LOW TESTOSTERONE FUNCTIONAL TESTING
(hCG Testicular Stimulation Test - TST)

Q: Why should testing for low Testosterone (T) be performed by doing *testicular functional testing?*
A: Assuming all standard low testosterone (T) tests and medical history have not provided the answer why your T levels are low then direct *functional testing* of the testes should be performed to determine the capacity to produce T. The answer will help determine T production capacity of the Leydig cells in the testes. The **gold standard** is to stimulate the testis to assess Leydig cell function.

Q: Why not just treat low T numbers after basic lab tests?
A: It is most important that the **Testicular Stimulation Test (TST)** be done first rather than immediately going on Testosterone Replacement Therapy (TRT) just because the T numbers are low. Otherwise you may never know if your low T is from testicular failure or other causes. TRT can cover up the cause of low T.

Q: What are Leydig Cells?
A: Leydig cells are only found in the testes and are the only cells of significance in the body to produce testosterone. They are also called testicular *interstitial cells* since they are found in the testes between sperm producing cells.

Q: What is hCG and how does it work?
A: Human chorionic gonadotropin (hCG) chemically is a polypeptide -glycoprotein molecule, which acts like the anterior pituitary hormone called luteinizing hormone (LH). Luteinizing hormone is the normal primary activator for T synthesis by the Leydig by acting on cell receptors. Human chorionic gonadotropin is an analog to LH (acts like LH and fits into Leydig cell receptors) and activates Leydig cells to make T. If the Leydig cells are sufficient in number and are functional you should see an increase in serum T.

Q: Where does hCG come from?
A: hCG is made by the placenta and is derived from human pregnancy urine. It is commonly sold as under brand names such as Novarel, Pregnyl or as a generic compound made by compounding pharmacies. The package insert for the hCG brand name Novarel says: *For Intramuscularly (IM) Use Only.* However the current standard is to inject through the skin *subcutaneously (SQ)* for longer action and better effects.

Q: What is a positive or negative hCG Testicular Stimulation Test?
A: After 10 or 11 injections of hCG over 30 to 33 days the following total T (TT) responses may be approximately anticipated.

a. <u>Strongly Positive Response:</u>
   The Leydig cells have the capacity to work very well and total T levels may rise 2-3 times from baseline. A 300 ng/dl baseline T may rise to 600-900 ng/dl.

b. Moderately Positive:
   Increase of 50 -75 % - baseline T of 300 rises to about 450-525 ng/dl.
c. Minimal Positive:
   Increase of 25-35 % - a T of 375-405 ng/dl.
d. Negative:
   No significant T change from baseline. A negative T response may mean there is significant Leydig cell functional failure and or low number of functional cells. Often the sperm producing cells are also affected.

Sometimes a second stimulation test is needed to confirm results.

Q: What are the contraindications for use of hCG?
A: Prostate cancer or other androgen dependent-neoplasm's. **Women are not to use this protocol** since it is meant for men only.

Q: What are some of the side effects of hCG?
A:
POSITIVE
There can be significant positive mood and quality of life feeling with use of hCG. This may occur even when the T levels are not greatly elevated. Those with functional Leydig cells can experience increased libido, morning erections, better erections and greater energy. Even pain levels may diminish with hCG use. The reasons are not well understood.

The *alpha subunit* of hCG is essentially identical to alpha subunits of luteinizing hormone (LH), follicle-stimulating hormone (FSH) and the alpha subunit of thyroid-stimulating hormone (TSH). The beta subunits differ. It is my opinion that the *beta subunit* of hCG has a novel effect.

NEGATIVE
There can be hypersensitivity reaction with local or systemic effects such as pain at injection site, redness, hives, and shortness of breath. It is not clear whether these reactions are from the polypeptide hormone or the benzyl alcohol in the dilutant.
Since androgens may induce fluid retention hCG should be used with caution in patients with cardiac or renal disease, epilepsy, migraine, or asthma. Reported have been: headache, irritability, restlessness, fatigue, edema, gynecomastia, pain at reaction site and other.

There have been sporadic reports of testicular tumors in healthy young men receiving hCG for infertility. The causative relationship has not been established.

Indications and Usage (from Novarel package insert):
hCG HAS NOT BEEN DEMONSTRATED TO BE EFFECTIVE ADJUNCTIVE THERAPY IN THE TREATMENT OF OBESITY. THERE IS NO SUBSTNATIAL EVIDENCE THAT IT INCREASES WEIGHT LOSS BEYOND THAT RESULTING FROM CALORIC RESTRICTION, THAT IT CAUSES A MORE "NORMAL" DISTRIBUTION OF FAT OR IT DECREASES THE HUNGER ASSOCIATED WITH CALORIE-RESTRICTED DIETS.