



G^{DX} Genova Diagnostics
Innovative Testing for Optimal Health

Adrenal – Thyroid Diagnostics


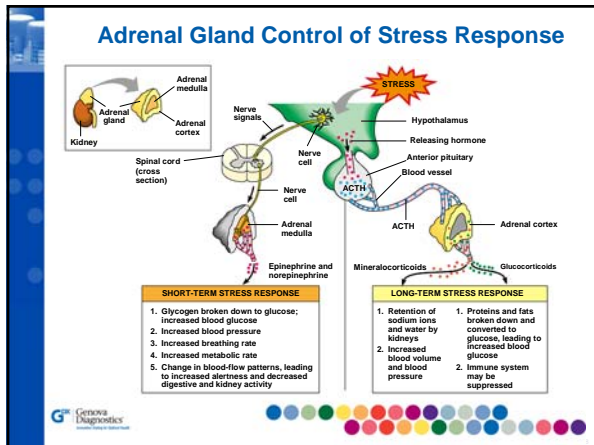
Dr. Nigel Abraham
 Scientific Director
 08th – 10th September 2009



“The adrenal glands are the glands of stress but are the first glands to fail under stressful conditions”
 (Hans Selye)




“A large percentage of what we think of when we discuss stress related problems are problems of excessive stress responses”.
 (Dr. Robert Sapolsky)

Effects of Stress

- Life events such as divorce, job loss, relocation and death in the family are associated with an increased risk of breast cancer. 10,808 Finnish women assessed over 15 years.
- Immunologic function or hormone balance.


March 1st 2003 *am J Epidemiol* 2003;157:414-423.



Why Physicians Do Not Recognise Adrenal Fatigue.

It is not looked for.


- Physicians have been taught that the only deficiency of the adrenal glands is Addison’s disease, near or total failure of the adrenal glands.
- So unless the adrenal glands are failing (Addison’s disease), they are not considered in the diagnosis



Why Physicians Do Not Recognise Adrenal Fatigue.

It is not properly diagnosed when the S&S are present.

- The common S&S of adrenal fatigue are not the classic S&S of adrenal failure (Addison’s) and so are not recognised by the doctor.
- Subtle endocrine disorders often do not progress to the more classic S&S but continue as vague and seemingly unrelated symptoms for years.
- Because of their close interrelationship, more than one endocrine gland is often involved.
- Furthermore, the same symptoms can result from disorders of different endocrine glands.



Why Physicians Do Not Recognise Adrenal Fatigue.

Laboratory tests are not properly used or understood.

- If doctors do suspect a problem with the adrenal glands, they usually order the wrong tests.
- The usual lab tests have excessively broad reference ranges, making accurate diagnosis difficult.
- Statistical norms are confused with physiological norms.
- There are no reference ranges for optimal functioning or allowance for biochemical individuality.
- Diurnal or cyclic hormonal variations may not be provided as part of standard reference ranges.



Salivary Diagnostics

- For many years saliva has been used as a biological fluid for the detection of different biomarkers such as electrolytes, hormones, drugs and antibodies.
- Sample collection is non invasive, painless and very convenient.
- Can be collected at any time, and where blood collection is difficult or inadvisable.
- Saliva is, in effect, the specimen of choice in a variety of health measurements



Salivary Diagnostics

- Steroid hormone assessment from saliva allows specific determination of biologically active or 'free' fraction of target hormone.
- This fraction represents 1 – 5% of the steroid total concentration in serum.
- There is currently no reliable immunoassay for the measurement of such 'free' fractions in serum
- Assays need to be extremely sensitive as the concentration of such fractions are significantly lower than the analyte in serum.



Hormones in Saliva: Mode of Entry and Consequent Implications for Clinical Interpretation

Russ F. Vining, Rebecca A. McKinley, and Richard G. Symcox

Assays of hormones in saliva would be more convenient than those in blood, but there is no information on the route by which hormones enter saliva, information that would provide insight into the clinical value of such assays. We have determined the mode of entry of various hormones into saliva. The results suggest that unconjugated steroids enter saliva by diffusing through the cells of the salivary glands and that

- Unconjugated steroids enter saliva by diffusing through the cells of the salivary glands and that their concentration in saliva does not depend on the rate of saliva production.
- We conclude that the salivary concentration of unconjugated steroids reflect the concentration of free (nonprotein-bound) steroids in plasma

may also be clinically useful. Many recent studies have been concerned with the relationship between concentrations of various steroid hormones in serum and plasma (1, 2), but there has been little discussion of the route by which steroids or other hormones enter saliva. We have measured the relative concentrations of free and total steroid concentrations and between unconjugated and conjugated steroids in serum and saliva of several hormones. Steroid hormones and drug metabolites. We believe the results might be useful in the interpretation of steroid assays in saliva. The results also have implications for the clinical usefulness of measuring these compounds in saliva.

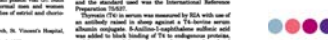
Materials and Methods

Collection of Samples

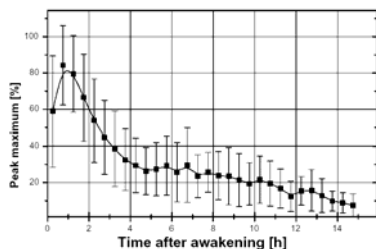
While sleeping under a clean gown, subjects collected saliva directly into a small plastic vial (3). Each specimen was obtained from normal men and women except that four men for the studies of cortisol and dehydro-

epiandrosterone were from healthy pregnant women, all of whom were delivered at term. Urine (4) and saliva (5) were collected from subjects with mild gingivitis by driving the piece into a fissure and applying a disposable cotton-gauze directly to the junction between teeth and gum. Urine (4) and saliva (5) were collected by aspirating into a syringe. Parotid saliva was obtained by placing a cannula

