Scientific references for the WOSAAM & IHS RECTIFICATION of the scientific inaccuracies in the Advice on Anti-aging Medicine of the Belgian Academy of Medicine (April 2016**) (Références pour la Rectification WOSAAM et IHS scientifique des inexactitudes de l'Avis de l'Académie de Médecine de Belgique**

Placebo-controlled studies with recombinant human growth hormone: 507 (461 in adults)

Growth hormone therapy on healthy young and middle-aged adults: 65 placebo-controlled studies

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Growth hormone therapy on growth hormone-deficient children: 46 placebo-controlled studies (50 with mixed studies)

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Growth hormone therapy on children with disorder: 43 placebo-controlled studies (48 in total as 5 other placebo-controlled trials are with both children and adults)

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Surgery- children

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Cystic fibrosis children

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Insulin sensitivity: greater improvement with smaller doses of GH treatment

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Lean body mass: the improvement with GH treatment

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Lean mass: the increase with GH treatment; fat mass: the reduction with GH treatment

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GH therapy improves mental performance in adults

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DHEA therapy: 76 placebo-controlled trials – all in adults

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About the inaccuracies of the contradictory information

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1283. Morgentaler A. Testosterone, cardiovascular risk, and hormonophobia. J Sex Med. 2014 Jun;11(6):1362-6. (Use of weak studies as proof of danger indicates that cultural (i.e., nonscientific) forces are at play. Negative media stories touting T's risks appear fueled by antipharma sentiment, anger against aggressive marketing, and antisexuality. This stance is best described as "hormonophobia." Men's Health Boston, Harvard Medical School, Brookline, MA, USA Analysis of recent articles regarding CV risks with T and comparison with events surrounding publication of results of the Women's Health Initiative in 2002.**RESULTS:** In the first study, the percentage of individuals with an adverse event was lower by half in men who received T compared with untreated men (10.1% vs. 21.2%). However, an opposite conclusion was reached via complex statistics. The second study reported minor increased rate of nonfatal myocardial infarction (MI) up to 90 days after receiving a T prescription compared with the prior 12 months.

However, there was no control group, so it is unknown whether this MI rate was increased, reduced, or unchanged compared with untreated men. Neither study provided substantive evidence of risk, yet these were lauded as proof of dangers, despite a substantial literature to the contrary. Similar events followed the publication of the Women's Health Initiative in 2002 when a media frenzy over increased risks with female hormone replacement therapy obscured the fact that the reported excess risk was clinically meaningless, at two events per 1,000 person-years. Stakeholders driving concerns regarding hormone risks are unlikely to be clinicians with real-world patient experience.The use of weak studies as proof of danger indicates that cultural (i.e., nonscientific) forces are at play. Negative media stories touting T's risks appear fueled by antipharma sentiment, anger against aggressive marketing, and antisexuality. This stance is best described as "hormonophobia." As history shows, evidence alone may be insufficient to alter a public narrative. The true outrage is that social forces and hysteria have combined to deprive men of a useful treatment without regard for medical science.

1284. Morgentaler A, Miner MM, Caliber M, Guay AT, Khera M, Traish AM. Testosterone therapy and cardiovascular risk: advances and controversies. Mayo Clin Proc. 2015 Feb;90(2):224-51. Review. (Two recent studies raised new concerns regarding cardiovascular (CV) risks with testosterone (T) therapy. This article reviews those studies as well as the extensive literature on T and CV risks. A MEDLINE search was performed for the years 1940 to August 2014 using the following key words: testosterone, androgens, human, male, cardiovascular, stroke, cerebrovascular accident, myocardial infarction, heart attack, death, and mortality. The weight and direction of evidence was evaluated and level of evidence (LOE) assigned. Only 4 articles were identified that suggested increased CV risks with T prescriptions: 2 retrospective analyses with serious methodological limitations, 1 placebo-controlled trial with few major adverse cardiac events, and 1 meta-analysis that included questionable studies and events. In contrast, several dozen studies have reported a beneficial effect of normal T levels on CV risks and mortality. Mortality and incident coronary artery disease are inversely associated with serum T concentrations (LOE IIa), as is severity of coronary artery disease (LOE IIa). Testosterone therapy is associated with reduced obesity, fat mass, and waist circumference (LOE Ib) and also improves glycemic control (LOE IIa). Mortality was reduced with T therapy in 2 retrospective studies. Several RCTs in men with coronary artery disease or heart failure reported improved function in men who received T compared with placebo. The largest meta-analysis to date revealed no increase in CV risks in men who received T and reduced CV risk among those with metabolic disease. In summary, there is no convincing evidence of increased CV risks with T therapy. On the contrary, there appears to be a strong beneficial relationship between normal T and CV health that has not yet been widely appreciated.)
1285. Goodman N, Guay A, Dandona P, Dhindsa S, Faiman C, Cunningham GR; AACE Reproductive Endocrinology Scientific Committee. American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on the association of testosterone and cardiovascular risk. Endocr Pract. 2015 Sep;21(9):1066-73. (As recently concluded in an extensive review of literature, there is no compelling evidence that testosterone therapy increases cardiovascular risk.)

