Fertility and Conception: Changes During the Past 30 Years Support the Need for Naturopathic Care

Dr. Pamela Frank, ND, Dr. Amber Moore, ND, Dr. Stefanie Trowell, ND and Dr. Morgan Winton, ND

Research on U.S. and Canadian populations indicates that all aspects of procreation, from conception through delivery, have been in a state of unfavourable decline over the last 30 years. Declining sperm counts, increasing ovulatory dysfunction, miscarriage and rising rates of caesarean section rates prevail. As naturopathic doctors, understanding the pathophysiology behind the deterioration in human reproduction will enhance our ability to counter societal, environmental and lifestyle factors that are contributing to our waning ability to reproduce.

Fertility Rates

The definition of infertility may involve some intentional form of family planning or only require unsuccessful conception after a set period of time. Typically in Canada, and for the purposes of this article, the term "infertility" refers to a lack of conception after a period of sexual intercourse without contraception (12 months for women who are under 35 years, 6 months for women over 35 years). Regardless of the definition used, the prevalence of infertility is undoubtably increasing. In fact, infertility affects approximately 16% of Canadian couples.^{19,20} This is nearly double the prevalence of infertility 20 years ago (8.5% in 1992) and triple that of 30 years ago (5.4% in 1984).²⁰ It is estimated that infertility affects over 1.25 million couples in Canada,²¹ a very unfavourable trend in both the male and female population.

Male Factor Infertility

In spite of the focus on female factor infertility, male factor infertility accounts for almost half of infertility cases.¹ During the past 50 years, sperm levels have declined from 113 million/mL in 1940 to 66 million/mL in 1990.² There are several theories to this multifactorial problem, most significantly the role of estrogens in the environment, the effect of oxidative stress on spermatogenesis, and the increase in sexually transmitted disease.³

Researchers from Washington State University have recently reported seeing effects on sperm from environmental estrogens, such as estradiol and biphenol A (BPA) exposure. Significant quantities

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of estradiol are found in the urine of women on oral contraceptives, which then passes through waste systems untreated and into our tap water.⁵ Certain herbicides and pesticides contribute to xenoestrogen exposure. BPA has also been shown to disrupt thyroid hormones, suppress aromatase activity, and act as an androgen antagonist.⁴ Men with detectable urine BPA had more than four times the risk of lower sperm count and more than twice the risk of lower sperm motility.⁶ Once an egg was fertilized by the sperm in question, development to blastocyst and pregnancy rates seemed to be the same regardless of whether the sperm was from men with or without high urinary BPA.7 This is contrary to the fact that we have seen that high urinary BPA can result in higher than average DNA fragmentation in sperm.⁷ With the use of assisted reproductive techniques, including in-vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), the effect of BPA on sperm can be overcome.7 Of course this doesn't help those trying naturally to conceive. Phthlates are another very common chemical that people are exposed to on a daily basis which can decrease all sperm parameters.8

Low intake of dietary folic acid and zinc were correlated with lower motility, low vitamin E with poor morphology, and lower overall antioxidant intake was associated with poor sperm concentration and motility. Overall sperm concentration in the lower dietary antioxidant intake group was 28.6 million/mL vs 50.77 million/mL in the higher intake group, percent motility was 29.5 vs 59.4 and percent normal morphology was 38.4 vs 50.9.¹⁰ Positive associations were also observed between dietary vitamin C intake and overall sperm count and concentration, between dietary vitamin E and motility, and between dietary beta-carotene and sperm concentration and motility.¹⁰ There is a positive association between dietary intakes of vitamin C, lycopene, and beta-carotene on motility. Furthermore, overall semen volume increased with higher dietary intakes of vitamin C.^{10,11}

The consumption of high fat foods, such as full fat dairy and meats may hurt sperm results due to the increased presence of lipophilic xenoestrogens which can concentrate in higher fat foods, whereas increasing fruits and vegetables was shown to help semen parameters. All parameters except total semen volume were better in the lower fat/higher fruit and vegetable group, most notably the percent of normal sperm morphology for the high fat group was about 3.7% compared with 22.3% in the lower fat/higher fruit and vegetable diet group.¹² Trans-fat consumption is inversely linked to overall lower semen parameters, including ejaculate volume. The lowest trans-fat consumers had on average 100 million sperm/mL whereas the highest trans-fat group had 3 million sperm/mL.¹³

Studies show that anti-oxidant supplementation can improve pregnancy rates and live birth rates in couples at fertility clinics.¹⁴ More specifically, taking vitamin E 400 mg every day and selenium 225 mcg every day for 3 months improved sperm motility.¹⁵ A metaanalysis of CoEnzyme Q-10 (ubiquinol) supplementation showed an overall increase in sperm seminal concentration and motility.¹⁶ Furthermore in 2012, a study showed that using 200 mg every day of ubiquinol for 26 weeks increased sperm concentration by 81.6%, motility by 31.7% and morphology by 24%.¹⁷ Taking 200 mcg of selenium plus 600 mg N-acetyl-cysteine every day showed a statistically significant increase in concentration, motility, and morphology of sperm.¹⁸

Female Factor Infertility

The female contributes significantly to the fecundity of the couple, and when comparing the prevalence of infertility in female partners over the past 3 decades, the numbers are on the rise. In 1984, a woman had about a 5% chance of experiencing infertility regardless of reproductive age; however in 2010, women aged 18 to 29 years had a 7.0-13.7% risk of infertility while women aged 40 to 44 years had a 14.3-20.7% risk.^{19,20} The impact of this number grows substantially when we consider that female factors account for nearly 50% of infertility cases.²¹ Female infertility can be grouped into 3 categories: ovulatory dysfunction, tubal pathology and pelvic concerns. Of these, ovulation dysfunction contributes considerably to female infertility and has been markedly affected by lifestyle changes by Canadian women.

