CFAS Consensus Document for the Investigation of Infertility
By First Line Physicians

Opinions and views expressed herein are those of, and have been reviewed by, the editorial advisors and participants and do not necessarily reflect the opinions and views of Berlex Canada Inc., Canadian Fertility and Andrology Society and Klick Healthcare Communications Inc.
Infertility is a medical condition revolving around a couple’s inability to conceive after one year of unprotected intercourse. It is also an area of medicine overly imbued with emotion and misinformation. Our goal is to provide first line medical practitioners with a clear sequence of considerations and investigations once infertility has been identified in a relationship where pregnancy is desired by both partners. It is important to note that infertility is frequently multi-factorial in nature and that it is extremely important to perform a complete workup on both partners before initiating therapy. The following summary of infertility investigations reflects the CFAS consensus on the investigation of the infertile couple at the basic level, identification of the appropriate individuals to perform the evaluations and appropriate points of referral to an infertility specialist. Reproductive health care providers desiring more information are referred to the appropriate World Health Organization (WHO) manuals.

TABLE OF CONTENTS

Algorithm .................................................. 2
Introduction ................................................. 5
History Taking and Physical Exam for Infertility ............................... 5
Unexplained Infertility ........................................ 6
Male Infertility ................................................. 7
Ovulation ........................................................ 8
Tubal-Peritoneal Factors ..................................... 9
Uterine ............................................................ 10
Cervical Factors and Infertility – Prevalence and Impact ..................... 11
Resources for Physicians ..................................... 12
Glossary ........................................................ 13
Abbreviations and Acronyms .................................. 22
References ..................................................... 23
Appendix I – Unexplained Infertility Prognosis ................................. 25
Investigation of Infertility By First Line Physicians

**DIFFICULTY CONCEIVING**

- If infertile
- If conditions preclude pregnancy
- High-risk factors

**CHECK**

- History and physical if appropriate
- Advice regarding smoking and drinking cessation/moderation
- Stress
- Intercourse (timing)
- Address issue of counseling
- Referral earlier if undue anxiety

**HISTORY**

- History and physical if appropriate
- Advice regarding smoking and drinking cessation/moderation
- Stress
- Intercourse (timing)
- Address issue of counseling
- Referral earlier if undue anxiety

**REMEMBER**

- Female rubella status
- Folic acid
- If female BMI >30 advise weight loss
- Drug History (include recreational drugs, herbal and nutritional supplements)
- Occupational history
- Cervical smear history

**ADVISE**

- Regular intercourse two or three times a week

**BASIC EVALUATION**

- If infertile
- If conditions preclude pregnancy
- High-risk factors

**FEEMALES**

- Consider referral at 18 months or earlier if:
  - Over 35 years of age
  - Amenorrhea/oligo-menorrhea
  - Previous abdominal/pelvic surgery
  - Abnormal pelvic exam
  - Pain

**TESTS**

- Confirm ovulation
- Do not measure thyroid function or prolactin if regular cycles
- Do not measure hormones if regular cycles
- Discourage long-term use of LH kits + BBT charts
- Test for STDs/chlamydial antibodies
- Evaluate tubal patency (HSG)

**MALES**

- Consider referral at 18 months or earlier if:
  - Previous genital pathology
  - Previous urogenital surgery
  - Previous STD
  - Varicoceles
  - Significant systemic illness
  - Abnormal genital exam

**TESTS**

- semen
  - Arrange for semen analysis to be sent to laboratory used by clinic to which patient is referred
  - Repeat if abnormal

**REMEMBER**

- Female rubella status
- Folic acid
- If female BMI >30 advise weight loss
- Drug History (include recreational drugs, herbal and nutritional supplements)
- Occupational history
- Cervical smear history

- **TESTS**
  - Ovulation
    - Confirm ovulation
    - Do not measure thyroid function or prolactin if regular cycles
    - Do not measure hormones if regular cycles
    - Discourage long-term use of LH kits + BBT charts
    - Test for STDs/chlamydial antibodies
    - Evaluate tubal patency (HSG)
  - Semen
    - Arrange for semen analysis to be sent to laboratory used by clinic to which patient is referred
    - Repeat if abnormal
**Investigation of Infertility By First Line Physicians**

**HISTORY TAKING AND PHYSICAL EXAM FOR INFERTILITY**

In the initial interview, medical history and physical examination of an infertile patient, the family doctor or gynecologist should try to answer the following three questions:

1. Are there factors that may be corrected to create an optimal setting for pregnancy or others that may contraindicate the planned pregnancy?
2. What is causing infertility in this couple?
3. What impact is this couple's inability to conceive having on the partners and on their relationship?

**FEMALES**
- If any test results abnormal, refer to dedicated specialist infertility clinic
- Suggestion for referral letter

**MALES**
- Can defer referral if history, examination and investigations normal in both partners and duration of infertility <18 months
- Suggestion resources

Folic acid supplementation of 0.4 mg/day is recommended while the couple is trying to conceive and during the first trimester of the pregnancy in order to decrease the chance of neural tube defects. The physician should inquire about the use of drugs, alcohol, over-the-counter medications and complementary remedies (e.g., herbal or homeopathic). Both partners should be advised to give up smoking or recreational drugs and to minimize alcohol consumption. Women should consider refraining from alcohol consumption once they become pregnant.

Obesity may seriously complicate conception and pregnancy; a supervised weight-loss program should be recommended whether the patient is ovulatory or not. Blood pressure should be checked, Pap smear done, and endocervical culture performed to rule out asymptomatic sexually transmitted disease (STD), especially if invasive tests such as hysterosalpingography (HSG) are to be conducted. Testing for human immunodeficiency virus (HIV), hepatitis B and hepatitis C should also be offered when appropriate.

**Key statements**

1. Infertility investigation should begin after 12 to 18 months of unprotected intercourse. Specific factors may mandate earlier investigation.
2. Infertility causes stress and stress may influence therapy.
3. Couples’ expectations from infertility investigation will vary.

In Canada, 8% of couples where the female partner is 15 to 45 years of age, experience infertility. In essence, they have not conceived after 12 months of intercourse without contraception. The monthly conception rate of couples at peak fertility is around 20%. Thus, in a normal population, approximately 60% of couples will achieve pregnancy within 6 months, 80% within 12 months, and 90% within 18 months. In couples where the woman is under age 35, it is reasonable to begin investigation after 12 to 18 months of unprotected sexual exposure. However, individual circumstances may prevail that mandate earlier investigation, such as, the female partner is 35 years old or greater, menstrual abnormality, or history of pelvic disease or surgery. Inability to conceive may be a source of distress for many couples. The desire to have a child varies from one couple to another, as does the willingness to commit to investigation and treatment of infertility. Therefore, it is essential to tailor the process to meet the couple’s needs and expectations. Each step, in the management of infertility should involve education and counselling so that the couple understands the rationale for testing and has realistic expectations for treatment. Both partners should begin evaluation concurrently.

**Management**

- Discuss results with couple
- Re-evaluate couple’s expectations
- Offer referral
- Plan for ongoing support in primary care after referral
2. Identify possible causes of infertility

Ovulation problems

Regular menses occurring every 25 to 35 days are almost always associated with ovulation, while irregular menses may indicate ovulatory problems. Pelvic examination is usually normal in ovulatory women, although the cervical mucus will typically stay abundant and clear. If an ovulatory problem is identified at the medical history, thyroid mass, galactorrhea and hirsutism should be ruled out during the physical examination.

Endometriosis

Endometriosis may be associated with dysmenorrhea, especially if dysmenorrhea is secondary, progressive and asymmetric. Deep dyspareunia and premenstrual spotting may also suggest endometriosis. When endometriosis is suspected, the most relevant findings at the gynecologic exam are painful nodules in the posterior cul-de-sac or asymmetry of the utero-sacral ligaments.

Pelvic Inflammatory Disease

A history of STD or intrauterine contraceptive device (IUCD)-associated complications previous pelvic surgery or multiple sexual partners are associated with an increased risk of pelvic inflammatory disease (PID). The gynecologic exam is often normal, although a pelvic mass may be found if hydrocolpos are present. Clinical cervicitis may also be evident.

3. Acknowledge that infertility may create significant personal and interpersonal stress. Infertility may be the first significant test of a relationship and may require ongoing counselling and support. Professional counselling may be indicated.

