1. Curr Nutr Rep. 2018 Sep;7(3):97-106.

**Nutritional Ketosis for Weight Management and Reversal of Metabolic Syndrome.**

Gershuni VM, Yan SL, Medici V

PURPOSE OF REVIEW: The goal of this paper is to review current literature on

nutritional ketosis within the context of weight management and metabolic

syndrome, namely, insulin resistance, lipid profile, cardiovascular disease risk,

and development of non-alcoholic fatty liver disease. We provide background on

the mechanism of ketogenesis and describe nutritional ketosis.

RECENT FINDINGS: Nutritional ketosis has been found to improve metabolic and

inflammatory markers, including lipids, HbA1c, high-sensitivity CRP, fasting

insulin and glucose levels, and aid in weight management. We discuss these

findings and elaborate on potential mechanisms of ketones for promoting weight

loss, decreasing hunger, and increasing satiety. Humans have evolved with the

capacity for metabolic flexibility and the ability to use ketones for fuel.

During states of low dietary carbohydrate intake, insulin levels remain low and

ketogenesis takes place. These conditions promote breakdown of excess fat stores,

sparing of lean muscle, and improvement in insulin sensitivity. PMID: 30128963

2. Obes Surg. 2018 Aug 18.

**The Efficacy of Energy-Restricted Diets in Achieving Preoperative Weight Loss for Bariatric Patients: a Systematic Review.** Naseer F, Shabbir A, Livingstone B, Price R, Syn NL, Flannery O

In bariatric practice, a preoperative weight loss of at least 5% is recommended.

However, the hypocaloric diets prescribed vary and no consensus exists. This

study examined the efficacy of preoperative diets in achieving 5% weight loss.

From a systematic literature search, eight randomised controlled trials (n = 862)

were identified. Half of the trials used a "very-low-calorie diet" whilst the

rest employed a "low-calorie diet". Only five diets achieved ≥ 5% weight loss

over varying durations and energy intakes. By inference, compliance with a

700-1050 kcal (2929-4393 kJ) diet, consisting of moderate carbohydrate, high

protein and low/moderate fat, for 3 weeks is likely to achieve 5% weight loss. A

low-carbohydrate diet (< 20 g/day) may achieve this target within a shorter

duration. Additional research is required to validate these conclusions. PMID: 30121854

3. Obes Surg. 2018 Aug;28(8):2215-2224.

**A 4-Week Preoperative Ketogenic Micronutrient-Enriched Diet Is Effective in Reducing Body Weight, Left Hepatic Lobe Volume, and Micronutrient Deficiencies in Patients Undergoing Bariatric Surgery: a Prospective Pilot Study.**

Schiavo L, Pilone V, Rossetti G, Barbarisi A, Cesaretti M, Iannelli A

BACKGROUND: Before bariatric surgery (BS), moderate weight loss, left hepatic

lobe volume reduction, and micronutrient deficiency (MD) identification and

correction are desirable.

OBJECTIVES: The objective of this study was to assess the safety and the

effectiveness of a 4-week preoperative ketogenic micronutrient-enriched diet

(KMED) in reducing body weight (BW), left hepatic lobe volume, and correcting MD

in patients scheduled for BS.

MATERIALS AND METHODS: In this prospective pilot study, a cohort of morbidly

obese patients (n = 27, 17 females, 10 males) with a mean body mass index (BMI)

of 45.2 kg/m2 scheduled for BS underwent a 4-week preoperative KMED. Their BW,

BMI, fat mass (FM), fat-free mass (FFM), resting metabolic rate (RMR), left

hepatic lobe volume, micronutrient status, and biochemical and metabolic patterns

were measured before and after the 4-week KMED. Patient compliance was assessed

by validated questionnaires (3-day estimated food records and 72-h recall).

Qualitative methods (5-point Likert questionnaire) were used to measure diet

acceptability and side effects.

RESULTS: All patients completed the study. We observed highly significant

decreases in BW (- 10.3%, p < 0.001, in males; - 8.2%, p < 0.001, in females),

left hepatic lobe volume (- 19.8%, p < 0.001), and an amelioration of patient

micronutrient status. All patients showed a high frequency of acceptability and

compliance in following the diet. No adverse side effect was reported.

CONCLUSION: This study demonstrates that a 4-week preoperative KMED is safe and

effective in reducing BW, left hepatic lobe volume, and correcting MD in obese

patients scheduled for BS. PMID: 29502279

4. Surg Obes Relat Dis. 2018 Jul;14(7):1013-1019.

**Metabolic effects, safety, and acceptability of very low-calorie ketogenic dietetic scheme on candidates for bariatric surgery.** Pilone V, Tramontano S, Renzulli M, Romano M, Cobellis L, Berselli T, Schiavo L

BACKGROUND: Previous studies have demonstrated significant advantages from a

preoperative dietetic regimen for candidates to bariatric procedure.

OBJECTIVES: Evaluation of safety, efficacy, and acceptability of a very

low-calorie ketogenic diet in patients before bariatric surgery.

SETTING: University Hospital.

METHODS: A standardized 30-day sequential preoperative diet regimen has been

analyzed, optimizing metabolic response with gradual carbohydrate reintroduction.

Patients were given a dedicated KetoStationkit, for use during the first 10 days

of the scheme, followed by a hypocaloric scheme for 20 days. The study group

underwent routine laboratory tests and anthropometric measurements (percent

weight loss, body mass index, waist circumference) at enrollment (T0), after 10

days (T1), and after 30 days (T2). Ketone body levels were measured in the plasma and urine.

RESULTS: Between January 2015 and September 2015, 119 patients were included in

the study. Mean body mass index was 41.5 ± 7.6 kg/m2. Weight, body mass index,

and waist circumference at T0 and T1, T0 and T2, and T1 and T2 decreased

significantly (P<.05). A bioelectrical impedance assay determined a significant

reduction in visceral fat at T1 and T2. We observed a significant (P<.05)

improvement in several clinical parameters, including glycemic and lipid profile

parameters. We also observed a mean 30% reduction in liver volume. The majority

of patients declared satisfied or very satisfied. The adverse effects were mild,

of short duration, and not clinically relevant.

