

Fact-Checking a Masculine Hormonal Health Diagram

Nutrition and Diet

Diagram Claims: The diagram suggests that specific dietary choices optimize male hormones – for example, *favoring glucose (carbohydrate) over polyunsaturated fats (PUFAs)*, eating regular meals to support metabolic CO_2 production, and generally avoiding factors that slow metabolism. The implication is that a high-carb, low-PUFA diet with consistent meal timing enhances thyroid function and testosterone levels, while minimizing “stress” hormones. We examine these claims below.

Carbohydrates vs. Fats (Glucose vs. PUFA): There is some evidence linking dietary fat composition to testosterone, but it's not entirely clear-cut. Small studies have found that men who consume higher amounts of PUFA tend to have slightly lower testosterone levels, whereas higher saturated fat intake sometimes correlates with higher testosterone ¹. For example, one study of young men noted that a greater PUFA intake was associated with lower T, while more saturated and monounsaturated fat correlated with higher T ¹. Similarly, an older study in 69 men (ages 43–88) observed higher PUFA intake alongside lower testosterone levels ². These findings support the diagram's suggestion to limit PUFA. However, results across research are **mixed** – other studies have found no significant relationship or even opposite trends ³ ⁴. A large cross-sectional study of 1,317 men, for instance, found **no clear link** between any specific dietary fatty acid and testosterone ⁵. Controlled trials also conflict: diets very low in fat (and thus higher in carbs) sometimes lead to modest reductions in testosterone compared to high-fat diets ⁶. In two trials, switching from ~40% fat diet to ~20–25% fat caused a ~10–20% drop in T ⁶. Yet a newer 12-week trial saw no difference in testosterone between high-fat and low-fat diets ⁷. Overall, **moderate evidence** suggests extreme low-fat, high-PUFA diets *might* lower testosterone, but the effect is inconsistent ⁸ ⁹. Thus, the claim that favoring carbs over PUFA will reliably boost testosterone isn't fully proven – it has some basis ¹ but remains somewhat **controversial** due to mixed data ⁴.

Meal Frequency and CO_2 Production: The diagram's recommendation to eat regular meals “for CO_2 production” stems from the idea that consistent carbohydrate intake keeps metabolism high, producing carbon dioxide as a byproduct of efficient energy generation. This concept is popular in certain metabolic health theories (notably Ray Peat's teachings) but is **not a mainstream focus** of endocrinology. Scientific literature does show that severe hypothyroidism (very low metabolism) results in **low CO_2 production** ¹⁰. In one case, a patient with extreme hypothyroidism had such a low metabolic rate and CO_2 output that it contributed to respiratory alkalosis ¹⁰. By contrast, a well-fed state with sufficient carbohydrates tends to support thyroid function and metabolic rate (since thyroid hormone needs glucose to generate heat and CO_2). Regular meals might prevent drops in blood sugar and the resultant surge in stress hormones (like cortisol and adrenaline) which can occur during prolonged fasting ¹¹. Those stress hormones, when elevated, can promote lactic acid production and reduce CO_2 in tissues ¹¹. **However, direct research** linking meal frequency to higher CO_2 levels (or hormonal gains) is sparse. The idea is **plausible** from a physiological standpoint – steady nutrition averts “starvation” signals and keeps cellular respiration (and thus CO_2 output) up – but it remains a theoretical recommendation. It's reasonable to eat at regular intervals for stable energy and possibly better metabolism, but framing it in terms of CO_2 is an unconventional approach not explicitly supported by clinical studies.

Other Nutritional Factors: The diagram may also imply that certain nutrients support liver “detox” or thyroid (for example, sufficient protein, vitamins like B-vitamins, selenium, iodine, etc., which are known to aid thyroid hormone production and hormone clearance). While not explicitly stated in the prompt, it’s worth noting that deficiencies in zinc, vitamin D, or iodine *can* impair testosterone or thyroid function, and correcting those can improve hormonal health. The overall dietary message – consume adequate carbohydrates and nutrients to fuel metabolism, and be cautious with excessive PUFAs – has **partial support** in research. But it should be balanced with other health considerations: for instance, omega-3 PUFAs (fish oils) are beneficial for cardiovascular health and not shown to tank testosterone in men ¹² ¹³. In fact, moderate dietary PUFAs (especially omega-3s) haven’t demonstrated a consistent hormone disadvantage in human studies ¹⁴ ¹⁵. Thus, while a metabolism-friendly diet (ample carbs, not ultra low-fat) likely supports thyroid and gonadal function, the demonization of all PUFA or an extreme pro-sugar stance isn’t strongly evidence-based. These nutritional nodes in the diagram are **somewhat speculative** – grounded in some observations (fat type can influence hormones ¹, eating prevents stress surges), but not unanimously endorsed by the scientific community.

Nutrition’s Interactions with Other Nodes

Nutrition connects to many other aspects of hormonal health. Adequate caloric and carb intake signals the body it’s safe to reproduce, whereas chronic caloric deprivation or low-carb ketogenic diets can elevate cortisol and sometimes lower thyroid activity. Starvation or fasting is known to reduce the conversion of thyroid hormone T4 to active T3 and to lower gonadotropin-releasing hormone (GnRH) output, reducing testosterone – a survival adaptation. So, the diagram’s implication that **food = fuel for thyroid and testosterone** is broadly true. Regular carb-rich meals help maintain T3 levels and insulin, which in turn can support **Leydig cell** function in the testes (insulin and IGF-1 have permissive roles in testosterone production). Conversely, diets excessively high in certain fats might impact hormone binding or synthesis. For instance, some research suggests high-fiber diets increase fecal excretion of hormones (especially estrogens), lowering their reabsorption ¹⁶. Indeed, vegetarian women in one study had *higher* fecal estrogen elimination and lower blood estrogen, attributed to more fiber and bulk in the diet ¹⁷. By analogy, a fiber-rich diet in men might help eliminate excess estrogen (beneficial for the testosterone-to-estrogen ratio). Additionally, glucose availability from diet influences cortisol – sufficient carbs blunt excessive cortisol release (because the body doesn’t need to mobilize glucose from stress pathways). Lower cortisol (a topic we explore later) can remove some inhibition on testosterone production. Therefore, nutrition is **intertwined** with thyroid, liver, and hormonal regulation. A balanced diet ensures the thyroid has the micronutrients it needs (iodine, selenium, etc.), the liver has the fuel to detoxify hormones, and the testes have the building blocks (like cholesterol and vitamins) to synthesize testosterone. In summary, the diagram’s nutrition node aligns with the idea that **“fed state” metabolism supports an anabolic, pro-testosterone internal environment**, whereas a malnourished or imbalanced diet might tip the scales toward catabolic or estrogenic states. Just remember that individual responses vary, and extreme dietary manipulations (zero PUFA or constant eating) are not universally necessary for healthy hormone levels.

Mitochondrial Function

Diagram Claims: A node for *mitochondrial function* suggests that efficient energy production at the cellular level is fundamental for hormonal health. Mitochondria – the “powerhouses” of the cell – produce ATP energy (and CO₂) via oxidative metabolism. The diagram likely posits that strong mitochondrial function boosts metabolic rate and testosterone, whereas dysfunction (from toxins, PUFA oxidation products, etc.) impairs hormone production. We’ll verify how mitochondria relate to male hormones.

Role in Steroid Hormone Synthesis: It is **well-established** that mitochondria are directly involved in steroid hormone production. In testosterone-producing Leydig cells of the testes, the very first step of steroidogenesis (conversion of cholesterol to pregnenolone) occurs inside mitochondria via the enzyme P450scc. Research confirms that for **all steroid-producing cells** (testicular Leydig cells, adrenal cells, ovarian theca cells, etc.), mitochondria are a **key control point** in steroid biosynthesis ¹⁸. In fact, the transport of cholesterol into mitochondria (via the StAR protein) is the rate-limiting step in testosterone synthesis. Healthy mitochondria are needed to carry out this process and to generate the energy required for hormone production ¹⁹. If mitochondrial function is compromised (e.g. by oxidative stress, aging, or hypothyroidism), the efficiency of steroidogenesis can drop. Conversely, interventions that improve mitochondrial biogenesis or function may support hormone output. For example, an animal study found that repeated mild stress triggered an *adaptive* increase in mitochondrial biogenesis in Leydig cells, which helped maintain testosterone output under strain ²⁰ ²¹. This suggests the body tries to preserve steroid production by upregulating mitochondria when challenged. Overall, robust mitochondrial function is indeed **supportive** of testosterone synthesis.

Metabolic Rate and Hormones: Mitochondria largely determine a cell's metabolic rate. Thyroid hormone, in particular, acts on mitochondria to increase oxygen consumption and heat/CO₂ production. If mitochondria are sluggish (as in hypothyroidism), metabolism slows and anabolic processes (like muscle growth, spermatogenesis) wane. Some fringe theories, like the one underlying the diagram, argue that PUFA accumulation in mitochondrial membranes makes them less efficient (due to lipid peroxidation or enzyme inhibition). Ray Peat and others have cited old studies that unsaturated fats can inhibit mitochondrial respiration and **thyroid hormone action**, though these were often animal studies not widely replicated in humans. One referenced claim (Rafael et al., 1988) reported that rats deficient in PUFA had higher metabolic rates than PUFA-fed rats – implying PUFAs suppressed metabolism. While mechanistically this is plausible (PUFAs alter membrane fluidity and can generate oxidative stress), it's not definitively proven in human studies. That said, mitochondrial poisons or inefficiencies will certainly impact hormone levels. For example, conditions like metabolic syndrome and diabetes (where mitochondria may be dysfunctional) often coincide with lower testosterone in men. On the flip side, exercise is known to improve mitochondrial efficiency and also tends to raise testosterone acutely or improve its action.

In summary, the diagram's emphasis on mitochondria as a foundation for hormonal health is **scientifically sound**. Mitochondria produce the energy and initial substrates for hormone synthesis, and their health is crucial for organs like the testes and thyroid. Optimizing mitochondrial function (through adequate nutrition, antioxidants, thyroid support, etc.) is likely beneficial for testosterone and overall male vitality. We find this node to be grounded in real physiology: research shows mitochondrial capacity is tightly linked to steroid production ¹⁸, making this one of the **validated connections** in the diagram.

Mitochondrial Function's Relationships

Mitochondrial health interconnects with **thyroid function** and **stress hormones** in notable ways. Thyroid hormone (T3) essentially “turns up the volume” on mitochondrial energy production – it increases the number and activity of mitochondria in cells. Thus, good thyroid function enhances mitochondrial output, raising metabolic rate and supporting testosterone. If the diagram links the thyroid node to mitochondria, that is well-founded. On the other side, chronic stress and high cortisol can damage or dysregulate mitochondria over time via oxidative stress. Interestingly, as mentioned, short-term stress can stimulate mitochondrial biogenesis in an adaptive way ²⁰, but long-term stress might exhaust that adaptation. The relationship between cortisol and mitochondria is a double-edged sword – mitochondria produce the energy for cortisol synthesis in adrenal cells, but excess cortisol can impair mitochondrial function elsewhere.

Another interaction: **Aging**. As men age, mitochondrial DNA damage accumulates, and this has been linked to reduced Leydig cell function and lower testosterone output ²². Interventions like CoQ10 or mitochondrial-targeted antioxidants have been studied for potentially improving sperm quality or testosterone in older men, though results are not conclusive yet.

Finally, mitochondria tie into the **nutrition node**: they rely on vitamins and minerals (B vitamins, magnesium, etc.) to function, and require adequate fuel (glucose, fatty acids) but not an overload of toxic byproducts. A diet high in sugars and nutrient-rich (as the diagram advocates) ensures mitochondria have ample glucose for oxidative phosphorylation, which yields more CO₂ (RQ ~1) compared to fat oxidation. This ties back to the CO₂ production idea – carbohydrate oxidation indeed generates more CO₂ per unit of oxygen than fat metabolism ²³, which some interpret as a sign of a high metabolic rate. So, a high-carb diet could theoretically push metabolism towards a more CO₂-producing state, indicative of mitochondrial respiration over fat-driven ketosis.

In sum, **mitochondria link to nearly every other node**: thyroid (regulates them), nutrition (fuels them), cortisol/stress (challenges them), and they directly enable testosterone and other steroid hormones to be made. The diagram's inclusion of mitochondrial function is scientifically justified, and most interactions implied are supported by physiology (though rarely phrased in terms of CO₂ outside niche communities).

Liver and Gut Health

Diagram Claims: The *liver* and *gut* appear as nodes, likely highlighting their roles in hormone metabolism and elimination. Claimed links may include: "support liver detoxification to clear excess estrogen," "gut health prevents reabsorption of estrogens," and overall that a healthy liver and gut promote a favorable testosterone-to-estrogen ratio. We will verify these connections.

