



**Estrategia de Búsqueda:** únicamente se han incluido los estudios que se han encontrado en Pubmed, que sean Randomized Controlled Trials, hechos en humanos y de los que dispongamos como mínimo el abstract.

("meal frequency" OR "Frequent feeding" OR "regular meal" OR "Frequent meal" OR "regular feeding" OR "meal pattern" OR ("increased frequency" AND eating) OR (Nibbling AND gorging)) (1-22)

## Reference List

1. **Stote KS, Baer DJ, Spears K, Paul DR, Harris GK, Rumpler WV et al.** A controlled trial of reduced meal frequency without caloric restriction in healthy, normal-weight, middle-aged adults. *Am J Clin Nutr* 2007; 85: 981-8.

Keywords: Adipose Tissue/Adult/Analysis of Variance/Biological Markers/blood/Blood Chemical Analysis/Blood Pressure/Body Composition/Cholesterol/Circadian Rhythm/Cross-Over Studies/Eating/Energy Intake/Female/Humans/Hunger/Hydrocortisone/Male/metabolism/Middle Aged/physiology/Pilot Projects/Risk Factors/Time Factors

Abstract: **BACKGROUND:** Although consumption of 3 meals/d is the most common pattern of eating in industrialized countries, a scientific rationale for this meal frequency with respect to optimal health is lacking. A diet with less meal frequency can improve the health and extend the lifespan of laboratory animals, but its effect on humans has never been tested. **OBJECTIVE:** A pilot study was conducted to establish the effects of a reduced-meal-frequency diet on health indicators in healthy, normal-weight adults. **DESIGN:** The study was a randomized crossover design with two 8-wk treatment periods. During the treatment periods, subjects consumed all of the calories needed for weight maintenance in either 3 meals/d or 1 meal/d. **RESULTS:** Subjects who completed the study maintained their body weight within 2 kg of their initial weight throughout the 6-mo period. There were no significant effects of meal frequency on heart rate, body temperature, or most of the blood variables measured. However, when consuming 1 meal/d, subjects had a significant increase in hunger; a significant modification of body composition, including reductions in fat mass; significant increases in blood pressure and in total, LDL-, and HDL-cholesterol concentrations; and a significant decrease in concentrations of cortisol. **CONCLUSIONS:** Normal-weight subjects are able to comply with a 1 meal/d diet. When meal frequency is decreased without a reduction in overall calorie intake, modest changes occur in body composition, some cardiovascular disease risk factors, and hematologic variables. Diurnal variations may affect outcomes



2. **Jackson SJ, Leahy FE, Jebb SA, Prentice AM, Coward WA, Bluck LJ.** Frequent feeding delays the gastric emptying of a subsequent meal. *Appetite* 2007; 48: 199-205.

Keywords: Adult/Appetite/Breath Tests/Carbon Isotopes/Cross-Over Studies/diagnostic use/Eating/Gastric Emptying/Humans/Male/Middle Aged/Octanoic Acids/physiology/Time Factors

Abstract: To assess the suitability of the <sup>13</sup>C-octanoic acid breath test for measuring gastric emptying in circumstances other than the post-absorptive state, a preliminary study was performed where 6 hourly spaced isoenergetic meals preceded the determination of gastric emptying of a subsequent 2 MJ meal. Emptying was measured in three individuals on four separate occasions, with a reproducibility of 8%. A crossover study was then conducted to test the hypothesis that meal frequency can modulate the gastric emptying of a subsequent meal, with the potential to influence appetite regulation. Sixteen subjects were fed to energy balance, receiving food either as 2 isoenergetic meals 3 h apart or 6 isoenergetic meals fed hourly. Gastric emptying of a subsequent 2 MJ meal was investigated. Visual analogue scales were used throughout to assess appetite. The maximum rate of gastric emptying was unchanged but the onset of emptying was delayed by the more frequent feeding pattern. There was no significant difference in subjective appetite before or after the test meal. In conclusion, short-term increases in feeding frequency delayed the gastric emptying of a subsequent meal, but significant effects on post-meal appetite could not be demonstrated

3. **Taylor KA, Barr SI.** Provision of small, frequent meals does not improve energy intake of elderly residents with dysphagia who live in an extended-care facility. *J Am Diet Assoc* 2006; 106: 1115-8.

Keywords: Aged/Aged,80 and over/complications/Cross-Over Studies/Deglutition Disorders/Dehydration/diet therapy/Drinking/Eating/Energy Intake/Feeding Behavior/Female/Humans/Male/Malnutrition/physiology/prevention & control/Skilled Nursing Facilities/Time Factors

Abstract: Malnutrition and dehydration are potential consequences of dysphagia, a common swallowing disorder among elderly individuals. Providing smaller, more frequent meals has been suggested (but not demonstrated) to improve energy intake among this group. Accordingly, this study was designed to assess whether the same energy content in five vs three daily meals would improve energy intake. Thirty-seven residents of an extended-care facility, aged older than 65 years, previously evaluated for dysphagia, and receiving a texture-modified diet, agreed to participate in a crossover study with random assignment to three or five meals during an initial 4-day study period, followed by the opposite meal pattern in a second period. Six were excluded from analysis, as their medical condition deteriorated before or during the study. Food and fluids consumed by participants during each study period were weighed before and after each meal. Average energy intakes were similar between the three- and five-meal patterns (1,325+/-207 kcal/day vs 1,342+/-177 kcal/day, respectively; P=0.565); fluid intake was higher with five meals (698+/-156 mL/day) vs three (612+/-176 mL/day; P=0.003). Because offering five daily feedings



did not improve energy intakes when compared with three, dietitians caring for this vulnerable group might need to consider other nutrition intervention strategies

4. **Farshchi HR, Taylor MA, Macdonald IA.** Beneficial metabolic effects of regular meal frequency on dietary thermogenesis, insulin sensitivity, and fasting lipid profiles in healthy obese women. *Am J Clin Nutr* 2005; 81: 16-24.