CONCLUSION: Our results confirm the acceptability, safety, and significant

advantage of a very low-calorie ketogenic diet for reducing weight and liver

volume of patients in preparation for bariatric surgery. PMID: 29785940

5. Eur J Nutr. 2018 Jun;57(4):1301-1312.

**Overweight and diabetes prevention: is a low-carbohydrate-high-fat diet recommendable?** Brouns F

In the past, different types of diet with a generally low-carbohydrate content

(< 50-< 20 g/day) have been promoted, for weight loss and diabetes, and the

effectiveness of a very low dietary carbohydrate content has always been a matter

of debate. A significant reduction in the amount of carbohydrates in the diet is

usually accompanied by an increase in the amount of fat and to a lesser extent,

also protein. Accordingly, using the term "low carb-high fat" (LCHF) diet is most

appropriate. Low/very low intakes of carbohydrate food sources may impact on

overall diet quality and long-term effects of such drastic diet changes remain at

present unknown. This narrative review highlights recent metabolic and clinical

outcomes of studies as well as practical feasibility of low LCHF diets. A few

relevant observations are as follows: (1) any diet type resulting in reduced

energy intake will result in weight loss and related favorable metabolic and

functional changes; (2) short-term LCHF studies show both favorable and less

desirable effects; (3) sustained adherence to a ketogenic LCHF diet appears to be

difficult. A non-ketogenic diet supplying 100-150 g carbohydrate/day, under good

control, may be more practical. (4) There is lack of data supporting long-term

efficacy, safety and health benefits of LCHF diets. Any recommendation should be

judged in this light. (5) Lifestyle intervention in people at high risk of

developing type 2 diabetes, while maintaining a relative carbohydrate-rich diet,

results in long-term prevention of progression to type 2 diabetes and is

generally seen as safe. PMID: 29541907

6. JAMA. 2018 Jan 16;319(3):215-217.

**Interest in the Ketogenic Diet Grows for Weight Loss and Type 2 Diabetes.** Abbasi J.

PMID: 29340675

7. Diabetes Metab Syndr. 2017 Nov;11 Suppl 1:S385-S390.

**Induced and controlled dietary ketosis as a regulator of obesity and metabolic syndrome pathologies.**

Gibas MK, Gibas KJ

A worsening epidemic of diabetes and its precursor, metabolic syndrome (MetS) is

engulfing America. A healthy individual, with proper glucose regulation has an

ability to switch between burning fat and carbohydrates. It has been suggested

that signaling errors within this homeostatic system, characterized by impaired

switching of substrate oxidation from glucose to fat in response to insulin, can

contribute to the etiology of metabolic syndrome and occurs before the

development of type II diabetes. Glucose regulation with restored insulin

sensitivity facilitated through clinically regulated, benign dietary ketosis

(BDK), may significantly reduce, regulate and reverse the adverse pathologies

common to MetS and obesity. The study assessed if prolonged maintenance of

induced and controlled physiological, dietary ketosis, would reverse pathological

processes induced by MetS including a reduction in fasting triglycerides, BMI

(body mass index) and body fat mass (BFM), weight, a significant decrease and/or

normalization of hemoglobin A1c (HgA1c) and an increase in resting metabolic rate

(RMR) and blood ketones. A group of 30 adults, previously diagnosed with MetS by

their primary care physician, were randomly prescribed to one of three groups: a

sustained ketogenic diet with no exercise, standard American diet (SAD) with no

exercise or SAD with 3-5 days per week of exercise (30 min.). The results

demonstrated that the change over time from week 0 to week 10 was significant

(p=0.001) in the ketogenic group for weight, body fat percentage, BMI, HgA1c and

ketones. All variables for the ketogenic group out-performed those of the

exercise and non-exercise groups, with five of the seven demonstrating

statistical significance. PMID: 28433617

8. Curr Opin Endocrinol Diabetes Obes. 2017 Oct;24(5):315-319

**Dietary guidelines in type 2 diabetes: the Nordic diet or the ketogenic diet?**

Magnusdottir OK, Gunnarsdottir I, Birgisdóttir BE.

PURPOSE OF REVIEW: To highlight recent developments in research regarding

nutrition therapies for type 2 diabetes mellitus (T2DM) with a focus on the

different approaches of the Nordic diet and the ketogenic diet.

RECENT FINDINGS: Recent short-term studies have revealed that similar beneficial

outcomes are seen after different dietary treatments for T2DM, with different

approaches resulting in comparable weight loss and impacts on metabolic factors.

SUMMARY: More individualized approaches in nutrition therapy should be considered

for T2DM patients and clinical guidelines should reflect this. More studies,

especially long-term studies, are urgently needed on the impacts of the diets on

different health parameters. Such studies should be prioritized because of the

high and increasing prevalence of T2DM and because dietary changes may have

greater benefits than previously thought. Furthermore, studies that focus on

patient compliance to different types of diets, and personal and environmental

factors that may affect compliance, are needed. PMID: 28723705

9. J Postgrad Med. 2017 Oct-Dec;63(4):242-251.

**Ketogenic diet in endocrine disorders: Current perspectives.**

Gupta L, Khandelwal D, Kalra S, Gupta P, Dutta D, Aggarwal S

Ketogenic diet (KD) is a high-fat, adequate-protein, and low-carbohydrate diet

that leads to nutritional ketosis, long known for antiepileptic effects and has

been used therapeutically to treat refractory epilepsy. This review attempts to

summarize the evidence and clinical application of KD in diabetes, obesity, and

other endocrine disorders. KD is usually animal protein based. An empiric

vegetarian Indian variant of KD has been provided keeping in mind the Indian food

habits. KD has beneficial effects on cardiac ischemic preconditioning, improves

oxygenation in patients with respiratory failure, improves glycemic control in

diabetics, is associated with significant weight loss, and has a beneficial

impact on polycystic ovarian syndrome. Multivitamin supplementations are

recommended with KD. Recently, ketones are being proposed as super-metabolic

fuel; and KD is currently regarded as apt dietary therapy for "diabesity." PMID: 29022562

10. Int J Obes (Lond). 2017 Aug;41(8):1224-1231.

**Timeline of changes in appetite during weight loss with a ketogenic diet.**

Nymo S, Coutinho SR, Jørgensen J, Rehfeld JF, Truby H, Kulseng B, Martins C

BACKGROUND/OBJECTIVE: Diet-induced weight loss (WL) leads to increased hunger and

reduced fullness feelings, increased ghrelin and reduced satiety peptides

concentration (glucagon-like peptide-1 (GLP-1), cholecystokinin (CCK) and peptide

YY (PYY)). Ketogenic diets seem to minimise or supress some of these responses.

The aim of this study was to determine the timeline over which changes in

appetite occur during progressive WL with a ketogenic very-low-energy diet (VLED).

