

HOW SIMPLE HORMONE TRACKING CAN HELP WOMEN PLAN THEIR PREGNANCY



Foreword by William Ledger

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We live in a time in which people have more control over their lives than ever before. We are used to instant electronic interaction and to accessing global information at the swipe of a finger. Modern healthcare is coming to terms with this fundamental social change and is learning how best to help the knowledgeable and smart generation Y. Pregnancy planning is a good example of how things have changed over the past 20 years. Previously, people met and fell in love. At the point they decided to start a family, they stopped use of contraception and then more or less left things to chance. If pregnancy did not occur quickly they may have borrowed a book from the library to read about the menstrual cycle, and might have bought a thermometer to check their basal body temperature. Many were reticent to talk to their doctor about such personal issues and would try for many months before plucking up courage to discuss their difficulty with anyone outside their family.

Many women approach things differently today. They will research conception and pre-conception management on the web, and take control of the initial steps while still using contraception. They may know about folic acid and vitamin D supplementation, know their blood group and rubella immunity, have had a health check-up and a cervical smear, and reduced alcohol intake. When they decide to stop their contraception they expect to conceive quickly and if this does not happen, will seek help online or from a health professional.

Part of this more planned approach to pregnancy involves the woman understanding her individual menstrual cycles. Everyone is different and women cannot rely on population

averages to understand their own fertility. Understanding when they ovulate is one of the easiest steps that women can take to understanding their fertility, and ovulation tests are the easiest way for women to accurately predict when they will ovulate. Conventional LH tests give couples 1-2 days advanced warning of ovulation. Clearblue have also developed more advanced products that give women even more information.

The Clearblue Advanced Fertility Monitor is the best device available to meet the needs of women who want to understand their fertility. It gives easy to understand, accurate and reliable personal information with the minimum of fuss, and helps women conceive quickly and easily without the stress of worrying about possible infertility that even a few months of trying without success can bring. We know that enthusiasm for and enjoyment of sex can rapidly wane when attempts at conception fail, bringing pressure on the relationship. In addition, women are older when they first try to conceive and so cannot afford to be as relaxed about time to conception as in earlier generations. This is particularly important when the couple plan two or three children.

The Clearblue Advanced Fertility Monitor is a device of its time and has a wide application for women who wish to conceive as quickly as possible and who want to understand how their body works. I'm happy to recommend it to my patients.

Professor William Ledger has a relevant financial relationship with Swiss Precision Diagnostics as a Clearblue Consultant and Advisory Board Member.



INTRODUCTION

Becoming pregnant is often not straightforward. It is estimated that one in seven couples in the UK¹, and approximately one in six women in the USA have difficulty conceiving².

Couples are often pro-actively planning their family, particularly as in recent decades, more women have been choosing to wait until they are older before they begin, when their fertility is already decreasing.

“ I see more professional women who have delayed having children, this has definitely increased over the last 5 years.

UK GP³

Once a couple starts trying to conceive, they expect and want pregnancy to happen quickly. More than half of women expect to become pregnant within 6 months, with younger women tending to expect it to happen more quickly. However, in a study of over 1,400 women who had planned their most recent pregnancy, 30-44% found it took longer than expected⁴.

There are many factors that can cause or contribute to difficulty conceiving. A common, and easily remedied, factor is mistiming of intercourse⁵. As many as 1 in 2 couples may be trying to conceive at the wrong time, because they don't know when their most fertile days are⁶.

There are a limited number of days in each cycle when a woman can become pregnant, known as the fertile window⁷. Many women have limited knowledge of this. In a study with over 5,000 women across 5 countries, 39-46% of women in the UK, USA and Spain either didn't know when they could conceive, or believed they could conceive any day in their cycle⁴. Another study showed that many women who were trying to conceive and actively seeking information about their fertility remained unaware of the timing of their fertile window⁸.