Unconjugated steroid in serum and saliva was determined by RIA as previously described (2). The conjugated fraction of both cortisol and cortisone in saliva was determined by measuring the radioactivity of the steroid after hydrolysis of the steroid with serum glucocorticoid-inducible protein (SGIP) (6). The steroid was then measured by RIA as previously described (2). Serum corticosteroids were measured by RIA with the use of an automatic that bound equally the whole molecule of corticosteroids and its free alcohol, but showed only a 10% free fraction with human lymphocyte cytochrome P-450 (7). The assay included a second antibody preparation step to separate free and bound corticosteroids and was described elsewhere (8). Preparation (9,10). Salivary cortisol was measured by RIA with use of an antibody raised in sheep against a 7 α -bromo serum albumin conjugate. A cortisol-corticosterone mixture was added to saliva. Binding of ³H to corticosteroids and



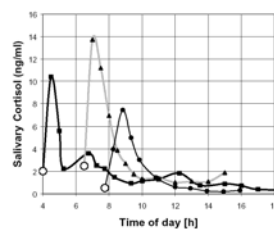
Mean Diurnal Cortisol in Saliva



Highest levels found 30 to 90 minutes after average wake up time.



Diurnal Rhythm of Salivary Cortisol, different wake-up times



- Normal Cortisol concentration in human saliva during the day is highly dynamic.
- Diurnal profiles of three individuals showing typical Cortisol peak in the morning.
- This is not dependent upon the absolute time and not influenced by daylight.
- It is dependent on wake-up timing of each individual.



Salivary cortisol response to awakening in chronic fatigue syndrome

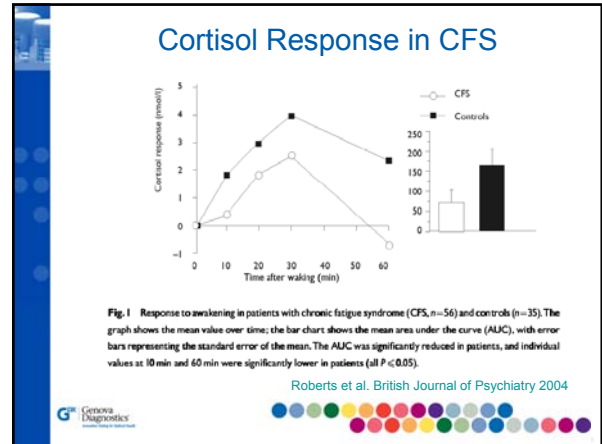
ANDREW G. ROBERTS, SIMON WICKHAM, NIGEL CHADLER, ANDREW PANOPOLGOS and ANTHONY J. CLEARE

• Found evidence of impaired function of the hypothalamic-pituitary-adrenal (HPA) axis in chronic fatigue syndrome (CFS) using a more naturalistic test undertaken in a home setting.

• The HPA axis responses were not affected by the presence or absence of comorbid depression.

• Changes to the HPA axis may represent one of the biological factors contributing to the maintenance of fatigue and other symptoms in CFS.

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Cortisol Awakening Response (Saliva)

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Salivary Cortisol and DHEA - Age Group 14 - 40

Sample	Time	Result	Increase	Optimal Range
Sample 1	00 mins	3.0	0.0	0.0
Sample 2	+ 10 mins	4.3	1.3	> 1.0
Sample 3	+ 20 mins	9.5	2.5	> 3.0
Sample 4	+ 30 mins	4.9	1.6	> 4.1
Sample 5	+ 40 mins	3.0	0.0	> 2.3

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Babies inherit 9/11 mums' stress

NEWS

Pregnant women who witnessed the World Trade Center attacks on 9/11 passed on biological signs of stress to their babies, researchers suggest.

It may be that stress has an effect on the developing brain of a foetus.

Scientists from Edinburgh and New York say tests on infants when they were a year old showed they had low levels of the stress hormone cortisol.

Their mothers also showed low cortisol levels, a sign someone is affected by PTSD the researchers say. (Journal of Clinical Endocrinology and Metabolism.)

The researchers will follow the babies as they grow up to see if those with lower cortisol levels go on to develop psychological disorders.

Previous research, which had largely focused on children of Holocaust survivors, also found low cortisol levels in the offspring.

However, scientists then concluded the finding was due to the stress of hearing their parent describe their experiences, or living with a parent who was distressed or anxious.

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Absence of a normal Cortisol Awakening Response (CAR) in adolescent males with Asperger

• In addition to abnormalities in social and communication development, a 'need for sameness' and 'resistance to change' are features of autistic spectrum disorders.

• Our ability to react to change is modulated by the hypothalamic-pituitary-adrenal (HPA) axis, a feature of which is a dramatic increase in cortisol upon waking, the Cortisol Awakening Response (CAR).

• Whilst a significant CAR was evidenced in the control group, this was not the case for those with AS.

• The implication is that individuals with AS may have an impaired response to change in their environment due to a refractory HPA axis.

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The Stress of Life

Hans Selye, 1956

- General adaptation syndrome (stress response):
- The body's non specific response to generic unpleasantness.
- The impact of the "usual and customary" stresses of everyday life, as well as the cumulative impact, over time, of unusual and extreme stress.
- The body's ongoing efforts to restore its balance in the face of both acute and chronic stress.

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Three Stages of Selye's Stress Response. The General Adaptation Syndrome

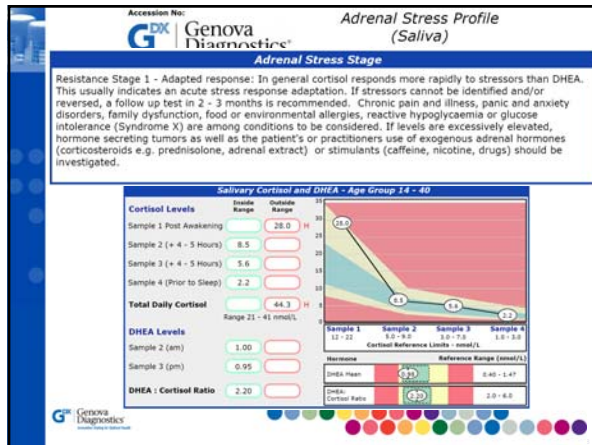
- Second stage: Resistance and adaptation: Intensification of the body's defensive efforts to fend off (resist) the stressor or to make whatever internal adjustments are necessary to live with (adapt to) the stressor.
- Adaptation: sustained increases of corticosteroids and alarm molecules, with alterations in glucose tolerance, blood pressure, thyroid hormone, and sex hormone metabolism

If you can't beat (resist) it, then join (adapt to) it!



