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Application of nutrient essentiality criteria to dietary carbohydrates

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Abstract

The purpose of the present review is to describe how human physiology at very low carbohydrate intakes relates to the criteria for nutritional essentiality. Although we did not limit ourselves to one particular type or function of carbohydrates, we did primarily focus on glucose utilisation as that function was used to determine the recommended daily allowance. In the general population, the human body is able to endogenously synthesise carbohydrates, and does not show signs of deficiency in the absence of dietary carbohydrates. However, in certain genetic defects, such as glycogen storage disease type I, absence of dietary carbohydrates causes abnormalities that are resolved with dietary supplementation of carbohydrates. Therefore, dietary carbohydrates may be defined as conditionally essential nutrients because they are nutrients that are not required in the diet for the general population but are required for specific subpopulations. Ketosis may be considered a physiological normal state due to its occurrence in infants in addition to at very low carbohydrate intakes. Although sources of dietary carbohydrates can provide beneficial micronutrients, no signs of micronutrient deficiencies have been reported in clinical trials of low-carbohydrate ketogenic diets. Nonetheless, more research is needed on how micronutrient requirements can change depending on the dietary and metabolic context. More research is also needed on the role of dietary fibre during a low-carbohydrate ketogenic diet as the beneficial effects of dietary fibre were determined on a standard diet and several studies have shown beneficial effects of decreasing non-digestible carbohydrates.

Key words: **Essential nutrients: Nutrient deficiency: Dietary carbohydrates: Ketogenic diets: Ketosis**

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Introduction

The potential issue of inadequate dietary carbohydrate intake was examined by the United States National Academy of Medicine (formerly Institute of Medicine) in its determination of recommended daily allowance for carbohydrates[1]. However, since that time there has been increasing interest in and use of carbohydrate-restricted diets, particularly the low-carbohydrate ketogenic diet (LCKD) which is defined as <50 g of carbohydrates or <10 % of energy derived from carbohydrates per d[2]. This is probably due to the increasing prevalence of diabetes and obesity given that a LCKD has been shown to be efficacious for the treatment of these health conditions[2–4]. Carbohydrate restriction is not recommended by some authorities, such as the Dietary Guidelines for Americans, but there is an apparent lack of evidence that it is harmful, that carbohydrates are essential to human nutrition, or that a LCKD cannot provide all the essential nutrients[5]. Therefore, we decided to re-examine the potential issues of inadequate carbohydrate intake or dietary carbohydrate deficiency.

We performed the following search without restrictions in language or other criteria 'essential AND carbohydrate AND deficien* NOT transferrin NOT glycoprotein' on PubMed yielding 2764 results on 27 November 2017. However, upon abstract review, we were unable to find indication of any significant disease or dysfunction caused by lack of dietary carbohydrates. Therefore, thoughts of systematic review were abandoned, and we instead decided to narratively review how human physiology at very low carbohydrate intakes relates to the criteria for nutritional essentiality. Dietary carbohydrates consist of a wide variety of sugars, oligosaccharides, starches and dietary fibre as well as performing a wide variety of functions in the body in addition to energy metabolism. Although we did not limit ourselves to one particular type or function of carbohydrates, we did primarily focus on glucose utilisation as that function was used to determine the recommended daily allowance[1]. We also included both the general population and specific sub-populations in relation to answering the question of nutritional essentiality.

The concept of nutritional essentiality

A nutrient is any substance normally consumed as a constituent of food which provides energy, which is needed for growth, development or maintenance of life, or which a deficit will cause

Abbreviations: FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; LCKD, low-carbohydrate ketogenic diet.

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characteristic physiological changes to occur[6]. The concept of nutritional essentiality was only firmly established less than 100 years ago and arose from observations that certain diseases could be prevented by the inclusion of a nutrient in the diet[7–10]. There is a difference between physiological essentiality and nutritional essentiality. Physiological essentiality represents a substance that is indispensable for life, whereas nutritional essentiality represents a substance that is indispensable in the diet[7]. For example, cholesterol is physiologically essential, but need for it can be met by endogenous production so it is not nutritionally essential. The criteria for nutritional essentiality are as follows[7,11,12]:

(1) The substance is required in the diet for growth, health and survival.
(2) Its absence from the diet or inadequate intake results in characteristic signs of a deficiency disease and, ultimately, death.
(3) Growth failure and/or characteristic signs of deficiency are prevented only by the nutrient or a specific precursor of it, not by other substances.
(4) Below some critical level of intake of the nutrient, growth response and/or severity of signs of deficiency are proportional to the amount consumed.
(5) The substance is not synthesised in the body and is therefore required to be obtained from the diet for some critical function throughout life.

