

Module 1 – Overview of role of a dietitian in fertility

Learning Objectives:

At the end of this module you should be able to:

1. Explain what Early Life Nutrition is and why it's important
2. Comprehend the process of how babies are made from a physiological perspective
3. Understand the current medical options for fertility assistance and a basic understanding of how they work

Genetic programming

"In September 1944, trains in the Netherlands ground to a halt. Dutch railway workers were hoping that a strike could stop the transport of Nazi troops, helping the advancing Allied forces.

But the Allied campaign failed, and the Nazis punished the Netherlands by blocking food supplies, plunging much of the country into famine. By the time the Netherlands was liberated in May 1945, more than 20,000 people had died of starvation.

The Dutch Hunger Winter has proved unique in unexpected ways. Because it started and ended so abruptly, it has served as an unplanned experiment in human health. Pregnant women, it turns out, were uniquely vulnerable, and the children they gave birth to have been influenced by famine throughout their lives." Carl Zimmer, The New York Times, 2018 ¹

As time went on a paradox was noticed. People who had been in utero during the 'Dutch Famine':

- were more overweight than average,
- in middle age, they had higher levels of triglycerides and LDL cholesterol,
- had higher rates of such conditions as metabolic syndrome, diabetes and schizophrenia.
- experienced a 10% increase in mortality after 68 years.²

The outcome of the 'Dutch Famine' was one of the key triggers for research into genetic programming or 'epigenetics' to be undertaken. Epigenetics is defined as 'changes in gene function that do not involve changes in the DNA sequence' or essentially how a fetus's environment (including nutrition) can impact the expression of particular genes in the future. Dr Bas Heijmans, geneticist at Leiden University Medical Center in the Netherlands was quoted as saying "How on earth can your body remember the environment it was exposed to in the womb — and remember that decades later?".²

What is ELN?

Early Life Nutrition is the period of time from pre-conception through to toddlerhood, also known as the 'first 1,000 days'. A growing body of evidence shows that the first one thousand days of a baby's life provides a critical window of opportunity where a healthy environment, in particular, diet and lifestyle can positively influence lifelong health. Research has identified vulnerable time periods both prior to conception and during pregnancy where exposure to environmental factors can trigger adaptations in the growing fetus.³ While these effects may be adaptive in the short term, they may also be associated with adverse outcomes in childhood and later life, including a greater risk of obesity, type 2 diabetes, heart disease and allergy. Therefore, identifying vulnerable periods in fetal development provides an important opportunity for parents, and health professionals to intervene and optimise future health outcomes.

Egg and sperm health

"The first 1000 days" traditionally refers to 270 days of pregnancy, plus the first two years of a child's life (730 days). However, more recent research also shows that the health and lifestyle of the mother and the father during the six months (180 days) before they conceive a baby is essential – after all, the egg and sperm will provide the genetic material for the developing foetus.⁴ So, it actually all adds up to 1,180 days– but let's not be pedantic!

Epigenetic changes

Epigenetic changes to DNA include methylation and histone modification. Methylation adds "tags" to human DNA that influences whether a gene is a gene turned on or off. Histone modifications affect how tightly the DNA is wrapped around histones. When histones are tightly wound, genes may not be accessible for activation. Epigenetic changes do not alter the DNA sequence but are heritable. At conception, most epigenetic information is "wiped" from the genome however some of these changes remain and are inherited, even across generations.

From ovulation to conception

Remember what you learnt in sex education classes about how a baby is made? We didn't think so! Watch this brief video to understand the process of ovulation to conception:

<https://www.youtube.com/watch?v=QnyeMf05X2g>

As you can see, conception is much more than about sex. The process of conception is a complex interplay between a range of hormones, processes and growth. However, in simplistic terms, there are 5 key processes that need to occur for healthy conception:

1. The client needs healthy sperm (module 2)
2. The client needs a healthy egg (module 3)
3. The client needs ovulation (when the egg is released from the ovary) to occur (preferably at a timely manner) (module 4)
4. The egg and the sperm need to join together to create an embryo
5. The embryo needs to implant into the uterus (module 5).

Terminology for a fertilized egg

Although often called an embryo, there are in fact many names for a fertilized egg:

Zygote – when an egg is first fertilized by sperm in the fallopian tubes (or in a petri dish) it becomes a zygote. A zygote is a single cell that contains all the 46 chromosomes needed to become a human.

