The Clearblue Fertility Monitor is:

Accurate - 99% accurate in detecting the LH surge in urine

Unique - provides daily fertility status by measuring two urinary hormones – LH and E3G

Effective - helps women to conceive more quickly

Simple to use - convenient and easy to interpret

Trustworthy - from Clearblue, the world's leading brand in home pregnancy and fertility testing

Proven - to increase the chance of conception by 89%

Clearblue

For more information about the Clearblue Fertility Monitor, please visit our websites:

www.clearblue.com

www.swissprecisiondiagnostics.com

SPD Swiss Precision Diagnostics GmbH

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Clearblue Professional Series: ROW-FM v1.0 – December 2010

Clearblue

Clearblue Fertility Monitor

Proven to increase the chance of conception by 89%

Clearblue Professional Series

About Clearblue

Clearblue® is the world's leading brand in home pregnancy and fertility testing. Consumers trust the Clearblue brand because it delivers the accurate information they want. The Clearblue product range is built on a strong foundation of peer-reviewed science and consumer understanding. Clearblue products are also trusted and recommended by doctors, many of whom recognise that Clearblue is supported by 25 years of expertise, quality, and innovation in consumer diagnostics.

Contents

Clearblue Fertility Monitor

There are a limited number of days each cycle when a woman can become pregnant. As more and more women today are choosing to have children later in life, when the ability to conceive is declining, they are increasingly finding it difficult to get pregnant when they want to. The Clearblue Fertility Monitor is a unique innovation that is proven to increase the chance of conception by 89%.[1] It accurately and naturally identifies those days leading up to and including ovulation when intercourse can lead to pregnancy.

As the pioneer of rapid immunoassay technology, Clearblue has further developed this technology to produce a unique dual hormone assay. This rapid assay innovation, combined with microelectronics, resulted in a breakthrough in home use conception aids, the Clearblue Fertility Monitor. By monitoring urinary hormone levels it accurately and reliably identified more fertile days than using LH alone, displaying clear daily information about a woman's personal level of fertility.

By detecting changes in the levels of two key fertility hormones using urine Test Sticks, the Clearblue Fertility Monitor can accurately identify the days when a woman is most likely to conceive.

Technology in the palm of her hand

The Clearblue Fertility Monitor consists of a handheld Monitor and disposable Test Sticks, which can identify a woman's fertile period by tracking the changing levels of estrone-3-glucuronide (E3G)*, the urinary metabolite of estradiol, and luteinising hormone (LH).

The Monitor reads the Test Sticks to identify changes in the hormone levels that control fertility.

The software within the Monitor collects and evaluates the data to identify and show the woman her daily Fertility Status: Low, High or Peak.

*Estrogen-3-glucuronide, E3G, is recognised by the World Health Organization as a principal metabolite of estradiol.[2] The urinary levels of E3G correspond to the serum levels of estradiol.[3]

Evaluating the fertile period

The chances of conception increase in the days preceding ovulation

In the 1980s, a World Health Organization task force evaluated the use of urine tests (including LH and E3G) to identify the fertile phase.[2] In more recent years, Wilcox and colleagues have studied the timing of the fertile window in the menstrual cycle of 221 women. They found that the fertile window was 6 days long, ranging from 5 days prior to the estimated day of ovulation (EDO) to the EDO itself. Results showed that in every cycle in which conception occurred, there was intercourse at least once in this 6-day period and none of the cycles in which no intercourse occurred in this period resulted in pregnancy.[4]

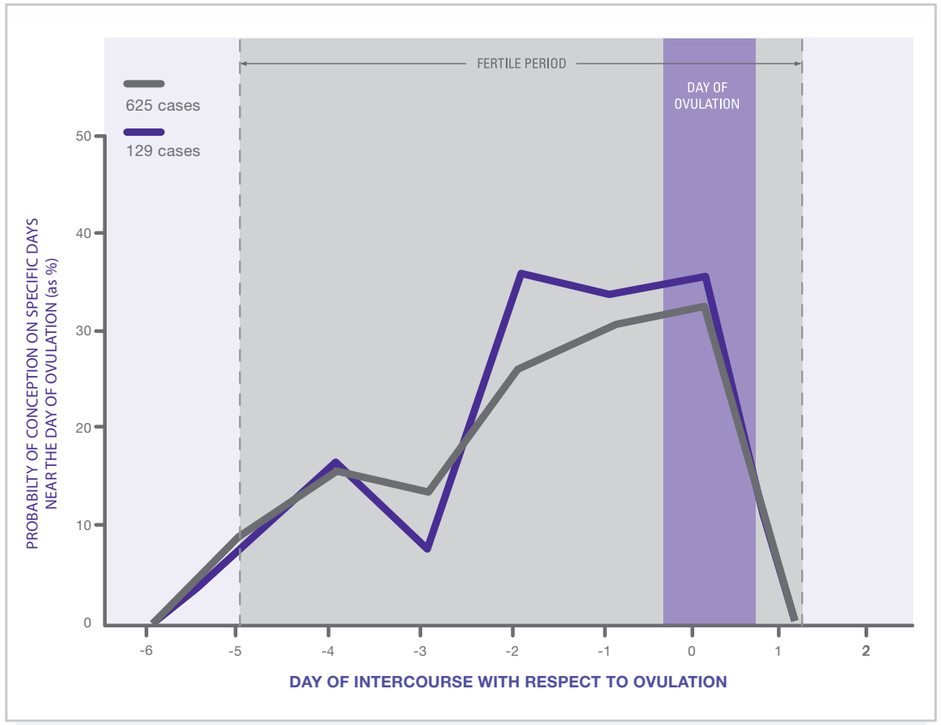

Figure One: Data from 129 ovulatory cycles in which a single act of intercourse led to pregnancy were used to calculate the probability of conception, and data from the statistical model applied to 625 ovulatory cycles. Adapted from Wilcox *et al* (1995).[4]

The duration of the fertile period is determined by the viability of the sperm in the days preceding ovulation and the lifespan of the ovum

- It is generally accepted that sperm can survive for up to 5 days in sperm-supportive cervical mucus
- Ova typically survive for 12–24 hours after ovulation.

