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Review Article

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Eat Your Fats, Skip the Carbs: Here's Why. A Dietary Fat Metabolic Journey

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Abstract

Sadly, much of our population is plagued by metabolic derangements which trace back to dysregulated sugar and fat metabolism. To better understand the importance of dietary fat and how to allow it to work to our health advantage, its necessary to revert back to the basics of fat metabolism and hyperglycemic-induced post prandial de novo fatty acid synthesis and up-regulation of inflammatory cytokines. Fats are necessary, and though this review is not addressing hormonal or nervous system lipid metabolism integration nor higher detailed serum lipid analysis, the take home message is healthy fat metabolism is not only possible, but energetically efficient, and recommended.

Keywords: Fat Metabolism; De Novo Fatty Acid Synthesis; Hyperglycemia; Nfkb

Introduction

Sadly, much of our population is plagued by metabolic derangements which trace back to dysregulated sugar and fat metabolism. There is a positive shift occurring for low carbohydrate and ketogenic slash Mediterranean dietary lifestyles with higher fats and proteins, and higher intake of vitamin/mineral rich sources of produce. To better understand the importance of dietary fat and how to allow it to work to our health advantage, its necessary to revert back to the basics of fat metabolism. Physiology before pathophysiology.

Lipids serve important physiological roles. Dietary fats are an energy source as well as serve the necessary requirement of nutritionally providing the essential fatty acids our body cannot synthesize such as the long chain fatty acids, linoleic acid omega-6 and alpha linolenic acid omega-3 [1-3]. There are additional essential fat-soluble vitamins including A/D/E/K which our body rely on for multiple physiological, biochemical, and epigenetic roles which also must be ingested. Several of these essential fat-soluble vitamins are also well known pleiotrophic molecules interacting in diverse and complex inter-related vital functions [4,5]. Additionally, lipids form our cell membranes providing hydrophobic barriers [1] but also serve as communicators with their hierarchy of cytokine chemical mediators upon stimulation [3,6,7]. Fatty acids generate important prostaglandins and participate in wound healing while other lipids act as precursors such as cholesterol and its role as a precursor for steroid hormones [1-3]. The brain relies on extensive amounts of lipids for regulatory actions and communication [8]. Fat catabolism serves as the energy source during intermittent periods of fasting [1,9] whether dietarily/lifestyle-chosen such as decreased caloric intake for optimal health or unplanned stress states of starvation. Dietary fats are necessary and serve physiological optimal roles and are best when paired with low carbohydrate.

Dietary digestive-enzyme digested fats

Dietary lipid digestion occurs sequentially with 3 different lipases beginning with lingual lipase at the back of the tongue, continues with gastric lipase in the stomach, then pancreatic lipase once chyme is released into the duodenum of the upper small bowel. The lingual and gastric lipases primarily degrade lipid TAGs of short- and medium-chain fatty acids meaning less than 12 carbons. Hepatic and/or gallbladder secreted bile emulsifies the lipids once in the duodenum increasing their surface area to allow the pan-

creatic lipases maximal exposure alongside the tumbling action of peristaltic waves. The pancreatic lipase primarily degrades the fatty acids in positions 1 and 3 of the TAG generating two free fatty acids and the 2-monoacylglycerol TAG remnant. Pancreatic juice also contains a large amount of phospholipase-A2 for degradation of dietary or bile phospholipids; recalling bile contains significant amounts of phosphatidylcholine, conjugated bile salts, and hepatic free cholesterol. The enterocyte brush border binds the micelles for absorption of the digested free fatty acids and 2-monoacylglyercol TAG degradation products, free cholesterol, as well as fat-soluble vitamins A/D/E/K, then the bile acids separate and continue to the ileum for reabsorption. The micelle hydrophobic lipid ensemble itself is not absorbed.

Dietary fats intestinally degraded in the lumen get resynthesized inside the enterocyte back into lipid molecules reforming triacyl glycerides (TAGs) and phospholipids, and dietary cholesterols get esterified then all get packaged into the chylomicron to be released into the lymphatic system. The dietary short- and medium-chain fatty acids do not require bile emulsification nor uptake into chylomicrons, instead they are directly absorbed across the enterocyte directly into the hepatic portal circulation and attached to albumin as free fatty acids (FFA) [1-3,10]. Dietary fats in the chylomicrons travel from the intestinal lymph into the thoracic duct to be discharged into the left subclavian vein for entry into the bloodstream where they travel to peripheral tissue and are utilized primarily by skeletal muscle and adipocytes but do not cross the blood brain barrier and not utilized by the brain [1]. However, short- and medium-chain fatty acids can cross the BBB and are a great alternative fuel source [10].