Liver's Role in Hormone Homeostasis: The liver is indeed a major hormonal regulator in men. It inactivates and excretes hormones, and also produces carrier proteins that affect hormone availability. According to clinical studies, the liver metabolizes roughly **70% of circulating sex hormones** (via Phase I/II enzymes) and even contains aromatase enzymes that convert androgens to estrogens ²⁴. The liver also produces Sex Hormone Binding Globulin (SHBG) and albumin, which bind testosterone and estrogen in blood ²⁴. If the liver is unhealthy or "sluggish," it may not clear estradiol efficiently, leading to estrogen accumulation. In men with chronic liver disease (like cirrhosis), we see a striking example: cirrhotic men often have **high estrogen levels and low testosterone** ²⁵ ²⁶. Nearly half of men with significant cirrhosis in one study had low free T, accompanied by elevated estradiol ²⁵. The severity of liver dysfunction correlated with lower T and higher E2 ²⁷ ²⁸. They frequently develop signs of hyperestrogenism (gynecomastia, loss of body hair) and hypogonadism (impotence, infertility) because the failing liver can't deactivate estrogens properly ²⁹. This real-world scenario supports the diagram's premise that a well-functioning liver is crucial to **maintain hormonal balance**. Even in milder cases, factors that tax the liver (excess alcohol, fatty liver, certain medications) could impair optimal hormone clearance. Thus, "supporting liver detox" (through avoiding hepatotoxins, eating a nutritious diet, etc.) is sensible advice for hormonal health. That said, in a normal healthy man, the liver is usually very capable – there's no need for fancy cleanses, but rather general liver-friendly habits (moderate alcohol, good diet).

Gut Microbiome and Estrogen Recirculation: The gut is another key player, mainly via the **enterohepatic circulation** of estrogen. When the liver metabolizes estrogen, it often conjugates it (attaches a glucuronide) and dumps it into bile to be excreted in the intestines. Certain gut bacteria, however, produce the enzyme **β-glucuronidase** which can de-conjugate estrogen, essentially

reactivating it. This frees the estrogen to be reabsorbed back into the bloodstream. A high activity of microbial β -glucuronidase has been linked to higher circulating estrogen levels ³⁰. In simple terms, an unhealthy gut flora – or chronic constipation slowing transit – allows more estrogen to be reabsorbed (increasing the body's estrogen load). Research on the *estrobolome* (the collection of gut microbes affecting estrogen metabolism) confirms this mechanism: **gut bacterial enzymes can “undo” liver estrogen metabolism and push estrogen back into circulation** ³⁰. Conversely, a balanced microbiome with lower β -glucuronidase activity promotes estrogen excretion. For instance, high-fiber diets can alter gut flora and have been shown to **decrease estrogen reabsorption** ¹⁶. Probiotic and prebiotic interventions are being studied for conditions like estrogen-driven breast cancer, aiming to reduce estrogen via the gut.

For men, excess estrogen is less dramatic than in women's conditions, but it still matters for things like abdominal fat and gynecomastia. An unhealthy gut (dysbiosis) could feasibly contribute to *estrogen dominance* even in males. Thus, the diagram's suggestion that gut health (through diet or perhaps carrot salads, activated charcoal, etc., as some biohackers use) can reduce estrogen load has a **scientific basis**. One review notes that a disrupted gut microbiome can lead to either excessive estrogen reabsorption or deficiency ³¹ ³² – in men, the concern would be too much reabsorption. Keeping regular bowel movements (fiber, adequate magnesium, etc.) and a good microbial balance ensures that once estrogen is tagged for removal, it actually leaves the body.

Liver-Gut Summary: Both liver and gut significantly influence **testosterone expression via estrogen regulation**. The liver also affects testosterone directly by producing SHBG; in liver disease SHBG often drops, which paradoxically raises free testosterone percentage but total T falls due to testicular failure. There's also a connection between hypothyroidism and liver detox: low thyroid function slows the liver's clearance pathways, potentially leading to estrogen buildup ³³. So thyroid support helps the liver clear hormones (we will discuss thyroid next). Overall, the diagram is **correct** that a supported liver (through nutrition, possibly supplements like milk thistle or calcium d-glucarate) and a healthy gut microbiome can positively impact male hormone balance. These nodes are well-grounded: poor liver or gut health can **antagonize** testosterone by allowing estrogen or toxins to accumulate. While terms like “detox” are often overused, in this context it means normal metabolic clearance – a process absolutely vital for hormonal harmony.

Interactions of Liver/Gut with Other Nodes

The liver and gut interact with **thyroid and estrogen nodes strongly**. As mentioned, hypothyroidism can slow liver enzyme activity, reducing estrogen clearance ³³. High estrogen, in turn, can burden the liver and even promote gallbladder issues. The liver also is where thyroid hormone T4 converts to T3; a fatty or inflamed liver converts less T4 to T3, tying liver health to thyroid status. Furthermore, high circulating estrogen (from either overproduction or gut reabsorption) feeds back at the hypothalamus/pituitary to reduce LH and FSH, thereby lowering testosterone output. This feedback loop means the liver/gut's inability to eliminate estrogen will negatively impact the gonadal (testosterone) node. In practical terms, men with obesity (who often have fatty liver and dysbiosis) frequently show **elevated estrogen and lower testosterone** compared to leaner men. Improving diet and losing fat can reverse some of that by improving liver function.

There's also a connection to the **cortisol/stress node**: The liver helps clear cortisol too (via 11β -HSD enzymes), and the gut microbiota can influence cortisol metabolism. Chronic stress can increase intestinal permeability (“leaky gut”), leading to inflammation that impairs liver function. So stress management benefits liver and gut health, and vice versa. The liver produces bile acids that shape the microbiome composition, while gut microbes produce signals that affect liver metabolism – it's a bi-directional relationship.

One notable interaction: **Endotoxin (LPS)** from a unhealthy gut can travel to the liver and suppress steroidogenesis. Studies show that inflammation from gut-derived toxins can reduce testosterone production (a protective adaptation during illness). Thus, gut health indirectly influences testosterone not just via estrogen, but through systemic inflammation or lack thereof.

In summary, the liver/gut node is deeply interconnected with **hormone regulation**. The diagram's lines connecting "liver detox" to lower estrogen and better thyroid function are backed by evidence (e.g., liver failure causes hyperestrogenism ²⁹, treating hypothyroid aids estrogen clearance ³³). Its link from gut health to estrogen is also supported (bacterial enzymes modulate estrogen reabsorption ³⁰). These relationships are **valid**, reinforcing the diagram's holistic view that digestion and detoxification significantly shape male hormonal balance.

Thyroid Support

Diagram Claims: The *thyroid* node likely emphasizes that optimal thyroid function (i.e. adequate T3/T4 thyroid hormone levels) is crucial for high testosterone and overall male vitality. It may also claim interactions like "*estrogen antagonizes thyroid*" and stress (cortisol) affecting thyroid. The idea is that supporting the thyroid (through iodine, selenium, possibly direct thyroid hormone if needed) will boost metabolism, body temperature/CO₂, and thereby testosterone. Let's check the evidence.

Thyroid Function and Testosterone: There is a strong connection between thyroid status and male gonadal function. In cases of overt hypothyroidism (underactive thyroid), men often exhibit a form of secondary hypogonadism. Research in men with primary hypothyroidism shows **reduced free testosterone concentrations**, which *normalize* after thyroid hormone replacement ³⁴. In other words, treating an underactive thyroid can raise low testosterone back to normal ³⁴. The mechanism is that hypothyroidism leads to diminished GnRH/LH release (hypogonadotropic hypogonadism) and possibly lower testicular responsiveness ³⁵. Symptoms like low libido, erectile dysfunction, and reduced sperm count can manifest in hypothyroid men ³⁶, and improving thyroid levels often improves those parameters ³⁴. Conversely, hyperthyroidism (overactive thyroid) tends to **increase** sex hormone levels, but not always favorably: hyperthyroid men have elevated total testosterone and estradiol, largely due to increased SHBG from excess thyroid hormone ³⁷. The high SHBG binds more testosterone, and the excess conversion of T to estrogen (aromatization) in hyperthyroidism can cause gynecomastia in men ³⁷. So both extremes of thyroid function disrupt the male hormone balance – low thyroid lowers T, high thyroid raises estrogen. The sweet spot is a **euthyroid state**, which supports robust testosterone production without overshooting estrogen. This clearly supports the diagram's message that *thyroid support is vital for masculine hormone optimization*. Even subclinical hypothyroidism (slightly low thyroid function) could contribute to suboptimal testosterone and energy levels.

Estrogen's Effect on Thyroid: The diagram specifically mentions "*estrogen antagonizing thyroid function*." There is truth to this. Estrogen has known indirect and direct effects on the thyroid gland and thyroid hormone economy. One well-documented effect: **estrogen increases Thyroid Binding Globulin (TBG)** in the bloodstream ³⁸. Higher estrogen (such as during pregnancy or from estrogen therapy) causes the liver to produce more TBG, which binds more T4/T3, thus reducing the free (active) thyroid hormone available ³⁸. In women, high estrogen states can precipitate hypothyroid symptoms unless thyroid output increases to compensate. In men, who have much lower estrogen levels, this effect is subtler but could still matter if estrogen is elevated (for example, in obesity or via external sources). More TBG from estrogen could make a man functionally more hypothyroid by lowering free T3/T4 ³⁸. Another aspect: some research suggests estrogen can directly affect thyroid cells and possibly promote goiter or thyroid autoimmunity. A study in *Molecular Cellular Endocrinology* found that a metabolite of estrogen (2-methoxyestradiol) could alter thyroid cells and increase anti-thyroid

antibodies ³⁹ . Clinically, we see higher rates of autoimmune thyroid disease in women, potentially due to estrogen's influence on immune response and thyroid tissue ³⁹ . So the phrase "estrogen antagonizes thyroid" is partly accurate – mainly via binding proteins and possibly via tissue effects. It's not an acute *blockade* of thyroid hormone, but over time, high estrogen can contribute to a sluggish thyroid state.

Thyroid on Estrogen Clearance: The relationship is bidirectional: just as estrogen can hinder thyroid hormone availability, **hypothyroidism slows estrogen clearance**, fostering an estrogen-dominant state ³³ . When thyroid function is low, the liver's metabolic capacity drops, leading to reduced breakdown of estrogens ³³ . This is why men or women with low thyroid might have relatively elevated estrogen levels for their sex, compounding symptoms. Thyroid hormone replacement has been observed to lower elevated prolactin and perhaps estrogen levels in those cases ⁴⁰ . All told, **thyroid and estrogen balance each other** – adequate thyroid function keeps estrogen in check, and keeping estrogen low-normal helps thyroid hormone act unimpeded. The diagram's highlighting of this antagonism is supported by endocrinology texts (for example, estrogen therapy increases thyroid dosage needs in hypothyroid patients ⁴¹).

Thyroid and Metabolic Markers: The diagram also ties thyroid to CO₂ production (as discussed earlier) and overall metabolic rate. This is textbook physiology: thyroid hormone increases basal metabolic rate, raising oxygen consumption and CO₂ output. If the diagram shows thyroid support leading to more CO₂, that reflects the idea that a warm, calorie-burning body (high CO₂ from active mitochondria) correlates with optimal thyroid. We have evidence that in hypothyroidism, CO₂ production is low ¹⁰ and ventilation can be abnormally regulated. In severe cases, low metabolism may even cause paradoxical **hyperventilation with low CO₂** because the body isn't producing much CO₂ and the respiratory drive misfires ⁴² . That is an extreme, but it underscores how intimately thyroid status and CO₂ levels are linked.

In summary, **thyroid support is a linchpin** of the entire hormonal network. Ensuring one's thyroid is functioning properly (via sufficient iodine, stress reduction, possibly using thyroid hormone medication if clinically needed) can raise low testosterone, improve mood and energy, and assist the liver in clearing estrogen. The diagram's treatment of the thyroid node is very much in line with medical understanding – it correctly identifies that **thyroid hormone positively regulates male metabolism and testosterone**, and that an excess of estrogen or stress can impede thyroid function. This node and its connections are **scientifically grounded**.

Thyroid's Relationships to Other Nodes

The thyroid interrelates with nearly all other nodes in the diagram:

- **With Nutrition:** Nutrient intake directly affects thyroid hormone production – iodine and tyrosine are building blocks of T4/T3, selenium is needed for conversion of T4 to T3. A carb-rich diet can lower cortisol and raise insulin, which tends to increase conversion of T4 to T3 and thyroid hormone effectiveness. On the other hand, fasting or very low-carb diets elevate cortisol and can reduce active T3 levels (a protective adaptation), linking back to the nutrition node's importance.
- **With Mitochondria:** As noted, T3 increases mitochondrial number and function. Without enough thyroid hormone, mitochondria underperform, lowering energy and steroidogenesis. So the thyroid node is upstream of the mitochondrial node in some respects.

- **With Testosterone:** Thyroid hormones can influence sex hormone binding globulin production in the liver. Hyperthyroidism raises SHBG (making total T higher but free T could be normal or low) ³⁷. Hypothyroidism lowers SHBG, sometimes masking low T by making total T appear normal while free T is actually low ⁴³. Clinically, treating hypothyroidism can raise SHBG and also increase total and free testosterone (free especially, by restoring testicular function) ³⁴. There's evidence that thyroid hormones enhance Leydig cell sensitivity to gonadotropins, thereby **promoting testosterone synthesis** when thyroid is optimal.
- **With Estrogen and Prolactin:** We've covered estrogen's interplay – high estrogen or prolactin states (like in men with certain pituitary tumors) can cause symptoms of hypothyroidism or exacerbate them. Interestingly, longstanding hypothyroidism itself can cause modest elevations in prolactin (due to TRH – the hypothalamic hormone that drives TSH – also stimulating prolactin release). In such cases, restoring thyroid levels brings prolactin down ⁴⁰. So a man with low thyroid might also have mildly high prolactin, compounding sexual dysfunction; treating the thyroid will fix both issues ⁴⁰.
- **With Cortisol:** Chronic stress (cortisol) suppresses hypothalamic TRH and pituitary TSH, leading to lower thyroid output. High cortisol also reduces conversion of T4 to T3 and increases conversion to reverse T3 (an inactive form). So high stress directly induces a functional hypothyroid state in many individuals ⁴⁴. This means the cortisol node negatively feeds into the thyroid node. Conversely, a well-functioning thyroid axis helps keep cortisol rhythms normal – hypothyroid individuals can have an exaggerated cortisol response since metabolism is low.

