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CFAS Consensus Document for the Investigation of Infertility

By First Line Physicians

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CANADIAN FERTILITY AND ANDROLOGY SOCIETY
SOCIÉTÉ CANADIENNE DE FERTILITÉ ET D'ANDROLOGIE

Canadian Society for Reproductive Medicine and Sciences
Société canadienne de médecine et des sciences de la reproduction

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PREFACE

Roger Pierson, MS, PhD
Serge Bélisle, MD, FRCSC, MSc

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.

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DIFFICULTY CONCEIVING

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- If conditions preclude pregnancy
- High-risk factors

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

Advise regular intercourse two or three times a week

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

BASIC EVALUATION

FEMALES

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

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)

MALES

Consider referral at 18 months or earlier if:

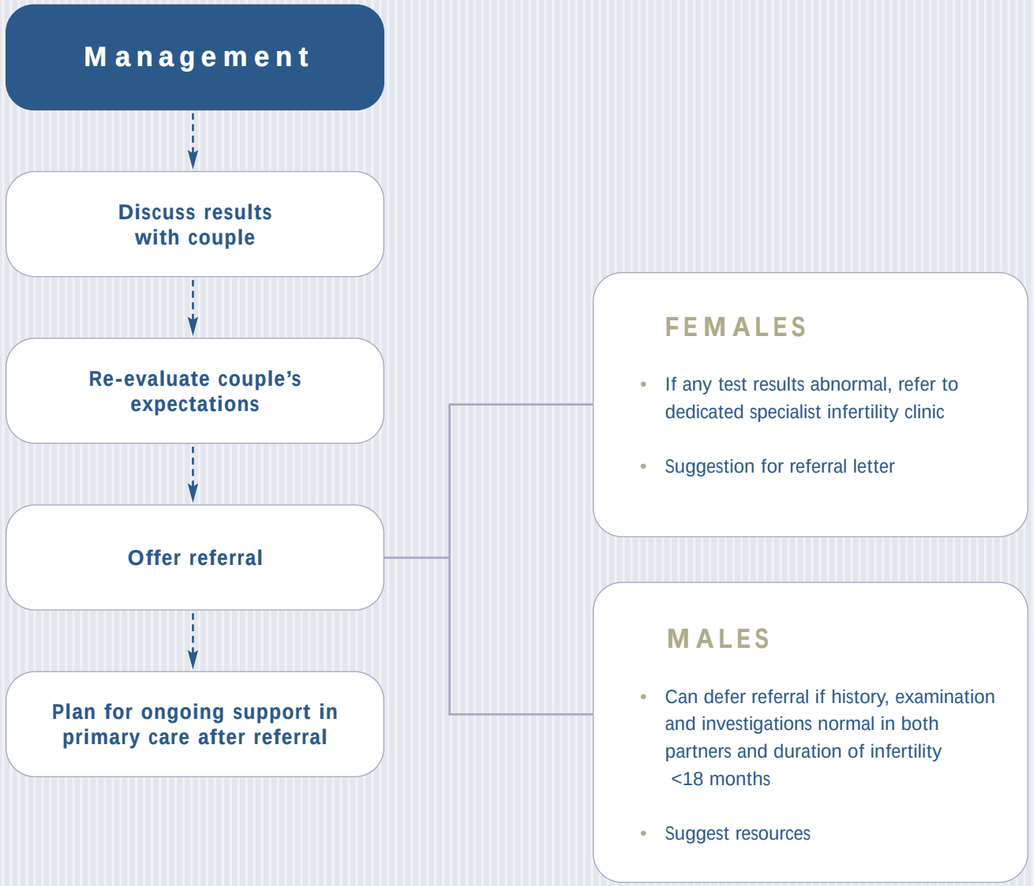
- Previous genital pathology
- Previous urogenital surgery
- Previous STD
- Varicocele
- Significant systemic illness
- Abnormal genital exam

TESTS

Semen

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

ALGORITHM



INTRODUCTION

SERGE BÉLISLE, MD, FRCSC, MSc

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.[1] 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.

HISTORY TAKING AND PHYSICAL EXAM FOR INFERTILITY

RODOLPHE MAHEUX, MD, FRCSC

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?

