The clinical content of preconception care: preconception care for men

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Little attention has been given to men's preconception health and health care. This paper reviews the key elements of an approach to optimizing the preconception health status of men. Preconception care for men is important for improving family planning and pregnancy outcomes, enhancing the reproductive health and health behaviors of their female partners, and preparing men for fatherhood. Most importantly, preconception care offers an opportunity, similar to the opportunity it presents for women, for disease prevention and health promotion in men. Currently, no consensus exists on service delivery of preconception care for men—who should provide preconception care to whom, where, when, and how, and there are significant barriers to this care including the organization, financing, training, and demand. Finally, much more research on the content and how to effectively market and implement preconception care for men is needed.

Key words: father, health promotion, preconception, risk assessment

In 2005, the Centers for Disease Control and Prevention (CDC) and 35 partner organizations convened a national summit and issued a set of recommendations to promote preconception care in the US. While passing recognition was given to the importance of preconception health promotion "among both men and women," the focus was on women. To date, little attention has been given to men's preconception health and health care.

The belated recognition of men in our efforts parallels efforts to involve men in reproductive health initiatives internationally, which has only gradually recognized that men should be legitimate targets for sexual and reproductive health promotion, and that men should play direct, active, and constructive roles as part of a broader reproductive health agenda.[1] Several international initiatives have taken place with themes such as "Men as Partners in Reproductive Health."[2] In the US, there has been a steady increase in research and programs on men's health and family involvement, but these have not heretofore been conceptualized in a preconception health context. We believe that there are several distinct reasons why preconception care for men is important.

First, as with women, improving men's preconception health is critical for ensuring that all pregnancies are planned and wanted. Men are critical partners in family planning, and until the advent of modern assisted reproductive technologies (ART), necessary partners. The CDC's first Preconception Care recommendation encourages all women, men, and couples to have a reproductive life plan.[3] Men's contribution to the family planning partnership means addressing the utilization, access, and efficacy of male fertility control, including barrier methods and hormonal agents; and not assuming that all reproductive responsibility (and biologic risk) is held by women. Although many assume men are not interested in or supportive of family planning and contraceptive usage, most recent research shows that this is untrue.[4] Men's preconception care should encourage men to positively influence their own and their partner's contraceptive decision making.

Second, improving men's preconception health can result in improved pregnancy outcomes by enhancing men's biologic and genetic contributions to the pregnancy conception. Sperm DNA can get damaged in many ways, including exposures to tobacco, alcohol, drugs (eg, anabolic steroids), caffeine, poor diet, radiation and chemotherapy, and testicular hyperthermia. Medical conditions such as diabetes mellitus, varicoceles, and epididymitis, if left untreated, can also reduce sperm count and quality. A growing number of xenobiotics, including 1,2-dibromo-3-chloropropane, nonylphenol, polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), dioxins, phthlates and acrylamide, have been shown to cause oxidative stress and DNA damage to the sperm. Such damage usually results in infertility, subfertility, or spontaneous abortions. However, pregnancy may still be possible despite some degree of DNA damage, and can result in birth defects and even childhood cancers. Because new sperm is made every 42-76 days, damaged sperm can be replaced within 3 months of mitigated exposures. Thus, preconception care offers a window of opportunity to improve sperm quality.

Third, preconception care for men can result in improved reproductive health biology for women. Preconception care for men offers an opportunity for

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screening and treatment of sexually transmitted infections (STIs), including gonorrhea, syphilis, human immunodeficiency virus (HIV), and others, as well as environmental toxins. STI treatment of women only, without treatment of their partners, is doomed to failure. Preconception care also provides the opportunity to address men's behaviors that might result in undesired and unplanned pregnancies, including intimate partner violence, rape, drinking/drug usage, and multiple sexual partners, among others. Violence against women prevention programs have proven beneficial, albeit limited in number and evaluative quality.[1]