Current clinical guidance in the UK states that people who are concerned about their fertility should be informed that vaginal sexual intercourse every 2 to 3 days optimises the chance of pregnancy¹. If this advice is followed properly, intercourse should take place during the fertile window. However, the most fertile days could still be missed, and the advice may be considered too demanding and not followed correctly. When women accurately identify their fertile window and target sexual intercourse accordingly, they are more likely to conceive naturally, more quickly⁹.

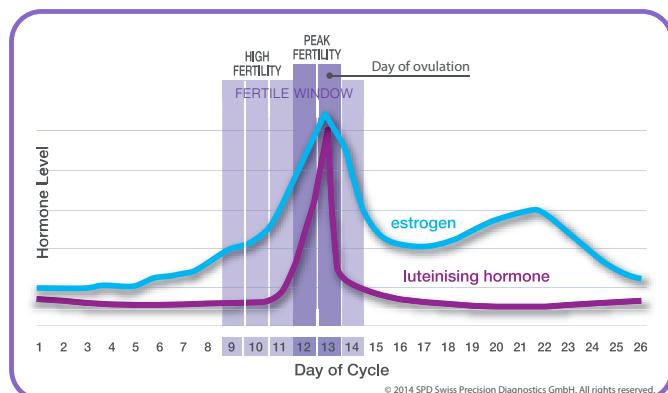
This booklet explains the hormonal changes that control ovulation, and the scientific basis for how simple hormone tracking is an accurate way to help women identify their fertile window. This enables them to time intercourse on the days in their cycle when they are most likely to conceive.

HORMONAL CONTROL OF OVULATION

The menstrual cycle is controlled by four hormones that are present in plasma - the anterior pituitary gonadotropins, follicle stimulating hormone (FSH) and luteinising hormone (LH), and the gonadal sex hormones, estrogen and progesterone¹⁰. The levels of these hormones change throughout the menstrual cycle and, amongst other things, control ovum development and ovulation^{10,11}.

There are various forms of estrogen and the principle active form is estradiol. Plasma estradiol is the major physiological determinant of the onset of the fertile window. Estradiol levels gradually rise in the early stage of the woman's cycle, reaching a threshold that triggers a sudden increase in LH, termed the LH surge. The LH surge is necessary for ovulation to occur^{11,12}. It is the best indicator of impending ovulation, which typically occurs 24-36 hours after the LH surge starts.

FIGURE 1:
Typical hormone levels during the menstrual cycle



HOW LONG DOES A WOMAN'S FERTILE WINDOW LAST?

Fertilisation of an ovum can only take place after ovulation has occurred. The maximum duration of the fertile window is therefore determined by the lifespan of the sperm in the days preceding ovulation, and the lifespan of the ovum after ovulation^{7,13,14}.

It is generally accepted that sperm can survive for around 5 days in the sperm-supportive cervical mucus that is present during the fertile window⁷. Therefore the fertile window starts around 5 days before ovulation occurs. Unfertilised ova typically survive for 12-24 hours^{13,14}, so the fertile window ends within 24 hours of ovulation.

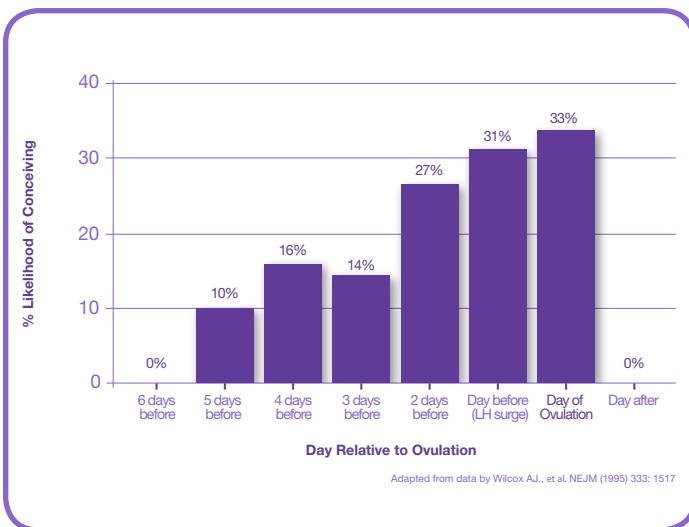
The fertile window therefore typically lasts for up to 6 days⁷, although this varies between women and between cycles¹⁵. The chances of conception increase in the days leading up to ovulation, with peak fertility being the day before, and on the day of ovulation.