Recommendations for general practitioners

- With less than two years duration of unexplained infertility the prognosis is good even without therapy, unless the female partner is more than 35 years of age.
- With more than three years duration of infertility, or with female partners more than 35 years of age, consider initiating therapy if that is the wish of the couple.

UNEXPLAINED INFERTILITY

JOHN COLLINS, MD, FRCSC, FACOG, FRCOG

Key statements

- Only some of the causes of infertility are known.
- Unexplained infertility due to unknown causes requires empiric therapy.
- Although no cause is apparent, unexplained infertility may be difficult to treat successfully.

After a conventional diagnostic assessment, up to 30% of infertile couples have unexplained or “idiopathic” infertility. The conventional infertility diagnostic tests evaluate ovulation, sperm production and fallopian tube patency. Although this conventional assessment of infertility may seem limited, even the most sophisticated array of diagnostic tests cannot reveal the defect causing infertility in many patients, with these causes remaining undiagnosed at this time. Evaluations of antisperm antibodies, postcoital tests, endometrial biopsy, and assessments for the presence of adhesions and evidence of pelvic endometriosis do not appear to add appreciably to the prognosis or lead to effective treatment. Infertility will therefore be unexplained in normal couples with low fecundity, in couples where female age is a contributing factor, and in couples with a defect in fecundity that cannot be detected by currently available testing.

Although the infertility is unexplained, the prognosis is far from normal. Compared with the 20% to 25% monthly fecundity that would be expected in normal fertile couples, monthly fecundity in untreated couples with unexplained infertility is less than 3%. Increasing age of the female partner and longer duration of infertility are poor prognostic factors.

Because the therapy for unexplained infertility is empiric, and offering empiric therapy is less satisfying, clinicians may feel pressure to use additional diagnostic tests even when such tests have no more than marginal predictive value. Consideration should be given to the usefulness of these tests with respect to whether the results change the prognosis or lead to effective therapy. For example, in a randomized trial, the postcoital test did not change prognosis or treatment choices.

A diagnosis of unexplained infertility can be based on the results of a conventional assessment of infertility, including an evaluation of ovulation, sperm production and fallopian tube patency. An empiric treatment program will generally include intrauterine insemination and stimulated ovulation, the only known treatments for diagnosable or non-diagnosable defects in ovulatory and cervical function in women with normal findings in the conventional assessment.

MALE INFERTILITY

JOHN E. GRANTHYRE, MD, FRCSC

Key statements

- Initial male infertility evaluation is simple and should precede invasive female evaluation.
- Successful treatment can often occur without IVF/ICSI.

Approximately one third of infertility problems are completely male in origin, and in another 20%, the male contributes to the problem. In spite of this, physicians dedicated to treatment of male infertility are not available in many fertility clinics. Patient encounters are time consuming and fraught with emotion, and treatments for the man are often disappointing. Fortunately, men are, in many ways, more easily investigated than women. Those who need specialized attention can be identified and referred early in the infertility investigation.

Once a couple wishes to proceed with fertility investigations, the male partner should be present and participating. Even if no male factor is identified, his presence will help support his partner through their difficult ordeals and help to minimize any sense of blame.

Because the therapy for unexplained infertility is empiric, and offering empiric therapy is less satisfying, clinicians may feel pressure to use additional diagnostic tests even when such tests have no more than marginal predictive value. Consideration should be given to the usefulness of these tests with respect to whether the results change the prognosis or lead to effective therapy. For example, in a randomized trial, the postcoital test did not change prognosis or treatment choices.

The overall plan of conventional treatment should proceed from the simplest level and should not presume that early application of the highest level treatment modalities is the best approach. Issues of safety, efficacy and cost-effectiveness must be balanced.

Endometriosis may be associated with dysmenorrhea, especially if dysmenorrhea is secondary, progressive and asymmetric. Deep dyspareunia and premenstrual spotting may also suggest endometriosis. When endometriosis is suspected, the most relevant findings at the gynecologic exam are painful nodules in the posterior cul-de-sac or asymmetry of the utero-sacral ligaments.

Pelvic Inflammatory Disease

A history of STD or intrauterine contraceptive device (IUCD)-associated complications previous pelvic surgery or multiple sexual partners are associated with an increased risk of pelvic inflammatory disease (PID). The gynecologic exam is often normal, although a pelvic mass may be found if hydrocolpos are present. Clinical cervicitis may also be evident.

3. Acknowledge that infertility may create significant personal and interpersonal stress. Infertility may be the first significant test of a relationship and may require ongoing counselling and support. Professional counselling may be indicated.

Recommendations for general practitioners

- With less than two years duration of unexplained infertility the prognosis is good even without therapy, unless the female partner is more than 35 years of age.
- With more than three years duration of infertility, or with female partners more than 35 years of age, consider initiating therapy if that is the wish of the couple.

UNEXPLAINED INFERTILITY

JOHN COLLINS, MD, FRCSC, FACOG, FRCOG

Key statements

- Only some of the causes of infertility are known.
- Unexplained infertility due to unknown causes requires empiric therapy.
- Although no cause is apparent, unexplained infertility may be difficult to treat successfully.

After a conventional diagnostic assessment, up to 30% of infertile couples have unexplained or “idiopathic” infertility. The conventional infertility diagnostic tests evaluate ovulation, sperm production and fallopian tube patency. Although this conventional assessment of infertility may seem limited, even the most sophisticated array of diagnostic tests cannot reveal the defect causing infertility in many patients, with these causes remaining undiagnosed at this time. Evaluations of antisperm antibodies, postcoital tests, endometrial biopsy, and assessments for the presence of adhesions and evidence of pelvic endometriosis do not appear to add appreciably to the prognosis or lead to effective treatment. Infertility will therefore be unexplained in normal couples with low fecundity, in couples where female age is a contributing factor, and in couples with a defect in fecundity that cannot be detected by currently available testing.

Although the infertility is unexplained, the prognosis is far from normal. Compared with the 20% to 25% monthly fecundity that would be expected in normal fertile couples, monthly fecundity in untreated couples with unexplained infertility is less than 3%. Increasing age of the female partner and longer duration of infertility are poor prognostic factors.

Because the therapy for unexplained infertility is empiric, and offering empiric therapy is less satisfying, clinicians may feel pressure to use additional diagnostic tests even when such tests have no more than marginal predictive value. Consideration should be given to the usefulness of these tests with respect to whether the results change the prognosis or lead to effective therapy. For example, in a randomized trial, the postcoital test did not change prognosis or treatment choices.

A diagnosis of unexplained infertility can be based on the results of a conventional assessment of infertility, including an evaluation of ovulation, sperm production and fallopian tube patency. An empiric treatment program will generally include intrauterine insemination and stimulated ovulation, the only known treatments for diagnosable or non-diagnosable defects in ovulatory and cervical function in women with normal findings in the conventional assessment.

Recommendations for general practitioners

- With less than two years duration of unexplained infertility the prognosis is good even without therapy, unless the female partner is more than 35 years of age.
- With more than three years duration of infertility, or with female partners more than 35 years of age, consider initiating therapy if that is the wish of the couple.

UNEXPLAINED INFERTILITY

JOHN COLLINS, MD, FRCSC, FACOG, FRCOG

Key statements

- Only some of the causes of infertility are known.
- Unexplained infertility due to unknown causes requires empiric therapy.
- Although no cause is apparent, unexplained infertility may be difficult to treat successfully.

After a conventional diagnostic assessment, up to 30% of infertile couples have unexplained or “idiopathic” infertility. The conventional infertility diagnostic tests evaluate ovulation, sperm production and fallopian tube patency. Although this conventional assessment of infertility may seem limited, even the most sophisticated array of diagnostic tests cannot reveal the defect causing infertility in many patients, with these causes remaining undiagnosed at this time. Evaluations of antisperm antibodies, postcoital tests, endometrial biopsy, and assessments for the presence of adhesions and evidence of pelvic endometriosis do not appear to add appreciably to the prognosis or lead to effective therapy. Infertility will therefore be unexplained in normal couples with low fecundity, in couples where female age is a contributing factor, and in couples with a defect in fecundity that cannot be detected by currently available testing.

Although the infertility is unexplained, the prognosis is far from normal. Compared with the 20% to 25% monthly fecundity that would be expected in normal fertile couples, monthly fecundity in untreated couples with unexplained infertility is less than 3%. Increasing age of the female partner and longer duration of infertility are poor prognostic factors.