1. Pre-pregnancy considerations

It is appropriate to consider and discuss the risk of future pregnancy to mother and offspring (i.e., high-risk pregnancy, advanced maternal age) before initiating infertility treatment. The rubella status of the female partner is an important point to assess before any pregnancy; vaccination should be offered if negative and the patient should be advised not to become pregnant within one month of immunization.

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.

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 hydrosalpinges 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.

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.[2] 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 undiscovered 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.[3]

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%.[4,5] Increasing age of the female partner and longer duration of infertility are poor prognostic factors.[5]

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.[6]

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.

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.

MALE INFERTILITY

JOHN E. GRANTMYRE, 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.[7] 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 ordeal and help to minimize any sense of blame.

In the man, a history of previous pregnancy or failed attempts is relevant. Previous surgery involving the testicles (particularly if undescended), inguinal surgery that could obstruct the vas, or other pelvic procedures should be noted. Usually a history of chemotherapy or radiation treatment will be volunteered, but even exposure to lesser toxins such as herbicides, pesticides, marijuana and alcohol can result infertility problems. In addition, inflammations of the testicle such as epididymitis, orchitis or traumatic injury can cause atrophy or epididymal obstruction.

Drugs such as sulfasalazine, spironolactone, or nitrofurantoin should be switched to safer alternatives. Hot baths may affect sperm production and, although the data supporting underwear choice is weak, many patients have already switched from briefs to boxer shorts or are not wearing underwear by the time they present at clinic.

The examination of men with a potential fertility problem is difficult as subtle changes of the epididymis, testicular veins or vas deferens are only obvious after considerable clinician experience. Although most male fertility specialists believe varicoceles are an important cause of poor sperm quality and function, the use of scrotal ultrasound is operator dependent and not recommended for routine evaluation. Nonetheless, a basic assessment of virilization, observing male habitus and hair distribution, a penis with a normally located meatus and testes of roughly normal dimensions, will provide ample initial information.

Early in the investigation of the couple, a comprehensive semen analysis should be performed according to current WHO standards after giving the patient careful instructions.[8] The man must have three days of abstinence, collect the specimen directly into the container provided by the laboratory and, ideally, deliver the specimen immediately to the lab. Many men will ‘save up’ if not instructed otherwise, waiting for more than three days to maximize their count. This will often falsely lower the evaluation of sperm motility.

If an abnormality is detected in the bulk semen characteristics in terms of sperm density or motility, serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone and prolactin should be ordered at the time of referral. Ideally, the blood specimen should be drawn at between 8 and 10 in the morning when testosterone levels are highest.

On occasion, ‘specialized’ sperm testing will be required, but it is surprising how many tests have come and gone without significant impact on patient care (e.g., hamster egg penetration test, computerized semen analysis, postcoital test, mucus penetration test).

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.[8] 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.[9] Identification of these sperm masquerading as WBCs can avoid unnecessary treatment of infection. Patients with unexplained infertility, failure to fertilize at 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).[10]

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 rerouted, and sperm aspirated in those who cannot be reconstructed.[11] Those having sperm retrieval can have cryopreservation of sperm with no effect on eventual fertilization. Most sperm retrievals will be dependent on IVF using ICSI and should have genetic screening and counselling as necessary.

The use of intra-uterine insemination (IUI) in the treatment of male infertility is more controversial. Most centres will limit IUI to those men who have >5 million motile sperm (after sperm processing) and with younger partners.

Unfortunately, clear outcome measures are not available for treating male factor with IUI and the indications vary from centre to centre. The advent of ICSI has provided high fertilization rates even with very low numbers of frozen sperm. What is less clear is at what point one should proceed to ICSI since sperm quality worsens. As the safety concerns are lessened by reassuring follow-up of ICSI children, there is a trend toward ICSI use whenever any semen abnormality is present or previous fertilization has been sub-optimal.

Genetic causes of male infertility are now being discovered. These include an association between azoospermia due to congenital absence of the vas deferens "CBAVD" associated with defects of the cystic fibrosis gene. Microdeletions in the lower aspect of the Y chromosome result in problems ranging from oligospermia to azoospermia. These genetic conditions carry risk of disease transmission to offspring produced by ICSI.