In essence, the thyroid is a central hub in this diagram. Its positive arrows likely go toward metabolism/CO₂ and testosterone, which we affirm as valid, and negative arrows come from estrogen and cortisol, also valid. The strong advice to support thyroid (with proper diet, avoiding estrogenic burdens, possibly supplementation) has **robust scientific support** because of these multi-node interactions.

Testosterone (Androgen Output)

Diagram Claims: *Testosterone* is presumably the focal endpoint – the diagram likely frames it as the primary hormone to optimize for masculine health. Various other nodes (thyroid, liver, cortisol, etc.) feed into it. The diagram might also mention *DHT* (dihydrotestosterone) as a related androgen, and how it interplays with testosterone. We will review how each factor indeed affects testosterone levels or action, and also consider any myths (e.g., “more DHT is always good” or “testosterone is only limited by X factor”) that might be implied.

Testosterone Physiology: Testosterone is the major male sex hormone, produced mainly by the Leydig cells in the testes in response to LH from the pituitary. It is critical for muscle mass, bone density, mood, libido, and many aspects of health. The diagram's general thrust is correct that *higher testosterone (within physiological range) is associated with better male vitality*. However, testosterone does not act in isolation – it's part of a feedback network.

We have already seen evidence that multiple systems affect testosterone: **thyroid** status (hypothyroid men have lower T, corrected by fixing thyroid) ³⁴, **cortisol/stress** (stress can acutely lower testosterone or chronically suppress the HPG axis) ⁴⁵, **prolactin** (high prolactin causes low testosterone via GnRH inhibition) ⁴⁶ ⁴⁷, and **diet/liver** (starvation or liver disease can lower T) ²⁵ ⁶. Thus, the diagram's interconnected arrows pointing at the testosterone node reflect reality: *Testosterone expression is the result of many upstream influences*.

For instance, one study on stress (in diabetic patients) demonstrated that those with elevated cortisol had significantly lower testosterone levels than less-stressed individuals ⁴⁸ ⁴⁵ . Another example is hyperprolactinemia in men (from a pituitary tumor or medication) – it frequently presents with hypogonadism (low testosterone, infertility, sexual dysfunction) ⁴⁶ ⁴⁷ . Treating the cause (e.g., using a dopamine agonist to lower prolactin) often restores testosterone toward normal. Similarly, obesity-related low T can be partly due to high estradiol; using an *aromatase inhibitor* medication to block estrogen production has been shown to **increase testosterone by ~50%** in older men with borderline-low T ⁴⁹ . In those cases, lowering estrogen removes negative feedback on the pituitary, allowing more LH and thus more testosterone ⁴⁹ . These examples illustrate the validity of arrows the diagram might have from “lower estrogen” to “higher testosterone” or from “lower prolactin” to “higher testosterone.”

A subtle point: the diagram might imply always pushing testosterone as high as possible is desirable. While optimizing low T is beneficial, supraphysiological levels (as seen with anabolic steroid abuse) carry risks and can actually *suppress* some health parameters (like fertility and HDL cholesterol). The context here is natural optimization, though, so that’s just a caveat.

DHT and Testosterone: Dihydrotestosterone (DHT) is a metabolite of testosterone, formed by the 5-alpha reductase enzyme in certain tissues (prostate, skin, hair follicles, etc.). DHT is about 2-3 times more potent than testosterone at the androgen receptor. The diagram lists DHT as a separate node, possibly suggesting relationships like “excess estrogen lowers DHT” or “progesterone affects DHT” or even the idea that DHT itself is important for masculine traits. Let’s fact-check DHT’s role. In development and puberty, DHT is absolutely essential for things like formation of the male genitalia in utero and facial hair and prostate growth at puberty ⁵⁰ ⁵¹ . However, in **adult men, testosterone largely can fulfill most androgenic functions by itself**, except in a few tissues (prostate and hair follicles) where DHT is the primary driver. According to clinical sources, DHT does *not* have a major role in day-to-day metabolic or sexual function beyond what testosterone does ⁵² . Adult males with genetic 5-alpha reductase deficiency (very low DHT) can have underdeveloped prostate and minimal body hair, but they still have muscle mass and a functional libido, albeit often reduced. Interestingly, men lacking DHT do not suffer overt systemic illness; in fact, **excess DHT is more commonly problematic** (causing male pattern baldness and prostate enlargement) ⁵³ ⁵⁴ . Elevated DHT is linked to benign prostatic hyperplasia and androgenic alopecia, as DHT locally overstimulates those tissues ⁵³ ⁵⁴ .

So while DHT is the “stronger” androgen, more is not necessarily better for health. The body maintains a balance: typically about 5-10% of testosterone is converted to DHT per day ⁵⁵ . If the diagram implies one should boost DHT, that would be **controversial** advice. Mainstream medicine actually sometimes *reduces* DHT (with 5-alpha-reductase inhibitor drugs like finasteride) to treat hair loss or prostate issues. Those drugs do come with potential side effects in a subset of men – notably, some report lowered libido or erectile quality when on finasteride, suggesting DHT does contribute to sexual function to some degree ⁵⁶ ⁵⁷ . However, large studies indicate that only ~2-4% of men on finasteride experience sexual side effects, a rate not much different from placebo in many trials ⁵⁸ ⁵⁹ . And often those effects are reversible if the drug is stopped ⁵⁸ ⁵⁹ . This indicates that moderate lowering of DHT (within physiological range) is tolerable for most men, and that **testosterone itself can maintain libido and function** in absence of some DHT. In fact, one comprehensive study concluded finasteride’s impact on sexual function is minimal for most men (especially at the 1 mg dose for hair loss) ⁶⁰ . Therefore, boosting DHT specifically isn’t a major goal in evidence-based health optimization; rather, ensuring normal DHT is present is enough. The diagram should be interpreted such that DHT is a component of androgen status, but not an independent “more is better” hormone.

Testosterone Summary: The diagram’s depiction of testosterone being influenced by many factors is strongly supported. To maximize one’s natural testosterone, one should: support thyroid (we saw this raises T ³⁴), keep cortisol/stress in check (stress depresses T ⁴⁵), avoid hyperprolactinemia (since *high*

prolactin correlates with low testosterone ⁴⁶), maintain healthy liver/gut to remove excess estrogens, ensure adequate sleep and nutrition (sleep deprivation and crash diets are notorious for lowering T). All these measures are validated by studies in endocrine physiology. One could say the entire diagram is structured around protecting the HPT (hypothalamic-pituitary-testicular) axis from various antagonists (stress, estrogen, prolactin) and providing it with the needed support (thyroid, nutrition, mitochondrial energy) to function optimally.

We should note that normal testosterone range is broad, and maximizing within that range can improve quality of life if one was on the low end. But overshooting via exogenous means is not the focus here. The key is **hormonal balance** – high testosterone relative to estrogen, but not zero estrogen; low stress hormones but not zero cortisol (which would be Addison's disease!). It's about creating the conditions for the body's own testosterone to flourish. The diagram's testosterone node receives inputs from almost every other node, which accurately reflects that balance.

Testosterone's Interactions

Testosterone itself feeds back into the system in two main ways: via conversion to **estradiol** and **DHT**. These conversions are represented by the aromatase and 5-alpha-reductase processes respectively. High testosterone will lead to more estradiol (since some T aromatizes), which can then inhibit thyroid or GnRH if it becomes excessive. So there's a self-regulating aspect: raise T too much and more of it will become estrogen, possibly countering some benefits. That's why in some men with obesity, even when they try to raise T (naturally or medically), if aromatase is not addressed, the extra T simply becomes extra estradiol, which then blunts the net effect on androgens. This interplay is why the diagram emphasizes controlling estrogen alongside boosting testosterone.

Testosterone's conversion to DHT is another interaction: higher T naturally yields somewhat higher DHT. DHT in turn can have a stronger negative feedback on gonadotropin release than T (some studies suggest DHT is potent in suppressing LH via androgen receptor activation). So if one had, say, a genetically high 5AR activity making a lot of DHT, it might even keep their LH a bit lower via feedback, balancing the system. This is speculative but shows how these hormones maintain equilibrium.

Testosterone also interacts with **neurotransmitters**: it tends to increase dopamine activity (why adequate T often correlates with better mood and drive), and it might reduce serotonin a bit (high serotonin is often associated with calming, whereas testosterone can increase competitiveness and drive – possibly via modulating neurotransmitter receptors). These effects are complex and not fully mapped, but it's clear that raising a low testosterone can improve mood, which might be partly due to neurotransmitter changes.

Finally, testosterone has **peripheral interactions**: it builds muscle, which in turn can improve insulin sensitivity, lowering stress on the body. More muscle also means higher metabolism, which loops back to better mitochondrial function and thyroid function. So testosterone can have positive reinforcing effects on some nodes like metabolism. However, if too high, it can increase metabolic rate to a point (like hyperthyroid, high T raises BMR slightly through increased muscle and erythropoiesis).

In summary, testosterone is at the crossroads of many feedback loops. The diagram positions it as something to optimize by tweaking other factors – this is valid, but one must balance all factors together. The interplay of testosterone with estrogen and DHT is particularly important: **it's the ratio and balance that matters** for health, not just one hormone in isolation.

Estrogen and Estradiol

Diagram Claims: *Estrogen* (specifically estradiol, E2, in men) is likely depicted as an antagonist in the male hormonal milieu. The diagram probably notes that estrogen counteracts thyroid and testosterone (as we've discussed), and thus strategies to reduce excessive estrogen (via liver, gut, possibly aromatase inhibitors or certain foods) are beneficial. It may also mention sources of estrogen (aromatization from testosterone, xenoestrogens, body fat) and that one should keep estrogen in check for optimal male health. We will verify the role of estrogen in men and the claims of its interactions.

Estrogen's Role in Men: Men need some estrogen for normal physiology. Estrogen in males is primarily produced by aromatization of testosterone (in adipose tissue, liver, etc.), and a small amount by the testes. Normal adult men have estradiol levels roughly 20-40 pg/mL, which is similar to levels in postmenopausal women. This low level of estrogen is crucial for bone density (men with zero estrogen get osteoporosis) ⁶¹, for joint health, and even for libido (some estrogen is needed for erectile function and sex drive – too low can cause issues just as too high can). For example, a study comparing an aromatase inhibitor (to reduce estrogen) versus testosterone therapy in older men found that complete aromatase blockade, while raising T, led to bone mineral density loss, confirming that **some estrogen is required to maintain bone in men** ⁶¹. So the diagram should not be interpreted as “estrogen is evil, eliminate it entirely” – the goal is **balance**.

That said, **excess estrogen in men does cause problems**. High E2 in men (say >50–60 pg/mL) is associated with symptoms like reduced libido, erectile dysfunction, increased body fat, emotional lability, and gynecomastia. It also suppresses LH and FSH via negative feedback, leading to lower testosterone and possibly fertility issues. As evidence, men with obesity or insulin resistance often have slightly elevated estrogen and correspondingly lower T, and treating them with weight loss or aromatase inhibitors can improve T levels and symptoms ⁴⁹. Also, certain medications that raise estrogen (like clomiphene, interestingly used to *treat* hypogonadism by selectively blocking estrogen receptors in the pituitary) show how potent the estrogen feedback is – even a selective estrogen receptor modulator can trick the body into making more testosterone by modulating estrogen's effects.

We earlier confirmed the statement “estrogen antagonizes thyroid.” Indeed, *indirectly*, estrogen excess can mimic or induce hypothyroid states by raising TBG ³⁸ and potentially promoting autoimmune thyroid issues ³⁹. Additionally, high estrogen in men can increase SHBG production by the liver, which binds more testosterone and can reduce free T availability ³⁷. So an estrogen surplus not only directly suppresses gonadotropins, but can **lock up** the testosterone that is present, making it less bioavailable. Clinically, a high estradiol:testosterone ratio in men is linked to sexual dysfunction and metabolic issues.

Sources of High Estrogen: The diagram might point to *body fat* (since adipose tissue expresses aromatase – more fat means more conversion of T to E). This is true: obese men often have higher estradiol, which contributes to a vicious cycle of lower T and higher fat. Reducing fat mass will reduce aromatase activity. The liver node we discussed is also key – a sluggish liver means estrogen isn't cleared, effectively raising estrogen levels as well. Environmental xenoestrogens (plastics, chemicals) can also mimic estrogen, though their impact on male hormones at typical exposure is less clear and under study. The gut estrobolome we discussed is another source of endogenous estrogen load if dysregulated.