Fourth, preconception care for men can result in improved reproductive health practices and outcomes for women. Men can be a vital source of support or stress for women during pregnancy, birth, and parenting. Men often play a controlling/gatekeeper role in decisions around prenatal care, delivery services, and other health-seeking behaviors. While paternal permission for access to modern reproductive health services is not a major issue in the US, this is not true all over the globe. Men also play important roles in fostering or discouraging important maternal health behaviors such as smoking, drinking, physical fitness, and healthy nutrition. Women who live with a smoking partner, for example, are less likely to reduce smoking than women who live with a nonsmoking partner,[5] not to mention the impact of secondhand smoke on the developing fetus. Men's preconception care therefore offers an opportunity to promote male support of women's positive reproductive health and health care-seeking practices.

Fifth, preconception care for men can result in their own improved capacity for parenthood and fatherhood. Men have critical roles to play as a parent during pregnancy and post childbirth to ensure healthy families and children. Men's maturation to be an effective parent (and even to be present) should begin with preconception care. There is a great deal of literature on men's development and men's conceptions of their roles in parenthood, which heretofore has not usually been conceived of as starting in the preconception period, but could and should be. Efforts to address gender and development, including programs to change men's (and especially adolescent men's) social or gender norms, can be conceptualized as men's preconception health programs. Male understanding of his roles and responsibilities as a parent has the capacity to evolve over the course of prepregnancy, pregnancy, and birth.

Sixth, preconception care can be a venue for enhancing the health of men through access to primary health care. A man's health is an issue of importance both for himself and for his capacity to be a parent. Topics such as paternal depression, smoking behavior, physical fitness, nutritional status, etc, all impact on his own health and his parenting/spousal responsibilities. Increasing obesity, for example, is directly associated with increasing male infertility.[6] Preconception care offers an opportunity for disease prevention and health promotion among men, similar to the opportunity among women—that can have an impact on his lifetime health and the nation's reproductive health overall.

As defined by the CDC Select Panel, preconception care is a set of interventions that aims to identify and modify biomedical, behavioral, and social risks to women's health or reproductive outcomes through prevention and management. This definition can be applied to preconception care for men if the focus is changed from "women's health" to "men's health." The basic components of preconception care for women consist of 1) risk assessment, 2) health promotion, and 3) clinical and psychosocial interventions. A model framework of the content of preconception care for men, which can be applied in clinical practice, is outlined below.

Risk Assessment

The primary objective of risk assessment is to identify ongoing problems that need to be addressed.

Reproductive life plan

Risk assessment begins with evaluation of the couple's reproductive life plan. As defined by the CDC, a reproductive life plan is a set of personal goals about having (or not having) children based on personal values and resources, and a plan to achieve those goals. The patient is queried as to whether he plans to have any (more) children, and how long he and his partner plan to wait. If they plan to wait less than a year, the patient should return for a full preconception assessment. If greater than a year, the patient should continue to receive recommended age-appropriate preventive health services, but the provider should make sure that he and his partner are using effective contraception, and update their reproductive life plan at every routine visit.

Past medical and surgical history

The provider should inquire about the patient's past medical and surgical history, including any ongoing medical conditions that may impair his reproductive health. Several medical conditions have been associated with reduced sperm quality, including obesity, diabetes mellitus, varicocele, and sexually transmitted infections. In men with diabetes mellitus type 1, it has been demonstrated that semen volume, motility, and morphology are all significantly lowered compared to controls; furthermore, diabetic men with unsatisfactory glycemic control had lower sperm count, motility, velocity, and viability characteristics than men with satisfactory glycemic control.[7] In terms of male reproductive function, diabetes can affect more than just sperm quality: in a study of 541 diabetic patients, 35% reported erectile dysfunction, with associations found between impotence and age, retinopathy, peripheral and autonomic neuropathy, and treatment with either insulin or an oral medication.[8]

Medications

The patient's past and current medication use, including prescription, nonprescription and herbal products, should be reviewed. A number of medications can affect sperm count and quality, including alkylating agents, calcium channel blockers, cimetidine, colchicine, corticosteroids, cyclosporine, erythromycin, gentamicin, methadone, neomycin, ni-

trofurantoin, phenytoin, spironolactone, sulfasalazine, tetracycline, and thioridazine. Any medication use, including over-the-counter medications, should be guided by a risk-benefit calculus weighing benefits for men's health against known or potential risks to offspring.