The chylomicrons now in blood circulation rapidly distribute primarily dietary TAGs to the skeletal muscle and adipocytes via help from Lipoprotein Lipase which solubilizes the fatty acids during the lipolysis for tissue uptake leaving the chylomicron remnants less rich in TAG and more so left with dietary cholesterol and is delivered for uptake into the liver as a chylomicron remnant via attachment to hepatic receptors. Following a meal, the skeletal muscles metabolize dietary fats and adipocytes esterify and package them back into TAGs for storage as energy reserves. Post-prandially in adipocytes, in addition to lipid uptake and storage, glucose uptake is metabolized to Acetyl CoA then converted into fatty acids for TAG storage as well; adipocyte lipogenesis of glucose and FA for TAG storage is enhanced post prandially by insulin. Dietary short- and medium-chain fatty acids direct from the intestine are either utilized for energy via beta-oxidation or altered forming different length fatty acids. Chylomicron remnant dietary cholesterol is used to replenish bile or packaged into VLDL for release into circulation. The liver is then responsible to manage dietary exogenous and nutrient-excessive endogenous fatty acids which are packaged hepatically into TAGs which get packaged into VLDLs released into the bloodstream to ultimately be converted to circulating LDLs.

Therefore, the fate of dietary fats is determined by post prandial tissue uptake for beta-oxidation conversion to ATP as intracellular energy primarily non-adipose, the adipose take-up the delivered fat for storage, and the remainder returns to the liver to be packaged into VLDL for peripheral tissue distribution and conversion in circulation to the LDLs. Of importance during the well fed post-prandial euglycemic state is the understanding and appreciation of all excess nutrients including carbohydrate, protein, and fat have a fate of being packaged by the liver into VLDL and HDL to be released into circulation; excess nutrients are defined as dietary intake of any combination of carbohydrate, protein, fat in excess of the body's energy demands. Therefore, post-prandial moving towards the 2 hour post-meal post-absorptive state, hepatic de novo fatty acid synthesis includes the following sources: exogenous dietary short- and medium-chain fatty acids direct from intestine to liver, returning exogenous dietary TAGs and cholesterols from chylomicron remnants, as well as endogenous de novo TAGs from nonlipid glucose and amino acid precursors from excess nutrient intake. Carbohydrate and simple sugars stimulate de novo fatty acid synthesis post prandially after carbohydrate-rich and simple sugar-rich meals. Dietary fat in combination with total meal caloric intake beyond the body's energy demands becomes packaged and stored. Dietary fat with low to no carbohydrate is the body's fuel source and will be shunted into beta-oxidation for conversion to energy as ATP. Fat catabolism generates significantly more energy molecules of ATP per lipid molecule catabolized compared to glucose catabolism and is a more efficient energy system.

Ultimately, the hepatic pool of TAGs along with dietary and recirculating cholesterol and phosholipids from intestinal dietary influx or recirculating chylomicron remnants as well as lipid/cholesterol contents of returning LDL and HDL, and fat-soluble vitamins are all together packaged into these large, dense VLDLs. The VLDLs are released into the blood circulation and TAGs are rapidly delivered to and taken up by peripheral tissues via the Lipoprotein Lipase, at which point the VLDL is then termed an IDL with a short lifespan, before the exact same molecule which was the VLDL then the IDL, becomes the circulating LDL. The size and content of the original VLDL is influenced by the type of dietary fat ingested (saturated/trans/essential polyunsaturated n3 or n6 fats) as well as the amounts of each of the latter, still plus the amount of nonlipid excess nutrient beyond the body's energy needs converted to fats such as carbohydrate and protein as nonlipid glucose and amino acid. Since the VLDL becomes the circulating LDL, dietary choices quality and quantity significantly influence the circulating population of LDL and determine the state of health or potential towards its well-known cardiovascular associated risk [1-3,11].

