Vitamin D Deficiency in Metabolic Syndrome Patients.

Dr. Maria Aziz¹ and Dr. K.S. Yadav².

¹Director, Pri-Med Care, Lewisville Texas 75067 USA.
²Principal, RGCP, Bhopal, INDIA.

Abstract

Vitamin D has an essential role in calcium metabolism and bone health. Vitamin D3 or cholecalciferol is synthesized from 7-dehydrocholesterol or provitamin D3, by sunlight ultraviolet radiation to the skin. 7-dehydrocholesterol is subsequently hydroxylated in the liver and then in the kidney to produce 1,25-(OH)₂D₃, the active metabolite that binds to specific receptors (VDR) in target tissues, mainly bone and intestine. Other tissues, such as the immune and cardiovascular system, have also VDR. Vitamin D deficiency can induce rickets in children and osteomalacia and osteoporosis in adults. A possible inverse association between vitamin D levels and the prevalence of metabolic syndrome has been proposed. Vitamin D deficiency increases the risk of type 1 diabetes, insulin resistance, and hypertension, key components of this syndrome. This clinical research study focuses on correlation between Vitamin D and Metabolic syndrome.

Introduction:

The prevalence of common obesity has become a public health concern in many countries as phenomenological approaches to the understanding of pathogenesis have failed to achieve any long term effect on prevention or treatment.

There is evidence for a central control mechanism which maintains body-weight to a set-point by the regulation of energy intake and energy expenditure through homeostatic pathways. It is suggested that common obesity occurs when the set-point is raised and that accumulation of fat mass functions to increase body size. Larger body size confers a survival advantage in the cold ambient temperatures and food scarcity of the winter climate by reducing surface area to volume ratio and by providing an energy store in the form of fat mass. In addition, it is suggested that the phenotypic metabolic and physiological changes observed as the metabolic syndrome, including hypertension and insulin resistance, could result from a winter metabolism which increases thermogenic capacity. Common obesity and the metabolic syndrome may therefore result from an anomalous adaptive winter response.

The stimulus for the winter response is proposed to be a fall in vitamin D. the synthesis of Vitamin D is dependent upon the absorption of radiation in the ultraviolet-B range of sunlight. At ground level at midlatitudes, UV-B radiation falls in the autumn and becomes negligible in winter. Vitamin D in the form of is the stimulus for the winter consists of an accumulation of fat mass (obesity) and the induction of a winter metabolism (the metabolic syndrome). Vitamin D deficiency can account for the secular trends in the prevalence of obesity and for individual differences in its onset and severity. It may be possible to reverse the increasing prevalence of obesity by improving vitamin D status.

In accord with this hypothesis, many studies have been done across the globe, most of which have found a negative correlation between vitamin D level and BMI. These studies were done in populations belonging to a particular region. In this context there is scarcity of data on Indian population and no such Indian study could be traced.
Present study will provide valuable information regarding relation of vitamin D level with obesity and metabolic syndrome in Indian population.

Aims & objectives:-
1. To determine mean serum 25 OH Vitamin D level in apparently healthy Indian population & to estimate prevalence of vitamin D deficiency in apparently healthy Indian population.
2. To determine mean serum 25 OH vitamin D level in patients suffering from metabolic syndrome & to estimate prevalence of vitamin D deficiency in patients of metabolic syndrome.
3. To determine correlation between metabolic syndrome & vitamin D deficiency.
4. To establish correlation between serum 25 OH vitamin D level and BMI, waist circumference, mean blood pressure, Fasting Blood Sugar, HDL cholesterol & Triglyceride level.

Material & methods:-
Study Design:-
• Cross Sectional, Case Control, Observational study.

Source of cases & controls:-
• Patients from OPD and wards of Hamidia Hospital, their attendants and other healthy volunteers.

Case:-
• One who meets IDF criteria for Metabolic Syndrome and has BMI>30.0

Control:-
• One who meets none of the five parameters of Metabolic Syndrome and has BMI<25.0

Inclusion Criteria:-
1. Willing to participate in study
2. Age between 15 to 65 years.

Exclusion Criteria
1. Suffering from any chronic renal, hepatic, cardiac, gastrointestinal, skeletal, or endocrine disease (except diabetes).
2. Suffering from any acute critical illness.
3. Those on calcium or vitamin D supplementation.

Methodology:-
Cases and controls were evaluated for following
1. Body Mass Index
2. Waist Circumference
3. Supine Blood Pressure
4. Serum HDL Cholesterol Level
5. Serum triglyceride Level
6. Serum 25OHvitD Level
Serum 25OHvitD levels were measured by Radio Immuno Assay (RIA).

Analysis of Data:-
Mean serum 25 OH vitamin D level of cases and controls were calculated and the significance of difference of two means calculated by applying unpaired student’t’ test. Correlation drawn between 25 OH vitamin D level & Body Mass index using PEARSON’s correlation coefficient.

Correlation drawn between 25 OH vitamins D level & fasting blood sugar using PEARSON’s correlation coefficient. Correlation drawn between 25 OH vitamin D level & serum HDL cholesterol level using PEARSONS correlation coefficient. Correlation drawn between 25PJ vitamin D :eve; & serum triglyceride level using PEARSONS correlation coefficient.
Observation & results:

Table 1: Comparison of mean serum 25 OH vitamin D, BMI, waist circumference, mean blood pressure, F.G.S., HDL cholesterol & serum triglyceride level between cases & controls.

|                          | Cases      | Controls   |
|--------------------------|------------|------------|
| 25 OH vitamin D (ng/ml)  | 21.34      | 26.94      |
| FBS (mg/dl)              | 106.36     | 90.64      |
| HDL Cholesterol (mg/dl)  | 47.64      | 53         |
| S. Triglycerides (mg/dl) | 158.56     | 101.44     |
| BMI (kg/m²)              | 32.988     | 21.772     |
| Waist Circumference (cms)| 101.96     | 74.04      |
| Blood Pressure (mm Hg)   | 100.276    | 90.848     |

Tabular representation mean serum 25 OH vitamin D was less in cases (21.34 ng/ml) than in control (26.94 ng/ml). Mean FBS, HDL cholesterol, Triglycerides, BMI< Waist circumference & blood pressure in cases was 106.36 mg/dl, 47.64 mg/dl, 158.56 mg/dl, 32.988 kg/m², 101.96 cms & 100.276 mm Hg respectively while those in controls was 90.64 mg/dl, 53 mg/dl, 101.44 mg/dl, 21.772 kg/m², 74.04 cms & 90.848 mm Hg respectively.