Keywords: Adult/blood/Blood Glucose/Body Mass Index/Cholesterol/Cross-Over Studies/Diet/Eating/Energy Intake/Energy Metabolism/Female/Humans/Insulin/Lipids/metabolism/Middle Aged/Obesity/Satiation

Abstract: **BACKGROUND:** Although a regular meal pattern is recommended for obese people, its effects on energy metabolism have not been examined. **OBJECTIVE:** We investigated whether a regular meal frequency affects energy intake (EI), energy expenditure, or circulating insulin, glucose, and lipid concentrations in healthy obese women. **DESIGN:** Ten women [x +/- SD body mass index (in kg/m<sup>2</sup>): 37.1 +/- 4.8] participated in a randomized crossover trial. In phase 1 (14 d), the subjects consumed their normal diet on 6 occasions/d (regular meal pattern) or followed a variable meal frequency (3-9 meals/d, irregular meal pattern). In phase 2 (14 d), the subjects followed the alternative pattern. At the start and end of each phase, a test meal was fed, and blood glucose, lipid, and insulin concentrations were determined before and for 3 h after (glucose and insulin only) the test meal. Subjects recorded their food intake on 3 d during each phase. The thermogenic response to the test meal was ascertained by indirect calorimetry. **RESULTS:** Regular eating was associated with lower EI (P < 0.01), greater postprandial thermogenesis (P < 0.01), and lower fasting total (4.16 compared with 4.30 mmol/L; P < 0.01) and LDL (2.46 compared with 2.60 mmol/L; P < 0.02) cholesterol. Fasting glucose and insulin values were not affected by meal pattern, but peak insulin concentrations and area under the curve of insulin responses to the test meal were lower after the regular than after the irregular meal pattern (P < 0.01 and 0.02, respectively). **CONCLUSION:** Regular eating has beneficial effects on fasting lipid and postprandial insulin profiles and thermogenesis

5. **Lundin EA, Zhang JX, Lairon D, Tidehag P, Aman P, Adlercreutz H et al.** Effects of meal frequency and high-fibre rye-bread diet on glucose and lipid metabolism and ileal excretion of energy and sterols in ileostomy subjects. *Eur J Clin Nutr* 2004; 58: 1410-9.

Keywords: administration & dosage/Adult/Aged/Bile Acids and Salts/blood/Blood Glucose/Bread/C-Peptide/Cholesterol/Colitis,Ulcerative/Cross-Over Studies/Diet/Dietary Fiber/drug effects/Energy Metabolism/Feeding Behavior/Female/Humans/Ileostomy/Ileum/Insulin/Lipid Metabolism/Lipids/Male/metabolism/Middle Aged/physiology/Secale cereale/secretion/Sterols/surgery/urine



**Abstract:** **OBJECTIVE:** To investigate the effect of a rye, high-fibre diet (HFD) vs a wheat, low-fibre diet (LFD), meal frequency, nibbling (Nib, seven times a day) or ordinary (Ord, three times a day), and their combined effects on blood glucose, insulin, lipids, urinary C-peptide and ileal excretion of energy, cholesterol and bile acids in humans. **DESIGN:** LFD period with Nib or Ord meal frequency followed by an HFD diet with Nib or Ord meal frequency in randomized, crossover design. **SETTING:** Outpatients of ileostomy volunteers were called for an investigation in research ward. **SUBJECTS:** A total of 10 subjects (two female subjects, age 34 and 51 y; eight males, mean age 54.4 y, range 43-65 y) participated in the experiment. All subjects were proctocolectomized for ulcerative colitis (mean 16.0 y, range 8-29 y before the study). **INTERVENTION:** In total, 10 ileostomy subjects started with LFD for 2 weeks, the first week on either Nib (five subjects) or Ord (five subjects) and the second week on the other meal frequencies, in a crossover design, followed by a wash-out week, and continued with HFD period for 2 weeks in the same meal frequency manner. All foods consumed in both Nib or Ord regimens were identical and a high-fibre rye bread was used in the HFD period and a low-fibre wheat bread in the LFD period. **MAIN OUTCOME MEASURES:** Day-profiles of blood glucose, insulin and lipids, blood lipids before and after dietary intervention, and excretion of steroids in the effluents and C-peptide in the urine. **RESULTS:** During the Nib regimen, plasma glucose and insulin peaks were lower at the end of the day with HFD compared with LFD. Urinary C-peptide excretion was significantly higher in the day-time on LFD compared with HFD (LFD-Ord vs HFD-Ord,  $P < 0.01$ ; LFD-Nib vs HFD-Nib,  $P < 0.01$ ). Plasma free-cholesterol, total cholesterol, triglycerides and phospholipids were significantly higher ( $P < 0.05$ ) after LFD than after HFD with the Nib regimen. A higher excretion of energy ( $P < 0.05$ ) and chenodeoxycholic acid ( $P < 0.05$ ) were observed with HFD compared with LFD regardless of meal frequency. A higher daily excretion of cholic acid, total bile acids, cholesterol, net cholesterol and net sterols ( $P < 0.05$ ) was observed on HFD compared with LFD with the Nib regimen. **CONCLUSIONS:** An HFD decreased insulin secretion measured as a decreased excretion of C-peptide in urine and as decreased plasma insulin peaks at the end of the day during a Nib regimen. The smoother glycaemic responses at the end of the day during a Nib regimen may be a consequence of a second meal phenomenon, possibly related to the nature of dietary fibre complex