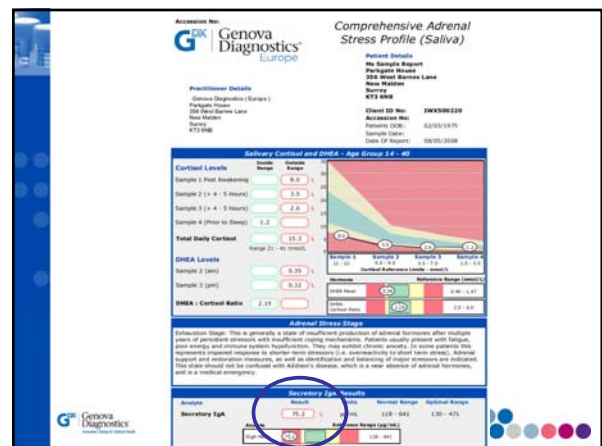
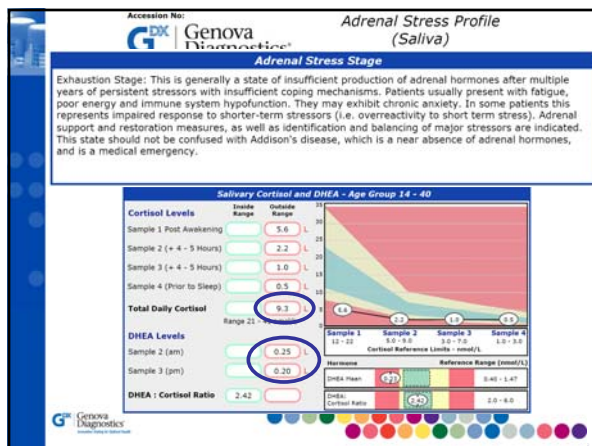
Stress Responses of Cortisol & DHEA

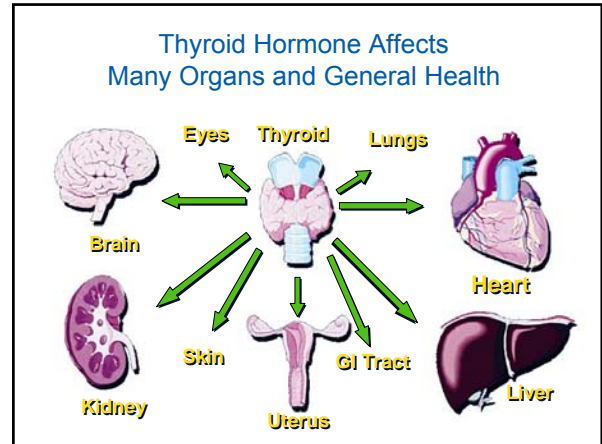
- When forced to respond to continued, chronic stress the adrenal glands enter a compensated phase in which production of hormones is divergent.
- Because of the difference in response to ACTH, the production of DHEA falls as Cortisol remains elevated.
- Later phases of compensated response result in a continued fall in DHEA production, followed by a fall in Cortisol, leading to a state of adrenal exhaustion.



Three Stages of Selye's Stress Response. The General Adaptation Syndrome

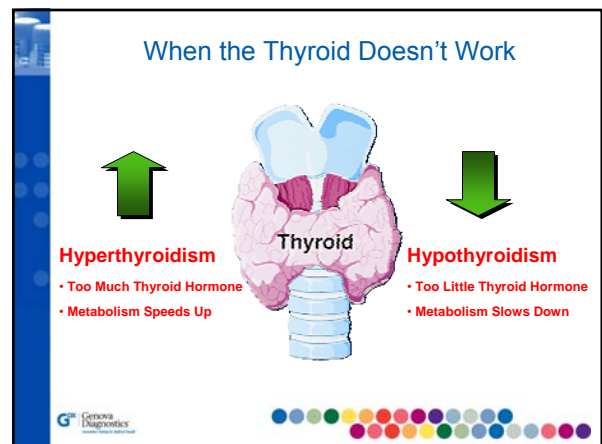
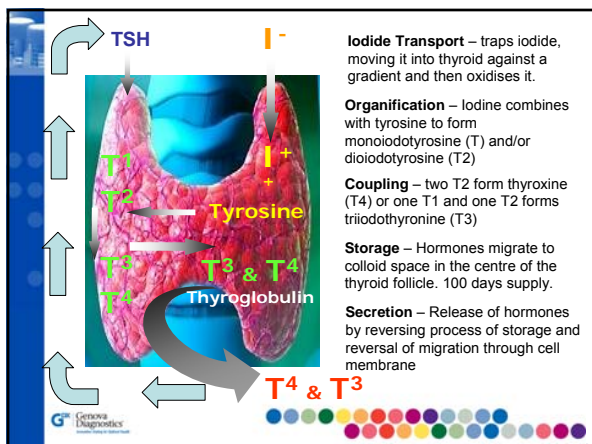
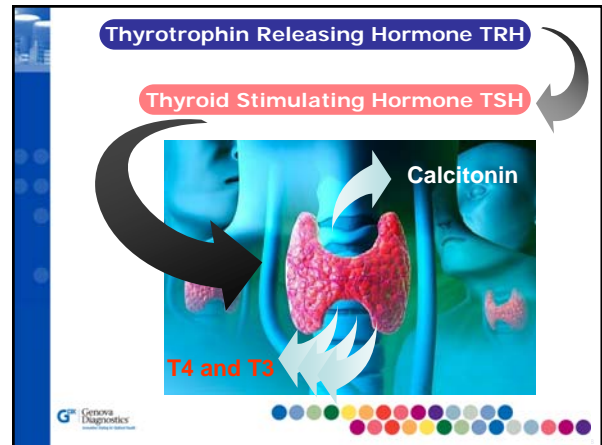
- Third Stage: Exhaustion, breakdown, and collapse. No longer able to adapt, the body will collapse, accompanied by progressive deterioration in structure and function. Final stage of dyshomeostasis, and chronic illness.
- Exhaustion: degenerative diseases as a result of the adverse influence of sustained high levels of corticosteroids and alarm molecules





Who Has Thyroid Disease?