Graph 1
Comparison of mean serum 25 OH vitamin D, BMI< Waist circumference, Mean Blood Pressure, F.B.S., HDL Cholesterol & Serum Triglyceride Level between cases & controls.
Graphic representation-mean serum 25 OH vitamin D was less in cases (21.34 ng/ml) than in controls (26.94 ng/ml). Mean FBS, HDL cholesterol, Triglycerides, BMI< Waist circumference & flood pressure in cases was 106.36 mg/dl, 47.64 mg/dl, 158.56 mg/dl, 32.988 kg/m², 101.96 cms & 100.276mm Hg respectively while those in controls was 90.64 mg/dl, 101.44 mg/dl, 21.772 kg/m², 74.04 cms & 90.848 mm Hg respectively.

Table -2Comparison of mean serum 25 OH vitamin D Level between males & females

| Mean Serum 25 OH vitamin D level between Males & Females (in ng/ml) |
|-----------------|-----------------|
| Males           | 22.26           |
| Females         | 23.2            |

Mean serum 25 OH vitamin D level in males was 22.26 ng/ml and in females was 23.2 ng/ml. The difference was not statistically significant.3

Table -3Comparison of mean serum 25 OH vitamin D in cases & controls

| Study Group | Mean Serum 25 OH Vitamin D Level (ng/ml) |
|-------------|------------------------------------------|
| Cases       | 21.34                                    |
| Controls    | 26.94                                    |
Mean serum 25 OH vit D level in cases (21.34 ng/ml) was less than those in controls (26.94 ng/ml). The significance of difference between both means was calculated using students unpaired ‘t’ test. ‘t’ value was 2.02 which was significant at 5% level but was not significant at 1% level (0.05>p<0.01).

Table – 4
Comparison of 25 OH vitamin D deficiency in cases & control

| Study Group | No.(%) of subjects deficient in 25 OH Vitamin D |
|-------------|---------------------------------------------|
| Cases       | 11 (44%)                                    |
| Controls    | 6 (24%)                                     |

11 cases out of 25 (44%) and 6 controls out of 25(24%) were 25 OH vitamin D deficient. This categorical data was assessed by chi-square test, which was not statistically significant (p>0.01)

Inverse relation between serum 25 OH vit D & serum triglyceride level. PEARSONS correlation coefficient between serum 25 OH vit D & serum triglyceride level was -0.3824 and p>0.01.

Direct relation between serum 25 OH vit D & serum HDL cholesterol level. PEARSONS correlation coefficient between serum 25 OH vit D & serum HDL cholesterol level was 0.2266 and p>0.01.

Inverse relation between serum 25 OH vit D & FBS. PEARSONS correlation coefficient between serum 25 OH vit D & FBS is -0.3854 and p<0.01.

Inverse relation between serum 25 OH vitamin D & waist circumference. PEARSONS correlation coefficient between serum 25 OH vit D & waist circumference was -0.54 and p<0.01.

Inverse relation between serum 25 OH vitamin D &BMI. PEARSONS correlation coefficient between serum 25 OH vit D &BMI was -0.56 and p<0.01.

Inverse relation between serum 25 OH vitamin D &Mean Supine B.P. PEARSONS correlation coefficient between serum 25 OH vit D &Mean Supine B.P. was -0.3838 and p<0.01.

Discussion:-
For the last two to three decades vitamin D deficiency has been associated with obesity and metabolic syndrome. Many studies have been done to establish association between vitamin D levels and occurrence of obesity/metabolic syndrome. According to a publication 22 years back[168]. Body weight increases with higher latitude with lower altitude ad in winter. Different explanations exist for all three associations but vitamin D provides a parsimonious explanation as vitamin D decreases with higher latitude, lower altitude and with winter. In a south Carolina study[169] all obese subjects had vitamin D levels (<2.2 ng/ml) lower than non obese subjects (>8ng/ml). These two studies suggested a inverse relation between vitamin D level and obesity but no causal relationship was explained and no insight into the pathogenesis was made. However, these landmark publications set the stage for further studies to establish this apparent relationship between vitamin D level and obesity.

In present study patients of metabolic syndrome had lower serum 25 OH vitamin D levels than healthy controls the difference was statistically significant at 5% level 44% of patients of metabolic syndrome were vitamin D deficient as compared t 24% of healthy controls. These results were similar to previous studies of Reis et al[79], Lu et al[80] & Kim et al[81].
Serum 25 OH vitamin D had inverse correlation with BMI. The correlation coefficient was -0.56 and the association was statistically significant at 1% level. This is similar to findings of two previous studies done in Norway by Kamycheva et al[94] & Lagunova et al[95].

Serum 25 OH vitamin D had inverse correlation with waist circumference. The correlation coefficient was -0.54 and the association was statistically significant at 1% level. This correlates well with the study done by Elizondo et al[96].

Serum 25 OH vitamin D had inverse correlation with FBS, mean B.P. and serum triglyceride level & a direct correlation with HDL cholesterol. The Pearson's correlation coefficient was -0.3854, -0.3838, -0.3824 & 0.2266 respectively. The association of FBS, mean B.P. and serum triglyceride level with serum 25 OH vitamin D level was significant at 1% level which correlates well with the studies of Kamycheva et al[94] & Lagunova et al[95]. The correlation between HDL cholesterol & serum 25 OH vitamin D level could not reach statistical significance which contrasts with the study of Kamycheva et al[94] & Lagunova et al[95], the reason for this contrast could be a small study group of present study (which results in a lower ‘t’ value for a particular correlation coefficient).

Present study suggests that 24% of apparently healthy Indian people have lower than reference serum 25 OH vitamin D level while 40% of patients of metabolic syndrome have vitamin D deficiency, however the study group is too small to draw inference for a vast country like India & these findings need confirmation by large scale study involving various population groups across the country. Whether this incidentally detected deficiency is clinically significant or not, can’t be said at this time & weather it should be corrected by vitamin D supplementation is not clear but probably it warrants a low threshold for checking serum vitamin D levels, should the clinical situation suggests vitamin D deficiency. Further prospective studies are needed to make situation clearer.

Serum 25 OH vitamin D levels were significantly low in patients of metabolic syndrome. This observation is consistent with previous studies done elsewhere. Weather it is low 25 OH vitamin D level contributing to metabolic syndrome or is it the other way round is not clear. To establish a cause and effect relationship, further prospective studies are required.

If prospective studies reveals that vitamin D deficiency is causally related to obesity and metabolic syndrome, then it might be possible to reduce the prevalence of obesity and metabolic syndrome globally by vitamin D supplementation.