Nutrient essentiality is a characteristic that varies by animal species, not by nutrient. The currently established essential nutrients for humans are water, energy, essential amino acids (histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine), essential fatty acids (linoleic and α-linolenic acids), vitamins (ascorbic acid, vitamin A, vitamin E, vitamin K, thiamine, riboflavin, niacin, vitamin B_6, pantothenic acid, folic acid, biotin and vitamin B_{12}), minerals (Ca, P, Mg and Fe), trace minerals (Zn, Cu, Mn, iodine, Se, Mo and Cr), electrolytes (Na, K and Cl) and ultra-trace minerals (As, B, Si, Ni and V)[7,12–14]. However, this list is still subject to debate. For example, arachidonic acid and DHA may actually be essential whereas linoleic and α-linolenic acids may not be essential[15]. Additionally, the role of ultra-trace minerals is still being investigated[16,17].

The category of conditionally essential nutrients describes nutrients not ordinarily required in the diet but must be supplied exogenously to specific populations who do not synthesise them in adequate amounts, such as in prematurity, pathological states or genetic defects[7,8,18]. The criteria of conditional essentiality are as follows[7,8,19]:

(1) Decline in the plasma or tissue level of the nutrient below the normal range.
(2) Appearance of chemical, structural or functional abnormalities.
(3) Correction of both of these by dietary supplementation of the nutrient.

Carnitine, taurine, arginine, cysteine, glycine, choline, glutamine, proline, serine and tyrosine are all generally classified as conditionally essential nutrients[8,19–27]. Vitamin D is sometimes classified as an essential nutrient but is better classified as a conditionally essential nutrient due to its ability to be adequately synthesised in the body in the presence of unconstrained UVB sunlight exposure[28,29]. As further evidence accumulates, it is likely that more nutrients will be found to be conditionally essential.

The need for essential or conditionally essential nutrients may be influenced by the presence of precursor substances, presence of inhibitors, imbalances with other nutrients, drug usage and genetic defects[7,8]. These conditions alter the amount that must be consumed, but do not alter the basic requirement. For example, the presence of phytic acid in the diet impairs Zn absorption and therefore increases the necessary amount of Zn consumption[1,7].

If the definition of essential and conditionally essential nutrients were broadened to include nutrients that provided a desirable effect on health, then the specificity of the current definition would be lost[7]. Therefore, it would be clearer to categorise nutrients with a biological effect without meeting criteria for essentiality or conditional essentiality as desirable for health, physiological modulators or bioactive substances[7,30]. For example, fluoride in low doses protects teeth from dental caries[7,31].

Physiological response during very low carbohydrate intake

The recommended daily allowance for carbohydrates is 130 g/d in order to ensure sufficient glucose for the brain[1]. However, when carbohydrate intake is less than 130 g/d, the body is able to meet the energy needs of the brain with endogenously produced glucose and ketone bodies. Ketone bodies can be produced up to a rate of 2·5 mmol/min, at which point negative feedback via insulinotropic and other effects prevents a further increase in rate and acidosis[32]. Ketone body oxidation also becomes saturated at a rate of 2·5 mmol/min with higher utilisation by muscle at lower concentrations and higher utilisation by the brain at higher concentrations[32].

Ketone bodies cross the blood–brain barrier to provide energy to the brain, reducing total body glucose demand to only 22–28 g/d[1]. The body continues to utilise glucose at a higher rate than this, though, as the body is able to endogenously produce 80 g/d or more of glucose from protein-derived amino acids, TAG-derived glycerol, recycled lactate, recycled pyruvate and ketone bodies themselves[1,33,34]. These processes do not cease during higher levels of carbohydrate intake, and, importantly, the metabolism of TAG and protein sources can be endogenous or exogenous[35]. In fact, if ample exogenous protein is supplied, ketogenesis significantly decreases as glucose can be produced endogenously at a rate that meets the energy needs of the brain[34]. Nonetheless, ketone bodies are oxidised for energy more efficiently than glucose, and it has therefore been proposed that ketone bodies may be beneficial in hypoxic brain injury[36–38]. There is also recent evidence that ketone bodies can act as cellular signalling molecules in addition to metabolites, but the relevance of this is yet to be determined[39–41].