6. **Farshchi HR, Taylor MA, Macdonald IA.** Regular meal frequency creates more appropriate insulin sensitivity and lipid profiles compared with irregular meal frequency in healthy lean women. *Eur J Clin Nutr* 2004; 58: 1071-7.

**Keywords:** Adolescent/Adult/Aged/analysis/Area Under Curve/blood/Blood Glucose/Cardiovascular Diseases/Cholesterol/Cross-Over Studies/Diet/Eating/Energy Metabolism/etiology/Feeding Behavior/Female/Humans/Insulin/Lipids/metabolism/physiology/Risk Factors/Time Factors

**Abstract:** **OBJECTIVE:** To investigate the impact of irregular meal frequency on circulating lipids, insulin, glucose and uric acid concentrations which are known cardiovascular risk factors. **DESIGN:** A randomised crossover dietary intervention study. **SETTING:** Nottingham, UK--Healthy free-living women. **SUBJECTS:** A total of nine lean healthy women aged 18-42 y



recruited via advertisement. INTERVENTION: A randomised crossover trial with two phases of 14 days each. In Phase 1, subjects consumed their normal diet on either 6 occasions per day (regular) or by following a variable meal frequency (3-9 meals/day, irregular). In Phase 2, subjects followed the alternative meal pattern to that followed in Phase 1, after a 2-week (wash-out) period. Subjects were asked to come to the laboratory after an overnight fast at the start and end of each phase. Blood samples were taken for measurement of circulating glucose, lipids, insulin and uric acid concentrations before and for 3 h after consumption of a high-carbohydrate test meal. RESULTS: Fasting glucose and insulin values were not affected by meal frequency, but peak insulin and AUC of insulin responses to the test meal were higher after the irregular compared to the regular eating patterns ( $P < 0.01$ ). The irregular meal frequency was associated with higher fasting total ( $P < 0.01$ ) and LDL ( $P < 0.05$ ) cholesterol. CONCLUSION: The irregular meal frequency appears to produce a degree of insulin resistance and higher fasting lipid profiles, which may indicate a deleterious effect on these cardiovascular risk factors. SPONSORSHIP:: The Ministry of Health and Medical Education, IR Iran

7. **Farshchi HR, Taylor MA, Macdonald IA.** Decreased thermic effect of food after an irregular compared with a regular meal pattern in healthy lean women. *Int J Obes Relat Metab Disord* 2004; 28: 653-60.

Keywords: Adolescent/Adult/Aged/Anthropometry/Appetite/Cross-Over  
Studies/Diet/Eating/Energy Intake/Energy Metabolism/Feeding  
Behavior/Female/Humans/Oxidation-Reduction/physiology/Satiation

Abstract: OBJECTIVES: To investigate the impact of irregular meal frequency on body weight, energy intake, appetite and resting energy expenditure in healthy lean women. DESIGN: Nine healthy lean women aged 18-42 y participated in a randomised crossover trial consisting of three phases over a total of 43 days. Subjects attended the laboratory at the start and end of phases 1 and 3. In Phase 1 (14 days), subjects were asked to consume similar things as normal, but either on 6 occasions per day (regular meal pattern) or follow a variable predetermined meal frequency (between 3 and 9 meals/day) with the same total number of meals over the week. In Phase 2 (14 days), subjects continued their normal diet as a wash-out period. In Phase 3 (14 days), subjects followed the alternative meal pattern to that followed in Phase 1. Subjects recorded their food intake for three predetermined days during the irregular period when they were eating 9, 3 and 6 meals/day. They also recorded their food intake on the corresponding days during the regular meal pattern period. Subjects fasted overnight prior to each laboratory visit, at which fasting resting metabolic rate (RMR) was measured by open-circuit indirect calorimetry. Postprandial metabolic rate was then measured for 3 h after the consumption of a milkshake test meal (50% CHO, 15% protein and 35% fat of energy content). Subjects rated appetite before and after the test meal. RESULTS: There were no significant differences in body weight and 3-day mean energy intake between the regular and irregular meal pattern. In the irregular period, the mean energy intake on the day when 9 meals were eaten was significantly greater than when 6 or 3 meals were consumed ( $P=0.0001$ ). There was no significant difference between the 3 days of the regular meal pattern. Subjective appetite measurement showed no significant differences before and after the test meal in all visits. Fasting RMR showed no significant differences over the experiment. The overall thermic effect of food (TEF) over the 3 h after the test meal was significantly lower after the irregular meal pattern ( $P=0.003$ ). CONCLUSION: Irregular meal frequency led to a lower







9. **Taylor MA, Garrow JS.** Compared with nibbling, neither gorging nor a morning fast affect short-term energy balance in obese patients in a chamber calorimeter. *Int J Obes Relat Metab Disord* 2001; 25: 519-28.

