

### **The Lowdown on Progesterone**

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Progesterone is a hormone naturally produced by the female reproductive tract. Many trans women believe it has value in the physical transition process and particularly in relation to the development of breast tissue. However, in the trans arena, there is much misinformation about its benefits, little information on its adverse effects and little understanding of its action in the genetic female.

#### **Progesterone Physiology**

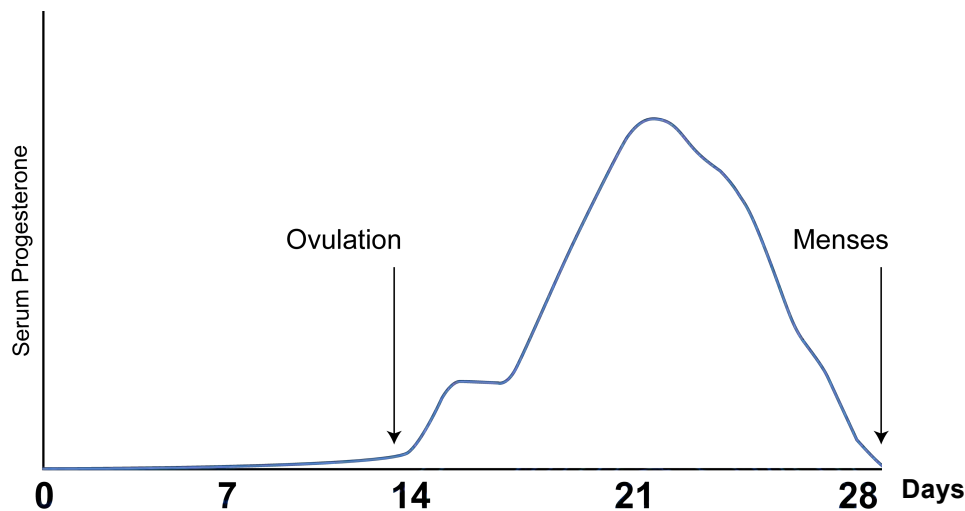
Prior to the start of menstruation – usually around 12 years old<sup>1</sup> – girls do not have any appreciable level of progesterone. In the early years of menstruation, oestrogen levels fluctuate but the typical monthly profile is not yet established and periods tend to be irregular in frequency and duration. Early cycles do not result in ovulation, i.e. no egg is released from the ovary.

After 2 years of non-fertile menstruation – at around 14 years old – ovulation starts to occur and an egg is released from the ovary.

Only when this occurs, do progesterone levels begin to rise from their low baseline during the second two weeks of the menstrual cycle (Figure 1).

They are highest during the week prior to menstruation and rapidly decline contributing to the stimulus for bleeding to occur. However, the average levels of progesterone during the full monthly cycle are very low.

**Figure 1: Progesterone levels in the 28 day menstrual cycle, once ovulation has started, at approximately 14 years old.**



It can therefore be seen that in genetic women, there is no progesterone before approximately 14 years of age. Consider this fact with the stages of natural breast development.

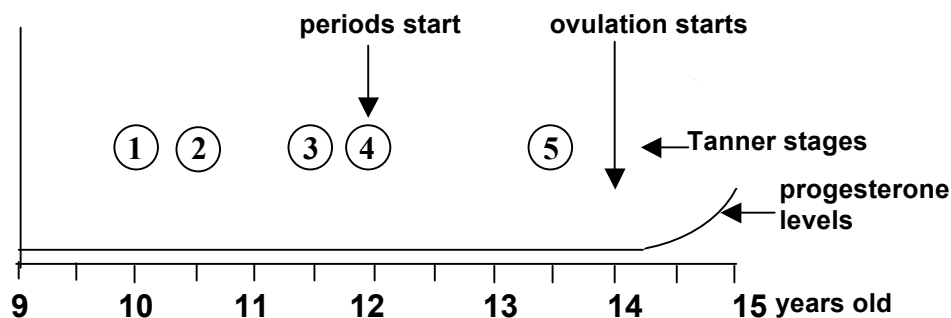
<sup>1</sup> Chronological ages given throughout this paper are all based on averages. The variation in start times of menses is wide and varies between populations.

### **Breast Development**

The *average* age at which a genetic girl commences breast development is 10 years old and occurs according to well-defined milestones called Tanner stages.