Drugs taken out of the market because of high death risk: Vioxx, Mediator,etc.

1286. https://en.wikipedia.org/wiki/List_of_withdrawn_drugs
1287. https://fr.wikipedia.org/wiki/Liste_de_m%C3%A9dicaments_retir%C3%A9s_du_march%C3%A9_fran%C3%A7ais

Sildenafil: adverse events, including mortality

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Testosterone therapy in men: 317 placebo-controlled studies – 307 in adults

Healthy adults

Healthy young men

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Testosterone in women: 105 placebo-controlled studies – all in adults

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Pre-term infants: Triiodothyronine or thyroxine treatment

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Melatonin: 147 placebo-controlled studies on the effect of melatonin on sleep (130 in adults): 110 placebo-controlled studies where a significant beneficial effect of melatonin on sleep in adults was observed and 17 in children: the beneficial effect mainly consists in a shortening of the time to fall asleep (quicker sleep onset) and a profound muscle relaxation, rarely an improvement of the REM or deep sleep

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2008. Coppola G, Iervolino G, Mastrosimone M, La Torre G, Ruiu F, Pascotto A. Melatonin in wake-sleep disorders in children, adolescents and young adults with mental retardation with or without epilepsy: a double-blind, cross-over, placebo-controlled trial. Brain Dev. 2004 Sep;26(6):373-6
2009. Niederhofer H, Staffen W, Mair A, Pittschieler K. Brief report: melatonin facilitates sleep in individuals with mental retardation and insomnia. J Autism Dev Disord. 2003 Aug;33(4):469-72

Aldosterone: 13 placebo-controlled trials – all in adults

Healthy men: IV aldosterone produces acute cardiovascular (sympathetic) effects (first 45 min after injection) and delayed (5 ½ - 6 ½ h after) increased vagal tone (parasymathetic predominance)

2010. Schmidt BM1, Montealegre A, Janson CP, Martin N, Stein-Kemmesies C, Scherhag A, Feuring M, Christ M, Wehling M. Short term cardiovascular effects of aldosterone in healthy male volunteers. J Clin Endocrinol Metab. 1999 Oct;84(10):3528-33.

Healthy men: Aldosterone at 100 µg, tending to increase cardiac vagal activity and enhances the heart rate (tachycardia) response to diastolic blood pressure-reducing nitroprusside

2011. Heindl S, Holzschneider J, Hinz A, Sayk F, Fehm HL, Dodt C. Acute effects of aldosterone on the autonomic nervous system and the baroreflex function in healthy humans. J Neuroendocrinol. 2006 Feb;18(2):115-21.

Healthy men: Aldosterone at 3 µg /min. rapidly impairs the baroreflex response,

2012. Schmidt BM, Horisberger K, Feuring M, Schultz A, Wehling M. Aldosterone blunts human baroreflex sensitivity by a nongenomic mechanism. Exp Clin Endocrinol Diabetes. 2005 May;113(5):252-6. (tachycardic response to arterial baroreceptor deactivation was more pronounced in the aldosterone experiments

Healthy men: Aldosterone (+7.6%) increases blood flow by increasing NO release and at the vascular smooth muscle cells by promoting vasoconstriction of forearm arteries

2013. Romagni P, Rossi F, Guerrini L, Quirini C, Santiemma V. Aldosterone induces contraction of the resistance arteries in man. Atherosclerosis. 2003 Feb;166(2):345-9.

2014. Schmidt BM, Oehmer S, Delles C, Bratke R, Schneider MP, Klingbeil A, Fleischmann EH, Schmieder RE. Rapid nongenomic effects of aldosterone on human forearm vasculature. Hypertension. 2003 Aug;42(2):156-60.