SUBJECTS/METHODS: Thirty-one sedentary adults (18 men), with obesity (body mass

index: 37±4.5 kg m-2) underwent 8 weeks (wks) of a VLED followed by 4 wks of

weight maintenance. Body weight and composition, subjective feelings of appetite

and appetite-related hormones (insulin, active ghrelin (AG), active GLP-1, total

PYY and CCK) were measured in fasting and postprandially, at baseline, on day 3

of the diet, 5 and 10% WL, and at wks 9 and 13. Data are shown as mean±s.d.

RESULTS: A significant increase in fasting hunger was observed by day 3 (2±1%

WL), (P<0.01), 5% WL (12±8 days) (P<0.05) and wk 13 (17±2% WL) (P<0.05).

Increased desire to eat was observed by day 3 (P<0.01) and 5% WL (P<0.05).

Postprandial prospective food consumption was significantly reduced at wk 9

(16±2% WL) (P<0.01). Basal total PYY was significantly reduced at 10% WL (32±8

days) (P<0.05). Postprandial active GLP-1 was increased at 5% WL (P<0.01) and CCK

reduced at 5 and 10% WL (P<0.01, for both) and wk 9 (P<0.001). Basal and

postprandial AG were significantly increased at wk 13 (P<0.001, both).

CONCLUSIONS: WL with a ketogenic VLED transiently increases the drive to eat up

to 3 weeks (5% WL). After that, and while participants are ketotic, a 10-17% WL

is not associated with increased appetite. However, hunger feelings and AG

concentrations increase significantly from baseline, once refeeding occurs. PMID: 28439092

11. Endocr Pract. 2017 Jun;23(6):649-656.

**LIMITED CARBOHYDRATE REFEEDING INSTRUCTION FOR LONG-TERM WEIGHT MAINTENANCE FOLLOWING A KETOGENIC, VERY-LOW-CALORIE MEAL PLAN.** Chang JJ, Bena J, Kannan S, Kim J, Burguera B, Kashyap SR.

OBJECTIVE: Weight-loss maintenance following very-low-calorie meal plans is

poorly studied. This report describes weight-loss efficacy and predictors of

weight-loss maintenance of a ketogenic, very-low-calorie meal plan

(protein-sparing modified fast, PSMF) in people with obesity.

METHODS: A total of 127 consecutive adults in the PSMF meal plan (27.2 ± 19.5

weeks) and 48 adults on a conventional, hypocaloric meal plan (23.6 ± 20.8 weeks)

were retrospectively studied for percent weight change from baseline to end of

intervention and at 6, 12, and 24 months postintervention. Baseline factors were

analyzed for correlations with weight-loss maintenance.

RESULTS: At end of intervention, weight loss from baseline was greater for the

PSMF group compared to the conventional intervention group (-12.4% vs. -2.6%;

P<.001) but was similar between groups by 12 months postintervention. PSMF

subjects who attended follow-up visits to receive instruction on gradual and

limited carbohydrate refeeding after ketosis saw significant weight loss at the

end of PSMF compared to those who did not follow-up to receive instruction

(-17.5% vs. -8.0%; P<.001) and maintained greater weight loss through 12 months

post-PSMF (-9.8% vs. -1.5%; P<.001). Higher baseline body mass index correlated

with less weight loss at 12 months post-PSMF (P = .035).

CONCLUSION: PSMF results in effective short-term weight loss of more than 5% from

baseline weight. Follow-up for limited carbohydrate refeeding instruction is

important for weight-loss maintenance up to 2 years after initial weight loss.

ABBREVIATIONS: BMI = body mass index; PSMF = protein-sparing modified fast. PMID: 28225305

12. Nutrients. 2017 May 19;9(5). pii: E517.

**Effects of Ketogenic Diets on Cardiovascular Risk Factors: Evidence from Animal and Human Studies.**

Kosinski C, Jornayvaz FR

The treatment of obesity and cardiovascular diseases is one of the most difficult

and important challenges nowadays. Weight loss is frequently offered as a therapy

and is aimed at improving some of the components of the metabolic syndrome. Among

various diets, ketogenic diets, which are very low in carbohydrates and usually

high in fats and/or proteins, have gained in popularity. Results regarding the

impact of such diets on cardiovascular risk factors are controversial, both in

animals and humans, but some improvements notably in obesity and type 2 diabetes

have been described. Unfortunately, these effects seem to be limited in time.

Moreover, these diets are not totally safe and can be associated with some

adverse events. Notably, in rodents, development of nonalcoholic fatty liver

disease (NAFLD) and insulin resistance have been described. The aim of this

review is to discuss the role of ketogenic diets on different cardiovascular risk

factors in both animals and humans based on available evidence. PMID: 28534852

13. Eur Rev Med Pharmacol Sci. 2017 May;21(9):2274-2289.

**Efficacy and safety of very-low-calorie ketogenic diet: a double blind randomized crossover study.**

Colica C, Merra G, Gasbarrini A, De Lorenzo A, Cioccoloni G, Gualtieri P, Perrone MA, Bernardini S, Bernardo V

OBJECTIVE: To verify safety respect to weight loss, cardiometabolic diseases of

short-term Very low-calorie ketogenic diets (VLCKDs, <800 kcal day-1).

PATIENTS AND METHODS: Randomized cross-over trial with placebo. The study had no.

2 dietary treatment (DT), conducted in two arms: (1) VLCKD1 in which 50% of

protein intake is replaced with synthetic amino acids; (2) VLCKD2 with placebo.

The VLCKDs (<800 kcal day-1) were different in term of protein content and

quality each arm lasted three weeks (wks). Between the two arms a 3-wks washout

period was performed to avoid additive effects on DT to follow. At the baseline,

at start and end of each arm, all the subjects were evaluated for their health

and nutritional status, by anthropometric analysis, body composition (Dual X-ray

Absorptiometry (DXA), Bioimpedentiometry, biochemical evaluation, and Peroxisome

Proliferator-Activated Receptor γ (PPAR) γ expression by transcriptomic analysis.

