

# Infertility evaluation and management

## *Strategies for family physicians*

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### ABSTRACT

**OBJECTIVE** To review family physicians' role in investigation and management of infertile couples.

**QUALITY OF EVIDENCE** MEDLINE and PubMed were searched using the MeSH headings infertility, advanced maternal age, polycystic ovarian syndrome, clomiphene citrate, and insulin sensitizers. Bibliographies of review articles and textbooks were also searched. Review articles, randomized trials, observational studies, and case series are cited.

**MAIN MESSAGE** Approximately 8% of Canadian couples have difficulty conceiving. Mother's age significantly affects ability to conceive. Infertility assessment focuses on ovulatory dysfunction, tubal factors, sexual factors, and male factors. Women older than 35 years more than 12 months infertile; women younger than 35 more than 18 months infertile; women likely to have such problems as anovulation, tubal disease, or endometriosis; women whose partners' semen tests abnormal; and women who request referral should be referred. Patients treated with clomiphene citrate should be aware of its potential side effects.

**CONCLUSION** Family physicians have an important role in preconception counseling. Detailed and focused assessment facilitates initial investigations and treatment and can identify couples who could benefit from referral for further assessment.

### RÉSUMÉ

**OBJECTIF** Examiner le rôle du médecin de famille (MF) dans l'investigation et le traitement des couples infertiles.

**QUALITÉ DES PREUVES** Une recherche a été effectuée dans MEDLINE et dans PubMed à l'aide des rubriques *MeSH infertility, advanced maternal age, polycystic ovarian syndrome, clomiphene citrate* et *insulin sensitizers*. Des bibliographies de manuels et d'articles de revue ont également été répertoriées. Les articles cités sont des revues, des essais randomisés, des études d'observation et des séries de cas.

**PRINCIPAL MESSAGE** Environ 8% des couples canadiens éprouvent de la difficulté à procréer. L'âge de la mère est souvent un facteur important de la difficulté à concevoir. Dans l'évaluation d'une infertilité, on s'attardera davantage aux dysfonctions ovulatoires, aux facteurs tubaires, aux facteurs d'ordre sexuel et au partenaire mâle. Une consultation en spécialité est conseillée dans les cas suivants lorsqu'une femme de plus de 35 ans est infertile depuis plus de 12 mois; lorsqu'une femme de moins de 35 ans l'est depuis plus de 18 mois; lorsqu'il y a une possibilité d'anovulation, de maladie tubaire ou d'endométriose chez la femme ou d'anomalie du liquide séminal chez le partenaire; et lorsque la femme le demande. Les patientes traitées au citrate de clomifène doivent être avisées des effets indésirables potentiels.

**CONCLUSION** Le MF joue un rôle important pour conseiller les couples qui désirent procréer. Devant une infertilité, une évaluation détaillée et bien dirigée facilite l'investigation et le traitement, et peut permettre d'identifier les couples susceptibles de bénéficier d'une évaluation spécialisée additionnelle.

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*Cet article a fait l'objet d'une évaluation externe.*

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**I**nfertility is defined as failure to conceive after 1 year of unprotected intercourse. Approximately 8% of Canadian couples have difficulty conceiving.<sup>1</sup> The prevalence of infertility appears to be increasing; many women are postponing childbearing for social, professional, financial, or psychological reasons.

Increased awareness and availability of modern treatments that assist couples to conceive and the decreased supply of infants for adoption have led more couples to seek infertility therapy. While the inability to conceive distresses many couples, they differ in their willingness to undergo intensive investigation and treatment for infertility.

Women often discuss fertility concerns initially with their family physicians. Family physicians have an important role in initial evaluation of infertility, particularly in counseling patients before they become pregnant about ways to optimize pregnancy outcome and about the relationship between age and infertility. Sometimes a focused history identifies simple problems or solutions to improve fertility, and sometimes individual circumstances encourage earlier evaluation or referral to a specialist. Ongoing support and acknowledging the stress of infertility are also important.

