

Understanding Blood Tests - Pregnancy/Fertility Monitoring *by Beth Anne Ary M.D*

Blood tests are the most common and most important method of monitoring pregnancy-- both assisted pregnancies, and unassisted. In most kinds of [assisted reproduction](#), blood tests become especially important. They become a major part of the experience. This is because in assisted conception, timing becomes crucial, and blood tests (together with ultrasound scans) provide the information to help assess this timing. The tests also provide continuous feedback on each cycle.

The monitoring process varies slightly from one type of assisted conception to another. With different types the process might be on the lookout for different events, and might be looking at different chemicals and different hormones. In order to write in a specific manner, we will write about IVF-ET cycles (identical for monitoring purposes to GIFT cycles).

The Purpose of Monitoring Blood Levels

In IVF-ET and GIFT cycles the purpose of monitoring blood levels is:

- to be certain that there is an adequate, but not excessive response to the hormones. These hormones (gonadotropins) would be Pergonal, Humegon or Metrodin.
- to time oocyte (egg) retrieval.
- to be sure that as many mature oocytes as possible are retrieved.
- to watch for changes in hormone levels. Particularly those hormones that are thought to indicate, or to cause poor oocyte quality.

To answer these questions, a number of different tests could be done. No patient would receive all these tests-- excessive testing can be stressful, and thus 'counterproductive'. Instead, tests would be done to measure for one or another of three different hormones. These three are estradiol ("E2"), luteinizing hormone ("LH"), and progesterone.

Estradiol: What It Is and What It Tells Us.

The level of estradiol is measured in almost every blood sample taken during the monitoring of almost every type of assisted pregnancy. It is arguably the most informative of the three tests. Because of this, we will spend more time and space on estradiol. Don't worry-- the other two won't be nearly as long.

Estradiol is a hormone that stimulates the lining of the uterus, causing the lining to grow, and to make itself ready for embryo arrival. (This is not estradiol's only function, but for us, it's the important one). Estradiol is tied into pregnancy by it's method of production: oocytes (eggs) contain follicles. These developing follicles contain 'granulosa cells'. These granulosa cells synthesize the estradiol and release it into the blood circulation.

This means that more follicles produce more estradiol. This helps measure how many follicles are actively developing. The longer they continue to develop, the longer the estradiol level continues. As they develop, the level continues to rise. This rise can further indicate that the oocyte within the follicles is reaching its maturity.

An example of the use of estradiol level is when it is measured during down-regulation cycles. In down-regulation we expect low levels of estradiol: below 30pg/ml. If levels are not this low, this suggests that the ovaries are not yet suppressed, and that the down-regulation should continue a little longer, until they actually are suppressed.

Estradiol And Ultrasound Scans

Blood estradiol is also used in combination with ultrasound scans. Taken together they help indicate how (and if) the ovaries are responding to stimulation. Is there a response? Is it adequate? Is it excessive? To tell us this, the blood level has to be viewed in relation to the stage of pregnancy and the day in the cycle in which the level is being taken.

For example, a level of 1500 pg/ml on day eleven might be considered acceptable in a stimulated cycle, as reflecting the presence of a reasonable number of mature follicles. However, if this level were present on day eight, it would be considered unacceptably high. It would almost certainly reflect the presence of an excess of follicles. At this stage (day eight) they would still be Immature ones. Their quantity, however, would suggest that continued stimulation would carry an unacceptable risk of developing OHSS-- ovarian hyperstimulation syndrome.

Don't Expect Easy Comparison

Before we continue, one important point: levels of estradiol are not the same from person to person. They cannot simply be compared from one to another. People vary-- everyone is slightly different, and everyone responds to a different degree. Some more so than others. A level that is dangerously high in one person-- or dangerously low in a second-- might be normal and healthy for a third. This is why blood levels can't just simply be compared. It's also why blood levels can't always be interpreted with complete certainty in the first cycles. Without prior cycles to 'calibrate' the levels, the meaning of a level can only be determined as to what it usually means-- what it 'probably', or perhaps even 'almost certainly' means.

Despite individual variation, estradiol level does provide very useful information.

A Rough Rule-of-Thumb for Good Estradiol Levels.

Exact figures are not possible. As a rough guide, however, a level in the range of 150 to 500 pg/ml is generally considered reasonable for the eighth day of a stimulated cycle. An approximate doubling of this level every 48 hours is considered promising, as a sign of continued good follicle development.

When the Estradiol Level Stays Flat or Begins to Fall.

Occasionally, the level of estradiol fails to rise during a cycle, or even falls. If this

happens it strongly suggests that the follicles are not responding appropriately, and that the oocytes within will not be of good quality. Under these circumstances our advice is almost invariably to cancel the cycle, because a change in stimulation protocol may yield more oocytes-- and healthier ones-- in a later attempt.

Low Estradiol Not Always a Problem

A more common situation is when the level is low in the early part of the cycle. The choice then is to either carry on with the same amount of stimulation, to increase the amount of stimulation, or to cancel the cycle. This decision has to be based on a number of factors. These include:

the previous response to stimulation
chronological age
how low the level is
the ultrasound appearance of the ovaries
is there a pressing need to ensure that an optimal number of oocytes are obtained, as in the case for couples with male factor infertility?

How It All Comes Together with Estradiol.

It should be clear from all of the above that estradiol levels do not tell the entire story by themselves. One level leads us to advise a couple to cancel. The same level in another couple leads us to suggest continuing.

