



REVIEW

# Dietary fat, insulin sensitivity and the metabolic syndrome

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## KEYWORDS

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**Summary** Insulin resistance is the pathogenetic link underlying the different metabolic abnormalities clustering in the metabolic syndrome. It can be induced by different environmental factors, including dietary habits. Consumption of energy-dense/high fat diets is strongly and positively associated with overweight that, in turn, deteriorates insulin sensitivity, particularly when the excess of body fat is located in abdominal region. Nevertheless the link between fat intake and overweight is not limited to the high-energy content of fatty foods; the ability to oxidize dietary fat is impaired in some individuals genetically predisposed to obesity.

Insulin sensitivity is also affected by the quality of dietary fat, independently of its effects on body weight. Epidemiological evidence and intervention studies clearly show that in humans saturated fat significantly worsen insulin-resistance, while monounsaturated and polyunsaturated fatty acids improve it through modifications in the composition of cell membranes which reflect at least in part dietary fat composition. A recent multicenter study (KANWU) has shown that shifting from a diet rich in saturated fatty acids to one rich in monounsaturated fat improves insulin sensitivity in healthy people while a moderate  $\omega$ -3 fatty acids supplementation does not affect insulin sensitivity. There are also other features of the metabolic syndrome that are influenced by different types of fat, particularly blood pressure and plasma lipid levels. Most studies show that  $\omega$ -3 fatty acids reduce blood pressure in hypertensive but not in normotensive subjects while shifting from saturated to monounsaturated fat intake reduces diastolic blood pressure. In relation to lipid abnormalities  $\omega$ -3 fatty acids reduce plasma triglyceride levels but in parallel, increase LDL cholesterol. Substitution of unsaturated fat for saturated fat not only reduces LDL cholesterol but contributes also to reduce plasma triglycerides in insulin resistant individuals.

In conclusion, there is evidence available in humans indicating that dietary fat quality influences insulin sensitivity and associated metabolic abnormalities. Therefore, prevention of the metabolic syndrome has to be targeted: (1) to correct overweight by reducing the energy density of the habitual diet (i.e., fat intake) and

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(2) to improve insulin sensitivity and associated metabolic abnormalities through a reduction of dietary saturated fat, partially replaced, when appropriate, by monounsaturated and polyunsaturated fats.

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## Introduction

Insulin sensitivity is a key function for the human body since it plays a crucial role in the development of diseases that have become very common in modern society and significantly influence duration and quality of life. Its relevance for human health derives from its being at the interface between genetic and environmental factors regulating a number of functions involved in intermediary metabolism, body fat deposition, blood flow in the cardiovascular system and many others. In this context, the relationship among these different functions is complex and often it is not possible to identify the exact sequence of events responsible for the development of impaired insulin sensitivity.

Insulin resistance is an important risk factor for type 2 diabetes and is often associated with other metabolic abnormalities and cardiovascular risk factors; moreover, it has been proposed as an independent risk factor for cardiovascular disease.<sup>1</sup> As a matter of fact, it represents the pathogenetic link underlying the different metabolic abnormalities clustering in the so-called metabolic syndrome. There is no internationally agreed definition of the metabolic syndrome, which is generally considered as an association of impaired glucose regulation (Impaired Glucose Tolerance, IGT or Impaired Fasting Glucose, IFG) or type 2 diabetes, hypertension, hypertriglyceridemia, low HDL and central obesity;<sup>2,3</sup> a recent statement from the National Cholesterol Education Panel (NCEP) of USA attempts to define diagnostic criteria for the Metabolic Syndrome based exclusively on these clinical parameters.<sup>4</sup> On the basis of this definition the prevalence of the metabolic syndrome is around 25% of the general population and is not different in males and females, but it may vary with genetic background.<sup>5</sup>

Insulin sensitivity can be modulated by different environmental factors, mainly dietary habits. The influence of diet on insulin sensitivity is mediated by its energy content and nutrient composition, in particular by different types of dietary fatty acids. The aim of this review is to evaluate the relationship between amount and composition of dietary fat with insulin sensitivity as well as with the development of the metabolic syndrome.