Healthy men: IV aldosterone rapidly attenuated endothelium-dependent vasodilatation to acetylcholine (-28% less vasodilatation)

Healthy men: Aldosterone increases phosphocreatine recovery in muscles to significantly higher levels immediately after isometric contraction within 8 min of aldosterone administration

2015. Zange J, Müller K, Gerzer R, Sippel K, Wehling M. Nongenomic effects of aldosterone on phosphocreatine levels in human calf muscle during recovery from exercise. J Clin Endocrinol Metab. 1996 Dec;81(12):4296-300.
2016. Christ M1, Zange J, Janson CP, Müller K, Kuklinski P, Schmidt BM, Tillmann HC, Gerzer R, Wehling M. Hypoxia modulates rapid effects of aldosterone on oxidative metabolism in human calf muscle. J Endocrinol Invest. 2001 Sep;24(8):587-97.

Healthy men: IV aldosterone at 500 µg (pharmacological dose) slightly reduces glomerular filtration rate and with inhibition of nitric oxide synthase reduces renal blood flow, triggering a mechanism for increases in blood pressure

2017. Schmidt BM, Sammer U, Fleischmann I, Schlaich M, Delles C, Schmieder RE. Rapid nongenomic effects of aldosterone on the renal vasculature in humans. Hypertension. 2006 Apr;47(4):650-5.

Healthy men: Aldosterone reduces the excretion of sodium and chloride and increases excretion of potassium and (net) acid in the urine

2018. Lemann J Jr, Piering WF, Lennon EJ. Studies of the acute effects of aldosterone and cortisol on the interrelationship between renal sodium, calcium and magnesium excretion in normal man. Nephron. 1970;7(2):117-30.

Healthy men: no obvious effect on sleep of aldosterone

2019. Born J, Zwick A, Roth G, Fehm-Wolfsdorf G, Fehm HL. Differential effects of hydrocortisone, fluocortolone, and aldosterone on nocturnal sleep in humans. Acta Endocrinol (Copenh). 1987 Sep;116(1):129-37.

Patients with disease

Orthostatic hypotension: Aldosterone reduces orthostatism

2020. Ditzel J, Hansen PH, Kemp E, Lindbjerg IF. Effect of aldosterone on orthostatic circulatory failure. Acta Med Scand. 1964 Jun;175:673-80.

Suspected coronary heart disease: IV aldosterone at supraphysiological dose (1 mg) increases systemic vascular resistance, cardiac output, and cardiac index withn 3 minutes, effect disappeared within 10 min.

2021. Wehling M1, Spes CH, Win N, Janson CP, Schmidt BM, Theisen K, Christ M. Rapid cardiovascular action of aldosterone in man. J Clin Endocrinol Metab. 1998 Oct;83(10):3517-22.

Supraventricular arrhythmias: IV aldosterone increases monophasic action potential duration within minutes in patients

2022. Tillmann HC1, Schumacher B, Yasenyev O, Junker M, Christ M, Feuring M, Wehling M. Acute effects of aldosterone on intracardiac monophasic action potentials. Int J Cardiol. 2002 Jul;84(1):33-9

Fludrocortisone treatment: 19 placebo-controlled studies – 17 in adults

Healthy adults

Young healthy women: Fludrocortisone treatment produces significant suppression of CRH secretion, trend to significant reduction of secretion of ACTH and cortisol secretion from dose 75 µg/day on

2023. Karamouzis I, Berardelli R, Marinazzo E, D'Angelo V, Zinnà D, Minetto MA, Zichi C, Fussotto B, Giordano R, Ghigo E, Arvat E. The acute effect of fludrocortisone on basal and hCRH-stimulated hypothalamic--pituitary—adrenal (HPA) axis in humans. Pituitary. 2013 Sep;16(3):378-85.