The fertile period can be identified by tracking two key hormones

Changes in hormonal levels control the fertile period

The menstrual cycle is controlled by the anterior pituitary gonadotrophins (follicle stimulating hormone and luteinising hormone) and the gonadal sex hormones (estrogen and progesterone).[5] Changing plasma hormone levels throughout the menstrual cycle control ovum development and ovulation.[6]

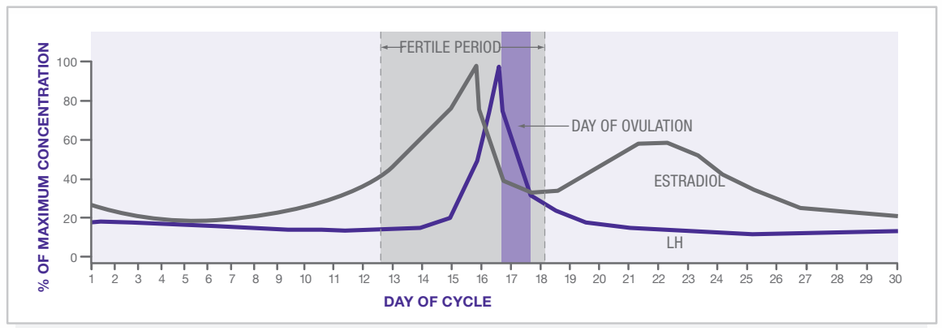

Figure Two: Mean changes in the concentration of hormones in peripheral venous plasma (expressed as a percentage of their maximum value relative to the day of the LH surge). Adapted from Collins (1985).[7]

Plasma estradiol is the major physiological determinant of the onset of the fertile period

Estradiol stimulates secretion of cervical mucus that is favourable for the survival and transport of sperm. The rise in estradiol corresponds closely to the appearance of sperm-supportive cervical mucus.[6]

Estradiol levels gradually rise in the early stage of the woman's cycle, reaching a threshold that triggers a sudden increase in LH – the LH surge.[6]

The LH surge is the best indicator of impending ovulation

The LH surge causes the dominant follicle to rupture and release a mature ovum. Ovulation typically occurs 24–36 hours after the LH surge.

Ovulation does not take place in the absence of an LH surge.[8]

Monitoring hormonal changes through urine tests

The Clearblue Fertility Monitor employs patented technology. In the Clearblue Fertility Monitor, this technology has been developed into a unique dual hormone assay for E3G and LH.

Ultrasound studies of follicular rupture have confirmed that the LH surge detected in urine occurs approximately 24–36 hours before ovulation. This is consistent with the detection of the LH surge in plasma.[8]

Rapid assay technology

In the Test Stick, monoclonal antibodies conjugated to blue latex particles are used to detect and identify LH and E3G in the urine.

After urine sampling*, blue lines form on the Test Stick. The Monitor uses optical technology to measure the intensity of these blue lines to track the levels of LH and E3G present in the urine.

The luteinising hormone assay

The assay is based on a "sandwich" principle, where the LH molecule forms a "sandwich" between the two antibodies specific for LH (Figure 3). One antibody is attached to the latex particles and the other is immobilised on the Test Stick strip in a line within the Test Stick window. Each antibody binds to a different part of the LH molecule, enabling both to bind simultaneously.

Therefore, as the amount of LH increases in the urine sample, the intensity of the blue latex line formed in the Test Stick window increases as well.

*First urine of the day.

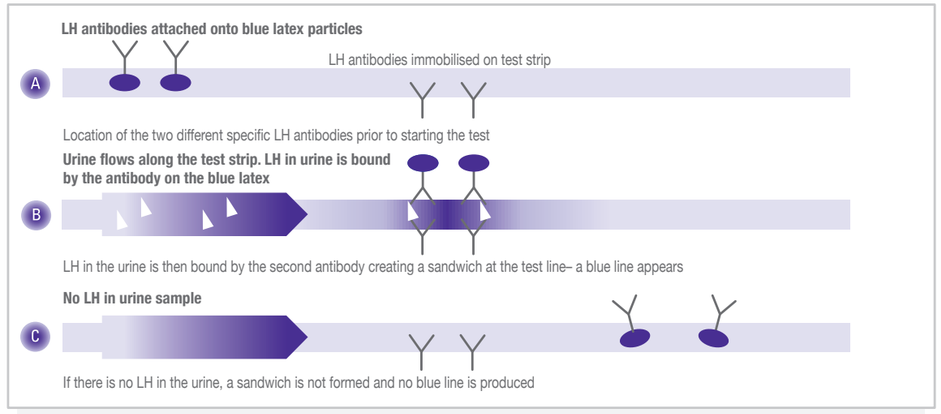

Figure Three: Non-competitive immunoassay for LH, based on the "sandwich" principle.

The estrone-3-glucuronide assay

E3G is a much smaller molecule than LH and cannot accommodate the two antibodies necessary for a sandwich assay format, so a "competitive" format is used. In this case, the antibody specific to E3G is coated onto the latex particles and an E3G-protein conjugate is coated onto the Test Stick strip as a second line in the Test Stick window. At low concentrations of E3G in the urine, the antibody-coated particles are able to bind to the E3G on the test strip producing a blue test line. As E3G levels increase in the urine, more antibody-coated particles bind to the urinary E3G and fewer are available to bind to the E3G on the test strip. Therefore, as E3G concentrations increase, the intensity of the blue test line decreases (Figure 4).

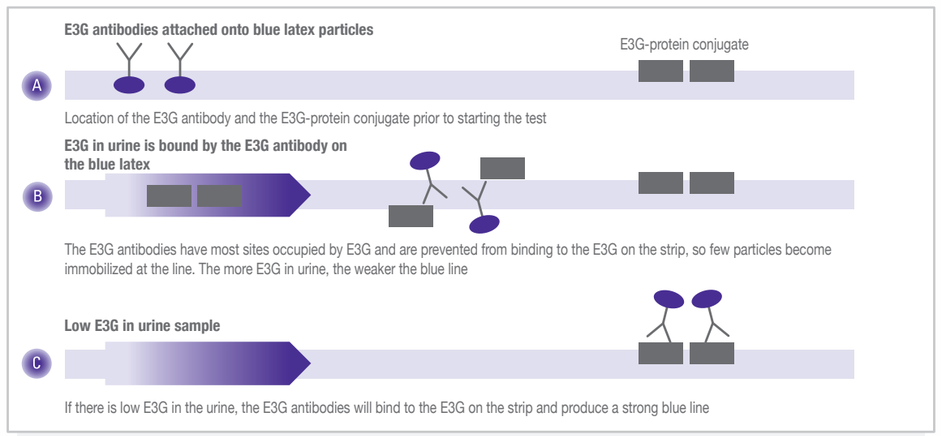

Figure Four: Competitive assay for E3G (simultaneous with LH assay).

