Dear Health Professionals:

The FDA has numerous warnings about the dangers of selective serotonin re-uptake inhibitors ("SSRI") antidepressant medications, including warnings that people can get worse on these drugs, hallucinate when being put on these drugs, and become suicidal either while taking them or while trying to discontinue them. One must follow the dosage recommendations for supplemental 5-HTP, using less and exercising caution if also using serotonin receptor agonists. Quitting SSRI antidepressant medications cold turkey is dangerous, and instead one should wean off carefully and slowly, if so desired.

Accumulated metal toxins are known to cause thyroid imbalances and even cancers, for which the elderly are often placed on thyroid supplements, but activation of thyroid hormone (T_4) to triiodothyronine (T_3) requires thiol-dependent deiodination, and metals poison thiols. Thus, simple supplementation with T_4, alone, is often inadequate for correcting thyroid imbalances in the toxic and elderly, who have accumulated a lifetime of toxic metal exposures:

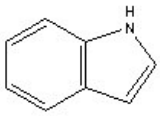
http://www.vitaletherapeutics.org/ipreface.htm http://www.vitaletherapeutics.org/disrtatn.htm

Low thyroid hormone, alone, can cause serious health problems, and any rebound to high thyroid status, even diurnally, can cause anxiety, so imbalances in diurnal biosynthesis, activation, and metabolic degradation can adversely affect health:

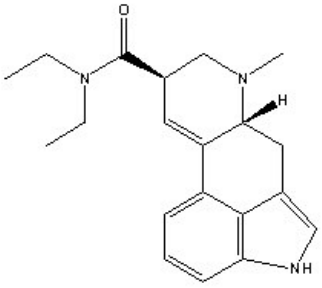
Hypothyroidism--psychosis, delusions, dementia, mania, "myxedema madness", "myxedema coma", mental disturbance, slowness, marked latency of response, alteration of mood and affect, mild delirium, facetiousness, jocularity with croaking voice, depression, retardation, schizophrenia, paranoid delusions, hallucinations, dominant frequency slowing in EEG, decreased cerebral blood flow and oxygen utilization, seizures, permanent brain damage, sensitivity to depressant actions of drugs....that act on the central nervous system, diminished turnover of drugs with elevated blood levels, and peripheral myxedema neuritis.

Hyperthyroidism--emotional lability, anxiety, "tension", over-reactiveness, poor ability to concentrate, restlessness, tremor, sleep disturbance, frank psychosis, with the elderly in particular becoming depressed, withdrawn, and apathetic with loss of appetite; severe cases can present delirium, coma, "organic brain damage", organic deficit in part reversible, personality disturbance, and stress. (From: Symptoms of thyroid imbalance from Reichlin, Seymour, Neuroendocrinology in “Textbook of Endocrinology,” 5th ed., R. H. Williams, M.D., Ed., W. B. Saunders Company, Philadelphia, Penn., 1974, pp. 821, 822.)

Exact mechanisms for drug action are sometimes not known or not disclosed. Chemical similarities of Xanax®, Prilosec®, Aricept®, and even LSD to natural indoles like tryptophan (an amino acid from protein in our diets), and the serotonin (the "feel good" hormone) and melatonin (the sleep hormone) derived naturally, therefrom, indicate that indole drugs variously alter tryptophan's use for making these natural hormones, and their subsequent distribution, use, and degradation. Symptoms of withdrawal from these non-nutritive drugs, often confirm this.



Indole

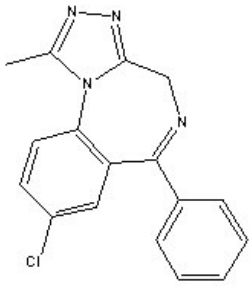


LSD ("Mind-control" indole can cause **insomia**!)

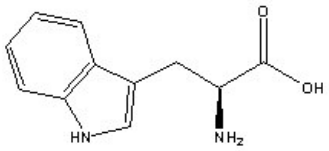
Symptom (Xanax)	%	Symptom (^10mg Aricept)	%	Symptom (Another SSRI)	%
Insomnia	**29.5**	**Nausea**	**19**	**Naseau**	**21**
Light-headedness	19.3	Diarrhea	15	Dry Mouth	20
Anxiety	**19.2**	**Insomnia**	**14**	**Somnolence**	**18**
Fatigue & Tiredness	**18.4**	**Fatigue**	**8**	**Insomnia**	**15**
Involuntary Movement	17.3	Vomiting	8	Sweating Increased	11
Headache	17.0	Muscle Cramps	8	Tremor	8
Naseau/Vomiting	16.5	Anorexia	7	Diarrhea	8

Decreases in melatonin manifest as insomnia and rebound from drug withdrawal, involving melatonin and the

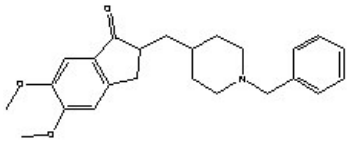
thyroid axis, can result in either anxiety or sleepiness. Such adverse withdrawal symptoms contribute to drug dependencies.