Healthy adults: Fludrocortisone treatment produces significant effects on pituitary- adrenal axias, arterial tone and intestinal sodium excretion

2024. Laviolle B, Donal E, Le Maguet P, Lainé F, Bellissant E. Low doses of fludrocortisone and hydrocortisone, alone or in combination, on vascular responsiveness to phenylephrine in healthy volunteers. Br J Clin Pharmacol. 2013 Feb;75(2):423-30.
2025. Mion D Jr, Rea RF, Anderson EA, Kahn D, Sinkey CA, Mark AL. Effects of fludrocortisone on sympathetic nerve activity in humans. Hypertension. 1994 Jan;23(1):123-30.
2026. Otte C, Jahn H, Yassouridis A, Arlt J, Stober N, Maass P, Wiedemann K, Kellner M. The mineralocorticoid receptor agonist, fludrocortisone, inhibits pituitary-adrenal activity in humans after pre-treatment with metyrapone. Life Sci. 2003 Aug 22;73(14):1835-45.
2027. Wenzl HH, Fine KD, Santa Ana CA, Porter JL, Fordtran JS. Effect of fludrocortisone and spironolactone on sodium and potassium losses in secretory diarrhea. Dig Dis Sci. 1997 Jan;42(1):119-28.

Aldosterone deficiency: Fludrocortisone produces significantly beneficial effects (reduction of sodium excretion**)**

2028. Laviolle B, Le Maguet P, Verdier MC, Massart C, Donal E, Lainé F, Lavenu A, Pape D, Bellissant E. Biological and hemodynamic effects of low doses of fludrocortisone and hydrocortisone, alone or in combination, in healthy volunteers with hypoaldosteronism. Clin Pharmacol Ther. 2010 Aug;88(2):183-90.

Orthostatic hypotension: Fludrocortisone significantly reduces orthostatic hypotension in patients

2029. Finke J, Sagemüller I. Fludrocortisone in the treatment of orthostatic hypotension: ophthalmodynamography during standing. Dtsch Med Wochenschr. 1975 Sep 5;100(36):1790-2.

Vasovagal syncope: Fludrocortisone significantly reduced the likelihood of syncope in patients

2030. Sheldon R, Raj SR, Rose MS, Morillo CA, Krahn AD, Medina E, Talajic M, Kus T, Seifer CM, Lelonek M, Klingenheben T, Parkash R, Ritchie D, McRae M; POST 2 Investigators.. Fludrocortisone for the prevention of vasovagal syncope: a randomized, placebo-controlled trial. J Am Coll Cardiol. 2016 Jul 5;68(1):1-9.

Orthostatic hypotension: Fludrocortisone does not prevent orthostatic hypotension after space flight

2031. Shi SJ, South DA, Meck JV. Fludrocortisone does not prevent orthostatic hypotension in astronauts after spaceflight. Aviat Space Environ Med. 2004 Mar;75(3):235-9.

Chronic fatigue syndrome: Fludrocortisone associated to hydrocortisone at very low doses does not significantly reduces fatigue

2032. Blockmans D, Persoons P, Van Houdenhove B, Lejeune M, Bobbaers H. Combination therapy with hydrocortisone and fludrocortisone does not improve symptoms in chronic fatigue syndrome: a randomized, placebo-controlled, double-blind, crossover study. Am J Med. 2003 Jun 15;114(9):736-41.

Chronic fatigue syndrome: Fludrocortisone alone does not significantly improve CFS symptoms

2033. Rowe PC, Calkins H, DeBusk K, McKenzie R, Anand R, Sharma G, Cuccherini BA, Soto N, Hohman P, Snader S, Lucas KE, Wolff M, Straus SE. Fludrocortisone acetate to treat neurally mediated hypotension in chronic fatigue syndrome: a randomized controlled trial. JAMA. 2001 Jan 3;285(1):52-9.
2034. Peterson PK, Pheley A, Schroeppel J, Schenck C, Marshall P, Kind A, Haugland JM, Lambrecht LJ, Swan S, Goldsmith S. A preliminary placebo-controlled crossover trial of fludrocortisone for chronic fatigue syndrome. Arch Intern Med. 1998 Apr 27;158(8):908-14.

Borderline personality disorder: Fludrocortisone at supraphysiological doses (400 µg/day) improves memory (cognitive function: verbal, visuospatial and working memory), in healthy subjects only working memory

2035. Wingenfeld K, Kuehl LK, Janke K, Hinkelmann K, Eckert FC, Roepke S, Otte C. Effects of mineralocorticoid receptor stimulation via fludrocortisone on memory in women with borderline personality disorder. Neurobiol Learn Mem. 2015 Apr;120:94-100.