Keywords: Adult/Calorimetry/Diet/Eating/Energy Intake/Energy  
Metabolism/Exercise/Fasting/Feeding Behavior/Female/Food/Humans/metabolism/Middle  
Aged/Obesity

Abstract: OBJECTIVE: To test if a diet of 4.2 MJ/24 h as six isocaloric meals would result in a lower subsequent energy intake, or greater energy output than (a) 4.2 MJ/24 h as two isocaloric meals or (b) a morning fast followed by free access to food. DESIGN: Subjects were confined to the Metabolic Unit from 19:00 h on day 1 to 09:30 h on day 6. Each day they had a fixed diet providing 4.2 MJ with three pairs of meal patterns which were offered in random sequence. They were: six meals vs two meals without access to additional foods (6vs2), or six meals vs 2 meals with access to additional food (6+vs2+), or six meals vs four meals (6+vsAMFAST). In the AMFAST condition the first two meals of the day were omitted to reduce daily intake to 2.8 MJ and to create a morning fast, but additional food was accessible thereafter. Patients were confined in the chamber calorimeter from 19:00 h on day 2 until 09:00 h on day 4, and then from 19:00 h on day 4 to 09:00 h on day 6. The order in which each meal pattern was offered was balanced over time. MEASUREMENTS: Energy expenditure (chamber calorimetry), spontaneous activity (video) and energy intake (where additional foods were available) during the final 24 h of each dietary component. SUBJECTS: Ten (6vs2), eight (6+vs2+) and eight (6+vsAMFAST) women were recruited who had a BMI of greater than 25 kg/m<sup>2</sup>. RESULTS: From experiment 6vs2 the difference between energy expenditure with six meals (10.00 MJ) and two meals (9.96 MJ) was not significant (P=0.88). Energy expenditure between 23:00 h and 08:00 h ('night') was, however, significantly higher (P=0.02) with two meals (9.12 MJ/24 h) compared with six meals (8.34 MJ/24 h). The pattern of spontaneous physical activity did not differ significantly between these two meal patterns (P>0.05). Total energy intake was affected by neither meal frequency in experiment 6+vs2+ (10.75 MJ with six, 11.08 MJ with two; P=0.58) nor a morning fast in experiment 6+vsAMFAST (8.55 MJ/24 h with six, 7.60 MJ with AMFAST; P=0.40). The total diet of subjects who had a morning fast tended to have a lower percentage of total energy from carbohydrate (40%) than when they had six meals per 24 h (49%) (P=0.05). Subsequent energy balance was affected by neither meal frequency (6vs2; P=0.88, 6+vs2+; P=0.50) nor a morning fast (P=0.18). CONCLUSIONS: In the short term, meal frequency and a period of fasting have no major impact on energy intake or expenditure but energy expenditure is delayed with a lower meal frequency compared with a higher meal frequency. This might be attributed to the thermogenic effect of food continuing into the night when a later, larger meal is given. A morning fast resulted in a diet which tended to have a lower percentage of energy from carbohydrate than with no fast

10. **Speechly DP, Buffenstein R.** Greater appetite control associated with an increased frequency of eating in lean males. *Appetite* 1999; 33: 285-97.  
Keywords: Adult/Appetite/Appetite Regulation/blood/Blood Glucose/Eating/Feeding



Behavior/Humans/Hunger/Insulin/Male/metabolism/physiology/Questionnaires/Satiety  
Response/Time Factors

