Endocrine System Health

Text adapted from
Textbook of Natural Medicine 3rd Edition
Pizzorno & Murray 2006
Learning Outcomes

On successful completion you will be able to:

• Explain the major pathophysiologies of the endocrine system

• Describe in detail the functions of different aspects of the endocrine system

• Evaluate orthodox medical testing and treatment for endocrine system disorders

• Outline nutritional therapy approaches to supporting major endocrine glands including the thyroid, pancreas and adrenal glands.
Endocrine System

- The endocrine system includes **8 major glands** throughout your body which make **20 major hormones**.

- Hormones are chemical messengers which travel through the bloodstream to target specific tissues or organs.

- Hormones work slowly and affect body processes from head to toe. These include:
  - Growth and development
  - Metabolism: Digestion, elimination, breathing, blood circulation and maintaining body temperature
  - Sexual function
  - Reproduction
  - Mood
Hormones

• Hormones are very specific in their action.

• They circulate in our body, with each hormone having target cells it communicates with.

• The message will only be passed on to those cells with receptors that recognise the specific hormone.

• These cell receptors need nutrients for their production and maintenance.
Endocrine Glands

The endocrine glands secrete hormones which regulate various functions throughout the body.

- Pituitary gland
- Thyroid and parathyroid glands
- Adrenal glands
- Pancreas
- Ovaries (female)
- Testes (male)

Accessed (14/01/2010)
Factors Affecting Hormonal Balance

- Glands can over or under secrete hormones.
- Glands can secrete ‘faulty’ hormones.
  - e.g. Due to poor quality of raw materials (precursor nutrients).
- If circulation is poor, hormones fail to reach target tissues.
- Feedback mechanism may be faulty.
  - This is when the message saying 'stop' fails to get through.
- Issues with the breakdown and excretion of 'used' hormones.
Endocrine Disorders

The most common endocrine disorders that present in practice are:

- Thyroid disorders:
  - Hypothyroidism
  - Hyperthyroidism

- Pancreatic disorders:
  - Diabetes mellitus type 1
  - Diabetes mellitus type 2
Thyroid Gland - Anatomy

Cricoid cartilage
Thyroid gland
Parathyroid glands

http://adam.about.com/reports/Thyroid-gland.htm
The function of the thyroid gland is to create the thyroid hormones.
- Tetraiodothyronine (T4)
- Triiodothyronine (T3).

Thyroid cells are the only cells in the body which can absorb iodine.

These cells combine iodine and the amino acid tyrosine to make T3 and T4.
Thyroid Hormone Production

- T3 and T4 are then released into the blood and are transported throughout the body where they control metabolism – the conversion of oxygen and calories to energy.

- Every cell in the body depends upon thyroid hormones for regulation of their metabolism.

- The normal thyroid gland produces about 80% T4 and about 20% T3, however, T3 possesses about four times the hormone "strength" as T4.
Thyroid Hormone Production

• The thyroid gland is under the control of the pituitary gland.

• When the level of thyroid hormones (T3 & T4) drops too low, the pituitary gland produces **Thyrotropin / Thyroid Stimulating Hormone (TSH)** which stimulates the thyroid gland to produce more hormones.

• Under the influence of TSH, the thyroid will manufacture and secrete T3 and T4 thereby raising their blood levels.

• The pituitary senses this and responds by decreasing its TSH production.
Thyroid Hormone Production

• The pituitary gland itself is regulated by the hypothalamus.

• The hypothalamus is part of the brain and produces **TSH Releasing Hormone (TRH)** which tells the pituitary gland to stimulate the thyroid gland - release TSH.
Thyroid Hormone

• An excess of thyroid hormones: **Hyper**thyroidism
  – Over stimulates the body, resulting in increased heart rate, anxiety, and weight loss.

• A lack of thyroid hormones: **Hypo**thryoidism
  – Can cause depression, sluggishness, weight gain, and heart failure.

• Hyperthyroidism is rare (affecting about 1 % of the population), while mild, subclinical hypothyroidism may be much more common than most people think.
Hypothyroidism occurs when the thyroid gland:

- Produces too little thyroid hormone – *primary hypothyroidism*.
- A lack of thyroid hormone secretion due to the failure of either:
  - adequate TSH secretion from the pituitary gland – *secondary hypothyroidism*.
  - A lack of TSH-releasing hormone (TRH) from the hypothalamus – *tertiary hypothyroidism*.
- Decreased conversion from T4 to T3.
- An overproduction of reverse T3 (*Wilson's syndrome*).
- When the body is not efficiently using thyroid hormone.
Hypothyroidism

- The most common cause is autoimmune thyroid disease - *Hashimoto’s thyroiditis*

- *Subclinical hypothyroidism*, also referred to as mild hypothyroidism
  - defined as **normal serum free T4** levels with **slightly high serum TSH** concentration

- More common in **females** than in males, with reports of prevalence 2 - 8 times higher in females.

- Most prevalent in **elderly** populations, with 2% - 20% of older age groups having some form of hypothyroidism.
Hypothyroid Signs and Symptoms

• Hypothyroidism commonly manifests as a **slowing** in physical and mental activity but may be asymptomatic.

• S/S are often subtle and neither sensitive nor specific.

• Classic S/S - such as *cold intolerance, puffiness, decreased sweating, and coarse skin* - previously reported in 90% - 97% of patients may actually occur in **only 50% - 64%** of younger patients

• Many of the more common symptoms are **nonspecific** and difficult to attribute to a specific cause.

• The diagnosis of hypothyroidism is based on clinical suspicion and **confirmed by laboratory testing**.
Hypothyroid Symptoms

- Fatigue, loss of energy, lethargy
- Weight gain
- Decreased appetite
- Cold intolerance
- Dry skin
- Hair loss
- Sleepiness
- Muscle pain, joint pain, weakness in the extremities
- Depression
- Emotional liability, mental impairment

- Forgetfulness, impaired memory, inability to concentrate
- Constipation
- Menstrual disturbances, impaired fertility
- Decreased perspiration
- Paresthesia and nerve entrapment syndromes
- Blurred vision
- Decreased hearing
- Fullness in the throat, hoarseness
Hypothyroid Symptoms

More specific to Hashimoto thyroiditis:

• Feeling of fullness in the throat

• Painless thyroid enlargement

• Exhaustion

• Neck pain, sore throat, or both

• Low-grade fever
Hypothyroid Signs

- Hypothermia
- Weight gain
- Slowed speech and movements
- Dry skin
- Jaundice
- Pallor
- Coarse, brittle, straw-like hair
- Loss of scalp hair, auxiliary hair, pubic hair, or a combination
- Dull facial expression
- Coarse facial features
- Periorbital puffiness
- Macroglossia

- Goitre
- Hoarseness
- Decreased systolic blood pressure and increased diastolic blood pressure
- Bradycardia
- Pericardial effusion
- Abdominal distension, ascites is uncommon.
- Non-pitting oedema (myxedema)
- Pitting oedema of lower extremities
- Hyporeflexia with delayed relaxation, ataxia, or both
Hypothyroid Causes

- About 95% of all cases of overt hypothyroidism are primary.
- In the past, the most common cause of hypothyroidism was iodine deficiency.
  - Iodine deficiency leads to hypothyroidism or the development of an enlarged thyroid gland (i.e. a goitre), or both.
  - Goitres are estimated to affect more than 200 million people worldwide.
  - In all but 4% of these cases, the cause is an iodine deficiency.
  - Iodine deficiency is now quite rare in industrialised countries due to the addition of iodine to table salt.
  - Adding iodine to table salt began in the US in Michigan, where in 1924 the goitre rate was an incredible 47%.
  - Few people in the United States are now considered iodine deficient, yet some still develop goitres.
  - These goitres are probably a result of the excessive ingestion of goitrogens-foods that block iodine utilisation.
Hypothyroid Causes

Goitrogens - foods that block iodine utilisation include:

- The Brassica family: turnips, cabbage, broccoli, Brussels sprouts, mustard, kale, cauliflower
- Cassava root
- Soybeans
- Peanuts
- Pine nuts
- Millet

• Cooking usually inactivates goitrogens.
Autoimmune:

- The most frequent cause of acquired hypothyroidism is autoimmune thyroiditis - Hashimoto thyroiditis.

- The body recognises the thyroid antigens as foreign, and a chronic immune reaction ensues, resulting in lymphocytic infiltration of the gland and progressive destruction of functional thyroid tissue.

- Up to 95% of affected individuals have circulating antibodies to thyroid tissue.

- Antimicrosomal or antithyroid peroxidase (anti-TPO) antibodies are found more commonly than antithyroglobulin antibodies (95% vs 60%). These antibodies may not be present early in the disease process and usually disappear over time.
Hypothyroid Causes

Postpartum thyroiditis:

• Up to **10%** of postpartum women may develop lymphocytic thyroiditis in the **2 - 10 months** after delivery.

• The frequency may be as high as **25%** in women with type 1 diabetes mellitus.

• The condition is usually transient (2 - 4 months) and can require a short course of treatment with *levothyroxine (LT4)*, but postpartum patients with lymphocytic thyroiditis are at **increased risk of permanent hypothyroidism**.
Hypothyroid Causes

• **Subacute granulomatous thyroiditis**: Inflammatory conditions or viral syndromes may be associated with transient hyperthyroidism followed by transient hypothyroidism (de Quervain or painful thyroiditis, subacute thyroiditis). These are often associated with fever, malaise, and a painful and tender gland.

• **Drugs**: Medications such as amiodarone, interferon alpha, thalidomide, lithium, and stavudine have been associated with primary hypothyroidism.
Hypothyroid Causes

• Latrogenic:
  
  – Use of radioactive iodine for treatment of Graves disease generally results in permanent hypothyroidism within one year of therapy. The frequency is much lower in patients with toxic nodular goitres and those with autonomously functioning thyroid nodules. Patients treated with radioiodine should be monitored for clinical and biochemical evidence of hypothyroidism.