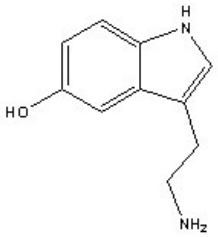
Xanax®



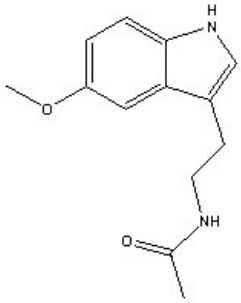
Tryptophan



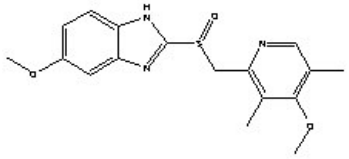
Aricept®



Serotonin

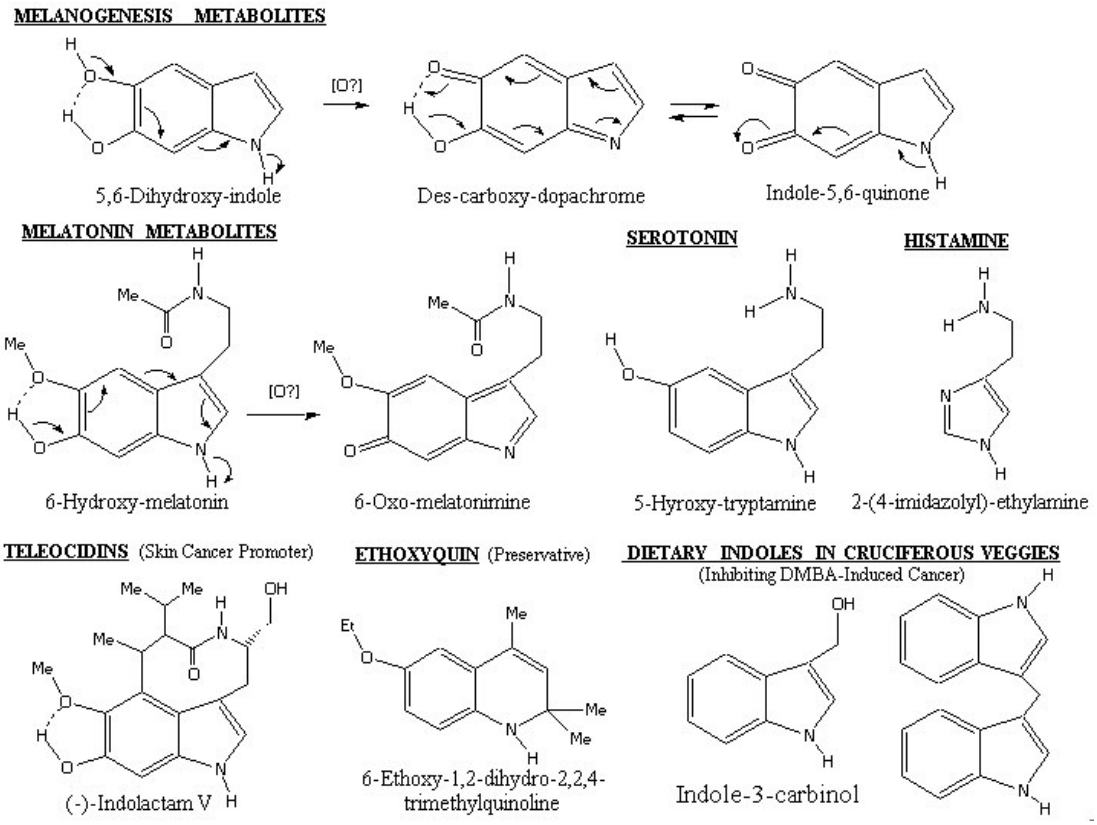


Melatonin

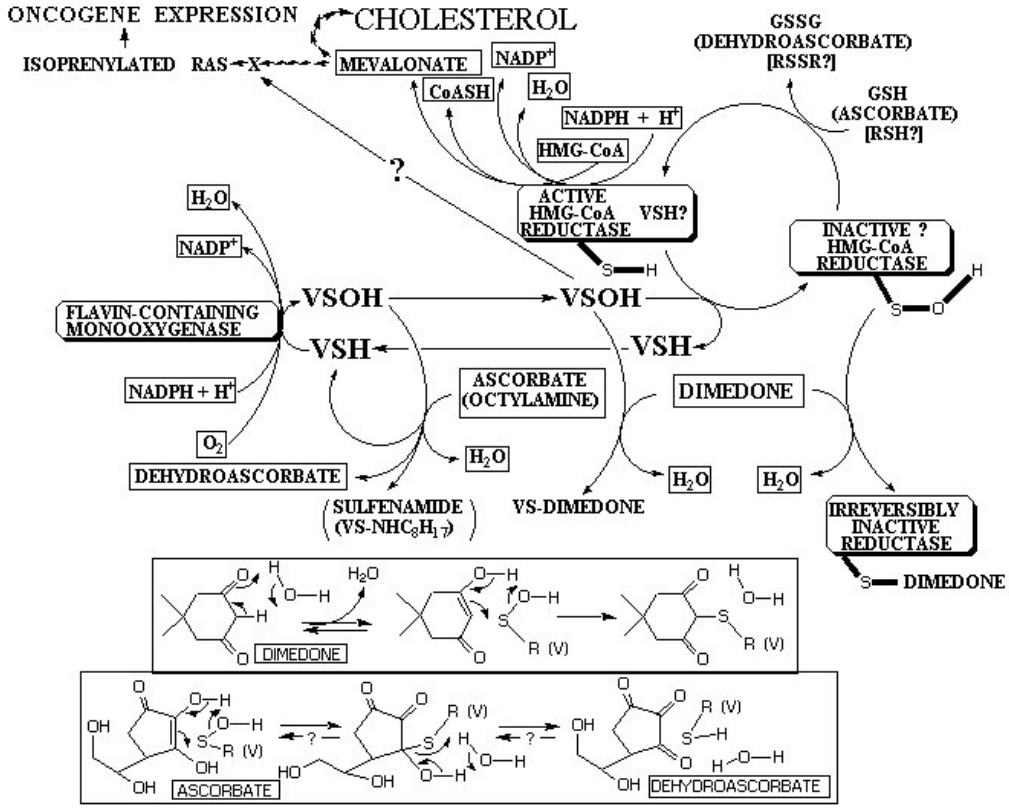


Prilosec®

Other non-nutritive indoles cause cancer and other health problems (http://www.vitaletherapeutics.org/vtlindol.htm):

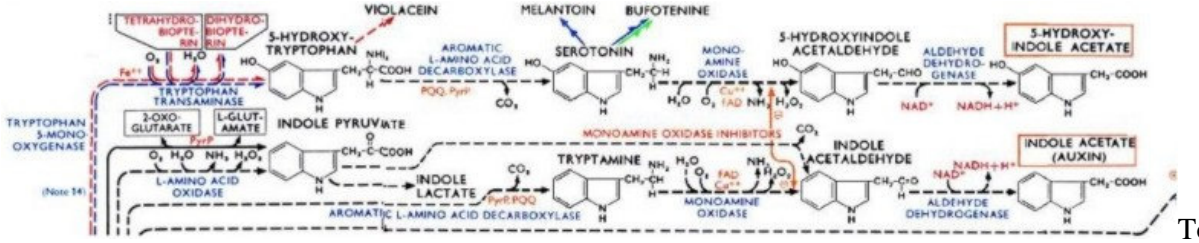


Melatonin appears metabolically necessary for increasing both the monooxygenase receptor for vitaletheine and vitaletheine (VSH), both of which have been implicated in all steps of thyroid hormone (T_4) biosyntheis and its thiol-dependent, biological activation by deiodination from T_4 to T_3 (http://www.vitaletherapeutics.org/vtlhmgmo.htm):



Thus, diurnal cycling of melatonin production is an important driving force that helps regulate the diurnal or circadian daily oscillations in the thiol and disulfide ratio (See Isaacs, J.T. and Binkley, F. Cyclic amp-dependent control of the rat hepatic glutathione disulfide-sulfhydryl ratio. Biochim. Biophys. Acta, 498: 29-38, 1977):

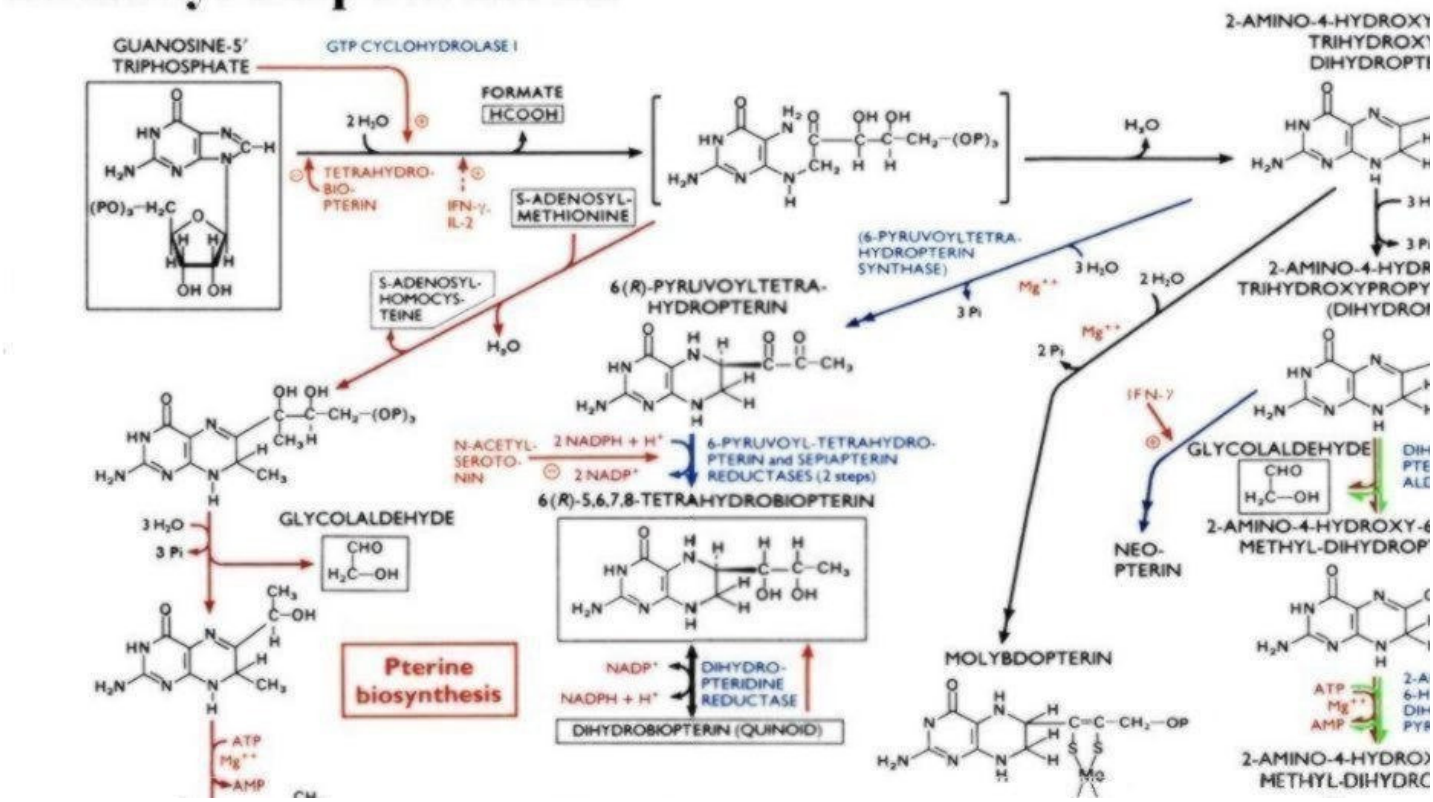
TRYPTOPHAN'S METABOLISM TO SEROTONIN AND MELATONIN AS WELL AS TO MORE PROBLEMATIC SUBSTANCES



To carcinogen

TRYPTOPHAN (A "nutritional" amino acid from dietary protein!)

Fortunately, **apple pectin** or **pomace** helps to channel the tryptophan from the protein in our diets into the more beneficial serotonin (the 5-HTP or "feel good" hormone) and melatonin (sleep hormone), and away from metabolic carcinogens. Without melatonin, produced when the body gets 6 to 8 hours of sleep in the dark, dirunal increases in this key drug-metabolizing enzyme and receptor for vitaletheine, along with associated increases in specific humoral (antibody) responses against existing immune challenges, are far less likely, leaving the body to cope with only its cell-mediated immunity. This has disastrous consequences for ones ability to make neurotransmitters, since such cell-mediated immune responses are heavily dependent upon interferon-gamma and IL-2, two proliferative cytokines that tend to switch metabolism to neopterin biosynthesis and away from the biopterin and tetrahydrobiopterin biosynthesis needed to make nearly all of our neurotransmitters. Avian flu victims reportedly die from cytokine storm, *sic*., an over-reliance upon cell-mediated immunity:



Neurotransmitter deficit from compromised humoral immunity could be prevented or remedied by eliminating pathological infections, including latent or subclinical ones (viral, bacterial, parasitic, mycotic, etc.), but this is notoriously difficult in nursing homes and managed care facilities. Triclosan-containing, antibacterial soaps also are used institutionally that adversely affect the thyroid hormone axis and lower body temperature, http://www.vitaletherapeutics.org/vtltclxn.htm:

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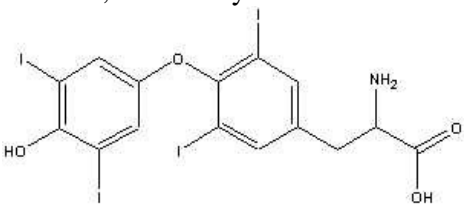
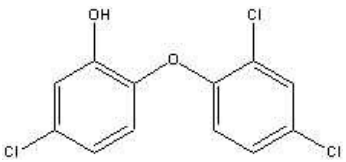
Triclosan's Antagonism of Thyroxine and T3: Wilson's Syndrome?