RESULTS: After VLCKD1 were reduced: Body Mass Index (BMI) (Δ%=-11.1%, p=0.00),

Total Body Water (TBW) (p<0.05); Android Fat Percentage (AFP) (Δ%=-1.8%, p=0.02);

Android Fat Mass (AFM) (Δ%=-12.7%, p=0.00); Gynoid Fat Mass (GFM) (Δ%=-6.3%,

p=0.01); Intermuscular Adipose Tissue (IMAT) (Δ%= -11.1%, p=0.00); Homeostasis

Model Assessment of Insulin Re-sistance (HOMA-IR) (Δ%=-62.1%, p=0.01). After

VLCKD1 a significant increase of uricemia, cre-atinine and aspartate

aminotransferase (AST) (respectively Δ%=35%, p=0.01; Δ%=5.9%, p=0.02; Δ%=25.5%,

p=0.03). After VLCKD2 were reduced: BMI (Δ%=-11.2%, p=0.00); AFM (Δ%=-14.3%,

p=0.00); GFM (Δ%=-6.3%, p=0.00); Appendicular Skeletal Muscle Mass Index (ASMMI)

(Δ%=-17.5%, p=0.00); HOMA-IR (Δ%=-59,4%, p=0.02). After VLCKD2, uricemia

(Δ%=63.1%, p=0.03), and Vitamin D levels (Δ%=25.7%, p=0.02) were increased. No

significant changes of car-diovascular disease (CVD) indexes were observed after

DTs. No significant changes of PPARγ lev-el in any DTs.

CONCLUSIONS: 21-days VLCKDs not impair nutritional state; not cause negative

changes in global measurements of nutritional state including sarcopenia, bone

mineral content, hepatic, renal and lipid profile. PMID: 28537652

14. J Med Internet Res. 2017 Feb 13;19(2):e36.

**An Online Intervention Comparing a Very Low-Carbohydrate Ketogenic Diet and Lifestyle Recommendations Versus a Plate Method Diet in Overweight Individuals With Type 2 Diabetes: A Randomized Controlled Trial.**

Saslow LR, Mason AE, Kim S, Goldman V, Ploutz-Snyder R, Bayandorian H, Daubenmier J, Hecht

BACKGROUND: Type 2 diabetes is a prevalent, chronic disease for which diet is an

integral aspect of treatment. In our previous trial, we found that

recommendations to follow a very low-carbohydrate ketogenic diet and to change

lifestyle factors (physical activity, sleep, positive affect, mindfulness) helped

overweight people with type 2 diabetes or prediabetes improve glycemic control

and lose weight. This was an in-person intervention, which could be a barrier for

people without the time, flexibility, transportation, social support, and/or

financial resources to attend.

OBJECTIVE: The aim was to determine whether an online intervention based on our

previous recommendations (an ad libitum very low-carbohydrate ketogenic diet with

lifestyle factors; "intervention") or an online diet program based on the

American Diabetes Associations' "Create Your Plate" diet ("control") would

improve glycemic control and other health outcomes among overweight individuals

with type 2 diabetes.

METHODS: In this pilot feasibility study, we randomized overweight adults (body

mass index ≥25) with type 2 diabetes (glycated hemoglobin [HbA1c] 6.5%-9.0%) to a

32-week online intervention based on our previous recommendations (n=12) or an

online diet program based around a plate method diet (n=13) to assess the impact

of each intervention on glycemic control and other health outcomes. Primary and

secondary outcomes were analyzed by mixed-effects linear regression to compare

outcomes by group.

RESULTS: At 32 weeks, participants in the intervention group reduced their HbA1c

levels more (estimated marginal mean [EMM] -0.8%, 95% CI -1.1% to -0.6%) than

participants in the control group (EMM -0.3%, 95% CI -0.6% to 0.0%; P=.002). More

than half of the participants in the intervention group (6/11, 55%) lowered their

HbA1c to less than 6.5% versus 0% (0/8) in the control group (P=.02).

Participants in the intervention group lost more weight (EMM -12.7 kg, 95% CI

-16.1 to -9.2 kg) than participants in the control group (EMM -3.0 kg, 95% CI

-7.3 to 1.3 kg; P<.001). A greater percentage of participants lost at least 5% of

their body weight in the intervention (10/11, 90%) versus the control group (2/8,

29%; P=.01). Participants in the intervention group lowered their triglyceride

levels (EMM -60.1 mg/dL, 95% CI -91.3 to -28.9 mg/dL) more than participants in

the control group (EMM -6.2 mg/dL, 95% CI -46.0 to 33.6 mg/dL; P=.01). Dropout

was 8% (1/12) and 46% (6/13) for the intervention and control groups, respectively (P=.07).

CONCLUSIONS: Individuals with type 2 diabetes improved their glycemic control and

lost more weight after being randomized to a very low-carbohydrate ketogenic diet

and lifestyle online program rather than a conventional, low-fat diabetes diet

online program. Thus, the online delivery of these very low-carbohydrate

ketogenic diet and lifestyle recommendations may allow them to have a wider reach

in the successful self-management of type 2 diabetes. PMID: 28193599

15. J Clin Endocrinol Metab. 2017 Feb 1;102(2):488-498.

**Body Composition Changes After Very-Low-Calorie Ketogenic Diet in Obesity Evaluated by 3 Standardized Methods.**

Gomez-Arbelaez D, Bellido D, Castro AI, Ordoñez-Mayan L, Carreira J, Galban C, Martinez-Olmos

Context: Common concerns when using low-calorie diets as a treatment for obesity

are the reduction in fat-free mass, mostly muscular mass, that occurs together

with the fat mass (FM) loss, and determining the best methodologies to evaluate

body composition changes.

Objective: This study aimed to evaluate the very-low-calorie ketogenic (VLCK)

diet-induced changes in body composition of obese patients and to compare 3

different methodologies used to evaluate those changes.

Design: Twenty obese patients followed a VLCK diet for 4 months. Body composition

assessment was performed by dual-energy X-ray absorptiometry (DXA),

multifrequency bioelectrical impedance (MF-BIA), and air displacement

plethysmography (ADP) techniques. Muscular strength was also assessed.

Measurements were performed at 4 points matched with the ketotic phases (basal,

maximum ketosis, ketosis declining, and out of ketosis).

Results: After 4 months the VLCK diet induced a -20.2 ± 4.5 kg weight loss, at

expenses of reductions in fat mass (FM) of -16.5 ± 5.1 kg (DXA), -18.2 ± 5.8 kg

(MF-BIA), and -17.7 ± 9.9 kg (ADP). A substantial decrease was also observed in

the visceral FM. The mild but marked reduction in fat-free mass occurred at

maximum ketosis, primarily as a result of changes in total body water, and was

recovered thereafter. No changes in muscle strength were observed. A strong

correlation was evidenced between the 3 methods of assessing body composition.