This paper reviews the initial workup of infertile couples, describes basic infertility investigations, and suggests guidelines for referral to gynecologists or infertility specialists. Some simple treatments can be initiated by family physicians, such as use of clomiphene citrate and insulin sensitizers for women with polycystic ovarian syndrome (PCOS). Finally, the indications, costs, and success rates of various infertility treatments will be briefly reviewed.

### Quality of evidence

A large body of literature describes causes, investigations, and treatment of infertility. English-language journals indexed in MEDLINE and PubMed were searched for relevant articles using the following MeSH headings: infertility (causes, investigation, treatment); advanced maternal age; PCOS; clomiphene citrate; and insulin sensitizers. References in retrieved articles were reviewed for potentially

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relevant articles not identified through database searches. Articles cited include review articles, randomized trials, prospective and retrospective cohort or case-control studies, observational studies, and case series.

Data from observational cohort studies (level III evidence)<sup>2</sup> identify etiologic factors associated with infertility. Data from both retrospective and prospective cohort and case-control studies (level II-2 evidence)<sup>2</sup> evaluate particular investigations for infertility. Frequently cited studies in the infertility literature, as well as best evidence from reviews by well-known experts and consensus statements from the Canadian Fertility and Andrology Society (CFAS), the American Society for Reproductive Medicine (ASRM), and the Royal College of Obstetrics and Gynaecology (RCOG) were also reviewed and cited where relevant (level III evidence). This paper focuses primarily on investigation of infertility, rather than treatment. Papers on treatment of infertility were predominantly prospective cohort studies (level II evidence) and one well-designed randomized controlled trial (level I evidence).

### Preconception counseling

Women in their reproductive years often see their physicians regularly for routine gynecologic assessment, renewal of oral contraceptive prescriptions, or other health concerns. Visits offer opportunities for physicians to discuss reproductive plans and give information on promoting optimal pregnancies and helping couples conceive on their own.

All women should be aware of certain information before trying to conceive. A serum rubella titre should be measured to confirm immunity and booster vaccination given if necessary 1 month before attempted pregnancy.<sup>3</sup> All women considering pregnancy should take folic acid (0.4 mg/d minimum) to reduce the chances of having babies with neural tube defects (level I evidence).<sup>4</sup>

It is also important to counsel women about smoking cessation, weight control, and avoiding alcohol and other drugs during pregnancy. Smoking has been associated with impaired fertility, ectopic pregnancy, spontaneous abortion, and poor pregnancy outcomes.<sup>5</sup> Women who smoke are 3.4 times more likely to experience a 1-year delay in conception compared with non-smokers.<sup>6</sup> Exposure to second-hand smoke is also a concern. Extremes of weight and body fat can also influence fertility and increase risk of ovulatory dysfunction.<sup>7</sup> Recreational drugs, such as marijuana, inhibit GnRH secretion in both male

and female patients and increase risk of infertility.<sup>8</sup> Over-the-counter medication, such as nonsteroidal anti-inflammatory drugs (NSAIDs), can interfere with ovulation by blocking oocyte release.<sup>9</sup>

Information about identifying ovulation, optimal timing of intercourse in relation to ovulation, and reasonable time frames in which couples can expect to conceive can be offered to women trying to conceive. The monthly conception rate of couples at peak fertility is 20% to 25%.<sup>10</sup> In a normally fertile population, about 60% of couples conceive within 6 months, 80% within 12 months, and 90% within 18 months.<sup>10</sup> The likeliest time for conception is from 2 days before ovulation to the day of ovulation.<sup>11</sup>

Infertility can result in severe emotional stress. Couples often describe the "hope and despair" cycle, as they hope each month that they will finally conceive, then despair when once again it does not happen. Men and women experience the stress and grief of infertility quite differently; this can create substantial personal and marital stress. Treatments are physically, emotionally, and financially draining. Family physicians can provide ongoing support and counseling, and can refer patients for counseling if necessary.