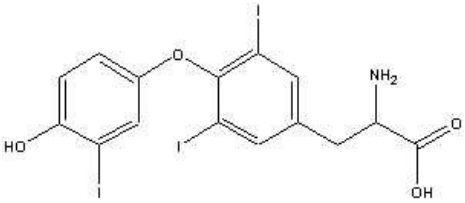
Structural considerations and the following abstract raise concerns about Triclosan interfering with thyroid hormone metabolism in the body, thereby lowering body temperature, and producing a variety of metabolic imbalances associated with poor thyroid hormone utilization. Wilson's Syndrome, supposedly a new thyroid disorder, could very well have environmental causes.



THYROXINE--Thyroid Hormone



TRICLOSAN--Antibacterial added to soaps, dishwashing liquids, toothpastes, etc.



ACTIVATED THYROXINE or T3 (3,5,3'-Triiodothyronine)

J Toxicol Environ Health 1983 Aug-Sep;12(2-3):245-53

The acute toxicity of penta-, hexa-, and heptachlorohydroxydiphenyl ethers in mice.
Miller TL, Lorusso DJ, Walsh ML, Deinzer ML
The acute intraperitoneal LD50 values of various hydroxychlorodiphenyl ethers (HO-ClX-DPEs; X = 5-7) in mice have been determined. The acute toxicities observed were on the order of, or slightly less than, that observed previously for 2-hydroxy-2',4,4'-trichlorodiphenyl ether (2-HO-Cl3-DPE; Irgasan DP-300; Triclosan), a commonly used bactericide. However, the acute toxicities determined for these compounds were substantially less than have been observed for HO-Cl9-DPEs and pentachlorophenol. The **HO-ClX-DPEs HAD A MARKED HYPOTHERMIC EFFECT**, similar to that produced by 2-HO-Cl3-DPE. Symptomatology following exposure to the HO-ClX-DPEs (X = 5-7) suggested a NONSPECIFIC DEPRESSANT EFFECT on the central nervous system.
PMID: 6655733, UI: 84090302
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Thus, published, peer-reviewed scientific articles implicate various medications and chemicals provided to the elderly as producing and aggravating "thyroid conditions", which logically results in many if not all of the alleged increases in disorientation and other mental problems associated with "aging", provided ***supra***. Such "routine treatments" can become counterproductive to their health without the routine monitoring of thyroid, mineral balance, and hypertension status. For this literature review, Donepezil is the generic term for Aricept®; paroxetine is the generic term for Paxil®; Synthroid® is T_4 and not T_3, the makers of Synthroid® losing a court case in which they tried to squelch research showing that their T_4 was no better than other thyroid medications when properly applied. The already activated "T_3" form, not supplied by Synthroid®, is more commonly supplied in glandular, natural extract, or compounding pharmacy formulas. Lower doses of Paxil®, *infra*, seem to give better responses to T_3 (and not necessarily "Synthroid®") supplementation:

Bentue-Ferrer D, Tribut O, Polard E, Allain H. **Clinically significant drug interactions with cholinesterase inhibitors: a guide for neurologists.** CNS Drugs. 2003;17(13):947-63. Review.
".....**donepezil** and antipsychotics (which results in the appearance of **parkinsonian symptoms**)....Care must be taken to reduce the risk of inducing central (excitation, agitation) or peripheral (e.g. bradycardia, loss of consciousness, digestive disorders) hypercholinergic effects via drug interactions with **cholinesterase inhibitors**.....need for prudent prescription, particularly when cholinesterase inhibitors are given in **combination** with psychotropics or antiarrhythmics. Possible interactions involving other often coprescribed antidementia agents (e.g. memantine, antioxidants, cognitive enhancers) remain an open area requiring particularly prudent use....**the blood-brain barrier becomes porous in the elderly, resulting in drug availability to the CNS being increased**. Finally, several **age-related diseases increase vulnerability to and lower the susceptibility threshold for drug-related adverse effects**, irrespective of their mechanism....**donepezil** and galantamine selectively inhibit AchE.....**Donepezil** is highly protein bound. It is **largely metabolised by CYP3A4 and CYP2D6**.....**The most frequently observed mechanisms underlying drug-drug interactions involve a pharmacokinetic phenomenon, often involving the CYP enzymes.** All steps of drug absorption, distribution, metabolism or excretion can be involved. The consequence is a modified serum concentration of one or more of the agents implicated in the interaction.....CYP3A4 is the primary route of donepezil metabolism.....As **donepezil is also metabolised by CYP2D6**, the **effects of the association are smaller than those produced by ketoconazole for other agents sharing the CYP3A4 pathway**.....**Donepezil**, galantamine and tacrine are **partly metabolised by CYP2D6**.....two case metabolic inhibitor of CYP1A2 have been published by Carrier....Two elderly patients taking **paroxetine, a potent CYP2D6 inhibitor, at a dosage of 20 mg/day experienced more severe than expected gastrointestinal and psychiatric symptoms after they received concomitant donepezil 5 mg/day;** however, it cannot be excluded that this possible interaction represents a pharmacodynamic one, as both drugs share the risk of gastrointestinal and psychiatric adverse reactions..... **Carrier L. Donepezil and paroxetine: possible drug interaction [letter]. J Am Geriatr Soc 1999; 47: 1037**.....**Several case reports of an interaction between a ChEI and an antipsychotic have been published**.....Sprung et al.[81] described a **complex interaction** in a patient with unrecognised atypical pseudocholinesterase, treated with **donepezil 5mg daily**, who received suxamethonium 100mg as part of general anaesthesia for surgery.....Hooten and Pearlson[86] reported a case of **delirium** that occurred in a 71-year-old woman given tacrine 20mg and ibuprofen 600 mg/day simultaneously....."

Louise Carrier MD FRCP(C)**. DONEPEZIL AND PAROXETINE: POSSIBLE DRUG INTERACTION**
Journal of the American Geriatrics Society - Volume 47, Issue 8 (August 1999)
LETTERS TO THE EDITOR
".....**Donepezil** hydrochloride is a selective inhibitor of acetylcholinesterase marketed for the treatment of mild to moderately severe Alzheimer's disease (AD).....**adverse events reported were associated with the digestive (nausea, vomiting, diarrhea, anorexia) and nervous systems (dizziness, fatigue)**.....**the number of patients who discontinued was increased to 16% in the donepezil 10 mg/day group**.....**elimination half-life of about 70 hours**.....protein-bound and **metabolized by the liver via the cytochrome P450 system 2D6 and 3A4 isoenzymes**.....**paroxetine** and sertraline **are potent in vitro inhibitors of the cytochrome P450 2D6 isoenzyme**..... The clinical significance of this effect is still poorly understood. Two case reports of a possible **interaction between donepezil and paroxetine are described**."

"Mr. A. is a 78-year-old man with a 3-year history of progressive **memory loss** and **dysphasia**.....**paroxetine 20 mg/day**.... **When donepezil was introduced at 5 mg/day, Mr. A. complained of severe** diarrhea, flatulence, and **insomnia**. **Donepezil was reduced to 5 mg every second day**, with **diarrhea and flatulence persisting**. These **side effects did not subside with time** although he took donepezil for more than 2 months. **Symptoms resolved when donepezil was stopped**.
Mrs. B. is a 67-year-old housewife diagnosed with moderate Alzheimer's disease ..... **20 mg of paroxetine** daily for the past 3 years for the treatment of **dysphoria** and **anxiety** exacerbated by the cognitive impairment. **Donepezil was introduced at 5 mg/day, but her husband stopped the medication after just 8 days because she had become increasingly agitated, confused, and aggressive**, which she had never been before. **Donepezil was reintroduced at a dose of 5 mg every second day, but she again became rapidly confused, irritable, and verbally aggressive.**
These two patients presented with AD and a mood disorder, a frequent occurrence.....**Inhibition of the cytochrome P450 system may lead to elevated plasma levels of co-administered drugs that are metabolized by these isoenzymes** ..... **clinicians should be aware of a possible drug interaction between SSRIs** fluoxetine, **paroxetine** and sertraline, **potent cytochrome P450 2D6 isoenzyme inhibitors, and donepezil which is metabolized in the liver by this same isoenzyme**. An **elevated plasma level of donepezil may in turn increase the risk for more severe adverse reactions**.....**even at a very low dose (2.5 mg donepezil daily equivalent) they experienced moderately severe side effects**....."