Conclusion: The VLCK diet-induced weight loss was mainly at the expense of FM and

visceral mass; muscle mass and strength were preserved. Of the 3 body composition

techniques used, the MF-BIA method seems more convenient in the clinical setting. PMID: 27754807

16. Br J Sports Med. 2017 Jan;51(2):133-139.

**Evidence that supports the prescription of low-carbohydrate high-fat diets: a narrative review.** Noakes TD, Windt J

Low-carbohydrate high-fat (LCHF) diets are a highly contentious current topic in

nutrition. This narrative review aims to provide clinicians with a broad overview

of the effects of LCHF diets on body weight, glycaemic control and cardiovascular

risk factors while addressing some common concerns and misconceptions. Blood

total cholesterol and LDL-cholesterol concentrations show a variable, highly

individual response to LCHF diets, and should be monitored in patients adhering

to this diet. In contrast, available evidence from clinical and preclinical

studies indicates that LCHF diets consistently improve all other markers of

cardiovascular risk-lowering elevated blood glucose, insulin, triglyceride, ApoB

and saturated fat (especially palmitoleic acid) concentrations, reducing small

dense LDL particle numbers, glycated haemoglobin (HbA1c) levels, blood pressure

and body weight while increasing low HDL-cholesterol concentrations and reversing

non-alcoholic fatty liver disease (NAFLD). This particular combination of

favourable modifications to all these risk factors is a benefit unique to LCHF

diets. These effects are likely due in part to reduced hunger and decreased ad

libitum calorie intake common to low-carbohydrate diets, allied to a reduction in

hyperinsulinaemia, and reversal of NAFLD. Although LCHF diets may not be suitable

for everyone, available evidence shows this eating plan to be a safe and

efficacious dietary option to be considered. LCHF diets may also be particularly

beneficial in patients with atherogenic dyslipidaemia, insulin resistance, and

the frequently associated NAFLD. PMID: 28053201

17. Eur Rev Med Pharmacol Sci. 2017 Jan;21(2):329-345.

**Effects of very-low-calorie diet on body composition, metabolic state, and genes expression: a randomized double-blind placebo-controlled trial.** Merra G, Gratteri S, De Lorenzo A, Barrucco S, Perrone MA, Avolio E

OBJECTIVE: Very low-calorie diets (VLCDs, < 800 kcal day-1) and Ketogenic diet

(KD) are generally used as part of integrated intervention, medical monitoring

and a program of lifestyle modification, to improve a multitude of clinical

states. The effect of three different very low calories KD (VLCKD), with (VLCKD1)

or without (VLCKD2,3) synthetic amino acid replacement of the 50% protein intake,

were analyzed after weight loss.

PATIENTS AND METHODS: The clinical study used a cross-over randomized

double-blind placebo-controlled trial. Obese subjects, who were eligible for the

study, were randomly (R) divided into three groups: one intervention group (IG)

and two control groups (CG1 and CG2). We comprehensively analyzed body

composition, serum metabolites, superoxide dismutase (SOD1), nuclear factor

kappa-light-chain-enhancer of activated B cells (NfKB), Chemokine (C-C Motif)

Ligand 2 (CCL2) gene expression.

RESULTS: After VLDKDs a significant decreased in BMI was observed. TBF (kg)

significantly decrease after VLCKD1 and VLCKD3. After VLCKD2, a reduction of

waist circumference (p = 0.02), FM L2-L5 (p < 0.05) was observed. After VLCKD1

reduction of IMAT (p = 0.00), LDL-C (p = 0.00) and HDL-C (p = 0.00) were

observed. No significant changes of GH, ESR, and fibrinogen were highlighted. CRP

(p = 0.02) reduced significantly after VLCKD3. Significant modulation of SOD1

expression (p = 0.009), CRP and decrease of glucose levels (p = 0.03) were

obtained after VLCKD3.

CONCLUSIONS: This is the first study that analyzes comprehensively body

composition, metabolic profile, and inflammation and oxidative stress genes

expression after VLCKD. Our results show the efficacy of VLCKD with synthetic

aminoacidic protein replacement, for the reduction of cardiovascular risk,

without the development of sarcopenia and activation of inflammatory and

oxidative processes. PMID: 28165552

18. Endocrine. 2016 Dec;54(3):681-690.

**Obesity treatment by very low-calorie-ketogenic diet at two years: reduction in visceral fat and on the burden of disease.** Moreno B, Crujeiras AB, Bellido D, Sajoux I, Casanueva FF

The long-term effect of therapeutic diets in obesity treatment is a challenge at

present. The current study aimed to evaluate the long-term effect of a very

low-calorie-ketogenic (VLCK) diet on excess adiposity. Especial focus was set on

visceral fat mass, and the impact on the individual burden of disease. A group of

obese patients (n = 45) were randomly allocated in two groups: either the very

low-calorie-ketogenic diet group (n = 22), or a standard low-calorie diet group;

(n = 23). Both groups received external support. Adiposity parameters and the

cumulative number of months of successful weight loss (5 or 10 %) over a 24-month

period were quantified. The very low-calorie-ketogenic diet induced less than 2

months of mild ketosis and significant effects on body weight at 6, 12, and 24

months. At 24 months, a trend to regress to baseline levels was observed;

however, the very low-calorie-ketogenic diet induced a greater reduction in body

weight (-12.5 kg), waist circumference (-11.6 cm), and body fat mass (-8.8 kg)

than the low-calorie diet (-4.4 kg, -4.1 cm, and -3.8 kg, respectively;

p < 0.001). Interestingly, a selective reduction in visceral fat measured by a

specific software of dual-energy x-ray absorptiometry (DEXA)-scan (-600 g vs.

-202 g; p < 0.001) was observed. Moreover, the very low-calorie-ketogenic diet

group experienced a reduction in the individual burden of obesity because

reduction in disease duration. Very low-calorie-ketogenic diet patients were 500

months with 5 % weight lost vs. the low-calorie diet group (350 months;

p < 0.001). In conclusion, a very low-calorie-ketogenic diet was effective 24

months later, with a decrease in visceral adipose tissue and a reduction in the

individual burden of disease. PMID: 27623967

19. Br J Nutr. 2016 Feb 14;115(3):466-79.

**Effects of low-carbohydrate diets v. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomised controlled trials.** Mansoor N, Vinknes KJ, Veierød MB, Retterstøl K

The effects of low-carbohydrate (LC) diets on body weight and cardiovascular risk

are unclear, and previous studies have found varying results. Our aim was to

conduct a meta-analysis of randomised controlled trials (RCT), assessing the

effects of LC diets v. low-fat (LF) diets on weight loss and risk factors of CVD.