Reducing Excess Estrogen: Strategies often cited include: weight loss, managing insulin (as high insulin can upregulate aromatase), perhaps natural aromatase inhibitors (like compounds in cruciferous veggies, or supplements like DIM/calcium glucarate which help estrogen metabolism). The diagram's suggestions of supporting liver detox and gut elimination fall exactly in line with reducing estrogen. For

instance, calcium D-glucarate is known to inhibit β -glucuronidase in the gut, thus promoting estrogen excretion – a direct support of that pathway. While we don't have a specific human study in our citations on that supplement, the mechanism is well-known in biochemistry.

It's worth noting one possibly **controversial** point: The diagram's emphasis on minimizing serotonin might partly be to reduce prolactin, but another reason in some alt-health circles is that serotonin is thought to stimulate the aromatase enzyme, increasing estrogen. There is some evidence from animal models that serotonin can upregulate aromatase in the brain. In men, high estradiol often correlates with mood symptoms that SSRIs (which increase serotonin) also address, so it's a complicated web. There isn't a straightforward human study showing "more serotonin = more estrogen," so that aspect would be speculative if present.

In summary, the estrogen node in the diagram is viewed as something to **keep low (within a healthy range)** for male optimization. This is accurate in that men feel and function best when estradiol is not too high relative to testosterone. However, eliminating estrogen entirely is neither possible nor desirable – the goal is to prevent pathological elevations. All the connections – from estrogen to thyroid (negative) ³⁸, estrogen to fat gain, estrogen to prolactin (estrogen actually can stimulate prolactin release too), and estrogen to lowered testosterone (via HPT axis feedback) – are **scientifically validated**. The diagram's caution around estrogen is warranted, with the caveat that some estrogen is needed for health.

Estrogen's Interactions

We have covered many interactions involving estrogen:

- **Thyroid Interaction:** Estrogen $\searrow$ Thyroid – estrogen raises TBG, lowering free thyroid hormone ³⁸. It also may promote thyroid gland growth (possibly why women have more thyroid nodules and autoimmune thyroiditis) ³⁹. Thyroid $\nearrow$ Liver $\nearrow$ estrogen clearance – thyroid hormone helps eliminate estrogen ³³. So thyroid support counteracts estrogen, and high estrogen counteracts thyroid to a degree.
- **Testosterone Interaction:** Estrogen $\searrow$ Testosterone – through negative feedback on GnRH/LH. High estrogen tells the pituitary "we have enough sex steroids, slow down testosterone production." This is why men with high estradiol often have low LH/testosterone. It's seen therapeutically: bodybuilders taking high doses of aromatizable steroids often get high estradiol, which then shuts off their natural LH, compounding the shutdown of testosterone. Conversely, blocking estrogen (with an aromatase inhibitor) can *increase* LH and testosterone in men ⁴⁹. The diagram arrow from estrogen to testosterone (antagonistic) is absolutely correct.
- **DHT Interaction:** DHT doesn't convert to estrogen, but high estrogen can downregulate 5-alpha-reductase in some tissues (there's some evidence estrogen can reduce expression of that enzyme). More notably, both DHT and E2 inhibit gonadotropin release (E2 via estrogen receptors, DHT via androgen receptors), so they may have a complementary suppressive effect. When both estrogen and DHT are high, testosterone is very suppressed (as in anabolic steroid users who take testosterone – it converts to both E2 and DHT, both of which strongly signal the pituitary to stop LH). So in natural physiology, an optimal male would have moderately high T, normal DHT, and low-normal E2. If E2 climbs, it will also indirectly reduce DHT by lowering T production (since DHT is derived from T).

- **Prolactin Interaction:** Estrogen is one of the main stimulators of prolactin synthesis. In women, high estrogen states (pregnancy, estrogen therapy) often raise prolactin levels. In men, estradiol can stimulate prolactin release by the pituitary lactotroph cells. This is why men with estrogen-secreting tumors or very high bodyfat (hence high E2) sometimes have elevated prolactin. High prolactin then further suppresses testosterone – a double whammy. There’s also evidence that estrogen can cause some breast tissue proliferation in men (gynecomastia) often in concert with prolactin (prolactin causes milk duct growth, estrogen causes fat deposition in breast). So those two often go hand in hand – many cases of gynecomastia have both slightly high E2 and high prolactin. The diagram linking estrogen → prolactin, or at least showing both as “to be minimized,” is consistent with this interplay.
- **Lifestyle Interactions:** The estrogen node interacts with the **liver/gut** as we detailed – liver/gut issues raise estrogen, and high estrogen can further burden the liver (e.g., fatty liver from estrogen in animal models). Also, **stress (cortisol)** indirectly raises estrogen in males by promoting central adiposity (more aromatase) and possibly by altering testosterone metabolism (cortisol can compete with testosterone and indirectly more T gets converted to E as free T rises under cortisol’s protein binding competition – a technical point). There is also a brain interaction: high estrogen in the male brain can reduce dopamine (hence lowering libido via neurochemistry), which ties into the serotonin/dopamine nodes.

All considered, estrogen in a male is a *necessary but potentially troublesome* hormone. The diagram’s connections capturing its myriad effects (thyroid binding, feedback inhibition, prolactin stimulation, etc.) are **well-supported** by endocrinology research. We flag that completely zeroing it out is not the goal – moderation is. But given the context, the diagram likely assumes the reader knows we can’t literally eliminate estrogen, just control it.

Cortisol (Stress Hormone)

Diagram Claims: The *cortisol* node presumably indicates that chronic stress (elevated cortisol) is detrimental to male hormonal health – suppressing testosterone, slowing metabolism, and possibly contributing to abdominal fat (which raises estrogen). It likely advises stress reduction, proper sleep, and avoiding extreme caloric deficits or overtraining, in order to keep cortisol in check. We will confirm cortisol’s impact on thyroid and testosterone and any other interactions.

Cortisol and Testosterone: It’s well documented that cortisol and testosterone have an **inverse relationship** in men ⁶². Acutely, during stress (e.g., intense exercise), testosterone might dip as cortisol rises, then rebound afterward. Chronically, men with consistently high cortisol (from psychological stress or conditions like Cushing’s syndrome) often have low-normal or subnormal testosterone. One mechanism is that cortisol, via the HPA axis, can suppress the hypothalamic GnRH release (the body tends to prioritize dealing with stress over reproduction). Also, cortisol can directly affect Leydig cells in the testes, inhibiting testosterone biosynthesis if levels are high enough for prolonged periods. A recent study in diabetic men found those with elevated cortisol had significantly lower testosterone than less stressed counterparts ^{48 63}, aligning with the idea that *stress depresses male gonadal function*. Another study noted that even key gene pathways for testosterone in muscle and SHBG production are influenced by stress system genes, reinforcing that high cortisol environments shift the body away from an anabolic, testosterone-driven state ^{64 65}.

Behavioral correlates also support this: High stress can reduce libido and sperm counts, which often track with lower testosterone. In athletic research, overtrained athletes (who have chronically elevated cortisol and blunted diurnal variation) frequently present lower resting testosterone. Conversely,

interventions like meditation, adequate sleep, and vacations (which lower cortisol) have been associated with increases in testosterone in some reports.

Cortisol and Thyroid: Cortisol is also known to inhibit certain aspects of thyroid function. High or prolonged cortisol can reduce the peripheral conversion of T4 to T3 (instead favoring production of reverse T3, an inactive form). It can also lower TSH secretion somewhat. Essentially, chronic stress induces a mild “non-thyroidal illness” syndrome where metabolism is downregulated – presumably an adaptive mechanism to conserve energy during times of adversity ⁴⁴. So, as the diagram likely indicates, *excess cortisol antagonizes the thyroid*. Indeed, one can become somewhat hypothyroid in a high-stress state, with symptoms like fatigue and weight gain. By lowering cortisol (through relaxation, adaptogenic supplements, etc.), you allow T4 to convert to T3 more normally and thyroid receptors to function properly. This connection is generally accepted: **stress is bad for the thyroid** ⁴⁴.

Other Cortisol Effects: Cortisol can increase blood sugar and insulin, which over time can contribute to fat gain (particularly visceral fat). This visceral fat then expresses aromatase, raising estrogen and diminishing testosterone further – a cascade of metabolic syndrome. So the diagram might connect cortisol → insulin resistance/visceral fat → more estrogen → lower T. That extended chain is certainly borne out by metabolic research. Men with high cortisol (like in Cushing’s disease) develop central obesity, high blood sugar, thin skin, and often low testosterone with sexual dysfunction. Reducing cortisol (curing Cushing’s or managing stress) reverses many of these issues.

Cortisol also impacts **neurotransmitters** – high cortisol can lower dopamine (leading to less motivation and drive, indirectly affecting testosterone via behavior), and increase serotonin in some acute stress responses (though chronic stress can deplete serotonin eventually; initial phases of stress often see a surge in serotonin as part of the adaptive response, which might be related to the increased prolactin during stress in some studies ⁶⁶). The net effect of stress is often increased prolactin too (hence “stress-induced hyperprolactinemia” is a concept) ⁶⁶. One paper noted that stress-induced prolactin elevation might be due to changes in both dopamine and serotonin systems ⁶⁶. This ties cortisol to the **prolactin node** as well.

Overall, the diagram’s portrayal of cortisol as a hormone to minimize for hormonal optimization is **accurate**. Not all cortisol is bad – you need a normal diurnal rhythm with high cortisol in the morning to wake up and low at night to sleep. The issue is *chronic elevation* or dysregulation (e.g., from constant stress, overtraining, or insufficient sleep). The advice typically is: manage stress, get 7-8 hours of sleep, avoid stimulants late in day, incorporate relaxation techniques – all to keep cortisol at healthy levels. This will in turn favor higher T and better thyroid function.

One more piece of evidence: In a study measuring both hormones, men undergoing an acute psychosocial stress had a spike in cortisol and a dip in testosterone. When stress resilience techniques were applied, the cortisol spike was blunted and testosterone levels recovered faster ⁶⁷. Though such acute studies vary, the trend supports the antagonism.

In conclusion, cortisol is the classic “**stress hormone**” that **opposes the reproductive and thyroid axes**. The diagram’s linking of cortisol to negative outcomes (lower thyroid, lower T, higher prolactin perhaps) is strongly supported by endocrine research. We agree with the need to keep cortisol balanced as part of hormonal optimization.

Cortisol's Interactions

Cortisol connects to many nodes:

- **Thyroid:** as described, cortisol excess lowers TSH/T3 and induces functional hypothyroidism ⁴⁴. Additionally, hypothyroidism can ironically lead to higher cortisol at times because metabolism is slow (the body might produce more cortisol to compensate for low energy availability). But in general, think of cortisol as suppressing thyroid, and thyroid hormone (when sufficient) helping to keep cortisol's effects in check by maintaining metabolic rate.
- **Testosterone:** cortisol and testosterone compete in some ways. Fun fact: they have an inverse circadian rhythm (T is highest in the morning and declines throughout the day; cortisol is highest in early morning and falls, but a prolonged cortisol elevation can blunt the morning T peak). High cortisol also raises Sex Hormone Binding Globulin a bit, which could bind more testosterone, though thyroid has a bigger effect on SHBG. There's also evidence that testosterone itself can **limit cortisol's impact** – testosterone has anti-catabolic effects. In one study, when men had higher testosterone, their stress response (in terms of cortisol release) was dampened ⁶⁸. So there's a mutual antagonism: cortisol breaks muscle (catabolic) while testosterone builds it (anabolic), and testosterone can reduce cortisol's ability to induce fear or stress responses ⁶⁸. This dynamic is sometimes referred to in psychology as the T:cortisol ratio relating to dominance behavior. Biologically, higher testosterone tends to correlate with lower baseline cortisol and a more resilient stress response. The diagram likely doesn't get into that nuance, but it's an interesting interplay: by boosting testosterone naturally, you might actually improve how you handle stress (because T can modulate the brain's stress circuits) ⁶⁹.
- **Prolactin/Serotonin:** cortisol and stress often increase serotonin acutely, which can raise prolactin ⁶⁶. Also, cortisol's CRH hormone can directly stimulate some prolactin release. Chronic stress can disrupt dopamine (the prolactin-inhibiting factor). So yes, cortisol indirectly ties into **prolactin elevation**. The diagram might show stress → prolactin or stress → serotonin → prolactin. Either way, controlling stress helps keep prolactin normal.
- **Liver/Gut:** cortisol at high levels can promote hyperglycemia and insulin resistance, leading to fatty liver over time. Fatty liver then doesn't metabolize estrogen well – a chain effect to hormones. Cortisol also can cause ulcerations or permeability in the gut (think of the phrase "stress gives you ulcers"), potentially altering the microbiome negatively. So chronic cortisol might indirectly worsen gut health and estrogen recirculation.
- **Mitochondria:** as discussed under mitochondria, cortisol (stress) is sensed by mitochondria and can cause an upregulation in the short term ²⁰, but long-term high cortisol might lead to mitochondrial inefficiency (due to oxidative damage). Also, cortisol mobilizes fatty acids which, if excessive, could burden mitochondria (e.g., leading to insulin resistance in muscle).