Carlos Rojas-Fernandez PharmD. **DRUG INTERACTIONS AND DONEPEZIL** Journal of the American Geriatrics Society - Volume 48, Issue 5 (May 2000) -
LETTERS TO THE EDITOR
".....Dr. Carrier hypothesizes that **inhibition of cytochrome P-450 (CYP 450) 2D6 by paroxetine may have been responsible for donepezil toxicity observed in two of her patients**.....**we agree with Dr. Carrier's comments**..... **Donepezil seems to be metabolized by two isoforms of CYP 450, namely 2D6 and 3A4**, as well undergoing glucuronidation.....**5 to 10% of white persons lack the functional 2D6 isoenzyme and are thus classified as poor metabolizers (PMs)**.....**CYP 3A4 can be inhibited by various drugs (as can CYP 2D6) as well as by grapefruit juice.** .....**the isoform primarily responsible for the metabolism of donepezil (i.e., 2D6 or 3A4) is not yet known**..... Co-administration with ketoconazole resulted in nonsignificant changes in pharmacokinetics on Day 1 of therapy, whereas **significant increases in maximum drug concentration (26.8%) and area under the curve (26.4%) were noted after 7 days of therapy** ..... **donepezil is also metabolized by CYP 2D6** ..... It is clear that **additional human studies (metabolic and drug-drug interaction studies) are needed** ..... **it is unknown whether simply inhibiting CYP 2D6 with paroxetine would result in significant increases in plasma levels of donepezil as this potential drug interaction has not been adequately studied** ..... **the observed effects may be congruent with recent case reports of worsening behavioral symptoms with donepezil** ..... **we agree with Dr. Carrier that clinicians must always be cautious and "keep their eyes open" whenever a new psychotropic medication is prescribed to patients with Alzheimer's disease who are receiving donepezil, or vice versa** ..... **we should not complacent when using psychotropic medications**....."

Agid O, Lerer B. **Algorithm-based treatment of major depression in an outpatient clinic: clinical correlates of**

response to a specific serotonin reuptake inhibitor and to triiodothyronine augmentation.
Int J Neuropsychopharmacol. 2003 Mar;6(1):41-49.
"Clinicians who treat major depression are faced with a bewildering choice of antidepressants. Given that all have a lag period before they are effective.....Non-responders to this dose receive augmentation with triiodothyronine (T3, 25-50 mug).....Ninety patients commenced open-label **treatment with 20 mg SSRI** (fluoxetine, n=81; **paroxetine, n=9**)".....**Raising the SSRI dose to 40 mg for a further 2 wk was effective in only 5 patients (16.6%).....Addition of T_3 was effective in 10 out of 16 women (62.5%)" .....Although values were within the normal range, patients who responded to T_3 had higher serum thyroid-stimulating hormone levels than those who did not. .....40% of patients will not respond to initial treatment with an SSRI even when the dose is increased to 40 mg/d**; that **severity of depression may be an important predictor of response.....T_3 may be useful as an augmenter of response in SSRI non-responders**..... **The effect of T3 may be related to thyroid function even within the normal range**...."

Dorota £ojkoa and Janusz K. Rybakowski. **l-thyroxine augmentation of serotonergic antidepressants in female patients with refractory depression.**
"..... **no history of thyroid axis disturbances** ..... **were also not taking drugs which might influence thyroid axis. Their free triiodothyronine (fT_3), free thyroxine (fT_4), and thyroid-stimulating hormone (TSH) values before thyroxine addition were within the normal range** ..... **clinical efficacy of l-thyroxine augmentation of serotonergic antidepressants in female patients with refractory depression, reflected by remission following 4 weeks of thyroxine addition in nearly 2/3 of treated subjects.....it is mainly T_3 that has been used in treatment-refractory depression**.....Our results point to a **significant therapeutic effect of addition of therapeutic dose of thyroxine (100 µg/d) to antidepressants in refractory depressed female patients. All these patients were euthyroid**.....**Our study was an open one and the number of patients studied was relatively small that can constitute main limitations.** ..... **addition of moderate dose of l-thyroxine may be a successful augmentation strategy in female treatment-resistant depressed patients in whom the effect of serotonergic antidepressant had been unsatisfactory. Furthermore, such strategy may be efficient despite of the lack of disturbances of thyroid axis in such patients.** "

Konig F, Hauger B, von Hippel C, Wolfersdorf M, Kaschka WP. **Effect of paroxetine on thyroid hormone levels in severely depressed patients.** Neuropsychobiology. 2000;42(3):135-8.
....." **The present study showed a significant reduction of 11. 2% in thyroxine during treatment with 20 mg paroxetine in 25 severely depressed patients.....**"
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Other factors are known to contribute the health problems in the elderly, which improper use of drugs complicate:
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Rozzini L, Vicini Chilovi B, Bellelli G, Bertoletti E, Trabucchi M, Padovani A. **Effects of cholinesterase inhibitors appear greater in patients on established antihypertensive therapy.** Int J Geriatr Psychiatry. 2005 Jun;20(6):547-51.
"........**Antihypertensive medications in AD patients treated with AChEis are associated with an independent improvement on cognition after 40 weeks of treatment.** Copyright # 2005 John Wiley & Sons, Ltd..... **There is increasing evidence that hypertension may contribute to the development of cognitive impairment and dementia** (Skoog et al., 1996; Birkenhager et al., 2004; Staessen et al., 2004)......."

Mossello E, Tonon E, Caleri V, Tilli S, Cantini C, Cavallini MC, Bencini F, Mecacci R, Marini M, Bardelli F, Sarcone E, Razzi E, Biagini CA, Masotti G. **Effectiveness and safety of cholinesterase inhibitors in elderly subjects with Alzheimer's disease: a "real world" study.** Arch Gerontol Geriatr Suppl. 2004;(9):297-307
".....**mild to moderate AD**.....**Compared to the other drugs, donepezil was associated with a lower incidence of withdrawals due to adverse events.** ..... **In conclusion, in this sample of elderly subjects with mild to moderate AD, treated with ChEI, a small but significant decline in cognitive and functional status was observed after 9 months**..... **No significant difference in cognitive outcome was found between drugs, while donepezil was better tolerated**....."

Kapaki E, Paraskevas GP, Mantzou E, Papapostolou A, Alevizaki M, Vassilopoulos D. **Thyroid function in patients with Alzheimer disease: implications on response to anticholinesterase treatment.**
Alzheimer Dis Assoc Disord. 2006 Oct-Dec;20(4):242-7
".....**Increasing evidence supports an extensive interrelationship between thyroid hormones and the cholinergic system, which is selectively and early affected in Alzheimer disease (AD)** ..... **(4 mo) treatment with donepezil**.....**All subjects were clinically euthyroid**. **Patients presented with higher fT4 and anti-thyroperoxidase levels, as compared with the controls. Significant reduction in T4, fT3 , fT4 , and anti-thyroperoxidase levels were observed 4 months after treatment. Responders had higher T4 and fT4**, than **nonresponders**, followed by **significant reductions after treatment**. **..... direct effect on hormone release from the thyroid gland and/or increased conversion of T4 to T3 within the brain**. **Higher T4 and fT4 levels before treatment might predict a favorable response** to **donepezil treatment**.....**Thyroid hormones are essential for normal brain maturation and function**.1 Increasing evidence also supports an extensive interrelationship between thyroid hormones and the cholinergic system, which is selectively and early affected in AD.2 **Hypothyroidism is accompanied by neurologic symptoms that might, in a way, resemble those observed in AD**.....Autoimmune thyroid disorders, such as Hashimoto thyroiditis, share with AD the involvement of some common **inflammatory mediators**.....pharmacologic management of AD and cholinesterase inhibitors (ChEIs) are the treatment of choice for these patients.17 However, **only about 50% of patients have been shown to benefit from this treatment approach**;....."There was **no history of thyroid disease or of any other major ailment in any of the patients**. **None of the patients had received or was under treatment with cognitive-enhancing drugs or antidepressants**.....**4 months on 5mg of donepezil** .....**Thyroid Status and AD Many studies have demonstrated a relationship between thyroid dysfunction and mood or cognitive disorders.** .....**increase of fT4 and anti-TPO anti-bodies in AD patients as compared to the controls**. **Elevated serum levels of T4 and fT4 have also been reported in depression, a condition closely linked to AD**..... **Lower fT4 levels in donepezil treated AD patients have been found to be associated with fear and fatigue**.....**elevated numbers of autoantibodies in possible AD with cerebrovascular disease**.....**AchE Inhibition Effects on TFTs Significant reduction in T4, fT4, fT3, and anti-TPO levels were observed 4 months after treatment, indicating interplay between TFTs and donepezil treatment**.....**most beneficial to cognition and other neuropsychologic functions of treated patients, within the first 6 months of administration followed by a gradual decline**..... **responders presented with higher T4 and fT4 levels before treatment**, and **had statistically significant reductions after treatment** .....**T3 supply of the brain depends, almost entirely, on cellular uptake and intracellular deiodination of thyroxin.** .....**Deiodinase activities and thyroid hormone concentrations in the CNS have been reported to be affected by tricyclic antidepressants**.....**we cannot exclude a possible function of donepezil in the regulation of deiodinase activity in the brain**.....**higher fT3 levels were observed between 6 and 12 months of ChEIs treatment**.....AD patients present with **increased fT4 levels and anti-TPO titers**. Relatively **higher serum concentration of (f)T4 may predict a favorable response to donepezil treatment**, and **serum levels of (f)T4 decrease in responders** but not in nonresponders....."

Balkan S, Yaras N, Mihci E, Dora B, Agar A, Yargicoglu P. **Effect of donepezil on EEG spectral analysis in Alzheimer's disease.** Acta Neurol Belg. 2003 Sep;103(3):164-9.
".....These findings show that **donepezil exerts a positive effect on EEG in AD by decreasing delta activity and increasing alpha and beta activity**. The increase in **theta activity after treatment may reflect a therapeutic shift of delta activity to theta activity**...."