### Age and fertility

Natural fertility declines with age. Physically, the optimal time for women to conceive is in their late teens and early 20s. For a variety of social, professional, financial, or psychological reasons, however, many women delay pregnancy until well into their 30s. One third of women who delay pregnancy until after age 35 and at least half of the women who delay until after 40 will have some difficulty conceiving.<sup>12</sup> Mean time to conception (ie, the time at which 50% of women have conceived) increases with age from 4 months in women younger than 30 to 9 months in women older than 35.<sup>13</sup> Incidence of spontaneous abortion almost doubles among women in their late 30s, compared with women younger than 30.<sup>14</sup> Women have accepted an increased risk of chromosomal abnormalities after age 35, yet few are aware of the effect of age on fertility and are surprised when conception does not occur on cue.

The ASRM recently launched a campaign to increase awareness among both the public and health care providers of the effect of age on fertility. Many women have been falsely reassured by the growing availability of assisted reproductive technologies (ART), believing that these treatments will overcome the effects of age, but the success of ART also

declines dramatically with increasing maternal age. It is important that women be aware of this.

### Infertility assessment

The main causes of infertility are related to ovulatory dysfunction; blocked or damaged fallopian tubes; and abnormalities of sperm number, motility, or morphology (Table 1).<sup>15</sup>

**Table 1. Causes of infertility**

CAUSE	%
Tubal or pelvic factors (blocked or damaged tubes because of pelvic adhesions or endometriosis)	35
Male factors (abnormalities of sperm number, motility, morphology)	35
Ovulatory dysfunction (infrequent or no ovulation)	15
Unexplained	10
Unusual (fibroids, polyps, uterine anomalies)	5

*Data from Speroff et al.<sup>15</sup>*

For couples presenting with infertility or concern about their failure to conceive, a focused history and physical examination help to identify factors that could affect fertility. Questions should focus on four main areas: ovulatory dysfunction, risk factors for tubal infertility, sexual factors, and male or sperm factors. Physical examination of women includes assessment of body mass index, thyroid, breasts, and signs of hyperandrogenism (hirsutism, acne, acanthosis nigricans). A Pap smear should be done if indicated, along with a bimanual examination to search for signs of endometriosis or pelvic adhesions, such as a fixed retroverted uterus, adnexal masses or tenderness, and uterosacral ligament thickening, nodules, or tenderness.

**Ovulatory dysfunction.** A history of regular menses every 24 to 35 days associated with premenstrual molimina (breast tenderness, bloating, cramping, mood changes) is compatible with ovulation in at least 95% of women.<sup>12,16,17</sup> If ovulation is in doubt, it can be confirmed using basal body temperature (BBT) charting, by using ovulation predictor kits, or by measuring the serum progesterone level in the midluteal phase<sup>17</sup> (level III evidence). A history of very irregular cycles suggests anovulation, which needs further evaluation for its various causes, including PCOS, hyperprolactinemia, thyroid dysfunction, premature ovarian failure, and hypothalamic dysfunction (eg, eating disorder, excessive exercise)<sup>17</sup> (level III evidence).

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Charting the BBT can help women with regular cycles predict their "most fertile times." Progesterone is thermogenic, acting on the thermoregulatory centre in the hypothalamus to reset the BBT in the luteal phase to 0.3° to 0.5°C higher than the follicular phase. A rise in BBT occurs 2 or 3 days after ovulation and is an indirect assessment of ovulation because it reflects adequate progesterone production by the corpus luteum. Optimal timing for intercourse is 5 days before until 2 days after the predicted day of ovulation. Chances of conception are highest when intercourse is timed to the periovulatory period, specifically from 48 hours before until 24 hours after ovulation<sup>11</sup> (level II evidence).