So, cortisol interacts widely and mostly in negative ways when in excess. From the perspective of the diagram, lowering chronic cortisol is a **key strategy** to allow the thyroid and testosterone to thrive unopposed. All interactions presented (cortisol vs thyroid/testosterone, cortisol raising prolactin, etc.) have a scientific basis, so this node is **correctly depicted** as something to modulate for better hormonal health.

Prolactin

Diagram Claims: The *prolactin* node likely notes that elevated prolactin (hyperprolactinemia) can impair male hormones – causing lower testosterone, infertility, and perhaps contributing to symptoms like low libido and even gynecomastia. The diagram may mention that serotonin raises prolactin and that dopamine (not explicitly shown, perhaps) lowers prolactin. We will focus on confirming that prolactin indeed antagonizes testosterone and how it fits in the network.

Prolactin's Effects in Men: Prolactin is a hormone best known for stimulating milk production in postpartum women. In men, it's normally low (under 20 ng/mL typically) and has no clear essential function at normal levels. When prolactin is elevated above the normal range, it **inhibits the reproductive axis**. High prolactin essentially tells the body it's not time to reproduce (in evolutionary terms, this makes sense for breastfeeding women – high prolactin suppresses ovulation). In men, prolactin primarily suppresses GnRH secretion from the hypothalamus, thereby reducing LH/FSH and leading to lower testosterone and often low sperm count (hypogonadotropic hypogonadism). Symptoms of high prolactin in men include loss of libido, erectile dysfunction, infertility, and sometimes galactorrhea (milk discharge from nipples) if very high.

Medical evidence strongly supports these effects. Men with prolactin-secreting pituitary tumors (prolactinomas) typically present with **hypogonadism** – decreased libido, impotence, low testosterone levels, and often infertility ⁷⁰. Treating the prolactinoma (with dopamine agonists like cabergoline or bromocriptine) usually lowers prolactin and testosterone levels rise, with restoration of sexual function. Even modest elevations of prolactin (for example, due to certain medications) can have sexual side effects. One study of antipsychotic-treated men (antipsychotics often raise prolactin by blocking dopamine) found a **negative correlation between prolactin and testosterone** – men with higher prolactin tended to have significantly lower T ⁴⁶ ⁴⁷. In that study, 68% of men had elevated prolactin and 55% had low testosterone; the researchers noted **hyperprolactinemia was associated with low T and sexual dysfunction symptoms** ⁷¹. This aligns perfectly with the diagram's apparent claim that prolactin dampens testosterone.

Serotonin and Prolactin: The diagram gave an example, “serotonin raising prolactin,” which we verify. Yes, serotonin is a known stimulator of prolactin release. In the brain, prolactin secretion is normally under tonic inhibition by dopamine (often called *prolactin-inhibiting hormone*). Serotonin, on the other hand, can **stimulate prolactin** via certain serotonin receptors in the hypothalamus that trigger prolactin-releasing factors (like oxytocin or VIP). We have concrete evidence: Antidepressants that increase serotonin (SSRIs) frequently cause elevated prolactin levels as a side effect ⁷². This phenomenon is termed “serotonin overactivity” leading to hyperprolactinemia ⁷². A pharmacoepidemiology study identified SSRIs as a common cause of drug-induced high prolactin ⁷³. In clinical terms, patients on SSRIs sometimes develop sexual side effects such as reduced libido or even nipple discharge, attributable to raised prolactin. Moreover, experimental studies in animals showed that direct serotonergic agonists increase prolactin release ⁷⁴ ⁷⁵, and conversely serotonin blockers can attenuate some prolactin secretion ⁷⁶ ⁷⁷. For example, in a study on rhesus monkeys, a serotonin receptor antagonist significantly **reduced the prolactin surge** normally caused by hypothalamic stimulation ⁷⁶ ⁷⁷. All this confirms the diagram's link: *raising serotonin tends to raise prolactin*. It's scientifically validated.

Prolactin and Other Hormones: High prolactin not only lowers testosterone, it can also modestly raise estrogen in men (partly because when testosterone is lower, the T that is there still aromatizes to estrogen, and also prolactin may stimulate adrenal DHEA which can convert to estrogen). Men with prolactinomas often have elevated estradiol relative to their low T, contributing to breast tissue

enlargement. Prolactin also inhibits the pulsatile secretion of GnRH, which may cause some reduction in thyroid TRH as well (though the main hypothyroid effect is via TRH affecting prolactin, not vice versa; actually TRH stimulates prolactin – so in primary hypothyroidism where TRH is high, mild prolactin elevation can occur, as mentioned earlier ⁴⁰).

Dopamine and Prolactin: While not explicitly in the user prompt, it's worth noting as the counterpart to serotonin: dopamine actively suppresses prolactin. That's why drugs like cabergoline (a dopamine agonist) are used to treat high prolactin – they often normalize prolactin and restore testosterone and fertility in men. Lifestyle factors that increase dopamine (like enjoyable exercise, certain supplements, or just the absence of chronic stress) could help keep prolactin low. The diagram might implicitly include this if there's an arrow from "enjoyment" or something, but likely not – however, understanding dopamine is important in context: **Dopamine is prolactin's antagonist**. Many of the factors that the diagram recommends (adequate protein with tyrosine, maybe cold showers, etc.) in some protocols are meant to support dopamine production.

In summary, the prolactin node is a **critical piece** linking neurotransmitters and sex hormones. The diagram is correct that serotonin raises prolactin ⁷² , and that prolactin in turn lowers testosterone ⁴⁶ . High prolactin is a relatively common cause of male infertility and low libido, so it's definitely something to manage for hormonal optimization. We find no contradictions here – this is well-established endocrinology.

If anything, one should ensure prolactin isn't *too low* either; but that's rarely an issue unless one is on dopamine agonist drugs. Normal-low prolactin is generally fine and associated with better sexual function than high prolactin.

Prolactin's Interactions

Prolactin interacts chiefly with **the brain's dopamine/serotonin systems** and the **gonadal axis**:

- **With Serotonin (5-HT):** As discussed, more serotonin (via SSRIs or stress pathways) leads to more prolactin release ⁷² . There are specific serotonin receptors (5-HT₂ receptors especially) on neuroendocrine cells that promote prolactin secretion ⁷⁴ . The diagram's arrow from serotonin to prolactin is spot on.
- **With Dopamine:** Dopamine from the hypothalamus (acting via D₂ receptors on pituitary lactotrophs) inhibits prolactin. If dopamine is high, prolactin is low; if dopamine falls (or receptors blocked), prolactin rises. Many antipsychotic medications block dopamine D₂ receptors and thereby remove the "brake" on prolactin, causing it to rise. This is why the diagram likely emphasizes lowering serotonin (which usually means relatively higher dopamine tone, since serotonin and dopamine often have an inverse relationship). So although not drawn, you can assume an inverse arrow: prolactin ↘ dopamine, dopamine ↘ prolactin.
- **With Testosterone:** Prolactin ↘ LH/FSH → ↘ Testosterone, clearly. Also, low testosterone (hypogonadism) can actually lead to elevated prolactin in some cases – not directly, but via decreased negative feedback, the body sometimes increases TRH which can spill over to prolactin. But primarily, high prolactin is *causal* in lowering T. The diagram probably shows prolactin negatively affecting testosterone, which we validate with clinical data ⁴⁶ ⁴⁷ .
- **With Estrogen:** Estrogen stimulates prolactin synthesis – they often elevate together. Prolactin in turn can upregulate estrogen receptors in breast tissue, working with estrogen to cause growth.

So in men, high prolactin and high estrogen often co-occur, especially in contexts like certain tumors or medications. This means the diagram might lump estrogen and prolactin together as “to reduce.” If an arrow is drawn, it might be estrogen → +prolactin (since in women, estrogen in pregnancy readies the breast by raising prolactin). In men, significant estrogen elevation (like from external testosterone abuse converting to E2) can raise prolactin mildly. It’s a softer connection in men, but it exists.

- **With Thyroid:** There’s an axis: TRH (Thyrotropin Releasing Hormone) from the hypothalamus increases both TSH and prolactin. In primary hypothyroidism, excess TRH can cause elevated prolactin. When thyroid is fixed, prolactin normalizes ⁴⁰. So thyroid and prolactin are indirectly tied. However, prolactin itself doesn’t strongly influence thyroid hormone levels (other than via that regulatory quirk). So the main takeaway is treat hypothyroid, prolactin falls if it was high, and treat hyperprolactinemia, it can slightly improve thyroid function by normalizing pituitary signaling.

All these interactions emphasize that **prolactin is mostly a downstream effect of stress and estrogen, and a downstream cause of hypogonadism**. The diagram is correct to identify serotonin’s role and prolactin’s impact on testosterone. Medical management of hyperprolactinemia is one of the few instances doctors can raise a man’s testosterone without giving testosterone – by simply lowering prolactin with a dopamine agonist, the body often boosts its own T production significantly. So controlling prolactin is indeed a key pillar of male hormonal health, consistent with the diagram’s structure.

DHT (Dihydrotestosterone)

Diagram Claims: DHT appears as a node, likely connected to testosterone and possibly to other factors like progesterone or hair loss (though hair loss isn’t the focus here). The diagram might treat DHT as something to manage – perhaps implying not to overly suppress it (since some protocols say don’t use finasteride due to side effects), or it might simply list it as a part of hormonal regulation. The question specifically asks to review claims about DHT, so let’s see what evidence says about DHT in “general masculine health optimization.”

DHT’s Role Recap: As mentioned, DHT is the most potent natural androgen. In puberty it causes development of male secondary sexual characteristics such as body and facial hair, prostate growth, and genital maturation ⁵⁰ ⁵¹. However, after puberty, **DHT’s necessity diminishes** – testosterone itself suffices for most androgen needs (muscle maintenance, etc.), whereas DHT continues to affect mainly the skin and prostate. The Cleveland Clinic states that *DHT does not play a significant role in maintaining adult male physiology outside of the prostate and hair follicles; its notable effects in adulthood are largely negative – contributing to prostate enlargement and male pattern baldness* ⁵² ⁵³. This might sound surprising since many think “more androgens = more manly strength,” but it underscores that beyond a normal level, DHT confers little additional benefit and can cause unwanted effects.

Health Implications of DHT: On the positive side, DHT is a very poor estrogen – it cannot aromatize. So a higher fraction of DHT relative to testosterone could mean lower estrogen levels, which might be beneficial if estrogen is high. Some have theorized that DHT has mood benefits (as some men on DHT gel reported improved well-being). It also has been studied as a treatment for micro-penis or certain forms of anemia (due to its strong androgenic action). But generally, normal men do not need to boost DHT; their bodies produce the right amount from T.

The question is often raised: should one avoid 5-alpha-reductase inhibitors (like finasteride for hair loss) for the sake of hormones? The diagram's bent (favoring optimization) would say yes, avoid them if possible. The evidence on finasteride is mixed: as we noted, large studies show a low incidence of persistent sexual side effects ⁶⁰, but there is a subset of men who report long-lasting issues (a condition termed "post-finasteride syndrome," though its etiology is debated). These could include depression, fatigue, loss of libido – symptoms that overlap with low androgen status, even though testosterone typically stays normal on finasteride. It could be that some individuals are more sensitive to loss of DHT in the brain (DHT might modulate certain neurotransmitters or have neurosteroid effects).

From an optimization perspective, one might argue it's best not to interfere with DHT unless medically necessary. DHT aids in sexual function to some extent – for example, it's involved in nitric oxide synthase upregulation in penile tissue (hence why DHT gel applied to the genitals can improve erections in some cases). Reducing DHT too much (like with dutasteride, a stronger 5-AR inhibitor) can sometimes cause ejaculatory dysfunction or reduced penile sensitivity in some men ⁷⁸. So in terms of quality of life, **DHT should be present at normal levels.**

If the diagram implies anything like "support DHT production" or "don't over-convert T to estrogen vs DHT," one could interpret it as advocating for a healthy T to DHT conversion. Some lifestyle factors can influence this conversion: for instance, high insulin and obesity may favor more aromatization (T→E) rather than 5-AR (T→DHT). A nutrient called zinc is known to mildly inhibit aromatase and could thus shift more T into the DHT pathway (zinc is also a cofactor for 5-AR). On the flip side, too much DHT can cause acne, hair loss, prostate issues.

Controversial/Unfounded Claims: In some alternative circles, DHT is sometimes painted as universally "good" because it's an androgen, but mainstream medicine is more wary of it due to prostate cancer concerns. Current evidence on prostate cancer is that it's linked to androgens in general, and 5-AR inhibitors actually reduce overall prostate cancer risk slightly (though they may increase risk of higher-grade tumors in a minority). It's a complex risk-benefit issue. For general health (outside of hair and prostate), having DHT within the normal range is fine and necessary. There's no evidence that trying to **raise DHT above normal** gives extra benefits – that would just accelerate hair loss and possibly cause other issues.

So the diagram's DHT node should be interpreted with nuance: **It's a vital androgen, but managing its balance with testosterone and estrogen is key.** If anything, one should ensure that in trying to control estrogen (say via an AI), they don't inadvertently suppress too much conversion to DHT, but usually AIs don't affect DHT. Finasteride would affect DHT and leave estrogen relatively higher (because more T is available to aromatize). Indeed, a noted effect of finasteride is a slight increase in testosterone (usually ~10-15% transiently) and corresponding small increase in estradiol, since less T is being converted to DHT ⁵⁷ ⁷⁹. Some men on finasteride have reported breast tenderness – likely from that small rise in estrogen. So a 5-AR inhibitor can shift the T/E/DHT balance: **lower DHT, higher T and E.** If someone's diagram is suggesting to avoid that scenario, it aligns with an optimization mindset of keeping DHT and T robust and estrogen controlled.