Ovulation disorders account for 40% of female factor infertility.²² The possible causes of dysfunctional ovulation include: aging, diminished ovarian reserve, endocrine disorders, polycystic ovary syndrome (PCOS) and lifestyle modifiers (e.g., tobacco use, alcohol intake, unhealthy weight and diet). Of these causes, there have been numerous trends over the years that are unfavourable for female fertility.

The past few decades have seen an increase in maternal age when attempting first pregnancy. Female age as a risk factor for infertility is well understood, with female fertility declining precipitously after the age of 35.^{23, 24} Delayed childbearing may be due to a rise in the number of women earning higher education or joining the paid workforce; however, irrespective of cause, both males and females are waiting longer before marriage or cohabitation. The result is an increased proportion of first-born children among women aged 35 and over, from 3% in 1984 to 11% in 2011^{20,21} and over 380,000 couples seeking medical assistance for conception.²⁰ The answer to this age problem is far from clear cut. Women should attempt conception earlier in their reproductive years; however, until financial security and career growth favour young mothers, this trend is unlikely to change in the foreseeable future without more education for women regarding factors that affect their fertility.

In addition to the impact of advanced female age, modifiable factors such as obesity have been shown to adversely affect female fertility. This is particularly relevant for Canadian women, as 45% are considered overweight, with nearly 20% of those women being obese - more than 5 times that in 1981.^{24,25} Excess weight affects reproductive functioning women from the hypothalamus to the ovarian follicle. Additionally, obese women are 3 times more likely to suffer infertility than women with a normal body mass index (BMI).²⁶

However, it is not all bad news for Canadian women. The percentage of women achieving moderate physical activity levels has increased over the past ten years, from 43 to 52%.²⁷ During this time, average daily energy intake has reduced slightly (the calories equate to that in a large banana), which should equate to a relative negative caloric balance, but this follows a decade of indulgence and women continue to eat more calories than they expend. From 1991 to 2002, daily energy intake increased 18%, with fat consumption increasing the most.^{28,29} Similarly, carbohydrate intake increased 18%, primarily in the form of pasta, specialty breads and cereal-based snacks.²⁹ This is a concerning trend since ovulatory infertility risk is increased with elevated consumption of processed carbohydrates and there has been a direct correlation observed between ovulatory infertility and consumption of high glycemic index foods.³⁰ Considering these dietary trends, a moderate level of activity appears inadequate for Canadian women to maintain a healthy BMI. In fact, obesity is the most modifiable risk factor for fertility and has been found to have the greatest impact among women younger than 35 years of age.³⁰

Ovulatory dysfunction is associated with other modifiable lifestyle choices, including smoking and alcohol use. The prevalence of smoking has been declining since the 1980s, from over 35 to 18% of Canadian women smoking cigarettes, with the proportion of heavy or moderate female smokers decreasing by more than 10% in the past decade alone.^{20, 31} This is significant as women who smoke are 1.6 times more likely to have fertility issues than non-smokers and are less likely to have successful IVF treatments.²⁰ Unfortunately, over the same time period, the prevalence of heavy drinking more than doubled amongst women aged 20–34 years, from 9 to 20% ^{20,32}. These factors, as well as excess body weight, promote free radical production and are thought to contribute to poor oocyte quality, DNA damage and female infertility.³³

Female factor fertility also involves the health of the fallopian tubes and other pelvic structures. Tubal factor infertility accounts for approximately 30% of female infertility cases²⁰ and of this, it is estimated that 64% is attributable to untreated *Chlamydia trachomatis* infections,²¹ a concerning finding since the chlamydial infection rate in Canada has increased 71% for women 20–24 years of age in the past 10 years.²⁰ The remaining 30% of causative factors for female infertility include endometriosis, uterine complications and cervical abnormalities.²⁰ These factors are affected, but associated to a lesser extent, by current trends in Canadian society and infertility risk factors previously discussed.

Miscarriage Rates

While there is some disparity when assessing miscarriage statistics over the years, research suggests that rates of miscarriage are on the rise in North America, increasing by approximately 1% per year.³⁴ Current estimations note that 15-20% of known pregnancies result

in miscarriage,³⁵ and women with a history of miscarriage are at higher risk of repeat miscarriages.³⁶ Some researchers speculate that increased use of home pregnancy tests and artificial reproductive technologies (ART) may have artificially elevated miscarriage rates by bringing increased awareness to early pregnancies and miscarriages that would have previously gone undetected³⁵ yet the likely influence of other factors must not be discounted.

The most common cause of miscarriage is chromosomal abnormalities, in part correlated to advanced maternal and paternal age.³⁷ The risk of miscarriage begins to rise in women after age 30, with increasing risk with advancing age;³⁹ paternal age appears to exhibit a similar trend.³⁸ A trend towards women having children later in life³⁹ suggests that this may have a role in rising miscarriage rates.