Family history and genetic risks

Genetic risk assessment should be based on family history, paternal age, and ethnicity. A 3-generation family history of genetic disorders should be obtained, as certain disorders (sex-linked or autosomal recessive) may skip generations. A number of genetic disorders, such as cystic fibrosis, Klinefelter syndrome, Kartagener syndrome, and polycystic kidney disease, may impair fertility and sperm quality. In a review article on Klinefelter syndrome, the study authors collected data consistent with symptomatic azoospermia, and only 8.4% of their adult patients had spermatozoa in their ejaculate, out of the 69.3% of their population that were willing and able to provide an ejaculate sample.[9] A small study of pre- and peripubertal boys with Klinefelter syndrome found that half (7) of the subjects had no spermatogonia; this study also found an association between the beginning of puberty and loss of spermatogonia.[10]

In an early study of adult men with cystic fibrosis, all patients examined had azoospermia. The study authors also pointed to a high number of abnormal sperm forms seen.[11] Obstructive azoospermia of males with cystic fibrosis is due to a condition known as congenital absence of the vas deferens.[12,13]

Discussion of paternal age-related decline in sperm quality may help inform the couple's reproductive life planning, as many men are not aware of the growing body of evidence linking paternal age to schizophrenia in the offspring. In a Swedish cohort study, the offspring's risk for schizophrenia had a hazard ratio of 1.47 for each 10-year increase in paternal age, even after adjustment for familial schizophrenia history, socioeconomics, birth exposures, and early parental death.[14] Another cohort study revealed that the relative risk for offspring with schizophrenia increases with every 5-year increase in paternal age, culminating in fathers of 50 and over having an adjusted relative risk of 2.96.[15] Furthermore, these authors indicated that for fathers 30-35 years, 1 out of 99 offspring are estimated to have schizophrenia, compared to 1 out of 47 for fathers aged 50 or older.

If the patient belongs to an ethnic group at increased risk for certain genetic disorders (eg, Ashkenazi Jews, African Americans, Southeast Asians, and Mediterranean), the provider should screen the patient if his partner's genetic screen is positive or unknown. For mixed couples, the partner at increased genetic risk based on ethnicity should be screened first.

Social History

The patient's social history, including potential occupational exposures, should be reviewed. Ongoing exposures to metals, solvents, endocrine disruptors, and pesticides at work can impair sperm quality, which may lead to infertility, miscarriage, and birth defects. The patient may obtain a copy of the Material Safety Data Sheet (MSDS) of any chemical exposure at work from his employer, for review for potential reproductive toxicity.

Risk Behaviors

The patient's major and potential risk behaviors, including tobacco, alcohol, drug use, and hobbies, should be reviewed.

Tobacco use has been associated with decreased sperm count and abnormal sperm morphology, motility, and fertilizing capacity. Recent evidence suggests that nicotine and other chemicals in cigarettes can also induce oxidative damage to sperm DNA.

The effects of alcohol use on sperm quality are unclear. Some studies have shown that moderate drinking may be protective against DNA damage, perhaps in part due to the antioxidant effect of some alcoholic beverages.[16] Other studies have shown that alcohol may be damaging to sperm DNA. The data are clearer on heavy drinking (> 2 drinks a day). In a study of alcoholics in an addiction treatment center, testosterone level, semen volume, sperm count, and the number of sperm with normal morphology and motility were lower among alcoholic than nonalcoholic men.[17] The CAGE questions can be easily used to screen for alcohol abuse.