Because the therapy for unexplained infertility is empiric, and offering empiric therapy is less satisfying, clinicians may feel pressure to use additional diagnostic tests even when such tests have no more than marginal predictive value. Consideration should be given to the usefulness of these tests with respect to whether the results change the prognosis or lead to effective therapy. For example, in a randomized trial, the postcoital test did not change prognosis or treatment choices.

A diagnosis of unexplained infertility can be based on the results of a conventional assessment of infertility, including an evaluation of ovulation, sperm production and fallopian tube patency. An empiric treatment program will generally include intrauterine insemination and stimulated ovulation, the only known treatments for diagnosable or non-diagnosable defects in ovulatory and cervical function in women with normal findings in the conventional assessment.

Recommendations for general practitioners

- With less than two years duration of unexplained infertility the prognosis is good even without therapy, unless the female partner is more than 35 years of age.
- With more than three years duration of infertility, or with female partners more than 35 years of age, consider initiating therapy if that is the wish of the couple.
Sperm morphology performed using the standardized technique of ‘Tygerberg’ ‘strict criteria’ morphology as recommended by WHO must be performed by a skilled technician in an andrology laboratory where this is practiced regularly.10 Staining of white blood cells (WBCs) in the semen using the immunoperoxidase stain is important as, most often, round cells present are, in fact, immature sperm.11 Identification of these sperm misclassifying as WBCs can lead to incorrect treatment of infection.12 Patients with unexplained infertility, failure to fertilize in vitro fertilization (IVF), or with isolated poor motility should have direct sperm antibody testing. Significant antibody levels can be successfully treated using IVF with intracytoplasmic sperm injection (ICSI).13

Once toxins and drugs have been avoided or adjusted, and hormonal conditions treated (rare in men), male infertility becomes either surgical or dependent on reproductive technologies. No effective empiric treatment exists to improve sperm quality. Varicoceles should be ligated in those with semen abnormalities, ductal obstructions should be repaired or resected, and sperm aspirated in those who cannot be reconstructed.14 Those having sperm retrieval can have cryopreservation of sperm with or without effect on eventual fertilization. Most sperm retrievals will be dependant on IVF using ICSI and should have genetic screening and counseling as necessary.

Ovulation

Ovulation is a prerequisite for conception. Ovulatory disorders occur in 15% to 25% of all infertile couples, ranging from mild cycle irregularity to amenorrhea.15 Confirmation of ovulation is a requisite part of the infertility investigation; however, prediction of the timing of ovulation may be of more practical importance for couples attempting to plan intercourse during the most fertile period.16

Diagnostic tests

A history of regular 24 to 35 day menses is consistent with ovulation in 97% of cases.17 Conversely, a clear history of oligomenorrhea or amenorrhea is strongly predictive of anovulation. When cycles are irregular, ovulation induction to regulate the cycle is more appropriate than tests to detect any sporadic ovulations that may occur naturally. When ovulatory status is uncertain or while monitoring therapy, ovulation may be confirmed by mid-luteal phase progesterone levels, ovulation predictor kits or basal body temperature charts. A mid-luteal phase serum progesterone level greater than 10 nmol/L confirms the presence of a corpus luteum and provides presumptive evidence of ovulation.18 Optimal timing of the sample (midway between ovulation and the next menses) may be difficult, especially with irregular menses. Because progesterone secretion is both pulsatile and parabolic during the luteal phase, low or borderline values may be encountered due to the vagaries of sampling.

Ovulation prediction kits also provide indirect evidence of ovulation by detecting the mid-cycle luteinizing hormone (LH) surge.19

Kits are widely available and may be helpful in timing of intercourse, although cost may become a factor for some couples. False negative or uninterruptible results often occur and are difficult to investigate.

Documentation of a biphasic basal body temperature (BBT) chart for one to three months provides presumptive evidence of ovulation and allows a cursory assessment of timing of intercourse and luteal phase length. However, it is not uncommon to see monophasic or uninterruptible BBT charts in ovulatory women. More prolonged use of BBTs rarely provides additional information and can become a frustrating process. Follicular ultrasound examinations are expensive and time-consuming and are generally reserved for the monitoring of ovulation induction or insemination cycles in a tertiary care setting. Endometrial biopsies are not part of the routine investigation of infertile couples. There is controversy regarding the prevalence and relevance of luteal phase defects, and there are no data to show that therapy is effective. Accordingly, where luteal phase defect is a consideration, it should be managed as unexplained infertility.

TUBAL-PERITONEAL FACTORS

ELLEN M. GREENBLATT, MD, FRCSC

Complete or partial tubal obstruction and/or peritubal/peritoneal adhesions are a significant cause of infertility (approximately 30%), either alone or in combination with other subfertility factors.20 These conditions are generally secondary to sexually transmitted disease (STD) exposure, previous pelvic/abdominal surgery, previous peritonitis, or endometriosis. The most common tests to evaluate tubal patency include hysterosalpingography (HSG), laparoscopy with chromotubation, and more recently, sono-hysterosalpingography (SHG) with or without the use of achoehancing agents for sono-salpingography. HSG is generally accepted as the traditional, least invasive and most cost effective method of evaluation of tubal patency in low-risk women. HS is useful in demonstrating proximal or distal tubal obstruction, salpingitis isthmica nodosa, evaluation of tubal diameter, and demonstration of normal tubal mucosal rugae. It also allows concurrent evaluation of the uterine cavity. Findings suggestive of peritubal adhesions may be implied by localization of contrast media or delayed spill. False positives for proximal tubal obstruction are approximately 15%. The concept of ovarian reserve as measured by Day 3 FSH and estradiol assays should be examined; however, there is no value in the routine determination of LH, follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), prolactin or androgens in infertile women with regular ovulatory menses in the absence of galactorrhea. In women withovulatory disorders, TSH and prolactin measurements are indicated, as well as an FSH level, to rule out premature ovarian failure (high FSH) or hypogonadotropic hypogonadism (very low FSH).

Androgens measurements are of little value unless there is evidence of hirsutism or virilization.

Recommendations

• Regular 23 to 35 day menses are strongly suggestive of ovulation. If in doubt, confirmation can be obtained with tubal phase serum progesterone levels or BBTs.
• There is little value in the use of BBTs for more than three months.
• There is no value in the routine measurement of LH, FSH, TSH, prolactin or androgens in women with regular menses and no galactorrhea or hirsutism.
Surgical ablation of minimal-to-mild endometriosis in the context of infertility only modestly improves pregnancy rates. Therefore, laparoscopy, if elected, should be performed under conditions where therapeutic procedures (folds of adhesions, ablation of endometriosis) can be applied at the initial procedure. Because of the invasive nature of laparoscopy, it is recommended as a first-line evaluation of tubal peritoneal factors only in patients in whom history and/or physical examination are suggestive of tubal or peritoneal disease (history of STD, intrauterine device [IUD] use, peritonitis, previous ectopic pregnancy, signs/symptoms suggestive of endometriosis). Laparoscopy may also be considered for further diagnosis/therapy of otherwise unexplained infertility, with consideration first being given to how findings may or may not impact management strategies.

Sonohysterography (SHG) and hysterosalpingo-contrastsonography (HyCoSy) combine the ability to evaluate the uterine cavity accurately, as well as confirm tubal patency (of at least a single tube). Preliminary results with laparoscopic comparison yielded a concordance of 85.6%, sensitivity of 90.4%, specificity of 70.3%, positive predictive value of 91.2%, and negative predictive value of 68.2%. Advantages of SHG over HSG include lack of gonadal irradiation and more accurate evaluation of the uterine cavity. This technique is likely to gain in importance with further evaluation and accessibility.

**Summary:**

1. Tubal/peritoneal factors are a common cause of infertility and should be addressed early in the infertility evaluation.

2. The appropriate test for evaluation of tubal patency (HSG, laparoscopy/hysteroscopy) should be determined based on individual patient characteristics that include age, duration of infertility, gynecologic history that would suggest tubal/peritoneal disease, and symptoms/signs on physical examination suggestive of endometriosis.

3. Although laparoscopy with chromotubation remains the ‘gold standard’, it should be undertaken in a setting in which the ability to offer therapy at the same time is available.

4. New sonographic procedures (SHG, HyCoSy) may, with time, replace HSG as the first-line procedure in evaluation of tubal patency/uterine cavity in low-risk patients.