Modifiable lifestyle factors also contribute to pregnancy maintenance. Obesity research findings parallel that of infertility, with one metaanalysis showing a 67% increased chance of miscarriage with a BMI >25,40 whereas other research shows that being underweight also increases miscarriage risk.^{41,42} Observational research also suggests an increased risk of miscarriage with caffeine intake >200mg/day (equivalent to 1-2 cups of coffee or black tea),43 alcohol intake42 and cigarette smoke, both in active smokers and via second hand exposure.44,45 As described previously, there have been some significant changes in these factors that contribute to oxidative stress. Oxidant-induced endothelial damage is thought to play a role in spontaneous abortion by impairing placental vascularization and inducing phospholipid modifications.⁴⁶ These changes are linked to anti-phospholipid syndrome, a hyper-coagulability condition associated with recurrent miscarriage. Additionally, preliminary research has demonstrated an association between low vitamin B6 and early pregnancy loss.⁴⁷ Weight loss,⁴⁸ aerobic exercise⁴⁹ and fish oil⁵⁰ have been shown to decrease risk of miscarriage in those with identified thrombotic risk factors.

Stress and its effect on the immune system plays a major role in maintaining a pregnancy. Women with recurrent miscarriage appear to have higher Th1/Th2 ratios⁵¹ and an enhanced pro-inflammatory immune system response as evidenced by increases in TNF-alpha, IL-17⁵² as well as decreased immune regulation via Treg cells.⁵³⁻⁵⁵ A large U.S. population-based survey tracked individual's perceived stress between 1983 and 2009, finding we are up to 30% more stressed than society was 30 years ago. Women and those under age 35 were found to be at higher risk.⁵⁶ Positive associations between high stress and miscarriage have been shown in many studies.⁵⁷ Preliminary research suggests that corticotropin releasing hormone (CRH) and other stress hormones can cause uterine mast cell activation and resultant miscarriage.58 The role of adrenaline, noradrenaline and acetylcholine on uterine vascularization and contractility,⁵⁹ increased TNF-alpha and inflammation,⁶⁰ as well as the interplay between cortisol demands and progesterone values⁶¹ also have been proposed. Addressing mental health in patients going through a miscarriage is prudent. A large body of evidence suggests that miscarriage is associated with increased stress, anxiety and/or depression^{62,63} and that this risk may be lessened by counselling as well as exploration for cause of miscarriage.^{64,65}

Environmental endocrine disruptors and toxins have become increasingly prevalent in our modernizing society and could in part explain trends towards increased miscarriage rates. BPA is a known xenoestrogen and exposure has been correlated with an increased relative risk of miscarriage.⁶⁶ Observational studies also demonstrate some evidence that exposure to pesticides,⁶⁷ anaesthetic gases,⁶⁸ radiation,⁶⁹ certain industrial solvents and electromagnetic fields may confer increased risk,⁷⁰ albeit research is preliminary in this field.

Thyroid Function: T3 and T4 have direct stimulatory effects on trophoblast function⁷¹ and estrogen and progesterone release from placental tissue.⁷² Low thyroid function has been shown to increase miscarriage rates in a number of studies,⁷³ even with modestly increased TSH values >1.5mIU/ml.⁷⁴

Conventional treatments to prevent miscarriage include aspirin or heparin for proposed or diagnosed thrombophilia, human chorionic gonadotrophin (hCG), progesterone, immunotherapies including intravenous immunoglobulin and bed rest. Of these, only aspirin or heparin for diagnosed antiphospholipid syndrome⁷⁶ and progesterone for recurrent miscarriage⁷⁵ have good supported efficacy according to Cochrane reviews.

Natural Birth Rates

Despite the increased risks of maternal mortality and infant morbidity and mortality,⁷⁷ rates of caesarean delivery (CD) have steadily increased over the past 20 years and vary widely; on average anywhere from 16-60%⁷⁸ in developed nations. Such a wide variation in C-section rates would imply a lack of consensus as to which conditions warrant CD and that some of these surgical interventions may be unnecessary.

The rate of caesarean deliveries in Canada jumped from 17.5% of deliveries in 1994–1995 to 23.7% in 2002–2003^{79,80} and again grew to 28% in 2010-2011.⁸² The World Health Organization's recommended rate of caesarean delivery, published in 1985, is 10-15%.⁸³ The three primary reasons cited for CD were dystocia (abnormal or difficult labour and delivery), elective (including previous C-section) and breech presentation.⁸⁴ According to the National Consensus Conference on Aspects of Caesarean Birth, dystocia is the indication for approximately one-half of all primary caesarean sections.

Labour dystocia is an ill-defined term that is subject to interpretation. As the primary cause of caesarean section, dystocia warrants critical examination. Zhang et al. in 2010 demonstrated that labor progresses substantially slower than what was historically taught.⁸⁵ Their data indicated that labour may take over 6 hours to progress from 4 to 5 cm dilation and over 3 hours to progress from 5 to 6 cm dilation.⁸⁵ Despite this revised information, decisions about labour progression and management are still being based on Friedman's curve, a plot of cervical dilation that dates back to 1955.⁸⁶ Influences on labour progression include: unripe cervix, contracted pelvis, cervical scarring, macrosomia, fetal malposition, hypotonic or uncoordinated contractions, analgesia/anesthesia, fear and anxiety.⁸⁷





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Other contributing factors to caesarean delivery include: maternal obesity,⁸⁸ induction of labour (15% CD in induction vs 8% CD in spontaneous delivery),⁹⁴ thyroid autoimmunity (abnormal TSH/ positive anti-Tg)⁸⁹ women over 45 who conceived via ART,⁹⁰ anterior placental location, advanced maternal age,⁹¹ adenomyosis,⁹² acute maternal bleeding⁹³ and fetal indications such as fetal weight, multiple gestation, intra-uterine growth restriction, abnormal or indeterminate fetal heart rate, oligohydramnios, placental abruption, macrosomia and post-term pregnancy.^{94,95}