High carb and hyperglycemic effect on fatty acid de novo synthesis

How is a carbohydrate-rich meal, a glucose breakdown product, turning into a totally different molecule, converting into a fat lipid? Post prandial carbohydrate rich meals and fasting hyperglycemia generate a high energy state in hepatic mitochondria where glucose underwent cytosolic glycolysis conversion to pyruvate, pyruvate transferred into the mitochondria to be converted into Acetyl-coA, which got condensed with oxaloacetate (OAA) forming Citrate. This is an up-regulated TCA cycle with excess intermediates entering the electron transport chain (ETC) for generation of ATP. Therefore, this is a mitochondrial state of high Citrate and high ATP which signals time to switch to de novo fatty acid synthesis. De novo fatty acid synthesis occurs in the hepatocyte and the fatty acids get packaged as mono-, di-, or tri-acylglerols (TAG) or can be altered by forming unsaturated fatty acids with double bonds and elongated by adding more carbons. The hyperglycemic, high energy hepatic mitochondrial state signals the Citrate to then exit the mitochondrial, and instead of continuing into the TCA cycle for entry into the ETC for further conversion to ATP, it exits to enter fatty acid de novo synthesis. The hepatic mitochondrial Citrate transfers across the mitochondrial membrane and once back in the cytosol reforms Acetyl-coA and OAA where the fate of Acetyl-coA is condensed with a CO2 by Acetyl-CoA Carboxylase-Biotin forming Malonyl-CoA, the building block of de novo fatty acids along with B3-Niacin derivative NADPH and ATP. After the Acetyl-CoA Carboxylase condenses Acetyl-coA with CO2 forming the original Malonyl-CoA carbon unit, the growing FA chain sequentially adds 5 more Malonyl-CoA units via Fatty Acid Synthase. The end product is the 16:0 saturated long chain fatty acid Palmitate. Elevated levels of Malonyl-CoA also inhibits FA beta-oxidation. The Fatty Acid Synthase does not extend further than the 16:0 Palmitate long chain saturated fatty acid, however desaturation and elongation occur in different hepatic organelles with specific enzymes for different end products. This process is Biotin and Niacin dependent and requires energy as ATP [1-3].

If hyperglycemia occurs post prandially from a carbohydrate-rich meal, hepatic de novo fatty acid synthesis is stimulated and generates a long chain Palmitate fatty acid of 16 carbons. An individual with chronic hyperglycemia will demonstrate higher amounts of hypertriglyceridemia with excess Palmitate in the core of their serum lipid VLDL upon advanced lipid analysis [1]. This same process occurs for individuals who avoid dietary fat [12].

Recall, dietary lipids get transferred to primarily skeletal muscle and adipocytes, among other tissues, for transfer of chylomicron TAG-rich delivery after meals, and the circulating chylomicron remnants return dietary lipids and cholesterol to the liver to be repackaged into VLDLs. Post prandial hyperglycemia as excess glucose signals the liver to convert the excess glucose into Acetyl-coA and shunt its formation into a fatty acid then further lipid processing occurs for final packaging into VLDL to be released for storage as peripheral fat accumulation; and is an energy-requiring process. The alternative to not having hyperglycemia and carbohydrate-rich meals, is fat catabolism, lipid catabolic beta-oxidation for generation of significant amounts of ATP, and no stimuli for lipogenesis nor lipo-storage. An excellent way to support optimal fat metabolism is through the supplementation of the conditionally-essential amino acid Carnitine to support its vital role in the Carnitine Shuttle for fat transfer between cytosol and mitochondria for fat catabolism and its high energy production of ATP through beta-oxidation [1-3]. Supplementing with L-Carnitine (ALCAR) significantly improves fat metabolism [13], and pairs well with the potent antioxidant and intrinsic Alpha Lipoic Acid (ALA) [14]. Together they significantly improve metabolism at the core of ATP generation.

Summary

Avoid hyperglycemia. Hyperglycemia is oxidative stress [15-18]. To determine the inflammatory response following a high glycemic meal a study was conducted on 10 young lean healthy men. A meal consisting of 50 g of glucose induced a spike in post prandial inflammatory markers and an up-regulation of pro-inflammatory NFkB; worse from white bread compared to pasta. It was found in lean healthy individuals, in the post-absorptive state the inflammatory response recovered [15]. Unfortunately, that is not the case in unhealthy pro-inflammatory hyperglycemic individuals.

Hyperglycemia is a primary source of endothelial dysfunction [15-18]. The excess glucose and its up-regulation of NFk B causes excessive free radicals and inflammatory cytokines which by themselves induce endothelial dysfunction. Inflammatory cytokines from activated macrophages/leukocytes in the intima lesions of atherosclerosis and inflammatory cytokines from hyperglycemia-induced NF-kB are both sources of NADPH-oxidase stimulation resulting in generation of superoxides and all induce e NOS uncoupling, oxygen and nitrogen free radicals, and vasoconstriction [17,18]. In conclusion, Node and Inoue sum it up exquisitely, "Postprandial hyperglycemia is characterized by hyperglycemic spikes that induce endothelial dysfunction, inflammatory reactions and oxidative stress, which may lead to progression of atherosclerosis and occurrence of cardiovascular events. There is evidence that postprandial hyperglycemia, but not fasting hyperglycemia, independently predicts the occurrence of cardiovascular events [18].

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