Ray Peat's Newsletter

March 2001

Mary Shomon interview

Mary Shomon: Why do women with treated hypothyroidism frequently still have inappropriately high levels of cholesterol and high triglycerides, and what can they do to help lower these levels?

RP: Often it's because they were given thyroxine, instead of the active thyroid hormone, but hypertriglyceridemia can be caused by a variety of things that interact with hypothyroidism. Estrogen treatment is a common cause of high triglycerides, and deficiencies of magnesium, copper, and protein can contribute to that abnormality. Toxins, including some drugs and herbs, can irritate or stimulate the liver to produce too much triglyceride. T3, triiodothyronine, is the active thyroid hormone, and it is produced (mainly in the liver) from thyroxine, and the female liver is less efficient than the male liver in producing it, as is the female thyroid gland. The thyroid gland, which normally produces some T3, will decrease its production in the presence of increased thyroxine. Therefore, thyroxine often acts as a "thyroid anti-hormone," especially in women. When thyroxine was tested in healthy young male medical students, it seemed to function "just like the thyroid hormone," but in people who are seriously hypothyroid, it can suppress their oxidative metabolism even more. It's a very common, but very serious, mistake to call thyroxine "the thyroid hormone."

Nov. 6, 2000, email interview with Mary Shomon for her website:
www.thyroid.about.com/library/weekly/aa110800c.htm
References weren't included in the interview.

High cholesterol is more closely connected to hypothyroidism than hypertriglyceridemia is. Increased T3 will immediately increase the conversion of cholesterol to progesterone and bile acids. When people have abnormally low cholesterol, I think it's important to increase their cholesterol before taking thyroid, since their steroid-forming tissues won't be able to respond properly to thyroid without adequate cholesterol.

MS: You feel that progesterone can have anti-stress effects, without harming the adrenal glands. Is progesterone therapy something you feel is useful to many or most hypothyroid patients? How can a patient know if she needs progesterone? Do you recommend blood tests? And if so, at what point in a woman's cycle?

RP: Estrogen blocks the release of hormone from the thyroid gland, and progesterone facilitates the release. Estrogen excess or progesterone deficiency tends to cause enlargement of the thyroid gland, in association with a hypothyroid state. Estrogen can activate the adrenals to produce cortisol, leading to various harmful effects, including brain aging and bone loss. Progesterone stimulates the adrenals and the ovaries to produce more progesterone, but since progesterone protects against the catabolic effects of cortisol, its effects are the opposite of estrogen's. Progesterone has antiinflammatory and protective effects, similar to cortisol, but it doesn't have the harmful effects. In hypothyroidism, there is a tendency to have too much estrogen and cortisol, and too little progesterone.

The blood tests can be useful to demonstrate to physicians what the problem is, but I don't think they are necessary. There is evidence that having 50 or 100 times as much progesterone as estrogen is desirable, but I don't advocate

"progesterone replacement therapy" in the way it's often understood. Progesterone can instantly activate the thyroid and the ovaries, so it shouldn't be necessary to keep using it month after month. If progesterone is used consistently, it can postpone menopause for many years.

Cholesterol is converted to pregnenolone and progesterone by the ovaries, the adrenals, and the brain, if there is enough thyroid hormone and vitamin A, and if there are no interfering factors, such as too much carotene or unsaturated fatty acids.

Progesterone deficiency is an indicator that something is wrong, and using a supplement of progesterone without investigating the nature of the problem isn't a good approach. The normal time to use a progesterone supplement is during the "latter half" of the cycle, the two weeks from ovulation until menstruation. If it is being used to treat epilepsy, cancer, emphysema, multiple sclerosis, migraine or arthritis, or something else so serious that menstrual regularity isn't a concern, then it can be used at any time.

MS:: What supplements do you feel are essential for most people with hypothyroidism?

RP: Because the quality of commercial nutritional supplements is dangerously low, the only supplement I generally advocate is vitamin E, and that should be used sparingly. Occasionally, I will suggest limited use of other supplements, but it is far safer in general to use real foods, and to exclude foods which are poor in nutrients. Magnesium is typically deficient in hypothyroidism, and the safest way to get it is by using orange juice and meats, and by using epsom salts baths; magnesium carbonate can be helpful, if the person doesn't experience side effects such as headaches or hemorrhoids.