We've already discussed levels that are low. When levels are high, we have the same choice: change the stimulation (reduce it), or cancel the cycle. The criteria to consider are the same as for low levels. The one additional factor is that with high levels we also think carefully about OHSS (ovarian hyper-stimulation syndrome). When assessing the risk of OHSS we look to previous cycles, if there are any. Any suggestions from these cycles of OHSS problems would quite definitely weigh heavily towards cancelling the cycle.

When the decision is to proceed, levels of estradiol continue to be monitored. If they continue to exceed acceptable levels, even with reduction in stimulation, we might reassess the cycle, and once again advise cancelling. If however they do return to normal levels, then the cycle will continue.

What is the limit of acceptable estradiol level? Acceptable levels vary-- it's not possible to give a definite, absolute number. However, any level of 4000 pg/ml or above does require careful consideration. Levels that are much in excess of this usually do lead to cancellation, though not always.

What about the lower limit? This too involves many factors. However, if the estradiol level has not reached a minimum of 600pg/L (**** beth-- should this be per liter, or per ml?***), then our usual policy is to discontinue the cycle. In practice we usually don't proceed unless the ultrasound shows three or more mature follicles. Since estradiol levels and the total number of follicles are related (as discussed in the beginning of this essay), this by itself eliminates most of the possibility for levels at or below this lower limit. Three or more mature follicles will, under most circumstances, secrete enough estradiol by themselves to give a level in excess of this minimum.

Do bear in mind that the above are only a rough, rule-of-thumb guides, however. They

can and do vary depending on individual circumstance.

Luteinizing Hormone, or "LH": What Is It and What Does It Do?

Before the introduction and widespread use of drugs such as Lupron, assessment of luteinizing hormone was at least as important, if not more important, than estradiol levels. It remains an important test for anyone undergoing any cycle where Lupron or Synarel (GnRH agonist) is not being used. This is because, without Lupron, an early unwanted LH surge may occur.

LH Surges (note: the next entry implies that an LH surge is desirable, and necessary. This entry implies that it isn't. How do the two reconcile? is early=bad, but near end=necessary?)

A surge in the level of LH may cause undesirable changes in egg quality, or cause early egg release. Both of these decrease the chance of pregnancy. Regimens such as Clomid, Clomid/Pergonal cycles, or "straight" Pergonal, Metrodin or Humegon cycles all must include urine LH testing (for instance, Ovuquick, or ClearPlan Easy). If a sudden rise in the level of LH is detected (often termed "an LH surge"), this indicates that the process leading to ovulation and release of the oocyte has begun. It is this process that is blocked, in the vast majority of cases, by the use of Lupron. Unfortunately, there is no way of knowing when a rise in the level of LH actually begins, except for testing blood or urine every three to four hours. This makes it virtually impossible to accurately time egg retrieval. This timing is necessary to be certain that the oocytes are mature. Because of this problem, the cycle is usually canceled if an LH surge is detected.

Progesterone: The Last of the Three

Progesterone is secreted by the corpus luteum complex, a complex that forms in the follicle once the oocyte has been released. (Or, more accurately, it forms once there has been an LH surge). One of progesterone's major functions is to act on the uterine lining that the estradiol hormone has primed to become receptive to embryo implanting. Progesterone is synthesized in small amounts in developing follicles, so low levels can be detected at most times during the stimulation phase of treatment.

If the levels of progesterone rise during monitoring, however, it indicates that follicle development is not proceeding smoothly, and that the oocytes, if they are recoverable, may be of poor quality and may result in poor quality embryos.

What is considered an acceptable level of progesterone? Unfortunately, this is a matter of considerable controversy. To further complicate things, the level varies according to the stage of the cycle. So, the acceptable level also varies. A high level on day 10, for instance, is much more likely to indicate a problem than a high level anytime during the early stages, such as day one through five. Indeed, it is common when "flare" protocols are being used for progesterone levels to rise dramatically in the first few days of the cycle, but to then fall, most of the time, to reasonable levels within a few days. This is common and appears to have little effect, if any, on the outcome.

Since the role of progesterone is crucial in ensuring adequate preparation of the uterine lining, we usually check the level prior to "natural cycle" frozen embryo transfers, if we are monitoring for the LH surge. If the levels are considered inadequate we usually advise supplementation in the form of progesterone suppositories. In frozen embryo transfer cycles, or in any cycle where Lupron is used, progesterone must be supplemented because the body's own production will be reduced.

Final Words

Decisions made during monitoring are complex and based on many considerations. These make it difficult or impossible to establish hard-and-fast rules. It also means that the advice given to one couple might contradict the advice given to another couple, even though their circumstances might appear similar, or even appear 'identical'.

Circumstance can also change with age, and with ongoing treatment. Advice from one cycle may not match advice in later cycles-- even when the results of monitoring appear identical. Even when, in fact, they are identical.

To decide to cancel a cycle is a difficult decision. There's a lot of hope tied up with each cycle, and the decision to cancel can be a disappointment-- or a cause for anxiety. It can be a blow to one's hopes and spirit, cause distress and . Understand, however, that the decision to cancel a cycle can sometimes lead to a better chance of success in a future cycle. Please also understand from this essay some of the reasons, some of the thinking, and some of the criteria behind the recommendation to cancel or to continue.

IVF nurses can help. Still, when possible, we advise 'going to the source'-- seek the advice of a physician when possible. A physician offers not just explanation, they can also discuss the implications, and how these might or might not affect any future treatment.

May luck be with you, along with our best wishes for success.

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