  – Thyroidectomy.

  – External neck irradiation (for head and neck neoplasms, breast cancer, or Hodgkin disease) may result in hypothyroidism and require monitoring.
Hypothyroid Causes

- **Rare** causes include inborn errors of thyroid hormone synthesis.

- **Iodine deficiency or excess**: Worldwide Iodine deficiency is the most common cause of hypothyroidism.
  
  - Excess iodine, as in radiocontrast dyes, amiodarone, health tonics, and seaweed, inhibits iodide organification and thyroid hormone synthesis.
  
  - Most healthy individuals have a physiologic escape from this effect; however those with abnormal thyroid glands may not. These include patients with autoimmune thyroiditis, surgically treated Graves hyperthyroidism (subtotal thyroidectomy) and prior radioiodine therapy.
Thyroid Assessment

UK serum thyroid hormone normal values:

- **TSH**: 0.4 to 4.5
  - TSH rises when the thyroid is struggling

- **TT4**: 50 to 160
  - Thyroid hormones bound to proteins.

- **Free T4**: 10 to 24
  - T4 not bound to proteins.

- **Free T3**: 4 to 8.3
  - T3 not bound to proteins.
Thyroid Assessment

According to a study reported in Lancet various “normal” TSH ranges may actually be associated with adverse health outcomes (Dayan CM et al 2002):

• TSH greater than 2.0:
  – Increased 20-year risk of hypothyroidism and increased risk of thyroid autoimmune disease.

• TSH greater than 4.0:
  – Greater risk of heart disease.

• TSH between 2.0 and 4.0:
  – Cholesterol levels decline in response to T4 therapy.
Thyroid Assessment

- An elevation in TSH with a normal T4 level is generally considered as *subclinical*.
- In conventional circles, treatment is not government recommended unless the TSH is greater than 10 (although GPs frequently recommend treatment from TSH 4 and above).
- Given the importance of adequate thyroid hormone to human health, our recommendations should be more aggressive.
- The American Thyroid Association recommends TSH screening every 5 years beginning at age 35.
Reverse T3

• Reverse T3 (RT3) can also be included into the Total Thyroid Screen on request or carried out separately (See Genova Diagnostics).

• RT3 is primarily produced from monodeiodiation of thyroxin in the peripheral tissue rather than by direct secretion by the thyroid gland.

• **Physical, mental and environmental stresses** can inhibit the deiodinating enzyme, causing less T4 to be converted to T3, thus decreasing the amount of active thyroid hormone available to the cells.

• More T4 is then shunted towards rT3 causing an elevation in rT3.

• When a patient produces excessive levels of rT3 they will usually present with hypothyroid symptoms.
Thyroid Assessment

Functional Assessment:

- Measures thyroid hormone's effect on the body – the resting metabolic rate is controlled by the thyroid gland

- According to Broda Barnes, the normal basal body temperature is 97.6° F to 98.2° F / 36.5 C to 36.8 C

- However, Barnes' approach can also be in error, as a low basal metabolic rate could also indicate nutritional deficiencies, inadequate physical activity, etc., while fever from an infection or other disease can result in an inaccurately high body temperature.
Barnes Temperature Test:

• If using a non-digital thermometer, shake the thermometer to below 35°C and place it by your bed before going to sleep at night.

• On waking, place the thermometer in you armpit for a full 10 minutes. It is important to make as little movement as possible. Lying and resting with you eyes closed is best. Do not get up until the 10 minutes test is complete. If using a digital thermometer, await the beep to show temperature recoding is complete.

• After 10 minutes, read and record the temperature and date.

• Record the temperature for at least three mornings in a row – preferably at the same time of day. Menstruating women must perform the test from the second, third and fourth day of menstruation onwards. Men and postmenopausal women can perform the test on any days.
Thyroid Assessment

Suspected hypothyroidism

Clinical and blood evaluation

- Laboratory test normal
  - Basal body temperature
    - Normal
      - Normal thyroid
        - Supplement with selenium and/or consider trial of low-dose natural thyroid
    - Low
      - Functional hypothyroidism

- Free T<sub>4</sub> low, TSH high
  - Primary hypothyroidism
    - Treat with thyroid hormones

- Free T<sub>4</sub> normal, TSH slightly to moderately elevated
  - Subclinical hypothyroidism
    - Thyroid peroxidase antibodies
      - Negative
        - TSH > 2.5
          - 3 month trial with thyroid hormones
            - Improvement
              - Continue
            - No improvement
              - Discontinue
          - Treat with thyroid hormones
      - Positive
        - If no response, treat with thyroid hormones

- Free T<sub>4</sub> low, TSH normal or low
  - Secondary hypothyroidism
    - Treat with pituitary support

Copyright © 2005, 1999, 1993 by Elsevier Ltd.
Orthodox Medical Treatment

• Almost always begins with synthetic T4 drugs, including *Synthroid* and *Levoyxl* (levothyroxine sodium).

• Low doses are usually used at first because a rapid increase in thyroid hormone may result in cardiac damage (Arnow WS 1995).

• For some patients, hypothyroidism symptoms persist despite standard T4 therapy.

• A combination therapy, using levothyroxine administered at the same time as T3. One such combination option is a drug called *Thyrolar*, which combines synthetic T3 and T4 in a fixed 4:1 ratio.
  – Caution should be used, however, in administering T3 to people over age 50 because of the increased risk of cardiac problems due to increased levels of T3.
Nutritional Support - Non Immune

- Begin with optimisation of the nutrients needed not only for thyroid hormone production, but also for the critical cellular conversion of T4 to T3.
  - Iodine: Required for thyroid hormone formation
  - Tyrosine: Required for thyroid hormone formation
  - Zinc: Conversion of T4 to T3
  - Copper: Conversion of T4 to T3
  - Selenium: Thyroid hormone synthesis, activation, and metabolism
  - Vitamin C and E: Reduce the oxidative stress caused by hypothyroidism
  - B vitamins: Riboflavin (B2), niacin (B3), and pyridoxine (B6)
Nutritional Support – Iodine

• Care must be taken if using iodine in conjunction with thyroid hormones regarding an additive effect - monitor symptoms.

• Iodine deficiency is now being recognised in the UK, USA and Australia.

• In 2002, the United Nations Children’s Fund announced a pledge to eliminate iodine deficiency in the world by 2005 citing it is a major cause of psychiatric and learning disabilities⁴.

• Of all the World Health Organisation regions, Europe continues to have the lowest coverage of iodised salt and nearly half of all school-age children have inadequate iodine intakes ².

• Once consumed, dietary iodine is easily absorbed and is subsequently converted to iodide ion (I⁻).

• Approximately 80% is sequestered by the thyroid gland for the synthesis of thyroxine.

• The result of iodine deficiency, or with decreased status, thyroxine cannot be made, which may ultimately result in thyroid dysfunction.

• Iodine deficiency results when iodide intake is < 20 μg/day. With iodine deficiency, an increase in serum TSH, and a significant decrease in both serum T4 and free T4 has been noted.

Iodine Toxicity

• Excess iodine is typically excreted via the urine and output can be measured.

• Goitre may result from excess iodine due to thyroid hyperactivity.

• High amounts of iodine from sources such as excess iodised salt, vitamin, cough medications, kelp tablets may also cause:
  – Rapid pulse, nervousness, headaches, fatigue, a ‘brassy’ taste in the mouth, excessive salivation, gastric irritation and hypothyroidism.

"24-hour iodine / iodide load test"

• A specified oral dose of iodine / iodide is given and urine is collected for the subsequent twenty-four hours.

• The test is based on the concept that the body has specific and saturable mechanisms to take up iodine / iodide.

• When maximal retention is attained, the percentage of an iodine / iodide load that is retained decreases and the percentage urinary excretion increases.
  – The percentage excretion is calculated by dividing the patient’s mg/24-hour iodine results by the oral iodine / iodide dosage (mg) provided on the requisition form by the practitioner, then multiplied by 100. The iodine excretion value represents iodine plus iodide oxidised to iodine. The load test requires a complete twenty-four hour urine collection.

• Available via Doctor’s Data
  – Phone: 0871 218 0052

Nutritional Support – Tyrosine

• Care should be taken if using tyrosine in conjunction with thyroid hormones regarding an additive effect - monitor symptoms.
• Critical precursor of the thyroid hormones thyroxine (T4) and triiodothyronine (T3).
• In the thyroid gland, these hormones are synthesised from the precursor protein thyroglobulin.
• The thyroglobulin protein is a large protein, especially rich in tyrosine residues that are reacted with iodine to produce the respective thyroid hormones.
• Tyrosine is also a precursor to catecholamines; dopamine, epinephrine etc. which may have an effect on mental function, including cognitive function.
• Use of tyrosine in hypothyroid is not fully backed by research.
• Dosage:
  – 150 mg per kilogram body weight recommended
  – The recommended therapeutic daily dose of tyrosine is regarded to be anywhere between 1-10 grams daily for adults
Three different selenium-dependent iodothyronine deiodinases (types I, II, and III) can both activate and inactivate thyroid hormones, making selenium an essential micronutrient for normal development, growth, and metabolism.

Furthermore, selenium is found as selenocysteine in the catalytic centre of enzymes protecting the thyroid from free radicals damage.

Adequate selenium nutrition supports efficient thyroid hormone synthesis and metabolism and protects the thyroid gland from damage by excessive iodide exposure.