Reeves RR, Struve FA, Patrick G.T**he effects of donepezil on quantitative EEG in patients with Alzheimer's disease.**
Clin Electroencephalogr. 2002 Apr;33(2):93-6.
".....Treatment was associated with **no significant differences between the pre- and post-treatment QEEGs** for (1) absolute power (all four frequency bands), (2) percent relative power (all four frequency bands), (3) total mean frequency, (4) mean frequency for theta and beta, (5) absolute power asymmetry across homologous electrode pairs (all four frequency bands), and (6) interhemispheric coherence across homologous electrode pairs (all four

frequency bands). There were **significant decreases in mean alpha and delta frequencies** that were consistent across broad electrode arrays except for an **increase in the delta frequency** at T3...."

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Even the use of paroxetine or donezapine, separately, is known to affect thyroid function, including adversely:

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Lojko D, Rybakowski JK. **l-thyroxine augmentation of serotonergic antidepressants in female patients with refractory depression.** J Affect Disord. 2007 Feb 6; [Epub ahead of print]

".....**no history of thyroid axis disturbances** and had **T_3, T_4, and thyroid-stimulating hormone (TSH) values within the normal range**. The antidepressants preceding thyroxine augmentation were serotonergic antidepressants (clomipramine - 11 patients, **paroxetine - 5 patients**, fluoxetine - 1 patient).....**moderate dose of l-thyroxine may be a successful augmentation strategy in female depressed patients in whom the effect of serotonergic antidepressant had been unsatisfactory. It may be efficient despite of the lack of disturbances of thyroid axis in such patients**....."

Brouwer JP, Appelhof BC, Peeters RP, Hoogendijk WJ, Huyser J, Schene AH, Tijssen JG, Van Dyck R, Visser TJ, Wiersinga WM, Fliers **Thyrotropin, but not a polymorphism in type II deiodinase, predicts response to paroxetine in major depression.** E. Eur J Endocrinol. 2006 Jun;154(6):819-25.

"..... **paroxetine treatment** ..... Ninety-eight outpatients with major depression (DSM-IV) .....overall treatment response was 48 of 98 patients (49%). **After exclusion of patients with subclinical hypothyroidism and/or TPO antibodies** (n = 16), **higher serum TSH significantly predicted response** ..... **Higher serum TSH was associated with response to paroxetine in patients with major depression**....."

Abraham G, Milev R, Stuart Lawson J. **T_3 augmentation of SSRI resistant depression**. J Affect Disord. 2006 Apr;91(2-3):211-5. Epub 2006 Feb 17.

".....**failed to show satisfactory antidepressant response after a minimum of six weeks adequate treatment** were recruited.....**thyroid-stimulating hormone (TSH) value within the normal range**.....started on 25 microg of T_3 and the dose was increased to 50 microg within a week when tolerated; they continued the combination of T_3 and the SSRI for a minimum of three weeks..... **4 were taking citalopram (mean dose = 50 mg/day)**.....**one patient was on 40 mg of paroxetine**. ..... T_3 augmentation was associated with a statistically significant drop ($p < .003$) in the mean HAMD at end of the three weeks compared to baseline scores. Five patients (42%) showed >or=50% improvement on HAMD scores, with three achieving full remission (HAMD scores<or=7) at the end of the study. There were no reliable differences between responders and non-responders in baseline HAMD scores, number of previous antidepressant trials, gender or Deltamax TSH. **.....** **T_3 augmentation resulted in improvement of mood scores. The responders' rate of 42%** in our study is **comparable to the response rates reported using T_3** ..... **the remaining 11 patients tolerated the addition of T_3 very well. With the availability of T_3, a viable, safe, inexpensive and effective augmentation treatment, the recent trend of replacing T_3 with other novel strategies appears unwarranted**...."

Appelhof BC, Brouwer JP, van Dyck R, Fliers E, Hoogendijk WJ, Huyser J, Schene AH, Tijssen JG, Wiersinga WM.

Triiodothyronine addition to paroxetine in the treatment of major depressive disorder.

J Clin Endocrinol Metab. 2004 Dec;89(12):6271-6.

"There is evidence that thyroid hormone **T_3 increases serotonergic neurotransmission**. .....**efficacy of T_3 addition** to **paroxetine** in major depression. One hundred thirteen patients with major depressive disorder were randomly assigned to 8 wk of double-blind outpatient treatment with low-dose T_3 (25 microg), high-dose T_3 (25 microg twice daily), or placebo in addition to **paroxetine 30 mg daily**. A total of 106 patients .....**these results do not support a role for T_3 addition to selective serotonin reuptake inhibitors in the treatment of nonrefractory major depressive disorder**. On the contrary, **more adverse reactions occurred in T_3-treated patients**....."

Chow TW, Mendez MF. **Goals in symptomatic pharmacologic management of frontotemporal lobar**

degeneration.
Am J Alzheimers Dis Other Demen. 2002 Sep-Oct;17(5):267-72.
".....**Paroxetine addressed anxiety and repetitive, ritualistic behaviors**. **Depression was resistant to treatment.** Valproic acid and quetiapine calmed agitated subjects without exacerbating Parkinsonism. **Donepezil has not emerged as a beneficial medication for this group of subjects**....."

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Drugs, especially when improperly combined, can aggravate health problems and be misinterpreted as "aging phenomena":

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Carcenac D, Martin-Hunyadi C, Kiesmann M, Demuynck-Roegel C, Alt M, Kuntzmann F. **[Extra-pyramidal syndrome induced by donepezil]** Presse Med. 2000 May 20;29(18):992-3. French.
".....**severe gait disorders were observed in 3 patients with Alzheimer's dementia treated with donepezil**. **This drug was associated with paroxetine** or a neuroleptic. **In 2 of the 3 cases, the extra-pyramidal effects disappeared when donepezil was discontinued**. **DISCUSSION: Extra-pyramidal syndromes in elderly subjects with cognitive impairment are difficult to interpret. The possible causes include interactions between acetylcholinesterase inhibitors, neuroleptics and serotonine reuptake inhibitors and Lewy body dementia**....."

Kieszek S. **[Trials and perspectives in pharmacotherapy of Alzheimer's disease]**
Psychiatr Pol. 1999 May-Jun;33(3):331-40. Review. Polish.
"..... **donepezil** and **Gingko Biloba** as well as nimodipine **improved mental functions** ..... **Behavioral symptoms often associated with dementia, like depression, anxiety, irritability, delusions, aggressiveness were treated with**: olazepine, risperidone, haloperidol, clozapine, fluoxetine, **paroxetine**, sertraline, trazodon, dezypramine, lithium, benzodiazepines, carbamazepine and valproic acid. **Drugs with strong anticholinergic effects**, such as amitriptyline or imipramine **should not be administered**....."

Asnis GM, De La Garza R 2nd. **Interferon-induced depression in chronic hepatitis C: a review of its prevalence, risk factors, biology, and treatment approaches.** J Clin Gastroenterol. 2006 Apr;40(4):322-35.
".....Combination treatment with pegylated interferon **(IFN)-alpha plus ribavirin** ..... **one of the most common side effects of this regimen is depression**. **Whereas IFN-alpha has been found to induce depression in chronic myelogenous leukemia, melanoma, and renal cell carcinoma, CHC patients may be especially prone to develop IFN-induced depression.** .....**Thyroid disorders and anemia (as well as other medical conditions) have also been associated with IFN exposure and may account for some incidences of depression** in CHC patients..... **brief description is provided of potential biological mechanisms of IFN-induced depression ..... proinflammatory cytokines**....."

Agid O, Shalev AY, Lerer B.**Triiodothyronine augmentation of selective serotonin reuptake inhibitors in posttraumatic stress disorder**. J Clin Psychiatry. 2001 Mar;62(3):169-73.
....."**"Addition of triiodothyronine (T_3) to ongoing antidepressant treatment is considered an effective augmentation strategy in refractory depression.** .....T_3 (25 microg/day) was added to treatment with a selective serotonin reuptake inhibitor (SSRI) (**paroxetine** or fluoxetine, **20 mg/day for at least 4 weeks and 40 mg/day for a further 4 weeks**) of 5 patients who fulfilled DSM-IV criteria for PTSD but **not for major depressive disorder** ..... **In 4 of the 5 patients, partial clinical improvement was observed with SSRI treatment at a daily dose of 20 mg with little further improvement when the dose was raised to 40 mg/day**. **This improvement was substantially enhanced by the addition of T_3.** .....**T_3 augmentation of SSRI treatment may be of therapeutic benefit in patients with PTSD, particularly those with depressive symptoms.** ....."

Stern RA, Davis JD, Rogers BL, Smith KE, Harrington CJ, Ott BR, Jackson IM, Prange AJ Jr.
Preliminary study of the relationship between thyroid status and cognitive and neuropsychiatric functioning in euthyroid patients with Alzheimer dementia. Cogn Behav Neurol. 2004 Dec;17(4):219-23.
".....**Mild alterations of thyroid hormone levels, even in the normal range, are associated with changes in**

mood and cognitive functioning in older, nondemented adults, and lower concentrations of thyroid hormones have been shown to be associated with an increased risk for cognitive decline ..... Twenty-eight euthyroid patients with AD on donepezil underwent evaluation of thyroid status..... **statistically significant associations between FT_4 concentrations and self-reported feelings of fear and fatigue**. **Fear and fatigue were /negatively/ correlated with FT_4**. .....preliminary study support a relationship between thyroid status and neuropsychiatric symptoms in euthyroid individuals with AD, with **lower concentrations of FT_4 associated with fear and fatigue**....."