The intensity of the blue line is measured optically by the monitor in order to establish the levels of E3G and LH in the urine sample. A sophisticated algorithm collects this information, along with menstrual cycle characteristics, into a simple-to-understand indicator of fertility level.

How the Clearblue Fertility Monitor increases the chances of conceiving

To increase chances of conception, it is beneficial to identify as many fertile days as possible so that additional opportunities where intercourse may result in pregnancy are not missed. Identifying the fertile days before ovulation occurs would be expected to result in higher conception rates.[9] Indeed, the Clearblue Fertility Monitor has been proven to increase the chances of conception in a randomised controlled trial.[1] The Clearblue Fertility Monitor provides a more accurate indication of fertile days than any other home method. Most women will be given 1–5 days of High Fertility before they reach their Peak Fertility status.[10]

Identifying days of High Fertility

Tracking E3G in the urine will typically show most women 1–5 days of High Fertility prior to Peak Fertility.[10] High Fertility indicates that the level of E3G is rising. At this time, the woman has an increased chance of conceiving because sperm can survive longer in her reproductive tract. High Fertility is also indicated by the Monitor for one day after Peak Fertility. The Monitor is proven to detect changes in urinary levels of LH and E3G which coincide with laboratory measurements by quantitative immunoassay in defining the potentially fertile period.[11] In a study of 54 couples, who were seeking conception assistance, over four cycles, the Monitor declared a median number of fertile days of 7 and more than 60% of cycles had between 1 and 5 days warning of the Peak Fertility. At least one act of intercourse was reported in the fertile window in over 96% of cycles and the four cycle, cumulative lifetable pregnancy rate was found to be 39.5%.[12]

Identifying days of Peak Fertility

Peak Fertility indicates that the Clearblue Fertility Monitor has detected the LH surge, the best indicator of impending ovulation.[2] The Monitor can predict ovulation accurately when compared to serum hormone measurements and vaginal ultrasound scans.[13] In 150 cycles the measurement of urinary hormones by the Monitor correlated very closely to serum levels and ovulation was detected by ultrasound during 2 days of Peak Fertility in 91% of cycles.[13]

The Clearblue Fertility Monitor offers a woman:

- A proven method to help them conceive more naturally
- The most advanced home method available
- A more accurate indication of more fertile days than any other home method
- An unmistakably clear indication of Fertile Status every day (Low, High or Peak)
- Notification of High Fertility – those additional fertile days which precede the LH surge
- Advance notice of Peak Fertility, so couples can plan intercourse at their convenience

} entire fertile window

Giving most women 1–5 days of High Fertility before they reach their Peak Fertility[10]

In a laboratory analysis of daily urine samples from 352 menstrual cycles, the mean percentage of menstrual cycles which showed 1–5 days of High Fertility before Peak Fertility was 60%.[10]

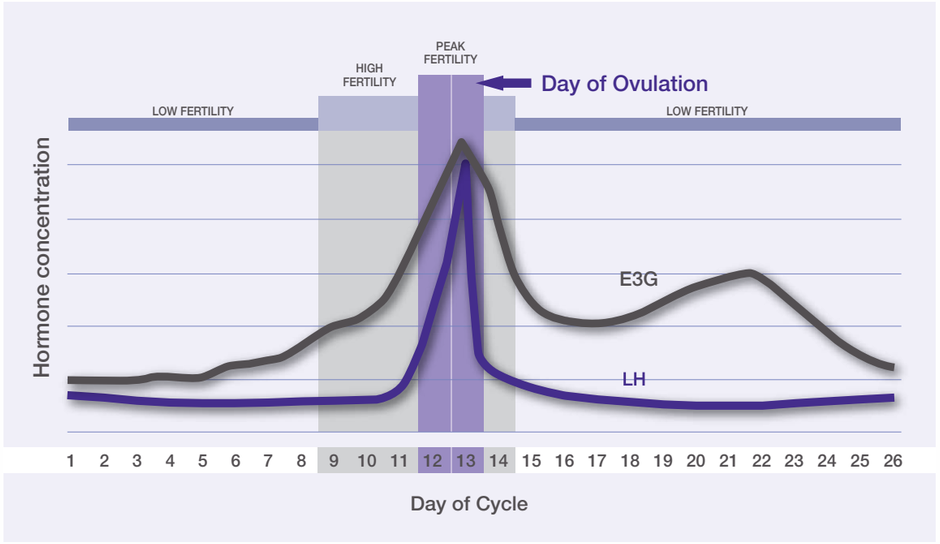

Figure Five: Schematic of typical hormone levels in urine throughout a cycle.

Duration of the fertile period as measured by the Clearblue Fertility Monitor

In a laboratory analysis of daily urine samples from 352 menstrual cycles, the mean duration of the combined High and Peak Fertility days was 6.01 ± 2.33 days, and most commonly 5 days.[10]

Of these menstrual cycles, all of which demonstrated an LH surge, 62% had between 3 and 6, and over 85% between 3 and 8, days of combined High and Peak Fertility.[10]

A woman is unlikely to conceive as a result of sexual intercourse on a Low Fertility day.

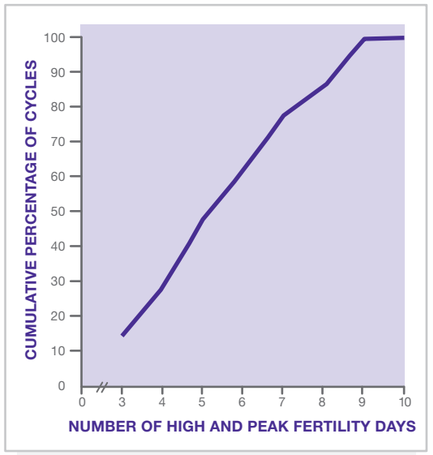

Figure Six: % of cycles and the corresponding number of High and Peak Fertility days.