**Key statements**

- 1. Cervical factors are a rare cause of infertility.
- 2. The postcoital test lacks validity since it is unable to predict prognosis or direct therapy.
- 3. There is no role for routine in vivo or in vitro testing for cervical factor infertility since available treatments for unexplained infertility will overcome any possible cervical factors.

- It is likely that cervical mucus plays a key role in sperm migration from the vagina into the uterus and in sperm retention within cervical crypts. Prior cervical trauma (conization) or current vaginitis or cervicitis may have a negative impact on volume or quality of cervical mucus.

**CERVICAL FACTORS AND INFERTILITY – PREVALENCE AND IMPACT**

**Recommendations**

Apart from uterine adhesions, there is no evidence linking the treatment of uterine abnormalities with improved fertility. Because hysteroscopy and laparoscopy are invasive procedures, they should only be performed if less invasive procedures such as HSG and HyCoSy are abnormal.

**Postcoital test**

Traditionally a diagnosis of cervical factor infertility was made when a postcoital test, late in the follicular phase, failed to show the required number of motile sperm several hours after intercourse. Cervical mucus taken from the cervical os 2 or 3 hours after intercourse was tested for spinning (stetchability), fermenation, and for the presence of sperm. The presence of motile sperm in cervical mucus showed good correlation with a normal semen analysis, however, the presence or absence of motile sperm showed little correlation with the outcome of infertility. Positive postcoital tests, in particular, often produced misleading results and frequently resulted in the prescription of therapies that did nothing to improve fertility (such as condoms for six months to reduce the exposure to presumed seminal allergens or high doses of corticosteroids).

- The value of routine postcoital testing (PCT) in the workup of the infertile couple has been seriously challenged. While the presence of clear watery cervical mucus with numerous motile sperm is obviously reassuring, both absence and presence of sperm within cervical mucus should not be misconstrued as evidence supporting a cervical factor for infertility. Many women of proven fertility may fail to demonstrate a so-called “normal” PCT test and controversy remains about what, in fact, is “normal.”

- **Transvaginal or pelvic ultrasound scanning of the uterus** is useful to identify congenital anomalies and uterine fibroids and may assist in diagnosing adenomyosis. The test can be performed at any time during the menstrual cycle.

**Recommendations**

- Apart from uterine adhesions, there is no evidence linking the treatment of uterine abnormalities with improved fertility. Because hysteroscopy and laparoscopy are invasive procedures, they should only be performed if less invasive procedures such as HSG and HyCoSy are abnormal.

**CERVICAL FACTORS AND INFERTILITY – PREVALENCE AND IMPACT**

**Key statements**

- Cervical factors are a rare cause of infertility.
- The postcoital test lacks validity since it is unable to predict prognosis or direct therapy.
- There is no role for routine in vivo or in vitro testing for cervical factor infertility since available treatments for unexplained infertility will overcome any possible cervical factors.

- It is likely that cervical mucus plays a key role in sperm migration from the vagina into the uterus and in sperm retention within cervical crypts. Prior cervical trauma (conization) or current vaginitis or cervicitis may have a negative impact on volume or quality of cervical mucus.

- The presence of antisperm antibodies in cervical mucus is rare and the interpretation of tests to establish this diagnosis remains controversial. The true incidence of abnormalities of cervical mucus is unknown because there are no universally accepted criteria for establishing the diagnosis. Even in studies with strict criteria for postcoital testing, poor inter-observer and intra-observer reproducibility occurs. It is likely that abnormalities of cervical mucus production contribute to unexplained infertility in a small percentage of couples. Current therapies for unexplained infertility (such as ovulation induction and intratubal insemination) would overcome cervical factors contributing to infertility in most circumstances.

- **Surgical ablation of minimal-to-mild endometriosis in the context of infertility only modestly improves pregnancy rates.** Therefore, laparoscopy, if elected, should be performed under conditions where therapeutic procedures (folds of adhesions, ablation of endometriosis) can be applied at the initial procedure. Because of the invasive nature of laparoscopy, it is recommended as a first-line evaluation of tubal peritoneal factors only in patients in whom history and/or physical examination are suggestive of tubal or peritoneal disease (history of STD, intrauterine device [IUD] use, peritonitis, previous ectopic pregnancy, signs/symptoms suggestive of endometriosis). Laparoscopy may also be considered for further diagnosis/therapy of otherwise unexplained infertility, with consideration first being given to how findings may or may not impact management strategies.

- **Sonohysterography (SHG) and hysterosalpingo-contrastsonography (HyCoSy) combine the ability to evaluate the uterine cavity accurately, as well as confirm tubal patency (of at least a single tube).** Preliminary results with laparoscopic comparison yielded a concordance of 85.6%, sensitivity of 90.4%, specificity of 70.3%, positive predictive value of 91.2%, and negative predictive value of 68.2%. Advantages of SHG over HSG include lack of gonadal irradiation and more accurate evaluation of the uterine cavity. This technique is likely to gain in importance with further evaluation and accessibility.

- **Summary:**

1. Tubal/peritoneal factors are a common cause of infertility and should be addressed early in the infertility evaluation.

2. The appropriate test for evaluation of tubal patency (HSG, laparoscopy/hysteroscopy) should be determined based on individual patient characteristics that include age, duration of infertility, gynecologic history that would suggest tubal/peritoneal disease, and symptoms/signs on physical examination suggestive of endometriosis.

3. Although laparoscopy with chromotubation remains the ‘gold standard’, it should be undertaken in a setting in which the ability to offer therapy at the same time is available.

4. New sonographic procedures (SHG, HyCoSy) may, with time, replace HSG as the first-line procedure in evaluation of tubal patency/uterine cavity in low-risk patients.

- Traditionally a diagnosis of cervical factor infertility was made when a postcoital test, late in the follicular phase, failed to show the required number of motile sperm several hours after intercourse. Cervical mucus taken from the cervical os 2 or 3 hours after intercourse was tested for spinning (stetchability), fermenation, and for the presence of sperm.

- The presence of motile sperm in cervical mucus showed good correlation with a normal semen analysis, however, the presence or absence of motile sperm showed little correlation with the outcome of infertility. Positive postcoital tests, in particular, often produced misleading results and frequently resulted in the prescription of therapies that did nothing to improve fertility (such as condoms for six months to reduce the exposure to presumed seminal allergens or high doses of corticosteroids).

- The value of routine postcoital testing (PCT) in the workup of the infertile couple has been seriously challenged. While the presence of clear watery cervical mucus with numerous motile sperm is obviously reassuring, both absence and presence of sperm within cervical mucus should not be misconstrued as evidence supporting a cervical factor for infertility. Many women of proven fertility may fail to demonstrate a so-called “normal” PCT test and controversy remains about what, in fact, is “normal.”

**Key statements**

- Cervical factors are a rare cause of infertility.
- The postcoital test lacks validity since it is unable to predict prognosis or direct therapy.
- There is no role for routine in vivo or in vitro testing for cervical factor infertility since available treatments for unexplained infertility will overcome any possible cervical factors.

- It is likely that cervical mucus plays a key role in sperm migration from the vagina into the uterus and in sperm retention within cervical crypts. Prior cervical trauma (conization) or current vaginitis or cervicitis may have a negative impact on volume or quality of cervical mucus.

- The presence of antisperm antibodies in cervical mucus is rare and the interpretation of tests to establish this diagnosis remains controversial. The true incidence of abnormalities of cervical mucus is unknown because there are no universally accepted criteria for establishing the diagnosis. Even in studies with strict criteria for postcoital testing, poor inter-observer and intra-observer reproducibility occurs. It is likely that abnormalities of cervical mucus production contribute to unexplained infertility in a small percentage of couples. Current therapies for unexplained infertility (such as ovulation induction and intratubal insemination) would overcome cervical factors contributing to infertility in most circumstances.

**Recommendations**

- Apart from uterine adhesions, there is no evidence linking the treatment of uterine abnormalities with improved fertility. Because hysteroscopy and laparoscopy are invasive procedures, they should only be performed if less invasive procedures such as HSG and HyCoSy are abnormal.
Highly motile sperm have been found within the fibrinated ends of the tubes and in the peritoneal cavity of patients in whom only immotile sperm could be found within cervical mucus. \textsuperscript{14} Where prior cervical cessation or recurrent vaginal infection have raised concern about possible mucus problems assessment of mucus production may be appropriate (after treatment of any infection). The test must be precisely timed to the immediate preovulatory time (perhaps employing lutenizing hormone [LH] detection kits).