ADVANTAGES OF VAGINAL DELIVERY	DISADVANTAGES OF CAESAREAN SECTION		
1. Quicker recovery time and no scars (2 days or less hospitalization vs 4 for c-section)	1. Greater risk of pre-term delivery and concomitant complications for the infant		
2. Lower mortality risk for the mom and infant ^{99, 102}	2. Increased risk of complications of anesthesia, puerperal infection, and venous thromboembolism ⁹⁹		
 Lower risk of iatrogenic complications¹⁰² Birth occurs on the baby's schedule, when he or she is physically ready 	 Higher maternal mortality (3.6 times higher after caesarean than after vaginal delivery)⁹⁹ and infant mortality (69% increase¹⁰²) Greater risk of post-partum depression (more than six times the risk of developing postnatal depression three months 		
 Vaginal birth allows the child to acquire normal flora at delivery Better maternal-infant bonding and lower risk of post-partum depression¹⁰⁰ 			
	 postpartum¹⁰³) Greater likelihood of subsequent caesarean deliveries. In subsequent pregnancies, although there is a small risk of uterine rupture, blood transfusion and hysterectomy, women who attempt vaginal birth after caesarean have a much lower rate of mortality than women who have a subsequent elective caesarean. 		
	6. Greater incidence of allergies and asthma in children delivered by c-section ¹⁰¹		

Conclusion

The unfavourable trends for fertility, miscarriage and delivery witnessed over the past 30 years suggest the growing need for practitioners to prudently assess and treat hopeful parents with a slightly different emphasis than perhaps was done previously. Many of the factors negatively affecting procreation are lifestyle and environmental in nature; our modern world is affecting our waist sizes, stress levels, diet composition, toxin exposure and age of first conception, to name a few factors. Foundational naturopathic care for fertility involves appropriate investigation and intervention to address such risk factors, and highlights our integral role as health educators to maximize chances of successful reproduction.

Recommendations:

There are many specific treatments that reach beyond the scope of this article that would be indicated in treating infertility, reducing risk of miscarriage and encouraging a healthy labour. However, following are some key areas to assess for reproductive success.

NATUROPATHIC RECOMMENDATIONS TO	PRECONCEPTION & FERTILITY			
ADDRESS CHANGING CANADIAN HEALTH TRENDS	Male	<u>Female</u>	PREGNANCY	LABOUR & DELIVERY
Educate patients regarding importance of family planning at a younger age	age-related infertility	age-related infertility	miscarriage risk	
Counsel patients on proper nutrition, diet and exercise to achieve healthy BMI	sperm motility & morphology	oocyte quality & quantity	miscarriage risk	maternal weight affects type of delivery
Emphasize importance of practicing safe sex as a young adult and gynecological screening exams (especially STI swabs)	lowering sperm counts	tubal factor infertility		
Reduce exposure to environmental toxins, sources of BPA and xenoestrogens	sperm concentration & motility	endocrine disruption of ovulation	miscarriage risk	
Encourage healthy lifestyle choices, notably: - avoiding exposure to cigarette smoke - reducing consumption of alcohol	oxidative damage to sperm	oxidative damage to oocytes	risk of spontaneous miscarriage	
Screen for mental health concerns, such as high stress, anxiety or depression.	age-related infertility	oocyte quality & quantity	correlated with miscarriage	
Consider naturopathic intervention (e.g. nutraceutical, herbal, acupuncture) to improve hormone balance and fecunditity.	emphasis on antioxidants & specific nutrient deficiencies			
Evaluate thyroid function (TSH and anti-thyroglobulin antibodies) and treat discrepancies.		ovulatory dysfunction	TSH > 1.5-2 associated with miscarriage	Re-assess at 15-28 weeks gestation
Recommend doula care - the odds of non-indicated caesarean were 80-90% lower among doula-supported women. ¹⁰⁵				
Educate patients as to normal gestation period (particularly for nulliparous) and labour progression. Encourage women to labour in an upright position. ¹⁰⁴				reduce induction & caesarean deliveries
Recommend moxibustion at BL67 between 33-35 weeks gestation in women with breech presentation. ^{97,98}				

About the Authors

Pamela Frank, BSc (Hons), ND has 15 years of experience as a naturopathic doctor and 20 years as a medical laboratory technologist. She is Clinic Director of Forces of Nature Wellness in Toronto and was twice voted "Best Naturopath in Toronto". Pamela maintains a busy practice with particular expertise in women's health issues including natural conception and fertility. Other passions include her family, tennis, running, cycling, ballroom dancing, and healthy cooking. For more information www.NaturopathToronto.ca.

Stefanie Trowell, ND is a licensed naturopathic doctor practicing in Toronto, Ontario. After graduating from the Canadian College of Naturopathic Medicine, she achieved acceptance into the competitive Clinical Residency program, which has placed Stefanie at the heart of evidence-based medicine and research. In addition to her work at the College, Stefanie enjoys seeing patients in her private practice. She is passionate about optimizing health through prevention and management of chronic disease, with a special interest in fertility and cancer care, especially breast cancer. Prior to moving to Toronto, Stefanie graduated from the University of Saskatchewan with a High Honours Bachelors of Science in Physiology, where she assisted with research in neuroscience, endocrinology and reproduction. Stefanie now focuses her analytical brain and problem-solving skills on the complexity of hormonal health in women. She is a dedicated and caring doctor with a gentle approach who is committed to the health of her patients For more information, visit www.stefanietrowellnd.com.