## Data source

We performed a literature search on the Medline database on dietary fat and insulin sensitivity or metabolic syndrome through December 2003.

All together 159 papers were identified; among them we selected 39 papers based on an epidemiological (mostly prospective) design or on intervention trials; they represent the core source of information for this review.

## Dietary fat, body weight and insulin sensitivity

Obesity, especially if associated with abdominal adiposity, is an important determinant of insulin-resistance and represents the most important risk factor for type 2 diabetes and the metabolic syndrome. Laboratory experiments in animals and clinical studies in humans have repeatedly shown that dietary factors, particularly fat and energy intake are strongly and positively associated with body weight gain. Moreover, there is robust evidence from epidemiological (cross-sectional and longitudinal) studies to support that a high fat diet (energy-dense) is an independent risk factor for overweight.<sup>6</sup> However, weight gain in sedentary people is largely dependent on the overall balance between total energy intake and energy expenditure; in some cases, particularly in children and adolescents, also excessive consumption of energy dense carbohydrate rich foods (soft drinks) can be predictive of overweight.<sup>7</sup>

The link between fat intake and overweight is not limited to the high-energy content of fatty foods.

As a matter of fact, subjects prone to obesity show a reduced ability to oxidize dietary and endogenous fat and, in the presence of excessive energy intake, store fat in adipose tissue to an extent that exceeds the body's ability to oxidize it, leading to an expansion of body fat stores and weight gain.<sup>8</sup> Conversely, weight-stable obese individuals show high rates of fat oxidation, which is interpreted as an adaptation mechanism to prevent further, unlimited weight gain.<sup>9-12</sup> This mechanism of weight control also applies to obese

subjects undergoing a weight loss treatment, since a low rate of lipid oxidation at the end of the weight-reduction period is able to predict weight re-gain in the following years.<sup>13</sup>

The importance of overweight in relation to the risk of type 2 diabetes and the metabolic syndrome has been emphasized by intervention studies showing that a reduction of body weight decreases the incidence of diabetes and improves all abnormalities clustering in the metabolic syndrome. In addition, in individuals already affected by diabetes, weight loss reduces postabsorptive rates of hepatic glucose production thereby reducing fasting hyperglycaemia. Furthermore weight loss improves insulin sensitivity in peripheral tissues, particularly increasing the capacity of non-oxidative glucose metabolism.<sup>14,15</sup>

## Dietary fat and insulin sensitivity

### Fat intake

Observational studies do not allow to evaluate whether total fat intake can influence insulin sensitivity independently of its effects on body weight. In this respect intervention studies are much more informative. Attempts have been made to influence insulin sensitivity by changing in isoenergetic conditions the total amount of nutrients, in particular the amount of total fat and carbohydrates. Unfortunately only few well-controlled studies using the glucose clamp or the frequently sampled intravenous glucose tolerance test (FSIGT) to measure insulin sensitivity are available in the literature (Table 1).<sup>16–25</sup> However, these studies are consistent in showing that when total fat intake is changed between 20% and 40% of

the total energy intake no major effect is observed on insulin sensitivity.<sup>17,18,20,22–25</sup> The only two studies in which insulin sensitivity deteriorated in parallel with an increase in fat intake were the Chen Study (fat intake varied from 0% to 55%)<sup>16</sup> and the Lovejoy Study<sup>19</sup> in which fat composition also changed. In the study performed by our group a reduction of fat intake (monounsaturated fat) counterbalanced by an increased consumption of starchy foods, even slightly worsened insulin sensitivity. This was probably a consequence of glucotoxicity; in fact our study participants had diabetes and the increase in the carbohydrate load deteriorated their glycemic control, thus impairing their insulin sensitivity.<sup>21</sup>

### Dietary fat composition

In relation to the effects of dietary fat composition on insulin sensitivity there is considerable evidence in experimental animals that saturated fat impairs whereas  $\omega$ -3 fatty acids improve insulin action, and that monounsaturated and  $\omega$ -6 polyunsaturated fatty acids have less negative effect on insulin sensitivity than saturated fat.<sup>26</sup>