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As long as adequate exogenous TAG and protein are consumed, no loss of fat or lean mass occurs[42]. If exogenous TAG and protein are not adequately supplied, particularly during times of increased energy demand such as lactation, then a depletion of fat and lean mass occurs and can ultimately result in death[34,43,44]. Therefore, it is important to differentiate between the effects of energy restriction and carbohydrate restriction as they are not necessarily mutually inclusive even though carbohydrates are a common energy source. It may be hypothesised that very low carbohydrate intakes are detrimental to physical performance as carbohydrate intake contributes to glycogen stores. Although some studies support this, the majority of studies indicate that physical performance during a very low carbohydrate intake is no worse for many activities[45–58]. Long-term population data on safety are not available, but randomised controlled trials of very low-carbohydrate diets up to 2 years in length have indicated no serious adverse effects[59].

Ketosis in children

Long-term data are similarly limited in children, but ketogenic diets have been used since the 1920s in the treatment of drug-resistant epilepsy in children, and the risk of serious adverse events is considered low[60,61]. More recently, a LCKD has also been shown to be effective for weight loss in adolescents without adverse effects[62]. Moreover, it should be noted that ketosis is a natural state in child development from gestation to weaning even in the presence of carbohydrates[1,34,63,64]. In fact, the enzymes for metabolism of ketone bodies are more efficient in infants than adults, and gluconeogenesis is well developed even in premature infants[1,65–67]. Ketone bodies are also used during this time as precursors for the synthesis of brain structures and myelinogenesis in addition to their use as a source of energy[68,69].

Breast milk is considered optimal for newborn growth and development[70]. Breast milk contains carbohydrates in the form of lactose, which provides energy, and oligosaccharides, which serve as a prebiotic[1,71]. However, in infants with epilepsy as young as 1 month old, the use of ketogenic formula does not lead to growth failure or signs of deficiency[72–77]. It is also thought that breast milk is relatively insensitive to changes in maternal diet, but this has not been tested for a maternal energy-sufficient LCKD[78–80]. There are no studies of infant carbohydrate restriction in non-epileptic populations, but weaning onto meat-based diets seems to have a positive effect on growth, head circumference and psychomotor development in comparison with cereal-based diets[81–84]. Additionally, supplementation of animal-source foods improves growth and test scores in schoolchildren in the developing world, and early introduction of eggs improves growth and reduces stunting[85–89]. However, these effects may be due to micronutrient deficiencies found in the developing world or nutrients found in meat, such as Fe, Zn, vitamin B_{12}, fatty acids and protein[90,91].

In summary, the necessity of carbohydrates in growth is largely unexplored, but the limited evidence available suggests that children do not suffer from growth failure or acquire signs of deficiency at low carbohydrate intakes.

Dietary carbohydrates do not meet criteria for nutritional essentiality

Although carbohydrates are physiologically essential, they do not meet the criteria for nutritional essentiality for the following reasons:

(1) Dietary carbohydrates are not required in the diet for growth and survival.
(2) Absence of dietary carbohydrates does not result in a characteristic deficiency disease or death.
(3) Carbohydrates are synthesised in the body.

Populations where dietary carbohydrates may be conditionally essential

Although carbohydrates, particularly glucose, are not ordinarily required in the diet, they may be required exogenously in certain populations who do not synthesise them in adequate amounts due to a genetic defect or pathological state. For example, glycogen storage disease type I (von Gierke disease) results from a genetic defect in glucose-6-phosphatase, thereby preventing the liver from releasing glucose from gluconeogenesis and glycogenolysis into the blood stream[92,93]. Therefore, although ketosis can lower the requirement for glucose, the body may still be unable to produce and utilise a sufficient amount of glucose without exogenous intake of carbohydrate depending on the severity of the glucose-6-phosphatase enzyme defect. This meets the criteria for conditional essentiality for the following reasons:

(1) There is a decline in the plasma level of glucose below the normal range with appearance of functional abnormalities.
(2) There is correction of the plasma level and function by dietary supplementation.

There are several other genetic defects in fat and ketone body metabolism that cause functional abnormalities during low intake of dietary carbohydrates: carnitine deficiency, carnitine palmitoyltransferase (CPT) deficiency, carnitine translocase deficiency, pyruvate carboxylase deficiency, acyl-CoA dehydrogenase deficiency (long, medium and short chain), 3-hydroxyacyl-CoA deficiency, mitochondrial β-hydroxy β-methylglutaryl-CoA (HMG-CoA) synthase deficiency, mitochondrial HMG-CoA lyase deficiency, succinyl-CoA-3-oxoacid CoA transferase deficiency and β-ketothiolase deficiency[61,94–97]. Additionally, acute intermittent porphyria may become symptomatic during low intake of dietary carbohydrates[61,94]. Several, but not all, of these genetic disorders meet the aforementioned criteria for conditional essentiality. Nonetheless, they all have potentially dangerous complications during low carbohydrate intakes.