\section*{Resources for Physicians}

\textbf{JUSTINE ESPENANT, PAST EXECUTIVE DIRECTOR, INFERTILITY AWARENESS ASSOCIATION OF CANADA, INC. (IAAC)}

There are a variety of national and international resources and support groups available to specialists and primary care physicians, as well as their patients, in the area of infertility.

\section*{Domestic Resources & Support Groups}

- Canadian Fertility and Andrology Society (CFAS) A national organization of fertility specialists.
  (514) 524-9000 www.cfas.ca

- Infertility Awareness Association of Canada, Inc. (IAAC) A national voluntary health charity dedicated to offering support, education and awareness to individuals with infertility.
  1-800-263-2929 www.iaac.ca

- Canadian Health Network A national, bilingual Internet-based health information service, providing resources from health information providers from across Canada.
  www.canadian-health-network.ca

- Infertility Network A non-profit, charitable organization providing information on all aspects of infertility: medical treatments, psychological impact, adoption, child-free living, current legislation and advocacy efforts.
  416-691-3612 www.infertilitynetwork.org

- Planned Parenthood Federation of Canada (PPFC) A national, bilingual, non-profit organization of fertility specialists.
  (613) 241-4474 www.ppfc.ca

\section*{International Resources & Support Groups}

  (617) 623-0774 www.resolve.org

- International Council on Infertility Information Dissemination Inc. (NICID)
  www.nicid.org

- Human Fertilisation and Embryology Authority (HFEA) A statutory body, which regulates, licenses and collects data on fertility treatments such as IVF and donor insemination, as well as human embryo research. In the UK.
  www.hfea.gov.uk

- International Federation of Infertility Patient Associations office@child.org.uk

- American Society for Reproductive Medicine An American organization of fertility specialists.
  (205) 978-5000 www.asrm.org

- Eric Daiter, MD Board certified specialist, discusses infertility and reproductive endocrinology in free on-line guides.
  (908) 226-0250 www.drdaiter.com

- Polycystic Ovarian Syndrome Association A national non-profit organization operated by women with polycystic ovarian syndrome.
  (877) 775-PCOS www.pcossupport.org

- Ferti.net Worldwide Fertility Network A resource for fertility specialists, health care professionals and those who are interested in learning more about fertility-related issues and current treatments.
  www.ferti.net

- Fertility UK An educational service offering instruction/counseling in Fertility Awareness and Natural Family Planning for women and couples.
  www.fertilityuk.org

\section*{Glossary}

\textbf{PROVIDED BY DAVID MORTIMER, PHD, DZOA BIOMEDICAL, INC., VANCOUVER, BC}

Because many specialist, scientific and medical terms, including jargon, are used in everyday conversations in the Assisted Reproductive Technology (ART) laboratory, a glossary of common terms, abbreviations and acronyms are provided in this glossary. If someone uses a term that you do not know or understand, ask that person or someone else in the laboratory for clarification. Clear, concise and unambiguous communication is vital!

\textbf{Acrosin} A trypsin-like protease enzyme that is contained inside the sperm acrosome (actually in its zymogen form, proacrosin) and is released by the acrosome reaction. It is believed that acrosin softens the glycoprotein structure of the zona pellucida and thereby facilitates sperm penetration through to the oocyte, and hence fertilization.

\textbf{Acrosome} An organelle of the spermatozoon that covers the anterior-most region of the sperm head. It contains acrosin in its zymogen form, proacrosin. See also acrosome reaction.

\textbf{Acrosome reaction} A process whereby the sperm plasma membrane forms localized fusions with the underlying outer acrosome membrane to create fusions through which acrosin is released. The acrosome reaction (AR) is induced in capacitated spermatozoa after binding to the sperm receptor, ZP3, on the zona pellucida. It is an essential part of the fertilization process, both in vivo and in vitro. See also capacitation.

\textbf{Allele} The term for a version or copy of DNA. For genes carried on the chromosomes inside the cell nucleus there are two copies or “alleles” present, although more versions may exist within the population.

\textbf{Aneuploidy} The sampling of fluid from the amniotic or gestational sac, usually performed around 14 weeks of pregnancy to check the genetic normality of the fetus by determining its karyotype or for performing biochemical tests.

\textbf{Amplication} See polymerase chain reaction.

\textbf{Anoopeny} A genetic abnormality caused by the absence or presence of one or more chromosomes (e.g., an extra chromosome 21 causes Down Syndrome).

\textbf{ART} See assisted reproductive technology.

\textbf{Assisted Reproductive Technology}, the technical procedures underlying medically assisted conception.

\textbf{Assisted hatching} A micromanipulation process used to breach the zona pellucida and hence facilitate hatching of the blastocyst. Common approaches include the use of mechanical partial zona dissection (PZD), acid Tyrodes or a laser.

\textbf{Asthenozoospermia} A medical term often used to describe low or poor sperm motility. However, since it does not describe any particular presentation, it is not considered a useful scientific term, and should be avoided. See oligozoospermia, teratozoospermia and oligoasthenoteratozoospermia.

\textbf{Atresia} A process that occurs around the time of birth in mammals whereby the numbers of primordial follicles in the ovaries are greatly reduced.

\textbf{Azoospermia} The complete absence of spermatozoa in a man’s semen caused either by an obstruction or by failure to produce spermatozoa in the testes.

\textbf{Blastocoeel} The fluid-filled cavity inside the blastocyst.

\textbf{Blastocyst} The stage of development at which the embryo is able to undergo implantation. Human embryos should reach this stage on Day 5 after fertilization. A blastocyst comprises an outer layer of cells, the trophoblast, that line the inner cell mass and a cavity, the blastocoeel.

\textbf{Blastomere} A cell of a cleavage stage embryo (e.g., an 8-cell embryo has 8 blastomeres).

\textbf{Centromere} The central part of a chromosome. While this region does not contain any genes, it is highly specific for each chromosome allowing their identification using techniques such as FISH.

\textbf{Capacitation} The final stage of sperm maturation that normally occurs within the female tract after separation of the spermatozoa from the inhibitory decapacitation factors present in the seminal plasma.
It is also required for fertilization in vitro, and the process must be supported by the culture medium. Capacitating spermatozoa display hyperactivated motility and, once capacitated, spermatozoa have the capacity to fertilize the oocyte (i.e., they are able to bind to the sperm receptor on the zona pelliculosa, ZP3 and then undergo the acrosome reaction).

CASA Computer-aided sperm analysis, a technique that combines videomicrography with digital image analysis to analyze sperm movement patterns and derive kinematic measures that describe them. CASA technology is used to analyze sperm hyperactivation.

CFAS The Canadian Fertility and Andrology Society, the professional society in Canada comprising physicians, scientists, nurses and allied health professionals working in the field of reproductive medicine.

Chorionic villus sampling A CVS test is performed at about 10 weeks of pregnancy. Under ultrasound guidance a small sample of tissue is taken from the placenta for genetic testing, such as a karyotype.

Chromatin The complex formed by the DNA inside a cell's nucleus when it is combined with regulatory and structural proteins.

Chromosome The visible structure formed by a single long strand of DNA with its supporting and regulatory proteins. There are 46 chromosomes in the nucleus of every human cell, 22 pairs of "autosomes" (common to both sexes) and the two sex chromosomes, XX in a female and XY in a male.

Clearance The process of repeated cell division whereby the fertilized oocyte or zygote divides into 2 daughter cells (the 2-cell embryo), each of which then divides into two, giving a 4-cell embryo, and so on.

Clone An organism that is identical to another, in terms of both its phenotype and its genotypic.

Cloning The process whereby a clone is created.

COH See Controlled ovarian hyperstimulation.

Controlled ovarian hyperstimulation See stimulation.

Corona radiata The innermost granulosa cells around the oocyte inside the follicle. During oocyte maturation the corona radiata cells extend processes through the zona pellucida and contact the oolemma. Although these processes are withdrawn at the end of oocyte maturation, the corona cells remain with the oocyte after ovulation. See also cumulus and oocyte-cumulus complex.

Corpus luteum The structure in the ovary created by the luteinized follicle. It secretes progesterone and supports the luteal phase of the female cycle. See also luteinization.