- 27 million Americans have overactive or under-active thyroid glands, but more than half remain undiagnosed.
- More than 8 out of 10 patients with thyroid disease are women.
- Women are 5 to 8 times more likely than men to suffer from hypothyroidism.
- 15 to 20 % of people with diabetes and their siblings or parents are likely to develop thyroid disease. (compared to 4.5% of the general population).



Thyroid Regulation

Central regulation

- Of the HPT axis is well understood and characterised as primary or secondary hypothyroidism based on:
- TSH levels from pituitary
- T4 levels from the thyroid gland

Peripheral action

- Yet thyroxine is a peripherally acting hormone
- T4 is converted to T3 in the liver or kidney.
- T3 binds to nuclear receptors, up-regulating metabolic rate.
- 95% of all circulating T3 is of peripheral origin (liver or kidney).



Causes of Hypothyroidism

- Failure of Control (secondary or tertiary)
- Primary Failure
- Failure of Conversion of T4 → T3
- Receptor Uptake Failure (resistance)
- Adrenal Insufficiency

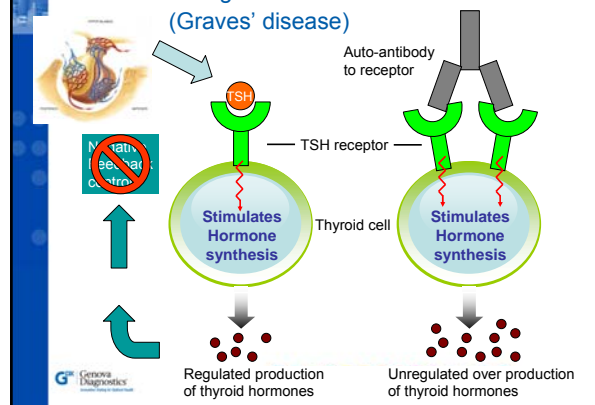


Anti –TG & Anti – TPO Antibodies

- Most sensitive measure to diagnose chronic thyroiditis
- Elevated in 85-90% of chronic thyroiditis patients
- Elevated in 97% of patients with Graves Disease or Hashimoto's thyroiditis
- Titres fall with successful treatment of either Graves or Hashimoto's



Stimulating Auto-antibodies (Graves' disease)

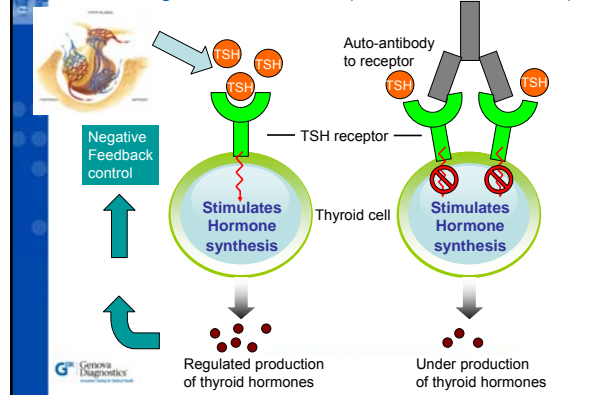


Hashimoto's Thyroiditis

- Autoimmune disease predominates in 30-50 year old women HLA-DR5 positive.
- Development of antibodies against peroxidase – antimicrobial antibodies and anti-thyroglobulin antibodies.
- Also antibodies against TSH receptor (mostly blocking antibodies).
- Increased incidence of other autoimmune diseases (SLE, Sjögren's).




Blocking Auto-antibodies (Hashimoto's disease)




Hashimoto's Thyroiditis

- Antibodies latch onto receptors within the thyroid, and may switch them on to promote over-activity, for a period of months or years.
- But sooner or later, this goes into reverse.
- The initial over-active phase may not occur, or is not noticed. Antibodies should always be looked for.
- Picture of progressive deterioration. Gland may enlarge or shrink.




Hashimoto's Thyroiditis - Cortisol

- The primary source of antigenic stimuli for the production of these autoantibodies is likely to be gut-derived antigens.
- Cortisol suppresses secretory immunoglobulin (sIgA) in the gastrointestinal tract, which leads to impaired gut antigen sampling.




Hashimoto's Thyroiditis - Cortisol

- Cortisol alters the consistency of the gastrointestinal mucosal barrier. The combined result of these effects is an enhanced immune response to gut-derived antigens and increased translocation of antigenic material to systemic circulation.
- Both of these processes could directly lead to the production of antibodies that would cross react to TSH receptors, leading to the development of Hashimoto's thyroiditis.



Therapeutic Strategies for Auto-Immune Diseases

- Reduce the total antigenic load:
 - Dysbiosis, Mycology, Parasitology
 - Food Intolerance assessment
 - Intestinal Permeability
- Calm Immune Responses:
 - Cod Liver Oil, Vitamin C, Quercetin
 - Vitamin E, DHEA (10-25 mg/d)



Commentary

THYROID INTERPRETATION GUIDELINES

Primary Hypothyroidism is **PROBABLE**. The likelihood increases if serum thyroglobulin are elevated (>4.52) and the total cholesterol levels are increased (>4.22)

Some of the clinical signs of hypothyroidism include:

1. Difficulty losing weight
2. Heridity sluggish, reduced initiative
3. Early fatigue, heavy during the day
4. Sensitive to cold, poor circulation (cold hands and feet)
5. Chronic constipation
6. Excessive hair loss and / or coarse hair
7. Morning headaches, wear off during the day
8. Loss of lateral 1/3 of eyebrow
9. Seasonal sadness

PROBABLE auto-immune thyroid disease.