OVULATION

MARGO FLUKER, MD, FRCSC

Ovulation is a prerequisite for conception. Ovulatory disorders occur in 15% to 25% of all infertile couples, ranging from mild cycle irregularity to amenorrhea.[5,12] 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.[13]

Diagnostic tests

A history of regular 24 to 35 day menses is consistent with ovulation in 97% of cases.[14] 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.[15] 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.[16]

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 uninterpretable 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.

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 (thyrotropin, TSH), prolactin or androgen levels in infertile women with regular ovulatory menses in the absence of galactorrhea. In women with ovulatory 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). Androgen 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 luteal 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 androgen levels in women with regular menses and no galactorrhea or hirsutism.

TUBAL-PERITONEAL FACTORS

ELLEN M. GREENBLATT, MD, FRCSC

Complete or partial tubal occlusion and/or peritubal/periovarian adhesions are a significant cause of infertility (approximately 30%), either alone or in combination with other subfertility factors.[17] 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, sonohysterography (SHG) with or without the use of echoenhancing agents for sonosalpingography.

HSG is generally accepted as the traditional, least invasive and most cost effective method of evaluation of tubal patency in low-risk women. HSG 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 loculation of contrast media or delayed spill. False positives for proximal tubal obstruction are approximately 15%.

The sensitivity and specificity of HSG for tubal patency are approximately 0.65 and 0.83, respectively. However, this method is less accurate for evaluating peritubal adhesions and peritoneal endometriosis not associated with tubal occlusion.[18,19,20] Selective fluoroscopic tubal cannulation can be performed as a therapeutic procedure if proximal tubal obstruction is demonstrated with HSG.

Laparoscopy with chromotubation is considered the gold standard for evaluation of tubal patency. It is the only accurate test for demonstrating peritubal/periovarian adhesions, fimbrial phimosis not causing tubal obstruction, and mild endometriosis not associated with tubal distortion. It is, however, a more invasive test, typically performed under general anesthesia. When performed with hysteroscopy, the uterine cavity can be evaluated concurrently. Although it is estimated that 49% of tubal/peritoneal disease would be missed by HSG alone[19,20] it is not clear to what extent identification of such abnormalities alters cumulative conception rates or eventual management.[19,21]

Surgical ablation of minimal-to-mild endometriosis in the context of infertility only modestly improves pregnancy rates.[22] Therefore, laparoscopy, if elected, should be performed under conditions where therapeutic procedures (lysis 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).[23,24] Preliminary results with laparoscopic comparison yielded a concordance of 85.8%, 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.[25]

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.

UTERINE

SALIM DAYA, MB

Although abnormalities of uterine anatomy are not common causes of infertility, evaluation of the uterine architecture provides useful information in the investigation of the female partner. The following methods are available:

a) Hysterosalpingography (HSG) –
(e.g., bicornuate uterus, septate uterus, etc.)

Congenital anomalies, structural abnormalities (e.g., intrauterine adhesions, endometrial polyps, submucous fibroids) and other acquired abnormalities may have an effect on pregnancy outcome and can be identified with HSG. Water-soluble or oil-based radio-opaque contrast material is used to delineate the uterine cavity. The ideal time to perform the procedure is between the end of menses and ovulation so that inadvertent irradiation of an early pregnancy is avoided. Prior administration of antibiotics to prevent pelvic inflammatory disease (PID) is still debatable.

b) Hysteroscopy

Direct visualization of the uterine cavity with the hysteroscope using a variety of distending media, such as saline, dextran and carbon dioxide, is an accurate method of evaluating the uterine cavity. However, the method is costly and invasive. Consequently, it is often reserved for use when the HSG is equivocal or when treatment is being planned (e.g., resection of septum, removal of polyp or fibroid, etc.)

c) Laparoscopy

Laparoscopy is useful when evaluation of the external architecture of the uterus is required. For example, when the HSG shows a bicornuate cavity, it is important to distinguish between a bicornuate uterus and a septate uterus so that the appropriate treatment can be planned.