Tanner Stage	Average. Age	
1	10	Increased nipple size
2	10 ½	Increased areola as well. Breast bud (small tender lump behind the nipple)
3	11 ½	Nipple – areola complex increases. Breast size increases
4	12	The areola is a separate mound above the breast
5	13 ½	The areola becomes confluent with the breast leaving only the nipple proud

**Figure 2: Tanner stages and approximate ages of development prompted by oestrogen**



It takes approximately two to three years to achieve the majority of breast growth at age 13. Until stage 4, the growth of the breast in a girl takes place with the same oestrogen level as an adult male, i.e. < 150pmol/litre, as periods have not yet started. (The reason teenage boys do not develop breasts is because testosterone inhibits the effect of oestrogen. The development of small breasts in teenage boys can occur; this is called gynaecomastia and is caused by the over-conversion of low levels of testosterone to oestrogen.)

As progesterone does not exist in genetic girls until age 14, it is clear that progesterone cannot possibly have any effect on breast development in the genetic female.

To be clear, there is no direct involvement of progesterone in determining the size of breasts. Oestrogen is the primary enabler of breast growth. And there is no reason to suppose that the development of the breast in trans women is different.

Puberty is a complex process and, in addition to oestrogen, there are many other hormones which regulate it. These include prolactin, insulin and growth hormone. Breast tissue is composed of 80% fat. Prior to puberty, girls have slightly more body fat than boys. Therefore, women have a head start in the breast fat accumulation race compared to the aspiring development in trans women. At puberty, the effect of oestrogen further increases fat deposition. An adult female has 10 – 15% more body fat than an adult male, of which a proportion is obviously on the breasts. The average breast size of a woman in the UK is a 'B' Cup. In fact, the average amount of breast growth in a trans woman is also an 'A /B' cup. However, the reason it does not look the same is due to the relatively larger frame of a trans woman.

The actions of progesterone in the natal female are:

- cerebral: causing mood change;
- uterine: to prepare the uterus for implantation;
- pregnancy: to maintain pregnancy;
- breast: enabling duct formation for lactation. N.b. Ducts are very small and contribute little to breast size.

The first of these effects is undesirable, and the latter three actions are not relevant in trans women who do not become pregnant and have no need for breastfeeding.

### **Myth**

There is a commonly perceived myth that progesterone increases breast size, or improves shape in the trans woman. This comes, in part, from a paper published some years ago documenting the microscopic appearance of breast tissue. It indicated that progesterone increased the size of the lactating ducts. Hence, this is in accordance with the functions detailed above. The paper is not saying that breasts are bigger.

### **Further facts about Progesterone**

Progesterone is produced in small quantities, in men and women, in the adrenal glands. It acts as a precursor to the formation of testosterone. ANY form of progesterone, whether naturally produced or artificially administered has the propensity for conversion into testosterone.

Commonly available progestones / progestins.

Levonorgestrel	(testosterone analogue)	Most androgenic
Norethisterone	(testosterone analogue)	
Mexdroxyprogesterone Acetate	(progesterone analogue)	
Dydrogesterone	(progesterone analogue)	Least androgenic
Drospirenone	(spironolactone derivative)	Antiandrogen
Cyproterone Acetate	(synthetic progesterone)	Antiandrogen

Progesterone reduces the effectiveness of oestrogen as it:

- a) increases the breakdown of oestrogen in the liver;
- b) reduces the number of oestrogen receptors in the breast (oestrogen must bind to receptors in order to work. Even if there are good oestrogen levels in the bloodstream, if there are no receptors, it cannot work);
- c) is converted into testosterone which inhibits the actions of oestrogen.

The following table shows the common side effects associated with progesterone; the **testosterone** derived effects of progesterone are **underlined**.

Bloating	Nausea	<b><u>Fluid retention</u></b>	<b><u>Body Hair Growth</u></b>
Breast tenderness	Headache	<b><u>Weight gain</u></b>	<b><u>Loss of head hair</u></b>
Dizziness	Drowsiness	<b><u>Acne</u></b>	<b><u>Increased cholesterol</u></b>
Depression	Itching	Jaundice	

Progesterone-only contraceptives stop menstruation and ovulation by inhibiting the actions of oestrogen. Therefore, high doses of progesterone in trans women will also inhibit the actions of oestrogen and thus hinder feminisation. All commercially available forms of progesterone are 'high doses' as they are made to inhibit the actions of oestrogen in natal women.