Culture medium (pl. = -di) A solution of various salts and nutrients designed to sustain gametes and embryos during their incubation in vitro. See also sequential media.

Cumulus The cumulus cells are specialized granulosa cells that surround the oocyte after ovulation as a structure called the cumulus oophorus. See also corona radiata and oocyte-cumulus complex.

CVS See chorionic villus sampling.

Cytogentic The study of genetics at the level of the chromosomes, usually by preparing a karyotype.

Cytoplasm The liquid contained inside each cell in which structural components (e.g., the nucleus and the mitochondria) are suspended and the enzymes and other substances are dissolved.

Cytotoxic The effect of a substance (e.g., antibody or chemical) that causes the death of a cell.

Decapacitation factor Substance(s) in seminal plasma that inhibit sperm capacitation.

Deletion An abnormality of a DNA molecule where one or more nucleotides is missing. If this occurs inside a gene it can cause a genetic defect that can affect the individual’s phenotype.

Diploid The usual number of chromosomes in an organism, 46 in humans.

Diplopermy Fertilization that involves a diploid spermatozoan, and results in the formation of a triploid zygote without the appearance of three pronuclei.

Dispermy Fertilization of an oocyte by two spermatozoa, and results in the formation of a triploid zygote with three pronuclei.

Deoxyribonucleic acid A molecule made up of a sequence of nucleotides, the order of which forms the genetic code of each individual animal or plant.

Dominant disorder A genetic defect that is expressed in the individual’s phenotype even if one only allele of the gene is abnormal.

Down syndrome A genetic disability (sometimes called “mongolism”) caused by the presence of a third copy of chromosome 21.

E2 See estradiol.

Embryo A word used loosely to describe these stages of the development of an animal from the fertilized oocyte (i.e., zygote) until the fetus (i.e., about the first 8 weeks of human development; the stages before implantation are sometimes referred to as the pre-embryo).

Embryo biopsy The procedure whereby one or two cells are removed from an embryo (usually performed at the 8-cell stage on Day 3 after fertilization) for genetic analysis.

Endometrium The lining of the uterus that undergoes cyclical changes and, a few days after ovulation, is receptive to the blastocyst.

Epididymis (pl. = -mides) A coiled tubular organ attached to the side of the testis where sperm maturation and storage takes place. It is anatomically and functionally divided into three regions, the “head” (caput epididymidis), “body” (corpus epididymidis; sperm maturation) and “tail” (cauda epididymidis; sperm storage).

Enzyme A protein molecule that acts as a catalyst for a specific biochemical reaction.

Estradiol The primary circulating estrogen. It is measured during stimulation to monitor follicular development.

Fecundity The chance of becoming pregnant per cycle of trying.

Fertility The state of being fertile (i.e., of having a child).

Fertilization The fusion of the male and female gametes, a spermatozoan with an oocyte, to create a new individual. A fertilized oocyte is termed the zygote.

Fetal Of or pertaining to the fetus.

Fetus The state of development between the embryo and birth (i.e., from 8 weeks after fertilization until delivery for humans).

FSH See fluorescent in-situ hybridisation.

Fluorescent in-situ hybridisation A technique using fluorescently tagged pieces of synthetic DNA (probes) to label particular regions of a chromosome so that it can be seen under a fluorescence microscope using ultraviolet light.

Follicle The structure inside the ovary where the oocyte develops. During each cycle several follicles begin growing although typically only one will regress (enter atresia) so that a single oocyte is released per cycle. With agedogenous gonadotrophin treatment these other follicles do not regress and multiple oocytes can be aspirated for use in IVF. See also cumulus and granulosa.

Follicle stimulating hormone The gonadotrophin secreted by the pituitary during the follicular phase of the female cycle. FSH stimulates the follicles to grow and the granulosa cells to produce estradiol.

Follicular phase The first half of the female cycle during which folliculogenesis occurs and estradiol is secreted by the granulosa cells.

Folliculogenesis The process of follicle growth, a part of oogenesis.

Fragile X syndrome A serious genetic disease caused by an abnormality of the X chromosome, specifically a variable expansion of a particularly fragile region. Females can carry this disease, but males are affected by it, causing developmental delays and mental retardation.

Free radicals See reactive oxygen species.

FSH See follicle stimulating hormone.

Gamete The generic term for a male or female germ cell, (i.e. the spermatozoon or oocyte).

Gametogenesis The process whereby gametes are produced. See oogenesis and spermatogenesis.

Gene A specific part of the DNA that contains the genetic code for a single molecule such as an enzyme or other protein.

Genome The entire genetic code of an individual cell or organism.

Genomics The study of the genome and gene expression.

Genotype The genetic description of an individual, as opposed to its physical description or phenotype.

Germinal vesicle A large, clear, circular nucleus visible inside the primary oocyte. Disappearance, or “breakdown” of the germinal vesicle (actually a prolonged late prophase stage of the first meiotic division) signals the primary oocyte’s resumption of meiosis.
Gonad  The male or female reproductive organ responsible for producing gametess (i.e., the testis and ovary).

Gonadotrophin Any hormone that switches on and supports the function of the male or female gonads (i.e., the testes and ovaries).

Granulosa  The granulosas cells surround the oocyte within the follicle. During the follicular phase of the female cycle they secrete estradiol, but in the luteal phase, they secrete progesterone. See also LH surge and luteinization. Specialized granulosa cells that form the oocyte-cumulus complex.

GV  See germinal vesicle.

GVBD  See germinal vesicle breakdown.

Haploid  The genetic state of having only half the usual number of chromosomes (i.e., 23 in humans). This state is achieved in the gametes by the process of meiosis.

Hatching  The term used to describe the process whereby the blastocyst is escaped from the zona pellucida prior to implantation. See also assisted hatching.

hCG  Human chorionic gonadotrophin (more correctly β-hCG), a hormone that is produced by the early embryo and the ovary to regulate the early stages of pregnancy. Testing for increased levels of β-hCG is the basis of a pregnancy test. As a pharmaceutical, hCG is also given to “trigger” ovulation in women undergoing ovarian stimulation for IVF.

Homeostasis  The physiological process(es) whereby the concentrations of something, or a physico-chemical state, is maintained inside a cell or organism within a required range.

Hyaluronic acid  A large polysaccharide (actually a glycosaminoglycan) that is the major constituent of the intercellular matrix, especially within the cumulus.

Hyaluronidase  The enzyme whose substrate is hyaluronic acid.

Hybridization  In this sense, the matching of two complementary strands of DNA.

Hyperactivated motility  A highly energetic pattern of sperm movement which, when seen under the microscope, often appears non-progressive. It is caused by the development of high curvature waves in the sperm tail that are propagated at high velocity along the tail (whip-like motility), usually with a short delay. This causes the sperm head to display wide lateral displacement, and hence move in a characteristic “thrashing” pattern. Its expression (hyperactivation) is associated with sperm capacitation and is generally believed to be essential for sperm penetration through the zona pellucida, and hence both in vivo and in vitro fertilization.

Hyperactivation  A change in the motility pattern of the spermatozoa associated with capacitation. See also hyperactivated motility.

ICSI  See intracytoplasmic sperm injection.

Implantation  The process whereby the blastocyst stage embryo burrows into the lining of the uterus, or endometrium, to establish a pregnancy.

Infertility  The state of being infertile, (i.e., not being able to conceive a child).

Inner cell mass  The part of the blastocyst that will give rise to the embryo proper, as opposed to the extra-embryonic membranes. See also trophoblast.

Interphase  The stage in the cell cycle where the chromosomes are not visible in their characteristic form within the nucleus. See also metaphase.

Intracytoplasmic sperm injection  A microinjection procedure whereby a single spermatozoon is inserted directly into the cytoplasm of the oocyte to achieve fertilization during IVF.

In-vitro culture  The incubation of fertilized oocytes (zygotes) in the laboratory through the process of cleavage, typically up to the blastocyst stage of development.

In-vitro fertilization  Literally, fertilization “in glass”. This technique, whereby oocytes and spermatozoa are mixed in the laboratory to achieve fertilization, is used as a treatment for infertility when the process cannot occur naturally inside the woman’s body.

In-vitro maturation  The maturation of immature oocytes in the laboratory attempting to duplicate the natural process that occurs within the follicle.