In man, there is indirect evidence that a higher saturated fat intake is associated with impaired insulin action. Several cross-sectional studies have examined the relationship between dietary fat and markers of insulin resistance (plasma insulin values) (Table 2).<sup>27–33</sup> The consistent finding is a positive association between saturated fat intake and hyperinsulinaemia, independently of body fat (in five of the seven studies).<sup>27–31</sup> Polyunsaturated fat intake was inversely associated with plasma insulin levels in one study<sup>30</sup> whereas linoleic acid intake was positively associated with fasting plasma insulin concentrations in another study.<sup>29</sup> The lack

**Table 1** Dietary fat and insulin sensitivity in healthy people (H) or in individuals with type 2 diabetes (D) or impaired glucose tolerance (IGT) = intervention studies: high fat vs. low fat.

Study	Fat content (%)	Subjects (n)	Duration (weeks)	Method	Relationship with insulin sensitivity
Chen et al. <sup>16</sup>	55 vs. 0	H (18)	1 × 2	FSIGT	↓
Swinburn et al. <sup>17</sup>	50 vs. 15	H (24)	2 × 2	FSIGT	↔
Borkman et al. <sup>18</sup>	50 vs. 20	H (8)	3 × 2	Clamp	↔
Lovejoy et al. <sup>19</sup>	50 vs. 20	H (31)	3 × 2	FSIGT	↓
Thomsen et al. <sup>25</sup>	40 vs. 30	H (16)	4 × 2	FSIGT	↔
Bisschop et al. <sup>20</sup>	83 vs. 41 vs. 0	H (6)	2 × 3	Clamp	↔
Parillo et al. <sup>21</sup>	40 vs. 20	D (10)	2 × 2	Clamp	↑
Garg et al. <sup>22</sup>	50 vs. 25	D (8)	2 × 3	Clamp	↔
Hughes et al. <sup>23</sup>	30 vs. 20	D/IGT (10/10)	12	Clamp	↔
Sarkkinen et al. <sup>24</sup>	40 vs. 34	D/IGT (17/14)	8	FSIGT	↔

FSIGT = frequent sampling intravenous glucose tolerance test (minimal model).

**Table 2** Relationship between dietary fat and insulin sensitivity in epidemiological (longitudinal) studies.

Study	Subjects (n)	Diet assessment	Method	Relationship with insulin sensitivity		
				Saturated	Unsaturated	Total fat
Maron et al. <sup>27</sup>	215	4-day food records	OGTT	↓	↓	↓
Parker et al. <sup>28</sup>	652	Food frequency questionnaire	OGTT	↓	n.e.	↓
Mayer et al. <sup>29</sup>	544	Food frequency questionnaire	OGTT	↓	↓	↓
Feskens et al. <sup>30</sup>	389	Dietary history	OGTT	↓	↑	↔
Marshall et al. <sup>31</sup>	1069	24 h diet recall		↓	↔	↔
Mayer-Davis et al. <sup>33</sup>	1173	Food frequency questionnaire	FSIGT	↔	↔	↔
Mooy et al. <sup>32</sup>	481	Semiquantitative food frequency questionnaire	OGTT	↔	↔	↔

FSIGT = frequent sampling intravenous glucose tolerance test (minimal model).

OGTT = oral glucose tolerance test.

n.e. = not examined.

**Table 3** Relationship between fatty acid composition of plasma/muscle lipids and insulin sensitivity in non-diabetic people.

Study	Subjects (n)	Source	Method	Relationship with insulin sensitivity	
				Saturated fat	Unsaturated fat
Pelikanova et al. <sup>34</sup>	11	Serum phospholipids	Clamp	↓	↑
Borkman et al. <sup>35</sup>	27	Muscle phospholipids	Fasting Insulin	↔	↑
Vessby et al. <sup>36</sup>	215	Serum cholesterol E.	Clamp	↓	↑
Pan et al. <sup>37</sup>	52	Muscle phospholipids	Clamp	↔	↑