For maximum accuracy, BBT should be measured immediately upon awakening in the morning, preferably at the same time each day. External factors, such as shift work, illness, or a room too cold or too hot, can alter the result and reduce accuracy. It is important to spend time reviewing use of these charts to ensure that couples understand them and that intercourse is being timed appropriately. Charts provide retrospective evidence of ovulation, so they are useful for predicting ovulation and timing intercourse in subsequent cycles, not for the cycle of charting, assuming cycles are fairly regular. Up to 3 months of charting is usually sufficient. Beyond that, some women become highly focused on their charts and find using them stressful, particularly if they are anovulatory.<sup>17</sup> Likewise, urinary ovulation detection kits are best used by women with regular cycles. Each kit usually comes with only five test sticks, and continued use by women with irregular cycles can become quite costly.

**Tubal factors.** Risk factors for tubal disease are history of sexually transmitted disease, pelvic inflammatory disease, previous pelvic surgery (especially ruptured appendix or surgery for Crohn's disease or ulcerative colitis), previous use of intrauterine devices, or endometriosis. One episode of pelvic inflammatory disease gives a 13% risk of tubal infertility. Risk increases to 36% and 75% with second and third infections, respectively.<sup>18</sup> Appendectomy for a ruptured appendix is associated with a four-fold increased risk of tubal infertility.<sup>19</sup> History of severe dysmenorrhea, dyspareunia, or pelvic pain or findings of a fixed retroverted uterus, thickening of the uterosacral ligaments, cul-de-sac nodularity, or pelvic tenderness during physical examination suggest endometriosis.

**Sexual factors.** Sexual intercourse is obviously essential for conception to occur naturally. Questions regarding timing and frequency of sexual intercourse are important. Conception is most likely to occur from 2 days before ovulation to the day of ovulation.<sup>11</sup> If couples are not making any particular effort to time intercourse around ovulation, then regular frequency of intercourse every 2 or 3 days (ie, two or three times weekly) should be encouraged. It is important to ask both partners about sexual dysfunction, particularly difficulties with erection or ejaculation, or dyspareunia that can limit sexual activity. Finally, use of lubricants should be discouraged, as many of the commercially available brands can impair sperm motility.<sup>20</sup>

**Male factors.** While it is often the woman who presents initially to discuss difficulties conceiving, infertility is a couple's problem. In at least one third of couples, infertility is attributable to a male factor.<sup>21</sup> Questions for men include previous paternity, history of testicular injury, torsion, surgery or infection (epididymitis, orchitis, prostatitis), undescended testicle, varicocele, and previous urinary tract or hernia surgery. Physical examination of male partners includes assessment of general appearance and masculinization and a genital examination looking for hypospadias, size and consistency of testes, and varicoceles<sup>22</sup> (level III evidence).

### Basic infertility investigations

Infertility investigations aim to assess three main areas: ovulation, tubal damage or dysfunction, and male factors. First-line investigations generally include a semen analysis and assessment of tubal patency, usually by hysterosalpingogram (HSG). Semen analysis is readily available in most communities. In some areas, HSGs are performed by family physicians or radiologists; other areas require referral to a gynecologist.

The need for blood tests is determined by the history; a battery of tests is rarely required. Routine random measurement of luteinizing hormone, follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), or prolactin in women with regular menstrual cycles and no galactorrhea or hirsutism is generally not useful. In women with ovulatory dysfunction identified on history, TSH and prolactin assessments are indicated, as well as FSH measurement to rule out premature ovarian failure or hypothalamic amenorrhea.<sup>17,23,24</sup> If necessary, a mid-luteal phase measurement of serum progesterone about

7 days after ovulation, or 7 days before an expected period, can confirm ovulation. A progesterone level of >10 nmol/L suggests ovulation. In women older than 35, FSH measured on cycle days 2 to 4 is useful to predict ovarian reserve. An FSH level > 15 IU/L suggests diminished ovarian reserve.<sup>12</sup> Routine measurements of serum androgens are not indicated in the absence of anovulation or clinical evidence of hyperandrogenism.<sup>17</sup>

Semen analysis is best performed after 72 hours of abstinence.<sup>25</sup> A longer period of abstinence results in increased sperm count, but reduced motility.<sup>26</sup> Normal semen parameters are shown in **Table 2**.<sup>27,28</sup> Limitations of semen analysis include individual fluctuations and an often substantial overlap between fertile and subfertile values. If results are abnormal, analysis should be repeated after 60 days, the time it takes for the testes to recover from any insult.<sup>15</sup> Persistent abnormalities, particularly of motility, require further assessment.