Abstract: Eight healthy males of age 22.9 $\pm$ 4.2 years (mean $\pm$ -SD) and body weight 73.26 $\pm$ 11.50 kg, with BMI of 23.11 $\pm$ 2.84 kg/m<sup>2</sup> underwent two different eating meal frequency patterns on 2 separate days. On both days they were fed approximately 33.3% of their average daily energy requirements as a breakfast pre-load meal: served either as a single meal (SINGLE) or divided into five equal portions (served hourly) (MULTI). Five and a half hours after the initial meal, an ad libitum meal was served. Venous blood was tested to determine plasma glucose and serum insulin concentrations every hour until the ad libitum lunch, and at 15-, 45- and 75-min after lunch. Visual analogue scales (VAS) were completed every hour until the ad libitum lunch, and at 15-, 45- and 75-min after lunch as a measure to determine hunger, appetite and satiety indices. Although both groups were fed isocaloric and identical macronutrient "breakfast pre-loads" (3450 $\pm$ 466 kJ), the SINGLE group consumed 26.6% more (p<0.02) energy in the ad libitum lunch (5111 $\pm$ 1502 kJ vs. 3752 $\pm$ 893 kJ) than the MULTI group did. The pre-load feeding pattern had no effect on blood glucose responses throughout the trial. Following the larger SINGLE pre-load, serum insulin concentration rose to a higher (p<0.01) level compared to the first of the MULTI pre-load meals (123.04 $\pm$ 61.51 microIU/ml vs. 37.30 $\pm$ 26.65 microIU/ml SINGLE vs. MULTI, respectively). Serum insulin rose to a higher (p<0.01) level following the fifth and final of the MULTI pre-load meals compared to the serum insulin levels in the SINGLE group at the same time into the trial (74.21 $\pm$ 51.64 microIU/ml vs. 24.98 $\pm$ 13.46 microIU/ml MULTI vs. SINGLE, respectively). Despite consuming more energy in the ad libitum lunch, the SINGLE group showed no difference in serum insulin concentration following the ad libitum lunch compared to the insulin response of the MULTI group. These data suggest that when the nutrient load was spread into equal amounts and consumed evenly through the day in lean healthy males, there was an enhanced control of appetite. This greater control of satiety when consuming smaller multiple meals may possibly be linked to an attenuation in insulin response although clearly both other physical (gastric stretch) and physiological (release of gastric hormones) factors may also be affected by the periodicity of eating

11. **Iwao S, Mori K, Sato Y.** Effects of meal frequency on body composition during weight control in boxers. *Scand J Med Sci Sports* 1996; 6: 265-72.

Keywords: Adult/Body Composition/Body Mass Index/Body Weight/Boxing/Creatine/Diet/Diet, Reducing/Energy Metabolism/Food/Food Habits/Humans/metabolism/methods/Methylhistidines/Myofibrils/physiology/urine/Weight Loss

Abstract: The effects of meal frequency on changes in body composition by food restriction were investigated. Twelve boxers were divided between a two meals day<sup>-1</sup> group (the 2M group) and a six meals day<sup>-1</sup> group (the 6M group). Both groups ingested 5.02 MJ (1200 kcal) day<sup>-1</sup> for 2 weeks. Although there was no difference in change of body weight by food restriction between the two groups, the decrease in lean body mass (LBM) was significantly greater in the 2M group than in the 6M group. The decrease in urinary 3-methylhistidine/creatinine was significantly greater in





the 6M group than in the 2M group. These results suggest that the lower frequency of meal intake leads to a greater myoprotein catabolism even if the same diet is consumed

12. **Murphy MC, Chapman C, Lovegrove JA, Isherwood SG, Morgan LM, Wright JW et al.** Meal frequency; does it determine postprandial lipaemia? *Eur J Clin Nutr* 1996; 50: 491-7.

Keywords: Adult/analogs & derivatives/analysis/blood/Blood Glucose/Cholesterol/Cholesterol,HDL/Cholesterol,LDL/Cohort Studies/Cross-Over Studies/Diet/Eating/Energy Intake/Fasting/Fatty Acids,Nonesterified/Female/Food/Gastric Emptying/Gastric Inhibitory Polypeptide/Glucagon/Humans/Insulin/Lipid Metabolism/Lipids/Lipoprotein Lipase/metabolism/physiology/Postprandial Period/Triglycerides

**Abstract:** **OBJECTIVE:** To determine the effect of altering meal frequency on postprandial lipaemia and associated parameters. **DESIGN:** A randomized open cross over study to examine the programming effects of altering meal frequency. A standard test meal was given on three occasions following: (i) the normal diet; (ii) a period of two weeks on a nibbling and (iii) a period of two weeks on a gorging diet. **SETTING:** Free living subjects associated with the University of Surrey. **SUBJECTS:** Eleven female volunteers (age 22 +/- 0.89 y) were recruited. **INTERVENTIONS:** The subjects were requested to consume the same foods on either a nibbling diet (12 meals per day) or a gorging diet (three meals per day) for a period of two weeks. The standard test meal containing 80 g fat, 63 g carbohydrate and 20 g protein was administered on the day prior to the dietary intervention and on the day following each period of intervention. **MAJOR OUTCOME MEASURES:** Fasting and postprandial blood samples were taken for the analysis of plasma triacylglycerol, non-esterified fatty acids, glucose, immunoreactive insulin, glucose-dependent insulinotropic polypeptide levels (GIP) and glucagon-like peptide (GLP-1), fasting total, low density lipoprotein (LDL)- and high density lipoprotein (HDL)-cholesterol concentrations and postheparin lipoprotein lipase (LPL) activity measurements. Plasma paracetamol was measured following administration of a 1.5 g paracetamol load with the meal as an index of gastric emptying. **RESULTS:** The compliance to the two dietary regimes was high and there were no significant differences between the nutrient intakes on the two intervention diets. There were no significant differences in fasting or postprandial plasma concentrations of triacylglycerol, non-esterified fatty acids, glucose, immunoreactive insulin, GIP and GLP-1 levels, in response to the standard test meal following the nibbling or gorging dietary regimes. There were no significant differences in fasting total or LDL-cholesterol concentrations, or in the 15 min postheparin lipoprotein lipase activity measurements. There was a significant increase in HDL-cholesterol in the subjects following the gorging diet compared to the nibbling diet. **DISCUSSION:** The results suggest that previous meal frequency for a period of two weeks in young healthy women does not alter the fasting or postprandial lipid or hormonal response to a standard high fat meal. **CONCLUSIONS:** The findings of this study did not confirm the previous studies which suggested that nibbling is beneficial in reducing the concentrations of lipid and hormones. The rigorous control of diet content and composition in the present study compared with others, suggest reported effects of meal frequency may be due to unintentional alteration in nutrient and energy intake in previous studies



13. **Vaz M, Turner A, Kingwell B, Chin J, Koff E, Cox H et al.** Postprandial sympatho-adrenal activity: its relation to metabolic and cardiovascular events and to changes in meal frequency. *Clin Sci (Lond)* 1995; 89: 349-57.