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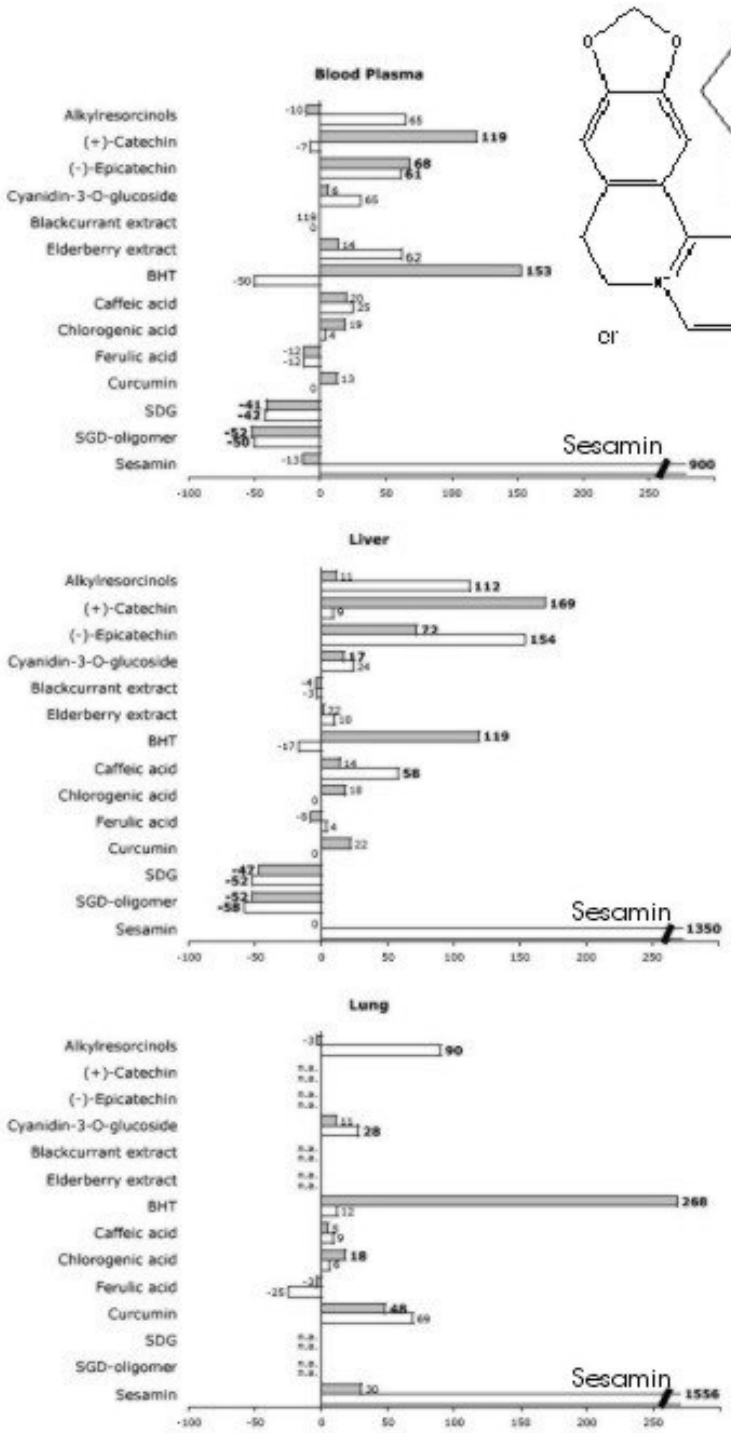

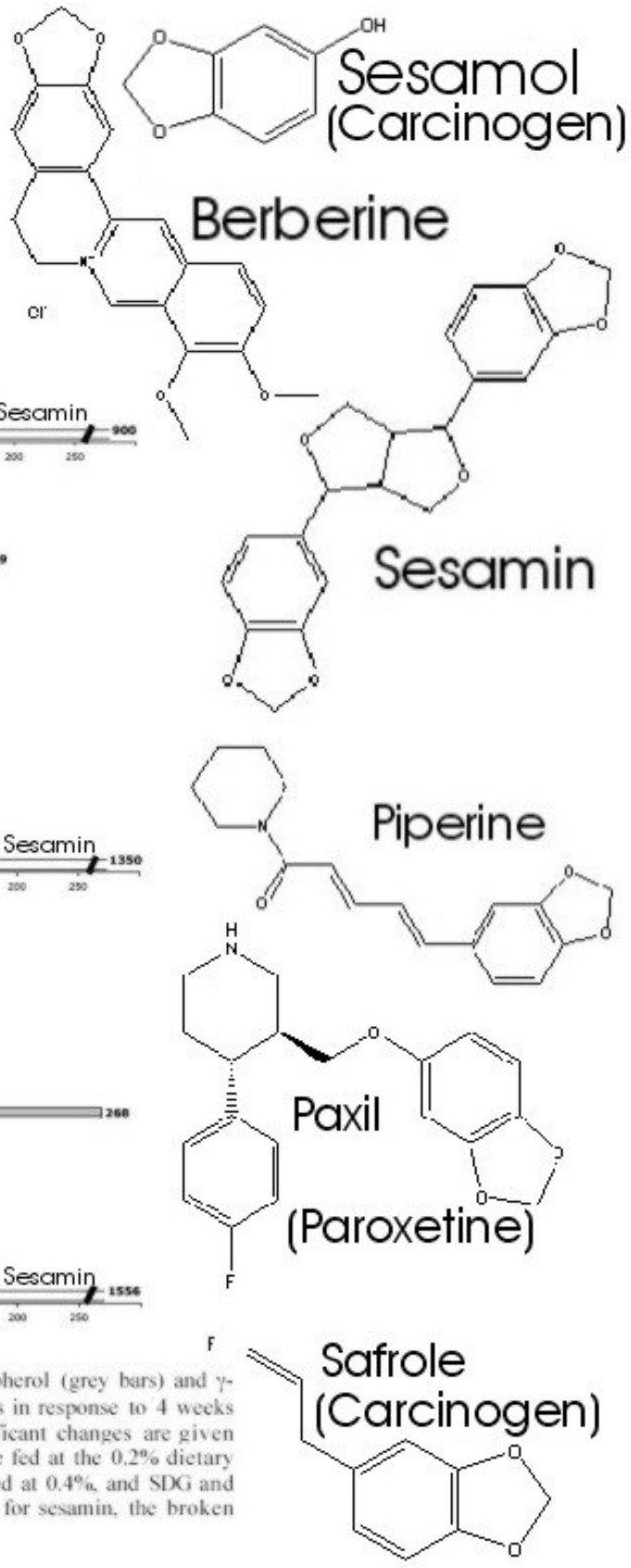

Figure 7. Changes (in percent) in the concentrations of α-tocopherol (grey bars) and γ-tocopherol (white bars) in blood plasma, liver, and lungs of rats in response to 4 weeks supplementation with phenolic compounds. Statistically significant changes are given in bold; n.a. = not analysed. All compounds and extracts were fed at the 0.2% dietary level, except alkylresorcinols, BHT, curcumin, and sesamin, fed at 0.4%, and SDG and its oligomer fed at 0.1% in the diet. Due to the extreme values for sesamin, the broken bars do not reflect the actual proportions.

34

NOTE: Many selective serotonin reuptake inhibitors, like Paxil®, have received major warnings from the FDA because of associated health problems and dependencies they create, including neurological ones, and due to the propensity for certain age groups to get more depressed and to commit suicide when taking these drugs or

withdrawing from them. Paxil® is chemically poised to interfere with a critical nutrient, now known to dramatically increase gamma- tocopherol levels more than any other tested antioxidant. Since gamma-tocopherol tends to protect neurological tissue enriched in unsaturated fatty acids, the poisoning of sesamin whether 1) by Paxil® (paroxetine), 2) by carcinogenic piperine from black pepper, 3) by berberine from certain herbs 4) by the carcinogenic sesamol found in sesame seed oil, or 5) by carcinogenic safrole.....has the potential for making neurodegenerative diseases relatively worse by their interference with the more beneficial dietary sesamin. Note this base sesamol- and safrole-like structures in various compounds, *supra*, both "good" and "bad":

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For some reason, such natural approaches to better health, or even combinations of natural approaches with conventional pharmaceutical approaches, do not receive widespread acceptance in American health practices, even when they appear to produce far better responses:

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Zhou ZL, Liang LZ, Yan YX. **[Clinical study of Reinhartdt and sea cucumber capsule combined with donepezil in treating Alzheimer's disease]**[Article in Chinese] Zhongguo Zhong Xi Yi Jie He Za Zhi. 2007 Feb;27(2):110-3.

"....efficacy and safety of **Reinhartdt and sea cucumber capsule (RSC)** combined with **donepezil** in treating Alzheimer's disease (AD), and its effect on **thyroid function** axis..... **improvement in the combined treatment group was more significant than that in the other two groups (P < 0.01). After 6 months of treatment, the levels of FT_3 and FT_4 in the combined treatment group were significantly changed (P < 0.01), but no significant change in all the thyroid hormones was found in the other two groups**..... **RSC combined with Donepezil in treating AD is effective and safe with no evident adverse reaction, better than single drug treatment, which may be through influencing the metabolism of thyroid hormones to improve the cognition function of AD patients**....."