Summary & conclusion:
In present study, patients of metabolic syndrome were found to have lower levels of 25 OH vitamin D levels than healthy population (mean serum level 21.34 ng/ml for cases & 26.94 ng/ml for controls, 44% of cases had vitamin deficiency as compared to 24% in controls). Serum 25 OH vitamin D level correlates inversely with BMI, waist circumference, FBS, serum triglyceride levels & mean supine B.P. The correlation of 25 OH vitamin D with waist circumference, BMI, FBS, Mean supine BP and serum triglycerides was statistically significant level. About 24% of healthy apparently healthy Indian population has lower than reference range 25 OH vitamin D level in this study while 40% of patients of metabolic syndrome had vitamin D deficiency the difference was not significant statistically, probably because of small study group.

Because of small study number of subjects included in this study, it is difficult to draw inference for a large population like India. Thus, a large study involving various population groups around the country is required to estimate true prevalence of vitamin D deficiency in India. If further studies reveal similar figures, then it might be possible to diagnose a large number of persons with subclinical vitamin D deficiency. Weather these persons with subclinical vitamin D deficiency will benefit from vitamin D supplement requires interventional prospective studies. It is thus concluded that vitamin D deficiency is associated with obesity & metabolic syndrome. However, a cause & effect relation cannot be established in this study & whether or not vitamin D supplementation can help reducing weight loss requires large randomized prospective studies.
Bibliography
1. Walter F., PhD. Boron (2003) “The Parathyroid Glands and Vitamin F”. Medical Physiology: A Cellular and Molecular Approach. Elsevier/Saunders. P. 1094.ISBN 978-1-4160-2328-9.
2. Institute of Medicine (IOM) Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride (1997) Access date: 2010-04-14.[1].
3. Joshi, D; Center, J; Eisman, J (2010). “Vitamin D deficiency in adults”. Australian Prescriber 33 (4) : 103-6.
4. Adams, J.S.; Hewison, M. (2010). “Update in Vitamin D”. Journal of Clinical Endocrinology & Metabolism 95 (2): 471-8 doi: 10.1210/jc. 2009-1773. PMID 20133466.
5. “Dietary Supplement Fact Sheet: Vitamin D”. National Institute of Health Office of Dietary Supplements.Retrieved 2010-04-11.
6. Dorland’s Illustrated Medical Dictionary, under Vitamin (Table of Vitamins).
7. History of Vitamin D University of California, Riverside, Vitamin D Workshop.
8. About Vitamin D Including Sections: History, Nutrition, Chemistry, Biochemistry, and Diseases. University of California Riverside
9. Vitamin D[2] – MayoClinic.com
10. Holick, MF (2004). Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease and osteoporosis". The American Journal of Clinical Nutrition 79 (3): 362-71 PMID 14985208.
11. UNRAVELING THE ENIGMA OF VITAMIN D U.S. Retrieved 2010-03-25.
12. “Windaus biography at” Nobelprize.org. 1959-06-09. Retrieved 2010-03-25.
13. Arvids A. Zeidonis; Mowery, David C; Nelson, Recharl R; Bhaven N. Sampat (2004). Irony tower and industrial innovation: university industry technology transfer before and after the Bayh-Dole Act in the United States. Stanford, Calif: Stanford Business Books. Pp. 39-40. ISBN 0-8047-4920-5.
14. Marshall, James (2005). Elbridge A. Stuart Founder of the Carnation Company. Kessinger Publishing P. 235. ISBN 1417988835.
15. Holick, MF (2004). “Sunlight and Vitamin D for bone health and prevention of autoimmune disease, cancers, and cardiovascular disease". The American Journal of clinical nutrition 80 (6 Suppl): 167S-88S. PMID 15585788. Free full text.
16. PubMed U.S. National of Medicine.
17. Vitamin D the Physicians Desk Reference. 2006 Thompson Healthcare.
18. Bijlsma, MF; Spek, CA; Zivkovic, D; Van De Water, S; Rezaee, F; Peppelenbosch, MP (2006). Repression of smootherned by Patched dependent (pro) vitamin D3 secretion. PLoS biology 4 (8); e232. Doi: 10.1371/journal. Pbio. 0040232. PMID 16895439.
19. Hedgehog signaling and Vitamin D Medscape.com. 2009-12-18. Retrieved 2010-03-25.
20. Schoenmakers, I; Goldberg, FR; Prentice, A (2008) “Abundant sunshine and vitamin D deficiency.”. The British journal of nutrition 99(6): 1171-3. Doi: 10.1017/S000711450889662 PMID 18234141.
21. Grant, WB; Holick, MF (2005) “Benefits and requirements of vitamin D for optimal health: a review” Alternative Medicine review 10 (2): 94-111. PMID 15989379.
22. Lerch, C; Meissner, T; Lerch, Christian (2007). “Interventions for the prevention of nutritional rickets in term born children” Cochrane database of systematic reviews (Online) (4): CD006164. Doi: 10.1002/14651858 CD0016164. Pub2 PMID 19743890.
23. Zargar, A.H.; Mithal, A; Wani, AI; Laway, BA; Masoodi, SR; Bashir, MI; Ganie, MA (2000) “Pseudovitamin D deficiency rickets-a report from the Indian subcontinent” Postgraduate Medical Journal 76(896): 369 Doi: 10.1017/S0007114500003949. PMID 10824056.
24. Gibbs, D (1994) “Rickets and the crippled child: an historical perspective”. Journal of the Royal Society of Medicine 87(12): 729-32. PMID 7503834.
25. Dunnigan, M (2003) “Commentary: John Snow and alum-induced rickets from adulterated London bread: an overlooked contribution to metabolic bone disease”Intentional journal of epidemiology 32 (3): 304 1. Doi: 10.1093/ije/dyg 160. PMID 12777415.
26. Pilleggi, V; De Luca, HF; Steenbock, H (1955). “The role of vitamin D and intestinal phytate in the prevention of rickets in rats on cereal diets*1” Archives of Biochemistry and Biophysics 58 (1): 194. Doi: 10.1016/0003-9861 (55)90106-5. PMID 13259690.
27. Ford, JA; Colhoun, EM; McIntosh, WB; Dunnigan, MG (1972). “Biochemical response of late rickets and osteomalacia to a chupatty-free diet” British medical journal 3 (5824): 446-7. Doi: 10.1136/bmj.3.5824.446. PMID 5069221.
28. Rajakumar, K (2003). “Vitamin D, cod-liver oil, sunlight, and rickets a historicalperspective”. Pediatrics 112 (2): e1325.doi: 10.1542/peds.112.2.e.132 PMID 12897318.
29. Oramasionqu, GE; Thacher, TD; Pam, SD; Pettifor, JM; Abrams, SA (2008). “Adaptation of calcium absorption during treatment of nutritional rickets in Nigerian children”. The British journal of nutrition 100(2): 3879. Doi: 10.1017/S0007114507001233. PMID 18197991.

