroids (associated with miscarriage and preterm birth) should be sought.
- Past history of sexually transmitted diseases, including the date and types of treatment should be noted.
- Previous reproductive history should be taken including any recurrent miscarriages, stillbirths, low birth weight, preterm births, congenital anomalies, antenatal problems and the mode, place, complications of delivery and type of contraception.
- All women who have had three consecutive miscarriages should be referred to a gynecologist or recurrent miscarriage

specialist for identification and management of any treatable cause (see Chapter 17 on recurrent miscarriages).

- The recurrence risk of an adverse outcome (e.g. miscarriage, intrauterine growth restriction, pre-eclampsia, congenital anomaly, perinatal death) should be discussed with women who have a history of these specific pregnancy complications.
- Genetic screening should be advised for couples who have had a previously abnormal fetus, three recurrent fetal losses or have a personal or family history of a genetic problem.

Family history (see Chapter 31)

- Enquiries should be made about family history of Tay Sachs disease (Ashkenazi Jews), sickle cell disease (Africans/Afro-Caribbeans, Afro-Americans, Asians), thalassemia (Mediterranean and Middle Eastern origins), cystic fibrosis, epilepsy, thrombophilia, hemophilia, congenital abnormalities, metabolic disorders and mental disorders.
- Certain ethnic minorities have a high prevalence of being heterozygous carriers of certain autosomal recessive disorders and both partners should be screened as this allows them to make informed decisions about having children.

Psychosocial problems

- It is important to screen for domestic violence, work-related issues, lack of support and financial issues that can be a barrier to preconception care²⁰.
- Women with mental health issues should be identified and actions taken to ensure they are under specialist care. Common

conditions necessitating referral are depression, bipolar affective disorder and schizophrenia, and history of postnatal depression²¹ (see Chapter 13).

- Women should be reassured that there is no indication to routinely stop tricyclic antidepressants or selective serotonin re-uptake inhibitors prior to or in early pregnancy.
- Women who are on mood stabilizing anti-epileptic drugs should be on 5 mg/day of folic acid preconceptionally and during first 3 months of pregnancy^{28,29}. This dose is higher than that universally recommended to other women.
- Lithium is highly teratogenic if taken in the first 12 weeks of pregnancy (risk of Ebstein's anomaly 4–12%) and should be given only if necessary by close monitoring of lithium levels. Schizophrenic women may be advised to continue maintenance therapy and discuss the relative risks/benefits of the selected agents.

Illicit drug use

- Cocaine use in pregnancy is associated with miscarriage, abortion, premature birth and low birth weight; opiate use is associated with growth restriction and preterm birth^{14,17,19,25}.
- All women addicted to heroin should be encouraged to enter a detoxification program.
- Intravenous drug abusers should be screened for hepatitis B, C and HIV, alcohol and tobacco use.
- A multidisciplinary approach is essential as is screening for sexually transmitted diseases.

Alcohol use

- It is important to elicit a detailed history of alcohol consumption in terms of amounts, duration and the propensity to binge drinking. Causes of subfertility in these women include reduced ovulation and endometriosis.
- Maternal consumption of 15 units/week is associated with a reduction in birth weight and in excess of 20 units/week is associated with intellectual impairment in the child.
- High levels of alcohol consumption during pregnancy result in the fetal alcohol syndrome (FAS), which includes growth retardation, mental retardation, facial anomalies and behavioral problems^{9,13,15,16,18}. It is seen in 33% of babies born to mothers who drink 18 units/day. There is no clear safe level of consumption. All women should be advised to reduce their alcohol intake if they are planning a pregnancy, although it has been posited that one or two drinks, once or twice a week, is unlikely to harm the fetus⁹.
- It is important to identify women who drink heavily and are likely to continue drinking throughout pregnancy so that appropriate help and support can be offered.

Smoking

- Approximately, 23% of women smoke in pregnancy, and they should be informed of the risks associated with smoking, which include miscarriage, stillbirth, growth restriction, preterm delivery and sudden infant death syndrome^{9,13,19}.
- All women who smoke should be counseled on the benefits of smoking cessation and offered resources to help them quit smoking. Women who quit before

pregnancy are less likely to relapse. Data on the use and relative risks of nicotine replacement therapy (NRT) in pregnancy are lacking.

- Bupropion should not be prescribed in pregnancy because of the lack of data on its safety in pregnancy.

Caffeine

- According to many publications, caffeine is the most widely consumed substance of abuse worldwide. The safe limit in pregnancy is thought to be 300mg/day, which is equivalent to three cups of brewed coffee. Caffeine is present in chocolate, cola and energy drinks as well as in coffee and tea. Approximately 20% of American adults consume more than 300mg of caffeine per day. Caffeine consumption of more than 250mg/day is associated with a modest, but statistically significant decrease in fertility^{9,19,22}.