### When do you refer?

A common question asked by primary care physicians is at what point they should refer infertile couples to specialists. **Table 3** provides some guidelines for referral.<sup>29</sup> *In women older than 35, serious consideration should be given to earlier referral for diagnosis and treatment, given the influence of age on fertility.*

### Infertility treatment

Most infertility treatments are beyond the scope of what is available in a family physician's office. Two circumstances, however, warrant consideration: women with anovulation due to PCOS, and both ovulatory and anovulatory women who use clomiphene citrate.

**Polycystic ovarian syndrome.** Polycystic ovarian syndrome is one of the most common endocrinologic disorders affecting women of reproductive age, and a very common cause of anovulatory infertility.<sup>30</sup> Approximately 60% of women with PCOS are obese. Many studies have demonstrated an improvement in ovulatory function (ie, resumption of ovulatory cycles) associated with weight loss and exercise. Losing as little as 5% to 10% of body weight can make a great difference.<sup>31</sup> It can also improve hyperandrogenic symptoms, such as hirsutism and acne; lipid profiles; and results of glucose tolerance tests. In patients with PCOS, weight loss should be encouraged for all of these reasons.

**Table 2. Normal semen parameters**

PARAMETER	VALUE
Volume	2-6 mL <sup>27</sup>
Concentration	>20 million/mL <sup>27</sup>
Motility	>50% with forward progression <sup>27</sup>
Morphology	>35% normal <sup>27</sup>
Total motile count (concentration X volume X % motility)	>20 million <sup>28</sup>

There has been considerable interest in the use of insulin-lowering agents among women with PCOS as a means to restore ovulation and reduce hyperandrogenemia and associated symptoms. The original work by Nestler et al<sup>32</sup> studied a group of 61 obese, clomiphene-resistant women with PCOS. Most of the women (89%) treated with metformin ovulated either spontaneously or in response to clomiphene citrate, but only 12% of the women treated with placebo did.

A recent review of the role of insulin-sensitizing medications in treatment of PCOS-associated

**Table 3. Guidelines for referral to infertility specialists**

#### Woman's age

- <35 with longer than 18 months' infertility
- >35 with longer than 12 months' infertility

#### Female partner

- History of endometriosis, pelvic inflammatory disease or sexually transmitted disease, or pelvic or abdominal surgery
- Amenorrhea or oligomenorrhea
- Pelvic pain
- Abnormal results from pelvic examination

#### Male partner

- Abnormal results of semen analysis
- History of sexually transmitted disease, urogenital surgery or pathology
- Varicocele or abnormal results from genital examination

#### Patient request or anxiety

*Data from Belisle and Pierson.<sup>29</sup>*

infertility supports use of metformin among clomiphene-resistant women (ie, women who have tried clomiphene citrate up to 150 mg, but have not ovulated)<sup>33</sup> (level I evidence). Use of metformin for initial treatment of infertility in women with PCOS, as an alternative to clomiphene citrate, has not been subjected to randomized studies. Many specialists are

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prescribing metformin for this reason, however, and adding clomiphene if spontaneous ovulation does not ensue within a reasonable time, usually 6 to 8 weeks at the full dose. As our knowledge increases, insulin-sensitizing drugs eventually might become the agent of choice for initial ovulation induction in PCOS.<sup>33</sup>

It is unnecessary to document insulin resistance before starting metformin; practically speaking, most women with PCOS can be considered insulin resistant.<sup>33</sup> The optimal dose of metformin is 500 mg three times daily. Patients should start with half a tablet (250 mg) daily, and gradually work up to the full dose as tolerated, to minimize gastrointestinal side effects. Metformin should be discontinued if women conceive.<sup>33</sup> Women should be advised that this is an “off-label” indication for this medication, although there is good evidence to support its use. Further research is ongoing and will determine the role of this medication in treating hyperandrogenism and reducing the risk of diabetes.