Amber Moore, ND is a graduate of the Canadian College of Naturopathic Medicine (CCNM), and is currently in the process of completing her clinical residency at CCNM. She is the cofounder of Nourish Integrative Health in midtown Toronto, a naturopathic clinic catering to the needs of women with a focus on infertility and breast cancer. Amber strives to be an advocate for her patients by employing a collaborative approach with a patient's health care team, and strongly believes in empowering her patients through health education. She has received additional training in women's health and naturopathic oncology during her clinical residency, and is licensed in intravenous therapy to provide comprehensive naturopathic care. For more information, visit www.nourishtoronto.com.

Morgan Winton, ND is a naturopathic doctor who has been practicing in Toronto's downtown core for over 10 years. She maintains a general practice, but has a special interest in fertility. She can be reached through her website at www.morganwinton.com.

Please see following page for References.

References

- Kumalic S, Pinter B. Review of Clinical Trials on Effects of Oral Antioxidants on Basic Semen and Other Parameters in Idiopathic Oligoasthenoteratozoospermia. *Biomed Res Int.* 2014: 426951
- Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. BMJ. 1992 Sep 12; 305(6854): 609-613. 2.
- Nat Rev Urol. 2014; advance online publication 21 October 2014; doi:10.1038/nrurol.2014.285
- Galloway T, Cipelli R, Guralnik J, et al. Daily Bisphenol A Excretion and Associations with Sex Hormone Concentrations: Results from the InCHIANTI Adult Population Study. *Environ Health Perspect*. 2010;118(11):1603-1608. 4.
- Vrooman LA, Oatley JM, Griswold JE, Hassold TJ, Hunt PA. Estrogenic Exposure Alters the Spermatogonial Stem Cells in the Developing Testis, Permanently Reducing Crossover Levels in the Adult. *PLoS Genet* 11(1): e1004949. doi: 10.1371/journal.pgen.1004949
- Li DK, Zhou Z, Miao M, et al. Urine bisphenol-A (BPA) level in relation to semen quality. Fertil Steril. 2011 Feb;95(2):625-30.e1-4. 6.
- Knez J, Kranvogl R, Breznik BP, Vončina E, Vlaisavljević V. Are urinary bisphenol A levels in men related to semen quality and embryo development after medically assisted reproduction? *Fertil Steril*. 2014 Jan;101(1):215-221.e5 7.
- Duty SM, Silva MJ, Barr DB, et al. Phthalate exposure and human semen parameters. *Epidemiology*. 2003 May;14(3):269-77. 8.
- Goldstone AE, Chen Z, Perry MJ, Kannan K, Louis GM. Urinary bisphenol A and semen quality, the LIFE Study. Reprod Toxicol. 2014 Nov 11;51C:7-13 9.
- Nadjarzadeh A, Mehrsai A, Mostafavi E, Gohari MR, Shidfar F. The association between dietary antioxidant intake and semen quality in infertile men. *Med J Islam Repub Iran.* 2013 Nov;27(4):204-9. Mínguz-Alarcón L, Mendiola J, López-Espín JJ, et al. Dietary intake of antioxidant nutrients is associated with semen quality in young university students. *Hum Reprod.* 2012 Sep;27(9):2807-14
- 12. Eslamian G, Amirjannati N, Rashidkhani B, Sadeghi MR, Hekmardoost A. Intake of food groups and idiopathic asthenozoospermia: a case-control study. *Hum Reprod.* 2012 Nov;27(11):3328-36.
- Chavarro JE, Mínguez-Alarcón L, Mendiola J, et al. Trans fatty acid intake is inversely related to total sperm count in young healthy men. *Hum Reprod.* 2014 Mar;29(3):429-40.
- Showell MG, Brown J, Yazdani A, Stankiewicz MT, Hart RJ. Antioxidants for male subfertility. *Cochrane Database Syst Rev.* 2011 Jan 19;(1)
- Keskes-Ammar L, Feki-Chakroun N, Rebai T, et al. Sperm oxidative stress and the effect of an oral vitamin E and selenium supplement on semen quality in infertile men. Arch Androl. 2003 Mar-Apr;49(2):83-94.
- Lafuente R, González-Comadrán M, Solà I, López G, Brassesco M, Carreras R, Checa MA. Coenzyme Q10 and male infertility: a meta-analysis. J Assist Reprod Genet. 2013 Sep;30(9):1147-56
- Nadjarzadeh A, Shidfar F, Amirjannati N, et al. Effect of Coenzyme Q10 supplementation on antioxidant enzymes activity and oxidative stress of seminal plasma: a double-blind randomised clinical trial. Andrologia. 2014 Mar;46(2):177-83
- Safarinejad MR, Safarinejad S. Efficacy of selenium and/or N-acetyl-cysteine for improving semen parameters in infertile men: a double-blind, placebo controlled, randomized study. J Urol. 2009 Feb;181(2):741-51 Bushnik T, Cook JL, Yuzpe AA, Tough S, Collins J. Estimating the prevalence of infertility in Canada. Hum Reprod. 2012: 27(3), 738–746.
- Tudiver S. Exploring Fertility Trends in Canada through a Gender Lens. Health Policy Research Bulletin. Health Canada, 2005: May (10); 7-10.
- 21. Bope ET, Kellerman RD. Conn's Current Therapy 2015. Elsevier, Inc. 2014. Accessed via Clinical Key.