Several recreational drugs have also been linked to male infertility, including marijuana, cocaine, and anabolic steroids. Marijuana has been shown to reduce testosterone production, sperm count, and semen quality. Cocaine has also been associated with decreased sperm count and abnormal sperm morphology and motility, and the effects can linger for up to 2 years from last use. Anabolic steroids can also reduce testosterone level and sperm quality. In a small study of 15 men who were using anabolic steroids, 11 had low testosterone level and 9 had no sperm production at all. Even after quitting, only 2 men resumed normal sperm production.[18]

A study of anabolic steroid use in bodybuilders and semen quality found that compared to a control group, the group of men using steroids exhibited lower sperm concentration and a lower amount of morphologically normal spermatozoa.[19] Patient steroid abuse gives the physician potential for positive intervention, as a study of 18 anabolic androgenic steroid and human chorionic gonadotrophin (HCG) users demonstrated that the mean sperm concentration more than doubled 6 months after cessation of steroid use.[20] This study also showed that the percent of spermatozoa with abnormal morphology was positively correlated with cumulative HCG dose taken.[20] CAGE questions can also be used to screen for recreational drug use.

Certain hobbies may expose the patient to reproductive hazards. Hobbies that involve refinishing furniture, repairing cars, painting, building models, or anything that requires the use of strippers, degreasers, or nonwater-based glues or paints may expose the patient to organic solvents. Hobbies that involve painting, pottery, making stained glass windows, or handling, shooting, or cleaning guns may expose the patient to lead or other heavy metals.

Nutrition

Nutritional screening should review current dietary patterns and use of restrictive diets. Both zinc and folate have antioxidant properties that counteract reactive oxygen species (ROS) and protect sperm against oxidative stress and DNA damage. In a randomized controlled trial of 99 fertile and 94 subfertile men, daily administration of 66 mg zinc sulfate and 5 mg folic acid significantly increased sperm concentration of the subfertile men, suggesting the importance of multiple nutrients impacting fertility; the study authors also found an increase in median percentage abnormal forms from 80-84%.[21] A study of 33 subfertile men from a male infertility clinic who received an intervention consisting of twice daily oral 220 mg zinc sulfate for 3 months significantly increased mean percentage progressive and total motility of sperm.[22] In a randomized controlled trial giving 250 mg zinc sulfate 2 times per day, investigators found that for asthenozoospermic men, 3 months of zinc therapy yielded increases in progressive motility of sperm, sperm count, and sperm membrane integrity, while decreasing percentage of nonmotile sperm.[23] An early study in which normospermic and oligospermic men were given 10 mg folic acid 3 times a day for 1 month found that treatment resulted in no change in sperm characteristics.[24]

Other antioxidants have also been used to treat male infertility, including vitamin C, vitamin E, selenium, glutathione, ubiquinol, carnitine, and carotenoids. However, the safety and efficacy of such treatments have not been clearly established. In 1 study, the combination of vitamins C and E at high doses resulted in sperm DNA damage in vitro, raising concerns about the potential harms of high-dose antioxidant supplementation.[25]

Mental Health

Routine screening for mental health disorders should be performed. Estimates of lifetime risk of major depression for men range from 1.4% in the Epidemiologic Catchman Area to 11% in the National Comorbidity Study. Recent evidence suggests that depression of the father during the postnatal development of their child was found to be significantly associated with poor childhood emotional and behavioral outcomes, even after adjusting for maternal depression and paternal depression during a different developmental stage of the child[26]; such long-term detriments can be averted with identification and referral of at-risk fathers-to-be for mental health services. Furthermore, depressed fathers can have a negative impact on the mother-child interaction behaviors, and are less likely to engage in certain father-child interactions, such as playing outdoors with their children.[27] On the other hand, fathers with good mental health have been shown to reduce the impact of a mother's depression on the child.[28]