MS: Do you feel that there are any special considerations, issues, or treatments for men with hypothyroidism?

RP: Thyroid supplements can be useful for prostate hypertrophy and some cases of impotence and infertility. Occasionally, a man who can't put on a normal amount of weight finds that a thyroid supplement allows normal weight gain. Leg cramps, insomnia and depression are often the result of hypothyroidism. Heart failure, gynecomastia, liver disease, baldness and dozens of other problems can result from hypothyroidism.

MS: Many people describe how they are clinically hypothyroid, with elevated TSH levels, but have extremely high pulse rates. Do you have any thoughts as to what might be going on in that situation?

RP: In hypothyroidism, thyrotropin-release hormone (TRH) is usually increased, increasing release of TSH. TRH itself can cause tachycardia, "palpitations," high blood pressure, stasis of the intestine, increase of pressure in the eye, and hyperventilation with alkalosis. It can increase the release of norepinephrine, but in itself it acts very much like adrenalin. TRH stimulates prolactin release, and this can interfere with progesterone synthesis, which in itself affects heart function.

I consider even the lowest TSH within the "normal range" to be consistent with hypothyroidism; in good health, very little TSH is needed. When the thyroid function is low, the body often compensates by over-producing adrenalin. The daily production of adrenalin is sometimes 30 or 40 times higher than normal in hypothyroidism. The adrenalin tends to sustain blood sugar in spite of the metabolic inefficiency of hypothyroidism, and it can help to maintain core body temperature by causing vasoconstriction in the skin, but it also disturbs the sleep and accelerates the heart. During the night, cycles of rising adrenalin can cause nightmares, wakefulness, worry, and a pounding heart. Occasionally, a person who has chronically had a heart rate of 150 beats per minute or higher, will have a much lower heart rate after using a thyroid supplement for a few days. If your temperature or heart rate is lower after breakfast than before, it's likely that they were raised as a result of the nocturnal increase of adrenalin and cortisol caused by hypothyroidism.

M.S.: You have written that for some people, there is a problem converting T4 to T3, but that

diet can help. You recommend a piece of fruit or juice or milk between meals, plus adequate protein, can help the liver produce the hormone. Can you explain a bit more about this idea and how it works?

R.P.: The amount of glucose in liver cells regulates the enzyme that converts T4 to T3. This means that hypoglycemia or diabetes (in which glucose doesn't enter cells efficiently) will cause hypothyroidism, when T4 can't be converted into T3. When a person is fasting, at first the liver's glycogen stores will provide glucose to maintain T3 production. When the glycogen is depleted, the body resorts to the dissolution of tissue to provide energy. The mobilized fatty acids interfere with the use of glucose, and certain amino acids suppress the thyroid gland. Eating carbohydrate (especially fruits) can allow the liver to resume its production of T3.

M.S.: You have recommended if supplemental T3 is used, a thyroid patients "nibble on a 10-15 mg Cytomel tablet throughout the day." Can you explain why? Would compounded time-released T3 as available in some compounding pharmacies do the same?

R.P.: Most hypothyroid people can successfully use a supplement that contains four parts of thyroxine for each part of T3, but some people need a larger proportion of T3 for best functioning. The body normally produces several micrograms of T3 every hour, but if a large amount of supplementary thyroid is taken in a short time, the liver quickly inactivates some of the excess T3. Taking a few micrograms per hour provides what the body can use, and doesn't suppress either the liver's or the thyroid's production of the hormone. I have only rarely talked to anyone who had good results with the so-called time-release T3, and I have seen analyses of some samples in which there was little or no T3 present. It is hard to compound T3 properly, and the conditions of each person's digestive system can determine whether the T3 is released all at once, or not at all. I don't think there is a valid scientific basis for calling anything "time-release T3."

I have been told that the company which now owns the Armour name and manufactures "Armour thyroid USP" has added a polymer to the formula, and I think this would account for the stories I have heard about its apparent inactivity. Some people have found that the tablets passed through their intestine undigested, so I think it's advisable to crush or powder the tablets.

M.S.: You feel that excessive aerobic exercise can be a cause of hypothyroidism. Can you explain this further? How much is too much?