- Aiken R J. Age, the environment and our reproductive future: linking baby boomers and the future of sex. *Reproduction*. 2014: 147, S1-11.
- Senzilet L, McCall D, Theriault J. Reproduction at Older Ages: The Health Implications. Health Policy Research Bulletin. Health Canada, 2005: May (10); 15-20.
- 24. Public Health Agency of Canada. Obesity in Canada. 2011. Available at: www.phac-aspc.gc.ca/hp-ps/hl-mvs/oic-oac/ adult-eng.php (1 February 2015, date last accessed). Statistics Canada. Overweight and obese adults (self-reported), 2012. catalogue no. 82-625-X 2013.(1 February 2015, date last accessed).
- Brewer CJ, Balen AH. Focus on Obesity: The adverse effects of obesity on conception and implantation. *Reproduction*. 2010: 140 (3) 347-364.
- 27. Statistics Canada. Physical activity during leisure time, 2012. catalogue no. 82-625-X 2013.(1 February 2015, date st accessed).
- Agriculture and Agri-Food Canada. The Canadian Consumer Behaviour, Attitudes and Perceptions Toward Food Products. Government of Canada. 2010. Available at: www.ats-sea.agr.gc.ca/can/5505-eng.htm#b (28 January 2015, date last accessed)
- Peng Y. Canadian Consumer Trends in Obesity and Food Consumption. Alberta Agriculture, Food and Rural Development, 2004. Available at: www1.agric.gov.ab.ca/\$department/deptdocs.nsf/all/sis8438 (28 January 2015, date last accessed)
- Jungheim ES, Travieso JL, Hopeman MM. Weighing the impact of obesity on female reproductive function and fertility. Nutr Rev. 2013: 71(0 1).
- Statistics Canada. Health at a Glance: Current smoking trends. catalogue no. 82-624-X 2012. (1 February 2015, date last accessed).
- Statistics Canada. Heavy drinking, 2013. catalogue no. 82-625-X. 2014. Available at: www.statcan.gc.ca/pub/82-625-x/2014001/article/14019-eng.htm (1 February 2015, date last accessed). Agarwal A, Aponte-Mellado A, Premkumar BJ, Shaman A, Gupta S. The effects of oxidative stress on female reproduction: a review. *Reprod Biol Endocrin*. 2012; 10, 49.
- Lang K, Nuevo-Chiquero A. Trends in self-reported spontaneous abortions: 1970-2000. Demography. 2012; 49(3), 989-1009.
- American College of Obstetricians and Gynecologists. Management of recurrent pregnancy loss. Int J Gynecol Obstet. 2002; 78(2),179-190.
- 36. Suzumori N, Sugiura-Ogasawara M. Genetic factors as a cause of miscarriage. Curr Med Chem. 2010; 17(29), 3431-7. 37. Risch HA, Weiss NS, Clarke EA, Miller AB. Risk factors for spontaneous abortion and its recurrence. Am J Epidemiol.
- 1988; 128(2), 420-30 Kleinhaus K, Perrin M, Friedlander Y, Paltiel O, Malaspina D, Harlap S. Paternal age and spontaneous abortion. Obster Gynecol. 2006; 108(2), 369-77.
- Mathews TJ, Hamilton BE. Delayed childbearing: more women are having their first child later in life. Center for Disease Control and Prevention: NCHS Data Brief. 21. (2009 Aug).
- Metwally M, Ong KJ, Ledger WL, Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. *Fertil Steril.* 2008 Sep; 90(3), 714-26.
- Arck P, Rucke M, Rose M, et al. Early risk factors for miscarriage: a prospective cohort study in pregnant women. *Reprod Biomed Online*. 2008 Jul; 17(1), 101-13.
- Maconochie N, Doyle P, Prior S, Simmons R. Risk factors for first trimester miscarriage--results from a UK-population-based case-control study. BJOG-Int J Obstet Gy. 2007 Feb;114(2), 170-86.
- Weng X, Odouli R, Li DK. Maternal caffeine consumption during pregnancy and the risk of miscarriage: a prospective cohort study. Am J Obstet Gynecol. 2008 Mar; 198(3), 279.
- George L, Granath F, Johansson AL, Annerén G, Cnattingius S. Environmental tobacco smoke and risk of spontaneous abortion. *Epidemiology*. 2006 Sep; 17(5), 500-5. Blanco-Muñoz J, Torres-Sánchez L, López-Carrillo L. Exposure to maternal and paternal tobacco consumption and risk of spontaneous abortion. *Public Health Rep.* 2009 Mar; 124(2), 317-22.
- Gupta S, Agarwal A, Banerjee J, Alverez JC. The role of oxidative stress in spontaneous abortion and recurrent pregnancy loss: a systematic review. Obstet Gynecol Surv. 2007 May; 62(5), 335-47.
- Ronnenberg AG, Venners SA, Xu X, Chen C, et al. Preconception B-vitamin and homocysteine status, conception, and early pregnancy loss. Am J Epidemiol. 2007 Aug; 166(3), 304-12.
- De Pergola G, Pannacciulli N. Coagulation and fibrinolysis abnormalities in obesity. J Endocrinol Invest. 2002 Nov; 25(10), 899-904.
- Hilberg T, Norwacki PE, Müller-Berghaus G, Gabriel HH. Changes in blood coagulation and fibrinolysis associated with maximal exercise and physical conditioning in women taking low dose oral contraceptives. J Sci Med Sport. 2000 Dec; 3(4), 383-90.
- Lazzarin N, Vaquero E, Exacoustos C, et al. Low-dose aspirin and omega-3 fatty acids improve uterine artery blood flow velocity in women with recurrent miscarriage due to impaired uterine perfusion. *Fertil. Steril.* 2009 Jul; 92(1), 296-300.