### **Optimising Breast Growth**

In the trans woman, breast growth occurs due to oestrogen. It is achievable at low plasma levels of oestrogen. It is thought that too high a dosage too soon can stunt breast development so that only the early Tanner stages are achieved causing a conical effect with poor nipple growth. In a pubertal girl, oestrogen levels increase very slowly over many months.

It is well known that the some trans women believe that more oestrogen is better. This would be feasible if the body had more oestrogen receptors, but unfortunately, there are not a great number of oestrogen receptors. However, they will soak up any available oestrogen from the bloodstream.

Therefore, genetic predisposition largely determines the number of receptors and thus the likelihood of breast growth. Oestrogen stimulates receptor synthesis with relatively low levels of oestrogen in the natal woman pre-menstruation. There is a strong argument for commencing at low dosage and gradually increasing towards typical adult female levels.

Breast growth takes 2-3 years as stated earlier. The body can only change slowly. Patience is required and the understanding that growth is also phasic that is, there are periods when it is active and periods when nothing occurs. N.b. breast / nipple tenderness does not always indicate growth is occurring.

Growth occurs because oestrogen induces formation of glandular tissue and fat. Glandular tissue is hard and nodular. It constitutes 20% of the size. 80% of breast size is due to the oestrogen induced accumulation of fat. Simplistically, in pubertal girls, the calories eaten will preferentially be laid down as fat, whereas in the pubertal boy, calories contribute to muscle accumulation. In the trans woman, the effect of the taking oestrogen is to help to re-dress this physiological difference.

Many women experience an increased appetite whilst taking oestrogen and those who feminise well tend to put on weight, typically ½ stone to a stone. As an oestrogen dominant individual, this will manifest as gaining fat, at least some of which will be laid down on the breasts (as long as there is the genetic predisposition) and some will accumulate on the hips / legs to create the rounded female shape.

Therefore, to optimise the development of the female shape, trans women should avoid excessive calorie restriction or large amounts of cardiovascular exercise at this point, because this will lead to a suboptimal outcome, particularly in individuals who are very lean to start with.

The bottom line is that oestrogen alone grows breasts as long as other factors are favourable.

### **Progesterone and Trans women**

Many trans women have a wish to take progesterone. For several reasons:

- 1) they feel they should because menstruating females have progesterone for two weeks in the month,
- 2) they think it will make their breasts bigger
- 3) they are influenced by their friends
- 4) they want to feel more like a genetic woman

With regard to 1) the average age of presentation of trans women is 42 years old. Natal women undergo the menopause at approximately 50 years old, after which time their progesterone is all but zero and their oestrogen levels are the same as a man. So if 1) were desirable, NO trans woman should be taking any progesterone, (or any oestrogen for that matter after the age of 50).

As already explained 2) is a fallacy.

Point 3) is a reflection of the pressure many trans women feel, and may put their friends under, having accepted as true the many postings on the internet on the topic of the benefits of

progesterone. The majority of what is written on the internet about hormones is rubbish. It is frequently written by non-medical people, who have copied and pasted their information from other uninformed sources. The advice is laden with myth, out of date information and personal opinion. Even the sites that seem to be written by 'doctors' are usually not actually medical doctors. A science PhD does not indicate medical competence.

Sites abroad are also seldom written by doctors and very few sources are written by any who have a reasonable degree of actual experience in dealing with the administration of hormones in trans people.

Point 4) is understandable but somewhat bizarre since most genetic women would prefer not to experience the effects of progesterone. Progesterone is largely what causes premenstrual tension (PMT). It greatly affects mood, causing a whole array of mood destabilising effects; anxiety, aggression, depression. The susceptible genetic woman will explain that these feelings are neither pleasant nor desirable. Feeling bloated and spotty with painful breasts just prior to a period is not welcomed by natal women. I believe trans women have a high placebo effect where this scenario is concerned.

### **Anecdotal Findings**

Many of my patients have reported their experience taking progesterone (not prescribed by me and usually before they see me).

Their experience falls into 3 categories:

- Some tell me it made no difference at all, neither good nor bad.
- Many describe the side effects, particularly on mood as well as the full complement of effects listed in table 3.
- Some report an increase in breast growth. In some individuals, this may be the case and I suspect that this is due to two things:
  - 1) The individual's appetite is greatly increased. This causes increased fat accumulation in a straightforward calorie excess dependent fashion.
  - 2) A sub-optimal oestrogen regime. Just because a person takes the dosages detailed on the internet, does not equate to an optimised regime. Many women do not absorb oestrogen well. There is no substitute for a professionally monitored oestrogen regime by someone who understands oestrogen physiology and drug administration. Oestrogen levels need interpretation in the context of the individual's observed effects, the regime administered and the dynamics of drug administration.