In 2002, a study was performed in 4 elementary schools chosen randomly in Białystok and in the Children's Outpatient Clinic of Endocrinology of the Specialist Regional Hospital. The study included 400 children aged 7-13 years from schools and 120 patients at the same age treated with KJ and/or thyroxine for minimum 12 months due to goitre in the Outpatient Clinic of Endocrinology. Basing on the assessment of the thyroid size as well as the criteria of WHO from 1997 year for body surface and sex, children were divided into 2 subgroups: with goitre and the thyroid gland within the norm. In both subgroups, blood samples were taken to determine concentrations of iron, selenium, copper and zinc.

Results: The mean concentration of selenium in the blood was statistically significantly lower in children with goitre in comparison with children with the thyroid gland within the norm (44.4 +/- 7.8 microg/L vs. 49.2 +/- 9.1 microg/L, p = 0.044)

Nutritional Support – Selenium

• In the study population of school children and the Outpatient Clinic of Endocrinology, almost half (45.5%) of patients with the lower serum concentration of iron (< 60 microg/dL) had goitre despite average 22-month therapy with KJ and/or thyroxine.

• Conclusion: Observed, in spite of proper iodine prophylaxis, 7% rate of goitre occurring in school children suggests factors other than iodine deficiency influence goitre development. The study proved that the low concentration of iron and/or selenium found in the serum of children with goitre, in spite of their treatment with KJ and/or thyroxine, may be additional factors influencing the effectiveness of this treatment.
Nutritional Support – Zinc

• Zinc is essential for thyroid hormone homoeostasis, with one particular role being the synthesis of thyrotropin releasing hormone (TRH).

• Zinc deficiency may lower 5-deiodinase activity, thereby contributing to lower T4 to T3 conversion.

• Zinc may also play a role in healthy genetic expression of thyroid hormone by influencing transcription factors that affect T3 nuclear receptor interactions.

Nutritional Support – Zinc

• Background and Aims: Zinc (Zn) is an essential element involved in many basic biochemical reactions in thyroid. The aims of present study is to evaluate the Zn status in biological samples and thyroid hormones levels in 60 goitrous male (GMPs) and 72 female patients (GFPs), before and after 6 months treatment with Zn supplementation and compared with non-goitrous subjects of both genders (M=106, F=120) of age range 16-30 years.

• Methods: The biological samples were analysed for Zn concentration using flame atomic absorption spectrophotometer, following their microwave assisted acid digestion. Quality control for the methodology was established with certified samples and with those obtained by conventional wet acid digestion method on the same CRMs and real samples.

Nutritional Support – Zinc

• Results: The results showed that the significantly lower mean values of Zn in serum, while high level urine samples of GMPs and GFPs were observed as compared to control subjects (p<0.005 and 0.007) respectively. The mean values of free triiodothyronine and thyroxin were found to be lower in goitrous patients of both genders than in the age matched healthy control (p<0.006 and 0.002) respectively, in contrast high mean values of thyroid stimulating hormone were detected in GMPs and GFPs (p<0.009).

• Conclusion: It was observed that Zn status and serum thyroid hormone levels were improved in goitrous patients after six months treatment with Zn supplementation.
Nutritional Support – Iron

- Iron deficiency impairs thyroid hormone synthesis by reducing activity of heme-dependent thyroid peroxidase.

- Iron-deficiency anaemia blunts and iron supplementation improves the efficacy of iodine supplementation.

- Restoring iron status may reduce need for thyroid medications.

- Iron supplementation may decrease the absorption of thyroid medication.


Withania (*Withania somnifera*) has long been used in the Ayurvedic tradition for the treatment of hypothyroid disorders, to regulate thyroid activity.

- Has been found in animal models to increase T4 concentrations, indicating it may stimulate the synthesis and/or release of T4 directly at the glandular level.
Nutritional Support – Non Immune

- Iodine: 150 micrograms (mcg) to 1.5 milligrams (mg) daily.
- Tyrosine: 500 to 2000 mg daily
- Selenium: 200 to 400 mcg daily
- Zinc: 30 to 60 mg daily
- Copper: 1 to 2 mg daily
- Vitamin E: 400 international units (IU) daily
  - with at least 200 mg gamma tocopherol
- Vitamin C: 2 to 3 grams daily
Nutritional Support – Non Immune

• Goitrogens to be limited:
  – Brassica family foods (turnips, cabbage, rutabagas, mustard greens, radishes, horseradishes), cassava root, soybeans, peanuts, pine nuts, and millet.
  – When eaten, these foods should be cooked to break down their goitrogenic constituents.
Goitrogens to be limited:

- Soy isoflavones may adversely affect thyroid function.
- The goitrogenic potential of soy has been shown in children fed with soy formula.
- Thyroid hormone biosynthesis may be affected by inhibiting thyroid peroxidase and tyrosine protein kinase.
- In a recent publication, Messina and Redmond reviewed 14 trials with the conclusion that, with only 1 exception, a soy-rich diet has only a mild hormonal effect. However, there is a clear correlation between some thyroid parameters and isoflavone levels.
Exercise is particularly important in a treatment program for hypothyroidism.

Exercise stimulates thyroid gland secretion and increases tissue sensitivity to thyroid hormone. Many of the health benefits of exercise may be a result of improved thyroid function.

The health benefits of exercise are especially important in overweight hypothyroid individuals who are dieting.

A consistent effect of dieting is a decrease in the metabolic rate as the body strives to conserve fuel.

Exercise has been shown to prevent the decline in metabolic rate in response to dieting.
Although synthetic hormones have become popular, many physicians (particularly naturopathic physicians) still prefer the use of desiccated natural thyroid, complete with all thyroid hormones, not just thyroxine.

Many people in the standard medical community believe that only T4 replacement is necessary because the body's peripheral tissues will reliably convert T4 to T3.

However, studies in rats whose thyroids were removed demonstrated that normal tissue levels of T4 and T3 were achieved only with an infusion of T4 and T3, and not by T4 alone.
Nutritional Support – Non Immune

• Desiccated thyroid is that it provides both T4 and T3, as well as relevant amino acids and micronutrients.

• The main drawback with natural thyroid is that it lacks consistency in results.

Hashimoto’s Thyroiditis

• More common in women than men (4:1).

• More common in whites than black persons (4:1).

• Incidence increases with age, increasing markedly after 45 and reaching a maximum after 60 years.

• Familial aggregation of Hashimoto’s and Graves’ diseases. Both diseases may be present in a family and cases of identical twins, one with each disease, have been reported.

• A cross-sectional community survey suggested that up to 3% of the population has minor degrees of thyroid failure associated with autoimmune thyroiditis.
Hashimoto’s is considered a **Th1 dominant** autoimmune condition

- Lymphocytes gradually destroy thyroid tissue.
- In the early inflammatory stages of the disorder patients may present with hyperthyroidism, but as the disease progresses, the damaged thyroid tissue is unable to produce sufficient thyroid hormone and hypothyroidism develops.
Hashimoto’s Thyroiditis

• Patients with Hashimoto's thyroiditis have antibodies to various thyroid antigens.
  – The most frequently detected of which include:
    • Anti – thyroid peroxidase (anti-TPO),
    • Antithyroglobulin (anti-Tg),
    • To a lesser extent, TSH receptor-blocking antibodies.

• 10-15% of patients with Hashimoto's thyroiditis may be antibody negative.
Hashimoto’s Thyroiditis - Aetiology / Risk Factors

- Major causative factors and risk factors that can contribute to the incidence of Hashimoto's include:
  - Pregnancy
  - Graves' disease
  - Positive family history of autoimmunity
  - Personal history of autoimmunity
  - Hyperoestrogenaemia: Excess oestrogen can decrease thyroid activity through increasing amounts of de-iodinase enzymes and increasing the number of pituitary T3 receptors, which inhibits TSH release.
Hashimoto’s Thyroiditis Support

- Thyroid replacement achieves two objectives in the autoimmune hypothyroid patient:
  - Decreased thyroid hormone levels can be normalised, and
  - Thyroid activity can be suppressed, thus decreasing autoimmune processes.

- Either desiccated or synthetic thyroid replacement may be used in high enough doses in order to decrease TSH levels at or near zero.

Food elimination, detoxification, and optimising GIT integrity may be useful treatment aimed at ameliorating a possible root factor of the antigenic autoimmune activity.

Assessment of adrenal function may also be warranted.

Turmeric (Curcuma longa) may be useful for its anti-inflammatory and antioxidant effects - 400 mg three times a day of curcumin capsules.

Selenium: 200 μg/day - especially in those patients who have high titres of anti-TPO antibodies.

Hashimoto’s Thyroiditis

- **Essential fatty acids** are anti-inflammatory and necessary for hormone production.

- The thyroid gland is very susceptible to toxins, especially toxic metals so reduce exposure to these and manage existing **heavy metal toxicity**.

- **Coleus (Coleus forskohlii):**
  - stimulates thyroid function by increasing cAMP.
  - TSH requires cAMP as a second messenger.
Hyperthyroidism

• A hypermetabolic condition associated with elevated levels of free thyroxine (FT$_4$) and/or free triiodothyronine (FT$_3$).

• Hyperthyroidism includes diseases that are a subset of thyrotoxicosis, that are caused by excess synthesis and secretion of thyroid hormone by the thyroid; they are not associated with exogenous thyroid hormone intake and subacute thyroiditis.

• Most clinicians, exclusive of endocrinologists, use the terms hyperthyroidism and thyrotoxicosis interchangeably.
Hyperthyroidism occurs when the thyroid gland produces excessive amounts of thyroid hormone, resulting in acceleration of the body’s metabolic rate.

- Hyperthyroidism causes the body's cells to burn fuel so rapidly that they waste much of it in the form of heat.

The ailment varies in severity.

Most cases can be treated effectively with medication.

Surgery may be necessary if conservative treatment fails.