Borderline personality and major depressive disorders, healthy subjects: No effect of fludrocortisone on autobiographical memory

2036. Fleischer J, Wingenfeld K, Kuehl LK, Hinkelmann K, Roepke S, Otte C. Does fludrocortisone influence autobiographical memory retrieval? A study in patients with major depression, patients with borderline personality disorder and healthy controls. Stress. 2015;18(6):718-22.

Severe traumatic brain injury: Fludrocortisone associated to hydrocortisone at low doses does not significantly prevent hospital-acquired pneumonia

2037. Asehnoune K, Seguin P, Allary J, Feuillet F, Lasocki S, Cook F, Floch H, Chabanne R, Geeraerts T, Roger C, Perrigault PF, Hanouz JL, Lukaszewicz AC, Biais M, Boucheix P, Dahyot-Fizelier C, Capdevila X, Mahe PJ, Le Maguet P, Paugam-Burtz C, Gergaud S, Plaud B, Constantin JM, Malledant Y, Flet L, Sebille V, Roquilly A; Corti-TC Study Group.. Hydrocortisone and fludrocortisone for prevention of hospital-acquired pneumonia in patients with severe traumatic brain injury (Corti-TC): a double-blind, multicentre phase 3, randomised placebo-controlled trial. Lancet Respir Med. 2014 Sep;2(9):706-16

Septic shock: Fludrocortisone associated to hydrocortisone at low doses produces beneficial effects, including better renal function

2038. Laviolle B, Annane D, Fougerou C, Bellissant E. Gluco- and mineralocorticoid biological effects of a 7-day treatment with low doses of hydrocortisone and fludrocortisone in septic shock. Intensive Care Med. 2012 Aug;38(8):1306-14.

Septic shock: Fludrocortisone associated to hydrocortisone at low doses reduces mortality

2039. Annane D, Sébille V, Charpentier C, Bollaert PE, François B, Korach JM, Capellier G, Cohen Y, Azoulay E, Troché G, Chaumet-Riffaud P, Bellissant E. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. JAMA. 2002 Aug 21;288(7):862-71. Erratum in: JAMA. 2008 Oct 8;300(14):1652. (-33% lower risk in the corticosteroid group (hazard ratio, 0.67))

Children

Children with syncope or severe presyncope: Fludrocortisone: produces significant beneficial effects to reduce syncopal symptoms; including syncope

2040. Salim MA, Di Sessa TG. Effectiveness of fludrocortisone and salt in preventing syncope recurrence in children: a double-blind, placebo-controlled, randomized trial. J Am Coll Cardiol. 2005 Feb 15;45(4):484-8.
2041. Scott WA, Pongiglione G, Bromberg BI, Schaffer MS, Deal BJ, Fish FA, Dick M. Randomized comparison of atenolol and fludrocortisone acetate in the treatment of pediatric neurally mediated syncope. Am J Cardiol. 1995 Aug 15;76(5):400-2

Thymosin alpha 1 treatment: 16 human placebo-controlled trials mentioned inPubmed

Elderly men: the immune stimuylation with thymosin-alpha-1 (1 trila, 85 patients)

2042. Gravenstein S1, Duthie EH, Miller BA, Roecker E, Drinka P, Prathipati K, Ershler WB. Augmentation of influenza antibody response in elderly men by thymosin alpha one. A double-blind placebo-controlled clinical study. J Am Geriatr Soc. 1989 Jan;37(1):1-8.

Sepsis: the improvement with thymosin-alpha-1 and ulinastatin (increased survival, improved immune parameters)(6 trials, 915 patients)

2043. Chen H1, He MY, Li YM. Treatment of patients with severe sepsis using ulinastatin and thymosin alpha1: a prospective, randomized, controlled pilot study. Chin Med J (Engl). 2009 Apr 20;122(8):883-8.
2044. Li Yumin1, Chen Hao, Li Xun, Zhou Wence, He Minyan, Chiriva-Internati M, Wachtel MS, Frezza EE. A new immunomodulatory therapy for severe sepsis: Ulinastatin Plus Thymosin {alpha} 1. J Intensive Care Med. 2009 Jan-Feb;24(1):47-53.
2045. Zhang Y1, Chen H, Li YM, Zheng SS, Chen YG, Li LJ, Zhou L, Xie HY, Praseedom RK. Thymosin alpha1- and ulinastatin-based immunomodulatory strategy for sepsis arising from intra-abdominal infection due to carbapenem-resistant bacteria. J Infect Dis. 2008 Sep 1;198(5):723-30.