Advantages of the Clearblue Fertility Monitor over other methods

The Clearblue Fertility Monitor has significant advantages over many other methods of aiding conception by accurately identifying the entire fertile window.[9] Calender calculations are unreliable for the purpose of timing intercourse to conceive, because women's cycles are known to vary from cycle to cycle and the day of ovulation itself is therefore variable. Most home ovulation tests only provide 1–2 days advance warning of ovulation, through identification of the LH surge, which limits the opportunity to have multiple acts of intercourse before ovulation. Another commonly used method, basal body temperature method (BBT) also has recognised limitations.[14-18] Use of BBT identifies ovulation after the event, so a woman uses retrospective information to predict her next ovulation. The efficacy of these methods is dependent upon very regular cycles. Ovarian follicular ultrasound by transvaginal scanning is highly accurate for identifying the approach and occurrence of ovulation, but it is a costly procedure with limited availability for routine use. The Clearblue Fertility Monitor has been shown to accurately predict ovulation when compared with serum hormone measurements and vaginal ultrasound scans.[13]

In a review of methods to time intercourse and achieve conception, the monitor was recommended as one of the two most appropriate methods to identify the entire fertile window for the purpose of achieving pregnancy.[9] The Clearblue Fertility Monitor has advantages over fertility charting of vaginal discharge for some women because it is proven to be easy to use[10] and through the use of innovative technology it is proven that it can have a positive impact on factors such as stress and anxiety for couples which can improve their confidence that a conception will happen.[19]

Clinical Validation of the Clearblue Fertility Monitor

The Clearblue Fertility Monitor was developed over several years and utilises state-of-the-art lateral flow technology linked to an electronic reader to deliver an easy to use, consumer-friendly home monitor. Throughout its development, and since launch, it has been subjected to a number of clinical studies to evaluate effectiveness both in measuring hormonal markers of the fertile phase, but also its effectiveness at helping women conceive.

The Clearblue Fertility Monitor has been shown to accurately predict ovulation when compared with serum hormone measurements and vaginal ultrasound scans.[11,13] (Figure 7). Through detection of the urinary E3G level, consistent with rising serum estradiol concentration, the monitor was able to alert a woman that her fertility status was High for 5 days prior to Peak Fertility. Peak Fertility, as indicated by the monitor on detection of urinary LH surge 1 day prior to ovulation, was confirmed by ultrasound.

In a study of 54 couples, who were seeking conception assistance, over four cycles, the Monitor declared a median number of fertile days of 7 and more than 60% of cycles had between 1 and 5 days warning of the Peak Fertility. At least one act of intercourse was reported in the fertile window in over 96% of cycles and the four cycle cumulative lifetable pregnancy was found to be 39.5%.[12]

In a study of over 600 women trying to conceive, 302 used the Clearblue Fertility Monitor and 347 women formed an equivalent control group trying to conceive. The pregnancy rate within the Clearblue Fertility Monitor group was significantly higher over the first 2 cycles of use, compared to women who were not using the Monitor.[1] The Clearblue Fertility Monitor was shown to increase the chance of conception by 89% in this study over 2 cycles of use (Figure 8).

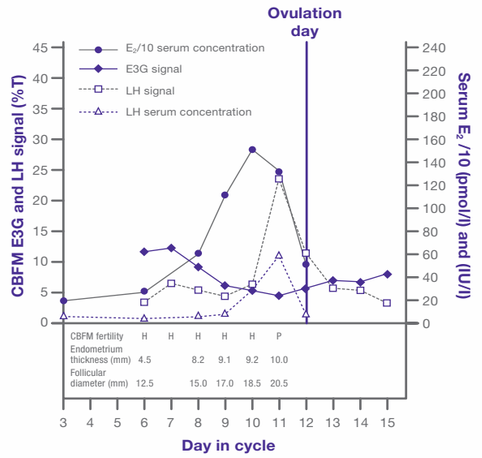

Figure Seven: Ovulation prediction using serum hormone measurements, vaginal ultrasound scans and the Clearblue Fertility Monitor.

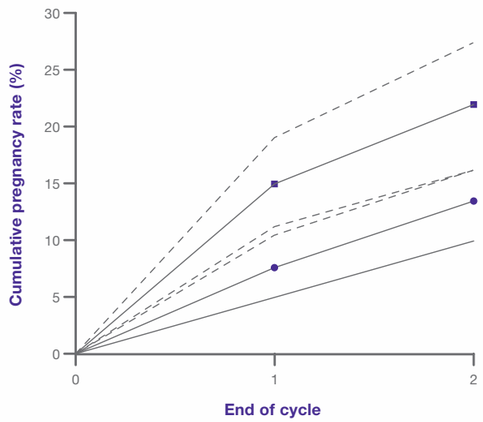

Figure Eight. Cumulative pregnancy rates over 2 cycles of use. Cumulative pregnancy rates at end of each cycle, with 95% confidence intervals, for women using (squares) or not using (circles) the Clearblue Fertility Monitor.

Summary information for your patients

On the morning after the start of her period, the woman presses the '*m*' Button to initiate that cycle of use. This also establishes the Testing Window which runs from 3 hours before to 3 hours after the time the '*m*' Button is set. The woman then simply looks at the Monitor every morning during the Testing Window and, through its display, it guides her through her cycle.

The Clearblue Fertility Monitor will indicate:

- The day of her cycle
- When a test is required
- Days of Low Fertility
- Days of High Fertility
- Days of Peak Fertility
- When the end of her cycle is approaching
- Where there is a system error.

Please note: always read the instructions provided in the package before using the Clearblue Fertility Monitor

In consumer studies:

- 100% of women found the instructions easy or reasonably easy to understand[10]
- 99% of women understood when to do a test[10]
- More than 97% of women correctly understood that they should have intercourse on days of High and Peak Fertility to increase their chances of conception[10]
- Over 90% of women found the Monitor easy or very easy to use in a study of over 300 women.[1]

In laboratory testing, the Clearblue Fertility Monitor has been shown to be 99% accurate in detecting the LH surge, in cycles tested where an LH surge had been identified by a reference method.

Why recommend the Clearblue Fertility Monitor?