Thyroiditis is the most common thyroid condition, leading to either hypothyroidism (Hashimoto's and sub-acute thyroiditis) or hyperthyroidism (Grave's disease). Hypothyroidism due to thyroiditis is the most common. Thyroiditis can present with normal, elevated, or decreased levels of thyroid hormone at any time.

Hashimoto's and Grave's disease the levels of auto-antibodies are significantly elevated. With sub-acute thyroiditis, the levels are usually normal or slightly increased.

Viral infection has been implicated in the etiology of sub-acute thyroiditis, including mumps virus, coxsackievirus and adenovirus. Bacteria also implicated include: Staph aureus, Strep pneumoniae & Strep pyogenes.


Peripheral Thyroid Function			
Analyte	Optimal Range	Reference Range	
FREE T3	4.4	3.8 - 6.0	2.8 - 6.5 pmol/L
FREE T4 FREE T3 RATIO	2.36	3.0 - 5.0	3.0 - 5.0

Thyroid Auto Immunity			
Analyte	Optimal Range	Reference Range	
THYROGLOBULIN	110	<40	0 - 40 IU/mL
PEROXIDASE (MICROSOMAL)	385	<25	0 - 35 IU/mL

**Case # 2 Mary
46 Y/O Female**


2002 total hysterectomy

- Followed by excessive weight gain >45lbs.
- Pallor & dark shadows.
- Severe fatigue. Neck, shoulders and lower back stiff and painful.
- Hands and feet always cold.
- Frontal headaches daily.
- Depression, poor concentration & memory.



Primary Thyroid Failure - Surgery

- Similar to major trauma with lasting effects.
- Cholecystectomy (gall bladder removed)
- Hysterectomy: Followed by weight gain, exhaustion. ? Hormonal communication between uterus and thyroid.
- Even sterilisation, D&C or termination of pregnancy may have this effect.
- Tonsillectomy: Shared blood supply with thyroid. Often leads to damage. Compensated for a while then deterioration in function.



Hypothyroid and Cholesterol

Case # 2 Mary
46 Y/O Female

Lipid Markers			
Measured Value	Result		Reference Range
Total Cholesterol	6.78	H	<=5.17 mmol/L
Total HDL (ρ_{0.2, 3})	0.90	L	>=1.03 mmol/L
Total LDL (ρ_{0.1, 1(ρ), 1(ρ)})	5.22	H	<=3.36 mmol/L
Total Triglycerides	4.52	H	<=2.26 mmol/L
Total VLDL (ρ_{0.1, 2, 3})	0.62		<=0.78 mmol/L
Calculated Values			
Non-HDL Cholesterol (ρ_{DL-VLDL})	5.84	H	<=4.14 mmol/L
Total Cholesterol : HDL Ratio	7.5	H	<=4.8

Hypothyroidism – Atherosclerosis

- A deposition of cholesterol within the arteries, leading to damage and narrowing.
- Low thyroid function is a bigger cause of cholesterol build up than diet !
- Cholesterol levels in low thyroid patients is almost always elevated.
- Triglycerides also elevated.
- These levels go down following treatment.

Hypothyroidism – Nervous Disorders

- Brain cells have more T3 receptors than any other tissue. So proper uptake is essential.
- Depression: 1/3 of depressed individuals may have unrecognised hypothyroidism.
- Loss of memory and thinking ability.

Accession No: **Genova Diagnostics Europe** **Total Thyroid Screen** **Case # 2 Mary 46 Y/O Female**

Practitioner Details: 1 W/D, Genova Diagnostics, Parkgate House, 305 West Barnes Lane, New Malden, Surrey, KT3 0NB

Patient Details: **Mary**

Client ID No: TWX500230
Accession No: TWX500230
Patients DOB: 46 Years
Sample Date: 18/03/2006
Date Of Report: 18/12/2007

Analyte	Result	Optimal Range	Reference Range
TOTAL THYROXINE (T4)	76.0	117	98 - 154 nmol/L
THYROID STIMULATING HORMONE (TSH)	3.60	0.5	0.4 - 4.0 mIU/L
FREE THYROXINE (T4)	19.5	12	10 - 22 pmol/L

Analyte	Result	Optimal Range	Reference Range
FREE T3	4.4	3.4	2.8 - 6.5 pmol/L
FREE T4 : FREE T3 RATIO	3.36	1.0	3.0 - 5.0

Analyte	Result	Optimal Range	Reference Range
THYROGLOBULIN I	110	<40	0 - 40 IU/ml
PEROXIDASE (MICROSOMAL)	385	<35	0 - 35 IU/ml

• She had had multiple tests for under-active thyroid always 'normal', by thyroid specialists.

• Normal Ranges ?
• Hypothyroid ?

What Is a Normal TSH Level?

- Most laboratories, the official "normal" reference range for the Thyroid Stimulating Hormone (TSH) blood test runs from approximately 0.5 to 5.0.
- In January 2003, by the American Association of Clinical Endocrinologists, that doctors "consider treatment for patients who test outside the boundaries of a narrower margin based on a target TSH level of 0.3 to 3.0."
- Late in 2002, National Academy of Clinical Biochemistry reported that: "In the future, it is likely that the upper limit of the serum TSH euthyroid reference range will be reduced to 2.5 mIU/L because more than 95% of rigorously screened normal euthyroid volunteers have serum TSH values between 0.4 and 2.5 mIU/L."