- Kheshtchin N, Gharagozloo M, Andalib A, et al. The expression of Th1- and Th2-related chemokine receptors in we with recurrent miscarriage: the impact of lymphocyte immunotherapy. Am J Reprod Immunol. 2010; 64, 104–112
- El-Far M., El-Sayed IH, El-Motwally Ael-G, et al. Tumor necrosis factor-alpha and oxidant status are essential participating factors in unexplained recurrent spontaneous abortions. *Clin Chem Lab Med.* 2007; 45(7), 879-83.
- Lee SK, Kim JY, Hur SE, et al. An imbalance in interleukin-17-producing T and Foxp3 regulatory T cells in women with idiopathic recurrent pregnancy loss. *Hum Reprod.* 2011 Nov; 26(11), 2964-71.
- Winger EE, Reed JL. Low circulating CD4(+) CD25(+) Foxp3(+) T regulatory cell levels predict miscarriage risk in newly pregnant women with a history of failure. *Am J Reprod Immunol.* 2011 Oct; 66(4), 320-8. Lee SK, Kim JY, Lee M, et al. Th17 and regulatory T cells in women with recurrent pregnancy loss. Am J Reprod Immunol. 2012 Apr; 67(4), 311-8.
- Cohen S, Jacnicki-Deverts D. Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, 2006, and 2009. J Appl Soc Psychol. 2012; 42(6), 1320–34.
- Neugebauer R, Kline J, Stein Z, et al. Association of stressful life events with chromosomal normal spontaneous abortion. Am. J. Epidemiol. 1996; 143(6), 588-96.
- Madhappan B, Kempuraj D, Christodoulou S, et al. High levels of intrauterine corticotropin-releasing hormone, urocortin, tryptase, and interleukin-8 in spontaneous abortions. *Endocrinology*. 2003 Jun; 144(6), 2285-90.
- Läpple M. Stress as an explanatory model for spontaneous abortions and recurrent spontaneous abortions. Zentralbl Gynakol. 1998; 110(6), 325-35.
- 60. Craig M. Stress and recurrent miscarriage. Stress. 2001 Sep; 4(3), 205-13.
- Arck P, Hansen PJ, Jericevic B, Piccinni MP, Szekeres-Bartho J. Progesterone during pregnancy: endocrine-immune cross talk in mammalian species and the role of stress. *Am J Reprod Immunol*. 2007; 58, 268–279.
- 62. Brier N. Anxiety after miscarriage: a review of the empirical literature and implications for clinical practice. Birth. 2004 Jun; 31(2), 138-42.
- Neugebauer R, Kline J, Shrout P, et al. Major depressive disorder in the 6 months after miscarriage. JAMA. 1997 Feb; 277(5), 383-8.
- Nikewic AV, Kuczmierczyk AR, Nicolaides KH. The influence of medical and psychological interventions on women's distress after miscarriage. J Psychosom Res. 2007 Sep; 63(3), 283-90.
- Nikcevic AV, Tunkel SA, Kuczmierczyk AR, Nicolaides KH. Investigation of the cause of miscarriage and its influence on women's psychological distress. Br J Obstet Gynaecol. 1999 Aug; 106(8), 808-13. 66. Lathi RB, Liebert CA, Brookfield KF, et al. Conjugated bisphenol A in maternal serum in relation to miscarriage risk.
- Fertil Steril, 2014 Jul; 102(1), 123-8. Blanco-Muñoz J, Aguilar-Garduño C, Gamboa-Avila R, et al. Association between PON1 genetic polymorphisms and miscarriage in Mexican women exposed to pesticides. *Sci Total Environ.* 2013; 449, 302-8.
- Boivin JF. Risk of spontaneous abortion in women occupationally exposed to anaesthetic gases: a meta-analysis. Occup Environ Med. 1997 Aug; 54(8):541-8.
- Shirangi A, Fritschi L, Holman CD. Maternal occupational exposures and risk of spontaneous abortion in veterinary practice. Occup Environ Med. 2008 Nov; 65(11), 719-25.
- Patelarou E, Kelly FJ. Indoor exposure and adverse birth outcomes related to fetal growth, miscarriage and prematurity—a systematic review. Int J Environ Res Public Health. 2014 Jun; 11(6), 5904-33.
- Maruo T, Matsuo H, Mochizuki M. Thyroid hormone as a biological amplifier of differentiated trophoblast function in early pregnancy. Acta Endocrinol (Copenh). 1991 Jul; 125(1), 58-66. Matuo H, Maruo T, Hayashi M, Mochizuki M. Modification of endocrine function of trophoblasts by thyroid hormone. Nihon Sanka Fujinka Gakkai Zashi. 1991 Nov; 43(11), 1533-8.
- Negro R, Schwartz A, Gismondi R, et al. Increased pregnancy loss rate in thyroid antibody negative women with TSH levels between 2.5 and 5.0 in the first trimester of pregnancy. *The Journal of Clinical Endocrinology & Metabolism.* 2010; 95(9), 44-48.
- Benhadi N, Wiersinga WM, Reitsma JB, et al. Higher maternal TSH levels in pregnancy are associated with increased risk for miscarriage, fetal or neonatal death. *Eur J Endocrinol*. 2009 Jun; 160(6), 985-91.
- 75. Haas DM, Ramsey PS. Progestogen for preventing miscarriage. Cochrane Database Syst Rev. 2013;10.
- de Jong PG, Kaandorp S, Di Nisio M, et al. Aspirin and/or heparin for women with unexplained recurrent miscarriage with or without inherited thrombophilia. *Cochrane Database Syst Rev.* 2014;7.