R.P.: I'm not sure who introduced the term "aerobic" to describe the state of anaerobic metabolism that develops during stressful exercise, but it has had many harmful repercussions. In experiments, T3 production is stopped very quickly by even "sub-aerobic" exercise, probably because of the combination of a decrease of blood glucose and an increase in free fatty acids. In a healthy person, rest will tend to restore the normal level of T3, but there is evidence that even very good athletes remain in a hypothyroid state even at rest. A chronic increase of lactic acid and cortisol indicates that something is wrong. The "slender muscles" of endurance runners are signs of a catabolic state, that has been demonstrated even in the heart muscle. A slow heart beat very strongly suggests hypothyroidism. Hypothyroid people, who are likely to produce lactic acid even at rest, are especially susceptible to the harmful effects of "aerobic" exercise. The good effect some people feel from exercise is probably the result of raising the body temperature; a warm bath will do the same for people with low body temperature.

M.S.: You feel that chronic protein deficiency is a common cause of hypothyroidism. How much protein should people get (as much as 70-100 grams a day?) and what types of protein, in order to prevent hypothyroidism?

R.P.: The World Health Organization standard was revised upward by researchers at MIT, and recently the MIT standard has been revised upward again by military researchers; this

is described in a publication of the National Academy of Sciences (National Academy Press, *The Role of Protein and Amino Acids in Sustaining and Enhancing Performance,* 1999). When too little protein, or the wrong kind of protein, is eaten, there is a stress reaction, with thyroid suppression. Many of the people who don't respond to a thyroid supplement are simply not eating enough good protein. I have talked to many supposedly well educated people who are getting only 15 or 20 grams of protein per day. To survive on that amount, their metabolic rate becomes extremely low. The quality of most vegetable protein (especially beans and nuts) is so low that it hardly functions as protein.

Muscle meats (including the muscles of poultry and fish) contain large amounts of the amino acids that suppress the thyroid, and shouldn't be the only source of protein.

M.S.: You talk about darkness and shorter days of winter as a stress. It's known that more thyroid hormone is needed by some patients during colder weather. Are there other things you recommend patients do to "winterproof" their metabolism?

R.P.: Very bright incandescent lights are helpful, because light acts on, and restores, the same mitochondrial enzymes that are governed by the thyroid hormone. In squirrels, hibernation is brought on by the accumulation of unsaturated fats in the tissues, suppressing respiration and stimulating increased serotonin production. In humans, winter sickness is intensified by those same antithyroid substances, so it's important to limit consumption of unsaturated fats and tryptophan (which is the source of serotonin). When a person is using a thyroid supplement, it's common to need four times as much in December as in July.

M.S.: You have reported that pregnenolone can be helpful for Graves' patients with exophthalmus. Can you explain further?

R.P.: Graves' disease and exophthalmos can occur with hypothyroidism or euthyroidism, as well as with hyperthyroidism. Pregnenolone regulates brain chemistry in a way that prevents excessive production of ACTH and cortisol, and it helps to stabilize mitochondrial metabolism. It apparently acts directly on a variety of tissues to reduce their retention of water. In the last several years, all of the people I have seen who had been diagnosed as "hyperthyroid" have actually been hypothyroid, and benefitted from increasing their thyroid function; some of these people had also been told that they had Graves' disease.

M.S.: You are a proponent of coconut oil for thyroid patients. Can you explain why?

R.P.: An important function of coconut oil is that it supports mitochondrial respiration, increasing energy production that has been blocked by the unsaturated fatty acids. Since the polyunsaturated fatty acids inhibit thyroid function at many levels, coconut oil can promote thyroid function simply by reducing those toxic effects. It allows normal mitochondrial oxidative metabolism, without producing the toxic lipid peroxidation that is promoted by unsaturated fats.

M.S.: Do you have any thoughts for thyroid patients who are trying to do everything right, and yet still can't lose any weight?

R.P.: Coconut oil added to the diet can increase the metabolic rate. Small frequent feedings, each combining some carbohydrate and some protein, such as fruit and cheese, often help to keep the metabolic rate higher. Eating raw carrots can prevent the absorption of estrogen from the intestine, allowing the liver to more effectively regulate metabolism. If a person doesn't lose excess weight on a moderately low calorie diet with adequate protein, it's clear that the metabolic rate is low. The number of calories burned is a good indicator of the metabolic rate. The amount of water lost by evaporation is another rough indicator: For each liter of water evaporated, about 1000 calories are burned.