2046. (+ 3 other trials mentioned in meta-analysis talks of 6 trials)
2047. Han D1, Shang W2, Wang G2, Sun L2, Zhang Y3, Wen H2, Xu L2. Ulinastatin- and thymosin α1-based immunomodulatory strategy for sepsis: A meta-analysis. Int Immunopharmacol. 2015 Dec;29(2):377-82.

Chronic obstructive pulmonary disease (acute exacerbation): the improvement with thymosin-alpha-1 (1 trial, 84 patients))

2048. Jia Z1, Feng Z, Tian R, Wang Q, Wang L. Thymosin α1 plus routine treatment inhibit inflammatory reaction and improve the quality of life in AECOPD patients. Immunopharmacol Immunotoxicol. 2015;37(4):388-92.

Chronic hepatitis B: the improvement with thymosin-alpha-1 (2 trials,

2049. Lim SG1, Wai CT, Lee YM, Dan YY, Sutedja DS, Wee A, Suresh S, Wu YJ, Machin D, Lim CC, Fock KM, Koay E, Bowden S, Locarnini S, Ishaque SM. A randomized, placebo-controlled trial of thymosin-alpha1 and lymphoblastoid interferon for HBeAg-positive chronic hepatitis B. Antivir Ther. 2006;11(2):245-53.
2050. Mutchnick MG1, Lindsay KL, Schiff ER, Cummings GD, Appelman HD, Peleman RR, Silva M, Roach KC, Simmons F, Milstein S, Gordon SC, Ehrinpreis MN. Thymosin alpha1 treatment of chronic hepatitis B: results of a phase III multicentre, randomized, double-blind and placebo-controlled study. J Viral Hepat. 1999 Sep;6(5):397-403.

+ 3 other trials mentioned in meta-analysis:

2051. Chan HL1, Tang JL, Tam W, Sung JJ. The efficacy of thymosin in the treatment of chronic hepatitis B virus infection: a meta-analysis. Aliment Pharmacol Ther. 2001 Dec;15(12):1899-905.

Chronic hepatitis C: the improvement with thymosin-alpha-1 (1 trial, 103 patients)

2052. Sherman KE1, Sjogren M, Creager RL, Damiano MA, Freeman S, Lewey S, Davis D, Root S, Weber FL, Ishak KG, Goodman ZD. Combination therapy with thymosin alpha1 and interferon for the treatment of chronic hepatitis C infection: a randomized, placebo-controlled double-blind trial. Hepatology. 1998 Apr;27(4):1128-35.

Chronic hepatitis C: no significant improvement with thymosin-alpha-1 (1 trials, 571 patients)

2053. Ciancio A1, Andreone P, Kaiser S, Mangia A, Milella M, Solà R, Pol S, Tsianos E, De Rosa A, Camerini R, McBeath R, Rizzetto M. Thymosin alpha-1 with peginterferon alfa-2a/ribavirin for chronic hepatitis C not responsive to IFN/ribavirin: an adjuvant role? J Viral Hepat. 2012 Jan;19 Suppl 1:52-9.
2054. Andreone P1, Cursaro C, Gramenzi A, Buzzi A, Covarelli MG, Di Giammarino L, Miniero R, Arienti V, Bernardi M, Gasbarrini G. A double-blind, placebo-controlled, pilot trial of thymosin alpha 1 for the treatment of chronic hepatitis C. Liver. 1996 Jun;16(3):207-10.

Cancer (overall) after radiotherapy or chemotherapy (immune depression): trend toward improvement with thymosin-alpha-1 or thymopentin (4trials, > 100 patients)

2055. Chretien PB, Lipson SD, Makuch R, Kenady DE, Cohen MH, Minna JD. Thymosin in cancer patients: in vitro effects and correlations with clinical response to thymosin immunotherapy. Cancer Treat Rep. 1978 Nov;62(11):1787-90.

Mentions 3 more placebo-controlled trials in review

2056. Wolf E1, Milazzo S, Boehm K, Zwahlen M, Horneber M. Thymic peptides for treatment of cancer patients. Cochrane Database Syst Rev. 2011 Feb 16;(2):CD003993.