Left untreated, hyperthyroidism is potentially fatal.
The condition can take 3 different forms:

- **Graves' Disease / diffuse toxic goitre (up to 85%)**
  - Appears as a goitre in the neck along with eye and skin changes.
  - An Th2 autoimmune condition.
  - It stems from an antibody that stimulates the thyroid to produce excessive amounts of thyroid hormones. In the process, the antibody overpowers the usual thyroid-stimulating hormone. The stimulation causes the thyroid to grow, creating a goitre.

- **Toxic Nodular Goitre (15-20%)**
  - One or more nodules (benign tumours) in the thyroid produce an excess of thyroid hormone.

- **Secondary Hyperthyroidism**
  - In this condition the pituitary gland stimulates the thyroid to overproduce thyroid hormones.
Graves disease is an organ-specific autoimmune disorder characterised by a variety of circulating antibodies
– Including common autoimmune antibodies, as well as anti-thyroid peroxidase (anti-TPO) and antithyroglobulin (anti-TG) antibodies.

The most important autoantibody is **thyroid-stimulating immunoglobulin (TSI)**.
– TSI is directed toward epitopes of the thyroid-stimulating hormone (TSH) receptor and acts as a TSH-receptor agonist. Similar to TSH, TSI binds to the TSH receptor on the thyroid follicular cells to activate thyroid hormone synthesis and release and thyroid growth (hypertrophy).
Hyperthyroidism - Risk Factors

- **Gender:**
  - Female-to-male ratio in published series is 7:1 to 10:1.

- **Stress:**
  - Recognised as a precipitating factor since Graves' disease was first recognised.

- **Genetics:**
  - HLA- B\(_8\) and HLA-DR\(_3\) in Caucasians; HLA-Bw\(_{35}\) in the Japanese; and, in the Chinese, HLA-Bw.

- **Left handedness:**
  - 1 study showed a statistically significant trend for left-handed people to manifest Graves' disease and other autoimmune diseases.
Hyperthyroidism - Risk Factors

• Smoking:
  – Estimate is comparatively less for smoking (1.5) than that associated with heredity (3.6) and negative life events (6.3)

• Iodine supplementation:
  – An interesting study evaluated the effects of mandatory consumption of iodised salt in a whole population of 267,330 inhabitants of Galicia. The incidence of thyrotoxicosis, diagnosed as elevated $T_4$ and suppressed TSH levels, increased throughout the whole study period, with 4.89 new cases per 100,000 population. The rate of increase for females (8.03) was much greater than for males (1.34). The increased incidence of thyrotoxicosis comprised both nodular and diffuse goitres. The authors concluded that dietary iodine supplementation in iodine-sufficient areas can increase the incidence of thyrotoxicosis in susceptible individuals.

• Mercury and cadmium exposure
Hyperthyroidism - Symptoms

- Nervousness
- Anxiety
- Increased perspiration
- Heat intolerance
- Tremor
- Hyperactivity
- Palpitations
- Weight loss despite increased appetite
- Reduction in menstrual flow or oligomenorrhea
Hyperthyroidism - Signs

- Hyperactivity
- Tachycardia or atrial arrhythmia
- Systolic hypertension
- Warm, moist, and smooth skin
- Lid lag
- Stare
- Tremor
- Muscle weakness
Hyperthyroidism – Orthodox Treatment

Radioactive iodine:

- A one-time oral dose of radioactive iodine (sodium iodide 131I) takes advantage of the thyroid’s affinity for iodine. The dose depends on the size of the thyroid and the findings of the radioactive iodine uptake test.

- The radioactive iodine becomes concentrated in the thyroid, destroying the hyperfunctioning tissue.

- The effects of the initial dose are checked after 2 to 3 months.

- Can cause hypothyroidism and is contraindicated in pregnancy.
Hyperthyroidism – Orthodox Treatment

• Thyroid depressants:
  – Alternatively, thyroid depressive drugs in tablet form, such as propylthiouracil and carbimazole, may be used to decrease production of thyroid hormone.
  – Typical starter doses usually bring hyperthyroidism under control within 6 to 12 weeks.

• Beta-blocking drugs:
  – Prescribed to help to control some of the symptoms of hyperthyroidism, particularly in a thyroid storm.
  – They slow heart rates, reduce tremors, and control anxiety.
  – However, they do not control abnormal thyroid function.
Hyperthyroidism – Nutritional Support

• The chief objective
  – Reduce symptoms while trying to re-establish normal thyroid status.

• Increase calories to compensate for the increase in metabolism and should be eaten in the form of small, frequent meals.

• Protein should be supplemented if the patient is nutritionally depleted.

• Reduce risk factors (i.e., stress, smoking, excess iodine intake) and increase rest.
  – Stress control is the single most important action the patient can take to assist normalisation of the thyroid
• Naturally occurring goitrogens:
  – The isothiocyanates are similar in action and structure to propylthiouracil
  – Remember that cooking inactivates
  – The highest levels of isothiocyanates are found in raw soymilk
  – In the Brassica family cabbage, and turnips usually contain the highest levels
    – 1/2 head of raw cabbage per day is the typical prescription

• Since iodine is found in kelp and other seaweeds, vegetables grown near the ocean, seafood, iodised salt and some nutritional supplements, these should be avoided.

• Do not supplement iodine
Antioxidants:
• Tissues exposed to high levels of thyroid hormone are known to be susceptible to free radical-mediated injury.
• Low antioxidant status is clearly prevalent in hyperthyroid patients.
• The degree of cell damage in Graves' disease is in direct correlation with the level of oxidative stress.
• Specifically focus on vitamins A, C, E and selenium.
  – Vitamin A: Potentially alters iodine metabolism
  – Vitamin C: Not appear to directly affect the course of this disease, supplementation seems warranted to help ameliorate the symptoms and metabolic effects.
  – Vitamin E: Reduce lipid peroxidation.
  – Selenium: Low selenium status in hyperthyroidism is well known.
Erythrocyte, serum and plasma antioxidant activities and the effects of propylthiouracil (PTU) treatment on these activities were studied in patients with toxic multinodular goitre.

The activities of the erythrocyte antioxidant enzymes (glucose-6-phosphate dehydrogenase, catalase, Cu/Zn-superoxide dismutase, selenium (Se)-dependent glutathione peroxidase and glutathione reductase) and the levels of erythrocyte Se, serum ceruloplasmin and plasma malondialdehyde were significantly higher while serum **vitamin E, plasma vitamin C and plasma Se were lower in hyperthyroid patients**.

PTU treatment, not for 1 but for 3 months caused a partial reversal of antioxidant activities to euthyroid levels. It is suggested that alterations in blood antioxidant activities following PTU treatment might be due to the antioxidant and/or antithyroid effect of this drug.
Hyperthyroidism – Nutritional Support

• Zinc:
  – Red blood cell zinc is decreased.
  – Hyperthyroidism also causes lower zinc assimilation by tissues after ingestion.

• L-carnitine:
  – Antagonist of thyroid hormone effect in peripheral tissues by inhibiting thyroid hormone entry into the nucleus of human and animal cells.

• Coenzyme Q10:
  – Found to be at low plasma concentrations.

• Calcium metabolism is altered in hyperthyroidism, and Graves patients are more susceptible to osteoporosis than ‘normal’.
Hyperthyroidism – Carnitine

- By experiments on cells (neurons, hepatocytes, and fibroblasts) that are targets for thyroid hormones and a randomized clinical trial on iatrogenic hyperthyroidism, we validated the concept that **L-carnitine is a peripheral antagonist of thyroid hormone action.** In particular, L-carnitine **inhibits** both triiodothyronine (T3) and thyroxine (T4) entry into the cell nuclei. This is relevant because thyroid hormone action is mainly mediated by specific nuclear receptors. In the randomized trial, we showed that **2 and 4 grams per day** of oral L-carnitine are capable of **reversing hyperthyroid symptoms** (and biochemical changes in the hyperthyroid direction) as well as **preventing (or minimizing) the appearance** of hyperthyroid symptoms (or biochemical changes in the hyperthyroid direction).

- A very recent clinical observation proved the usefulness of L-carnitine in the most serious form of hyperthyroidism: thyroid storm.

- Since hyperthyroidism impoverishes the tissue deposits of carnitine, there is a rationale for using L-carnitine at least in certain clinical settings.
Hyperthyroidism – Nutritional Support

• Decrease inflammation
  – Omega 3, quercetin, vitamin C, E, B3, B2 and D.

• Increase phase 2 liver detoxification
  – Specifically glucuronidation pathway to increase T4 excretion
    – Taurine, glycine, glutathione and cysteine

• Reduce sweating
  – Vitamins B1 and B5, choline

• Check for food sensitivity
Diabetes Mellitus (DM)

- A disorder characterised by an inability to properly transport and metabolise glucose.
- This inability can have a number of causes depending on the type of diabetes, but the final common pathway of all types is an elevated plasma glucose.
  - In type 1 diabetes / T1DM - formerly known as “juvenile onset” or “insulin-dependent”
    - Failure of insulin production in the pancreas.
  - In type 2 diabetes / T2DM
    - Insulin resistance and decreased sensitivity of the insulin receptor.
  - Gestational diabetes
    - Diabetes occurring during pregnancy.
Insulin Overview

- Essential to process carbohydrates, fat, and protein.

- Reduces blood glucose levels by allowing glucose to enter muscle cells and by stimulating the conversion of glucose to glycogen as a carbohydrate store \textit{glycogenesis}.

- Inhibits the release of stored glucose from liver glycogen - \textit{glycogenolysis}.

- Slows the breakdown of fat to triglycerides, free fatty acids, and ketones.

- Stimulates fat storage - \textit{lipogenesis}.