30. Fischer; PR; Rahman, A; Cimma, JP; Kyaw-Myint, TO; Kabir, AR; Talukder, K; Hassan, N; Manaster, BJ et al. (1999) “Nutritional rickets without vitamin D deficiency in Bangladesh”. Journal of tropical pediatrics 45 (5): 291-3 doi:10.1093/tropej/45.5.291. PMID 10584471.

31. Dunnigan, MG; Henderson, JB (1997). “An epidemiological model of privational rickets and osteomalacia”. The proceedings of the nutrition society 56 (3): 939-56. PMID 9483661.

32. Robertson, I; Ford, JA; McIntosh, WB; Dunnigan, MG (1981). “The role of cereals in the aetiology of nutritional rickets: the lesson of the Irish National Nutrition Survey 1943-8”. The British Journal of Nutrition 45(1): 17-22. Doi: 10.1079/BJN19810073. PMID 6970590.

33. Clements, M.R. (1989). “The problem of rickets in UK Asians” Journal of Human Nutrition and Dietetics 2: 105 doi: 10.1111/j.1365-277X.1989.tb00015.x.

34. Pettifor, JM (2004). “Nutritional rickets: deficiency of vitamin, calcium, or both?” The American Journal of clinical nutrition 80 (6 Suppl): 172SS-95. PMID 15585795.

35. Dunnigan, MG; Henderson, JB (1997). “An epidemiological model of privational rickets and osteomalacia”. The Proceedings of the Nutrition Society 56 (3): 939-56. PMID 9483661.

36. Dunnigan, Mathew G.; Henderson, Janet B.; Hole, David J.; Mawer, E. Barbara; Berry, Jacqueline L. (2007). “Meat consumption reduces the risk of nutritional rickets and osteomalacia”. British Journal of Nutrition 94(6): 983-91. Doi: 10.1079/BJN20051558. PMID 16351777.

37. “US National Institutes of Health National cancer Institute” Science. education.nih.gov. Retrieved 2010-08-24.

38. Weick, MT (1967). “A history of rickets in the United States” The American Journal of clinical nutrition 20 (11): 1234-41 PMID 4862158.

39. Gerrison, R., Jr., Somer, E., The nutrition desk reference (1997).

40. E. Melanie DuPuis., Nature's Perfect Food : How Milk Became American’s Drink (2002) ISBN 978-0814719381.

41. Teegarden, D; Lyle, RM; Proulx, WR; Johnston, CC; Weaver, CM (1999) “Previous milk consumption is associated with greater bone density in young women”. The American Journal of clinical nutrition69 (5): 1014-7. PMID 10232644.

42. Holick, MF (2003) “Vitamin D: A millennium perspective”. Journal of cellularbiochemistry 88 (2): 296-307. doi : 10.1002/jcb.10338. PMID 12520530.

43. Stewart B. Leavitt. “Vitamin D: A Neglected Analgesic for Chronic Musculoskeletal Pain” Pain-Topics.org retrieved 2009-03-25.

44. Straube, S; Andrew Moore, R; Derry, S; McQuay, HJ (2009) “Vitamin D and chronicpain” Pain 141 (12) : 103. Doi: 10.1016/j.pain.2008.11.010. PMID 1984336.

45. Amor, KT; Rashid, RM; Mirmirani, P (2010). “Does D matter? The role of vitamin D in hair disorders and hair follicle cycling” Dermatology online journal 16 (2): 3. PMID 20178699.

46. Melamed, ML; Muntner, P; Michos, ED; Uribarri, J; Weber, C; Sharma J; Raggi, P (2008) “Serum 25-Hydroxyvitamin D levels and the prevalence of peripheral arterial disease: results from NHANES 2001 to 2004” Arteriosclerosis, thrombosis, and vascular biology28 (6): 1179-85. doi : 10.1161/ATVBHA.108.165886. PMID 18417640.

47. Evatt, ML; Delong, MR; Khazai, N; Rosen, A; Triche, S; Tangpricha, V (2008). “Prevalence of vitamin D insufficiency in patients with Parkinson disease and Alzheimer disease”. Archives of neurology 65 (10): 1648-52. doi : 10.1001/archneur.65.10.1348. PMID 18852350.

48. Pittas, AG; Chung, M; Trikalinos, T; Mitri, J; Brendel, M; patel, K; Lichtenstein, AH; Lau, Jet al. (2010). “Systematic review : Vitamin D and cardiovascular outcomes” Annals of internal medicine 152(5): 307-14. doi : 1059/0003-4819-152-5-201003020-00009 (inactive 2010-03-25). PMID 201941237.

49. AzminaGovindji RD. “When its sunny, top up your vitamin D” Thelsmali.org. Retrieved 2010-07-01.

50. Ford, Loretta; Graham, Valerie; Wall, Alan; Berg, Jonathan (2006) “Vitamin D concentrations in an UK inner-city multicultural outpatient/ population”. Annals of Clinical Biochemistry (The Royal Society of Medicine Press Ltd.) 43 (6): 468-473 doi : 10.1258/000456306778904614.

51. Signorello, LB; Williams, SM; Zheng, W; Smit, JF; Long, J; Cai, Q. Hargreaves, MK; Hollis, BW et at. (2010). “Blood vitamin D levels in relation to genetic estimation of African ancestry”. Cancer epidemiology, biomarkers &prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of preventive Oncology 19 (9):2325-31 doi : 10.1158/1055-9965.EPI-10-0482. PMID 20647395.
52. Aloia, JF; Chen, DG; Chen, H (2010). “The 25 (OH) D/PTH Threshold in Black Women”. The Journal of clinical endocrinology and metabolism 95 (11) : 5069-73 doi : 10.1210/jc.2010-0610 PMID 20685862.

53. Wang, TJ; Zhang, F; Richards, JB; Kestenbaum, B; Van Meurs, JB; Berry, D; Kiel, DP; Streiten, EA et al. (2010) “Common genetic determinants of vitamin D insufficiency: a genome-wide association study” Lancet 376 (9736) : 180-8doi : 10.1016/S0140-6736(10)60588-0 PMID 20541252.

54. Bouillon, R (2010) “Genetic and environmental determinants of vitamin D status” Lancet 376 (9736) : 148-9 doi : 10.1016/S0140-6736(10)60635-6 PMID 20541253.

55. Wang, L; Manson, JE; Song, Y; Sesso, HD (2010) “Systematic review : Vitamin D and calcium supplementation in prevention of cardiovascular events” Annals of internal medicine 152 (5) : 315-23 doi 10.1059/0003-4819-152-5-201003020-00010 (inactive 2010-03-25) PMID 20194238.