of relationship between polyunsaturated fat consumption and markers of insulin sensitivity could depend on the difficulty of assessing the intake of unsaturated fat by dietary recall. The relationship between dietary fat composition and insulin sensitivity has been further supported by human studies using more accurate techniques to evaluate insulin resistance and objective markers of fat intake (measurement of serum/muscle lipid fatty acid profile) (Table 3).<sup>34-37</sup> These studies have shown consistently that increased unsaturated fat intake (as indicated by higher proportion of unsaturated fatty acids in plasma or muscle) is associated with an improved insulin sensitivity. Evidence is also available on the relationship between fatty acid composition in body tissues and incidence of diabetes.<sup>38</sup> A problem with these studies, however, is that most fatty acids are closely interrelated and, therefore, insulin resistance or an increased risk of type 2 diabetes are characterized by a fatty acid "pattern" in plasma or tissues rather than by the proportion of one or a few fatty acids.

The mechanisms linking dietary fat quality to insulin sensitivity are not completely understood; however, the effects of dietary fatty acids on this

biological function are believed to be mediated, at least partially, through the fatty acid composition of cell membranes. A specific fatty acids profile in cell membranes could influence insulin action through several potential mechanisms, including altered insulin receptor binding or affinity, and by influencing ion permeability and cell signalling.

Therefore, trying to summarize the results deriving from epidemiological studies, we can conclude that most studies show an association between a higher saturated fat intake and worsening of insulin sensitivity while the contrary is true for unsaturated fat. However, these associations do not necessarily imply a cause/effect relationship, which can be proven only by intervention studies.

The main studies evaluating the effects of dietary saturated fat versus unsaturated fat on insulin sensitivity in healthy and type 2 diabetic individuals utilizing an intervention trial design are listed in Table 4.<sup>39-45</sup> In most studies, changes in dietary fat quality had no effect on insulin sensitivity;<sup>39-42,45</sup> however, it is important to underline that these studies were performed in vary small groups of subjects and, generally, for a short period of time. Instead, two studies,<sup>43,44</sup> one performed in healthy

**Table 4** Effects of diet composition on insulin sensitivity-intervention studies: *Saturated vs. Unsaturated fat.*

Study	Subjects (n)	Duration (weeks)	Method	Fat change	Relationship with insulin sensitivity
Heine et al. <sup>39</sup>	Diabetic (14)	30 × 2	Insulin–glucose infusion	SAFA vs. PUFA	↔
Uusitupa et al. <sup>40</sup>	Healthy (10)	3 × 2	FSIGT	SAFA vs. MUFA	↔
Schwab et al. <sup>41</sup>	Healthy (10)	3 × 2	FSIGT	SAFA vs. PUFA	↔
Fasching et al. <sup>42</sup>	Healthy (10)	1 × 3	Clamp	SAFA vs. MUFA vs. PUFA	↔
Vessby et al. <sup>43</sup>	Healthy (162)	12 × 2	FSIGT	SAFA vs. MUFA	↓
Summers et al. <sup>44</sup>	Diabetic (6)	5 × 2	Clamp	SAFA vs. PUFA	↓
	Healthy (6)				
	Obese (5)				
Lovejoy et al. <sup>45</sup>	Healthy (25)	4 × 3	FSIGT	SAFA vs. MUFA vs. PUFA	↔

FSIGT = frequent sampling intravenous glucose tolerance test (minimal model).

SAFA = saturated fatty acids.

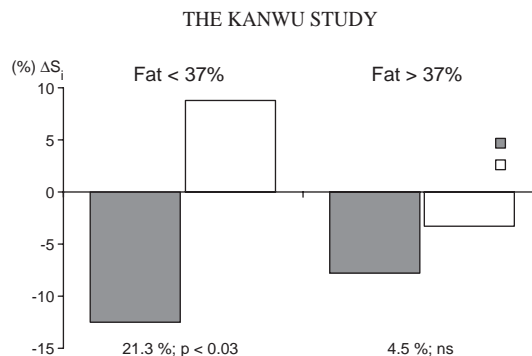
MUFA = monounsaturated fatty acids.