Further investigation into the genetic defects and pathological states where dietary carbohydrates are conditionally essential is still needed. For example, carbohydrate intake has traditionally been recommended for glycogen storage disease type III and V, but recently case reports have found symptomatic improvements using a LCKD[98,99]. Additionally, although CPT-Ia deficiency results in hypoketotic hypoglycaemia due to impaired fatty acid oxidation, this variant is present at a high frequency

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in the Inuit, whose traditional diet consisted of minimal plant food[100–102]. Similarly, further investigation is needed into the genetic defects and pathological states where dietary carbohydrate restriction may be the treatment of choice. For example, GLUT1 deficiency and pyruvate dehydrogenase deficiency have defects that prevent proper glucose utilisation, and diabetes characteristically has abnormally elevated blood glucose levels[61,94].

Circumstances where dietary carbohydrates may be desirable for health

Although dietary carbohydrates themselves are not essential, it is possible that sources of carbohydrates contain nutrients or properties unavailable from other food sources. The following sections will examine only two of many possibilities: micronutrients and dietary fibre.

Micronutrients

Starvation can lead to micronutrient deficiencies and potentially severe complications, including death[103]. Bariatric surgery can also lead to micronutrient deficiencies, including thiamine, vitamin B_{12}, Fe, Cu and fat-soluble vitamins[104,105]. The evidence for micronutrient deficiencies on a LCKD is less clear as few studies have reported on micronutrient status. A recent systematic review identified seven randomised control trials, two non-randomised control trials and one cross-sectional study reporting on micronutrient intake or status on carbohydrate-restricted diets[106,107]. Dietary intakes of thiamine, folate, Mg, Ca, Fe and iodine were noted to be reduced compared with baseline or control participants, but no adverse events related to micronutrient deficiencies were reported[106,107]. The majority of these trials were hypoenergetic and used dietary recall or dietary records to measure micronutrients, which has the potential for inaccuracies[108]. Only one trial both provided food to participants and was isoenergetic, and in this trial only Mg and iodine were reduced whereas thiamine increased and folate, Ca and Fe were unchanged[109]. In this same trial, serum folate levels increased despite no increase in dietary consumption; yet in another trial serum folate levels decreased[109,110]. Similarly, dietary intake of vitamin C has been reported to decrease but serum vitamin C levels have been reported to increase, indicating a need for assessment of biological markers of micronutrient status[111–114].

Since macronutrients, micronutrients and metabolic pathways all have interrelated connections, it is difficult to predict how a large change in diet would affect essential nutrients. Unexpectedly, scurvy does not seem to occur on a diet based solely on meat and fat[115]. The reason for this is unknown, but it may be due to vitamin C's interaction with glucose. Glucose appears to compete with the oxidised form of vitamin C for entry into cells and mitochondria[116–119]. Once inside the cell, glutathione, which is increased during a LCKD, appears to recover the function of vitamin C[120–122]. Vitamin C is also found in meat, so it may be possible that the requirement is simply sufficiently met[116]. However, there is a case report of a child developing scurvy while on a classical ketogenic diet for epilepsy, indicating a potential for deficiency when combined with epileptic medications or proprietary ketogenic formulas[123]. Nonetheless, it may be pertinent to re-examine micronutrient requirements on a LCKD because the current requirements were only defined to prevent deficiencies on a standard American diet.

Furthermore, how micronutrients interact with each other or are converted to their active form is still incompletely understood. As previously discussed, phytic acid, present in grains and other plant sources, inhibits the absorption of Zn and other minerals[7,31]. Some nutrients, such as β-carotene and α-linolenic acid, have low conversion rates to their active forms, thereby increasing the importance of consuming their respective active forms, which are found predominantly in animal sources of food[124–127]. Similarly the dietary reference values for vitamin K are exclusively based on vitamin K_1, but consumption of vitamin K_2 may play an important role in health[128]. Furthermore, vitamin K_2 seems to work in conjunction with vitamin A, vitamin D_3, Ca, P and Mg, indicating a highly complex interrelationship[129,130].