56. Vitamin D at the Marck Manual for Healthcare Professionals.

57. Lucas, JeenyA.; Bolland, Mark J; Grey, Andrew B; Ames, Ruth W.; Mason, Barbara H.; Horne, Anne M.; Gamble, Greg D; Reid, Ian R. (2005) “Determinants of Vitamin D status in older women living in a subtropical climate”. Osteoporosis international 16 (12) : 1641-8 doi : 10.1007/S00198-005-1888-2. PMID 16027959.

58. Bolland, M.J.; Grey, A.B.; Ames, R.W.; Mason, B.H.; Morne, A.M.; Gamble, G.D.; Reid, I.R. (2006). “Determinants of Vitamin D status in older men living in a subtropical climate” Osteoporosis International 17(12): 1742-8 doi : 10.1007/S00198-006-0190-2 PMID 16932872.

59. Field, A.E.; Coakley, EH; Must, A; Spadano, JL; Laird, N; Dietz, WH; Rimm, E; Colditz, GA (2001) “Impact of overweight on the risk of developing common chronic diseases during a 10 year period” Archives of Internal Medicine 161 (13). 1581-6 doi : 10.1001/archinte.161.13.1581. PMID 11434789.

60. Wortsman, J; Matsuoka, LY; Chen, TC; Lu, Z; Holick, MF (2000) “Decreased bioavailability of vitamin D in obesity”, The American journal of clinical nutrition 72 (3): 690-3. PMID 10966885.

61. Binkley N.; Novotny, R; Krueger, D; Kawahara, T; Daida, YG, Lensmeyer, G; Hollis, BW; Drezner, MK (2007) “Circulating vitamin D3 and 25-hydroxyvitamin D in humans: An important tool to define adequate nutritional vitamin D status”. The Journal of Steroid Biochemistry and Molecular Biology 103 (3-5): 631-4 doi: 10.1016/j.jsbmb.2006.12.066 PMID 17218096.

62. Melamed, M.L.; Michos, E.D.; Post, W.; Astor, B (2008) “25- Hydroxyvitamin D Levels and the Risk of Mortality in the General Population”. Archives of Internal Medicine 168 (15): 1629-37 doi: 10.1001/archinte.168.15.1629 PMID 18695076.

63. Michaelsson, K; Baron, JA; Sneliman, G; Gedeborg, R; Byberg, L; Sundstrom, J; Berglund, L; Arnlov, J et al. (2010) “Plasma Vitamin D and mortality in older men: a community based prospective cohort study”. The American Journal of clinical nutrition 92 (4) : 841-8 doi : 10.3945/ajcn.2010.29749. PMID 20720256.

64. Melamed, M.L.; Michos, E.D.; Post, W.; Astor, B. (2008). “25-Hydroxyvitamin D Levels and the Risk of Mortality in the General Population”. Archives of Internal Medicine 168 (15): 1629-37 doi 10.1001/archinte.168.15.1629 PMID 18695076.

65. Michaelsson, K; Baron, JA; Sneliman, G; Gedeborg, R; Byberg, L; Sundstrom, J; Berglund, L; Arnlov, J et al. (2010) “Plasma Vitamin D and mortality in older men: a community based prospective cohort study”. The American Journal of clinical nutrition 92 (4) : 841-8 doi : 10.3945/ajcn.2010.29749. PMID 20720256.

66. Tuohimaa, Pentti (2009). “Vitamin D and aging”. The Journal of Steroid Biochemistry and Molecular Biology 114 (1-2): 78-84 doi : 10.1016/j.jsbmb. 2008.12.020. PMID 19449397.

67. Keisala, Tiina; Minasyan, Anna; Lou, Yan-Ru; Zou, Jing; Kaleuff, Allan V.; Pyykko, Ilmari; Tuohimaa, Pentti (2009). “Premature aging in vitamin D receptor mutant mice”. The journal of steroid biochemistry and molecular biology 115(3-5): 91-7. Doi: 10.1016/j.jsbmb.2009.03.007 PMID 19500727.

68. Tuohimaa, P.; Keisala, T.; Minasyan, A.; Cachat, J.; Kaluuff, A. (2009). “Vitamin D, nervous system and aging”Psychoneuroendocrinology 34; S278-86 doi : 10.1016/j.psyneuen.2009.07.003 PMID 196600871.

69. Manya, H; Akasaka-Manya, K.; Endo. T.(2010) “Klotho protein deficiency and aging”. Geriatrics & Gerontology International 10:S80 doi : 10.111/j.1447-0594.2010.00596.x.PMID 20590845 edit/

70. Michaelsson, K; Baron, JA; Sneliman,k G; Gedeborg, R; Byberg, L; Sundstrom, J; Berglund, L; Arnlov, J et al. (2010). “Plasma vitamin D and mortality in older men: a community based prospective cohort study”. The American Journal of Clinical Nutrition 92(4): 841-8 doi : 10.3945/ajcn.2010.29749 PMID 20720256.

71. Medici, D.; Razzaque, M.S.; Deluca, S.; Rector, T.L.; Hou, B.; Kang, K.; Goetz, R.; Mohammadi, M. et al. (2008) “FGF-23-Klotho signaling stimulates proliferation and prevents vitamin D0 induced apoptosis”. The Journal of Cell Biology 182: 459 doi: 10.1083/jcb.200803024 edit.
73. Harrisons Textbook of Internal Medicine 17th edition-chapter 74 (2) Harrisons Textbook of Internal Medicine 17th edition-chapter 236 Jam.

74. CollNutr. 2002 Apr; 21 (2): 152s-155s.

75. Can J Public Heath, 2004 May-June:95(3): 179-83, J Periodontal 2003 May; 74(5):610-5, J Clin. EndocrinolMetab. 2004 June; 89(6)2583-9.

76. J Nutr. 137.2437-2442 Nov., 2007, Lisa M BodnarJanor M Cator, James M Robets, Hyagriv N Simhan.

77. Asia Pac J Clin. Nutr. 2004;13(suppl): 582. Asia Pac J Clin. Nutr.2004;13(suppl)565.

78. Asia Pac J Clin. J Nutr. 2004;13(suppl):582, Asia Pac J Clin, Nutr.2004;13(suppl)556.

79. J Nutr. 2003 Jan;133(1):103-6, E.Kamycheva, R.M. Joakimsen R. Jorde.

80. Eur Endocrinol. 2004 Aug;151(2):167-72.

81. Eur J endocrinol 2008 Jul;159(1):41-8 Epub2008 Apr21.

82. Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant D. For the Conference Participants. Definition of metabolic syndrome; report of the National, Heart, Lung, and Blood Institute/American Heart Association conference on scientific aspects related to definition. Circulation. 2004;109:433-438.