The presence of subserous fibroids can be ascertained and surgical removal can be performed if they are affecting tubal function or deforming the uterine cavity. When confronted with a bicornuate vs. septate uterus, a 3D-ultrasound or MRI may be considered in place of laparoscopy.

d) Sonohysterography (HyCoSy)

HyCoSy involving transvaginal ultrasound scanning is increasingly being used to evaluate the uterine cavity for congenital anomalies and structural and acquired abnormalities. A variety of contrast media can be used, including saline, sterile water and Echovist®.

e) Ultrasonography

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

ROBERT L. REID, MD, FRCSC

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. 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 occur.[26] 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 intrauterine insemination) would overcome cervical factors contributing to infertility in most circumstances.

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 8 hours after intercourse was tested for spinnbarkeit (stretchability), ferning and for the presence of motile sperm (criteria varied from 1 to 20 per high power field). The presence of motile sperm in cervical mucus showed a good correlation with a normal semen analysis, however, the presence or absence of motile sperm showed little correlation with the outcome of interest - pregnancy. Negative 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.[6,27] While the presence of clear watery cervical mucus with numerous motile sperm is obviously reassuring [26], the failure of sperm to remain motile within cervical mucus should not be misconstrued as evidence supporting a cervical factor for infertility.[28] Many women of proven fertility may fail to demonstrate a so-called "normal" PC test and controversy remains about what, in fact, is "normal".[29]

Highly motile sperm have been found within the fibriated ends of the tubes and in the peritoneal cavity of patients in whom only immotile sperm could be found within cervical mucus.[30] Where prior cervical conization 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 luteinizing hormone [LH] detection kits).

Outcome of treatment

Cervical factor infertility has been much overrated and, when diagnosed, is a significant cause of anxiety and hardship (cost and inconvenience of putative therapies) for infertile couples. Over 95% of pregnancies occurring in couples with this diagnosis occurred spontaneously at a time remote from the therapeutic intervention for cervical factor infertility.[31]

Resources for Physicians

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.

Domestic Resources & Support Groups

- Canadian Fertility and Andrology Society (CFAS)
  A national organization of fertility specialists.
  (514) 524-9009 ***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.
  416-691-3611 ***www.infertilitynetwork.org***
- Planned Parenthood Federation of Canada (PPFC)
  (613) 241-4474 ***www.ppfc.ca***

International Resources & Support Groups

- RESOLVE (The American National Infertility Association)
  An American self-help group for infertile couples.
  (617) 623-0774 ***www.resolve.org***
- International Council on Infertility Information Dissemination Inc. (INCIID)
  www.inciid.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.pcosupport.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/counselling in Fertility Awareness and Natural Family Planning for women and couples.
  www.fertilityuk.org

GLOSSARY

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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!

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***.

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***.

Acrosome reaction A process whereby the sperm plasma membrane forms localized fusions with the underlying outer acrosome membrane to create fenestrations 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***.

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.

Amniocentesis 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.

Amplification See ***polymerase chain reaction.***

Aneuploidy A genetic abnormality caused by the absence or presence of one or more ***chromosomes*** (e.g., an extra chromosome 21 causes ***Down Syndrome***).

AR See ***acrosome reaction.***

ART ***Assisted Reproductive Technology***, the technical procedures underlying medically assisted conception.

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.

Asthenozoospermia A medical term often used to described 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***.

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

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.

Blastocoel The fluid-filled cavity inside the ***blastocyst***.

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 enclose the ***inner cell mass*** and a cavity, the ***blastocoel.***

Blastomere A cell of a cleavage stage ***embryo*** (e.g., an 8-cell embryo has 8 blastomeres).

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***.

Capacitation The final stage of sperm maturation that normally occurs within the female tract after separation of the ***spermatozoon*** 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 pellucida, 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 biomedicine.

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.

Cleavage 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 ***genotype***.

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. = ***-dia***) 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***.

Cytogenetics 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 ***nucleotide*** 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.

Diplospermy ***Fertilization*** that involves a ***diploid spermatozoon***, and results in the formation of a ***triploid zygote*** without the appearance of three ***pronuclei***.