M.S.: You have talked about internal malnutrition as a problem for many thyroid patients, due to insufficient digestive juices and poor intestinal

movements. Are there ways patients who are treated for hypothyroidism can help alleviate this problem.

R.P.: The absorption and retention of magnesium, sodium, and copper, and the synthesis of proteins, are usually poor in hypothyroidism.

Salt craving is common in hypothyroidism, and eating additional sodium tends to raise the body temperature, and by decreasing the production of aldosterone, it helps to minimize the loss of magnesium, which in turn allows cells to respond better to the thyroid hormone. This is probably why a low sodium diet increases adrenalin production, and why eating enough sodium lowers adrenalin and improves sleep. The lowered adrenalin is also likely to improve intestinal motility.

M.S.: You've mentioned eggs, milk and gelatin as good for the thyroid. Can you explain a bit more about this?

R.P.: Milk contains a small amount of thyroid and progesterone, but it also contains a good balance of amino acids. For adults, the amino acid balance of cheese might be even better, since the whey portion of milk contains more tryptophan than the curd, and tryptophan excess is significantly antagonistic to thyroid function. The muscle meats contain so much tryptophan and cysteine (which is both antithyroid and potentially excitotoxic) that a pure meat diet can cause hypothyroidism. In poor countries, people have generally eaten all parts of the animal, rather than just the muscles--feet, heads, skin, etc. About half of the protein in an animal is collagen (gelatin), and collagen is deficient in tryptophan and cysteine. This means that, in the whole animal, the amino acid balance is similar to the adult's requirements. Research in the amino acid requirements of adults has been very inadequate, since it has been largely directed toward finding methods to produce farm animals with a minimum of expense for feed. The meat industry isn't interested in finding a diet for keeping chickens, pigs, and cattle healthy into old age. As a result, adult rats have provided most of our direct information about the protein requirements of adults, and since rats keep growing for most of their life, their amino acid requirements are unlikely to be the same as ours.

M.S.: Do you think the majority of people with hypothyroidism get too much or too little iodine? Should people with hypothyroidism add more iodine, like kelp, seaweeds, etc.?

R.P.: 30 years ago, it was found that people in the US were getting about ten times more iodine than they needed. In the mountains of Mexico and in the Andes, and in a few other remote places, iodine deficiency still exists. Kelp and other sources of excess iodine can suppress the thyroid, so they definitely shouldn't be used to treat hypothyroidism.

M.S.: What are your thoughts for Graves' disease/hyperthyroidism patients? Should they move ahead quickly to get radioactive iodine treatment, or are there natural things they might be able to try to temporarily – or even permanently – get a remission?

RP: Occasionally, a person with a goiter will temporarily become hyperthyroid as the gland releases its colloid stores in a corrective process. Some people enjoy the period of moderate hyperthyroidism, but if they find it uncomfortable or inconvenient, they can usually control it just by eating plenty of liver, and maybe some cole slaw or raw cabbage juice. Propranolol will slow a rapid heart. The effects of a thyroid inhibitor, PTU, propylthiouracil, have been compared to those of thyroidectomy and radioactive iodine. The results of the chemical treatment are better for the patient, but not nearly so profitable for the physician.

Besides a few people who were experiencing the unloading of a goiter, and one man from the mountains of Mexico who became hypermetabolic when he moved to Japan (probably from the sudden increase of iodine in his diet, and maybe from a smaller amount of meat in his diet), all of the people I have seen in recent decades who were called "hyperthyroid" were not. None of the

people I have talked to after they had radioiodine treatment were properly studied to determine the nature of their condition. Radioiodine is a foolish medical toy, as far as I can see, and is never a proper treatment.

REFERENCES

Endocrinol Jpn 1977 Jun;24(3):271-6 **Effect of thyrotropin releasing hormone on heart rate and visual evoked potentials in rats.** Tonoue. The effect of injection of 0.3 microgram of thyrotropin releasing hormone (TRH) into the third ventricle on heart rate and photically evoked potentials in the midbrain reticular formation in urethane-anesthetized rats was studied. TRH increased the heart rate and amplitude of the visual evoked potentials within a few minutes following injection. The intraventricular injections of LHRH, consituent amino acids of TRH and intraperitoneal TSH did not exert any effect. This indicates that TRH is effective in the central nerveous system in inducing tachycardia in the rat.