The Clearblue Fertility Monitor provides you with a unique innovation in fertility management that women can use at home to increase their chances of conception.

The Monitor:

- Is proven to increase the chances of conception by 89% in the first two cycles of use[1]
- Accurately predicts ovulation when compared with serum hormone measurements and vaginal ultrasound scans[13]
- Is proven to detect changes in urinary levels of LH and E3G which coincide with laboratory measurements by radioimmunassay and fluorescence immunoassay in defining the potentially fertile period[11,13]
- Is able to accurately identify the entire fertile window for the purpose of achieving pregnancy.[9] Mistiming intercourse is recognised as a significant factor in couples who have problems conceiving[20]
- Is able to help women conceive more quickly.[20]

For your patient, the Clearblue Fertility Monitor:

- Is a quick, simple and effective way to identify the most fertile days
- Indicates when to test and the level of fertility every day requiring no subjective interpretation
- Helps to reduce the worry and uncertainty couples may be experiencing when trying to conceive
- Works naturally, without drugs or invasive devices and procedures
- Can help couples conceive more naturally.

Recommending the Clearblue Fertility Monitor

Suitable patients for the Clearblue Fertility Monitor

The Clearblue Fertility Monitor is ideal for women who are proactively planning pregnancy. It is suitable for women whose natural cycle length normally lasts between 21 and 42 days. Women who have difficulty interpreting ovulation predictor test results or determining when to test will find the Monitor easy to use and easy to read.

Ensuring an effective performance

The Clearblue Fertility Monitor should not be recommended if the woman:

- Has experienced menopausal symptoms
- Is breast-feeding
- Has recently been pregnant (even if not carried to full term)
- Has impaired liver or kidney function
- Has polycystic ovarian syndrome
- Is taking antibiotics containing tetracyclines
- Is undergoing treatments which will affect her cycle (e.g. hormonal contraception including emergency contraception, certain fertility treatments, HRT)
- Clomiphene citrate may elevate estrogen levels and this may result in High Fertility being declared early in the cycle and more High Fertility days being displayed. In some cases the Fertility Monitor may not show Peak Fertility even when ovulation occurs.

Clinical support – published data

Increased pregnancy rate with use of the Clearblue Easy Fertility Monitor

Robinson JE, Wakelin M and Ellis JE. Fertility and Sterility 2007;87:329–334

Key Findings:

- Significantly higher pregnancy rates were achieved in women who were using the Clearblue Easy Fertility Monitor compared to women who were not using the Clearblue Easy Fertility Monitor, over the first two cycles of use
- The Clearblue Easy Fertility Monitor increases the chances of conception by 89% within first 2 cycles of use, based on a study of 302 women who used the Clearblue Easy Fertility Monitor for 2 cycles compared to a control group of 347 women who did not use the Clearblue Easy Fertility Monitor
- With conception most likely to occur in the 5–6 days leading up to ovulation, the Clearblue Easy Fertility Monitor provides a wider window of fertility at which to target intercourse in order to successfully achieve pregnancy
- Users find the device easy or very easy to use (90%) and convenient or very convenient (80%).

Mistiming of intercourse as a primary cause of failure to conceive: results of a survey on use of a home-use fertility monitor

Robinson JE and Ellis JE. Current Medical Research and Opinion 2007;23:301–306

Key Findings:

- A study of 196 women who had conceived using the fertility monitor showed that 91.9% conceived within 3 cycles of use. Conception aids were used by 84% of women prior to using the fertility monitor and 64.3% had consulted a physician to seek help in attempting to conceive.
- Average fertility treatment costs prior to using the fertility monitor were $6,637.
- A probable cause of failure to conceive in this group appeared to be mistiming of intercourse.

Prediction of ovulation by urinary hormone measurements with the home-use Clearblue Fertility Monitor: comparison with transvaginal ultrasound scans and serum hormone measurements

Behre HM, Kuhlage J, Gaßner C, *et al*. Human Reproduction 2000;12:2478–2482

Key Findings:

- Peak Fertility was detected by the Fertility Monitor in 135 of 149 ovulatory cycles (as confirmed by ultrasound).
- A serum LH surge was detected in 139/149 (93.3%) of these cycles.
- Ovulation occurred in 91.1% of the ovulatory cycles during the 2 Peak Fertility days and in 97.0% of these cycles during the 2 Peak Fertility days plus the 1 High Fertility day thereafter.
- The serum LH surge was detected 92.8% of the time during the Fertility Monitor's Peak Fertility period or one day before.

Results from the study led the author to conclude, "if a couple desiring children have intercourse on the first day of Peak Fertility, in 97% of cycles this time-point would be ideal for conception and clinical pregnancy."

Prediction of the potentially fertile period by urinary hormone measurements using a new home-use monitor: comparison with laboratory hormone analyses

Tanabe K, Susumu N, Hand K, *et al*. Human Reproduction 2001;16:1619–1624

The monitor LH and E3G measurements and corresponding fertility status were compared with serum oestradiol, serum LH, urinary E3G and urinary LH measurements in a population of normal healthy women.

Key Findings:

- There was agreement between the first day of peak fertility and the urinary LH peak day in 65.6% of cycles and detection 1 or 2 days before the urinary LH peak day in 31% as a result of the Monitor detecting the start of the LH surge. Overall surge detection by the Monitor was 96.6%.
- The median number of high and peak days was 8.
- The mean LH and E3G signals showed similar changes to the mean serum and urinary concentrations with both the peak mean LH and E3G signals occurring on day 0 the same day as the peak mean urinary LH and E3G concentrations measured by radioimmunoassay and fluorescence immunoassay respectively.

The authors concluded that the Monitor offers increased benefits over existing methods. By informing the woman that her fertility status is high, it provides more warning of her 2 day period of maximum fertility and in addition intercourse on the high fertility days themselves may lead to pregnancy.

Clinical support – articles

Timing Intercourse to Achieve Pregnancy: Current Evidence

Stanford JB, White GL and Hatasaka H. Obstetrics and Gynecology 2002;100:1333–1341.