- Inhibits the breakdown of protein and fat for glucose production in both liver and kidneys - \textit{gluconeogenesis}.
Diabetes Mellitus I / T1DM

• 10% of all cases.

• Primarily a failure of insulin production resulting from an autoimmune destruction of the pancreatic islet cells responsible for insulin secretion.

• **Antibodies** against pancreatic cells are found in approximately 85–90% of individuals with T1DM
  – The rate of **islet cell destruction** can be variable, being rapid in some individuals and slow in others.

• Autoimmune destruction of islet cells can be the result of:
  – A genetic predisposition, environmental factors, and in some cases, unknown causes.
Gestational Diabetes

• Abnormal maternal glucose regulation.

• Occurs in 3-10% of pregnancies.

• Accounts for 90% of cases of diabetes mellitus in pregnancy.

• Type II diabetes mellitus accounts for 8% of cases of diabetes mellitus in pregnancy, and given its increasing incidence.
  – Pre-existing diabetes mellitus now affects 1% of pregnancies.

• Studies suggest that the prevalence of diabetes mellitus (DM) among women of childbearing age is increasing.
  – Potentially attributable to more sedentary lifestyles, changes in diet, and the virtual epidemic of childhood and adolescent obesity that is presently evolving.
Diabetes Mellitus II / T2DM

• Non-insulin dependent diabetes.
• Accounts for the **vast majority** of patients with diabetes.
• The incidence is **rising rapidly** concurrent with the epidemic of obesity.
  – Approximately tripled over the past three decades.
• More alarming is the recent steady demographic shift in type 2 diabetes to younger populations.
• Associated with:
  – Microvascular (i.e., retinal, renal, possibly neuropathic)
  – Macrovascular (i.e., coronary, peripheral vascular)
  – Neuropathic (i.e., autonomic, peripheral) complications
Diabetes Mellitus II

• Do not have antibodies to their islet cells but become resistant to utilising the insulin they produce.
  – At least initially, insulin treatment is not required.

• Obesity plays a large role in the pathogenesis:
  – Contributes to insulin resistance.
  – A number of factors secreted by fat cells (leptin, tumor necrosis factor, and others) increase insulin resistance and thus interfere with the action of insulin.
Normal blood sugar ranges:

• For the majority of healthy individuals, normal blood sugar levels are as follows:
  – First thing in the morning, before breakfast: 80 to 120 mg/dl
  – Before other meals: 80 to 120 mg/dl
  – 2 hours after meals: 140 to 160 mg/dl
  – Before bed: 100 to 140 mg/dl
• Blood sugar ranges for people with diabetes.

• When being tested for diabetes, blood sugar levels will normally be taken after around eight hours of fasting. During this blood sugar levels are put into the following categories:
  – Normal: 70 to 100 mg/dl (5.6 mmol/l)
  – Prediabetes or Impaired Glucose Tolerance: 101 to 126 mg/dl (5.6 – 7 mmol/l)
  – Diagnosis of diabetes: More than 126 mg/dl (7 mmol/l)

• Classic symptoms of polyuria, polydipsia, and polyphagia.

• May also be associated with:
  – Fatigue, blurred vision, poor wound healing, periodontal disease, and frequent infections.
Diagnostic Summary

• Most patients are asymptomatic for years.

• Classic symptoms of:
  – Polyuria: Passage of large volumes of urine.
  – Polydipsia: Excessive thirst.
  – Polyphagia: Excessive hunger; abnormally strong desire to eat.

• May also be associated with:
  – Obesity, hypertension, acanthosis nigricans, candida infections, fatigue, decreased or absent light touch and temperature sensation, blurred vision, poor wound healing, periodontal disease, and frequent infections.
The "gold standard" in diagnosing diabetes remains the oral glucose tolerance test (GTT) because of its longstanding use. However, it is not the gold standard because it is the most accurate or convenient test but rather because of its longstanding use. In fact, according to some studies the GTT is significantly less reliable than fasting blood glucose, especially if combined with a glycosylated haemoglobin level (haemoglobin A1C / HgbA1C).
Major Complications of DM

• **Cardiovascular disease** - Adults with diabetes have death rates from cardiovascular disease about 2-4 times higher than adults without diabetes.

• **Hypertension** - About 75% of adults with diabetes have high blood pressure.

• **Retinopathy** - DM is the leading cause of blindness among adults.

• **Renal disease** - DM is the leading reason for dialysis treatment, accounting for 43% of new cases.

• **Neuropathy** - About 60%-70% of people with diabetes have mild to severe forms of nervous system damage. Severe forms of diabetic nerve disease are a major contributing cause of lower-extremity amputations.

• **Amputations** - More than 60% of lower-limb amputations in the US occur among people with diabetes.
Major Complications of DM

• **Periodontal disease** - Almost one third of people with diabetes have severe periodontal (gum) disease.

• **Pain** - Many diabetics fall victim to chronic pain due to conditions such as arthritis, neuropathy, circulatory insufficiency, or muscle pain (fibromyalgia).

• **Depression** - This is a common accompaniment of diabetes. Clinical depression can often begin to occur even years before diabetes is fully evident. It is difficult to treat in poorly controlled diabetics.

• **Autoimmune disorders** - Thyroid disease, inflammatory arthritis, and other diseases of the immune system commonly add to the suffering of diabetes.
# Differences Between T1DM and T2DM

<table>
<thead>
<tr>
<th>Features</th>
<th>T1DM</th>
<th>T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>Usually younger than 40 yr</td>
<td>Usually older than 40 yr</td>
</tr>
<tr>
<td>Proportion of all diabetics</td>
<td>&lt;10%</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Family history</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Appearance of symptoms</td>
<td>Rapid</td>
<td>Slow</td>
</tr>
<tr>
<td>Obesity at onset</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Insulin levels</td>
<td>Decreased</td>
<td>Normal-high initially, decreased after several yrs</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>Occasional</td>
<td>Often</td>
</tr>
<tr>
<td>Treatment with insulin</td>
<td>Always</td>
<td>Usually not required</td>
</tr>
</tbody>
</table>
Most medical texts, diabetes organisations, and medical doctors tend to consider type I diabetes primarily as a genetic disorder.

– Rather than acting as the primary cause, the genetic predisposition simply sets the stage for the environmental or dietary factor to initiate the destructive process.
– The very term *predisposition* clearly indicates that something else needs to occur: less than 10% of those with increased genetic susceptibility for T1DM actually develop the disease.

Dietary and other environmental factors are the chief factors that ultimately determine whether the disease develops.
Abnormalities of the gut immune system may play a fundamental role in the development of the immune attack on beta cells. It is interesting to consider that an underlying factor that may contribute to type I diabetes is poor protein digestion.

- Strong evidence implicates dietary factors like cow's milk and gluten as important triggers of the autoimmune process.

Viral infection, particularly of the gastrointestinal tract.

- Enteroviruses (e.g., polioviruses, coxsackieviruses, echoviruses) and rotavirus.

- All of these viruses replicate in the gut and cause stimulation of the intestinal immune system that may activate the insulin-specific immune cells to seek out and destroy beta cells.
T1DM – Risk Factor Theories

• Omega 3 deficiency:
  – Beta cells are destroyed by administering compounds that generate free radicals (e.g., nitrosamines and alloxan). One study found that feeding fish oil to experimental animals before treating them with the drug alloxan prevented the development of chemically induced type I diabetes. The mechanisms responsible for this effect are related to improved cell membrane function leading to enhanced antioxidant status and suppression of the formation of inflammatory compounds known as cytokines.

• Nitrates and nitrosamines:
  – Agricultural runoff from fertilisers and are in cured or smoked meats such as ham, hot dogs, bacon, and jerky to keep the food from spoiling.
T1DM – Risk Factor Theories

- Vitamin D deficiency:
  - In the most extensive of studies looking at vitamin D and type I diabetes, all pregnant women in northern Finland who were due to give birth in 1966 were enrolled (more than 12,000 women) and their children were monitored until December 1997.
  - Final analysis of 10,366 enrollees demonstrated that children who regularly took vitamin D, primarily from cod liver oil, had an 80% reduced risk of developing type I diabetes, while those who had vitamin deficiency actually had a 300% increased risk of developing the disease.
  - One study found that the use of vitamin D from cod liver oil during pregnancy significantly reduced the frequency of type I diabetes in their children.
  - Furthermore, studies looking at vitamin D status in the blood of newly diagnosed cases of type I diabetes are much lower in these patients than in healthy controls.
T1DM Treatment

Pharmaceutical Treatments:

• Insulin - available in short, medium and long duration forms, which can be used for baseline dosage and also as a bolus at mealtime. Alternative administration options such as inhalation are being developed.

• Early intervention in type I diabetes designed to affect the autoimmune or oxidative process theoretically may be capable of lengthening the "honeymoon" phase or even completely reversing the process.
  – Niacinamide / nicotinamide
  – Epicatechin
T1DM Treatment

• Carbohydrate counting is a method advised by the NHS for T1DM to improve insulin dosing.

• Approved online or short courses are available to patients. See the Diabetes UK website.

• Read more at: http://www.nursingtimes.net/nursing-practice/clinical-zones/diabetes/carbohydrate-counting-in-diabetes/5036209.article
Niacinamide / nicotinamide:

- In a retrospective study, the data from 25 patients with type 1 diabetes, who had been given at the initial diagnosis nicotinamide at a dose of **25 mg/kg body weight** along with **intensified insulin therapy** (IIT) for **2 years**, were analysed and compared to data from a control group given only IIT.

- The results indicated that the patients treated with nicotinamide + IIT or IIT alone did not significantly differ in terms of C-peptide secretion or insulin requirement.