Studies were identified by searching MEDLINE, Embase and Cochrane Trials. Studies

had to fulfil the following criteria: a RCT; the LC diet was defined in

accordance with the Atkins diet, or carbohydrate intake of <20% of total energy

intake; twenty subjects or more per group; the subjects were previously healthy;

and the dietary intervention had a duration of 6 months or longer. Results from

individual studies were pooled as weighted mean difference (WMD) using a random

effect model. In all, eleven RCT with 1369 participants met all the set

eligibility criteria. Compared with participants on LF diets, participants on LC

diets experienced a greater reduction in body weight (WMD -2·17 kg; 95% CI -3·36,

-0·99) and TAG (WMD -0·26 mmol/l; 95% CI -0·37, -0·15), but a greater increase in

HDL-cholesterol (WMD 0·14 mmol/l; 95% CI 0·09, 0·19) and LDL-cholesterol (WMD

0·16 mmol/l; 95% CI 0·003, 0·33). This meta-analysis demonstrates opposite change

in two important cardiovascular risk factors on LC diets--greater weight loss and

increased LDL-cholesterol. Our findings suggest that the beneficial changes of LC

diets must be weighed against the possible detrimental effects of increased

LDL-cholesterol. PMID: 26768850

20. High Blood Press Cardiovasc Prev. 2015 Dec;22(4):389-94.

**Middle and Long-Term Impact of a Very Low-Carbohydrate Ketogenic Diet on Cardiometabolic Factors: A Multi-Center, Cross-Sectional, Clinical Study.** Cicero AF, Benelli M, Brancaleoni M, Dainelli G, Merlini D, Negri R

INTRODUCTION: Obesity is a constantly growing illness in developed countries and

it is strictly related to cardiovascular (CV) diseases, i.e. the main cause of

mortality throughout industralised areas.

AIM: to test the ability of trained general physician to safely and effectively

prescribe a very-low carbohydrate ketogenic (VLCK) diet in clinical practice,

with a specific attention to the effect of this approach on overweight related CV

risk factors (anthropometric measures) blood pressure, lipid levels, glucose metabolism).

METHODS: The study has been carried out on a group of 377 patients scattered

across Italy and monitored during 1 year. The proposed VLCK diet is a nutritional

regimen characterized by low-fat and low- carbohydrates formulations and a

protein content of 1.2/1.5 g/kg of ideal body weight, followed by a period of

slow re-insertion and alimentary re-education.

RESULTS: All the predetermined goals-namely safety, reduction of body weight and

CV risk factors levels-have been reached with a significant reduction of body

weight (from baseline to 4 weeks (-7 ± 5 kg, p < 0.001), from 4 to 12 weeks (-5 ±

3 kg, p < 0.001), no changes from 12 weeks to 12 months; waistline (from baseline

to 4 weeks (-7 ± 4 cm, p < 0.001), from 4 to 12 weeks (-5 ± 7 cm, p < 0.001), no

changes from 12 weeks to 12 months; fatty mass (from baseline to 4 weeks (-3.8 ±

3.8 %, p < 0.001), from 4 to 12 weeks (-3.4 ± 3.5 %, p < 0.001), no changes from

12 weeks to 12 months; SBP from baseline to 3 months (-10.5 ± 6.4 mmHg, p <

0.001), no further changes after 1 year of observation).

CONCLUSION: the tested VLCD diet suggested by trained general physicians in the

setting of clinical practice seems to be able to significantly improve on the

middle-term a number of anthropometric, haemodynamic and laboratory with an

overall good tolerability. PMID: 25986079

21. Obes Rev. 2015 Jan;16(1):64-76.

**Do ketogenic diets really suppress appetite? A systematic review and meta-analysis.**

Gibson AA, Seimon RV, Lee CM, Ayre J, Franklin J, Markovic TP, Caterson ID, Sainsbury A.

Very-low-energy diets (VLEDs) and ketogenic low-carbohydrate diets (KLCDs) are

two dietary strategies that have been associated with a suppression of appetite.

However, the results of clinical trials investigating the effect of ketogenic

diets on appetite are inconsistent. To evaluate quantitatively the effect of

ketogenic diets on subjective appetite ratings, we conducted a systematic

literature search and meta-analysis of studies that assessed appetite with visual

analogue scales before (in energy balance) and during (while in ketosis)

adherence to VLED or KLCD. Individuals were less hungry and exhibited greater

fullness/satiety while adhering to VLED, and individuals adhering to KLCD were

less hungry and had a reduced desire to eat. Although these absolute changes in

appetite were small, they occurred within the context of energy restriction,

which is known to increase appetite in obese people. Thus, the clinical benefit

of a ketogenic diet is in preventing an increase in appetite, despite weight

loss, although individuals may indeed feel slightly less hungry (or more full or

satisfied). Ketosis appears to provide a plausible explanation for this

suppression of appetite. Future studies should investigate the minimum level of

ketosis required to achieve appetite suppression during ketogenic weight loss

diets, as this could enable inclusion of a greater variety of healthy

carbohydrate-containing foods into the diet. PMID: 25402637

22. Endocrine. 2014 Dec;47(3):793-805.

**Comparison of a very low-calorie-ketogenic diet with a standard low-calorie diet in the treatment of obesity.**

Moreno B, Bellido D, Sajoux I, Goday A, Saavedra D, Crujeiras AB, Casanueva FF.

The global prevalence of obesity has significantly increased in most

industrialized countries. Anti-obesity drugs are scarce, and indications to

change their life style are impractical. Therefore, to identify diets able to

produce significantly and maintained weight loss is mandatory. The present work

evaluated the efficacy of a very low-calorie-ketogenic (VLCK) diet in obesity. A

group of obese patients were randomized into two groups: the VLCK diet group and

a standard low-calorie diet (LC group). The follow-up period was 12 months. Both

groups received external support, counseling, to perform physical activity and

adhered to the diet. The VLCK diet induced a 30-45 days of mild ketosis and

significant effects on body weight within 15 days. At 2 months, the weight

reductions in the VLCK diet and LC diet groups were 13.6 ± 3.9 and 4.8 ± 2.7 kg,

respectively (p < 0.0001). At the end of the study, at 12 months, the weight

reductions were 19.9 ± 12.3 and 7.0 ± 5.6 kg, respectively (p < 0.0001), and more

than 88 % of patients in the VLCK diet group lost more of 10 % of their initial

weight. Lean mass was practically unaffected. The VLCK diet was well tolerated

and the side effects were moderate and transitory. In a group of obese patients,

the VLCK diet was significantly more effective than a standard LC diet. At one

year follow-up in the group with VLCK diet, most of the patients loss more than

10 % of their initial weight and lean mass was well preserved. PMID: 24584583

23. BMJ Open. 2014 Feb 5;4(2):e003505.

**Effect of a 6-month vegan low-carbohydrate ('Eco-Atkins') diet on cardiovascular risk factors and body weight in hyperlipidaemic adults: a randomised controlled trial.** Jenkins DJ, Wong JM, Kendall CW, Esfahani A, Ng VW, Leong