**Clomiphene citrate.** Clomiphene citrate is another option for ovulation induction in women with PCOS. It is also widely used for couples with unexplained infertility to induce multiple follicular development in a single cycle. In women with PCOS, ovulation and pregnancy rates with clomiphene are 80% to 85% and 30% to 40%, respectively. The usual starting dose is 50 mg daily from days 5 to 9 of the cycle.<sup>34</sup> Couples with unexplained infertility have a pregnancy rate per cycle of 2% to 3% without treatment.<sup>35</sup> With clomiphene, this rate is doubled to 4% to 5%.<sup>26</sup>

While clomiphene is fairly well tolerated, there are a few side effects about which both patients and physicians should be aware. The rate of multiple pregnancy is 8% to 10%. Nearly all multiple pregnancies

will be twins, but could be triplets or higher-order pregnancies.<sup>36</sup>

A less well-known effect of clomiphene is the potential for an antiestrogenic effect on the uterine lining, which occurs in 15% to 20% of women.<sup>37</sup> A thin endometrium is believed to affect implantation adversely and therefore reduce the chance of pregnancy.<sup>38</sup> It can easily be identified on transvaginal ultrasound before ovulation and is defined as an endometrial thickness of < 6 mm.<sup>38</sup> It tends to be a repetitive effect, so women diagnosed with this condition in their first cycle are not candidates for further clomiphene cycles.

Some women have a tendency to form ovarian cysts while taking clomiphene. This is likely related to the luteinized unruptured follicle syndrome, or the lack of oocyte release following the surge in luteinizing hormone. It can be prevented in most cases by administration of human chorionic gonadotropin (eg, Profasi) when lead follicles are 18 mm.<sup>39,40</sup>

Finally, many patients and physicians are concerned about the possible association between prolonged clomiphene use (ie, more than 12 cycles) and ovarian cancer.<sup>41</sup> This association has not been proven; nevertheless, it is recommended that use of clomiphene be limited to 12 lifetime cycles.<sup>36</sup> This is a reasonable number, particularly because the cumulative conception rate with clomiphene plateaus by the 12th cycle.<sup>36</sup> To reassure women who have taken or are taking clomiphene, it is useful to inquire about past oral contraceptive (OC) use, since OC use for longer than 2 years reduces the risk of ovarian cancer by at least 50%, virtually eliminating any risk associated with clomiphene.<sup>42</sup>

Because of the potential side effects associated with clomiphene therapy and the recommendation

**Table 4. Indications, costs, and success rates of common infertility treatments**

TREATMENT	INDICATION	COST PER CYCLE	SUCCESS RATE PER CYCLE (%)
CC	Oligo-ovulation or anovulation	\$50-150	10-15 <sup>36</sup>
CC	Unexplained		4-6 <sup>26</sup>
CC and IUI	Unexplained	\$150-300	8-10 <sup>26,43</sup>
SO and IUI	Unexplained	\$750-2000	18-20 <sup>43</sup>
IVF	Tubal factor	\$5000-8000	
IVF	Male factor		40 (<30 years) <sup>44</sup>
IVF	Endometriosis		35 (30-35) <sup>44</sup>
IVF	Unexplained		25 (35-39) <sup>44</sup>
IVF and ICSI	Male factor	\$8000-10 000	<15 (≥40) <sup>44</sup>

CC—clomiphene citrate, ICSI—intracytoplasmic sperm injection, IUI—intrauterine insemination, IVF—in vitro fertilization, SO—superovulation (ie, ovulation induction with gonadotropins).

to limit the total number of lifetime cycles, all patients taking clomiphene should be monitored in some way to assess their response to treatment. The optimal form of monitoring is with ultrasound, for at least one cycle, to assess follicular growth, to measure endometrial thickness, and to time intercourse appropriately around ovulation. If monitoring is unavailable, consider having patients maintain basal BBT charts and measuring a luteal phase progesterone level approximately 5 days after temperature rise as a presumptive confirmation of ovulation. Without ultrasound monitoring, the number of clomiphene cycles should probably be limited to three, and early referral should be considered before several of the patient's lifetime cycles have been used up.