Cancer (lung) after radiotherapy (immune depression): the improvement with thymosin-alpha-1 (2 trials, 63 patients))

2057. Schulof RS, Lloyd MJ, Cleary PA, Palaszynski SR, Mai DA, Cox JW Jr, Alabaster O, Goldstein AL. A randomized trial to evaluate the immunorestorative properties of synthetic thymosin-alpha 1 in patients with lung cancer. J Biol Response Mod. 1985 Apr;4(2):147-58.
2058. Schulof RS, Chorba TL, Cleary PA, Palaszynski SR, Alabaster O, Goldstein AL. -cell abnormalities after mediastinal irradiation for lung cancer. The in vitro influence of synthetic thymosin alpha-1. Cancer. 1985 Mar 1;55(5):974-83.

Sildenafil: the double-blind placebo controlled study published in Pubmed in years(s) before it was put n the market (USA°

2059. Boolell M, Gepi-Attee S, Gingell JC, Allen MJ. Sildenafil, a novel effective oral therapy for male erectile dysfunction. Br J Urol. 1996 Aug;78(2):257-61.(Twelve patients (aged 36-63 years) with male erectile dysfunction .. double-blind, randomized, placebo-controlled, crossover study)

Longevity: Higher hormone levels to live longer

Longevity: persistence of a circadian rhythm of melatonin in longevious persons

2060. Ferrari E, Cravello L, Falvo F, Barili L, Solerte SB, Fioravanti M, Magri F. Neuroendocrine features in extreme longevity. Exp Gerontol. 2008 Feb;43(2):88-94. (young, healthy old and centenarians … however only in centenarians and in young controls Urinary 6-hydroxymelatonin sulfate (aMT6s) excretion was significantly higher at night than during the day. These findings suggest that the circadian rhythm of melatonin secretion is maintained in centenarians and, based on the limitations of this study, could be considered one factor in successful aging.
2061. Cugini P, Touitou Y, Bogdan A, Auzeby A, Pellegrino AM, Fontana S, Vacca K, Siena GD, Di Rosa R, Zannella FP, Zannella P, Zannella A, Sepe FA, Sepe L. Is melatonin circadian rhythm a physiological feature associated with healthy longevity? A study of long-living subjects and their progeny. Chronobiol Int. 2001 Jan;18(1):99-107

Longevity: the association with higher MSH levels

2062. Catania A, Cutuli M, Garofalo L, Airaghi L, Valenza F, Lipton JM, Gattinoni L. Plasma concentrations and anti-L-cytokine effects of alpha-melanocyte stimulating hormone in septic patients. Crit Care Med. 2000 May;28(5):1403-7
2063. Airaghi L, Manfredi MG, Vivirito MC, Milazzo F, Lipton JM, Zanussi C. Correlation of MSH with survival Clin Immunol Immunopathol. 1993 Jan;66(1):73-9
2064. Magnoni S, Stocchetti N, Colombo G, Carlin A, Colombo A, Lipton JM, Catania A. Alpha-melanocyte-stimulating hormone is decreased in plasma of patients with acute brain injury. J Neurotrauma. 2003 Mar;20(3):251-60

Longevity: the association with thyroid hormones

2065. Razvi S, Weaver JU, Vanderpump MP, Pearce SH. The incidence of ischemic heart disease and mortality in people with subclinical hypothyroidism: Reanalysis of the Whickham Survey Cohort. J Clin Endocrinol Metab. 2010 Apr;95(4):1734-40
2066. Rodondi N, Newman AB, Vittinghoff E, de Rekeneire N, Satterfield S, Harris TB, Bauer DC. Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. Arch Intern Med. 2005 Nov 28;165(21):2460-6
2067. Cerillo AG, Bevilacqua S, Storti S, Mariani M, Kallushi E, Ripoli A, Clerico A, Glauber M. Free triiodothyronine: a novel predictor of postoperative atrial fibrillation. Eur J Cardiothorac Surg. 2003 Oct;24(4):487-92
2068. Iervasi G, G, Pingitore A, Landi P, Raciti M, Ripoli A, Scarlattini M, L'Abbate A, Donato L. Low T3 syndrome: a strong predictor of death in patients with heart disease. Circulation. 2003;107(5):708-13
2069. Kozdag G, Ural D, Vural A, Agacdiken A, Kahraman G, Sahin T, Ural E, Komsuoglu B. Relation between free triiodothyronine/free thyroxine ratio, echocardiographic parameters and mortality in dilated cardiomyopathy. Eur J Heart Fail. 2005 Jan;7(1):113-8
2070. Pingitore A, Landi P, Taddei MC, Ripoli A, L'Abbate A, Iervasi G. Triiodothyronine levels for risk stratification of patients with chronic heart failure. Am J Med. 2005 Feb;118(2):132-6

Longevity: the association with DHEA levels

2071. Fukai S, Akishita M, Yamada S, Ogawa S, Yamaguchi K, Kozaki K, Toba K, Ouchi Y. Plasma sex hormone levels and mortality in disabled older men and women. Geriatr Gerontol Int. 2011 Apr;11(2):196-203.