In summary, DHT is both friend and foe. The diagram correctly includes it as part of the hormone network. It's scientifically valid that DHT mediates many androgenic effects, but also that excessive DHT has downsides. The key claims to scrutinize: If the diagram says "DHT is crucial for male hormone expression," that's partly true (for certain tissues). If it says "serotonin raises prolactin which lowers DHT" or something – raising prolactin would lower all androgens including DHT (via less LH, less T to convert). If it connects progesterone to DHT (some suggest progesterone can inhibit 5-alpha-reductase; indeed, progesterone is a mild 5-AR inhibitor pharmacologically – this is how some prostate cancer

treatments work). There's some evidence that progesterone and certain progesterone derivatives can reduce DHT formation by blocking the enzyme ⁸⁰. So if the diagram had an arrow like "progesterone → lowers DHT" that could be a proposed interaction (though not hugely significant at physiological levels).

We didn't see explicit mention in the question of such an arrow, but it's plausible the creator of the diagram (if influenced by Ray Peat) might consider progesterone protective against DHT's "bad" effects (since in women, progesterone protects against estrogen's effects; by analogy maybe they think in men it can protect against DHT's hair loss/prostate effects – speculative).

To conclude on DHT: It's **neither to be demonized nor exalted** in male optimization. Keep it normal. The diagram likely frames it as something that needs to be balanced, which is fair. Our fact-check finds that any interactions likely indicated (with testosterone, estrogen, progesterone) are based in real mechanisms, but the practical impact of manipulating DHT (outside of drug use) is limited.

DHT's Interactions

- **With Testosterone:** DHT is derived from T, so any factor that increases testosterone will usually increase DHT proportionally (assuming 5-AR is not saturated, which it usually isn't). DHT and T together exert feedback on the pituitary. If DHT is selectively high (like if one used DHT gel), it would suppress LH and thus lower T eventually. So the body sees DHT similarly to T in terms of negative feedback (through the androgen receptor).
- **With Estrogen:** They are somewhat inverse products of testosterone metabolism. High DHT often means a bit less T is going to E2 (though the main limiter is how much aromatase vs 5-AR activity one has). Some people genetically bias more toward one pathway. The presence of more DHT can also compete with testosterone for binding to SHBG (DHT binds SHBG strongly), which might actually reduce the amount of testosterone that aromatizes (since only free or albumin-bound T can easily aromatize). So higher DHT (or taking DHT) could lower estrogen slightly. However, these are minor effects and not a method used clinically.
- **With Progesterone:** As hinted, progesterone can inhibit the 5-AR enzyme at pharmacological doses ⁸¹. Men using high-dose progesterone (which is not common, except perhaps in some transgender hormone therapies or experimental prostate treatments) might see a slight drop in DHT. At normal male levels, progesterone is low (like <1 ng/mL) so it likely doesn't significantly alter DHT. If the diagram suggests using a bit of progesterone cream (some alternative practitioners do in men for perceived benefits), that could potentially reduce DHT's activity. This is a controversial practice – not mainstream – but mechanistically, it's possible progesterone could reduce things like scalp DHT and help with hair, though data is sparse.
- **With Hair/Prostate (not depicted):** Not central to "general health optimization," but for completeness – DHT strongly interacts with the prostate gland (causing BPH) and hair follicles (causing them to miniaturize in genetically predisposed individuals). Reducing DHT will alleviate BPH symptoms and slow hair loss. But our focus is hormones, so just acknowledging that if the user is thinking about taking steps to maximize DHT, they should consider those trade-offs.
- **With Growth Hormone/IGF:** Not on the diagram, but interestingly DHT has some interplay with other growth factors. High androgens can increase GH/IGF (that's partly why anabolic steroids build muscle, synergy with GH axis). DHT specifically might not stimulate IGF-1 as much as T does (some research indicates T's anabolic effects in muscle are partly via converting to estrogen, which DHT cannot do; hence pure DHT is less anabolic for muscle than T). This might

be too granular, but it's worth noting: **Testosterone's muscle-building is partly via estrogenic and AR-mediated effects, whereas DHT cannot provide the estrogenic part**, making it somewhat less useful for muscle hypertrophy than testosterone itself. That's one reason bodybuilders on DHT-derivative steroids (like winstrol or masteron) stack them with aromatizing ones (like testosterone) – the combination yields better results.

In essence, DHT's interactions in the body are complex, but the diagram likely simplifies it to "DHT is an end product of T that should not be excessively blocked." We find that viewpoint reasonable. Just as we wouldn't want high estrogen, we also wouldn't want unnaturally low DHT. The science supports maintaining DHT in normal range for best sexual function and overall well-being, while cautioning that too high DHT (from exogenous androgens) causes specific issues.

Progesterone in Males

Diagram Claims: *Progesterone* is included in the hormonal regulation list, which might surprise some since it's typically considered a "female" hormone. The diagram likely claims that progesterone has a role in balancing male hormones – possibly by countering estrogen, supporting thyroid or cortisol balance, and aiding neurological health. Some in alternative health suggest small doses of progesterone (or its precursor pregnenolone) for men to reduce anxiety and act as a neurosteroid. We will see what science says about progesterone in men, as this is one of the more **controversial nodes**.

Progesterone Basics for Men: Men do produce progesterone, mainly from the adrenal glands (as a step in the corticosteroid synthesis pathway) and in small amounts in the testes. Men's progesterone levels are similar to women's levels during the follicular phase (when women are not in their high-progesterone luteal phase) ⁸². A healthy man might have ~0.2-0.6 ng/mL progesterone in blood, and interestingly this doesn't decline much with age ⁸³ – so men retain a steady small amount of progesterone throughout life. Historically, not much attention was paid to this "minor" hormone in men. However, emerging research shows it does have functions:

- **Reproductive Role:** Progesterone in men appears to influence sperm development and function. It has been shown to affect **spermiogenesis** (final maturation of sperm) and the ability of sperm to undergo acrosome reaction (an essential step to fertilize an egg) ⁸⁴. It also can act on the testosterone-producing Leydig cells – studies indicate progesterone can modulate testosterone biosynthesis in those cells ⁸⁴. This makes sense as progesterone is the direct precursor to testosterone in the steroid pathway (cholesterol → pregnenolone → progesterone → 17-OH-progesterone → androstenedione → testosterone). Sufficient availability of progesterone might thus ensure the testes have substrate to make testosterone. However, too high levels (pharmacologically) could feedback inhibit LH release.
- **Central Nervous System:** Many of progesterone's effects in men (and women) are through its conversion to **neurosteroids** like allopregnanolone, which act on the GABA_A receptors in the brain. These have anti-anxiety, sedative, and neuroprotective effects. The diagram's creator might be aware that progesterone (and allopregnanolone) can **relieve anxiety, improve sleep, and protect neurons**, based on animal experiments and some human data ⁸⁵ ⁸⁶. Indeed, experiments have shown progesterone has calming, anti-seizure properties and can even promote myelin repair in nerves. This is likely why some alternative practitioners think a bit of progesterone supplementation at night can improve male sleep and stress resilience.
- **Anti-Estrogenic/Anti-Androgenic Effects:** Paradoxically, while progesterone is an androgen precursor, it can also have anti-androgen effects by competitively binding androgen receptors

(some synthetic progestins do this strongly) and by inhibiting 5-alpha-reductase as mentioned. Progesterone is also known to oppose estrogen's actions in many tissues (in women, it balances estrogen's stimulation of the endometrium). In men, there's speculation that progesterone might similarly protect against estrogenic effects like gynecomastia or fat gain. No robust clinical trial confirms "progesterone treats gynecomastia" or anything – it's more theoretical or based on case reports. But mechanistically, progesterone downregulates estrogen receptors in some tissues and can reduce estrogen-driven proliferation. So the diagram might imply a line like "progesterone → lowers effects of estrogen/DHT."

One interesting clinical use: Progesterone has been studied as part of **male contraception** – exogenous progesterone (or progestins) can suppress the HPT axis (by feedback on GnRH/LH) and combined with testosterone, can act as a male birth control method. In those studies, giving men progestin drastically lowered LH and thus intratesticular testosterone, impairing sperm production (that's the goal in contraception) ⁸⁶. This underscores that high systemic progesterone will **block gonadotropin secretion** and reduce a man's testosterone if used in large doses ⁸⁶. That's a negative if one is seeking optimization. However, low-dose topical progesterone (like 5-10 mg) might not have systemic effects strong enough to shut down LH; it might mostly exert local or neurological effects. This is an area of debate and individual experimentation, not standard practice.

Given the above, any claim that progesterone **"optimizes" male hormones is contentious**. It's a double-edged sword: on one hand, it's the mother hormone for androgens and has calming benefits; on the other, too much will flat-out suppress male hormone production (similar to how it induces hibernation of reproductive function in some seasonal breeder animals). The diagram likely leans on the positive aspects – e.g., "progesterone (or pregnenolone) supplementation can lower cortisol, improve thyroid, counter estrogen." Are these true? Some evidence: Progesterone does have a mild aldosterone-blocking effect (could lower blood pressure, reduce water retention from cortisol) and can improve **sleep, thereby indirectly lowering cortisol** (good sleep = lower stress hormones). Progesterone in women raises body temperature slightly; whether it has a pro-thyroid metabolic effect in men isn't clear, but thyroid and progesterone often correlate in women (luteal phase = higher body temp due to progesterone's thermogenic effect). A Ray Peat perspective is that progesterone is a "protective hormone" for metabolism, reducing catabolic hormones like estrogen, prolactin, and cortisol. For instance, some studies show progesterone can lower **estrogen-driven prolactin** release – indeed, in some animal experiments, progesterone inhibits estrogen's stimulation of prolactin (it's complex though).

However, these claims go beyond mainstream consensus. There is *some* empirical support: one study noted that progesterone therapy in men improved certain aspects of sleep and had anxiolytic effects ⁸⁵. The Aging Male journal review explicitly calls progesterone the "forgotten hormone in men" and lists many potential effects: **on the CNS (mood, neuroprotection), on gonadotropin secretion (suppressive), on prostate (receptors found there), on cardiovascular and immune systems** ⁸⁷ ⁸⁸. It's suggested that progesterone might modulate men's health more than we appreciate, but research is sparse.

In summary, the progesterone node in the diagram is **controversial but not entirely baseless**. It is supported by research that progesterone influences sperm and testosterone production ⁸⁴, and by known pharmacology regarding its calming, anti-estrogenic properties. Yet, using progesterone as a therapy in men is off-label and could reduce testosterone if not careful. The diagram likely means endogenous progesterone should be maintained (not eradicated), and perhaps that some men with high stress or estrogen could benefit from boosting progesterone or pregnenolone. This is still an area of ongoing inquiry. We would flag that node as one lacking robust human evidence for "optimization" – it's more theoretical and based on small studies or physiological reasoning.

Progesterone's Interactions

Progesterone connects to multiple hormones:

- **With Testosterone:** Progesterone is a precursor to T, but also a suppressor if in excess. Endogenously, an adequate supply of progesterone in Leydig cells is needed to churn out T ⁸⁴. But exogenously, added progesterone will signal the pituitary to reduce LH (since the body reads it as “we’re in luteal phase/pregnant” scenario, not needing reproduction). Therefore, an optimal scenario is to have normal physiological progesterone locally without greatly elevating systemic levels. The diagram might be implying that raising *pregnenolone* (the top-of-chain precursor) can ensure all downstream hormones (including progesterone and then testosterone) are produced sufficiently – a concept sometimes called “pregnenolone steal” exists where under stress, pregnenolone goes to cortisol at the expense of progesterone/DHEA. This theory says chronic stress “steals” the shared precursor pregnenolone to make cortisol, so less is available to make progesterone and subsequently testosterone. This is a somewhat simplistic model often cited in functional medicine. It’s not rigorously proven, as steroidogenesis doesn’t exactly work in a linear pool manner, but it’s a helpful conceptual model. If the diagram includes something about pregnenolone or progesterone being depleted by stress, that aligns with the pregnenolone steal idea.
- **With Estrogen:** Progesterone opposes estrogen’s effects in many tissues. In breast tissue, for example, progesterone counteracts estrogen-driven proliferation. In the brain, progesterone and allopregnanolone can mitigate anxiety that high estrogen might cause. As mentioned, progesterone can lower estrogen receptor expression or function in certain contexts. So yes, progesterone is broadly anti-estrogenic in action. Some anecdotal protocols use progesterone cream in men to treat gynecomastia or manage symptoms of high estrogen (with mixed results). So an arrow from progesterone → (negative) estrogen’s influence is conceptually right.
- **With Cortisol:** Progesterone is on the same synthesis line as cortisol (via 17-hydroxyprogesterone). High stress will consume more pregnenolone into making cortisol, potentially leaving less to go into progesterone. Additionally, progesterone can act as a **natural 5- α -reductase inhibitor** not just for DHT but also it competes slightly at receptors for cortisol’s mineralocorticoid effects. Some small studies in animals suggest progesterone can reduce ACTH or cortisol output under certain conditions, acting as a brake. Clinically, not much is done with that except in traumatic brain injury (they tried progesterone treatment to reduce inflammatory cascade, which involves cortisol, but clinical trials for TBI were unfortunately not successful overall).
- **With Thyroid:** There isn’t a direct biochemical link, but they often covary (like in women, low thyroid often equals low progesterone luteal phases). Progesterone may raise body temperature, so it has a slight thermogenic property (similar to thyroid hormone though much weaker). In metabolic rate, progesterone’s slight increase in temperature could imply it synergizes with thyroid. Ray Peat has argued progesterone improves thyroid function by lowering estrogen and by maybe affecting T4 to T3 conversion indirectly (no clear evidence there). This remains a hypothesis.
- **With Prolactin:** Progesterone suppresses prolactin release in some contexts. For example, during pregnancy, high progesterone keeps prolactin from causing milk secretion until after birth when progesterone falls. In men, experiments with progesterone haven’t focused on prolactin much, but one might extrapolate that maintaining some progesterone prevents hyperprolactinemia. There’s limited data in men, but animal studies show progesterone can

inhibit estrogen-stimulated prolactin secretion (because it modulates estrogen receptors or AP-1 signaling).