Eur Heart J 1987 May;8 Suppl B:147-51 **Injection of thyrotropin releasing hormone into the locus coeruleus increases blood pressure.** Paakkari I, Siren AL, Nurminen ML, Svartstrom-Fraser M. Thyrotropin releasing hormone (TRH), 10 pmol kg-1 injected in the region of locus coeruleus, caused a rapid (within 1 min) rise of mean arterial pressure in **the urethane-anaesthetized rat. No clear-cut effects in heart rate or ventilation were observed. When TRH was injected into the lateral ventricle, a dose more than 10-fold higher was required to achieve a comparable rise in arterial pressure. It is concluded that TRH may have a physiological role in central cardiovascular regulation.**

Horm Metab Res 1987 Apr;19(4):164-7. **Cardiovascular, catecholamine and psychological responses to TRH in four types of affective disorder patients.** Kennedy B, Strassman RJ, Ziegler MG, Janowsky DS, Risch SC, Huey LY, Gillin JC When 500 micrograms of TRH is given intravenously, an increase in TSH, blood pressure, plasma catecholamines and positive emotions follows. Four groups of patients with major, minor or bipolar depression or schizoaffective disorder increased their TSH levels by similar amounts after TRH. The neurohormone also significantly increased diastolic blood pressure by 5.5 +/- 1.6 mm Hg, and decreased heart rate by 7.6 +/- 1.3 beats/min. There was a weak trend for bipolar depressives to have less cardiovascular response to TRH than the other **groups. Plasma norepinephrine (NE) was higher after TRH than after placebo. The NE response differed between patient groups (P = .0023) because of a smaller** response by major depressives. TRH decreased anger, tension and depression, and increased friendliness. Positive emotional responses were significantly greater in the bipolar depressives than in other groups. Forty-one other studies have found a subnormal TSH response does not distinguish between subtypes of the affective disorders, but cardiovascular, catecholamine and mood responses may do so.

Acta Physiol Scand 1983 Mar;117(3):427-37. **Effects of TRH and TRH analogues on the central regulation of breathing in the rat.** Hedner J, Hedner T, Wessberg P, Lundberg D, Jonason J Respiratory activity was studied in rats during light halothane anesthesia. Thyrotropin releasing hormone (TRH) and two TRH analogues: the desamidated form (TRH-OH) and gamma- butyrolactone- gamma-carbonyl-L-histidyl-L-prolinamide citrate (DN 1417) were administered intracerebroventricularly. TRH 0.5-5 micrograms induced a marked tachypnoea with a rapid onset and a duration of at least 20 min. DN 1417, a potent analogue of TRH with a very low TSH (thyroid stimulating hormone) releasing activity was more effective in stimulating respiratory frequency, while TRH-OH, regarded to have neither TSH releasing nor extra hypothalamic effects, at equimolar doses was unable to induce any changes in the respiratory pattern. When TRH was given into the fourth ventricle the dose response curve was slightly shifted to the left. In experiments employing the occluded breath technique, P0.1 was increased in the same magnitude as the mean inspiratory flow (VT/T1). The results also indicated an increase in the gain of the inflation reflex loop whereas the central bulbopontine setting for T1 and TTOT were not significantly changed. Local injection of TRH into the nucleus tractus solitarii induced a stimulation of respiratory frequency which was slower in onset compared to the response seen after injection into the lateral or fourth ventricles. Concomitantly to the respiratory changes, i.c.v. TRH **injection induced a hypocarbia and an alkalosis. No changes in blood pressure** or heart rate were seen. The respiratory stimulant effect of TRH could be potentiated by pretreatment with naloxone, methylatropine or a low dose of GABA. Haloperidol or propranolol did not significantly change the respiratory effects of TRH, while reserpine pretreatment seemed to blunt some of the ventilatory effects of TRH. It seems likely that TRH has few direct effects on brain stem neurones involved in the central regulation of respiration, but the main effects seem to be elicited in areas rostral to the brain stem. The respiratory stimulating effect of TRH is unrelated to TSH. Furthermore, other neurotransmitter systems might also be involved in modulation of the respiratory stimulation evoked by TRH.