Implications for Patients

- One study found that using a TSH upper normal range of 5.0, approximately 5% of the population is hypothyroid.
- However, if the upper portion of the normal range was lowered to 3.0, approximately 20% of the population would be hypothyroid

Causes of Hypothyroidism

- Failure of Control (secondary or tertiary)
- Primary Failure
- Failure of Conversion of T4 → T3
- Receptor Uptake Failure (resistance)
- Adrenal Insufficiency



Causes of Hypothyroidism Failure of Conversion

Cortisol ↓ DHEA ↓ Failure T4 → T3
 Cortisol ↑ C:D Ratio ↑ Excess T4 → rT3
 Deiodinase Enzymes ↓ Failure T4 → T3



Total Thyroid Screen

Central Thyroid Axis & Activity

Analyte	Result	Optimal Range	Reference Range
TOTAL THYROIDINE (T4)	8.8	17 - 100	50 - 154 nmol/L
THYROID STIMULATING HORMONE	3.5	0.5 - 2.5	0.4 - 4.3 mIU/L
FREE THYROIDINE (T4)	16.0	12 - 22	10 - 22 pmol/L

Peripheral Thyroid Function

Analyte	Result	Optimal Range	Reference Range
FREE T3	4.5	2.0 - 6.5	2.0 - 6.5 pmol/L
FREE T4 - FREE T3 RATIO	0.4	0.5 - 1.0	1.0 - 5.0

Thyroid Auto Immunity

Analyte	Result	Optimal Range	Reference Range
THYROGLOBULIN	<20.0	<10	0 - 40 IU/mL
PEROXIDASE (MICROSOMAL)	<10.0	<10	0 - 30 IU/mL

Commentary
 Reference range: The conventional or standard laboratory normal range designed to identify and compare disease states and patterns.
 Optimal range: The functional approach, orientated around changes in physiology and pathology. This results in a tighter range, increasing the ability to detect patients with changes in physiological function.

Case # 3 Amy 41 Y/O Female

- Recent history of depression, suicidal anxiety, ? bulimia.
- Weight < 6 stone.
- Severe symptoms of IBS.
- Obsessed with Detox.
- Coffee enemas X8 daily for 3 years.
- Husband threatening? Divorce because of symptoms.

Adrenal Stress Profile (Saliva)

Salivary Cortisol and DHEA - Age Group 41 - 50

Sample	Time	Cortisol (nmol/L)	DHEA (nmol/L)	C:D Ratio
Sample 1 (Wak)	08:00	15.5	1.5	10.3
Sample 2 (4 - 8 Hours)	12:00	5.5	0.5	11.0
Sample 3 (4 - 8 Hours)	16:00	3.4	0.4	8.5
Sample 4 (Prior to Sleep)	22:00	4.2	0.4	10.5
Total Daily Cortisol		52.7		

Adrenal Stress Index

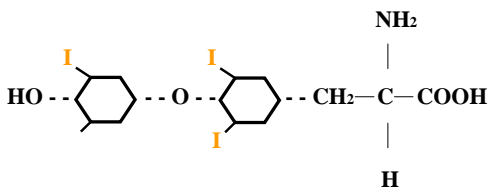
Sample	Time	Stress Index
Sample 1 (Wak)	08:00	0.13
Sample 2 (4 - 8 Hours)	12:00	0.10
Sample 3 (4 - 8 Hours)	16:00	0.12
DHEA / Cortisol Ratio		0.22

Case # 3 Amy 41 Y/O Female

- Long term severe stress.
- Elevated Cortisol inhibition of T4 to T3 conversion
- Production of rT3.

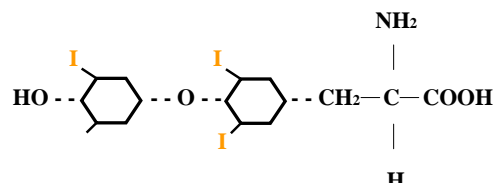
Structure of Thyroid Hormones

Take away one iodine atom and we have:



Structure of Thyroid Hormones

Take away a different iodine atom and we have:



Reverse T3

rT3 is the inactive form of T3. Has about 5% the activity of T4

Manufactured by the body for the recycling of Excess T3, T4 & Iodine

Causes of raised levels of rT3:

Stress

Illness, Starvation

Excess Adrenal Oestrogen



Factor Associated With ↓ T3 & ↑ rT3

Reduced T3

- Immune activation
- IL-6, TNF- α , IFN
- High Cortisol
- High Catecholamines
- High Free Radicals

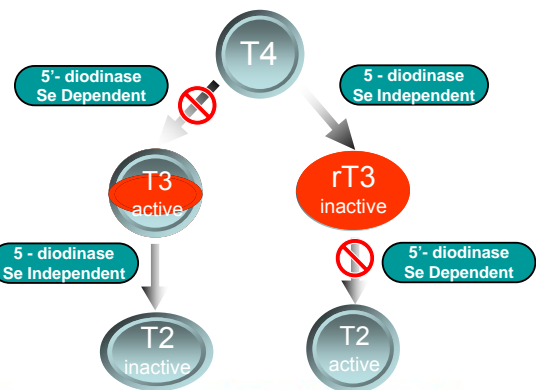
Increased rT3

- Aging
- Fasting
- Stress
- Prolonged Illness
- Toxic Metal Exposure
- Diabetes (1DDM)



5'- Deiodinase Inhibitors

- Selenium deficiency
- Cd, Hg, Pb toxicity – Se antagonists
- Stress – elevated Cortisol
- Chronic illness
- Inadequate protein, excess carbohydrate
- Compromised liver or kidney
 - Impaired glucuronidation
 - Impaired sulphation ?



Case # 3 Amy 41 Y/O Female

Comprehensive Thyroid Assessment



Patient: Amy
DOB: 41 years
Sex: F
MRN: 0001054579

Order Number: 9080181
Completed: June 13, 2007
Received: June 08, 2007
Collected: June 04, 2007
Module Number: A074796




Causes of Hypothyroidism

- Failure of Control (secondary or tertiary)
- Primary Failure
- Failure of Conversion of T4 → T3
- Receptor Uptake Failure (resistance)
- Adrenal Insufficiency



Causes of Hypothyroidism *Receptor Uptake Deficiency*

- Resistance at Receptor Site
- Reduction of Receptors or Desensitisation
- Environmental Toxins e.g. fluoride, mercury
- Prolonged Illness
- Genetic Predisposition



REVIEWS

Novel Insights into thyroid hormones from the study of common genetic variation

©2015 M. Cooper and Agnese Rebecchi
Approved: Effects of thyroid hormones in individual tissues are determined by many factors beyond their serum levels.