- Xie RH, Gaudet L, Krewski D, Graham ID, Walker MC, Wen SW. Higher Cesarean Delivery Rates are Associated with Higher Infant Mortality Rates in Industrialized Countries. *Birth.* 2015 Jan 17. Visser GHA. Women Are Designed to Deliver Vaginally and Not by Cesarean Section: An Obstetrician's View. Neonatology 2015; 107:8-13
- 79. Canadian Perinatal Health Report. 2003. Ottawa: Minister of Public Works and Government Services Canada; 2003.
- Health system performance. Health Indicators. Catalogue no. 82-221-XIE, Volume 2005, No. 3, Ottawa: Canadian Institute for Health Information; 2005.
- 81. Canadian Institute of Health Information (CIHI), Discharge Abstract Database.
- 82. Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2010. Natl Vital Stat Rep. 2011;60(2):1-25.
- 83. World Health Organization. Appropriate technology for birth. Lancet. 1985; 2: 436-7. 84. SOGC Clinical Practice Guidelines, No 296, Sept 2013.
- Zhang, J, Landy HJ, Branch, W, et al. Contemporary Patterns of Spontaneous Labor With Normal Neonatal Outcomes. Obstet Gynecol. 2010 Dec; 116(6): 1281–1287.
- 86. Friedman EA. Primigravid labor; a graphicostatistical analysis. Obstet Gynecol. 1955 Dec; 6(6):567-89.
- Kutlesić M, Kutlesić R. Epidural analgesia in labor: specific characteristics, dilemmas and controversies. Med Pregl. 2012 Sep-Oct;65(9-10):441-7.
- Dubourdeau AL, Berdin A, Mangin M, Ramanah R, Maillet R, Riethmuller D. Obesity and primiparity: Risky delivery? J Gynecol Obster Biol Reprod (Paris). 2015 Jan 17. pii: S0368-2315(14)00319-6. Saki F, Dabaghmanesh MH, Ghaemi SZ, Forouhari S, Omrani GR, Bakhshayeshkaram M. Thyroid autoimmunity in pregnancy and its influences on maternal and fetal outcome in Iran (a prospective study). *Endocr Res.* 2014 Oct 20:1-7.
- D. Jackson S. Hong C., Wang ET, Alexander C, Gregory KD, Pisarska MD. Pregnancy outcomes in very advanced maternal age pregnancies: the impact of assisted reproductive technology. *Fertil Steril*. 2015 Jan;103(1):76-80.
- Schimmel MS, Bromiker R, Hammernan C, et al. The effects of maternal age and parity on maternal and neonatal outcome. Arch Gynecol Obstet. 2014 Sep 17.
- Mochimaru A, Aoki S, Oba MS, Kurasawa K, Takahashi T, Hirahara F. Adverse pregnancy outcomes associated with adenomyosis with uterine enlargement. J Obstet Gynaecol Res. 2014 Nov 3.
- Weissmann-Brenner A, Haiman S, Ayala MM, et al. Maternal medical compromise during pregnancy and pregnancy outcomes. J Matern Fetal Neonatal Med. 2014 Aug 19:1-6.
- Rijal P. Identification of risk factors for cesarean delivery following induction of labour. J Nepal Health Res Counc. 2014 May;12(27):73-7.
- Parkes I, Kabiri D, Hants Y, Ezra Y. The indication for induction of labor impacts the risk of cesarean delivery. J Matern Fetal Neonatal Med. 2014 Dec 23:1-5.
- 96. SOGC Clinical Practice Guidelines, No 40, Oct 1995
- Vas J, Aranda-Regules JM, Modesto M, et al. Using moxibustion in primary healthcare to correct non-vertex presentation: a multicentre randomised controlled trial. *Acupunct Med.* 2013 Mar;31(1):31-8.
- Coyle ME, Smith CA, Peat B. Cephalic version by moxibustion for breech presentation. *Cochrane Database Syst Rev.* 2012 May 16;5:CD003928.
- Deneux-Tharaux C, Carmona E, Bouvier-Colle MH, Bréart G. Postpartum maternal mortality and cesarean delivery. Obstet Gynecol. 2006 Sep;108(3 Pt 1):541-8.
- 100. Swain JE, Tasgin E, Mayes LC, Feldman R, Constable RT, Leckman JF. Maternal brain response to own baby-cry is affected by cesarean section delivery. J Child Psychol Psychiatry. 2008 Oct; 49(10): 1042ry 32. 101. Pistiner M, Gold DR, Abdulkerim H, Hoffman E, Celedón JC. Birth by cesarean section, allergic rhinitis, and allergic sensitization among children with a parental history of atopy. J Allergy Clin Immunol. 2008 Aug;122(2):274-9.
- MacDorman MF, Declercq E, Menacker F, Malloy MH. Neonatal mortality for primary cesarean and vaginal births to low-risk women: application of an "intention-to-treat" model. *Birth*. 2008 Mar;35(1):3-8.
- 103.Boyce PM, Todd AL. Increased risk of postnatal depression after emergency caesarean section. *Med J Aust.* 1992 Aug 3;157(3):172-4.
- 104.Lawrence A, Lewis L, Hofmeyr GJ, Styles C. Maternal positions and mobility during first stage labour. Cochrane Database Syst Rev. 2013 Oct 9;10:CD003934.
- Kozhimanni KB, Attanasio LB, Jou J, Joarnt LK, Johnson PJ, Gjerdingen DK. Potential benefits of increased access to doula support during childbirth. *Am J Manag Care*. 2014 Aug 1;20(8):e340-52.