Embryo – the zygote divides in two and is now officially called an embryo. The embryo continues to divide to produce more and more cells.

Blastocyst – by day 5, the embryo becomes a blastocyst. A cavity forms inside the embryo and it breaks down its protective outer membrane enabling it to enter the uterus from the fallopian tube. This is known as ‘hatching’. (The blastocyst stage is especially important to know about for clients who are undergoing Assisted Reproductive Treatments as the day 5 blastocyst is when a ‘transfer’ occurs (from the petri dish into the woman’s uterus) or when the blastocyst is frozen for later use).

Chemical pregnancy – this term is used to describe the first five weeks of pregnancy (prior to ultrasound) when rates of miscarriage are at their highest. Approximately 75% of chemical pregnancies are believed to end in miscarriage.

Foetus – foetus is the term for a growing baby in a woman’s womb. The term foetus is usually used from 8 weeks gestation when the baby has all its major organs.

Infertility

‘Infertility’ is defined as not being able to get pregnant despite having frequent, unprotected sex for at least 12 months.⁵ It is estimated to impact between 8-12% of reproductive couples worldwide, with approximately 30% being attributed to male complications, 30% attributed to female complications, 30% attributed to both male and female complications and 10% unknown complications.

Subfertility is defined as any form of reduced fertility which may lead to a prolonged time for conception to occur.⁶

Obviously with such a complex process, there’s a lot that can go wrong. Over the next few modules, we’re going to delve down into each of the stages of conception to see how dietary modification can optimise fertility. However, there’s some physical issues that no amount of nutrition can fix! This is when your client will need to see a Fertility Specialist. Examples of physical issues may include:

Female

- Blocked fallopian tubes
- Pelvic adhesions
- Structural problems of the uterus (such as polyps)

Male

- Premature ejaculation
- Azoospermia (the male’s ejaculate doesn’t contain any sperm)
- Blockage or absence of tubes (vas deferens) due to injury or vasectomy so that sperm can’t get through.

Overview of fertility treatments

If you are working with clients with subfertility or infertility, it's important to have an understanding of the types of procedures that they may be having. It's also important to note that new technologies are emerging constantly, so it's essential to stay abreast of the latest advances.

Ovulation induction

Ovulation induction may be used by women who are not ovulating or not ovulating regularly.

Ovulation induction involves taking a hormone medication (orally or via injection) which stimulates the pituitary gland to produce FSH (Follicle Stimulating Hormone). This encourages the development of one or more follicles. When the follicles are large enough another hormone is administered which releases the egg from the follicle.

Ovulation induction treatments are taken for 5 days, starting on the 5th day of the menstrual period. Ovulation is expected to occur approximately 5-10 days after commencement.

You should know:

- Ovulation induction is commonly used as a first line treatment for women with PCOS
- Encourage sex during this time
- Ovulation induction is not recommended for more than 3 treatment cycles
- Weight loss in overweight women significantly increases its effectiveness
- Ovulation induction can increase rate of multiples
- Ovulation induction increases the risk of OHHS (Ovulation Hyperstimulation Syndrome)

Ovarian Hyperstimulation Syndrome

Ovarian hyperstimulation syndrome, or OHSS, is caused by taking injectable hormone medications to stimulate the development of eggs in your ovaries. It can cause rapid weight gain, abdominal pain, vomiting and shortness of breath.

The majority of women diagnosed with OHSS will experience a mild form of the syndrome, which usually resolves within 2 weeks. In about 20 per cent of women, the abdominal discomfort associated with OHSS can be quite uncomfortable and take up to a month to resolve.⁷

In about 2 per cent of women, the symptoms may become so severe, hospitalisation is necessary.

It's important to note that Ovarian Hyperstimulation Syndrome is just that – a SYNDROME. That means that it's a collection of symptoms, and the symptoms, and therefore the treatment will be slightly different for everyone. Most symptoms are treated medically, but there are a few dietary interventions that may be needed.

Most women will just have some nausea and bloating for a few days. Treat it like morning sickness (small, regular carbohydrate-rich meals, fresh air, adequate fluid intake, avoid extremely hot or cold foods, low fat etc).

If your patient's condition is worse and they have vomiting and fluid build-up, the main dietary intervention is to adjust their fluid intake. Depending upon their symptoms, you may either need to increase fluid intake OR reduce it. If they're vomiting profusely, they may be losing a lot of fluids and need to replace them, but if they are fluid overloaded, they may need to restrict them. If they are fluid overloaded, they may also require a low salt diet.⁸ This is why it's extremely important that client's receive personalised advice for their condition.

