

## The Low Down on Progesterone

Progesterone is a hormone naturally produced by the female reproductive tract. Many transwomen have questions about its value in the physical transition process.

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.

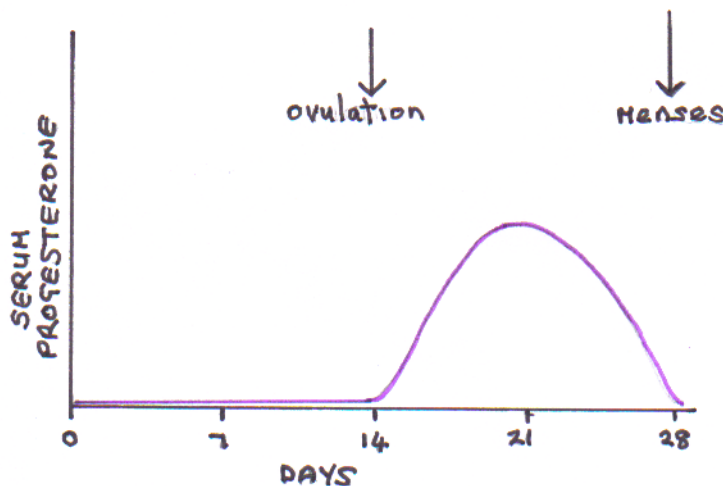
### Progesterone Physiology

Prior to menstruation, genetic girls do not have any appreciable level of progesterone.

The average age of the commencement of menstruation is around 12 years old and early cycles do not result in ovulation, i.e. no egg is released from the ovary.

Oestrogen fluctuates but the typical monthly profile of it is not yet established and periods tend to be irregular in frequency and duration. Progesterone is consistently at a very low level.

After 2 years of non-fertile menstruation, ovulation does start to occur and an egg is released from the ovary (average age 14). Only when this occurs, do progesterone levels begin to rise gradually from their low baseline during the second two weeks of the menstrual cycle. They are highest during the week prior to menstruation and rapidly decline contributing to the stimulus for bleeding to occur. Thus the average levels of progesterone during the full monthly cycle are somewhat low.



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

### 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.

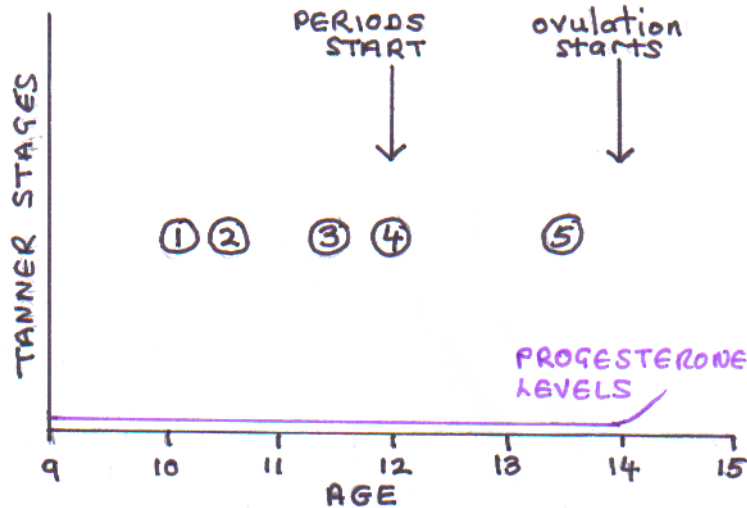
Tanner Stage	Age	
1	10	Increased nipple size
2	10 ½	Increased areola as well. Breast bud (small tender lump behind nipple)
3	11 ½	Nipple – areola complex increases. Breast size increases
4	12	The areola is a separate mound above the breast
5	13 ½	The areola becomes confluent with the breast leaving only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

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, 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 called gynaecomastia occurs due to 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.



There is no reason to suppose that the development of the breast in transwomen is different.

*To be clear, there is no direct involvement of progesterone in determining the size of breasts. Oestrogen is the primary enabler of breast growth.*

Puberty is a complex process and there are many additional 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, genetic women have a head start in the breast fat accumulation race compared to the aspiring development in transwomen.