In-vitro production  The combined processes of in-vitro fertilization and in-vitro culture whereby embryos are produced in the laboratory (i.e., IVF = IVM+IVF+IVC).

ISO  The International Standards Organization comprising representation from the national standards institutes of more than 90 countries worldwide. Among many other standards, this organization produces the family of quality standards known as “ISO 9000” or, more correctly to reflect the publication of revised standards in 2000, “ISO 9001:2000”. For service-oriented businesses (e.g., ART units) the relevant standards are “ISO 9001:2000” (manufacturers are covered by “ISO 9002:2000”), whereas for specific application in laboratories, they are the “ISO/IEC 17025” standards.

IVC  See in-vitro culture.

IVF  See in-vitro fertilization.

IVM  See in-vitro maturation.

IVP  See in-vitro production.

Karyotype  A preparation made from one or more cells in the laboratory to study whether an individual has a normal set of chromosomes. A normal male is 46 XY, while a normal female is 46 XX. See also Down syndrome and translocation.

Kinematics  Measurements that describe sperm movement patterns (e.g., hyperactivated motility), usually derived using CASA technology.

LH  See luteinizing hormone.

LH surge  A surge in LH secretion during the late follicular phase of the female cycle, caused by positive feedback of rising estradiol levels on the pituitary, that acts as the trigger for the final stages of oocyte maturation and ovulation.

Luteal phase  The second half of the female cycle, during which the luteinized follicle or corpus luteum secretes progesterone and implantation of the blastocyst into the endometrium lining the uterus occurs. See also luteinization.

Luteinization  The change in the granulosa cells of the follicle, induced by the LH surge, that causes their steroid hormone production to switch from estradiol to progesterone.

Luteinizing hormone  The gonadotrophin that causes luteinization of the granulosa cells. See also LH surge.

Medium or Media  Common terms for culture medium.

Messenger RNA  A molecule of RNA (mRNA) produced by transcription of a gene that carries the code for the product of that gene. This product is then produced by translation in the cytoplasm of the cell.

Metaphase  The stage in the cell cycle immediately before it divides where all the chromosomes are visible and arranged in a single plane ready for division so that one copy of each goes to each daughter cell. See also interphase.

Micro-epididymal sperm aspiration  A medical procedure whereby spermatozoa are aspirated from the epididymis, usually involving microsurgery.

Mitochondria  (pl. — mitochondria) structures inside every cell that resemble bacteria. These are sites of metabolism where carbohydrate is oxidized to release energy that is trapped as ATP for movement around the cell.

Mitosis  The usual process of cell division whereby a cell divides into two identical “daughter” cells (e.g., during cleavage of the embryo).

Mitotic index  The rate of cell division (mitosis) of a population of cells.

Molecular genetics  The study of genetics at the level of individual genes or the DNA itself.

mRNA  See messenger RNA.

mtDNA  The small amount of DNA that carries the genetic code of the mitochondrion. It is the only DNA outside the cell nucleus and codes for 13 genes, which are essential in metabolism, and are not coded for by the nuclear DNA of the chromosomes.

Muscular dystrophy  A group of neuromuscular diseases caused by specific genetic defects.

Mutation  A change in the sequence of nucleotides in a DNA strand. See also deletion, point mutation.

Nuclear transfer  The process by which the nucleus of one cell is removed and transferred into another cell; a basic technique used in cloning.

Oocyte  Developmental stage of the female gamete. The mature oocyte is the equivalent of the male spermatozoon, and, when fertilized, that will give rise to the embryo proper, as opposed to the extra-embryonic membranes. See also granulosa.

Oogenesis  Specialized granulosa cells that form the oocyte-cumulus complex.

Oocyte-Cumulus Complex  The group of specialized somatic cells associated with the oocyte. They secrete progesterone. See also granulosa.

Ovulation  The second half of the female cycle, caused by positive feedback of rising estradiol levels on the pituitary, that acts as the trigger for the final stages of oocyte maturation and ovulation.

Parthenogenesis  Any hormone that switches on and supports the function of the male or female gonads (i.e., the testes and ovaries).

Parthenogenesis  Any hormone that switches on and supports the function of the male or female gonads (i.e., the testes and ovaries).

Peptidases  Enzymes that act on polypeptides.

PGC  See pregranulosa cell.

PGD  See preimplantation genetic diagnosis.

Post-Implantation Genetic Diagnosis  A test that can be performed on preimplantation embryos to determine the presence of certain genetic disorders. See also PGD.

Preimplantation Genetic Diagnosis  A medical technique whereby embryos produced in the laboratory (i.e., IVF = IVM+IVF+IVC) can be tested for genetic abnormalities prior to implantation in the uterus. See also PGD.

Pregranulosa cell  An undifferentiated somatic cell that surrounds the oocyte within the follicle and will give rise to the granulosa cells that support the oocyte. See also granulosa and ovary.

Primary follicle  A small follicle which contains an immature oocyte (i.e., oogonia) in the ovary. See also secondary follicle.

Primary oocyte  The oocyte which emerges from the ovary and migrates to the surface of the ovary to undergo meiosis I, thereby becoming a secondary oocyte. See also meiosis.

Primary ovary  The ovary that contains the eggs (i.e., oogonia) at birth. See also ovary.

Primary spermatocyte  The male gamete that emerges from the testis and is destined to become a spermatozoon. See also spermatogenesis.

Primary spermatogonia  The primary spermatogonia are responsible for the production of spermatocytes and are not visible in their characteristic form that resemble bacteria. These are sites of metabolism where carbohydrate is oxidized to release energy that is trapped as ATP for movement around the cell.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.

Proliferation  The study of genetics at the level of individual genes or the DNA itself.
Nucleotide  One of the four base chemicals that make up the double helix of DNA (adenine, cytosine, guanine, thymine). The order in which the four nucleotides occur in a stretch of DNA is called its sequence and constitutes the genetic code.

Nucleus  The central part of each cell where the genetic code carried in the chromosomes reside.

OAT Syndrome  See oligoazoozoospermia.

OCC  See oocyte-cumulus complex.

Oestradiol  See estradiol.

OHSS  See ovarian hyperstimulation syndrome.

Oligoasthenozoospermia  A medical term often used to described low or poor sperm mobility combined with a low sperm concentration. However, since it does not describe any particular presentation, it is not considered a useful scientific term, and should be avoided. See also asthenozoospermia, oligozoospermia, and teratozoospermia.

Oligomucleotide  A small piece of synthetic DNA often used as a primer in the polymerase chain reaction. It comprises a highly specific sequence of nucleotides designed to recognize a particular region of a gene.

Oligozoospermia  An incorrect term, often used to describe a low sperm concentration. See oligozoospermia.

Oligozoospermia  The medical term for having a very low sperm count (defined by the WHO as <20x10⁶ spermatozoa per ml of semen).

Oocyte  The correct scientific term for the female gamete, often referred to as the “egg.”

Oocyte-cumulus complex  This structure, which is visible to the naked eye, comprises the oocyte, inside the zona pellicula, surrounded by the corona radiata cells and the cumulus oophorus; it is the structure found in follicular aspirates at oocyte retrieval.

Oocyte maturation  A process that occurs during folliculogenesis whereby the oocyte becomes too competent to undergo fertilization and support early embryonic development. It comprises both nuclear and cytoplasmic processes, the former is visible as germinal vesicle breakdown and entry into meiosis (which is arrested at the metaphase II stage so that it is a secondary oocyte that is released at ovulation), while the latter involves the production and storage of a variety of essential mRNAs that will control development from fertilization through the time when the embryonic genome is activated (on Day 3, at about the 8-cell stage, in human embryos). See also in-vitro maturation.

Point mutation  An abnormality of a DNA molecule where a single nucleotide is changed. If this occurs inside a gene it can cause a genetic defect that can affect the individual’s phenotype.

Polar body  A small cytoplasmic mass extruded by the oocyte during meiosis that contains a discarded set of chromosomes. The first polar body (1st PB) signals the completion of the first meiotic division and can be seen in the secondary oocyte; the second polar body (2nd PB) is extruded as a consequence of penetration of the oocyte by a spermatozoon and is an indication of fertilization.

Polymerase chain reaction  A molecular genetic technique that allows a single copy of a genetic sequence to be amplified geometrically to produce vast numbers of copies that can then be detected and analyzed. It uses a thermostable DNA polymerase enzyme and a repetitive sequence of temperature shifts in a “thermal cycler” machine to produce copies of a particular region of the genetic code located between a pair of carefully chosen primers.