OHSS seems to be more common in women with a healthy weight than women who are overweight. One study suggests that leptin may play a protective role in overweight women.⁹

Intrauterine Insemination (IUI)

Intrauterine insemination (also known as artificial insemination (AI)) is used to treat women who have normal, healthy fallopian tubes, but for some unknown reason, aren't able to conceive. This may be due to mechanical difficulties with intercourse (for example a man is unable to achieve an erection or has structural problems with his penis post trauma) or the male's semen has been frozen due to absence (e.g. death, travel or using donor sperm) or cancer treatments.

IUI involves insertion of semen through the female's cervix and into the uterus around the time of ovulation. An IUI can be performed during a natural menstrual cycle or in combination with ovulation induction.

Gamete Intrafallopian Transfer (GIFT)

GIFT was introduced as a more natural version of IVF. Instead of fertilization occurring in a culture dish in a laboratory, the woman's eggs are retrieved and inserted between two layers of sperm in fine tubing. The tubing is then fed into one of the woman's fallopian tubes where the egg and sperm are left to fertilize naturally. GIFT is not commonly used, however, it is sometimes used as an option for couples who don't want to use IVF (providing the woman's fallopian tubes are functioning).

In Vitro Fertilization (IVF)

The first baby conceived via In Vitro Fertilization (IVF) was born in 1980. Since then, over 5 million babies have been conceived via IVF worldwide¹⁰.

IVF is the process of fertilization where an egg is combined with sperm outside of the body, in vitro (i.e. In a test tube, which literally means 'in glass').

Usually women produce one egg per month ('per cycle'). In an IVF cycle, during the 'stimulation phase' Ovulation Induction occurs using 'superovulatory' drugs to stimulate the follicles to produce multiple eggs. The Fertility Specialist will monitor the growth of these follicles with blood tests and ultrasounds. Towards the end of the stimulation phase, a 'trigger injection' is given. This gets the eggs ready for ovulation.

Egg retrieval usually occurs at a hospital under general anaesthetic. The Fertility Specialist uses an ultrasound to guide a needle into each ovary to collect the eggs. The average number of eggs collected is 8-15. The procedure takes around 30 minutes.

If the couple are planning on using fresh sperm, the male will provide a sample on the morning of the egg retrieval. If they are planning on using frozen or donor sperm, the lab will prepare it. The sperm are washed in a cocktail of medications to slow down their movement so that scientists can view the sperm under a microscope. The sperm are graded in four levels of quality and the best sperm are identified for use.

The eggs and the sperm are placed together in a dish so that they can find each other naturally, the way they would inside the body.

When a sperm fertilizes an egg, it's put inside a special incubator to optimise growth. Some of the embryos hatch to become 5-day blastocysts. The embryos (blastocysts) will then be frozen or transferred into the woman's uterus.

A 'transfer' is similar to a pap smear. It takes about 5 minutes, there's no anaesthetic and then two weeks after the transfer the woman will have a blood test to measure her levels of Human Chorionic Gonadotropin (hCG) which indicates whether or not she is pregnant (known as 'the two week wait').

Intracytoplasmic Sperm Injection (ICSI)

Intracytoplasmic Sperm Injection (ICSI) is similar to IVF. It is used to overcome male fertility issues such as low sperm count, low sperm morphology or motility, anti-sperm antibodies or have previously had a vasectomy or unsuccessful vasectomy reversal. ICSI essentially follows the same procedures as IVF, except that instead of allowing sperm to naturally fertilize eggs in the dish, ICSI involves direct injection of a single sperm into each egg to achieve fertilization.

Preimplantation Genetic Testing (PGT)

Pre-implantation Genetic Testing (PGT), also known as Preimplantation Genetic Diagnosis (PGD) is a technique used to help people reduce their risk of passing on a known genetic condition. There are two types of PGT:

1. PGT for monogenic/single gene defects (PGT-M) is used to identify embryos that are not affected by a 'faulty' gene that can lead to disease.
2. PGT for chromosomal structural rearrangements (PGT-SR) is used to identify embryos that have the correct amount of genetic material.

In PGT, embryos are generated via IVF or ICSI and then one or two cells are removed from the embryo and screened for a specific genetic condition/s.

References

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