Key Findings:

- The Clearblue Fertility Monitor identifies the occurrence of ovulation clinically and also identifies a longer window of fertility than urinary luteinising hormone kits.
- Prospectively identifying the full window of fertility may lead to higher rates of conception.
- Proper information given early in the course of trying to achieve pregnancy is likely to reduce time to conception for many couples, and also reduce unnecessary intervention and cost.
- Prospective methods that identify the approach of ovulation before it occurs would be expected to result in higher conception rates.
- Calendar calculations are unreliable for the purpose of timing intercourse to conceive.
- Ovarian follicular ultrasound (by transvaginal scanning) is highly accurate for identifying the approach and occurrence of ovulation but its high cost and limited availability preclude its routine use for couples trying to achieve pregnancy.
- BBT rise occurs after ovulation making it nearly impossible to identify the days of fertility to achieve pregnancy within the same cycle.
- LH urinary kits are accurate at identifying the LH surge but the brief time window (1–2 days) prospectively limits the opportunity to have multiple acts of intercourse before ovulation.
- Physicians in a study in Missouri were most likely to recommend the initial steps of BBT or calendar calculations.
- This suggests that physicians in the US may currently be recommending methods that are less than optimal for timing intercourse to achieve pregnancy.

The authors recommended the Clearblue Fertility Monitor as one of the two most appropriate methods to identify the entire fertile window for the purpose of achieving pregnancy. The Monitor has advantages over fertility charting of vaginal discharge because of its high tech perception and ease of use.

Acceptability of a home monitor used to aid in conception: psychosocial factors and couple dynamics

Severy LJ, Robinson J, Findley-Klein C and McNulty J. Contraception 2006;73:65–71

Assessing the psychological acceptability of new technologies designed to assist couples achieve a desired pregnancy is a complex process. It has been suggested that three psychosocial domains of interest when studying couples trying to conceive are[†]

- A method's impact on the couple
- Their emotional status as they achieve, or fail to achieve, a pregnancy
- Acceptability of the technology.

The authors concluded that the Monitor offers increased benefits over existing methods. By informing the woman that her fertility status is high, it provides more warning of her 2 day period of maximum fertility and in addition intercourse on the high fertility days themselves may lead to pregnancy.

Measures relating to the impact of a new technology on the couple's relationship, their feelings relating to pregnancy status, and the process of conceiving were assessed in a study of couples using the Clearblue Fertility Monitor. Fifty-two couples participated in a four menstrual cycle study. Pregnancy status and daily logs of sexual activity were recorded. In addition, self completion questionnaires were collected from both male and female partners at the beginning of the study (before use of the Monitor), and at the end of each menstrual cycle during the study.

Results of the study indicated that psychological satisfaction with the new technology increased for couples achieving pregnancy. Baseline measures were the highest for couples eventually achieving a pregnancy, indicating that couples who entered the study with an optimistic attitude about conceiving were more likely to conceive than those who were not as optimistic.

Additionally, couples were twice as likely to achieve a pregnancy if the male's ratings of acceptability of the technology were similar to his perceptions of his partner's feelings about the technology. For couples not becoming pregnant, acceptability of the technology declined over time and the relationship became more strained.

Achieving a pregnancy is a complex process. The process can be enhanced by gaining knowledge of the woman's own reproductive functioning, which can lead to the proper timing of intercourse, therefore keeping stress, anxiety and couple strain to a minimum. The results of this study indicate that all of these factors seem to be positively impacted by use of the Clearblue Fertility Monitor.

[†]Cleland J, Hardy E, Taucher E (1990). Introduction of new contraceptives into family planning programs: Guidelines for social science research. Geneva: World Health Organization.

Clinical support – articles

Assessment of the Clearplan* Easy Fertility Monitor (CPEFM) in Couples Seeking Conception Assistance

Pouru P. Bhiwandiwalla, MD, Stan Williams, MD, Lawrence J Severy, PhD and Janet E. Jacobs, FIBS
Obstetrics & Gynecology, Volume 97, Number 4 (supplement), April 2001, 29S

Objective:

This study evaluated a new home-use Fertility Monitor designed to help couples increase their chances of conceiving.

Methods for data collection

CPEFM is an interactive system which is designed to identify those days in a woman's cycle when intercourse is most likely to lead to conception by predicting ovulation through the simultaneous measurement of urinary E3G and LH. Couples used the CPEFM for four menstrual cycles, or until they conceived. Couples completed coital logs and data from these logs were analysed in conjunction with data collected from the Monitor.

Results

54 couples were recruited. Average age of female volunteers was 32 years. 68% had been trying to conceive for a maximum of six months. 54% had not had previous pregnancy. 21 volunteers conceived during the trial. The cumulative lifetable pregnancy rate was 16.7% after one cycle, 31.5% after two cycles, 35.5% after three cycles and 39.5% after four cycles (95% confidence interval 26.3% to 52.8%). The CPEFM declared a median number of fertile days of 7. More than 60% of cycles had between 1 and 5 days warning of the CPEFM peak/LH surge day. At least one act of intercourse was reported in the CPEFM fertile phase in over 96% of cycles, while over 70% of cycles had between 2 and 5 acts of intercourse during this period. Over 91% of cycles had at least one act of intercourse during the period three days before the LH surge to two days after the LH surge (mode three). This six day fertile period has been previously recognised as the most likely time for a couple to conceive.

Conclusion

The four cycle, cumulative lifetable pregnancy was found to be 39.5%. CPEFM was demonstrated to be an easy-to-use method of predicting the days immediately preceding ovulation, when intercourse would most likely lead to conception.

*The Monitor name has since been changed to Clearblue Fertility Monitor.

Clinical support – Data on file

Laboratory analysis of performance of the Clearblue Fertility Monitor

Objective

To determine the accuracy of the Clearblue Fertility Monitor in detecting the LH surge.

Method

Daily urine samples were collected from 88 women of reproductive age for 185 menstrual cycles. The timing of the LH surge was identified for each cycle using a radioimmunoassay reference method.

Those cycles in which an LH surge had been identified (171) were tested using the Clearblue Fertility Monitor.

Results

A range of laboratory analyses has been carried out by SPD in order to build a database of information relating to the performance of the Clearblue Fertility Monitor. From this extensive database, the following conclusions can be drawn:

- The Clearblue Fertility Monitor provides a 99% accurate detection of the LH surge, the best marker of impending ovulation.
- The Clearblue Fertility Monitor will give the majority of women 1–5 days warning of their Peak Fertility.
- The Clearblue Fertility Monitor will typically identify up to 6 days of High and Peak Fertility.