Addendum:

http://www.fda.gov/cder/drug/infopage/escitalopram/ SSRIs/SNRI/Triptan and Serotonin Syndrome [issued 7/2006]

A *life-threatening condition called serotonin syndrome* can happen when medicines called selective serotonin reuptake inhibitors (SSRIs), such as Lexapro, and **medicines used to treat migraine headaches known as 5-hydroxytryptamine receptor agonists (triptans), are used together**.....

SSRIs/SNRI/Triptan and Serotonin Syndrome (7/2006) **A *life-threatening condition called serotonin syndrome (serious changes in how your brain, muscles and digestive system work due to high levels of serotonin in the body)* can happen when medicines called selective serotonin reuptake inhibitors (SSRIs), such as Lexapro, and medicines used to treat migraine headaches known as 5-hydroxytryptamine receptor agonists (triptans), are used together. Signs and symptoms of serotonin syndrome include the following:**

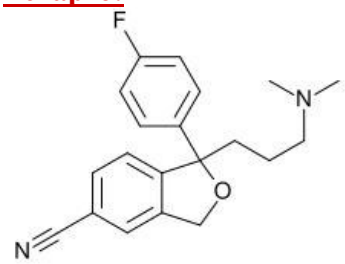
restlessness
diarrhea
hallucinations
coma
loss of coordination
nausea
fast heart beat
vomiting
increased body temperature
fast changes in blood pressure
overactive reflexes

Serotonin syndrome* may be more likely to occur when *starting or increasing the dose of an SSRI or a triptan*.** This information comes from reports sent to FDA and knowledge of how these medicines work. If you take migraine headache medicines, ask your healthcare professional if your medicine is a triptan. Before you take **Lexapro** and a triptan together, talk to your healthcare professional. If you must take these medicines together, be aware of the possibility of ***serotonin syndrome, and get medical care right away if you think serotonin syndrome is happening to you.

http://www.fda.gov/cder/drug/InfoSheets/HCP/paroxetineHCP.htm#triptan

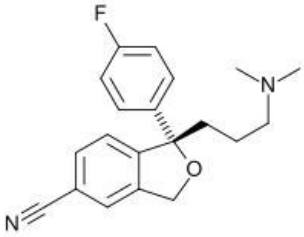
http://www.fda.gov/cder/drug/advisory/SSRI_SS200607.htm

NOTE:Celexa™, Cipramil™, Citrol™, Sipralexa™, Seropram™, Zetalo, Celepram™, Ciazil™, Zentius™, Cipram™ and Citalopram are the racemic versions without the specific stereochemistry of Lexapro!



Citalopram

Celexa™ (U.S., Forest Laboratories, Inc.), Cipramil™ , Citrol™, Sipralexa™ , Seropram™ (Europe and Australia), Zetalo (India), Celepram™, Ciazil™ (Australia), Zentius™ (South America, Roemmers) and Cipram™ (Denmark, H. Lundbeck A/S)



Lexapro® (Escitalopram or Cipralex®, Sipralexa®, and Seroplex®)

Escitalopram/Lexapro®/:

Wessels-van Middendorp AM, Timmerman L. **[Galactorrhoea and the use of selective serotonin reuptake inhibitors]**

[Article in Dutch]Tijdschr Psychiatr. 2006;48(3):229-34.

"...**citalopram**, because of a depressive episode. She developed symptoms of **galactorrhea**; there was a time relationship between **suspension of the treatment with citalopram and a reduction of the galactorrhea symptoms**. .... **under-supplementation of thyroid hormone and resultant hypothyroidism**. **Psychiatrists usually see galactorrhea in patients who are taking antipsychotics**. However, **few psychiatrists know that galactorrhea can also be caused by SSRIs**. **When a patient has symptoms of bilateral galactorrhea and has used an SSRI and when hyperprolactinemia has been found in laboratory tests** it is **probably advisable to stop the SSRI medication**....."

Masalova OO, Sapronov NS. **[The influence of cypramil on depressive disorders of behavior in young thyroidectomized male rats]**[Article in Russian] Eksp Klin Farmakol. 2006 Mar-Apr;69(2):6-9.

".....**selective serotonin re-uptake inhibitor cypramil (cipramil, citalopram**) has been studied in young male rats with thyroid hormone dysbalance induced by thyroidectomy. **Thyroidectomy increased the level of depressed behavior** in the Porsolt forced swim test and enhanced the expression of emotional behavior in the open-field test. **The replacement treatment of thyroidectomized rats with triiodothyronine (T_3) produced an antidepressant and anxiolytic effects**. The **chronic administration of cypramil** also produced an antidepressant action in the Porsolt test, the d**rug effect being more pronounced in the case of a combined treatment with cypramil and T_3 (synergism)**. ..... **drug effects were less pronounced in the case of joint administration with T_3**....."

Kalisova-Starkova L, Fisar Z, Paclt I, Hanus Z, Vevera J. **Red blood cell triiodothyronine uptake as membrane parameter of depression.** Physiol Res. 2006;55(2):195-204. Epub 2005 May 24.

"....24 patients with major depression were measured before treatment and after 1 month of treatment with **citalopram**. ..... **We concluded that the function of the membrane transporter for L-T_3 in RBC is changed in depression. This change is probably connected with alteration of membrane fluidity and/or transporter-lipid interactions. We did not find any normalization of the measured parameters after 1 month of treatment. The results show the importance of composition and physical properties of the lipid bilayer for**

transmembrane transport of L-T_3 and support the hypothesis that the HPT axis is in depression....."

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Rush AJ, Fava M, Wisniewski SR, Lavori PW, Trivedi MH, Sackeim HA, Thase ME, Nierenberg AA, Quitkin FM, Kashner TM, Kupfer DJ, Rosenbaum JF, Alpert J, Stewart JW, McGrath PJ, Biggs MM, Shores-Wilson K, Lebowitz BD, Ritz L, Niederehe G. **Sequenced treatment alternatives to relieve depression (STAR*D): rationale and design.**
Control Clin Trials. 2004 Feb;25(1):119-42.
"STAR*D is a multisite, prospective, randomized, multistep clinical trial of outpatients with nonpsychotic major depressive disorder. **The study compares various treatment options for those who do not attain a satisfactory response with citalopram, a selective serotonin reuptake inhibitor antidepressant**. The study enrolls 4000 adults (ages 18-75)...."

Flores G, Perez-Patrigeon S, Cobos-Ayala C, Vergara J. **Severe symptomatic hyponatremia during citalopram therapy--a case report.** BMC Nephrol. 2004 Jan 16;5:2.
"..... **Hyponatremia secondary to the syndrome of inappropriate secretion of antidiuretic hormone is an uncommon complication of treatment with the new class of antidepressant agents, the selective serotonin reuptake inhibitors. The risk of hyponatremia seems to be highest during the first weeks of treatment particularly, in elderly females and in patients with a lower body weight.** ..... **malaise, progressive confusion, and a tonic/clonic seizure two weeks after starting citalopram, 20 mg/day**. ..... **hyponatremia, serum hypoosmolality, urine hyperosmolarity, and an elevated urine sodium concentration**, leading to the **diagnosis of inappropriate secretion of antidiuretic hormone**. **Citalopram was discontinued and fluid restriction was instituted**. The patient was discharged after serum sodium increased from 124 mmol/L to 134 mmol/L. **Two weeks after discharge the patient denied any new seizures, confusion or malaise**. At that time his serum sodium was 135 mmol/L. ..... **Because the use of serotonin reuptake inhibitors is becoming more popular among elderly depressed patients** the present paper and other reported cases emphasize the **need of greater awareness of the development of this serious complication and suggest that sodium serum levels should be monitored closely in elderly patients during treatment with citalopram**....."

Kulikov AV, Jeanningro R. **The effects of hypothyroidism on 5-HT1A and 5-HT2A receptors and the serotonin transporter protein in the rat brain.** Neurosci Behav Physiol. 2001 Jul-Aug;31(4):445-9.
"The effects of hypothyroidism on 5-HTIA and 5-HT2A receptors and the serotonin transporter protein were studied in **thyroidectomized male Wistar rats** in two experimental groups: 1) animals kept on an **iodine-free diet hypothyroid rats**) and 2) animals kept on **thyroxine (15 microg/kg) for 21 days (giving normal thyroid hormone levels. euthyroid animals)**. **Sham-operated rats served as controls**. ..... significant **decreases in [^{3}H]ketanserin binding to 5-HT2A receptors in the frontal cortex in hypothyroid rats as compared with controls**; **this decrease was reversed by thyroxine treatment**. Thus, **losses of cortical 5-HT2A receptors appears to be the main consequence of hypothyroidism** at the level of the serotonin system of the brain....."