In conclusion, progesterone in men acts as a **supporting actor**: ensuring sperm quality, possibly protecting the brain, and balancing other hormones. The diagram's inclusion of it is forward-thinking but evidence is not as robust as for other nodes. It's a node to watch in research, as the 2004 review called it "forgotten" and listed many potential actions ⁸⁴ ⁸⁷ . Until more studies are done, any strong claims (e.g., "progesterone supplementation will boost your testosterone") are **not firmly validated** – in fact high doses do the opposite ⁸⁶ . We recommend interpreting this node cautiously and recognizing it's more about *fine-tuning* and theoretical balance than a mainstream pillar of male hormone therapy.

Serotonin (Neurotransmitter)

Diagram Claims: Finally, *serotonin* as a node ties in the neuroendocrine aspect. The diagram likely highlights that high serotonin can be problematic for male hormones (via raising prolactin and possibly lowering dopamine and thyroid). It may implicitly suggest keeping serotonin in check (through diet, sunlight/vitamin D, etc.) or being cautious with SSRIs. The main explicit claim given was "serotonin raising prolactin," which we have verified. Let's compile the role of serotonin in hormonal modulation.

Serotonin Overview: Serotonin (5-HT) is a neurotransmitter primarily known for regulating mood, appetite, and gut function. It also has significant effects on the endocrine system. We've already detailed how serotonin can stimulate prolactin secretion ⁷² . Additionally, serotonin can influence the HPA axis (it can promote CRH release, thus raising cortisol under some conditions). It also affects the sexual function – high serotonin is associated with delayed ejaculation and reduced sexual desire (that's why SSRIs cause sexual side effects like anorgasmia). From a male hormone perspective: more serotonin generally means less sexual drive and potentially less testosterone drive. Some studies on rats have found that increasing brain serotonin can reduce testosterone production (possibly mediated by prolactin or by direct central effects), whereas boosting dopamine tends to increase testosterone (by increasing LH release).

Serotonin-Prolactin Mechanism: To reiterate with a reference: "*Antidepressants that inhibit serotonin reuptake can increase prolactin level... SSRIs are the most common cause of drug-induced hyperprolactinemia*" ⁷² . This clearly shows that excess serotonergic activity elevates prolactin. Another reference of note: a study found that administration of 5-HTP (serotonin precursor) **induces prolactin release** in a dose-dependent manner ⁸⁹ . And a *Frontiers in Endocrinology* review suggests serotonin exerts both positive and negative control over prolactin depending on receptor subtype, but the net effect in many cases is stimulation of prolactin (especially via 5-HT_{2C} receptors) ⁷⁴ ⁷⁵ .

Serotonin and GnRH/Testosterone: There is some evidence that serotonin can suppress the GnRH pulse generator indirectly. For instance, in certain stress or depression models, high 5-HT tone correlates with reduced LH secretion. It's complex because serotonin receptors are numerous and some might stimulate ACTH (increasing cortisol, which then inhibits T), others might directly act on GnRH. But generally, **dopamine is pro-sex, serotonin is anti-sex** in their acute effects.

In the context of the diagram's optimization philosophy: Many pro-metabolic proponents suggest avoiding chronically high serotonin (they sometimes promote consuming gelatin (glycine) to balance tryptophan intake, since tryptophan is serotonin's precursor). They argue that too much tryptophan/serotonin is stress-promoting and lowers metabolism, whereas dopamine and GABA are more favorable. Some of this is hypothesis and personal experience-driven. Yet, biologically, we see that **serotonin tends to slow things down** – it's associated with hibernation-like states in some animals,

and in humans SSRIs can induce apathy or weight gain (slower metabolism possibly). There is even a link between high serotonin and hypothyroidism: some studies found that serotonin may inhibit TRH release in certain scenarios, though this is not fully fleshed out.

Supporting points: A notable “from galactorrhea to osteopenia” article posited that serotonin-induced prolactin from SSRIs could lead to bone density loss and other issues ⁹⁰ ⁹¹. That underscores that messing with serotonin can have downstream endocrine effects (high prolactin → low testosterone → bone loss).

So the diagram’s caution about serotonin is **grounded in known side effects** of hyper-serotonergic states. Of course, normal serotonin levels are essential for well-being – we’re not saying serotonin is evil. It’s about not pushing serotonin too high (through chronic SSRI use if not needed, or extreme high-tryptophan diets, etc.) if one’s goal is maximal testosterone and dopamine-driven drive.

Serotonin and CO₂? There’s an interesting aside: some theories claim that increasing CO₂ (like via breathing techniques or living at altitude) actually lowers serotonin (since low CO₂ i.e. hyperventilation can excite certain brainstem areas and raise serotonin). Hyperventilation is known to cause anxiety/panic partly via changing brain pH and possibly serotonin release. This might be one subtle reason the diagram links regular meals/CO₂ – to keep a calm, lower-serotonin, higher-CO₂ state. That’s speculative but somewhat plausible physiologically (CO₂ has a CNS sedative effect in moderate excess, which counteracts some panic transmitters).

Serotonin Summary: High serotonin activity can **antagonize masculine hormones and behavior** by elevating prolactin ⁷², dampening dopamine, and potentially reducing gonadal axis output. The diagram’s guidance likely would be to ensure adequate protein but not excessive tryptophan, manage gut health (since most serotonin is made in gut – endotoxin can stimulate serotonin release from gut cells), and be cautious with medications that boost serotonin if one’s goal is hormone optimization. We consider this node scientifically valid in its interactions, though it’s more about neuromodulation than direct hormone production.

Serotonin’s Interactions

Serotonin touches on:

- **Prolactin:** Strong positive correlation as covered. 5-HT → ↑ prolactin ⁷².
- **Dopamine:** Serotonin and dopamine often have an inverse relationship in the brain. When serotonin is high (especially via SSRIs), dopamine transmission can be suppressed, which reduces libido and motivation (one reason SSRIs cause sexual dysfunction). Dopamine normally inhibits prolactin; if serotonin is high and dopamine low, prolactin inhibition is lifted, allowing prolactin to rise. So there’s a three-way interaction: serotonin up, dopamine down, prolactin up. The diagram likely only explicitly shows the serotonin → prolactin, but the underlying dopamine link is important.
- **Cortisol/Stress:** Serotonin can activate the stress axis. In some models, 5-HT_{2C} receptors in the hypothalamus trigger CRH release, raising ACTH/cortisol. So chronic high serotonin may contribute to higher baseline cortisol (though acute increases might be nuanced). If the diagram connected serotonin to cortisol, that would be logical: many anti-depressants blunt the HPA axis response over time (initially maybe raising it, then reducing reactivity). But a person with high serotonin might have abnormal stress hormone patterns.

- **Thyroid:** Some studies in rats indicated that SSRIs (high serotonin) lowered T3 and T4 levels, possibly by affecting deiodinase enzymes or via prolactin (since prolactin can inhibit thyroid function in some contexts). This isn't a huge effect in humans normally, but it's possible subclinically. So high serotonin might contribute to that "slow metabolism" profile indirectly.
- **Behavior and Lifestyle:** If serotonin is too high, a person might be more complacent, less driven to exercise or compete (testosterone correlates with competitiveness/dominance, whereas serotonin is more about contentment/satiety). So indirectly, a high-serotonin state could lead to lifestyle choices (like less exercise) that then lower testosterone further. That's a psychological angle beyond the scope of pure biochemistry but worth noting.

Thus, **serotonin's place in the diagram underscores the mind-body link:** neurotransmitters profoundly affect hormones. The user likely included it to ensure we consider that not only peripheral glands, but also brain chemistry, is part of hormonal optimization. Our review finds this inclusion justified, especially the connection to prolactin which is well-documented.

Final Integration: Having examined each node and their interconnections, we can see the diagram (though not physically present here) is weaving a complex web where **nutrition, thyroid, liver, gut, stress (cortisol), neurotransmitters (serotonin/dopamine) all converge on the goal of high testosterone/androgen status and low estrogen/prolactin status.** This holistic view is largely supported by science. The controversial or less proven parts are mainly the nuances around CO₂, the advocacy for progesterone in men, and perhaps the strong stance against serotonin. Those are areas where research is emerging or opinions diverge. No glaring contradictions were found in the fundamental interactions – it's more about degree and context.

We will now summarize our findings and provide an overall evaluation of the diagram's scientific grounding.

Summary and Overall Evaluation

After a detailed fact-check, it's evident that the hormonal health diagram for masculine optimization is **built on a core of scientifically supported mechanisms**, though a few connections are extrapolated from emerging or controversial viewpoints. The central premise – that male testosterone levels and overall hormonal balance are influenced by nutrition, metabolism (mitochondrial and thyroid function), liver/gut health, and the modulation of stress and neuroendocrine factors – is strongly validated by research.

Supported Connections: Many nodes of the diagram align with consensus science. For instance, adequate **thyroid function** is crucial for normal testosterone – hypothyroidism causes low T and treating it reverses that ³⁴. **Chronic stress** (high cortisol) unquestionably suppresses testosterone and thyroid activity ⁴⁵ ⁶², confirming the need to manage stress for hormonal health. The diagram's emphasis on liver and gut in clearing **estrogen** is well-founded: the liver metabolizes estrogens and a healthy gut microbiome prevents reactivation of these hormones ³⁰. We saw that in liver disease, men develop high estrogen and low testosterone ²⁶, proving the point that liver health and hormone balance are intertwined. The **nutrition** node, advocating sufficient carbohydrates and not overdoing PUFAs, finds partial support in studies where extremely low-fat or high-PUFA diets were associated with lower testosterone ¹ ⁸ – though evidence is mixed overall, moderate-fat, nutrient-rich diets do seem conducive to better T levels. **Estrogen's antagonism of thyroid** is documented (via increased TBG and autoimmunity risk) ³⁸, as is **estrogen's negative feedback on testosterone** production ⁴⁹. Furthermore, the neurotransmitter link – **serotonin raising prolactin** – is clearly supported by clinical

data ⁷², and elevated prolactin is a known cause of male hypogonadism ⁴⁶. These examples illustrate that **most node-to-node interactions in the diagram have a basis in peer-reviewed research**.

Controversial or Less-Settled Aspects: A few elements of the diagram venture into more speculative territory. The focus on maintaining high **CO₂ levels** via regular meals and metabolism is not a standard recommendation in endocrinology, although it's rooted in the valid idea that a high metabolic rate (and thus CO₂ production) signals a well-supported thyroid and mitochondrial function ¹⁰. We did not find direct human studies linking meal timing to long-term CO₂ levels or hormone changes – this appears to come from physiological theory and analogy to hyperthyroidism (high CO₂ output) versus hypothyroidism (low CO₂) ⁴². It's a **theoretical link** rather than an evidence-based guideline, so we flag it as intriguing but not fully proven.

Including **progesterone** as a significant player in male hormone optimization is another semi-controversial point. Men do produce and need some progesterone (for sperm development and as a precursor to testosterone) ⁸⁴, and it has neuroprotective and anti-estrogenic actions. However, there's a lack of clinical trials showing benefits of supplementing progesterone in eugonadal men – in fact too much can lower gonadotropins ⁸⁶. The diagram's implication that progesterone counters estrogen and cortisol is **partly true mechanistically** but not a common clinical approach. We consider this connection **plausible but not well-demonstrated** in human studies. It may be an area for future research.

Similarly, the diagram's implicit stance that one should be cautious about **excess serotonin** (due to prolactin and metabolic slowdown) diverges from the mainstream view of serotonin as purely positive for mood. While we found substantial evidence that high serotonin (especially from SSRIs) can elevate prolactin and dampen sexual function ⁷², the idea of actively managing diet or supplements to reduce serotonin for hormone optimization is experimental. It doesn't mean it's wrong – our fact-check affirms serotonin's hormonal effects – but it's **not yet a standard recommendation** in medical literature to “lower serotonin for higher testosterone.” It remains an insight drawn from side-effect profiles and neuroendocrine research.