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

Deoxyribonucelic 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 those 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 ***spermatozoon*** 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).

FISH 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 all but one will regress (enter ***atresia***) so that a single oocyte is released per cycle. With exogenous ***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 ***gametes*** (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 granulosa 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 believed to escape from the ***zona pellucida*** prior to ***implantation***. See also ***assisted hatching***.

hCG Human chorionic ***gonadotrophin*** (more correctly ß-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 ß-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 concentration 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 (whiplash 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 ***spermatozoon*** 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 micromanipulation 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 maturation, ***in-vitro fertilization*** and ***in-vitro culture*** whereby embryos are produced in the laboratory (i.e., IVP = 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 9000:2000." For service-orientated 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 induces ***luteinization*** of the ***granulosa*** cells. See also ***LH surge***.

Medium or Media Common terms for ***culture medium***.

Meiosis A special type of cell division that occurs only during ***gametogenesis*** (i.e., ***oogenesis*** and ***spermatozogenesis***) and results in the daughter cells, the ***gametes***, having only half the usual number of ***chromosomes*** (i.e., being ***haploid***).

MESA See ***micro-epididymal sperm aspiration***.

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.

Mitochondrion (pl.= ***-dria***) 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***.

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 ***oligoasthenoteratozoospermia***.

OCC See ***oocyte-cumulus complex***.

Oestradiol See ***estradiol***.

OHSS See ***ovarian hyperstimulation syndrome***.

Oligoastheno-zoospermia A medical term often used to described low or poor sperm motility 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***.

Oligonucleotide 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 recognise a particular region of a gene.

Oligospermia 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 $<20x10^6$ 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 pellucida***, 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***.

Oocyte pickup See ***oocyte retrieval***.

Oocyte retrieval The stage in the IVF process when the ***oocyte***, more correctly the ***oocyte-cumulus complex*** (OCC) – usually several – are aspirated from the follicles of the ovary. Sometimes referred to as "***oocyte pickup"*** or "***OPU***."

Oogenesis The entire process whereby ***oocytes*** are produced in the ***ovary***.

Oolemma The plasma membrane of the ***oocyte***.

Ooplasm The ***cytoplasm*** of the ***oocyte***.

OPU See ***oocyte pickup*** or ***oocyte retrieval***.

Ovarian hyperstimulation syndrome
A complication of ovarian ***stimulation*** that can, in extreme cases, be fatal.

Ovary (pl. = ***ovaries***) The female ***gonad*** where the female ***gametes*** (***oocytes***) are produced inside ***follicles*** by the process of ***oogenesis***.

Ovulation The process whereby the (secondary) ***oocyte*** is released from the mature ***follicle*** on the surface of the ***ovary***.

Ovum The female ***gamete*** after completion of ***meiosis***. Since in humans (and many other mammals) the female gamete is released from the ovary as a ***secondary oocyte***, and the second meiotic division is not completed until after incorporation of the ***spermatozoon*** at ***fertilization***, the ovum stage never actually exists since at that time it is, strictly, already considered a fertilized oocyte, although not quite a ***zygote***.

Partial zona dissection A micromanipulation process used to breach the ***zona pellucida*** using a fine glass needle. See also ***assisted hatching***.

PCR See ***polymerase chain reaction***.

PGD See ***preimplantation genetic diagnosis***.

Phenotype The physical expression of the genetic makeup or ***genotype*** of an individual.

PN See ***pronucleus***.

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***.

Polymorphism 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***.

QA See ***quality assurance***.

QC See ***quality control***.

QI See ***quality improvement***.

Quality assurance Includes ***quality control***, 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***.

ROSI See ***round spermatid injection***.

ROSNI See ***round spermatid nucleus 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 ***spermatozoon***.

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

Round spermatid nucleus injection An experimental procedure for achieving ***fertilization***, similar to ***ICSI***, whereby the isloated ***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 "sperm functional assessment."

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

Seminiferous epithelium The epithelium lining the ***seminiferous tubules*** of the ***testis***. This is where ***spermatogenesis*** takes place.