Moreau X, Jeanningros R, Mazzola-Pomietto P. **Chronic effects of triiodothyronine in combination with imipramine on 5-HT transporter, 5-HT(1A) and 5-HT(2A) receptors in adult rat brain.**
Neuropsychopharmacology. 2001 Jun;24(6):652-62.
"Triiodothyronine (T_3) has been shown to accelerate and potentiate the clinical response to tricyclic antidepressant (TCA) treatment in depressive disorders. .....**combined administration of imipramine and T_3 for 7 days modified the density of 5-HT transporters and of 5-HT(1A) receptors**. On day 21, the combination did not change imipramine- or T_3-induced decrease in 5-HT transporter density whereas **it prevented imipramine-induced increase in 5-HT(1A) receptor density**. Whatever the treatment duration, imipramine-T_3 **combination potentiated imipramine-induced decrease in 5-HT(2A) receptor density**. On both day 7 and day 21, **T_3 given alone had no effects on the density of 5-HT(1A) and 5-HT(2A) receptors**. These data indicate that **T_3 is able to modulate the long-term adaptive changes which occur at the postsynaptic level of 5-HT neurotransmission after antidepressant treatment**....."

Kulikov A, Moreau X, Jeanningros R. **Effects of experimental hypothyroidism on 5-HT1A, 5-HT2A receptors, 5-HT uptake sites and tryptophan hydroxylase activity in mature rat brain1**. Neuroendocrinology. 1999 Jun;69(6):453-9.
".....**Surgically thyroidectomized male Wistar rats** received: (1) an **iodine-free diet to produce severe hypothyroidism**; (2) **hormonal replacement with 15 microgram/kg/day of thyroxine (T_4)** for 21 days to **normalize serum TH levels**, or (3) **hormonal replacement with 200 microgram/kg/day of T_4** for 14 days to produce an **excess of circulating THs**. **Sham-operated rats were used as controls**. ..... **hypothyroid rats had a significant decrease in Bmax of 3H-ketanserin binding to cortical 5-HT2A receptors compared to controls**. **Cortical 3H-ketanserin binding in thyroidectomized rats was normalized after replacement with low-dose T_4**. .... **decrease in cortical 5-HT2A receptors is the main neurochemical event underlying the impairing effect of hypothyroidism on 5-HT neurotransmission**....." --
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Many of these drugs absolutely should not be used in combination with aspirin and other pain relievers in the elderly, and the citalopram, not surprisingly, has been associated with hypothyroid responses, not good when one is trying to alleviate the "symptoms" of hypothyroidism noted, ***supra***.

This symptomology is aggravated in the elderly by additional hormonal deficiencies and adverse interactions. Progesterone is known to induce the monooxygenase receptor for vitaletheine, that is being recognized as being more and more important to proper regulation of bodily functions, metabolism, and even diurnal rythms.

Mol Pharmacol. 1981 Jan;19(1):134-9.
Changes in dimethylaniline N-oxidase activity of mouse liver and kidney induced by steroid sex hormones.
Duffel MW, Graham JM, Ziegler DM.

Ciba Found Symp. 1979;(72):191-204. Related Articles, Links
Studies on the nature and regulation of the cellular thio:disulphide potential.
Ziegler DM, Duffel MW, Poulsen LL.
Microsomal fractions separated from homogenates of liver, kidney and corpora lutea contain a monooxygenase (dimethylaniline monooxygenase [N-oxide forming], EC 1.14.13.8) that catalyses NADPH- and oxygen-dependent oxidation of cysteamine to cystamine. The monooxygenase purified to homogeneity from hog liver also catalyses oxygenations of diverse xenobiotics, but it does not catalyse oxidation of any other physiological sulphur- or nitrogen-containing compounds. All the available evidence indicates that cysteamine is the physiological substrate for the monooxygenase, and the oxidation of this thiol to the disulphide may be a significant source of disulphide maintaining the cellular thiol:disulphide potential. The concentration of protein-low molecular weight mixed disulphide is a function of this potential. Changes in concentration of this protein-mixed disulphide reflect changes in thiol:disulphide balance. At constant substrate concentrations the potential would depend primarily on activity of the cytosol glutathione reductase (NAD(P)H: oxidized-glutathione oxidoreductase, EC 1.6.4.2) relative to that of the membrane-bound monooxygenase. In hepatic tissue from adult mice and hamsters there is a correlation between the concentration of protein-mixed disulphide and the activity of the monooxygenase relative to the reductase. Hepatic glutathione reductase is relatively constant in mice, but the monooxygenase is much higher in the female than in the male. After gonadectomy monooxygenase activity decreases in the female and increases in the male. **Activities are restored to control levels by treating** males with testosterone and **females with progesterone**. Testosterone decreases and **progesterone increases activity**. These two hormones apparently regulate the level of this enzyme in hepatic tissue.

Progesterone levels drop in both men and women as we age:
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Peer-Reviewed Professional Journals
· Fitzpatrick, L. A., et al. Comparison of regimens containing oral micronized progesterone or medroxyprogesterone acetate on quality of life in postmenopausal women: a cross-sectional survey. J Women's Health Gen Med. 9(4):381-387, 2000.
A cross-sectional survey was conducted to examine quality of life (QOL) related to physiological, somatic, and vasomotor effects of changing progestin treatment from medroxyprogesterone acetate (MPA) to micronized

progesterone in postmenopausal women. 176 eligible women were currently using hormone replacement therapy (HRT) containing micronized progesterone for 1-6 months and had previously received HRT containing medroxyprogesterone acetate. QOL was assessed via telephone interview using the Greene Climacteric Scale and the Women's Health Questionnaire. When compared with the MPA-containing regimen, women using micronized progesterone-containing HRT experienced significant improvement in vasomotor symptoms, somatic complaints, and anxiety and depressive symptoms. Women reported improved perceptions of their patterns of vaginal bleeding and control of menopausal symptoms while on the micronized progesterone-containing regimen. Approximately 80% of women reported overall satisfaction with the micronized progesterone-containing regimen. A micronized progesterone-containing HRT regimen offers the potential for improved QOL as measured by improvement of menopause-associated symptoms.

· British Medical Journal. 290(6482):1617-1621, 1985.

This double-blind crossover trial showed that maximum improvement in PMS patients using supplemental progesterone occurred during the first month of treatment with progesterone.

Laypersons' Publications

· Dean, W. Natural progesterone: first choice. Vitamin Research News. 16(6), 2002.

The author proposes that the true underlying cause of many menopause-related disorders may be relative deficiency of progesterone, leading to estrogen dominance. With menopause, estrogens production declines by approximately 50%, while progesterone production declines by approximately 99%. This significantly increases the estrogens:progesterone ratio.

· Fowkes, S. Wm. Aromatase inhibtion and aging. Smart Life News. 7(1):1-6, 1999.

In women, progesterone levels decline to a far greater extent than the decline in estrogen. This decline occurs mainly after menopause.

· Lee, John R. What Your Doctor May Not Tell You About Menopause. Warner Books, May, 1996.

· Valentine, G. What women want to know about progresterone. Life Enhancement. November 2000.

· Live it up: women in perimenopause need not experience related symptoms. Life Extension. 7(10), 2001.

It is recommended that women using progesterone for the treatment of menopausal symptoms use 60 mg per day (in progesterone cream). Some women require two to three months of this therapy before results become apparent.

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This is exacerbated by increases in stress as friends and family members grow old, become morbidly ill, and die because cortisol is produced by the body in response to this stress, but cortisol binds to the same transport protein as progesterone, thereby limiting the distribution of a key beneficial hormone that is already in short supply. The net result is that the levels of monooxygenase receptor for vitaletheine, that would otherwise help to regulate many biochemical pathways in the body properly, declines with age, with drops in the levels of progesterone, and when stress and cortisol poison its distribution via progesterone's transport protein.

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Also known as: CBG; Corticosteroid Binding Globulin; Transcortin

Description

Cortisol Binding Globulin is a type of water-soluble endogenous Globulin that is synthesized by the Liver.

Biological Functions of Cortisol Binding Globulin

Hormones

CBG facilitates the transport of Cortisol and **Progesterone around the body via the Plasma within the Bloodstream**:

- CBG binds to Cortisol and Progesterone, transports them via the bloodstream and when in close proximity to a Cell, releases them for transport through the Cell Membrane into the Cytoplasm of Cells (where, if they then encounter the appropriate accessible Receptors they migrate into the Cell's Nucleus).
- 75% of the body's Cortisol is normally bound to CBG (20% of the remaining 25% of Cortisol is free to exert its effects on target Steroid Receptors):
- **When plasma Cortisol levels exceed 20 - 30 mcg/dl, Cortisol Binding Globulin becomes saturated, allowing the concentration of "free" Cortisol to rise sharply.**

These Substances may Increase the Production of Cortisol Binding Globulin

Hormones

Estrogens increase the production of CBG by the Liver.
These Factors may Increase the Body's Production of Cortisol Binding Globulin
Metabolism
Hyperthyroidism may increase the production of CBG by the Liver.
Sexual System
CBG production increases during Pregnancy.
These Ailments may Interfere with Cortisol Binding Globulin
Metabolism
Hypothyroidism may cause a decrease in the body's production of CBG.
Related Topics
Binding Proteins
- Cortisol
- Endogenous Globulins
- Progesterone

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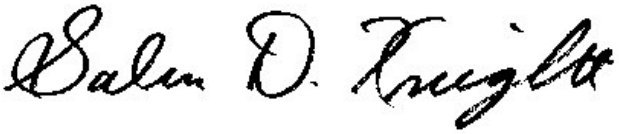
Thus, support of the monooxygenase pathway and the vitaletheine modulator pathway is critical for long, healthy, and productive lives.

Good Health!!



Galen D. Knight, pHd