OBJECTIVE: Low-carbohydrate diets may be useful for weight loss. Diets high in

vegetable proteins and oils may reduce the risk of coronary heart disease. The

main objective was to determine the longer term effect of a diet that was both

low-carbohydrate and plant-based on weight loss and low-density lipoprotein

cholesterol (LDL-C).

DESIGN, SETTING, PARTICIPANTS: A parallel design study of 39 overweight

hyperlipidaemic men and postmenopausal women conducted at a Canadian

university-affiliated hospital nutrition research centre from April 2005 to November 2006.

INTERVENTION: Participants were advised to consume either a low-carbohydrate

vegan diet or a high-carbohydrate lacto-ovo vegetarian diet for 6 months after

completing 1-month metabolic (all foods provided) versions of these diets. The

prescribed macronutrient intakes for the low-carbohydrate and high-carbohydrate

diets were: 26% and 58% of energy from carbohydrate, 31% and 16% from protein and

43% and 25% from fat, respectively.

PRIMARY OUTCOME: Change in body weight.

RESULTS: 23 participants (50% test, 68% control) completed the 6-month ad libitum

study. The approximate 4 kg weight loss on the metabolic study was increased to

-6.9 kg on low-carbohydrate and -5.8 kg on high-carbohydrate 6-month ad libitum

treatments (treatment difference (95% CI) -1.1 kg (-2.1 to 0.0), p=0.047). The

relative LDL-C and triglyceride reductions were also greater on the

low-carbohydrate treatment (treatment difference (95% CI) -0.49 mmol/L (-0.70 to

-0.28), p<0.001 and -0.34 mmol/L (-0.57 to -0.11), p=0.005, respectively), as

were the total cholesterol:HDL-C and apolipoprotein B:A1 ratios (-0.57 (-0.83,

-0.32), p<0.001 and -0.05 (-0.09, -0.02), p=0.003, respectively).

CONCLUSIONS: A self-selected low-carbohydrate vegan diet, containing increased

protein and fat from gluten and soy products, nuts and vegetable oils, had lipid

lowering advantages over a high-carbohydrate, low-fat weight loss diet, thus

improving heart disease risk factors. PMID: 24500611

24. Br J Nutr. 2013 Oct;110(7):1178-87.

**Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials.** Bueno NB, de Melo IS, de Oliveira SL, da Rocha Ataide T.

The role of very-low-carbohydrate ketogenic diets (VLCKD) in the long-term

management of obesity is not well established. The present meta-analysis aimed to

investigate whether individuals assigned to a VLCKD (i.e. a diet with no more

than 50 g carbohydrates/d) achieve better long-term body weight and

cardiovascular risk factor management when compared with individuals assigned to

a conventional low-fat diet (LFD; i.e. a restricted-energy diet with less than

30% of energy from fat). Through August 2012, MEDLINE, CENTRAL,

ScienceDirect,Scopus, LILACS, SciELO, ClinicalTrials.gov and grey literature

databases were searched, using no date or language restrictions, for randomised

controlled trials that assigned adults to a VLCKD or a LFD, with 12 months or

more of follow-up. The primary outcome was bodyweight. The secondary outcomes

were TAG, HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C), systolic and

diastolic blood pressure,glucose, insulin, HbA1c and C-reactive protein levels. A

total of thirteen studies met the inclusion/exclusion criteria. In the overall

analysis,five outcomes revealed significant results. Individuals assigned to a

VLCKD showed decreased body weight (weighted mean difference 20·91 (95% CI 21·65,

20·17) kg, 1415 patients), TAG (weighted mean difference 20·18 (95% CI 20·27,

20·08) mmol/l, 1258 patients)and diastolic blood pressure (weighted mean

difference 21·43 (95% CI 22·49, 20·37) mmHg, 1298 patients) while increased

HDL-C(weighted mean difference 0·09 (95% CI 0·06, 0·12) mmol/l, 1257 patients)

and LDL-C (weighted mean difference 0·12 (95% CI 0·04,0·2) mmol/l, 1255

patients). Individuals assigned to a VLCKD achieve a greater weight loss than

those assigned to a LFD in the longterm; hence, a VLCKD may be an alternative

tool against obesity. PMID: 23651522

25. Eur J Clin Nutr. 2013 Aug;67(8):789-96.

**Beyond weight loss: a review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets.** Paoli A, Rubini A

Very-low-carbohydrate diets or ketogenic diets have been in use since the 1920s

as a therapy for epilepsy and can, in some cases, completely remove the need for

medication. From the 1960s onwards they have become widely known as one of the

most common methods for obesity treatment. Recent work over the last decade or so

has provided evidence of the therapeutic potential of ketogenic diets in many

pathological conditions, such as diabetes, polycystic ovary syndrome, acne,

neurological diseases, cancer and the amelioration of respiratory and

cardiovascular disease risk factors. The possibility that modifying food intake

can be useful for reducing or eliminating pharmaceutical methods of treatment,

which are often lifelong with significant side effects, calls for serious

investigation. This review revisits the meaning of physiological ketosis in the

light of this evidence and considers possible mechanisms for the therapeutic

actions of the ketogenic diet on different diseases. The present review also

questions whether there are still some preconceived ideas about ketogenic diets,

which may be presenting unnecessary barriers to their use as therapeutic tools in

the physician's hand. PMID: 23801097

26. Br J Nutr. 2011 Jul;106(2):282-91.

**Effects of a high-protein, low-carbohydrate v. high-protein, moderate-carbohydrate weight-loss diet on antioxidant status, endothelial markers and plasma indices of the cardiometabolic profile.**

Johnstone AM, Lobley GE, Horgan GW, Bremner DM, Fyfe CL, Morrice PC, Duthie GG.