Keywords: Adult/analysis/blood/Blood Pressure/Cardiovascular  
Physiology/Eating/Epinephrine/Feeding Behavior/Heart  
Rate/Humans/Insulin/Male/metabolism/Norepinephrine/physiology/Postprandial  
Period/secretion/Sympathetic Nervous System

Abstract: 1. Sympatho-adrenal activity was measured after the consumption of a 3.15 MJ mixed meal. Whole-body noradrenaline spillover rates, forearm plasma noradrenaline spillover and adrenaline secretion rates were derived using isotope dilution methodology. Heart rate and blood pressure spectral analysis measurements were also made. The relation of sympathoadrenal activity to thermogenic and cardiovascular events was studied. Sympathetic nervous and thermogenic responses were measured for 120 min after the single 3.15 MJ meal and compared with those after three 1.05 MJ meals, given 30 min apart. 2. Whole-body and forearm plasma noradrenaline spillover, and the 0.1 Hz component of systolic pressure power all increased significantly postprandially, while the 0.1 Hz component of heart rate variability, an indirect index of cardiac sympathetic nervous activity, remained unaltered. Adrenaline secretion was unaltered postprandially. Whole-body plasma noradrenaline spillover and thermogenesis during the 120 min postprandial period were 37% and 36% higher after the single meal as compared with the multiple meals, although this was not statistically significant. 3. The sympathetic neural responses were delayed in relation to peak plasma insulin levels and sustained in the face of declining insulin levels. Energy expenditure increased significantly postprandially, but there was no direct quantitative relationship to plasma noradrenaline spillover. Forearm oxygen consumption did not increase postprandially despite significant increases in regional noradrenaline spillover. Thus, no close relation was demonstrated between postprandial sympathetic nervous activation and either insulin secretion or thermogenesis

14. **Jones PJ, Namchuk GL, Pederson RA.** Meal frequency influences circulating hormone levels but not lipogenesis rates in humans. *Metabolism* 1995; 44: 218-23.

Keywords: Adult/blood/Deuterium Oxide/Diet/Eating/Energy Intake/Gastric Inhibitory  
Polypeptide/Humans/Insulin/Male/Triglycerides

Abstract: To determine whether human lipogenesis is influenced by the frequency of meal consumption, 12 subjects were divided into two groups and fed isocaloric nutritionally adequate liquid diets over 3 days, either as three larger diurnal (n = 6) or as six small, evenly spaced (n = 6) meals per day. On day 2 (08:00 h) of each diet period, 0.7 g deuterium (D) oxide/kg body water was administered and blood was collected every 4 hours over 48 hours for measurement of plasma insulin and glucose-dependent insulinotropic polypeptide (GIP) levels. At each time point, the incorporation of D into plasma triglyceride fatty acid (TG-FA) was also determined by isotope ratio mass spectrometry after TG-FA extraction and combustion/reduction. Insulin and GIP levels



were elevated over daytime periods in subjects fed three versus six meals per day. Contribution of de novo synthesis to total TG-FA production was not significantly different for days 2 and 3 in subjects consuming three (6.56% +/- 1.32% and 6.64% +/- 2.08%, respectively) and six (7.67% +/- 2.29% and 7.88% +/- 1.46%, respectively) meals per day. Net TG-FA synthesis rates over days 2 and 3 were 1.47 +/- 0.33 and 1.55 +/- 0.53 g/d, respectively, for subjects fed three meals per day, and 1.64 +/- 0.47 and 1.69 +/- 0.30 g/d for subjects fed six meals per day. These findings suggest that consuming fewer but larger daily meals is not accompanied by increases in TG-FA synthesis, despite the observation of hormonal peaks

15. **Arnold L, Ball M, Mann J.** Metabolic effects of alterations in meal frequency in hypercholesterolaemic individuals. *Atherosclerosis* 1994; 108: 167-74.