PUFA = polyunsaturated fatty acids.

subjects and the other one in type 2 diabetic patients, obese and healthy people, show that a moderate substitution in the diet of saturated fat with unsaturated fat (monounsaturated in the study on healthy subjects and  $\omega$ -6 polyunsaturated in the one on diabetic patients) is able to improve significantly insulin sensitivity.

To this regard, the KANWU study by Vessby et al. is the only intervention trial on this topic, performed using adequate methodologies and a sufficiently large sample size (about ten times larger than any other study on this topic).<sup>43</sup> This study involved 162 healthy individuals from 5 different countries, randomly assigned to consume either high saturated fat or high monounsaturated fat diets without any change in other dietary constituents; a randomly selected subsample within each group was also given fish oil supplement (3.6g/day) or placebo. Insulin sensitivity—assessed by the Frequent Sampling Intravenously Tolerance Test (minimal model)—was significantly impaired on the saturated fatty acid diet (−10%,  $P = 0.05$ ) but remained unchanged on the monounsaturated fatty acid diet.

The KANWU study did not attempt to modify total fat intake; however if participants were stratified according to their habitual intake of total fat (above and below median), the effect of fat composition on insulin sensitivity was clearly different between the high and the low fat group. As a matter of fact, in the group consuming more than 37% energy as total fat (median of the study population), the difference between saturated fat and monounsaturated fat in relation to their effects on insulin sensitivity almost completely disappeared; conversely, in those consuming less



**Figure 1** The KANWU study: effects of changing dietary fat composition (high SAFA or high MUFA) on insulin sensitivity ( $S_i$ ) in relation to total fat intake during treatment (total fat <37 vs. >37%). SAFA gray column; MUFA white column. \* $P < 0.03$ .

than 37% energy as total fat, the difference between the two diets was even more striking (20.3%,  $P < 0.03$ ) (Fig. 1).

This suggests that the total amount of fat can influence insulin sensitivity and, possibly, the risk of type 2 diabetes only when it exceeds a threshold level that is between 35–40% of the total energy intake. This is in line with the many clinical studies presented above (Table 1) showing that alterations within a “reasonable” range of total fat intake (20–40%), are unlikely to have a major impact on insulin sensitivity.

In relation to the influence of dietary  $\omega$ -3 fatty acids on insulin sensitivity in humans, most intervention studies, based on a controlled design, have been performed in type 2 diabetic patients; they are listed in Table 5.<sup>46–51</sup> In all these studies supplementation with long-chain  $\omega$ -3 fatty acids

**Table 5** Controlled studies on the effects of supplementation of long chain  $\omega$ -3 fatty acids on insulin sensitivity (clamp) in type 2 diabetic patients.

Study	Subjects (n)	Fish oil dose (g/day)	Design	Duration (weeks)	Relationship with insulin sensitivity
Borkman et al. <sup>46</sup>	10	3	Cross-over	3 × 2	↔
Annuzzi et al. <sup>47</sup>	8	3	Cross-over	2 × 2	↔
Boberg et al. <sup>48</sup>	14	3	Cross-over	8 × 2	↔
McManus et al. <sup>49</sup>	11	3	Cross-over	12 × 2	↔
Rivellese et al. <sup>50</sup>	16	2.5	Parallel groups	26	↔
Lou et al. <sup>51</sup>	12	6	Cross-over	8 × 2	↔

**Table 6** Effects of a moderate  $\omega$ -3 fatty acid supplementation (3.6 g/day) on the phospholipid fatty acid composition of erythrocytes and insulin-mediated glucose disposal in type 2 diabetic patients.

	$\omega$ -3 Supplementation (n = 8)		Placebo (n = 8)	
	Baseline	After 6 months	Baseline	After 6 months
EPA (%)	0.7 ± 0.2	2.2 ± 0.3*	0.7 ± 0.1	0.6 ± 0.1
DHA (%)	5.1 ± 0.3	6.7 ± 0.2*	5.0 ± 0.4	4.7 ± 0.3
M (mg/kg/min)	4.04 ± 0.82	3.96 ± 0.50	3.5 ± 0.62	4.09 ± 0.49

EPA = eicosapentaenoic; DHA = docosahexaenoic; \* $P < 0.001$  vs. Baseline ( $M \pm SEM$ ).