83. American Heart Associations description of Syndrome X

84. Kogiso T. Moriyoshi Y, Shimizu S. Nagahara H. Shiratori K (March 2009) “High-sensitivity C-reactive protein as a serum predictor of nonalcoholic fatty liver disease based on the Alkaike Information Criterion scoring system in the general Japanese population”. J Gastroenterol 44(4): 131. doi :10.1007/s00535-009-0002-5. PMID 19271113.

85. Joslin EP. The prevention of diabetes mellitus.JAMA 1921; 76:79-84.

86. Kylin E. (Studies of the hypertension – hyperglycemia-hyperuricemia syndrome) (Ferman). Zentralbl Inn Med 1923;44: 105-27.

87. Vague J. La differantiation sexuually, facteur determinant des forms de l’obesitePresse Med 1947;30:339-40.

88. Avogadro A, Crepaldi G, Enzi G, Tiengo A. Associazione di iiperlipidemia, diabetemellito e obesita di mediogrado. ActaDiabetolLat1967;4:572-590.

89. Haller H. [Epidemiology and associated risk factors of jyperlipoproteinemia] (German). Z Gesamte Inn Med1997;32(8):124-8. PMID 883354.

90. Singer P. [Diagnosis of Primary hyperlipoproteinimias] (German) Z Gesamte Inn Med 1977;32(9): 129-33. PMID 906591.

91. Phillips GB. Sex hormones, risk factors and cardiovascular diseases. Am J Med 1978;65:7-11. PMID 356599.

92. Phillips GB. Relationship between serum sex hormones and glucose; insulin, and lipid abnormalities in men with myocardial infarction. Proc Natl AcadSci US A 1977;74:1729-1733. PMID 193114.

93. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes 1988;37:1595-607. PMID 3056758.

94. J Nutr. 2003 Jan; 133(1): 103-6 E Kamycheva, R.M. Joakimsen, R. Jorde.

95. Anticancer Res. 2009 Sep; 29(9): 3713-20 Lagunova Z, Porojniku AC, Lindberg F, Hexeberg S, Moan J.

96. Obesity (silver spring) 2010 sep;6, E Kamycheva, R.M. Joakimsen, R. Jorde.

97. VITAMIN D, WHO 2000 p.6.

98. Haslam DW, James WP (2005) “Obesity”. Lancet 366 (9492): 1197-1209 doi :10.1016/S0140-6736(05)67483-1. PMID 16198769.

99. VitaminD, WHO 2000 p.9.

100. Sweeting HN (2007) “Measurement and definitions of obesity in childhood and adolescence: A filed guide for the uninititated” Nutr. J: 32. doi:10.1186/1475-2891-6-32. PMID 17963490,PMC 2164947.

101. NHLBI P. xiv

102. Gray DS, Fujioka K. (1991) “Use of relative weight and Body Mass Index for the determination of adiposity” J ClinEpidemiol 44 (6): 545-50 doi:10.1016/0895-4356(91)90218-X, PMID 2037859.

103. “Healthy Weight: Assessing Your Weight : BMI : about BMI for Children and Teens”. Center for disease control and prevention Retrieved April 6, 2009.

104. Flegal KM, Ogden CL, Wei R, Kuczmarski RL, Johnson CL (June 2001), “Prevalence of overweight in US children comparison of US growth charts from the Centers for Disease Control and Prevention with other reference values for body mass index” Am J. Clin. Nutr. 73 (6): 1086-93. PMID 11382664.

105. Sturm R (July 2007) “Increases in morbid obesity in the USA 2000-2005” Public Health 121 (7) : 492-6 doi:10.1016/j.puhe.2007.01.006. PMID 17399752.