Keywords: administration & dosage/Adult/Aged/analysis/blood/Blood Glucose/Body Weight/C-Peptide/Cholesterol/Creatinine/Cross-Over Studies/Diet/Dietary Fats/Eating/Fasting/Female/Humans/Hypercholesterolemia/Insulin/Lipid Metabolism/Lipids/Male/metabolism/Middle Aged/Time Factors/Triglycerides

Abstract: It has been suggested that the metabolic consequences of a given diet may depend in part on the frequency with which meals are eaten. To investigate the effects of meal frequency on plasma lipid metabolism, 16 free-living hypercholesterolaemic men and women consumed their usual diet as 3 or 9 meals/day in random order for 4 weeks. Dietary macronutrient intake and body weight remained similar on the 2 regimens. Fasting plasma lipids were measured after 2, 3 and 4 weeks on each regimen and there were no significant differences in the fasting concentrations of plasma total, LDL, and HDL cholesterol, triglycerides, apolipoprotein A-I and B and the ratio of total: LDL and LDL:HDL cholesterol (HDL-C) on the two diets. The mean (+/- S.D.) fasting total cholesterol was 6.73 +/- 0.74 and 6.81 +/- 0.88 mmol/l on 3 and 9 meals/day, respectively and LDL-C was 4.77 +/- 0.66 and 4.87 +/- 0.78 mmol/l, respectively. There was also no significant variation in the response of plasma triglycerides or serum insulin to a high fat meal following a 3 week adaptation to regimens of 3 and 9 meals/day. Finally the 24 h urinary output of C-peptide was similar on each diet. The consumption of isoenergetic diets as 3 and 9 meals/day did not influence fasting plasma lipid levels, C-peptide excretion or the plasma triglyceride response to a high fat meal of a group of free living hypercholesterolaemic subjects

16. **Verboeket-van de Venne WP, Westerterp KR, Kester AD.** Effect of the pattern of food intake on human energy metabolism. *Br J Nutr* 1993; 70: 103-15.

Keywords: Adult/Body Composition/Body Mass Index/Body Temperature Regulation/Body Weight/Circadian Rhythm/Energy Intake/Energy Metabolism/Exertion/Feeding Behavior/Food/Humans/Male/metabolism/Middle Aged/physiology





Keywords: blood/Blood Glucose/Diabetes Mellitus, Type 2/Diet/Eating/Fatty Acids, Nonesterified/Female/Glycosuria/Humans/Insulin/Male/metabolism/Middle Aged/Time Factors/urine

Abstract: OBJECTIVE--We studied the effects of meal frequency on blood glucose, serum insulin, and FFAs in 12 NIDDM subjects. RESEARCH DESIGN AND METHODS--Subjects were assigned in random order to two 8-hr observation periods after an overnight fast. They received isocaloric diets with similar composition either as six small or as two large meals. At the end of each study period, an IVGTT was given. RESULTS--Two large meals induced an 84% greater maximum amplitude of glucose excursions than six small meals (6.1 +/- 0.5 vs. 3.3 +/- 0.5 mM,  $P < 0.005$ ) and higher insulin responses ( $P < 0.03$ ). The Kg response to an IVGTT did not differ in the two situations. The average FFA level was lowest in response to frequent meals ( $P < 0.02$ ). CONCLUSIONS--A higher meal frequency acutely subdues glucose excursions and reduces insulin and FFA levels during the daytime in older NIDDM subjects

19. **Brighenti F, Ciappellano S, Vuksan V, Rao AV, Wolever TM, Jenkins A et al.** Is colonic fermentation minimized by increasing meal frequency? *Eur J Clin Nutr* 1991; 45: 221-6.

Keywords: Acetates/administration & dosage/Adult/Analysis of Variance/blood/Colon/Diet/Dietary Carbohydrates/Dietary Fats/Fermentation/Food Habits/Humans/Intestinal Absorption/Lipid Metabolism/Male/metabolism/physiology

Abstract: It has been suggested that, although increasing meal frequency has metabolic advantages in terms of carbohydrate and lipid metabolism, the efficiency of small intestinal absorption may be enhanced, thus reducing the extent of colonic fermentation. Since this may be undesirable, we have tested whether increasing meal frequency reduces the amount of carbohydrate fermented into the colon. Accordingly, seven healthy male volunteers took, in random order, two identical 2-week metabolic diets divided into either seventeen or three meals daily. On day 13 of each period measurements were made throughout the day of breath H<sub>2</sub> and serum acetate, as markers of colonic fermentation. Mean levels of both breath H<sub>2</sub> and acetate were similar on both diets, being lower on nibbling by 3.2 +/- 0.8 ppm and 25 +/- 9  $\mu\text{mol/l}$  respectively (not significant). This study failed to demonstrate an effect of more efficient carbohydrate absorption with increased meal frequency

20. **Jenkins DJ, Wolever TM, Vuksan V, Brighenti F, Cunnane SC, Rao AV et al.** Nibbling versus gorging: metabolic advantages of increased meal frequency. *N Engl J Med* 1989; 321: 929-34.