IDENTIFYING THE ENTIRE FERTILE WINDOW INCREASES THE LIKELIHOOD OF CONCEPTION

Although conception is most likely to occur when intercourse takes place the day before, or on the day of ovulation, conception is possible throughout the fertile window¹⁶.

Identification of additional fertile days provides couples with more flexibility to plan intercourse around their busy lifestyles and also more opportunities to conceive, which may reduce the pressure that couples can experience when trying to conceive. Intercourse throughout the entire fertile window increases the probability of conception⁹, and women using the Clearblue Advanced Fertility Monitor to identify their entire fertile window were shown to almost double their chance of getting pregnant¹¹.

FIGURE 2:
Probability of conception with respect to ovulation



HOW CAN A WOMAN'S FERTILE WINDOW BE IDENTIFIED?

Although a 'typical cycle' is often stated to be 28 days, this varies between women, and between cycles. In fact 46% of menstrual cycles vary by 7 or more days¹⁷; this has a significant impact on the timing of ovulation from one cycle to the next. It is therefore often difficult for women to accurately predict their fertile window. A study amongst women trying to get pregnant found that only 13% correctly estimated their ovulation day, and only 55% of women estimated their day of ovulation within their fertile window⁸.

There are a variety of methods that may help women identify their ovulation day, and/or their fertile window. They vary in ease of use and accuracy.

Urinary hormone tests

Urinary levels of fertility hormones have been shown to closely mirror levels in plasma¹⁸. A woman's fertile window can therefore be identified by monitoring hormonal changes using urinary ovulation tests.

Traditional ovulation tests measure LH to detect the LH surge, and provide 1–2 days advance warning of ovulation. These tests are simple to use, and accurately pinpoint the best 2 days to conceive. The results are most often displayed as a control line and a test line appears when the LH surge occurs. However, unlike traditional line pregnancy tests, where any test line is considered to be positive, the test line on an ovulation test has to be compared with the control line and only indicates an LH surge when it is as dark, or darker than the control line. This can be difficult, and 1 in 4 women can misread the result^v.

Digital ovulation tests also detect the LH surge, giving 1-2 days advance warning of ovulation. Digital ovulation tests solve the difficulty of reading line tests, as the results are displayed digitally for greater accuracy¹⁹.

Ovulation tests are effective at helping more women conceive more quickly. In a recent study, 77% more women became pregnant when using digital ovulation tests, and pregnancy was achieved more quickly compared to women advised to have regular intercourse^{20, IV}.



The **Clearblue Digital Ovulation Test with Dual Hormone Indicator** is a more advanced ovulation test. In addition to measuring LH, it is the only ovulation test that also tracks changes in estrone-3-glucuronide (E3G)¹⁸. E3G is a urinary metabolite of estradiol, and has been recognised as a good measure of serum estradiol levels (World Health Organization 1983). Estradiol starts to rise before the onset of the LH surge, so tracking LH and E3G has significant advantages over many other methods of aiding conception because it is designed to identify more fertile days prior to ovulation⁹.

Clearblue Digital Ovulation Test with Dual Hormone Indicator typically identifies 4 or more fertile days – that's more than any ovulation test based on LH alone. Importantly, the additional days provide couples with the opportunity to proactively time multiple acts of intercourse before ovulation, to help women get pregnant sooner.