Physical Examination and Laboratory Testing

Physical examination and laboratory testing should be guided by clinical history. For example, men at increased risk for sexually transmitted infections should be offered screening for HIV, syphilis, and other STIs. The United States Preventive Services Task Force (USPSTF) recommends screening all adult men for high blood pressure and obesity; men aged 35 and older for lipid disorders (as well as men aged 20-35 with diabetes, family history of cardiovascular disease or familial hyperlipidemia, or multiple coronary heart disease risk factors); men with hypertension or hyperlipidemia for type 2 diabetes mellitus; and men aged 50 and older for colorectal cancer.[29] Routine screening for testicular cancer in young men or prostate cancer in men aged 50 and older ($\geq$ 45 for men at increased risk, eg, African Americans or those with family history of prostate cancer) may also be considered.

Health Promotion

Healthy weight and nutrition

There is a national epidemic of obesity. In 2003-2004, 62.2% of men aged 20-39 were overweight or obese, categorized as having a body mass index (BMI) of 25 or higher.[30] Males who are overweight or obese have been associated with lower testosterone level, poorer sperm quality, and reduced fertility, compared to nonoverweight or obese men; the odds of infertility increases by 10% for every 20 lbs overweight.[6]

An important objective of preconception care is to achieve healthy weight before conception. Clinical guidelines have been established for the identification, evaluation, and treatment of overweight and obesity. Men should be encouraged to set weight loss goals, to develop a plan to reach those goals, and to exercise at least 30 minutes a day on most days of the week. A referral to a nutritionist and/or a structured weight loss program may be useful. After successful weight loss, the likelihood of weight loss maintenance is enhanced by a program consisting of dietary therapy, physical activity, and behavior therapy, which should be continued until pregnancy.

Stress reduction and enhancing resilience

The impact of chronic stress on men's cardiovascular health has been well demonstrated; much less is known about the impact of chronic stress on men's reproductive health. Stress can disrupt hypothalamic-pituitary-gonadal functions, resulting in decreased steroidogenesis and spermatogenesis. Stress can also increase susceptibility to infection and inflammation, which may cause oxidative damage to sperm. However, the literature on stress and semen quality has been inconsistent. Stress has been shown to negatively impact semen quality variables for in vitro fertilization (IVF) patients and patients visiting andrology clinics,[30-34] but has also been shown to have no impact on semen quality for these patients.[35] Weekly time at job and stress have been shown to negatively impact sperm quality variables for fertile men,[36] but job strain and stress have also shown no impact on sperm for infertile men[37] and men of unknown fertility.[38] In other studies of unknown male fertility, stress levels were not associated with variables of sperm quality,[39] but acute stress stemming from an event like a family death,[40] or physiologic, psychological, and overall stress levels can impact sperm quality variables.[41]

It appears prudent to recommend steps that promote stress reduction and resilience in the context of male precon-

ception care. Elements to consider include regular exercise, adequate sleep, and balanced nutrition. Programs or selected readings that enhance the patient's emotional intelligence, capacity for interpersonal communication, and positive mental health should be helpful as well. As is recommended for women, men should be screened for the adequacy of their social support systems. Activities that strengthen social support should be encouraged.

Inflammation and immunization

Chronic inflammation can cause oxidative damage to sperm. Sources of chronic inflammation include chronic, untreated infections such as periodontal disease or STIs, stress, diet, and xenobiotics. Screening for such disorders or exposures should be included as a routine part of health promotion during preconception care.

The immunization status of men should be reviewed as part of a preconception evaluation, and appropriate vaccines should be offered. Immunization recommendations are updated annually by the CDC, the American College of Physicians (ACP), and the American Academy of Family Physicians (AAFP).