- However, glycosylated hemoglobin (**HbA1c**) was **significantly lower** 2 years after diagnosis in patients treated with nicotinamide + IIT (6.09% versus 6.989%, respectively).

- No adverse effects were observed in patients receiving nicotinamide. These results indicate that the addition of nicotinamide at diagnosis and continued for 2 years improves metabolic control as assessed by HbA1c.

- In both nicotinamide and control patients, no decline in C-peptide was detected 2 years after diagnosis, indicating that IIT preserves C-peptide secretion.
Niacinamide / nicotinamide:

- Patients with recent-onset type 1 diabetes were randomised to receive either nicotinamide (25 mg/kg body weight) alone or with vitamin E (15 mg/kg body weight).

- IIT was applied to both treatment groups. Patients diagnosed at an age of less than 9 years showed significantly reduced C-peptide levels compared with those aged over 9 years at diagnosis and at the 2-year follow-up, but there were no differences between the nicotinamide alone and the nicotinamide + vitamin E-treated groups.

- However, at 6 months, patients over 9 years of age treated with nicotinamide + vitamin E showed significantly higher C-peptide levels compared with the nicotinamide alone group.

- In both age groups and in the different treatment groups, C-peptide levels found at diagnosis were preserved 2 years later. It appears that children over the age of 9 years may benefit from the addition of vitamin E to nicotinamide and IIT.
Epicatechin

• Initially bark from the Malabar kino tree (Pterocarpus marsupium). This botanic medicine has a long history of use in India as a treatment for diabetes.

• Green tea (*Camellia sinensis*) extract appears to be a better choice than extracts of *P. marsupium*.
  – Exerts a broad range of beneficial effects.
  – Polyphenols exhibit significant antiviral activity against rotavirus and enterovirus-two viruses suspected of causing type I diabetes.
  – Considerably easier to find commercially than *P. marsupium*.

• Recommended dosages for children younger than age 6 is 50 to 150 mg; for children 6 to 12 years old, 100 to 200 mg; for children older than 12 years old and adults, 150 to 300 mg.

• The green tea extract should have a polyphenol content of 80% and be decaffeinated.
T1DM Support

• A diet high in fresh fruit (whole), vegetables (low GL), essential fatty acids and lean protein sources to provide essential phytonutrients, antioxidants to help to control inflammatory processes and support healthy nitric oxide production.
  – Relatively low in saturated/animal fat.
  – Emphasises on essential fatty acids.
  – High GL / refined carbohydrates should be avoided.
T1DM Support

• Regular aerobic exercise: Starting slowly and increasing as patient’s fitness improves
  - Has been shown to stimulate non-insulin dependant glucose transport into cells.

• Manage hypertension, lipids and obesity as they are significant risk factors.

• Smoking cessation is the highest priority in currently smoking patient.

• Patients with kidney damage should carefully monitor and in many cases reduce protein intake.
• Diabetes UK has for many years been calling for the establishment of active programmes to identify people with Type 2 diabetes early, to ensure appropriate diabetes care and treatment.

• Those at increased risk of Type 2 diabetes should be targeted as part of systematic case finding, annual health checks and Cardiovascular Disease Risk Management Programmes.

• The objectives of such initiatives are to reduce the numbers of people with undiagnosed diabetes, the burden of complications at diagnosis, the impact on the person with diabetes and the impact of diabetes on NHS resources.
• Diabetes UK/Dr Foster 2005 research has shown that 60% of localities in England have programmes in place to identify people with diabetes early.

• However, it is estimated that approximately 0.75 million people with diabetes remain undiagnosed in the UK.

• With the expectation that the number of people with diabetes will reach 3 million by the end of the decade, further action is needed to ensure that people with diabetes are identified early.
T2DM – Pathophysiology

1. Carbohydrate intake
2. Increased hepatic glucose production
3. Decreased peripheral glucose uptake
4. Decreased insulin secretion

Blood Glucose
T2DM – Risk Factors

- Family history of diabetes (i.e., parent or sibling with type II diabetes)
- Obesity (esp. truncal obesity)
- Increased waist-to-hip ratio
- Age-increasing age is associated with increased risk beginning at age 45 years
- Race/ethnicity (e.g., African American, Hispanic American, Native American/Canadian, Native Australian or New Zealander, Asian American, Pacific Islander)
- Previously identified impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)
- History of gestational diabetes (diabetes during pregnancy) or delivery of baby > 9 lb
- Hypertension (blood pressure > 140/90 mmHg)
- Triglyceride level >2.8 mmol/L
- Low adiponectin levels,
- Elevated fasting insulin levels
- Polycystic ovary syndrome (consider in any adult woman who is overweight with acne and infertility)
T2DM – Signs and Symptoms

Symptoms tend to appear gradually over a period of years, but once present may mimic some type 1 indicators. Type 2 diabetes is often asymptomatic (with elevated glucose found on routine exam), or an individual may present with:

- Hyperosmolar coma
- Polyuria and polydipsia
- Fatigue
- Blurred vision
- Vaginitis
- Candida infections of the skin
- Poor vision
- Pruritus
- Impotence
- Numbness or burning sensation of distal extremities
- Frequent or recurrent urinary infections
**T2DM – Treatment**

- **Sulfonylureas**: Stimulates insulin secretion and is therefore most valuable where there are still some functional pancreatic beta cells.
  - E.g. Glipizide, gliclazide, glibenclamide, and glimepiride

- **Biguanides**: Insulin sensitisers—they improve insulin action at target cells and reduce insulin resistance. Biguanides are very useful in later stages of type 2 diabetes when insulin secretagogues begin to fail.
  - E.g. Metformin (Glucophage)
  - Increase homocysteine production

- **Thiazolidinediones**: By improving insulin sensitivity to allow glucose to enter the cells, this class of medication when used in conjunction with insulin for type 2 diabetics will likely lower the amount of exogenous insulin needed.
  - Thiazolidinediones are effective reducers of HbA1C, but may increase LDL cholesterol and weight. However, they do tend to raise HDL cholesterol levels, improve endothelial cell function, preserve pancreatic beta cell function, and may decrease albumin secretion:
  - E.g. Rosiglitazone (Avandia), pioglitazone
## Treatment of Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th></th>
<th>monotherapy*</th>
<th>add</th>
<th>add</th>
</tr>
</thead>
<tbody>
<tr>
<td>obese</td>
<td>metformin</td>
<td>sulfonylurea</td>
<td>exenatide or insulin or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>glitazone</td>
</tr>
<tr>
<td>non-obese</td>
<td>sulfonylurea or metformin</td>
<td>metformin or sulfonylurea</td>
<td>exenatide or insulin or glitazone</td>
</tr>
<tr>
<td>elderly</td>
<td>low dose secretagogue</td>
<td>switch to simple insulin regimen</td>
<td>----</td>
</tr>
<tr>
<td>Asians</td>
<td>glitazone</td>
<td>metformin</td>
<td>sulfonylurea or insulin or exenatide**</td>
</tr>
</tbody>
</table>

*for symptomatic patients, may initially use secretagogue or insulin to rapidly decrease glucose

**exenatide not approved for use with glitazone
• **Eye Exam** - Annual eye exam with an ophthalmologist to screen for diabetic retinopathy.

• **Urine** - Annual urine screening for proteinuria with an appropriate test that measures microalbumin excretion.
  – Patients with an elevated urinary albumin excretion should be offered co-managed care with a conventional medicine provider to discuss the addition of an angiotensin converting enzyme (ACE) inhibitor to the patient’s treatment regimen.

• **Ketones** - Ketones appear in the urine when there is a severe deficiency in the availability or the activity of insulin; avoid ketoacidosis.

• **Blood Pressure** - Regular hypertension screening.

• **Lipid Profile** - Initial fasting lipid screening, repeated annually if elevated.
  - An ideal goal for low-density lipoprotein cholesterol (LDL) is <2.6 mmol/L.

• When adipocytes, particularly those around the abdomen, become full of fat, they secrete a number of biologic products; resistin, leptin, tumor necrosis factor, free fatty acids - that dampen the effect of insulin, impair glucose utilisation in skeletal muscle, promote glucose production by the liver, and impair insulin release by pancreatic beta cells.

• As the number and size of adipocytes increase, this leads to a reduction in the secretion of compounds that promote insulin action including a protein produced by fat cells known as adiponectin.
  – Adiponectin is not only associated with improved insulin sensitivity, but it also has anti-inflammatory activity, lowers triglycerides, and blocks the development of atherosclerosis.
The Third National Health and Nutrition Examination Survey (NHANES III) made it quite clear that diabetes is a disease of diet and lifestyle.

Results showed individuals with type II diabetes:

- 69% did not exercise at all or did not engage in regular exercise.
- 62% ate fewer than five servings of fruits and vegetables per day.
- 65% consumed more than 30% of their daily calories from fat.
- More than 10% of total calories from saturated fat
- 82% were either overweight or obese.
Lack of exercise is clearly established as a risk factor for development of diabetes in susceptible individuals.

A meta-analysis of 14 studies evaluating the impact of exercise on established diabetes found that exercise reduced HgbA1C from 8.3% to 7.6%—a significant decrease—even though it did not lead to a significant change in BMI.

Most experts agree that the exercise regimen recommended for those with diabetes should be aimed at both increasing cardio respiratory fitness and muscle strength.

4 hours total per week is generally agreed upon as a reasonable target.
T2DM – Support

• Food intake overview:
  – Low glycaemic load.
  – Moderate protein.
  – Monounsaturated fats such as olive oil, nuts, and nut oils and omega-3 fatty acids from fish protect.
  – High antioxidants - especially Vitamins C and E.
  – Low in pro-inflammatory foods.