- Effects of thyroid hormones in individual tissues are determined by many factors beyond their serum levels, including local deiodination and expression and activity of thyroid hormone transporters.
- intriguingly, most of these associations are independent of serum thyroid hormone levels, which highlights the importance of local regulation of thyroid hormones in tissues.
- Future research might reveal novel roles for thyroid hormones in obesity, cardiovascular disease, osteoporosis and depression and could have implications for interpretation of thyroid function tests and individualization of thyroid hormone replacement therapy.



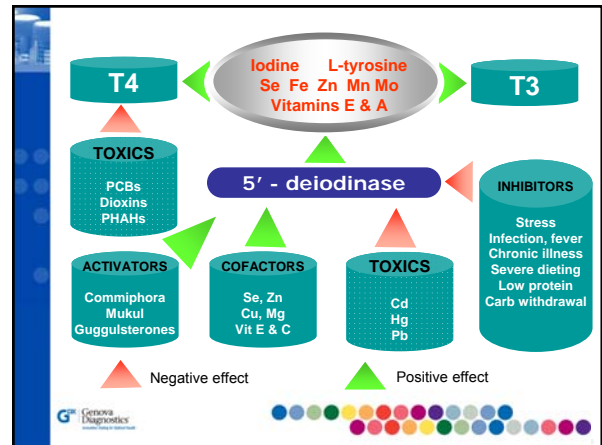


Table 3 | Association of deiodinase SNPs and serum thyroid hormone parameters

SNP	Free T ₄ level	T ₄ or free T ₄ level	T ₄ /T ₃ ratio	rT ₃ level	TSH level
In the DIO1 gene					
rs112092441 ^{13,14}	Increased	Decreased	Decreased	Increased	No effect seen
rs120950801 ¹⁴	No effect seen	Increased	Results of association not published	rT ₃ /T ₄ ratio decreased	No effect seen
rs22365441 ¹⁵	Decreased	Increased	Increased	Decreased	No effect seen
In the DIO2 gene					
rs2250141 ^{16,17,18}	No effect seen	No effect seen	No effect seen	No effect seen	No effect seen
rs128853001 ⁷	Decreased ^P	No effect seen	Increased ^P	Decreased ^P	No effect seen
In the DIO3 gene					
rs9450061 ¹⁹	No effect seen	No effect seen	No effect seen	No effect seen	No effect seen


^PEarly, not replicated findings. Abbreviations: rT₃, reverse T₃; SNP, single nucleotide polymorphism.

- Convincing evidence indicates a role of type 1 iodothyronine deiodinase (D1) in determining the serum T4:T3 ratio
- Preliminary evidence suggests associations between D2 variants and hypertension, psychological well-being and response to T3 or T4 treatment.

Causes of Hypothyroidism


- Failure of Control (secondary or tertiary)
- Primary Failure
- Failure of Conversion of T4 → T3
- Receptor Uptake Failure (resistance)
- Adrenal Insufficiency



Causes of Hypothyroidism *Adrenal Insufficiency*

Weakened Adrenal Response damages:

- Thyroid Hormone Production
- T4 → T3 Conversion
- Receptor Uptake
- Tissue Response
- Adrenal Oestrogen Production Balance



Adrenal & Thyroid Connection

- If thyroid hormone is not being produced nothing works properly – including the adrenal glands.
- Compounded by the fact that low thyroid output is a stress inducing situation.
- To cope with low thyroid output, the adrenals increase the level of cortisol.
- In time the adrenals begin to fail leading to low adrenal reserve.



Adrenal & Thyroid Connection

- General health, nutrition, lifestyle and other stresses all play a part.
- The length of time the thyroid problem has gone on for and how badly.
- The cause of the deficiency: Surgery & I131 a particular problem for adrenal glands.
- Supplementary thyroid hormone may itself cause stress if the system cannot cope, by using wrong dose or ignoring adrenal support.



Adrenal & Thyroid Connection

- Thyroxine T4 has to be converted to active T3 by action of 5'-deiodinase enzymes.
- In low adrenal reserve this process fails leading to toxic build up of unused and unstable T4.
- T3 has to be taken up by receptors within the cell wall, this uptake is degraded in adrenal insufficiency.
- The receptors become dormant or may disappear or become resistant.
- Even if T3 is available, the system can become toxic.



Adrenal & Thyroid Connection

- The optimal functioning of the adrenal glands is absolutely vital for correct Thyroid function.
- Equally as important is to provide adrenal support when low adrenal reserve is present.
- The failure of thyroid supplementation to restore normal health may well be due to a adrenal problem.



CLINICAL RESEARCH

Thyroid Insufficiency, Is TSH Measurement the Only Diagnostic Tool?