The Clearblue Fertility Monitor has been designed for women whose natural cycle lengths are between 21 and 42 days. Those women whose cycle lengths did not fall within range were excluded from the study.

Conclusion

In laboratory testing, the Clearblue Fertility Monitor detected the LH surge in 169/171 cycles, in agreement with a quantitative radioimmunoassay.

Consumer data on the Clearblue Fertility Monitor – Data on file

Objective:

To determine whether women could correctly understand and use the Clearblue Fertility Monitor.

Method

The Clearblue Fertility Monitor was used at home by 65 women contributing a total of 358 menstrual cycles, with a maximum of 6 cycles per woman. Self-reported diaries were kept recording general information about menses, when the women performed tests as requested by the Monitor and what their daily Fertility Status (Low, High or Peak) was. Daily urine samples were also collected and tested in the laboratory by trained personnel using the Clearblue Fertility Monitor.

Results

- The fertility status from home use of the Clearblue Fertility Monitor agreed with that of the laboratory on 98.8% of days (+/- 1 day) and 91.2% exact agreement
- The LH surge was accurately identified by the home users of the Monitor on 90.7% of cycles compared to the laboratory
- From cycle 2 onwards, the Monitor requested only 10 tests per cycle in 89% of cycles
- Users completed 95.4% of tests requested by the Monitor
- The Fertility Status was correctly recorded by users on 99.3% of days compared to the downloaded Monitor data
- 92.5% of users believed that the Clearblue Fertility Monitor showed the best time to conceive
- 100% of users found the Instruction Booklet very or reasonably easy to understand.

Clinical support – review articles

Estradiol: the physiological basis of the fertile period

Burger HG. International Journal of Gynecology and Obstetrics 1989;Suppl.1:5–9

Key Findings:

- Serum estradiol is the major physiological determinant of the onset and duration of the fertile period.

The ability to define this period by simple clinical means (e.g. by hormonal assays) and the explanation of all the mechanisms involved provide the basis for approaches to the regulation and management of infertility.

Review article: Hormonal indices of ovulation and the fertile period

Collins WP. Advances in Contraception 1985;1: 279–294

Key Findings:

- The mean concentration of plasma estradiol starts to rise about one week before the onset of the LH surge and reaches a maximum value on the day before the LH peak
- A rise in the level of estradiol in plasma or saliva, or a metabolite in urine, might be used to indicate the start of the probable fertile period
- A defined rise in plasma LH occurs, on average, 32 hours before ovulation, with a range of 24 to 56 hours
- By measuring hormone levels it is possible to develop algorithms to predict ovulation and identify the fertile period.

Human cervical mucus: Research update

Katz DF. American Journal of Obstetrics and Gynecology 1991;165:1984–1986

Key Findings:

- Cervical mucus regulates fertility as its physical properties change during the menstrual cycle
- Cervical mucus accepts, filters, prepares and releases sperm for successful transport to the egg and prospective fertilisation
- In general, the number and rate of penetration of sperm into cervical mucus are maximal during the periovulatory period when mucus viscoelasticity is minimal
- Sperm may, however, penetrate the more viscoelastic cervical mucus that occurs before ovulation

Preliminary data shows a correlation between preovulatory sperm penetrability and rising serum (or urinary) estrogen levels.

Clinical support – review articles

Timing of sexual intercourse in relation to ovulation

Wilcox AJ, Wienberg CR Baird DD. New England Journal of Medicine 1995;333:1517–1521

Key Findings:

- Results from this study indicated that all conceptions resulted from intercourse that occurred during a 6-day interval ending on the day of ovulation. When 129 menstrual cycles in which a single act of intercourse led to pregnancy were studied, the probability of conception ranged from 8% on the first day of the 6-day period up to 36% on the sixth day, the day of ovulation. When using the statistical model, the probability of conception ranged from 10% when intercourse occurred 5 days before ovulation to 33% when it occurred on the day of ovulation itself
- By analysing data on the day of ovulation (identified by means of hormone assays of daily urine specimens), and daily records of sexual intercourse, we found that all conceptions resulted from intercourse that occurred during a six-day interval ending on the day of ovulation.

Optimal use of infertility diagnostic tests and treatments

Crosignani PG, Rubin BL. Human Reproduction 2000;15:723–732

Key Findings:

- This workshop concluded that prediction of ovulation is useful in order to time intercourse during the most fertile period in those wishing to become pregnant. Evaluating the LH surge is the best single assay while measurement of LH plus preovulatory estrogen is the best prediction.

“It is possible to predict the fertile period and detect the LH surge through parallel assay of oestrone glucuronide and LH in the urine. While these urinary methods give a higher incidence of false negative results than radioimmunoassay or immunoradiometry in blood, they are accurate enough to have wide application in self-testing, both for enhancing fertility and for contraception.”

Clinical support – additional articles

World Heath Organization. Temporal relationships between indices of the fertile period. Fertility and Sterility 1983;39:647–655.

World Health Organization. A prospective multi-centre to develop universal immunochemical tests for predicting the fertile period in women. International Journal of Fertility 1985;30:18–30.

Catalan R, *et al*. Correlation between plasma estradiol and estrone-3-glucuronide in urine during the monitoring of ovarian induction therapy. International Journal of Fertility 1989;34:271–275.

Kerin JF, *et al*. Morphological and functional relations of Graafian follicle growth to ovulation in women using ultrasonic, laparoscopic and biochemical measurements. British Journal of Obstetrics & Gynaecology 1981;88:81–90.

Bourne TH, *et al*. Ultrasound studies of vascular and morphological changes in the human corpus luteum during the menstrual cycle. Fertility and Sterility 1996;65:753–758.

France JT, *et al*. Characteristics of natural conception cycles occurring in a prospective study of sex preselection: fertility awareness symptoms, hormone levels, sperm survival and pregnancy outcome. International Journal of Fertility 1992;37:244–255.

Lenton EA, *et al*. Problems in using basal body temperature recordings in an infertility clinic. British Medical Journal 1977;1:803–805.