Polymerophim  The existence of multiple versions of a particular gene or sequence of genetic code.

Pre-embryo  A non-scientific term commonly used in N. America to describe the embryo between the time of fertilization and implantation.

Preimplantation genetic diagnosis  Testing performed on the cleavage stage embryo or blastocyst involving embryo biopsy and analysis of one or two cells using genetic techniques such as FISH or PCR.

Primary oocyte  The stage of oogenesis when the female gamete undergoes the first meiotic division. See also meiosis.

Primer  A small piece of synthetic DNA with a highly specific code for a particular region of a gene that can be used to initiate the polymerase chain reaction.

Primordial follicle  A primitive stage of follicle within the ovary, especially numerous during the late fetal period. The number of primordial follicles is greatly reduced just around the time of birth by the process of atresia.

Probe  A piece of synthetic DNA, usually with a fluorescent tag, used to identify particular regions of the chromosomes, e.g. in the technique of FISH.

Progesterone  The hormone secreted by granulosa cells after luteinization, (i.e. during the luteal phase of the female cycle). It is often given to help support the luteal phase in cycles where cryopreserved embryos are replaced due to deficient corpus luteum activity.

Pronucleus  A structure formed during fertilization by the nuclear material contributed by each gamete, hence normal fertilization involves both a female pronucleus (created after extrusion of the second polar body) and a male pronucleus (formed, inside the ooplasm, from the decondensed chromatin of the sperm nucleus). A normal zygote has two pronuclei (2PN).

PZD  See partial zona dissection.

Quality control  Includes quality assurance, but is more expansive, encompassing quality control of the various component sub-processes and involving monitoring and control of the ultimate outcomes of the entire process.

Quality control  Involves establishing specifications for each aspect of a process, assessing the procedures involved in the process to determine conformance to those specifications, and taking any necessary corrective actions to bring procedures into conformance.

Quality cycle  A process within the framework of Total Quality Management whereby continuous cycles of quality assurance and quality improvement are undertaken.

Quality improvement  The process whereby a procedure is reviewed and quality management principles used to bring about improvements in the actual procedure itself and/or its outcome(s).

Reactive oxygen species  Damaging by-products of oxidative metabolism that can cause severe damage to cells, including their membranes and DNA. Also sometimes called “free radicals.”

Recessive disorder  A genetic defect that must be present in both alleles of a gene for it to be expressed in the individual’s phenotype.

Recombinant  In this case, a substance produced artificially using molecular genetic engineering, e.g. the gonadotrophin hormones used in controlled ovarian hyperstimulation for IVF.
Ribonucleic acid A molecule used in the transcription of DNA (e.g., messenger RNA).

RNA See ribonucleic acid.

ROS See reactive oxygen species.

ROS- See ROS.

ROS1? See reactive oxygen species injection.

Round spermatid A large, round, undifferentiated cell that is produced as a result of completion of the second meiotic division during spermatogenesis. The round spermatid enters spermiogenesis and differentiated into the spermatozoan.

Round spermatid injection An experimental procedure for achieving fertilization, similar to ICSI, whereby a round spermatid is injected into the oocyte. ROS1 has very poor success rates.

Round spermatid nucleus injection An experimental procedure for achieving fertilization, similar to ICSI, whereby the isolated nucleus from a round spermatid is injected into the oocyte. ROSNI has very poor success rates.

SART The Society for Assisted Reproductive Technologies, a section of the American Society for Reproductive Medicine (ASRM), which runs a registry for ART results to which many Canadian clinics also report.

Secondary oocyte The stage of oogenesis when the female gamete undergoes the second meiotic division (see also meiosis). In humans (and many other mammals), the female gamete is released from the ovary (ovulation) at this stage, hence the female gamete is not actually an ovum.

Second polar body The 2nd PB is extruded as a consequence of penetration of the oocyte by a spermatozoon and is an indication of fertilization.

Semen The male ejaculate, comprising spermatozoa and other cells suspended in a fluid the seminal plasma.

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Seminal plasma The liquid fraction of the semen, in which the spermatozoa are suspended. It is a mixture of secretions from the epidermis, prostate, seminal vesicles and other accessory glands of the male tract.

Semen analysis The process whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Seminal plasma The liquid fraction of the semen, in which the spermatozoa are suspended. It is a mixture of secretions from the epidermis, prostate, seminal vesicles and other accessory glands of the male tract.

Seminal plasma The liquid fraction of the semen, in which the spermatozoa are suspended. It is a mixture of secretions from the epidermis, prostate, seminal vesicles and other accessory glands of the male tract.

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Seminal plasma The liquid fraction of the semen, in which the spermatozoa are suspended. It is a mixture of secretions from the epidermis, prostate, seminal vesicles and other accessory glands of the male tract.

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Seminal plasma The liquid fraction of the semen, in which the spermatozoa are suspended. It is a mixture of secretions from the epidermis, prostate, seminal vesicles and other accessory glands of the male tract.

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”

Semen analysis The procedure whereby the characteristics of the semen are measured, (e.g., sperm concentration, motility, vitality, morphology). Sometimes referred to as a “seminal fluid analysis” or “SFA,” although this abbreviation is also used to mean “spem functional assessment.”
ABREVIATIONS AND ACRONYMYS

PROVIDED BY DAVID MORTIMER, PH.D., COZZA BIOMEDICAL, INC., VANCOUVER, BC

AAB American Association of Bioanalysts, the organization that board certifies lab directors in the USA
AH Assisted Hatching
AI Artificial Insemination (see also AID, AIH, DI, TDI)
AID Artificial Insemination by Donor (no longer used, see DI, TDI)
AIH Artificial Insemination by Husband
ART Assisted Reproductive Technology
ASABS Anti-Sperm Antibodies
BBT Basal Body Temperature
CASA Computer-Aided Sperm Analysis
CRYO Relating to cryopreservation
-D May be added to denote that donor spermatozoa were used, (eg., IVF-D)
DI Donor Insemination (formerly AID, see also TDI)
DM SOD Dimethylsulfoxide (a cryoprotectant used for freezing embryos)
ET Embryo Transfer
FET Frozen Embryo Transfer
FF Follicular Fluid (see also hFF)
GEOY Glycerol-Egg Yolk Citrate (a modified Ackerman's cryoprotectant medium used to freeze semen)
GIFT Gamete Intra-Fallopian Transfer (by laparoscopy, ultrasound or mini-laparotomy)
HEPES HEPES-buffered saline (a cryoprotectant used for freezing embryos)
HEPT Hamster Egg Penetration Test
hFF Human Follicular Fluid (see also FF)
HSA Human Serum Albumin
HTF Human Tubal Fluid (a culture medium used for IVF developed by Patricia Quinn)
HZA Hamster-Zona Assay (a variant sperm-zona binding test, see also ZBT)
IBT Immunoassay Test
ICSI Intracytoplasmic Sperm Injection
IUI Intra-Uterine Insemination
IVF In-vitro Fertilization
IVF-ET In-vitro Fertilization and Embryo Transfer
MDSDS Material Safety Data Sheet
OFC Oocyte Pick-Up or retrieval
PCT Post-Coital Test
PN Pronucleus
PvO Propanolol (a cryoprotectant used for freezing embryos)
PVP Polyvinylpyrolidone
ROS Reactive Oxygen Species (free radicals)
SCMC Sperm-Cavial Mucus Contact test
SPA Sperm Functional Assessment = Genisn-standen semen analysis
SMIT Sperm Mucus Interaction Test (usually in-vitro, cT, PCT)
SPA Sperm Penetration Assay (synonymous with HEPT)
TDT Therapeutic Donor Insemination (see DI)
Tytka-Yolk See TYG
TYG TEST-yolk-glycerol, a common cryoprotectant for semen
TW Thal Waich, a pre-treatment sperm assessment including sperm preparation
TZI Teratospermia Index, an assessment used in sperm morphology
US Ultrasound, sometimes US = ultrasound scan(ning)
WBC White Blood Cell or leucocyte
WHMIS Workplace Hazardous Materials Information System
WHO World Health Organization
ZBT Sperm-Zona Binding Test (see also HZA)
ZIFT Zygote Intra-Fallopian Transfer (by laparoscopy or ultrasound)

REFERENCES

REFERENCES CONTINUED...