Avoidance of harmful exposures

An increasing number of environmental exposures, including phthlates (a type of plasticizer used in food-can linings and many household products), acrylamide (produced during frying, baking, and overcooking), and pesticides and dioxins, have also been shown to cause sperm DNA damage. According to the National Institute for Occupational Safety and Health, male reproductive health can be negatively affected by the following workplace exposures: lead, dibromochloropropane, carbaryl, toluenediamine, dinitrotoluene, ethylene dibromide, plastic production (styrene and acetone), ethylene glycol monoethyl ether, welding, perchloroethylene, mercury vapor, heat, military radar, kepone (in large doses), bromine vapor (in large doses), radiation (in large doses), carbon disulfide, and 2, 4-dichlorophenoxy acetic acid.[42] Additional substances have been identified as potential causes of male infertility, including chlordecone, beta-chloroprene, lead azide, lead II thiocyanate, manganese, manganese tetroxide, tetraethyl lead, and tetramethyl lead.[43] Physical exposures like heat, sedentary work positions, and radiation have the potential to affect male fertility, though the evidence supporting a direct effect remains unclear.[44]

Clinical and Psychosocial Interventions

The integration of preconception care into the ongoing primary care of women is an acknowledged challenge for the recommendations of the CDC's Select Panel. However, an even greater challenge will be to apply the science and principles outlined in this paper to the primary care of men. Even when adequate access and health insurance coverage are available, men do not often seek primary care for their own health promotion and disease prevention. Obstetricians-gynecologists and other clinical professionals providing primary care to women can help by encouraging the woman's partner to seek such care. Additionally, the clinical content of male preconception health care must be integrated into both graduate and continuing medical education for both family medicine and general internal medicine physicians.

Preconception care also offers an opportunity to address the psychosocial needs of men before pregnancy and parenting. Three types of psychosocial services should be made available to men during preconception care: 1) social services, 2) clinical support, and 3) partner and parenting support. Social services may include financial literacy training or assistance with job placement to help men get ready to start a family. The preconception care visit can offer a platform for accessing these services. Men who have mental health problems including depression could benefit from some forms of psychological support and therapy. Many men can use some guidance on how to provide emotional support to their partners, with emphasis on strengthening their capacities for communication and nurturance. Similarly, most men can use some lessons to help them prepare for fatherhood, and preconception is a good time to start.

Recommendation. In spite of the challenges and barriers, we recommend that each male, planning with their partner to conceive a pregnancy, should undergo a comprehensive medical evaluation for the purposes of disease prevention and detection, and preconception education. Management should be optimized for any high risk behaviors or poorly controlled disease states prior to attempting conception. *Strength of recommendation:* B; *quality of evidence:* III.

Conclusion

In this paper, we have outlined the key elements of a comprehensive approach to optimizing the preconception health status of men. Preconception care for men is important for improving family planning and pregnancy outcomes, enhancing the reproductive health and health behaviors of their female partners, and preparing men for fatherhood. Most importantly, preconception care offers an opportunity, similar to the opportunity it presents for women, for disease prevention and health promotion in men.

However, we recognize that to improve preconception health and health care for men in the US, significant barriers must be overcome. Issues that need to be addressed include organization, financing, training, and demand. There is currently no consensus on service delivery of preconception care for men—who should provide preconception care to whom, where, when, and how. To ask busy clinicians to provide preconception care to men at every visit ("every man, every visit") may not be feasible, and some components of preconception care may not be indicated or appropriate for every man at every visit. Furthermore, preconception care for men is not currently a billable diagnosis under most health plans. Many clinicians who provide care to men are not trained to provide preconception care; most obstetricians-gynecologists are not trained to provide care for men. As a starting

point, each couple seeking infertility services should be encouraged to have the male partner medically evaluated by either a urologist or reproductive endocrinologist with an interest in andrology.

Perhaps the most difficult issue is a social marketing one. Men are notorious about not seeking preventive and primary health care. In order to make preconception care for men relevant to every man, targeted health messaging, the buy-in of partners and peers, cultural competency, and appropriate language will be critical. Further evidence is needed on how to effectively market and implement preconception care for men. Additionally, much more research is needed on men's preconception health; research in this newly identified area is virtually nonexistent. ■

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