**Indications, costs, and success rates.** Couples often wonder what to expect following referral to an infertility clinic or specialist. Infertility treatments range from fairly simple and inexpensive, such as ovulation induction with clomiphene citrate, to far more time-consuming, complicated, and expensive, such as in vitro fertilization and intracytoplasmic sperm injection. Generally speaking, the more complicated and expensive treatments are also more successful (Table 4<sup>26,36,43,44</sup>). Success rates are estimates, at best. Individual factors, such as maternal age, cause of infertility, and duration of infertility are important considerations factored into estimates of success for particular couples. These factors are also considered when treatment decisions are made. Costs are estimates based on the average costs for medications and treatment across Canada. Unfortunately, infertility treatment and medications are rarely covered by provincial health care or personal insurance plans.

### Conclusion

Family physicians are uniquely situated for counseling women in their reproductive years. Regular visits offer opportunities to discuss reproductive plans. Couples can be educated about ways to increase the chances of conception, lifestyle factors that can affect fertility, and the important effect of maternal age. A detailed and focused assessment will help facilitate initial investigations and treatment and will identify couples who could benefit from referral for further assessment. Finally, family physicians can provide ongoing support for couples dealing with the emotional, physical, and social stresses associated with infertility. ❖

### Editor's key points

- Family doctors' role in infertility begins by promoting healthy pregnancies: counseling about smoking, alcohol, weight, and recreational drugs; encouraging folic acid intake (0.4 mg/d); and checking for rubella immunity.
- Natural fertility declines with age; more women older than 35 have difficulty conceiving and have a higher rate of spontaneous abortions than younger women.
- Main causes of infertility are blocked or damaged fallopian tubes (35%), sperm abnormalities (number, motility, morphology) (35%), and ovulatory dysfunction (15%).
- Infertility investigation includes assessment of tubal patency and semen analysis. Blood tests are determined by history. For ovulatory dysfunction, thyroid-stimulating hormone, prolactin, follicle-stimulating hormone, and (occasionally) progesterone levels are useful.
- Referral to specialists is encouraged if women younger than 35 are infertile for more than 18 months or women older than 35 for more than 12 months. Signs of tubal damage or sperm abnormalities also indicate referral.

### Points de repère du rédacteur

- Devant un cas d'infertilité, le MF doit d'abord promouvoir une grossesse saine par des conseils sur le tabac, l'alcool, le poids corporel et les drogues à usage récréatif; il doit aussi encourager la prise d'acide folique (0,4 mg/d) et vérifier le taux d'anticorps contre la rubéole.
- La fertilité naturelle diminue avec l'âge; passé 35 ans, les femmes ont plus de difficulté à devenir enceinte et leur taux d'avortement spontané est plus élevé que chez les plus jeunes.
- Les principales causes d'infertilité sont les atteintes ou obstructions des trompes utérines (35%), les anomalies des spermatozoïdes (numération, motilité, morphologie; 35%) et les dysfonctions ovulatoires (15%).
- L'investigation inclut l'évaluation de la perméabilité tubaire et l'analyse du liquide séminal. Le choix des épreuves sanguines dépend de l'histoire. En cas de dysfonction ovulatoire, il peut être avantageux de mesurer la TSH, la prolactine, la FSH et (parfois) la progestérone.
- Les femmes de moins de 35 ans qui sont infertiles depuis plus de 18 mois et celles de plus de 35 ans qui le sont depuis au moins 12 mois devraient être dirigées en spécialité. Il en est de même lorsqu'il y a des signes d'atteinte tubaire ou d'anomalie des spermatozoïdes.

## Competing interests

None declared

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