Invest Ophthalmol Vis Sci 1989 Oct; 30(10): 2200-8. **Thyrotropin releasing hormone increases intraocular pressure. Mechanism of action.** Liu JH, Dacus AC, Bartels SP. Eye Research Institute of REtina Foundation, Harvard Medical School, Boston, Massachusetts. Intravenous injections of 1-100 micrograms thyrotropin releasing hormone (TRH) in rabbits elevated intraocular pressure (IOP). The 2-5 mm Hg increase of IOP lasted for less than 2 hr. No change of pupil size was observed. This IOP elevation was not due to a direct effect of TRH on ocular tissues since intravitreal injections of 0.1 and 1 micrograms TRH did not change IOP. Concentrations of thyroid stimulating hormone (TSH), triiodothyronine (T-3), epinephrine (Epi) and norepinephrine (NE) in the plasma were elevated at 30 min after an i.v. injection of 10 micrograms TRH. Plasma levels of prolactin and thyroxine were not changed. Bolus i.v.

injections of 0.1-1 micrograms TSH and 0.1-1 micrograms T-3, which would produce an equivalent increase of relevant hormones in the circulation, did not increase IOP. However, similar i.v. injections of 10-100 ng Epi and 100 ng NE caused a 1.5-3 mm Hg IOP elevation for 15-30 min. Thus, the IOP elevation following TRH administration probably is caused by the increase of circulating endogenous catecholamines and not by the stimulation of the TSH-thyroid hormone axis. Heart rate, but not blood pressure, was increased with 10 micrograms TRH. After unilateral transection of the cervical sympathetic trunk, the IOP elevation in the decentralized eye was larger than that in the intact eye. Topical treatment of 0.1% or 1% timolol in the decentralized eye inhibited the IOP elevations in both eyes, but 0.1% prazosin was not effective. **Topical 1% atropine and atropine given subcutaneously at 0.6 mg/kg decreased the bilateral IOP elevations. These observations indicate that beta-adrenergic and muscarinic mechanisms,** not an alpha-1-adrenergic mechanism, are involved.

Peptides 1990 Sep-Oct;11(5):939-44. **Selective cardiorespiratory activity of an iodinated analog of thyrotropin-releasing hormone (TRH).** Paakkari I, Jarvinen A, Vonhof S, Mannisto PT, Cohen LA, Labroo VM, Feuerstein G. The biological activity of thyrotropin-releasing hormone (TRH) and its analogs 4(5)-I-Im-TRH and 2,4(5)-I2-Im-TRH was assessed by means of their effects on: 1) the mean arterial pressure (MAP), 2) heart rate (HR), 3) ventilation minute volume (MV), 4) contractility of the rat duodenum, and 5) concentrations of thyrotropin (TSH) or prolactin (PRL) in serum. Also their binding to TRH-receptors in brain homogenates was studied. In urethane-anesthetized rats TRH ICV increased MAP, HR and MV. 4(5)-I-Im-TRH was equally as active as TRH on HR and MV but a significant elevation in MAP was observed only at a dose 100-fold to that of TRH. However, the maximal responses of 4(5)-I-Im-TRH and TRH did not differ. **In conscious rats, TRH 1A elevated MAP and HR** but 4(5)-I-Im-TRH was active on MAP only. 2,4(5)-I2-Im-TRH was devoid of cardiorespiratory activity. **TRH dose-dependently inhibited the contractions of the rat duodenum** while the iodinated analogs lacked such an activity. To induce a significant release of TSH several hundred times more of 4(5)-I-Im-TRH and over 1000 times more of 2,4(5)-I2-Im-TRH were needed as compared to TRH. The iodoanalogs elevated PRL levels only at doses 2000-fold higher than those of TRH. The iodoanalogs displaced [3H][3-Me-His2]TRH [(3H]MeTRH) from its binding sites at concentrations about 1000 times higher than those of TRH. Substitutions of the histidyl moiety of TRH in 4(5)-I-Im-TRH and 2,4(5)-I2-Im-TRH resulted in substantial loss of the endocrine activity. While the di-iodinated analog was **practically devoid of any biological activity the monoiodinated analog exerted similar cardiorespiratory activity to that of TRH.**