Consider this. In my past life:

If I weighed 57kg (9 stone) my breasts were less than an A-cup.

If I weighed 60kg, they were a proper A-cup.

If I weighed 63kg or over, I was a B-cup.

This was regardless of hormone status and only depended upon how much I ate or exercised.

### **The Problems Associated with Progesterone**

The forms of progesterone available to trans women are all DRUGS. Regardless of how they are taken or what they are called, these drugs are not the same as a naturally occurring progesterone hormone. ALL drugs have side effects.

The side effects of progesterone are significant and MUST NOT be dismissed.

Anyone with the following pre-existing conditions should be extremely cautious about taking progesterone.

Cautions	Epilepsy	High blood pressure
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	Migraine	Asthma
	Heart disease	Kidney disease
	Abnormal liver function	History of jaundice
	Thrombosis (DVT / PE)	Depression
	Diabetes	

Progesterone is contraindicated in people who have, or who have had, any of the following: liver dysfunction, breast cancer, heart disease, stroke, arterial disease.

In the natal woman, progesterone is given largely in three scenarios;

1. as a contraceptive;
2. to suppress menstrual blood loss;
3. to protect the uterus from developing cancer.

Trans women have none of these issues therefore, progesterone administration is not indicated.

With regard to protecting the uterus from cancer, this is the only reason a post menopausal woman is given progesterone as well as oestrogen as part of her hormone replacement therapy (HRT) regime. Otherwise, if there is no uterus, oestrogen only is given, regardless of patient age. The reason for not giving progesterone unless absolutely necessary, is because of the risk. The most serious of which are breast cancer and thrombosis.

Studies and observation show well documented evidence for a significant contribution from progesterone in the above. Of itself, oestrogen increases the risk of venous thrombosis and breast cancer. Progesterone further contributes independently of oestrogen.

For Thrombosis (DVT):

	50-59 years old	60-69 years old
No HRT	10 cases in 1000 women	20 in 1000
+ Oestrogen	11 in 1000	24 in 1000
Oestrogen + progesterone	15 in 1000	33 in 1000

These figures indicate that in the 50-59 age group, 4 more women in a 1000 will have a venous thrombosis when progesterone is part of their regime.

And for breast cancer:

	50-59 years old	60-69 years old
No HRT	14 in 1000	31 in 1000
+ Oestrogen	15 in 1000	31 in 1000
Oestrogen + progesterone	20 in 1000	35 in 1000

Venous thrombosis and breast cancer are obviously serious problems. Be aware that no one knows the true incidence of breast cancer in trans women. There are no data on this. Figures cannot be collected accurately as many women cease to attend gender clinics, and positive diagnoses in trans women (where the trans history is disclosed) are not, in any case, ascribed to a transgender category.

### **Another Myth**

It is wrong to believe that venous thrombosis will not occur if aspirin is taken.

**ASPIRIN WILL NOT PREVENT VENOUS THROMBOSIS.**

The clotting processes which occur in veins are different to those in the arteries. Aspirin protects the arteries.

## **Conclusion**

The above are the reason the risk-benefit ratio associated with progesterone renders it unethical to prescribe. The benefits of it are extremely limited and unproven.

Hormone protocols from well-informed gender clinics around the world do not routinely use progesterone and ethical doctors who are up to date in their knowledge will not prescribe it. It should NOT be self-prescribed and is only done by foolish, misinformed, risk taking individuals. The overall effect of it with regard to feminisation is a negative one.

If progesterone contributed to breast growth it would be evident in natal women when they take progesterone preparations. This is not the case. Any increase in breast size in natal women is due to general weight gain.

Therefore the same effect in feminisation can be gained by exercising less, and a modest degree of caloric over-consumption.

For those who wish bigger breasts, save your money, reduce the side effects and longer term risk and just eat more pies. Without making yourself obese, feminisation is greatly dependent on the oestrogen assisted accumulation of body fat which does not come out of the ether.

If you are disappointed with the eventual size of the breasts resign yourself to the fact that you may need a breast augmentation; a procedure increasingly sought by non-trans women and undertaken in 50% of trans women after two years on hormones.