Seminiferous tubules U-shaped tubules, lined by the ***seminiferous epithelium***, coiled inside separate lobes of the ***testis***. They are the sites of ***spermatogenesis***.

Sequence The order in which the four ***nucleotides*** (adenine, cytosine, guanine, thymine) occur in a stretch of ***DNA***, this constitutes the genetic code of a ***gene***.

Sequential media A series of ***culture media*** designed to support an ***embryo*** during the various stages of its development *in vitro*, from ***fertilization*** to the ***blastocyst*** stage.

SFA See ***semen analysis***.

Spermatogenesis The process of male ***gametogenesis*** that occurs in the ***seminiferous epithelium*** lining the ***seminiferous tubules*** of the ***testis***, whereby ***spermatozoa*** are produced. It includes cell divisions both by ***mitosis*** and ***meiosis*** as well as the differentiation process known as ***spermiogenesis***.

Spermatozoon (pl.= ***-zoa***) the correct scientific term for the male ***gamete***, often referred to by the lay term "sperm."

Spermiation The process whereby ***spermatozoa*** are released from the ***seminiferous epithelium*** into the lumen of the ***seminiferous tubules*** of the ***testis***.

Spermiogenesis The highly complex process of differentiation whereby the ***round spermatid*** becomes a ***spermatozoon***.

Sperm maturation A final process of maturation that spermatozoa undergo during passage through the ***epididymis***. Unless this process is completed, spermatozoa are unable to ***fertilize oocytes*** via a normal process of ***fertilization***, even *in vitro*.

Sterility The condition of being completely incapable of conceiving a child.

Stimulation The process by which multiple ***follicles*** are stimulated to grow, using ***gonadotrophin*** hormones, in a woman's ovaries in a single cycle so that multiple oocytes can be collected for ***IVF***. More correctly, this process should be referred to as ***controlled ovarian hyperstimulation*** (COH).

TESE See ***testicular sperm extraction***.

Testicular sperm Extraction A procedure whereby ***spermatozoa*** are retrieved from homogenized tissue obtained by ***testis biopsy***.

Teratozoospermia A medical term often used to described poor sperm morphology. 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 ***oligoasthenoteratozoospermia*** and ***Teratozoospermia Index***.

Teratozoospermia index Index of the degree of sperm abnormality. A high **TZI** value is highly predictive of sperm dysfunction and hence impaired fertilizing ability.

Total quality management A management philosophy that combines ***quality control***, ***quality assurance*** and ***quality improvement*** into a continuous, holistic process of achieving and improving upon best practice by iterations of the ***quality cycle***.

TQM See ***total quality management***.

Transcription The copying of a strand of ***DNA*** (or a part of one, e.g. a gene), by a transcriptase enzyme, to make messenger ***RNA***.

Transgenic An organism whose genotype has been modified by the insertion of a ***gene*** from another to produce individuals with one or more desired characteristics or traits.

Translation The decoding of a strand of ***RNA*** to produce a protein or "gene product."

Translocation A genetic defect caused by the transfer of a part of one ***chromosome*** with, or onto another. This abnormality may be balanced, if parts of two chromosomes are exchanged so that the individual has a complete set of genetic information, but if any part is missing or a third copy of any part is present then it is unbalanced and can cause a problem.

Triploid An abnormal genetic state caused by the combination of three haploid sets of ***chromosomes*** at ***fertilization***, usually revealed by the presence of three ***pronuclei*** in the ***zygote*** (typically caused by ***dispermy***), althpugh it can also be caused by ***diplospermy*** or retention of the ***second polar body***.

Trisomy A genetic defect caused by the presence of third copy of a ***chromosome*** (e.g., ***Down syndrome***).

Trophoblast The outer layer of cells of the ***blastocyst*** that will, after ***implantation***, give rise to the extra-embryonic membranes.

TZI ***Teratozoospermia Index***

Xenotransplantation The transplantation of tissues or organs between different species (e.g., pig and human).

X- and Y-bearing Spermatozoa Spermatozoa carrying ***X chromosomes*** will produce female offspring at ***fertilization***, while sperm carrying Y-chromosomes will produce male offspring (since all oocytes carry only the X chromosome).