• Reduce high GL/refined carbohydrates.
  – This can increase insulin sensitivity in some subjects, help with weight loss, lower blood lipids, and may even be of benefit in cancer risk reduction by decreasing insulin-like growth factor.
T2DM – Support

• Increase water soluble fibre.
  – Legumes, oat bran, nuts, seeds, Psyllium seed husks, pears, apples, and most vegetables.
  – Slow digestion and absorption of carbohydrates, thereby prevent rapid rises in blood sugar, thereby increasing the sensitivity of tissues to insulin.
  – > 50 mg / day

• Stress support
  – Higher stress levels are associated with higher blood glucose levels in both type I and type II diabetes.

• Monitor blood pressure, lipid profile and homocysteine.

• Education, education, education…..and support…. 
Legumes, specifically soybeans, associated with reduced risk of T2DM.

A study was conducted in a population-based prospective cohort of 64,227 middle-aged Chinese women with no history of type 2 diabetes mellitus (DM), cancer, or cardiovascular disease; these women were followed an average of 4.6 years.

Anthropometric measurements, in-person interviews, and validated food-frequency questionnaires were used to collect data.

An inverse association was observed between quintiles of total legume intake and three mutually exclusive legume groups (peanuts, soybeans, and other legumes) and type 2 DM incidence.

The multivariate-adjusted relative risk of type 2 DM for the upper quintile compared with the lower quintile was 0.62 (95% CI 0.51, 0.74) for total legumes and 0.53 (95% CI 0.45, 0.62) for soybeans. Although soy milk consumption was associated with a lower risk of type 2 DM, the association between other soy products and soy protein consumption with type 2 DM was not significant.
• Reduce saturated fat and trans fatty acids and optimise essential fats.
  – Reduced membrane fluidity can cause reduced insulin binding to receptors on cellular membranes or reduced insulin action or both.
  – A total intake of fats at less than 30% of calories, and a restriction in saturated fats to less than 10% of total calories have been shown to be effective dietary interventions in the prevention trials to date.
  – Data from the Nurses’ Health Study suggests that more emphasis on nuts as a source of monounsaturated and polyunsaturated fats may reduce risk of diabetes in women.
In vitro and in vivo animal studies have reported strong insulin-like or insulin-potentiating effects after cinnamon administration.

A double-blind study of 60 individuals with type 2 diabetes revealed a significant decrease in fasting serum glucose (18-29%), triglyceride (23-30%), low-density lipoprotein cholesterol (7-27%), and total cholesterol (12-26%) levels after they had taken cinnamon for 40 days.

The effective dosage was 1 g of cinnamon per day (roughly ¼ teaspoon), although some dosages were 6 g/d.
A follow-up to this study in postmenopausal women with type 2 diabetes failed to show benefit. In this study, patients were supplemented with either cinnamon (1.5 g/d) or a placebo. Before and after 2 and 6 weeks of supplementation, arterialized blood samples were obtained, and oral glucose tolerance tests were performed. Results indicated that there was no effect on whole-body insulin sensitivity, oral glucose tolerance, or blood lipids profile.

Failure to show effectiveness in the second study may have been related to insufficient levels of active components. It was originally thought that the active compound, a water-soluble compound known as methyl-hydroxy-chalcone polymer, was responsible for cinnamon's insulin-like effects; however, further research identified the active constituents as water-soluble polyphenol polymers, which are type A polymers consisting of mixtures of epicatechin and catechins.
T2DM – Support
Cinnamon

• In a double-blind study using a *water-soluble cinnamon* extract, positive results were shown again.

• A total of 79 patients with diagnosed diabetes mellitus type 2 not on insulin therapy but treated with oral hypoglycemic drugs or diet were randomly assigned to take a cinnamon extract or a placebo capsule three times a day for 4 months.

• The amount of aqueous cinnamon extract corresponded to 3 g of cinnamon powder per day. The mean absolute and percentage differences between the preintervention and postintervention fasting plasma glucose levels of the cinnamon and placebo groups were significantly different.

• There was a significantly higher reduction in the cinnamon group (10.3%) than in the placebo group (3.4%). No effect was seen on hemoglobin A₁c or lipid profiles.
T2DM – Support
Chromium

• A key constituent of the "glucose tolerance factor."
  – It works closely with insulin in assisting the uptake of glucose into cells. Without chromium, insulin's action is blocked and glucose levels are elevated.

• Its mechanism of action has been described as increasing insulin binding to cells due to increasing the number of insulin receptors.

• In vitro studies have also shown chromium to alter activity of phosphotyrosine phosphatase and phosphotyrosine kinase.
More than 20 clinical studies have focused on chromium supplementation in diabetes.

- In some of these studies in type II diabetes, supplementing the diet with chromium has been shown to decrease fasting glucose levels, improve glucose tolerance, lower insulin levels, and decrease total cholesterol and triglyceride levels while increasing HDL-cholesterol levels.

- Although there are also studies that have not shown chromium to exert much effect in improving glucose tolerance in diabetes, there is no argument that chromium is an important mineral in blood glucose metabolism.

- At this time, however, it appears that chromium supplementation is likely to produce meaningful improvements in glycaemic control only in people who are deficient in this essential trace element.
The largest double-blind, placebo-controlled trial of chromium involved 180 Chinese type 2 diabetics, randomised to placebo, 200 mcg, or 1,000 mcg of chromium picolinate daily for 4 months.

HgA1C levels significantly declined in both study groups at 4 months compared to placebo (placebo 8.5%, 200mcg 7.5%, 1,000 mcg 6.6%), yet the higher dose group also demonstrated significant improvements in fasting blood glucose levels, 2 hr oral glucose tolerance testing, and insulin and cholesterol levels.

A follow up open-label study on 833 Chinese diabetics using a similar form of chromium, followed for 10 months, found decreases in fasting and post-prandial glucose as well as decreased symptoms of fatigue, excessive thirst, and frequent urination.
The objective of the study was to provide a comprehensive evaluation of chromium (Cr) supplementation on metabolic parameters in a cohort of type 2 diabetes mellitus subjects representing a wide phenotype range and to evaluate changes in "responders" and "nonresponders."

After preintervention testing to assess dysglycemia, insulin sensitivity (assessed by euglycemic clamps), Cr status, and body composition, subjects were randomized in a double-blind fashion to placebo or 1000 mug Cr.

A substudy was performed to evaluate 24-hour energy balance/substrate oxidation and myocellular/intrahepatic lipid content. There was not a consistent effect of Cr supplementation to improve insulin action across all phenotypes.
Insulin sensitivity was negatively correlated to soleus and tibialis muscle intramyocellular lipids and intrahepatic lipid content. Myocellular lipids were significantly lower in subjects randomized to Cr.

At preintervention, responders, defined as insulin sensitivity change from baseline of at least 10% or greater, had significantly lower insulin sensitivity and higher fasting glucose and A(1c) when compared with placebo and nonresponders, that is, insulin sensitivity change from baseline of less than 10%.

Clinical response was significantly correlated (P < .001) to the baseline insulin sensitivity, fasting glucose, and A(1c).
There was no difference in Cr status between responder and nonresponders. **Clinical response to Cr is more likely in insulin-resistant subjects who have more elevated fasting glucose and A(1c) levels.**

Chromium **may reduce myocellular lipids** and **enhance insulin sensitivity** in subjects with type 2 diabetes mellitus who do respond clinically independent of effects on weight or hepatic glucose production. Thus, modulation of lipid metabolism by Cr in peripheral tissues may represent a novel mechanism of action.
Chromium is an essential mineral that appears to have a beneficial role in the regulation of insulin action and its effects on carbohydrate, protein and lipid metabolism. Chromium is an important factor for enhancing insulin activity. Studies show that people with type 2 diabetes have lower blood levels of chromium than those without the disease.

Insulin resistance, with or without the presence of metabolic syndrome, significantly increases the risk of cardiovascular disease. Insulin resistance is present in two serious health problems in women; polycystic ovarian syndrome (PCOS) and gestational diabetes.

Several studies have now demonstrated that chromium supplements enhance the metabolic action of insulin and lower some of the risk factors for cardiovascular disease, particularly in overweight individuals.
Chromium picolinate, specifically, has been shown to reduce insulin resistance and to help reduce the risk of cardiovascular disease and type 2 diabetes. Dietary chromium is poorly absorbed. Chromium levels decrease with age.

Supplements containing 200-1,000 mcg chromium as chromium *picolinate* a day have been found to improve blood glucose control. Chromium picolinate is the most efficacious form of chromium supplementation. Numerous animal studies and human clinical trials have demonstrated that chromium picolinate supplements are safe.
Diabetes is characterised by increased nutritional and oxidative stress. As individuals with diabetes typically have elevated levels of free radicals and oxidative compounds, they are much more likely to suffer from their damage. These highly reactive compounds bind to and destroy cellular compounds. They also greatly increase the inflammatory process by adding fuel to their destructive fire via increased formation of inflammatory mediators like C-reactive protein.

One of the critical goals in nutritionally supporting individuals with diabetes is to flood the body with a high level of antioxidant compounds to counteract the negative effects of free radicals and pro-oxidants. The implementation of this goal is achieved by using the recommendations given earlier, along with taking a flavonoid-rich extract and alpha lipoic acid.
Diabetes is a common metabolic disorder that is usually accompanied by increased production of reactive oxygen species or by impaired antioxidant defenses. Importantly, oxidative stress is particularly relevant to the risk of cardiovascular disease.

Alpha-lipoic acid (LA), a naturally occurring dithiol compound, has long been known as an essential cofactor for mitochondrial bioenergetic enzymes. LA is a very important micronutrient with diverse pharmacologic and antioxidant properties.
• Pharmacologically, LA improves glycaemic control and polyneuropathies associated with diabetes mellitus; it also effectively mitigates toxicities associated with heavy metal poisoning. As an antioxidant, LA directly terminates free radicals, chelates transition metal ions, increases cytosolic glutathione and vitamin C levels, and prevents toxicities associated with their loss.