Keywords: 3-Hydroxybutyric Acid/Adult/analysis/Apolipoproteins B/blood/Blood Glucose/C-Peptide/Cholesterol/Cholesterol, LDL/Diet/Dietary Carbohydrates/Eating/Fasting/Fatty Acids, Nonesterified/Food/Glucose Tolerance





Test/Humans/Hydrocortisone/Hydroxybutyrates/Insulin/Lipids/Male/metabolism/Middle Aged/secretion/Triglycerides/urine

**Abstract:** We studied the effect of increasing the frequency of meals on serum lipid concentrations and carbohydrate tolerance in normal subjects. Seven men were assigned in random order to two metabolically identical diets. One diet consisted of 17 snacks per day (the nibbling diet), and the other of three meals per day (the three-meal diet); each diet was followed for two weeks. As compared with the three-meal diet, the nibbling diet reduced fasting serum concentrations of total cholesterol, low-density lipoprotein cholesterol, and apolipoprotein B by a mean ( $\pm$  SE) of 8.5  $\pm$  2.5 percent (P less than 0.02), 13.5  $\pm$  3.4 percent (P less than 0.01), and 15.1  $\pm$  5.7 percent (P less than 0.05), respectively. Although the mean blood glucose level and serum concentrations of free fatty acids, 3-hydroxybutyrate, and triglyceride were similar during both diets, during the nibbling diet the mean serum insulin level decreased by 27.9  $\pm$  6.3 percent (P less than 0.01) and the mean 24-hour urinary C-peptide output decreased by 20.2  $\pm$  5.6 percent (P less than 0.02). In addition, the mean 24-hour urinary cortisol excretion was lower by 17.3  $\pm$  5.9 percent (P less than 0.05) at the end of the nibbling diet than at the end of the three-meal diet. The blood glucose, serum insulin, and C-peptide responses to a standardized breakfast and the results of an intravenous glucose-tolerance test conducted at the end of each diet were similar. We conclude that in addition to the amount and type of food eaten, the frequency of meals may be an important determinant of fasting serum lipid levels, possibly in relation to changes in insulin secretion

21. **Arnold L, Mann JI, Ball MJ.** Metabolic effects of alterations in meal frequency in type 2 diabetes. *Diabetes Care* 1997; 20: 1651-4.

**Keywords:** Aged/analysis/blood/Blood Glucose/Creatinine/Cross-Over Studies/Diabetes Mellitus, Type 2/Diet/diet therapy/Fasting/Female/Food/Food Habits/Glucose Intolerance/Humans/Insulin/Lipid Metabolism/Lipids/Male/metabolism/methods/Middle Aged/physiology

**Abstract:** **OBJECTIVE:** The effects of altering meal frequency on measures of glucose and lipid metabolism in type 2 diabetes were examined by comparing isocaloric dietary regimens in which daily food intake was provided by three or nine meals each day. **RESEARCH DESIGN AND METHODS:** A total of 13 free-living men and women with type 2 diabetes or persistently impaired glucose tolerance participated in a randomized crossover study in which three- and nine-meal regimens were followed for 4-week periods. Fasting plasma lipid and lipoprotein, glucose and insulin concentrations were measured at weekly intervals and glucose, insulin, and triglyceride responses following a 75-g glucose load at weeks 2 and 4 of each diet period. Dietary intake was also recorded during these weeks. **RESULTS:** Nutrient intakes and all measures of carbohydrate and lipid metabolism were similar on the three- and nine-meal regimens. **CONCLUSIONS:** This longer-term study could not confirm the potential benefits of increased meal frequency suggested by comparable 4-week studies in type 2 diabetic individuals and acute experiments in individuals with diabetes. However, as there were no adverse effects of consuming nine meals per day, it would seem appropriate that meal frequency in those with type 2 diabetes should be left to personal choice, provided that energy balance is maintained



22. **Jenkins DJ, Khan A, Jenkins AL, Illingworth R, Pappu AS, Wolever TM et al.** Effect of nibbling versus gorging on cardiovascular risk factors: serum uric acid and blood lipids. *Metabolism* 1995; 44: 549-55.

Keywords: Adult/analysis/blood/Blood Glucose/Cardiovascular Diseases/Cholesterol/Circadian Rhythm/Creatinine/Cross-Over Studies/Diet/Diuresis/epidemiology/Fasting/Feeding Behavior/Humans/Insulin/Lipids/Male/Middle Aged/Risk Factors/Uric Acid/urine

Abstract: Nibbling has been reported to decrease serum cholesterol under fasting conditions, as well as the incidence of cardiovascular disease. It has been suggested that these effects are partly attributable to reduced concentrations of serum insulin, which are also observed. However, data on the effects of nibbling on serum lipids throughout the day are not available, nor is it known how nibbling affects serum uric acid as a further insulin-related risk factor for cardiovascular disease. We have attempted to address these issues. Seven healthy men consumed identical diets in a randomized crossover design either as three meals daily (control) or as 17 meals daily (nibbling) for 2 weeks. On day 13, serum lipid levels were measured over the course of the day (12 hours) together with the 24-hour urinary excretion of mevalonic acid as an indicator of hepatic cholesterol synthesis. Concentrations of uric acid in serum and 24-hour urinary excretion of uric acid were also determined. Mean ( $\pm$  SE) percent treatment differences in day-long total, low-density lipoprotein (LDL), and non-high-density lipoprotein (HDL) cholesterol, and apolipoprotein (apo) B were significant, with lower values on the nibbling diet as compared with the control diet (8.1%  $\pm$  1.6%,  $P = .002$ ; 12.2%  $\pm$  2.6%,  $P = .005$ ; 10.1%  $\pm$  1.6%,  $P < .001$ ; and 9.9%  $\pm$  2.6%,  $P = .008$ , respectively). No significant difference was seen in the total to HDL cholesterol ratio or in urinary mevalonic acid excretion.(ABSTRACT TRUNCATED AT 250 WORDS)