Zona pelludica The glycoprotein structure that surrounds the ***oocyte***.

ZP See ***zona pellucida***.

ZP3 Zona protein 3, a glycoprotein that is believed to be the sperm receptor in the ***zona pellucida***.

Zygote The scientific term for a fertilized ***oocyte*** which then undergoes ***cleavage*** to form the 2-cell ***embryo*** or conceptus.

ABREVIATIONS AND ACRONYMS

PROVIDED BY DAVID MORTIMER, PhD, OOZOA 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 Reproduction 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)
DMSO	Dimethylsulphoxide (a cryoprotectant used for freezing embryos)
ET	Embryo Transfer
FET	Frozen Embryo Transfer
FF	Follicular Fluid (see also hFF)
GEYC	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	Hydroxyethylpiperazine ethanesulphonic acid, a zwitterionic buffer used in culture media so that elevated carbon dioxide levels are not required to maintain their pH
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 Patrick Quinn)
HZA	Hemi-Zona Assay (a variant sperm-zona binding test, see also ZBT)
IBT	Immunobead Test
ICSI	Intracytoplasmic Sperm Injection
IUI	Intra-Uterine Insemination
IVF	*In-vitro* Fertilization
IVF-ET	*In-vitro* Fertilization and Embryo Transfer
MSDS	Material Safety Data Sheet
OPU	Oocyte Pick-Up or retrieval
PCT	Post-Coital Test
PN	Pronucleus
PrOH	Propanediol (a cryoprotectant used for freezing embryos)
PVP	Polyvinylpyrrolidone
ROS	Reactive Oxygen Species (free radicals)
SCMC	Sperm-Cervical Mucus Contact test
SFA	Sperm Functional Assessment = Genesis-standard semen analysis
SMIT	Sperm Mucus Interaction Test (usually *in-vitro*, c/f. PCT)
SPA	Sperm Penetration Assay (synonymous with HEPT)
TDI	Therapeutic Donor Insemination (see DI)
Test-Yolk	See TYG
TYG	TEST-yolk-glycerol, a common cryoprotectant for semen
TW	Trial Wash, a pre-treatment sperm assessment including sperm preparation
TZI	Teratozoospermia Index, an assessment used in sperm morphology
US	Ultrasound; sometimes USS = 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)

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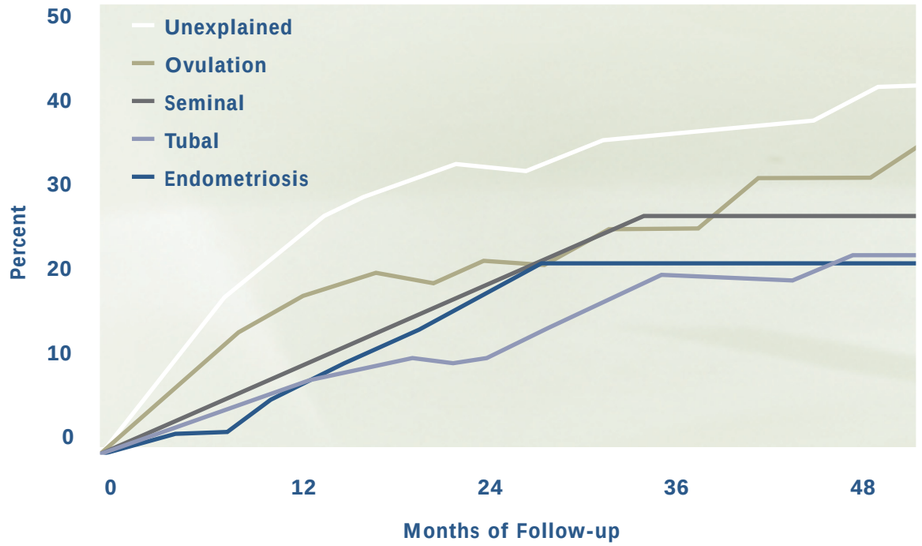
Unexplained Infertility Prognosis

LIVE BIRTH CONCEPTIONS, VARIOUS INFERTILITY DIAGNOSES



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