106. Kanazawa M, Yoshiike N, Osaka T, Numba Y, Zimmet P, Inoue S (December 2002). “Criteria and classification of obesity in Japan and Asia-Oceania”. Asia Pac J ClinNutr 11 Suppl8 : S732-S737 doi 10/1046j.1440-6047.11s8.19.x. PMID 12534701.
107. Bei-Fan Z; Cooperative Meta Analysis Group of Working Group on Obesity in China (December 2002) “Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults: study on optimal cut-off points of body mass index and waist circumference in Chinese adults”. Asia Pac J Clin Nutr 11 Suppl:8:S685-93 doi : 10.1046/j.1440-6047.11.s8.9.x. PMID 12534691.
108. Berrington de Gonzalez A, Hartge P, Cerhan JR, et al. (December 2010). “Body-mass index and mortality among 1.46 million white adults”. N. Engl. J. Med. 363(23): 2211-9 doi: 10.1056/NEJMoa100367. PMID 2121834.
109. Mokdad AH, Marks JS, Stroup DF, Gerberding JL (March 2004) “Actual causes of death in the United States, 2000” (PDF). JAMA291 (10).
110. Allison DB, Fontaine KR, Manson JE, Stevens J, VanItallie TB (October 1999). “Annual deaths attributable to obesity in the United States” JAVA 282 (16): 1530-8 doi: 10.1001/jama.282.16.1530. PMID 10546692.
111. Whitlock G, Lweington S, Sherliker P, et al. (March-2009) “Body Mass index and cause-specific mortality in 900000 adults: collaborative analyses of 57 prospective studies”. Lancet 373 (9669): 1083-96 doi : 10.1016/S0140-6736(09)60318-4 PMID 19299006.
112. Calle EE, Trun MJ, Petrelli JM< Rodriguez C, Heath CW (October 1999). “Body-mass index and mortality in a prospective cohort of U.S. Adults”. N. Engl. J. Med. 341 (15) : 1097-105 doi : 10.1056/NEJM199910073411501 PMID 10511607.
113. Pischon T, Boeing H, Hoffmann K, eta l. (November 2008) “General and abdominal adiposity and risk of death in Europe” N. Engl. J. Med. 359 (20) :2105-20 doi : 10.1056/NEJMoa0801891 PMID 19005195.
114. Manson JE, Willett WC, Stampfer MJ, et al. (1995) “Body weight and mortality among women” N. Engl. J. Med. 333(11): 677-85 doi : 10.1056/NEJM199500914333101 PMID 7637744.
115. Tsigosa Constantine; Mainer, Vojtech; BGasdevant, Arnaud; Finer, Nick; Fried, Martin; Mathus-Vliegen, Elisabeth; Micie, Dragan; Maislos, Maximo et al. (2008). “Management of Obesity in Adults : European Clinical Practice Guidelines”. The European Journal of Obesity 1 (2): 106-16, doi : 10.1159/000126822. PMID 20054170.
116. Fried M,Hainer V, Basdevant A, et al. (April 2007) “Inter-disciplinary European guidelines on surgery of severe obesity”. Int J Obes (Lond) 31 (4):569-77. Doi : 10.1038/sj.ijo.0803560 PMID 17325689.
117. Peeters A, Barendregt JJ, Willkens F, Mackenbach JP, AI Mamun A, Bonneux L (January 2003). “Obesity and severe obesity”. Int J Obes (Lond) 31 (4):569-77. Doi : 10.1038/sj.ijo.0803560 PMID 17325689.
118. Grundy SM (2004) “Obesity, metabolic syndrome, and cardiovascular disease” J. Clin. EndocrinolMetab. 89(6): 2595-600 doi : 10.1210/jc.2004-0372 PMID 15181029.
119. Seidell 2005 p.9
120. Bray GA (2004) “Medical consequences of obesity” J. Clin. Endocrinol.Metab. 89 (6): 2583-9 doi : 10.1210/jc.2004-0355 PMID 15181027.
121. Shoelson SE, Herrero L, Naaz A (May 2007) “Obesity, Inflammation, and insulin resistance” Gastroenterology 131 (6): 2169-80 doi : 1053/j.gastro.2007.03.059. PMID 17498510.
122. Shoelson SE, Lee J, Goldfine AB (July 2006) “Inflammation and insulin resistance” J.Clin. Invest. 116(7): 1793-801 doi : 10.1172/JCI29069. PMID 16823477, PMC 1483173.
123. Dentali F, Squizzato A, Agen W (July 2009). “The metabolic syndrome as a risk factor for venous and arterial thrombosis” SeminThromb. Hemost. 35 (5): 451-7 doi : 10.1055/s – 0029-1234140. PMID 19739035.
124. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L, INTERHEART study investigators (2004) “Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study)” : Case-control study Lancet 364 (9438): 937-52 doi : 10.1016/S0140-6736(04)17018-9 PMID 15364185.
125. Darvall KA, Sam RC, Silverman SH, Bradbury AW, Adam DJ (February 2007) “Obesity and thrombosis” Eur J VascEndovascSurg 33(2) 223-33 doi :10.1016/j.ejvs.2006.10.006 PMID 17185009.
126. Yosipovitch G, DeVore A, Dawn A (June 2007)“Obesity and the skin: skin physiology and skin manifestations of obesity”. J. Am. Acad. Dermatol. 56 (6) : 9001-16; quiz 917-20 doi : 10.1016/j.jaad.2006.12.004 PMID 17504714.
127. Hahler B (June 2006). “An overview of dermatological conditions commonly associated with the obese patient” Ostomy Wound Manger 52 (6) : 34-6, 38, 40 passim. PMID 16799182.
128. Arendas K, Qui Q, Gruslin A (June 2008). “Obesity in pregnancy : pre-conceptional to postpartum consequences” J. ObstetGynaecol Can 30 (6) 477-88. PMID 18611299.
129. Anand G, Katz PO (2008)“Gastroesophageal reflux disease and obesity” Rev GastroenterolDisord 8 (4) : 233-9. PMID 19107097.
130. Harney D, Patijn J (2007) “Meralgia paresthetica: diagnosis and management strategies”. Pain Med 8 (8): 669-77 doi : 10.1111/j.1526-4637.2006.00227.x. PMID 18028045.

131. Bigal ME, Lipton RB (January 2008) “Obesity and chronic daily headache”. Curr Pain Headache Rep 12(1): 56-61 doi : 10.1007/s11916-008-0011-8 PMID 18417025.

132. Sharifi- MOIlayousefi A, Yazdchi-Marandi M, Ayyamilou H, et al (February 2008) “Assessment of body mass index and hand anthropometric measurements as independent risk factors for carpal tunnel syndrome” Folia Morphol (Warsz) 67 (1): 36-42. PMID 18335412.

133. Beydoun MA, Beydoun HA, Wang Y, (May 2008) “Obesity and central obesity as risk factors for incident dementia and its subtypes: A systematic review and meta analysis” Obes Rev 9 (3): 204-18 doi : 10.1111/j.1467-789X.2008.00473.x. PMID 18331422.

134. Wall M (March 2008) “Idiopathic Intracranial Hypertension (pseudotumorcerebri)” Curr Neurol Neurosci Rep S (2) : 87-93 doi : 10.1007/s11910-008-0015-0. PMID 18460275.

135. Munger KL, Chitnis T, Ascherio A (2009) “Body size and risk of MS in two cohorts of US women” Neurology 73 (19) : 1543-50 doi : 10.1212/WML.0b013e3181cd06e0. PMID 19901245.

136. Calle EE, Rodriguez C, Walker – Thurmond K, Thun MJ (April 2003). “Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. Adults” N. Engl. J. Med. 348 (17): 1625-38 doi : 10.1056/NEJMoa021423. PMID 12711737.

137. Poulain M, Doucent M, Major GC, et al (April 2006). “The effect of obesity on chronic respiratory diseases: pathophysiology and therapeutic strategies” CMAJ 174 (9) : 1293-9 doi : 10.1503/cmaj.051299. PMID 16636330.PMC 1435949.

138. Choi HK, Atkinson K, Karison EW, Curhan G (April 2005). “Obesity weight change hypertension, diuretic use and risk of gout in men the health professionals follow up study” Arch. Intern. Med. 165 (7): 742-8. doi : 10.1001/archinte.165.7.742.PMID 15824292.

139. duker T, Visscher T, Picavet H (April 2008) “Overweight and health problems of the lower extremities: osteoarthritis, pain and disability” Public Health Nutr. 12 (3) : 1-10 doi : 10.1017/S1368980008002103. PMID 18426630.

140. Molenaar EA, Numans ME, van Ameijden EJ, Grobbee DE (November 2008) “Considerable comorbidity in overweight adults: results from the Utrecht Health Project” (in Dutch, Flemish). Ned Tijdschr Geneeskd 152 (45) : 2457-63. PMID 19051798.

141. Esposito K, Giugliano F, Di Palo C, Giugliano G, Marfella R, D’Andrea F, D’Armiento M, Giugliano D (2004). “Effect of lifestyle changes on erectile dysfunction in obese men: A randomized controlled trial” JAMA 291 (24): 2978-84 doi : 10.1001/jama.291.24.2978 PMID 15213209.

142. Hunskaar S (2008). “A systematic review of overweight and obesity as risk factors and targets for clinical intervention for urinary incontinence in women”. Urodyn. 27(8): 749-57 doi : 10.1002/uod.20635. PMID 18951445.