W. V. BAISSER MD, J. HERTOGHE MD, AND W. ECKHAUT MD

- **Results:** A score of the 8 main symptoms of hypothyroidism, serum thyroxine radio-immunoassay (T4-RIA), serum T4-RIA/thyroid binding globulin (TBG), 24h urine free triiodothyronine (T3) were considered before and after treatment.
- The score of these 8 main symptoms is a reliable expression of their illness in 97% of hypothyroid patients.
- 24h urine free T3 correlates better with the clinical status of hypothyroid patients than serum T4-RIA, and even better than T4-RIA/TBG.
- Other investigators were unable to find any correlation between serum thyroid stimulating hormone (TSH) or serum free T4 and thyroid symptoms. The dosage of natural desiccated thyroid (NDT) has a correlation with 24h urine T3.
- **Conclusions:** In this study symptoms of hypothyroidism correlate best with 24h urine free T3.

hormone (TSH) test, even the third generation procedure, as well as the serum free thyroxine (FT4) test, correlate poorly with the clinical status of the thyroid diseased patient. Therefore, we are interested in showing that another test, the 24h urine free triiodothyronine (T3) test, correlates well with the symptoms of thyroid disease. We started by comparing a list of generally accepted symptoms upon which to rely as an objective base reflecting the clinical status of the patient. We soon noticed that, from this extended list, a small series of the most frequently seen symptoms could be isolated. As a test for the reliability of our views, we compared this selected list of main symptoms before and after



Thyroid Hormones 24 Hour Urine

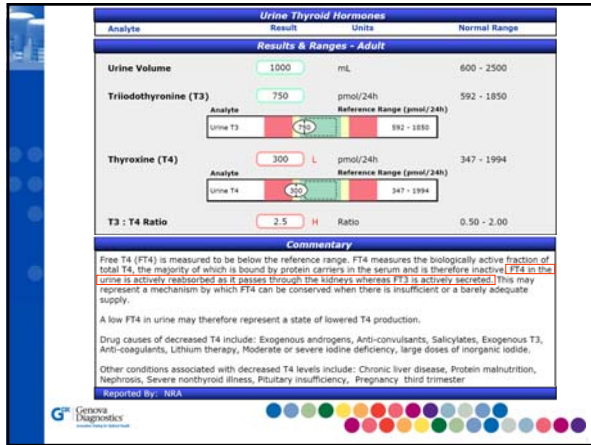
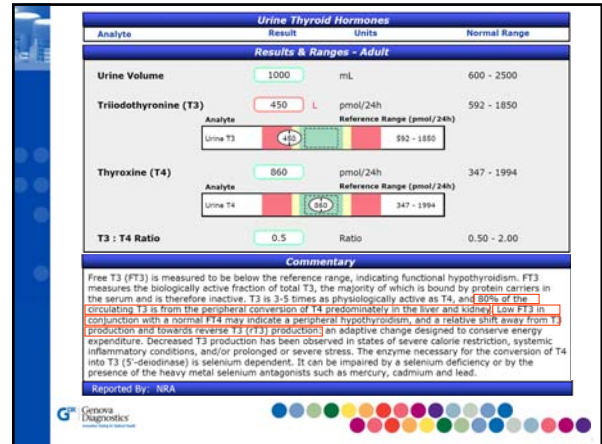
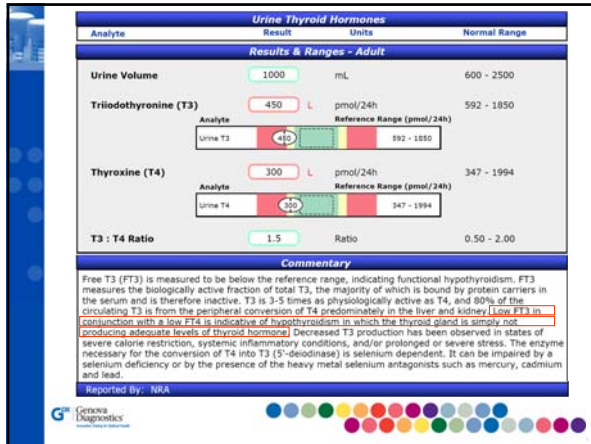
Commentary

The diagnosis of hypothyroidism is usually made almost exclusively from measurements of TSH and T4 levels found in blood tests. However this method is thought to be largely ineffective at diagnosing cases of mild hypothyroidism, more accurately termed 'thyroid dysfunction'. Hormone levels in urine, assesses tissue exposure to thyroid hormones over a 24-hour period. The urine thyroid test therefore serves as a valuable tool for detecting those patients that are suffering from thyroid dysfunction that may otherwise go undetected through standard blood tests.

Analyte	Result	Reference Range
Urine Volume	1000 mL	600 - 2000
Triiodothyronine (T3)	800 gpmol/24h	592 - 1830
Thyroxine (T4)	1000 gpmol/24h	347 - 1994
T3 : T4 Ratio	0.8	0.50 - 2.00



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Thyroid Patient Advocacy UK Dismissal of all other assays?

- There is a large body of evidence to support the use of 24 hour urine testing for thyroid dysfunction.
- Excellent papers are available to point out their efficacy but have been ignored.
- Analytical and clinical validation has been shown to anyone who will read it, or listen.
- The 24 hour urine thyroid function test is generally to be preferred over standard serum TFT because it shows the amount of thyroid being used, not simply how much is there – and perhaps not being used.

Lycopus europaeus (Gyposwort): Effects on the thyroidal parameters and symptoms associated with thyroid function
A.M. Baur^{1*}, A.R. Wabnitz², H. Schmidt-Layk³

- An observational study yielded no noticeable changes of thyroid parameters in the serum of humans treated with *Lycopus europaeus*, whereas a reduction of tachycardic episodes and an improvement of vegetative and psychic complaints was observed.
- The T4 excretion in urine is significantly increased in the *Lycopus europaeus* group as compared to the control group.
- This study shows for the first time a measurable change of thyroid-related hormone parameters in human beings.

Check list

- Thyroid function
- Adrenal function
- Sex hormones
- Comprehensive Digestive Stool Analysis -'leaky gut' & dysbiosis, malabsorption
- Food allergies and intolerances
- Poor liver detoxification.

To quote just one patient:

"The ignorance, arrogance and incomprehension of the medical doctors I have been subjected to in my search for diagnosis and treatment leaves me incandescent with rage. Even as a qualified health professional working for a major DGH I remain powerless to prevent the cumulative long term health risks associated with lack of treatment; I am voiceless, neutered, patronised, and crawling day-to-day through what used to be my vital and colourful life. I would give everything I have for an open minded and creative diagnostician, and more for a little compassion, but this seems to be entirely beyond the capability of the modern medic. God help us all."

Thank You!