Exercise

- Women who exercise regularly should be advised to continue such activity. On the other hand, those who are inactive should start a gentle exercise program. Inadequate levels of exercise associated with obesity may be a more common cause of anovulation than exercise associated anovulation.
- In some epidemiological studies, more than 7h/week of aerobic exercise is associated with ovulatory infertility and could be related to reduced progesterone levels and changes in the gonadotropin releasing hormone (GnRH), luteinizing hormone (LH) and follicle stimulating hormone (FSH) secretion⁹. Initiation of strenuous exercise in pregnancy should be avoided, including hot tubs and saunas.

Immunizations and infections

- Women of childbearing age should be asked for a history of any illness or immunizations.
- Non-pregnant women of childbearing age should receive all clinically indicated immunizations, preferably 1 month prior to conception.
- Having a clearly documented immunity to rubella is important, as primary rubella infection in the first 8–10 weeks of pregnancy can result in mental handicap, cataract, deafness, cardiac abnormalities and growth restriction in the fetus.
- Varicella infection in the mother during first 20 weeks of pregnancy can cause congenital varicella syndrome in the fetus. Varicella vaccine must not be given to pregnant women.
- Pregnant women are at increased risk of influenza infection complications. It is recommended that women who become pregnant during the influenza season receive the influenza vaccine, regardless of the stage of pregnancy. Pregnant women are also being encouraged to have swine flu vaccine.
- Patients at risk for hepatitis B infection (women with multiple sexual partners, parenteral drug users, household contacts, health care workers) should be offered hepatitis B vaccine.
- Women of childbearing age who are HIV positive should be offered preconceptional counseling with a HIV specialist.

Occupational and environmental exposure

- Questions about the woman's work, hobbies, pets and home environment can identify potential toxic exposures, such

as working with organic solvents, X-rays, radioactive substances, toxoplasmosis (from changing cat litter boxes) and using lead paint or solder used for decorating^{22–24}.

- Risks from potential hazards at home (e.g. pets), at work and from farm animals should be assessed.
- Any woman who thinks that her occupation may pose a risk to pregnancy should be advised to discuss this with her employer or occupational health department, if possible, before getting pregnant.

SUMMARY AND RECOMMENDATIONS

- All women of childbearing age should be offered preconceptional counseling and evaluation.
- The goals of preconceptional counseling are to identify risks to the woman and her pregnancy, educate the patient and initiate appropriate interventions.
- Good communication between primary and secondary care providers is vital to optimize a woman's health prior to conception and ensuring timely referral.
- A thorough history will help in identifying risk factors to the woman and her pregnancy.
- A pregnant woman with a BMI of greater 30kg/m² should be referred to dietician and specialist clinic.
- Women who are planning a pregnancy should be on folic acid 400 µg/day. Women who are diabetic or on antiepileptic medications should be on 5 mg of folic acid/day^{26–29}.
- An up-to-date cervical smear should have been taken.

- All women should be screened for hepatitis B, HIV, syphilis, rubella and varicella immunity.
- All medications should be reviewed and advice given on the use of over-the-counter medications.
- If applicable, advice should be given on stopping smoking, reducing alcohol intake, healthy eating and stopping illicit drug use. Psychosocial and domestic issues should be identified.
- Ethnic minorities should be screened for hemoglobinopathies and carrier state.
- Family history should be reviewed with referral for genetic counseling, if appropriate.
- Women with a history of recurrent miscarriages, stillbirth, pre-eclampsia or a previous small baby should be referred to an obstetrician/gynecologist or a specialist center for further investigations and discussion of recurrence risks.
- Women with chronic medical conditions should receive multidisciplinary care. Women with diabetes, chronic hypertension, renal or cardiac disease, thyroid problems, epilepsy or asthma should be advised to use effective contraception until seen by a specialist and plans for care have been discussed and put into practice.
- Women with mental health issues should be referred to a psychiatrist.
- Genetic counseling should be offered to all women with a previous abnormal fetus, personal or family history of genetic problems or a history of three recurrent miscarriages.
- A good occupational and environmental history should be sought to review all potential health and pregnancy hazards.