Arch Gen Psychiatry 1991 Feb;48(2):148-56. **Endocrine, cardiovascular, and behavioral effects of intravenous protirelin in patients with panic disorder.** Stein MB, Uhde TW Section on Anxiety and Affective Disorders, National Institute of Mental Health, Bethesda, Md 20892. The effects of protirelin administration on the anterior pituitary release of thyrotropin and prolactin were examined in 26 patients with panic disorder and 22 healthy volunteers. There were no differences observed in hormonal responses to protirelin between patients and controls. However, higher Beck Depression Inventory scores were associated with smaller baseline-corrected maximal changes in thyrotropin responses. Cardiovascular responses to protirelin did not differ between a subgroup of 15 patients with panic disorder and 15 age- and **sex-matched healthy controls. Although protirelin produced robust increases in heart rate and blood pressure, only one patient with panic disorder experienced** a panic attack during the infusion. The hormonal findings suggest that the presence of depressive symptoms may have a significant impact on various indexes of neuroendocrine responsivity and should be taken into consideration when looking at biologic measures in patients with panic disorder. The cardiovascular and behavioral findings do not support the hypothesis that all panic-producing stimuli are nonspecific and suggest that the induction of physical stimuli may be insufficient to produce panic attacks even in susceptible individuals.

Exp Clin Endocrinol 1992;99(3):143-6. **Time-related effects of thyrotropin-releasing hormone (TRH) on the pituitary-thyroid axis and extrathyroidal targets.** Nink M, Weber P, Krause U, Beyer J IIIrd. Thyrotropin-releasing hormone (TRH) is a tripeptide and acts as a stimulator of the pituitary-thyroid axis as well as having a great number of well defined extrathyroidal functions. Studies in experimental animals have shown, that TRH also has a role as a neuromodulator within the autonomous nervous system. In this study we analyzed the effects following peripheral administration of TRH (200 micrograms, 400 micrograms) in patients with endocrinological disorders and in healthy females and males. By means of a questionnaire, patients were asked about possible (side-) effects; ventilatory and cardiovascular monitoring was performed during steady state. The pulsatile TSH-secretion pattern was analyzed and thyroid and stress hormones were measured in the blood prior to and following TRH i.v. Frequent symptoms afer TRH were feeling of heat (58%), **stimulation of respiration (61%), palpitations (39%), micturition urge (52%) and restlessness (32%). Apparative monitoring demonstrated a short stimulation of respiration and an increase of heart rate. After 400 micrograms TRH i.v., blood levels of ACTH decreased slightly (p less than 0.01) but levels of T3, T4,** epinephrine, norepinephrine and cortisol remained unchanged (p greater than 0.05). TSH-levels were low during daytime and showed a surge at night.

Am J Cardiol 1994 Feb 15;73(5):374-8. **Usefulness of L-thyroxine to improve cardiac and exercise performance in idiopathic dilated cardiomyopathy.** Moruzzi P, Doria E, Agostoni PG, Capacchione V, Sganzerla P. "The short-term effects of L-thyroxine (100 micrograms/day, 10 patients) and placebo (10 patients) on idiopathic dilated cardiomyopathy were compared." **"A decrease in resting**

systemic vascular resistances and an increase in cardiac output ($p < 0.05$) were also observed. Cardiopulmonary effort parameters improved ($p < 0.05$) without hemodynamic changes at peak exercise. It is concluded that L-thyroxine short-term administration improves cardiac and exercise performance in patients with chronic heart failure, without modifying the adrenergic support to the heart and the circulatory parameters at peak exercise."

J Steroid Biochem 1983 Jul;19(1B):433-8. **Effects of anterior pituitary hormones and their releasing hormones on physiological and behavioral functions in rats.** Lin MT, Ho LT, Uang WN "The effects of direct administration of TRH, TSH, LHRH, LH, ACTH, GH, FSH and prolactin into cerebral ventricle system on metabolic, respiratory, cardiovascular and behavioral responses were assessed in unanesthetized rats, **Intraventricular administration of TRH, TSH, LHRH or LH caused hypothermia, decreased metabolism and/or cutaneous vasodilation at room temperature (22 degrees C)."** "In addition, intraventricular administration of TRH, LHRH or LH caused tachycardia, hypertension and a reduction in the epinephrine-induced reflex bradycardia." "Furthermore, following intraventricular administration of **TRH, but not TSH, LHRH, LH, FSH, GH, ACTH or prolactin three main categories of behavior were provoked: activity of normal type--forward locomotion stimulation, head and body rearing; stereotype activity--increased grooming and head swaying; and abnormal type behavior--tail elevation and piloerection in rats."**