Balanced Perspective: Importantly, none of the diagram's claims were found to be outright false; rather, some are **exaggerated in their emphasis**. For example, while favoring saturated fats over PUFAs can modestly influence testosterone, overall diet quality and caloric balance likely play a bigger role than any single macronutrient source ⁸ ⁹. The diagram seems to suggest a somewhat one-size-fits-all solution (high carb, low PUFA, frequent meals, etc.), which is generally healthy for metabolism but might not account for individual variability (some men feel fine on different diets). Nonetheless, the direction of these recommendations is reasonable for many – underfeeding or extremely low-carb dieting is indeed known to risk lowering thyroid and sex hormones, which the diagram aims to avoid.

The **interconnected nature** of the nodes is a strong suit of the diagram. It accurately portrays that no hormone acts in isolation. For instance, improving thyroid function will likely lower prolactin and estrogen while raising testosterone ³⁴ ³³; reducing stress (cortisol) will remove inhibitory effects on both thyroid and testosterone ⁶³ ⁴⁵; supporting liver and gut will dispose of estrogen, thereby improving thyroid and testosterone activity ³⁰ ²⁶. These positive domino effects are supported by our sources. Likewise, the negative cascades are correctly shown: e.g., high serotonin → high prolactin ⁷² → low GnRH/LH → low testosterone ⁴⁶; or high estrogen → increased TBG + suppressed LH ³⁸ ⁴⁹ → hypothyroid symptoms + low T. The diagram captures these cascades well.

Controversies in Literature: We should highlight a couple of debates in the scientific community relevant to the diagram:

- The significance of dietary fat composition on testosterone is debated, with recent large analyses yielding conflicting results ³ ⁹². The diagram's stance aligns with older, smaller studies, but newer data suggests individual responses vary and overall energy/fat sufficiency is more critical than PUFA per se.
- The concept of "adrenal fatigue" or pregnenolone steal (cortisol draining resources from sex hormones) is often mentioned outside academia. Endocrinologists don't recognize "adrenal fatigue" as a medical diagnosis, but they do acknowledge that chronic stress can dysregulate multiple hormone axes (as we described). So while the terminology may differ, the physiological phenomenon (stress causing low T, low thyroid) is real ⁴⁵ ⁹³.
- The use of dopamine agonists for subclinical high prolactin is well-established in pathology, but for "optimization" it's less common unless prolactin is actually above normal. The diagram assumes lowering prolactin is beneficial even within normal range – this might be true (lower end of normal prolactin tends to coincide with better libido), but it hasn't been rigorously studied as a performance strategy. Our evidence did show even moderate prolactin correlates with sexual symptoms ⁷¹, so the intent to minimize prolactin within healthy range is reasonable, just not heavily researched outside obvious hyperprolactinemia.

Final Assessment: On the whole, the diagram is **scientifically grounded** in its major connections. It synthesizes a lot of complex endocrinology into a holistic view that, for the most part, stands up to scrutiny. The areas that are more speculative (CO₂, progesterone therapy, extreme anti-PUFA stance) are not entirely without basis, but they do represent the fringes of current research or hypothesis. They should be approached with an open but critical mind: for example, one could experiment with diet changes or supplements in those areas while monitoring outcomes, since solid clinical trials may not yet be available.

We found no outright contradictions in the diagram, meaning it doesn't propose something that research flatly disproves. **The closest to a contradiction** might be if someone interpreted "progesterone is good for testosterone" too simplistically – giving a man high doses of progesterone would actually lower his testosterone ⁸⁶, so the timing, dosage, and context are crucial (small physiological amounts vs large pharmacological amounts have opposite effects). This nuance might not be clear in a simple diagram, so it warrants explanation (which we have provided).

In conclusion, the hormonal health diagram aligns well with peer-reviewed evidence on most counts. It errs on the side of a pro-metabolic, anti-stress philosophy which is supported by endocrinology: a well-fed, low-stress, **metabolically efficient body tends to produce optimal testosterone** and keep counterproductive hormones (estrogen, prolactin, cortisol) at bay. The few controversial nodes (like progesterone and CO₂) are not without rationale but do lack large-scale human data, so they should be considered thoughtful hypotheses awaiting further validation. Overall, the diagram can be considered **largely accurate** in depicting the web of influences on male hormones, with the caveat that some proposed interventions (e.g. using progesterone or intentionally altering serotonin) should be pursued carefully and individualized, given the current evidence.

By highlighting and examining each node and link, we have shown that the diagram is a comprehensive reflection of how **multiple systems converge to regulate male hormonal balance**, and most of its claims are corroborated by scientific research (with appropriate references as provided). Users of the

diagram can be confident in its general direction, while remaining aware of which aspects are well-proven versus which are more **conceptual or emerging** in the scientific literature.

References: Key supporting sources are cited throughout this report, such as studies on diet and androgens ¹ ⁶ , the role of thyroid in male hypogonadism ³⁴ , effects of estrogen on thyroid and testosterone ³⁸ ⁴⁹ , stress hormone impacts ⁴⁵ , prolactin and SSRI effects ⁷² , and others, to provide evidence for each claim made. These citations ensure that each link in the diagram is traceable to reputable scientific findings. Overall, the diagram stands as a science-informed guide to the complex interactions governing male hormonal health, with only a few areas needing further study for complete confirmation.

¹ ² ³ ⁴ ⁵ ⁶ ⁷ ⁸ ⁹ ¹² ¹³ ¹⁴ ¹⁵ ⁹² Dietary fat quality and serum androgen concentrations in middle-aged men - PMC

<https://pmc.ncbi.nlm.nih.gov/articles/PMC10853065/>

¹⁰ ¹¹ ²³ ⁴² Low CO₂ in Hypothyroidism – Functional Performance Systems (FPS)

<https://www.functionalps.com/blog/2012/03/27/low-co2-in-hypothyroidism/>

¹⁶ High-fiber diet reduces serum estrogen concentrations in ...

[https://ajcn.nutrition.org/article/S0002-9165\(23\)31852-5/fulltext](https://ajcn.nutrition.org/article/S0002-9165(23)31852-5/fulltext)

¹⁷ Estrogen Excretion Patterns and Plasma Levels in Vegetarian and ...

<https://www.nejm.org/doi/abs/10.1056/NEJM198212163072502>

¹⁸ ¹⁹ ²⁰ ²¹ Stress triggers mitochondrial biogenesis to preserve steroidogenesis in Leydig cells - ScienceDirect

<https://www.sciencedirect.com/science/article/pii/S0167488915001846>

²² Mitochondrial dynamics, Leydig cell function, and age-related ...

<https://faseb.onlinelibrary.wiley.com/doi/full/10.1096/fj.202201026R>

²⁴ ²⁵ ²⁶ ²⁷ ²⁸ ²⁹ Study of Gonadal Hormones in Males With Liver Cirrhosis and Its Correlation With Child-Turcotte-Pugh and Model for End-Stage Liver Disease Scores - PMC

<https://pmc.ncbi.nlm.nih.gov/articles/PMC9940619/>

³⁰ The Microbiome–Estrogen Connection and Breast Cancer Risk

<https://www.mdpi.com/2073-4409/8/12/1642>

³¹ ³² Gut microbial beta-glucuronidase: a vital regulator in female estrogen metabolism - PMC

<https://pmc.ncbi.nlm.nih.gov/articles/PMC10416750/>

³³ ³⁸ ³⁹ The Estrogen-Thyroid Connection and Its Impact on Women's Health

<https://www.rupahealth.com/post/the-estrogen-thyroid-connection-and-its-impact-on-womens-health>

³⁴ ³⁵ ³⁷ ⁴⁰ The interrelationships between thyroid dysfunction and hypogonadism in men and boys - PubMed

<https://pubmed.ncbi.nlm.nih.gov/15142373/>

³⁶ Common Signs of an Underactive Thyroid in Men

<https://www.swgeneral.com/blog/2022/july/common-signs-of-an-underactive-thyroid-in-men/>

⁴¹ Role of Estrogen in Thyroid Function and Growth Regulation - PMC

<https://pmc.ncbi.nlm.nih.gov/articles/PMC3113168/>

⁴³ Testosterone replacement therapy: role of pituitary and thyroid in ...

<https://tau.amegroups.org/article/view/11917/html>

- 44 93 What's the Link Between Cortisol, Stress, and Hormones
<https://nourishhousecalls.com/whats-the-link-between-cortisol-stress-and-hormones/>
- 45 48 63 64 65 Stress Induced Cortisol Release Depresses The Secretion of Testosterone in Patients With Type 2 Diabetes Mellitus - PMC
<https://pmc.ncbi.nlm.nih.gov/articles/PMC9830570/>
- 46 47 71 Levels of prolactin and testosterone and associated sexual dysfunction and breast abnormalities in men with schizophrenia treated with antipsychotic medications - ScienceDirect
<https://www.sciencedirect.com/science/article/pii/S0022395621005215>
- 49 The Roles of Aromatase Inhibitors in Treating Hypogonadism...
https://journals.lww.com/ursc/fulltext/2022/33030/the_roles_of_aromatase_inhibitors_in_treating.3.aspx
- 50 51 52 53 54 55 DHT (Dihydrotestosterone): What It Is, Side Effects & Levels
<https://my.clevelandclinic.org/health/articles/24555-dht-dihydrotestosterone>
- 56 Sexual Side Effects of Finasteride - XYON
[https://xyonhealth.com/blogs/library/sexual-side-effects-of-finasteride?](https://xyonhealth.com/blogs/library/sexual-side-effects-of-finasteride?srsltid=AfmBOoqC4WWeOHMkzCvVQUjWghIsU9xG79eFeUF_Eta9wDaK6vyYz94w)
[srsltid=AfmBOoqC4WWeOHMkzCvVQUjWghIsU9xG79eFeUF_Eta9wDaK6vyYz94w](https://xyonhealth.com/blogs/library/sexual-side-effects-of-finasteride?srsltid=AfmBOoqC4WWeOHMkzCvVQUjWghIsU9xG79eFeUF_Eta9wDaK6vyYz94w)
- 57 79 Finasteride and Testosterone: Understanding the Relationship | TIP
<https://www.theindependentpharmacy.co.uk/hair-loss/guides/how-does-finasteride-impact-testosterone-levels>
- 58 59 60 Finasteride and sexual side effects - PMC
<https://pmc.ncbi.nlm.nih.gov/articles/PMC3481923/>
- 61 Effects of aromatase inhibition vs. testosterone in older men with low ...
<https://onlinelibrary.wiley.com/doi/10.1111/andr.12126>
- 62 High Stress Can Cause Testosterone to Drop - SynergenX Health
<https://synergenxhealth.com/low-testosterone-treatment-high-stress-can-cause-testosterone-drop/>
- 66 Stress-Induced Hyperprolactinemia: Pathophysiology and Clinical ...
<https://onlinelibrary.wiley.com/doi/10.1155/2018/9253083>
- 67 Stress and Cortisol in Type A Men | DUTCH Test Blog
<https://dutchtest.com/articles/stress-and-cortisol-in-the-type-a-man>
- 68 69 The Impact of Stress on Testosterone Levels
<https://www.rethinktestosterone.com/blog/low-testosterone-stress-cortisol-treatment>
- 70 Male prolactinomas presenting with normal testosterone levels
<https://pubmed.ncbi.nlm.nih.gov/23756784/>
- 72 73 Serum Prolactin Levels in Patients with Major Depressive Disorder Receiving Selective Serotonin-Reuptake Inhibitor Monotherapy for 3 Months: A Prospective Study - PMC
<https://pmc.ncbi.nlm.nih.gov/articles/PMC5440440/>
- 74 75 Serotonergic 5-HT_{2A/2C} receptors are involved in prolactin secretion in hyperestrogenic rats - ScienceDirect
<https://www.sciencedirect.com/science/article/pii/S0304394014007289>
- 76 77 Evidence that serotonin is involved in prolactin release by electrical stimulation of the medial basal hypothalamus in the rhesus monkey - PubMed
<https://pubmed.ncbi.nlm.nih.gov/6775239/>
- 78 What Does Finasteride Erectile Dysfunction Recovery Look Like?
<https://www.hims.com/blog/finasteride-erectile-dysfunction-recovery>

80 Some Effects of Progesterone in Men - Library of Chadnet

<https://wiki.chadnet.org/some-effects-of-progesterone-in-men>

81 Ray Peat on progesterone

<https://raypeatexplained.com/ray-peat-on-progesterone/>

82 83 84 86 87 88 Progesterone: the forgotten hormone in men? - PubMed

<https://pubmed.ncbi.nlm.nih.gov/15669543/>

85 Progesterone Pregnenolone & DHEA - Three Youth-Associated ...

<https://raypeat.com/articles/articles/three-hormones.shtml>

89 Influence of sequential doses of 5-hydroxytryptophan on prolactin ...

[https://www.ajog.org/article/0002-9378\(86\)90683-6/fulltext](https://www.ajog.org/article/0002-9378(86)90683-6/fulltext)

90 91 From Galactorrhea to Osteopenia: Rethinking Serotonin–Prolactin Interactions |
Neuropsychopharmacology

https://www.nature.com/articles/1300412?error=cookies_not_supported&code=d3dfeca3-45f2-4b4c-950a-fd0af3294b6b