REFERENCES

1. Hamilton BE. Annual summary of vital statistics: 2005. *Pediatrics* 2007;119:345
2. Johnson K, Posner SF, Biermann J, et al. Recommendations to Improve Preconception Health and Health Care – United States A Report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. *MMWR Recomm Rep* 2006;55:1
3. Atrash H, Jack BW, Johnson K, et al. Where is the “W”oman in MCH?. *Am J Obstet Gynecol* 2008;199:S259
4. Jack BW, Atrash H, Coonrod DV, et al. The clinical content of preconception care: an overview and preparation of this supplement. *Am J Obstet Gynecol* 2008;199:S266
5. Adams MM, Bruce FC, Shulman HB, et al. Pregnancy planning and pre-conception counseling. The PRAMS Working Group. *Obstet Gynecol* 1993;82:955
6. Mills JL, Simpson JL, Driscoll SG, et al. Incidence of spontaneous abortion among normal women and insulin-dependent diabetic women whose pregnancies were identified within 21 days of conception. *N Engl J Med* 1988;319:1617
7. Anselmo J, Cao D, Karrison T, et al. Fetal loss associated with excess thyroid hormone exposure. *JAMA* 2004;292:691
8. Matalon ST, Blank M, Ornoy A, Shoenfeld Y. The association between anti-thyroid antibodies and pregnancy loss. *Am J Reprod Immunol* 2001;45:72
9. ACOG practice bulletin. Management of recurrent pregnancy loss. Number 24, February 2001. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet* 2002;78:179
10. Korenbrot CC, Steinberg A, Bender C, Newberry S. Preconception care: a systematic review. *Matern Child Health J* 2002;6:75
11. Leuzzi RA, Scoles KS. Preconception counseling for the primary care physician. *Med Clin North Am* 1996;80:337
12. Stubblefield PG, Coonrod DV, Reddy UM, et al. The clinical content of preconception care: reproductive history. *Am J Obstet Gynecol* 2008;199:S373
13. Shiono PH, Klebanoff MA, Rhoads GG. Smoking and drinking during pregnancy. Their effects on preterm birth. *JAMA* 1986;255:82

14. Li CQ, Windsor RA, Perkins L, *et al.* The impact on infant birth weight and gestational age of cotinine- validated smoking reduction during pregnancy. *JAMA* 1993;269:1519
15. Marbury MC, Linn S, Monson R, *et al.* The association of alcohol consumption with outcome of pregnancy. *Am J Public Health* 1983;73:1165
16. Alcohol consumption among pregnant and childbearing-aged women--United States, 1991 and 1995. *MMWR Morb Mortal Wkly Rep* 1997;46:346
17. Miller JM Jr, Boudreaux MC. A study of antenatal cocaine use--chaos in action. *Am J Obstet Gynecol* 1999;180:1427
18. Alcohol consumption among women who are pregnant or who might become pregnant--United States, 2002. *MMWR Morb Mortal Wkly Rep* 2004;53:1178
19. Floyd RL, Jack BW, Cefalo R, *et al.* The clinical content of preconception care: alcohol, tobacco, and illicit drug exposures. *Am J Obstet Gynecol* 2008;199:S333
20. Klerman LV, Jack BW, Coonrod DV, *et al.* The clinical content of preconception care: care of psychosocial stressors. *Am J Obstet Gynecol* 2008;199:S362
21. Frieder A, Dunlop AL, Culpepper L, Bernstein PS. The clinical content of preconception care: women with psychiatric conditions. *Am J Obstet Gynecol* 2008;199:S328
22. McDiarmid MA, Gardiner PM, Jack BW. The clinical content of preconception care: environmental exposures. *Am J Obstet Gynecol* 2008;199:S357
23. Fischbein A, Wallace J, Sassa S, *et al.* Lead poisoning from art restoration and pottery work: unusual exposure source and household risk. *J Environ Pathol Toxicol Oncol* 1992;11:7
24. Shaw GM. Adverse human reproductive outcomes and electromagnetic fields: a brief summary of the epidemiologic literature. *Bioelectromagnetics* 2001;(Suppl 5):S5
25. Stanton CK, Gray RH. Effects of caffeine consumption on delayed conception. *Am J Epidemiol* 1995;142:1322
26. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. 1. diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabetes Med* 1998;15:539-53
27. Casson IF, Clarke CA, Howard CV, *et al.* Outcomes of pregnancy in insulin dependent diabetic women: results of a 5 year population cohort study. *Br Med J* 1997;315:275-8
28. Adab N, Kini U, Vinten J, *et al.* The longer term outcome of children born to mothers with epilepsy. *J Neurol Neurosurg Psychiatry* 2004;75:1517-8
29. Crawford P, Appleton R, Betts T, *et al.* Best Practice guidelines for the management of women with epilepsy. *Seizure* 1999;8:201-17
30. Ono T, Guthold R, Strong K. WHO *Global Comparable Estimates*, 2005. Geneva: World Health Organization, 2005