**Table 7** KANWU study: effects of long-chain  $\omega$ -3 fatty acids supplementation (3.6 g/day) on insulin sensitivity (FSIGT) in healthy people.

	SAFA		MUFA	
	$\omega$ -3 (n = 41)	Placebo (n = 42)	$\omega$ -3 (n = 40)	Placebo (n = 39)
Baseline	4.0 ± 2.4	4.4 ± 2.3	5.0 ± 4.0	4.5 ± 2.6
After treatment	3.7 ± 2.3	4.0 ± 2.2	4.9 ± 3.8	4.8 ± 2.6

FSIGT = frequent sampling intravenous glucose tolerance test (minimal model) ( $M \pm SEM$ )  $\omega$ -3 vs. Placebo  $P = 0.48$  (ns).

did not induce any change in insulin sensitivity. However, most of them were conducted for periods of time too short to allow a real change in the composition of cell membrane phospholipids to occur; obviously, if dietary fat is able to modulate insulin action through modifications in cell membranes composition, the duration of the experiment is of crucial importance. To this regard, two studies have been performed in humans with such a duration as to allow a change in the composition of cell membranes to be observed: one was performed in a small group of type 2 diabetic patients with hypertriglyceridemia<sup>50</sup> and the other one in a large group of healthy individuals.<sup>43</sup> In the first study, which lasted 6 months, type 2 diabetic patients with hypertriglyceridemia were randomly assigned to two groups, one on fish oil supplementation

(2.5 g/day for the first 2 months and 1.7 g/day for the following 4 months) and the other one on placebo. After a period of 6 months, there was a significant change in the composition of phospholipid fatty acids in erythrocytes, which were significantly enriched in long-chain  $\omega$ -3 fatty acids in the group receiving fish oil. Nonetheless, insulin-mediated glucose utilization, evaluated by the clamp technique at baseline and at the end of the study period in the two groups of patients, was practically unchanged in both groups (Table 6).<sup>18</sup>

The other study related to this topic is the already mentioned KANWU study. Also in this study the  $\omega$ -3 fatty acid supplement did not influence insulin sensitivity in the whole study group, nor in those assigned to the saturated fat or the mono-unsaturated fat diet (Table 7).

### Effects of dietary fat composition on other features of the metabolic syndrome

Insulin resistance is strictly associated with the other metabolic abnormalities clustering in the metabolic syndrome. Among them the most important ones are related to lipoprotein metabolism and are characterized mainly by high triglyceride levels and low HDL cholesterol. Changes in dietary fat composition are clearly associated with significant changes in plasma lipoprotein levels (Table 8). However, the influence of dietary fat on lipoprotein metabolism is mediated by multiple mechanisms and therefore not always changes in plasma lipoproteins and insulin sensitivity occur in parallel. Moreover, there are very few studies evaluating the influence of dietary fat on lipoprotein metabolism specifically in individuals with the metabolic syndrome. In the presence of insulin resistance, replacement of saturated fat with unsaturated fat lowers not only LDL cholesterol but also VLDL triglycerides.<sup>17</sup> The effects on HDL cholesterol are less clear, possibly in relation to the type of unsaturated fat utilized. Trans fatty acids induce similar effects on plasma lipoprotein levels as those observed with saturated fat.<sup>52</sup> With respect to triglyceride metabolism, long-chain  $\omega$ -3 fatty acids are very powerful in reducing triglyceride levels in humans<sup>53</sup> despite the fact that they have no effect on insulin sensitivity. The reduction of triglyceride by long-chain  $\omega$ -3 fatty acids has been shown in hypertriglyceridemic individuals as well as in type 2 diabetic patients<sup>50</sup> and has been confirmed also in normotriglyceridemic people.<sup>43</sup> However, it is important to underline that this effect is associated with an increase in LDL cholesterol, not only in hyperlipidemic individuals, but also in normolipidemic people.<sup>54</sup>