The Clearblue Advanced Fertility Monitor is the most advanced home method to maximise a woman's chance of getting pregnant naturally. It is an innovative and unique handheld monitor with simple urine tests that are designed to identify the entire fertile window. The Monitor's touch-screen interface makes it even easier for a woman to track and understand her fertility; it advises her when to conduct a test, tracks E3G and LH levels, combines this information with the woman's menstrual cycle characteristics and recorded acts of intercourse, and can store and analyse data for up to 6 cycles at a time. Using a sophisticated algorithm, the monitor translates the data to give women easy to understand, comprehensive, personalised daily information that is unique to each cycle. This information can be recalled and shared with her healthcare professional via the calendar and cycle summary screens. Using the Clearblue Advanced Fertility Monitor has been clinically proven to increase the chance of conception by 89%ⁱⁱ.

" I always recommend the Clearblue Fertility Monitor to my patients as the most accurate and easy to use device available

UK Fertility Consultant³

In addition, the Clearblue Advanced Fertility Monitor is the only fertility monitor that can also test for pregnancy. The separate pregnancy tests can be used to detect hCG from 3 days before the period is due.^{vi}



Calendar calculations

Calendar calculations are simple, free, and the method women trying to conceive most commonly use to estimate when they are fertile⁴. Many see it as the 'first proactive step'³.

A vast range of downloadable apps are now available to help make it even easier for women to track their personal cycle calendar. These apps usually mark the predicted day of ovulation, based on population averages.

However, calendar calculations are unreliable because women's cycles vary and the day of ovulation is also variable. Almost 50% of women's cycles vary by 7 days or more, making it difficult to accurately identify the day of ovulation¹⁷. Women may rely on textbook definitions of the menstrual cycle, rather than understanding their own cycle⁸. In a study of 895 cycles from 101 women, which compared the calendar method with ovulation day calculated from the detection of urinary LH surge, the calendar method was found to identify appropriate fertile days in only 35% of the cycles tested²¹.

Basal body temperature (BBT)

After ovulation, progesterone levels start to increase, and this is associated with a slight increase in BBT. Therefore taking the temperature daily can indicate when ovulation has occurred. However, it has limitations as a prospective method because the temperature rise occurs post-ovulation i.e. after the end of the fertile period for that cycle. So a woman uses retrospective information to predict her next ovulation, which can vary from cycle to cycle²².

In addition women may find it inconvenient as BBT has to be measured at the same time each day before moving out of bed, and the results can be affected by every day events such as illness, drinking alcohol, and restless sleep. Studies have shown BBT predicts the most fertile days in only one third of cycles²², and many women give up quickly due to the inconvenience³.

Current UK clinical guidelines state that the use of basal body temperature charts to confirm ovulation does not reliably predict ovulation and is not recommended¹

Observation of cervical secretions

The consistency, volume and content of a woman's cervical mucus changes prior to ovulation to become more 'sperm friendly'. Monitoring the mucus can therefore provide prospective information about ovulation.

Immediately after menstruation a low level of viscous “infertile mucus” is secreted, which acts as a barrier to sperm. As ovulation approaches, the aqueous content increases; this abundant low viscosity, elastic “fertile mucous” aids sperm transport. Interpreting the changes in cervical secretions requires a level of training, is less accurate than monitoring the LH surge, and may not be acceptable to all women²³.

STRESS AND TRYING TO CONCEIVE

Deciding to try for a baby is an exciting time, but it can also be stressful. 6-12% of women willing to have children worry that it might take some time to be successful³, and if a couple fail to conceive within the time they expect, stress may increase.

It has also been suggested that timing intercourse around ovulation can be a cause of stress in itself. However, a randomised controlled trial demonstrated that the use of home ovulation tests by women trying to conceive does not adversely impact stress levels and can improve time to conception²⁰.

On the contrary, many women report that using ovulation tests can provide reassurance that they are ovulating and targeting intercourse around ovulation gives them a feeling of control.

“ [Confirms] Your body is working. ”³

“ Making me feel like I was doing something constructive - taking matters into my own hands. ”³

Many women actively seek information about their cycles when planning a pregnancy. In a study of over 3,800 women, 21-26% of women believe knowing when you are fertile is the single most important factor when trying to get pregnant. 1 in 3 women track their cycle before trying to conceive (particularly in the USA where 54% of women track their cycle before starting to try), over 50% of women have tracked their cycle whilst trying to conceive, and over a third of women targeted sex to their most fertile days when trying to conceive³.