• These diverse actions suggest that LA acts by multiple mechanisms both physiologically and pharmacologically. Its biosynthesis decreases as people age and is reduced in people with compromised health, thus suggesting a possible therapeutic role for LA in such cases.
Persistent hyperglycemia in diabetics is thought to trigger increased free radical mediated oxidative stress.

The data is mixed on Vitamin E and glycaemic control, with the largest study, a double-blind placebo-controlled crossover design of 53 type 2 diabetics with average HbA1C of 11.9%, finding no improvement using a 400 IU dose of an unspecified form of vitamin E. Other randomised studies using higher doses (up to 1200 IU) showed positive glucose lowering effects.

Typical dosage recommendations are 400 IU daily of mixed tocopherols, though higher doses may be more effective in diabetics.
• **Magnesium**
  – Functions as an essential cofactor involved in glucose oxidation and modulates glucose transport across cell membranes.
  – Considerable evidence indicates that diabetics should take supplemental magnesium, the reasons being that more than half of all people with diabetes show evidence of magnesium deficiency and magnesium may prevent some of the complications of diabetes like retinopathy and heart disease.
  – Magnesium levels are usually low in diabetics and lowest in those with diabetic complications like retinopathy and neuropathy.

• **Manganese**
  – Role in enzyme systems including glucose control and a role in super oxide dismutase.
Diabetes mellitus, insulin and zinc share an intricately complex relationship with both type 1 and type 2 diabetic patients often exhibiting lowered zinc status.

The primary mechanism behind this typical reduced zinc status is increased urinary zinc losses as a consequence of hyperglycaemia.

Zinc is suspected as having a significant role in normal insulin metabolism.
- This includes the ability to regulate insulin receptor intracellular events that determine glucose tolerance and the ability to support normal pancreatic reaction to a glucose load.
• Zinc is an essential factor in the formation of a variety of antioxidant enzymes, including superoxide dismutase, catalase and peroxidase.

• Compounding the low zinc status is the fact that diabetes mellitus is associated with an increased production of reactive oxygen species and a reduction in antioxidant defences.

• The result is oxidative stress that can compound the diabetic complications, potentially affecting the heart, vascular system, kidneys, retina and peripheral nerves.
While type 2 diabetes is not a disease of the liver, this organ is involved in blood sugar regulation. Moreover, the development of non-alcoholic fatty liver disease is often associated with metabolic syndrome, a precursor state to type 2 diabetes.

Milk thistle extract was found to be useful in type 2 diabetes in a recent clinical trial, with associated improvements in liver function (damage) tests.
- Can lead to improved glycaemic control, reduced transaminases and a better blood lipid profile.
# Support

<table>
<thead>
<tr>
<th>Natural Agent</th>
<th>Mechanism of Action</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-HTP</td>
<td>Increases serotonin, reduces food cravings[^24]</td>
<td>250 mg/d</td>
</tr>
<tr>
<td>Acupuncture</td>
<td></td>
<td>6 treatments, 20 weeks</td>
</tr>
<tr>
<td>Bilberry (Vaccinium myrtillus)</td>
<td>Repairs connective tissue, particularly in blood vessels[^1]</td>
<td>40-120 mg/d</td>
</tr>
<tr>
<td>Biotin</td>
<td>Collector for enzyme glucokinase, role in intracellular metabolism of glucose[^1]</td>
<td>5-20 mg/d</td>
</tr>
<tr>
<td>Bitter melon (Momordica charantia)</td>
<td>Increases hepatic glucose utilization, impedes glucose synthesis enzymes[^2]</td>
<td>100 mL aqueous extract daily</td>
</tr>
<tr>
<td>Capsaicin</td>
<td>Depletes substance P from sensory neurons[^1]</td>
<td>.175% cream daily</td>
</tr>
<tr>
<td>Carnitine</td>
<td>Antioxidant[^43]</td>
<td>0.5-1 g/d IM</td>
</tr>
<tr>
<td>Chromium</td>
<td>Increases insulin binding, receptor number, and phosphorylation; decreases insulin resistance and cholesterol[^198,^26]</td>
<td>200-1000 µg/d</td>
</tr>
<tr>
<td>Evening primrose (Oenothera biennis)</td>
<td>Metabolite of linoleic acid may be important in nerve membrane function[^1]</td>
<td>6 g/d</td>
</tr>
<tr>
<td>Fenugreek (Trigonella foenum graecum)</td>
<td>Increases insulin receptor activity, impairs glucose absorption[^1]</td>
<td>15-100 g/d</td>
</tr>
<tr>
<td>Fig (Ficus carica) leaf tea</td>
<td>Enhances cellular uptake of glucose[^11]</td>
<td>1 cup/d, 13 g decoction</td>
</tr>
<tr>
<td>Fish oil</td>
<td>Inhibits platelet aggregation, lowers triglycerides, may raise LDL; no adverse effect on Hbg A1c; with high fiber, decreases LDL; with statins, optimal improvement in apolipoprotein B metabolism[^2,^25]</td>
<td>4000 µg/d</td>
</tr>
<tr>
<td>Folate</td>
<td>Counteracts homocysteine increasing effect of metformin[^20]</td>
<td>.25 mg/d</td>
</tr>
<tr>
<td>Ginseng (Panax)</td>
<td>Stimulates glucose utilization and/or insulin release from the pancreas[^1,^26]</td>
<td>3000 mg/d</td>
</tr>
</tbody>
</table>

### Support

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Description</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ginseng</strong> (Panax)**</td>
<td>Stimulates glucose utilization and/or insulin release from the pancreas&lt;sup&gt;1,9&lt;/sup&gt;</td>
<td>3000 mg/d</td>
</tr>
<tr>
<td><strong>Gynostemma</strong> (Gynostemma sylvestre)**</td>
<td>Decreases glucose absorption from intestine, may regenerate beta cells, variable effect on insulin secretion&lt;sup&gt;4&lt;/sup&gt;</td>
<td>400 mg/d</td>
</tr>
<tr>
<td><strong>Holy basil</strong> (Ocimum tenuiflorum) leaves**</td>
<td>Improves beta cell function, enhances insulin secretion&lt;sup&gt;14&lt;/sup&gt;</td>
<td>2.5 g fresh leaf in 200 mL water daily</td>
</tr>
<tr>
<td><strong>Lipoic acid (best as alpha lipoic acid)</strong></td>
<td>Antioxidant, improves glucose tolerance, increases insulin sensitivity and glucose effectiveness&lt;sup&gt;24,27,35-39&lt;/sup&gt;</td>
<td>600-1200 mg IV, 400-500 mg BID PO</td>
</tr>
<tr>
<td><strong>N-acetyl cysteine</strong></td>
<td>Antioxidant, counterbalances endothelial oxidation&lt;sup&gt;62&lt;/sup&gt;</td>
<td>1200 mg/d</td>
</tr>
<tr>
<td><strong>Vanadium</strong></td>
<td>Insulin-like action, does not dramatically improve insulin sensitivity or glycemic control&lt;sup&gt;1,70&lt;/sup&gt;</td>
<td>50 mg BID (may be toxic at this dose)</td>
</tr>
<tr>
<td><strong>Vitamin B&lt;sub&gt;1&lt;/sub&gt;</strong></td>
<td>Normalizes deficiency state&lt;sup&gt;30&lt;/sup&gt;</td>
<td>320 mg/d</td>
</tr>
<tr>
<td><strong>Vitamin B&lt;sub&gt;2&lt;/sub&gt;</strong></td>
<td>Necessary for production of GTP, lipid-modifying dose can be safely used in diabetics&lt;sup&gt;64,85&lt;/sup&gt;</td>
<td>100 mg/d vitamin B&lt;sub&gt;2&lt;/sub&gt; plus 200 µg/d chromium, or 3000 mg/d vitamin B&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td><strong>Vitamin B&lt;sub&gt;5&lt;/sub&gt;</strong></td>
<td>Inhibits glycoylation of proteins&lt;sup&gt;1&lt;/sup&gt;</td>
<td>25-150 mg/d</td>
</tr>
<tr>
<td><strong>Vitamin B&lt;sub&gt;6&lt;/sub&gt;</strong></td>
<td><strong>-</strong></td>
<td>15-30 µg IM, 100 µg IV, 500 µg TID, oral methylcobalamin</td>
</tr>
<tr>
<td><strong>Vitamin B&lt;sub&gt;12&lt;/sub&gt;</strong></td>
<td>Methionine synthase enzyme cofactor&lt;sup&gt;35&lt;/sup&gt;</td>
<td>1000-3000 mg/d</td>
</tr>
<tr>
<td><strong>Vitamin C</strong></td>
<td>Antioxidant, inhibits accumulation of sorbitol, reduces glycoylation of proteins, preserves endothelial function, lowers urinary albumin excretion rate&lt;sup&gt;15,29,43&lt;/sup&gt;</td>
<td>100-1200 IU/d</td>
</tr>
</tbody>
</table>

<sup>1-6</sup>-HTP indicates 5-hydroxytryptophan; BID, twice daily; GTF, glucose tolerance factor; Hgb, hemoglobin; IM, intramuscular; IV, intravenous; LDL, low-density lipoprotein; PO, per os (by mouth); TID, 3 times daily.
T2DM – Support

• A 3 week hydrotherapy intervention had positive effect on diabetics.

• Hydrotherapy can increase blood flow to skeletal muscles.

• Hot tub hydrotherapy is suggested for diabetics who can’t exercise.

• Read more about this and other alternative therapies for diabetes sufferers [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3249697/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3249697/)