At puberty, the effect of oestrogen further increases fat deposition. An adult female is 10 – 15% more body fat than an adult male, of which a proportion is obviously on the breasts. The average breast size of a natal woman in the UK is a 'B' Cup.

In fact, the average amount of breast growth in a transwoman is also an 'A-B' Cup. However, the reason it does not look the same is due to the relatively larger frame of a transwoman.

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

The latter three actions are not relevant in transwomen who do not become pregnant and have no need for breastfeeding.

### Myth

There is a commonly perceived myth that progesterone increases breast size in the transwoman. This partly comes 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 the adrenals by men and women. 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 progesterones / progestins.

Levenorgestrel	(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-

- b) increases the breakdown of oestrogen in the liver
- a) 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).

The testosterone derived effects of progesterone lead to the underlined side effects

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

Progesterone only contraceptives stop menstruation and ovulation by inhibiting the actions of oestrogen. Therefore, high doses of progesterone in transwomen 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 transwoman, breast growth occurs due to oestrogen. It is achievable at modest plasma levels of oestrogen. It is thought that too high a dosage too soon can stunt breast development such that only the early Tanner stages are achieved causing a conical effect with poor nipple growth.

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

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 as 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. 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. In the pubertal boy, calories contribute to muscle accumulation.

In the transwoman, the effect of the given oestrogen helps to re-dress this physiological difference. Many women notice 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, excessive calorie restriction or large amounts of cardiovascular exercise at this point, 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 Transwomen

Many transwomen 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 transwomen 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 transwoman 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 sad reflection of the pressure many transwomen put their friends under and as equally sad case of gullibility from those who believe postings on the internet or succumb to peer pressure. The majority of what is written on the internet about hormones is rubbish. It is written by non-medical people, generally by transpeople who have copied and pasted their information from other trans sources. The advice is laden with myth, out of date information and personal opinion. Even the sites which seem to be written by 'doctors' are not actually medical doctors. In the UK, a PhD does not indicate medical competence. Sites abroad are also not written by many doctors and very few sources are written by any physician with a reasonable degree of actual experience in dealing with the management of hormonal administration 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 not pleasant nor desirable. Feeling bloated and spotty with painful breasts just prior to a period is not welcomed by natal women. I believe transwomen 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-

- i) Some tell me it made no difference at all, neither good nor bad.
- ii) Many describe the side effects, particularly on mood as well as the full complement of effects listed in table 3.
- iii) Some report an increase in breast growth. In some individuals, this may well be the case and I suspect that this is due to two things:

- 1). A sub-optimal oestrogen regime. Just because a person takes the dosages detailed on the internet, or more, as is often the case, this does not equate to an optimised regime. I have many patients who do not absorb oestrogen well regardless of however it is taken and further, those whose body does not respond for reasons outlined previously will not see results either.

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 individuals observed effects, the regime administered and the the dynamics of drug administration.

- 2) The individuals appetite is greatly increased. This causes increased fat accumulation in a straightforward fashion.

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 hormonal status and only depended upon how much I ate or exercised.

### The Problems Associated with Progesterone

The forms of progesterone available to Transwomen are all DRUGS. Regardless of how it is taken or what it is 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 pr-existing conditions should be extremely cautious about taking progesterone.

<u>Cautions</u>	Epilepsy	High blood pressure	Worsened by fluid retention
	Migraine	Asthma	
	Heart disease	Kidney disease	
	Abnormal liver function	History of jaundice	
	Thrombosis (DVT / PE)	Depression	
	Diabetes		

Progesterone is contraindicated in people with 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.

Transwomen 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 transwomen. Figures cannot be collected accurately as many women cease to attend gender clinics. The positive diagnoses are not ascribed to a transgendered category and many women may not disclose their status either.

#### Another Myth

The misinformed falsely reassure themselves that a venous thrombosis will not occur if they take aspirin. **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 genetic women and undertaken in 50% of transwomen.