WHY EXPERTS RECOMMEND OVULATION TESTS TO WOMEN ACTIVELY TRYING TO CONCEIVE

With a prevalence of up to 15.5% of couples unable to conceive after one year of unprotected intercourse²⁴, infertility affects a sizable proportion of the population; this adversely affects both the couple trying to conceive, and the healthcare system.

Ovulation tests are a simple step that can offer a range of practical and emotional benefits:

- **Takes the guess work out of timing intercourse:**

Ovulation tests help women identify the most fertile period of each cycle, which takes the guess work out of timing intercourse to achieve pregnancy. Recommendations to have intercourse regularly throughout the cycle can be emotionally demanding and can quickly lead to a ‘mechanical’ approach to intercourse whilst trying to conceive.

- **Reduced time to conception:** A study showed women using ovulation tests took on average 10% less time to become pregnant than women advised to have regular intercourse¹⁷. This helps avoid stress that couples may feel if it takes longer to become pregnant than they expect/hope. Reduced time to conception is particularly beneficial for older women who need to conceive quickly before they run out of time, and may otherwise need to enter the healthcare system to help them conceive.

- **Reassurance and control:** Knowing when to time intercourse for the best chance of achieving pregnancy can be very reassuring, and it helps couples feel more in control. Ovulation testing also helps women understand their own bodies better, which provides an emotional benefit of empowerment. Confirmation that they are ovulating regularly is reassuring, and discovering that even when they have a relatively regular menstrual cycle, the day of ovulation can vary by several days each month can be very enlightening.

“ The beauty of these monitors is that they reassure women that their cycles are normal. ”
UK Consultant Gynaecologist and Obstetrician³

- **Easy:** Many women find it easy to identify their fertile window by tracking urinary hormones. Other methods are less reliable (such as calendar calculations) and more difficult/inconvenient (such as basal body temperature).

- **Get help quicker:** If a woman is not ovulating regularly, identifying this early on is helpful both to her (as it will encourage her to seek the help of a healthcare professional earlier) and the healthcare provider (as it provides relevant information when considering the appropriate clinical course of action).

“ I would encourage all women planning to get pregnant to use ovulation tests – the improved understanding of their bodies is emotionally reassuring, and it will help improve their chances of achieving pregnancy more quickly. ”
Professor William Ledger, 2014

ABOUT CLEARBLUE®

Clearblue is the world's number one selling brand in home pregnancy and fertility tests^{III}. Our products are built on a strong foundation of peer-reviewed science and consumer understanding.

For more information about Clearblue,
visit www.clearblue.com.

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- II By 89% in the first 2 cycles of use. Robinson JE,Wakelin M and Ellis JE. Increased pregnancy rate with use of the Clearblue Easy Fertility Monitor. *Fertility & Sterility* (2007) 87(2): 329-334.
- III Based on international sales in nearly 20 countries compiled using independent market research data.
- IV Total 210 women. 2 menstrual cycles. Average 144 days for OT group, 160 days for control group. Not statistically significant for conception rates.
- V In a UK study of 72 women reading ovulation test results typical of normal cycles (2010).
- VI Clearblue recommends that you test from the day your period is due. However, the pregnancy hormone increases rapidly in early pregnancy and Clearblue can be used to test up to 3 days before your period is due. In clinical testing with early pregnancy samples Clearblue gave the following results: 74% of women received a 'Pregnant' result 3 days early, 91% of women 2 days early, 96% of women 1 day early. If you test early and get a 'Not Pregnant' result it is possible that the level of pregnancy hormone may not yet be high enough to be detected. You should test again when your period is due.
- VII Tiplady S., et. al Human Reproduction (2013) 28(1): 138-151 210 women. Not statistically significant for conception rates.