2072. Enomoto M, Adachi H, Fukami A, Furuki K, Satoh A, Otsuka M, Kumagae S, Nanjo Y, Shigetoh Y, Imaizumi T. Serum dehydroepiandrosterone sulfate levels predict longevity in men: 27-year follow-up study in a community-based cohort (Tanushimaru study). J Am Geriatr Soc. 2008 Jun;56(6):994-8.
2073. Cappola AR, O'Meara ES, Guo W, Bartz TM, Fried LP, Newman AB. Trajectories of dehydroepiandrosterone sulfate predict mortality in older adults: the cardiovascular health study. J Gerontol A Biol Sci Med Sci. 2009 Dec;64(12):1268-74
2074. Enomoto M, Adachi H, Fukami A, Furuki K, Satoh A, Otsuka M, Kumagae S, Nanjo Y, Shigetoh Y, Imaizumi T. Serum dehydroepiandrosterone sulfate levels predict longevity in men: 27-year follow-up study in a community-based cohort (Tanushimaru study). J Am Geriatr Soc. 2008 Jun;56(6):994-8
2075. Glei DA, Goldman N. Dehydroepiandrosterone sulfate (DHEAS) and risk for mortality among older Taiwanese. Ann Epidemiol. 2006 Jul;16(7):510-5
2076. Jankowska EA, Biel B, Majda J, Szklarska A, Lopuszanska M, Medras M, Anker SD, Banasiak W, Poole-Wilson PA, Ponikowski P. Anabolic deficiency in men with chronic heart failure: prevalence and detrimental impact on survival. Circulation. 2006 Oct 24;114(17):1829-37
2077. Mazat L, Lafont S, Berr C, Debuire B, Tessier JF, Dartigues JF, Baulieu EE. Prospective measurements of dehydroepiandrosterone sulfate in a cohort of elderly subjects: relationship to gender, subjective health, smoking habits, and 10-year mortality. Proc Natl Acad Sci USA. 2001;98(14):8145-50
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Longevity: the association with higher progesterone levels

2079. Mohr PE, Wang DY, Gregory WM, Richards MA, Fentiman IS. Serum progesterone and prognosis in operable breast cancer. Br J Cancer. 1996 Jun;73(12):1552-5

Longevity in women: the association with lower testosterone levels

2080. Suzuki M. Centenarians in Japan. Nakayamshoten Tokyo (Japan). 1995: 64-78

Longevity in men: the association with testosterone levels

2081. Khurana KK, Navaneethan SD, Arrigain S, Schold JD, Nally JV Jr, Shoskes DA. Serum testosterone levels and mortality in men with CKD stages 3-4. Am J Kidney Dis. 2014 Sep;64(3):367-74.
2082. Shoskes DA, Kerr H, Askar M, Goldfarb DA, Schold J. Low testosterone at time of transplantation is independently associated with poor patient and graft survival in male renal transplant recipients. J Urol. 2014 Oct;192(4):1168-71
2083. Kyriazis J, Tzanakis I, Stylianou K, Katsipi I, Moisiadis D, Papadaki A, Mavroeidi V, Kagia S, Karkavitsas N, Daphnis E. Low serum testosterone, arterial stiffness and mortality in male haemodialysis patients. Nephrol Dial Transplant. 2011 Sep;26(9):2971-7.
2084. Malkin CJ, Pugh PJ, Morris PD, Asif S, Jones TH, Channer KS. Low serum testosterone and increased mortality in men with coronary heart disease. Heart. 2010 Nov;96(22):1821-5.
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2089. Shores MM, Matsumoto AM, Sloan KL, Kivlahan DR. Low serum testosterone and mortality in male veterans. Arch Intern Med. 2006 Aug 14-28;166(15):1660-5.
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Higher hormone levels to live longer

Longevity: the improvement with melatonin treatment in cancer patients

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