About SPD Swiss Precision Diagnostics GmbH

SPD Swiss Precision Diagnostics GmbH is a world leader in the research, design, production and supply of advanced consumer diagnostic products. Our brands, such as Clearblue® and Persona®, are familiar in many countries, and are trusted for their accuracy and simplicity by women keen to know more about their own reproductive health. SPD brands are acclaimed for their pioneering innovation: Clearblue was the first brand to introduce a one-step pregnancy test, a one-minute test, a urine sample indicator, digitally displayed results and a Conception Indicator feature.

At SPD, we are committed to helping people make informed decisions about their health and well-being, through a continuing flow of new and inventive developments. Our research centre is at the sharp edge of innovation, and is fully engaged in the development of reliable diagnostic products for better health and personal self-care.

If you are a healthcare professional and wish to contact a member of the Clearblue support team about any product in the Clearblue range, please send an email to spdproductsupport@spdspark.com

Alternatively, you could write to us at:
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Switzerland
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References

1 Robinson JE *et al*. Increased pregnancy rate with use of Clearblue Easy Fertility Monitor. Fertility and Sterility 2007;87:329–334.

2 World Health Organization. Temporal relationships between indices of the fertile period. Fertility and Sterility 1983;39:647–654.

3 Catalan R *et al*. Correlation between plasma estradiol and estrone-3-glucuronide in urine during the monitoring of ovarian induction therapy. International Journal of Fertility 1989;34:271–275.

4 Wilcox AJ *et al*. Timing of sexual intercourse in relation to ovulation. New England Journal of Medicine 1995;333:1517–1521.

5 Martinez AR *et al*. Prediction and detection of the fertile period: the markers. International Journal of Fertility 1995;40:139–155.

6 Burger HG. Estradiol: the physiological basis of the fertile period. International Journal of Gynecology and Obstetrics 1989;Suppl 1:5–9.

7 Collins WP. Hormonal indices of ovulation and the fertile period. Advances in Contraception 1985;1:279–294.

8 Kerin JF *et al*. Morphological and functional relations of Graafian follicle growth to ovulation in women using ultrasonic, laparoscopic and biochemical measurements. British Journal of Obstetrics and Gynaecology 1981;88:81–90.

9 Stanford JB *et al*. Timing Intercourse to Achieve Pregnancy: Current Evidence.Obstetrics and Gynecology 2002;100:1333–41.

10 Data on file.

11 Tanabe K *et al*. Prediction of the potentially fertile period by urinary hormone measurements using a new home-use monitor: comparison with laboratory hormone analyses. Human Reproduction 2001;16:1619–1624.

12 Bhiwandiwalla PP *et al*. Assessment of the Clearplan Easy Fertility Monitor (CPEFM) in couples seeking conception assistance. Obstetrics and Gynecology 2001;97:29S.

13 Behre HM *et al*. Prediction of ovulation by urinary hormone measurements with the home use Clearblue Fertility Monitor: comparison with transvaginal ultrasound scans and serum hormone measurements. Human Reproduction 2000;12:2478–2482.

14 Lenton EA *et al*. Problems in using basal body temperature recordings in an infertility clinic. British Medical Journal 1977;1:803–805.

15 Matthews CD *et al*. Optimal features of basal body temperature recordings associated with conceptional cycles. International Journal of Fertility 1980;25:318–320.

16 Wetzels LC *et al*. Basal body temperature as a method of ovulation detection: comparison with ultrasonographical findings. Gynecologic and Obstetric Investigation 1982;13:235–240.

17 Yong EL *et al*. Simple office methods to predict ovulation: the clinical usefulness of a new urine luteinizing hormone kit compared to basal body temperature, cervical mucus and ultrasound. Australian and New Zealand Journal of Obstetrics and Gynaecology 1989;29:155–160.

18 Moghissi KS. Accuracy of basal body temperature of ovulation detection. Fertility and Sterility 1976;27:1415–1421.

19 Severy LJ *et al*. Acceptability of a home monitor used to aid in conception: psychosocial factors and couple dynamics. Contraception 2006;73:65–71.

20 Robinson JE and Ellis JE. Mistiming of intercourse as a primary cause of failure to conceive: results of a survey on use of a home-use fertility monitor. Current Medical Research and Opinion 2007;23:301–306.

Limitations on use

There are no products available that can guarantee success in achieving pregnancy. The Clearblue Fertility Monitor has been designed to assist in conception. It is NOT intended to be used for contraception.

The Clearblue Fertility Monitor is suitable for women whose natural cycle normally lasts between 21 and 42 days. The majority of women will need 10 Test Sticks in each cycle. However, women with irregular or long cycles may have to use 20 Test Sticks each cycle in order to detect their most fertile time.

Certain medical conditions and medications can adversely affect the performance of the Clearblue Fertility Monitor. Women who have menopausal symptoms, polycystic ovarian syndrome, impaired liver or kidney function, are pregnant or have recently been pregnant (even if not carried to full term), may get misleading results. Similarly misleading results may be obtained by women using antibiotics containing tetracyclines, hormonal treatments (e.g. hormonal contraception, hormone replacement therapy), fertility treatments containing human Chorionic Gonadotrophin (hCG) or Luteinising Hormone (LH), or any treatment that might affect their cycle. Clomiphene citrate may elevate estrogen levels and this may result in High Fertility being declared early in the cycle and more High Days being displayed, and in some cases the Monitor may not show Peak Fertility even when ovulation occurs. It is therefore recommended that women taking clomiphene citrate consult their doctor for advice before using the Clearblue Fertility Monitor. Women who have recently been breastfeeding, using hormonal treatments (e.g. hormonal contraception, including emergency contraception, fertility treatments, hormone replacement therapy), or any other treatment that might affect their cycle, may wish to wait until they have at least two natural menstrual cycles in a row (each lasting 21–42 days), before using the Clearblue Fertility Monitor.

Women who have recently been pregnant (even if not carried to full term) may still have hCG in their bodies. HCG can adversely affect the performance of the Clearblue Fertility Monitor. Therefore they are advised to wait until they have had at least two natural menstrual cycles in a row (each lasting 21–42 days), before using the Clearblue Fertility Monitor.

Women are advised to read the manufacturer's instructions for any medication they are taking before using the Clearblue Fertility Monitor, and to speak to their doctor if they need further advice.