In relation to blood pressure, it is important to consider that some epidemiological studies have found significant associations between fat intake and blood pressure levels, indicating that the consumption of saturated fat is associated with higher blood pressure levels, while the higher the intake of MUFA the lower is blood pressure.<sup>55,56</sup>

**Table 8** Effects of dietary fat composition on plasma lipoprotein levels.

	VLDL TG	LDL chol	HDL chol
SAFA	—↑	↑↑	—
MUFA	—	—	—↑
PUFA $\omega$ -6	↓	—	—↓
PUFA $\omega$ -3	↓↓	↑	—

Intervention studies in humans comparing the effects of saturated, monounsaturated, and polyunsaturated long-chain  $\omega$ -6 fat on blood pressure are few and give no consistent results. Conversely, studies with long-chain  $\omega$ -3 fatty acids seem to suggest that they are able to reduce blood pressure, but only in hypertensive people and in patients with vascular disease, with a dose-related effect.<sup>57</sup>

The multicenter KANWU Study, previously described, has shown that a moderate shift from saturated to monounsaturated fat reduces significantly diastolic blood pressure. On other hand, a moderate supplementation of long-chain  $\omega$ -3 fatty acids for 3 months had no effect on blood pressure.<sup>54</sup>

Summarizing the results of the intervention studies performed in humans, it is possible to conclude that the quality of dietary fat is able to influence insulin sensitivity as well as the other metabolic abnormalities linked to insulin-resistance. However, the effects are not always inter-related, suggesting multiple mechanisms of action.

All these data support the concept that in order to prevent the metabolic syndrome it may be appropriate to implement a reduction in the consumption of foods rich in saturated fat in favor of foods and vegetable oils rich in unsaturated fat, particularly monounsaturated fat, not only for their beneficial effects on LDL cholesterol, but also for their influence on insulin sensitivity and some of the related metabolic abnormalities.

### Conclusions

The metabolic syndrome occurs in individuals with impaired insulin sensitivity, therefore prevention of this condition has to be targeted (1) to improve insulin sensitivity and (2) to correct/prevent the associated metabolic and cardiovascular abnormalities.

However, while it is firmly established that weight reduction is a powerful measure to prevent the metabolic syndrome, long-term and sufficiently powerful (large sample size) intervention studies in humans are still needed to establish how changes in dietary fat composition can influence insulin sensitivity and the development of the metabolic syndrome. At present, on the basis of the best available evidence, the diet for prevention/treatment of the metabolic syndrome should be limited in the intake of saturated fat, for its known unfavorable effects on insulin sensitivity and blood pressure, as well as on plasma lipids. Individuals

with (or at risk of) the metabolic syndrome are excessively prone to cardiovascular diseases; therefore, in defining the "optimal diet" for these people the need to reduce as much as possible plasma cholesterol levels and, in particular, low-density lipoproteins (LDL), cannot be neglected. In this respect the reduction of saturated fat, which is beneficial for improving insulin sensitivity, is further reinforced since it contributes to lowering LDL. In addition, cholesterol intake has also to be reduced since it influences LDL concentrations and, more generally, the cardiovascular risk.<sup>58</sup>

Moderate amounts of monounsaturated fat could be permitted since they do not induce detrimental metabolic effects while the total amount of fat does not need to be drastically reduced, as advocated in the past in order to provide cardiovascular disease protection. It is now clear that, within certain limits, it is fat composition rather than the total amount of fat that really matters. Moreover, too much emphasis on the need to reduce total fat intake could lead people to increase their carbohydrate consumption with possible untoward effects on the features of the metabolic syndrome. Setting an upper limit for fat consumption around 35–40% of total energy intake is both realistic and biologically sound: so far, no clear clinical disadvantage has been demonstrated for diets deriving up to 40% of energy from fat, provided that the saturated type is kept low. Moreover, since in most western countries a large part of the population (between one-third and one half) consumes more than 40% energy as fat, the goal of not exceeding this limit is more feasible than any drastic fat reduction which could discourage both patients and physicians from trying to achieve it. Properly designed intervention studies with adequate sample size are urgently warranted to evaluate the clinical benefits of an appropriate nutritional approach to prevent/treat the metabolic syndrome.

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