143. Ejerblad E, Fored CM, Lindblad P, Fryzek J, McLaughlin JK, Nyren O (2006) “Obesity and risk for chronic renal failure”. J. Am. Soc. Nephrol. 17(6): 1695-702 doi : 10.1681/ASN.2005060638. PMID 16641153.

144. Makhshida N, Shah J, Yan G, Fisch H, Sabagh S, Sabsigh R (September, 2005) “Hypogonadism and metabolic syndrome: implications for testosterone therapy”. J. Urol. 174 (3) : 827-34 doi : 10.1097/01.JU.0000169490.78443.59 PMID 16093964.

145. Schmidt DS, Salahudeen AK (2007) “Obesity survival paradox-still a controversy?” Semin Dia 20 (6) : 486-92 doi : 10.1111/j.1526-392X.2007.00349.x. PMID 17991192.

146. U.S. Preventive Services Task Force (June 2003) “Behavioral counseling in primary care to promote a healthy diet recommendations and rationale” Am Fam Physician 67 (12):2573-6. PMID 12825847 [dead link].

147. Habbu A, Lakkis NM, Dokainish H (October 2006) “The obesity paradox: Fact or fiction?” Am. J. Cardiol. 98(7): 944-8, doi : 10.1016/j.amjcard.2006.04.039 PMID 16996880.

148. Romero-Corral A, Montori VM, Somers VK, et al (2006) “Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: A systematic review of cohort studies”. Lancet 368 (9536): 666-78 doi : 10.1016/S0140-6736 (06)692519. PMID 16920472.

149. Oreopoulos A, Padwal R, Kalantar-Zadeh K, Fonarow GC, Norris CM, McAlister FA (July 2008) “Body mass index and mortality in heart failure: A meta-analysis”. Am. Heart J. 156 (1) : 13-22 doi : 10.1016/j.ahj.2008.02.014. PMID 18585492.

150. Oreopoulos A, Padwal R, Norris CM, Mullen JC, Pretorius V, Kalantar-Zadeh K (February 2008). “Effect of obesity on short and long term mortality postcoronary revascularization: A metaanalysis” Obesity (Silver Spring) 15 (2) : 442-50 doi : 10.1038/oby.2007.36. PMID 18239657.
151. Diercks DB, Roe MT, Mulgund J et al. (July 2006) “The obesity paradox in non-ST segment elevation acute coronary syndromes: Results from the Can rapid risk stratification of Unstable angina patients suppress Adverse outcomes with early implementation of the American College of Cardiology/American Heart Association Guidelines Quality Improvement Initiative”. Am Heart J 152 (1) : 140-8 doi: 10.1016/j.ahj.2005.09.024. PMID 16824844.

152. Lau DC, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E (April 2007). “2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]” CMAJ 176 (8) :S1-13 doi: 10.1503/cmaj.061409. PMID 17420481.

153. Bleich S, Cutler D, Murray C, Adams A (2008). “Why is the developed world obese?” Annu Rev Public Health 29: 273-95 doi: 10.1146/annurev.publhealth.29.020907.090954 PMID 18173389.

154. Drewnowski A, Spector SE (January 2004). “Poverty and obesity: the role of energy density and energy costs” Am. J. Clin. Nutr. 79 (1) : 12-24 doi : 10.1093/ajcn/79.1.12 PMID 15068581.

155. Nestle M, Macobson MF (2000) “Halting the obesity epidemic: A public health policy approach”. Public Health Rep 115(1): 12-24 doi : 10.1093/iph/115.1.12 PMID 10968581.

156. James WP (March 2008). “The fundamental drivers of the obesity epidemic” Obes Rev 9 Suppl1 : 6-13 doi : 10.1111/j.1467-789X.2007.00432.x. PMID 18307693.

157. Keith SW, Redden DT, Katzmarzyk PT, et al. (2006). “Putative contributors to the secular increase in obesity: exploring the roads less traveled”. Int J Obes (Lond) 30 (11) : 1585-94 doi : 10.1038/sj.ijo.0803326. PMID 16801930.

158. Yang W, Kelly T, He J (2007) “Genetic epidemiology of obesity” Epidemiol Rev 29:49-61, doi:10.1093/epirev/mxm004. PMID 17566051.

159. Walley AJ, Asher JE, Froquel P (June 2009) “The genetic contribution to non-syndromic human obesity”. Nat. Rev Genet. 10(7) : 432-42, doi : 10.1038/nrg2594. PMID 19506576.

160. Falagas ME, Kompoti M (July 2006) “Obesity and Infection” Lancet Infect Dis 6 (7): 438-46, doi : 10.1016/S1473-3099(06)70523-0. PMID 16790384.

161. Flier JS (2004) “Obesity wars: Molecular progress confronts an expanding epidemic”. Cell 116(2): 337-50 doi:10.1016/S0092-8674(03)0108-X PMID 14744442.

162. Hamann A, Matthaei S (1996). “Regulation of energy balance by leptin” Exp. Clin.Endocrinol. Diabetes 104 (4): 293-300, doi : 10.1055/s-0029-1211457. PMID 886745.

163. Boulpaep, Emile L; Boron, Walter F. (2003). Medical Physiology: A cellular and molecular approach. Philadelphia: Saunders. Pp. 1227.ISBN 0-7216-3256-4.

164. Strychar I (January 2006). “Diet in the management of weight loss” CMAJ 174 (1) : 56-63, doi : 10.1503/cmaj.045037 PMID 16389240. PMC 1319349.

165. Shck SM< Wing RR, Klem ML, McGuire MT, Hill Jo, Seagle H (Arpril 1998) “Persons successful at long term weight loss and maintenance continue to consume a low energy, low fat diet”. J. Am Diet Assoc 98 (4): 408-13, doi: 10.1016/S0002-8223(98)00093-5. PMID 9550162.

166. Tate DF, Jeffery RW, Sherwood NE, Wing RR (1 April 2007) “Long term weight losses associated with prescription of higher physical activity goals. Are higher levels of physical activity protective against weight regain?” J. Am. Clin. Nutr. 85(4): 954-9 PMID 17413092.

167. Wing, Rena R; Phelan, Suzanne (1 July 2005) “Science-Based Solutions to Obesity: What are the Roles of Academia, Government, Industry, and Health Care? Proceedings of a symposium, Boston, Massachusetts, USA, 10-11 March 2004 and Anaheim, California, USA, 2 October, 2004”. Am J. ClinNutr. 82 (1 Suppl): 207S-273S. PMID 16002825.

168. Ann Hum Biol. 1988 Sep-Oct’ 15(5):353-64

169. Calcify Tissue Int. 1988 Oct; 43(4):199-201.