A decrease in micronutrient intake may be expected to occur with a decrease in energy intake. Although many micronutrients have a requirement related to body weight and growth rate, it may be relevant to consider micronutrient intake adjusted for energy intake because micronutrients involved in energy metabolism may have an intake requirement relative to energy intake[131]. For example, absolute intake of thiamin has been reported to decrease on a LCKD, as previously discussed, but its intake relative to energy intake has been reported to increase, resulting in a greater thiamin:energy ratio than if the subject's usual diet was reduced by the same amount of energy[132]. Nonetheless, there has been a case report of two children developing thiamin deficiency while on a classical ketogenic diet for epilepsy, again indicating a potential for deficiency when combined with epileptic medications or proprietary ketogenic formulas[133]. There is another case report of thiamin deficiency in a man supposedly following a low-carbohydrate diet but whose diet actually consisted of only rice crispies and chicken nuggets[134].

The bioavailability of micronutrients is relevant to consider, such as how haeme Fe is more readily bioavailable than non-haeme Fe[31]. Therefore, although absolute Fe intake has been reported to decrease on a LCKD, the intake of haeme Fe has been reported to increase[132]. Furthermore, the decrease in absolute Fe, as well as other nutrients such as iodine, may only be due to a decrease in foods that have been fortified with these nutrients but do not naturally contain them in significant amounts[111]. Although fortification of food has undoubtedly led to a decrease in the prevalence of micronutrient deficiencies, food sources naturally containing the same micronutrients may be preferable, but a framework for how dietary patterns and nutrients interact still needs to be determined[135,136].

It may also be relevant to consider how micronutrient intake compares among different dietary patterns. In trials comparing weight-loss diets, micronutrient intake is decreased in most groups for various micronutrients, although no signs of deficiency were reported[111,137]. Similarly in cross-sectional and hypothetical analyses, it appears that a standard diet and popular diet plans may not meet the recommended daily intake for

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several micronutrients, but conflicting reports exist[138–141]. Additionally, further research is needed to differentiate between nutrient intake needed to prevent deficiencies and nutrient intake needed for optimal health. For example, it has been proposed that subclinical Mg deficiency is a health concern for a vast majority of the population[142].

Dietary fibre

The National Academy of Medicine defines dietary fibre as intact plant non-digestible carbohydrates, functional fibre as isolated non-digestible carbohydrates that have beneficial effects in humans, and total fibre as the sum of dietary fibre and functional fibre[1,31]. Dietary and functional fibre are not essential nutrients, so potential health benefits were instead used to determine the recommended intake[1,31]. Specifically, adequate intake of total fibre was determined based on risk reduction of CHD primarily and risk reduction of diabetes secondarily[1,31]. The evidence for this is based on prospective studies showing a correlation between cereal fibre and CHD as well as intervention studies showing a reduction in serum cholesterol by viscous functional fibre[1,31]. Recent meta-analyses of prospective cohort studies are consistent with this, showing a reduced risk of cardiovascular mortality, and even all-cause mortality, with dietary fibre consumption[143–145]. However, no randomised controlled trials evaluating dietary fibre or cereals have reported on cardiovascular mortality[146,147]. Randomised controlled trials of dietary fibre, but not wholegrain cereals, have shown a reduction in total and LDL-cholesterol but there was also a decrease in HDL-cholesterol and an unclear risk of bias[146,147].

Although a reduction in dietary carbohydrates may lead to a reduction in dietary fibre, it may also be possible on a LCKD to consume an equal or even greater amount of dietary fibre than a standard diet due to consumption of fibrous vegetables. Furthermore, the role of dietary fibre was evaluated on a standard diet but has yet to be definitively tested or determined for a LCKD. Nonetheless, a LCKD has been shown to generally improve markers of CVD and diabetes in overweight populations[2–4,148–150]. This may be confounded by weight loss, as any diet that induces weight loss in overweight populations improves markers of CVD and diabetes, but a recent study indicates that some of these improvements may be independent of weight loss[151–153]. Specifically, it is thought that the decrease in plasma TAG, increase in HDL, and improved glycaemic control outweigh the potential increase in LDL[2–4,148–150,154]. It is beyond the scope of this article to evaluate the evidence for and against the relationship between serum cholesterol and CHD, but there have been several recent reviews on this matter[155–162]. Randomised controlled trials reporting on cardiovascular mortality are still needed, but this is not unique to a LCKD as dietary intervention trials sparsely report on mortality[163].