Indian J Physiol Pharmacol 1984 Apr-Jun;28(2):153-8 **A study of pituitary-thyroid function during exercise in man.** Sawhney RC, Malhotra AS, Gupta RB, Rai RM "Exercise induced modulations in circulatory T4, T3 and TSH were monitored in 14 healthy euthyroid male volunteers undergoing exercise on a bicycle ergometer at 750 KPM for 20 minutes." "Serum T4 exhibited a significant decrease (P less than 0.05) from 9.6 +/- 0.49 microgram/dl (mean +/- SE) to 8.3 +/- 0.47 microgram/dl at 20 min after the termination of the exercise, whereas a significant decrease (P less than 0.01) in T3 levels from 158 +/- 9 ng/dl to 144 +/- 8.2 ng/dl was recorded at 40 min after the termination of the exercise." "These observations suggest that hormone **secretion by the thyroid and its responsiveness to endogenous TSH are maintained after exercise. The decrease in circulatory T4 and T3 could be due to an increase in degradation of the hormones or may reflect a generalized adaptation phenomenon. The exact mechanism and significance of these alterations remains to be elucidated."**

Arch Intern Med 1984 Jun;144(6):1149-52 **Diagnostic dosages of protirelin (TRH) elevate BP by noncatecholamine mechanisms.** Zaloga GP, Chernow B, Zajtchuk R, Chin R, Rainey TG, Lake CR "While performing thyroid function tests, we noticed that protirelin (TRH) raised BP, and, therefore, we investigated the effect of diagnostic dosages of protirelin (500 micrograms) on plasma catecholamine levels and cardiovascular function in eight patients one day before, one day after, and four weeks following heart surgery. **Mean arterial pressure (MAP), heart rate (HR), plasma norepinephrine (NE), epinephrine (EPI), dopamine (DA), thyroid hormone (triiodothyronine [T3], thyroxine), and thyrotropin (TSH) levels were measured before and after the intravenous injection of protirelin. Protirelin increased MAP transiently from 88 +/- 2 to 103 +/- 3 mm Hg (before surgery), 86 +/- 4 to 102 +/- 4 mm Hg (one day after surgery), and 86 +/- 4 to 104 +/- 5 mm Hg (four weeks after surgery)."** "We conclude the following: (1) **diagnostic dosages of protirelin transiently elevate MAP and SVR by a noncatecholamine mechanism, (2) clinicians who perform protirelin tests should be aware of protirelin's transient pressor effects."**

Endocrinologie 1982 Jul-Sep;20(3):165-76. **Endocrine circadian time structure in the aged.** Nicolau GY, Haus E, Lakatua DJ, Bogdan C, Petrescu E, Sackett-Lundeen L, Berg HG, Ioanitiu D, Popescu M, Chioran C "Thirteen circadian rhythms in plasma hormone levels (ACTH, aldosterone, cortisol, C-peptide, insulin, DHEA-S, estradiol, LH, prolactin, 17-OH progesterone, testosterone, T4 and TSH) were studied in April 1981 in 25 males and 25 females 57 to 91 years of age, institutionalized at the Berceni Hospital for the aged." "In comparison with previous data from the Endocrine Rhythms Laboratory ("C. I. Parhon" Institute) and series of younger subjects studied in Minnesota (St. Paul-Ramsey Medical Center) as well as in comparison with data published from other centers, the aged **seem to experience an earlier arousal of their endocrine system which may be related to certain disturbances of old age e.g. of sleep."**

Clin Endocrinol (Oxf) 1988 Jul;29(1):63-75. **A double-blind cross-over 12-month study of L-thyroxine treatment of women with 'subclinical' hypothyroidism.** Nystrom E, Caidahl K, Fager G, Wikkelso C, Lundberg PA, Lindstedt G. "Twenty women, who had been randomly selected from women with subclinical hypothyroidism identified in a population study were treated with L-thyroxine and placebo in a double-blind cross-over design during 2 x 6 months." "Heart rate-corrected preejection period and symptom score **decreased (P less than 0.05). Four women starting with L-thyroxine showed a marked and prolonged (4-6 months) rise in thyrotrophin concentration during the subsequent placebo period, but remained clinically euthyroid." "Subclinical hypothyroidism is common among middle-aged and old women, and our findings indicate that approximately one woman in four with this 'subclinical' condition will benefit from L-thyroxine treatment."**

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