There are concerns that weight-loss (WL) diets based on very low carbohydrate

(LC) intake have a negative impact on antioxidant status and biomarkers of

cardiovascular and metabolic health. Obese men (n 16) participated in a

randomised, cross-over design diet trial, with food provided daily, at

approximately 8.3 MJ/d (approximately 70 % of energy maintenance requirements).

They were provided with two high-protein diets (30 % of energy), each for a

4-week period, involving a LC (4 % carbohydrate) and a moderate carbohydrate (MC,

35 % carbohydrate) content. Body weight was measured daily, and weekly blood

samples were collected. On average, subjects lost 6.75 and 4.32 kg of weight on

the LC and MC diets, respectively (P < 0.001, SED 0.350). Although the LC and MC

diets were associated with a small reduction in plasma concentrations of retinol,

vitamin E (α-tocopherol) and β-cryptoxanthin (P < 0.005), these were still above

the values indicative of deficiency. Interestingly, plasma vitamin C

concentrations increased on consumption of the LC diet (P < 0.05). Plasma markers

of insulin resistance (P < 0.001), lipaemia and inflammation (P < 0.05, TNF-α and

IL-10) improved similarly on both diets. There was no change in other

cardiovascular markers with WL. The present data suggest that a LC WL diet does

not impair plasma indices of cardiometabolic health, at least within 4 weeks, in

otherwise healthy obese subjects. In general, improvements in metabolic health

associated with WL were similar between the LC and MC diets. Antioxidant

supplements may be warranted if LC WL diets are consumed for a prolonged period. PMID: 21521539

27. Diabetologia. 2011 Apr;54(4):731-40.

**The effect of high-protein, low-carbohydrate diets in the treatment of type 2 diabetes: a 12 month randomised controlled trial.** Larsen RN, Mann NJ, Maclean E, Shaw JE.

AIMS/HYPOTHESIS: Short-term dietary studies suggest that high-protein diets can

enhance weight loss and improve glycaemic control in people with type 2 diabetes.

However, the long-term effects of such diets are unknown. The aim of this study

was to determine whether high-protein diets are superior to high-carbohydrate

diets for improving glycaemic control in individuals with type 2 diabetes.

METHODS: Overweight/obese individuals (BMI 27-40 kg/m(2)) with type 2 diabetes

(HbA(1c) 6.5-10%) were recruited for a 12 month, parallel design, dietary

intervention trial conducted at a diabetes specialist clinic (Melbourne, VIC,

Australia). Of the 108 initially randomised, 99 received advice to follow low-fat

(30% total energy) diets that were either high in protein (30% total energy, n =

53) or high in carbohydrate (55% total energy, n = 46). Dietary assignment was

done by a third party using computer-generated random numbers. The primary

endpoint was change in HbA(1c). Secondary endpoints included changes in weight,

lipids, blood pressure, renal function and calcium loss. Study endpoints were

assessed blinded to the diet group, but the statistical analysis was performed

unblinded. This study used an intention-to-treat model for all participants who

received dietary advice. Follow-up visits were encouraged regardless of dietary

adherence and last measurements were carried forward for study non-completers.

RESULTS: Ninety-nine individuals were included in the analysis (53 in high

protein group, 46 in high carbohydrate group). HbA(1c) decreased in both groups

over time, with no significant difference between groups (mean difference of the

change at 12 months; 0.04 [95% CI -0.37, 0.46]; p = 0.44). Both groups also

demonstrated decreases over time in weight, serum triacylglycerol and total

cholesterol, and increases in HDL-cholesterol. No differences in blood pressure,

renal function or calcium loss were seen.

CONCLUSIONS/INTERPRETATION: These results suggest that there is no superior

long-term metabolic benefit of a high-protein diet over a high-carbohydrate in

the management of type 2 diabetes. PMID: 21246185

28. Prog Lipid Res. 2008 Sep;47(5):307-18.

**Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome.** Volek JS, Fernandez ML, Feinman RD, Phinney SD.

Abnormal fatty acid metabolism and dyslipidemia play an intimate role in the

pathogenesis of metabolic syndrome and cardiovascular diseases. The availability

of glucose and insulin predominate as upstream regulatory elements that operate

through a collection of transcription factors to partition lipids toward anabolic

pathways. The unraveling of the details of these cellular events has proceeded

rapidly, but their physiologic relevance to lifestyle modification has been

largely ignored. Here we highlight the role of dietary input, specifically

carbohydrate intake, in the mechanism of metabolic regulation germane to

metabolic syndrome. The key principle is that carbohydrate, directly or

indirectly through the effect of insulin, controls the disposition of excess

dietary nutrients. Dietary carbohydrate modulates lipolysis, lipoprotein assembly

and processing and affects the relation between dietary intake of saturated fat

intake and circulating levels. Several of these processes are the subject of

intense investigation at the cellular level. We see the need to integrate these

cellular mechanisms with results from low-carbohydrate diet trials that have

shown reduced cardiovascular risk through improvement in hepatic, intravascular,

and peripheral processing of lipoproteins, alterations in fatty acid composition,

and reductions in other cardiovascular risk factors, notably inflammation. From

the current state of the literature, however, low-carbohydrate diets are grounded

in basic metabolic principles and the data suggest that some form of carbohydrate

restriction is a candidate to be the preferred dietary strategy for

cardiovascular health beyond weight regulation. PMID: 18396172

29. J Int Soc Sports Nutr. 2004 Dec 31;1(2):7-11.

**Metabolic effects of the very-low-carbohydrate diets: misunderstood "villains" of human metabolism.** Manninen AH

During very low carbohydrate intake, the regulated and controlled production of

ketone bodies causes a harmless physiological state known as dietary ketosis.

Ketone bodies flow from the liver to extra-hepatic tissues (e.g., brain) for use

as a fuel; this spares glucose metabolism via a mechanism similar to the sparing

of glucose by oxidation of fatty acids as an alternative fuel. In comparison with

glucose, the ketone bodies are actually a very good respiratory fuel. Indeed,

there is no clear requirement for dietary carbohydrates for human adults.

Interestingly, the effects of ketone body metabolism suggest that mild ketosis

may offer therapeutic potential in a variety of different common and rare disease

states. Also, the recent landmark study showed that a very-low-carbohydrate diet

resulted in a significant reduction in fat mass and a concomitant increase in

lean body mass in normal-weight men. Contrary to popular belief, insulin is not

needed for glucose uptake and utilization in man. Finally, both muscle fat and

carbohydrate burn in an amino acid flame. PMID: 18500949