The National Academy of Medicine also identifies satiety, laxation and fermentation as other properties of total fibre that were not used to determine the adequate intake[1,31]. Both dietary fibre and a LCKD seem to exert independent effects on satiety[164,165]. Dietary fibre can also contribute to satiety through decreasing energy density, which can lead to reduced energy intake[165]. However, the role of dietary fibre in laxation and fermentation is less clear as an increase in faecal weight does not necessarily equate with enhanced laxation and there appears to be no relationship between the level of dietary fibre intake and fermentation[1]. Although in the short term, there is a decrease in faecal butyrate on a LCKD, it may be premature to draw conclusions that this is necessarily detrimental as faecal butyrate does not account for absorbed butyrate or the butyrate-producing capacity of the colonic microbiome[166–169]. It is also untested if endogenous β-hydroxybutyrate production may compensate for colonic butyrate needs due to the structural similarity of the molecules.

Although colonic bacteria concentration decreases after initiation of a LCKD, it appears that it may normalise after several months[170]. The microbiome has been shown to rapidly and reliably change based on diet composition, possibly reflecting past evolutionary pressures[171]. This may be due to bacterial fermentation of dietary fibre being compensated for by fermentation of other components, such as glycoproteins and bile acids[172–174]. In fact, animal-derived non-digestible carbohydrates, such as those found in connective tissue, are considered to be functional fibre and are a part of the total fibre intake[1]. Although this change in fermentation has been argued to be detrimental to colon health, it may be premature to draw this conclusion as there is a lack of evidence from existing randomised controlled trials that dietary fibre decreases adenomatous polyps and diverticulosis[175–177]. The National Academy of Medicine also states that the relationship between fibre intake and colon cancer is currently unresolved and the available evidence is too conflicting to recommend an intake level based on the prevention of colon cancer[1]. The change in microbiome composition may even be beneficial to overall health as it is associated with weight loss in obese populations[178].

Additionally, although constipation has been noted as a side effect of a LCKD, a recent clinical trial showed drastic improvement in constipation by reducing dietary fibre intake[33,61,179]. A low-fibre diet may even be therapeutic for some bowel diseases[180]. Because insoluble and soluble fibre have differing effects on the bowels, it may be possible that there are differing types of constipation which are correspondingly resolved by either increasing or decreasing dietary fibre[181–186]. Another possibility is that dietary fibre is a marker of unrefined plant foods and that indigestibility alone does not necessarily confer all the same health benefits[1,187,188]. If so, then added fibre may not confer the same health benefits as unrefined plant foods.

It may also be possible that the apparent benefits of low-fibre diets are at least partially mediated by a decrease in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) since a decrease in FODMAP has been shown to improve symptoms of irritable bowel syndrome[189–194]. A maternal low-FODMAP diet has also been shown to reduce symptoms of colic in breastfed infants without gross changes in breast milk composition[195]. Although further research is needed to address the shortcomings of current trials using a low-FODMAP diet, a low-FODMAP diet is also being explored for the treatment of inflammatory bowel disease[196–201]. Interestingly, a low-FODMAP diet improves symptoms of irritable bowel syndrome despite a decrease in carbohydrate fermentation that is generally thought to be beneficial to health and an increase in protein fermentation that is generally thought to be detrimental to

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health[202–205]. Therefore, the interaction of fermentation and health may be more complex than previously thought, and it may be prudent to wait for more clinical trial data to determine the beneficial amount of dietary fibre.

Conclusion and limitations

In conclusion, the carbohydrate requirement of the human body can be met by endogenous synthesis without signs of deficiency in the absence of dietary sources in the general population. However, in certain rare genetic defects in metabolism, absence of dietary carbohydrates causes abnormalities that are resolved by dietary supplementation of carbohydrates, thus defining carbohydrates as conditionally essential nutrients. Ketosis may be considered a physiologically normal state due to its occurrence in infants, where it may contribute to brain development, in addition to its occurrence at very low carbohydrate intakes.

Although sources of dietary carbohydrates can provide beneficial micronutrients, no signs of micronutrient deficiencies have been reported in LCKD clinical trials. However, evidence in this area is limited and more research is needed on how micronutrient requirements can change depending on the dietary and metabolic context. More research is also needed on the role of dietary fibre during a LCKD as the beneficial effects of dietary fibre were determined on a standard diet and several studies have shown beneficial effects of decreasing non-digestible carbohydrates.

Our analysis and conclusions are subject to several limitations. As is inherent in any narrative review, it is possible that selection bias may have occurred. It is also possible that our interpretation may have been unintentionally biased due to subjectivity. However, human physiology at very low carbohydrate intakes and nutritional essentiality are broad areas that lack the controlled studies to allow quantitative systematic review.

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