Module 1. The history and future of sports nutrition

Unit 1.1 History

1.1.1 Where it all started

Greeks and Romans

It could be argued that sports nutrition started in paradise when Eve gave the apple to Adam to make him as strong as God. Nutrition has always intrigued humans. As far back as ancient Greece, nutrition has been linked to performance and health. It was Hippocrates (460 BC - ca. 370 BC) who said "If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health". The diet of most Greeks and Romans was predominantly vegetarian and consisted of cereals, fruit, vegetables and legumes, and wine diluted with water. When meat was eaten, the most common source was goat for Greeks and pork for Romans.

It is believed that the first documented information about a special diet of a Greek athlete was Charmis of Sparta. He is said to have trained on dried figs. There are other reports of figs being used as sports nutrition. Running was a big part of army training and there were professional runners who were used to send [*sic*] messages sometimes over long distances. The most well known runner was perhaps Pheidipphides, who has been linked to the origin of the marathon. Pheidipphides is said to have run from Athens to Sparta (240km) to ask the Spartans for help when Persians were about to destroy Athens. When the Spartans replied that they were just celebrating an annual ceremony and their laws did not permit them go to Athens to help, Pheidippides had to run back to convey the bad news.

"If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health." Hippocrates (460 BC - ca. 370 BC).

So, he ran a total of 480km and he would have used figs as one of his main energy sources. It was estimated that with his 50 kg, he expended 28,000

kcal. (112,000 kJ). He also supposedly ran from Marathon to Athens (40km) which later became the marathon distance at modern Olympic Games. However, whether this run actually took place is still debated. (Saltin & Jeukendrup, 2010, p. 9).

Olympic Games

According to Galen and other authors, at the end of the third century B.C., athletes believed that drinking herbal teas and eating mushrooms could increase their performance during competition in the ancient Olympic Games. There is also a report that states that a meat diet was introduced about the middle of the fifth century by Dromeus of Stymphalos, an ex-long-distance runner. Another account by Diogenes Laertius reports that Eurymenes of Samos consumed a meat diet recommended by his trainer, Pythagoras of Croton. However, by far the best accounts of athletic diet to survive from antiquity are those of Milo of Croton, a wrestler whose feats of strength became legendary and won the wrestling event at five successive Olympics from 532 to 516 B.C. His diet supposedly consisted of 9 kg (20 pounds) of meat, 9 kg (20 pounds) of bread and 8.5 L (18 pints) of wine a day. The validity of these reports from antiquity, however, must be suspect. Although Milo was clearly a large and powerful man, who possessed a prodigious appetite, basic estimations reveal that if he trained on such a volume of food, Milo would have consumed approximately 57,000 kcal (238,500 kJ) per day.

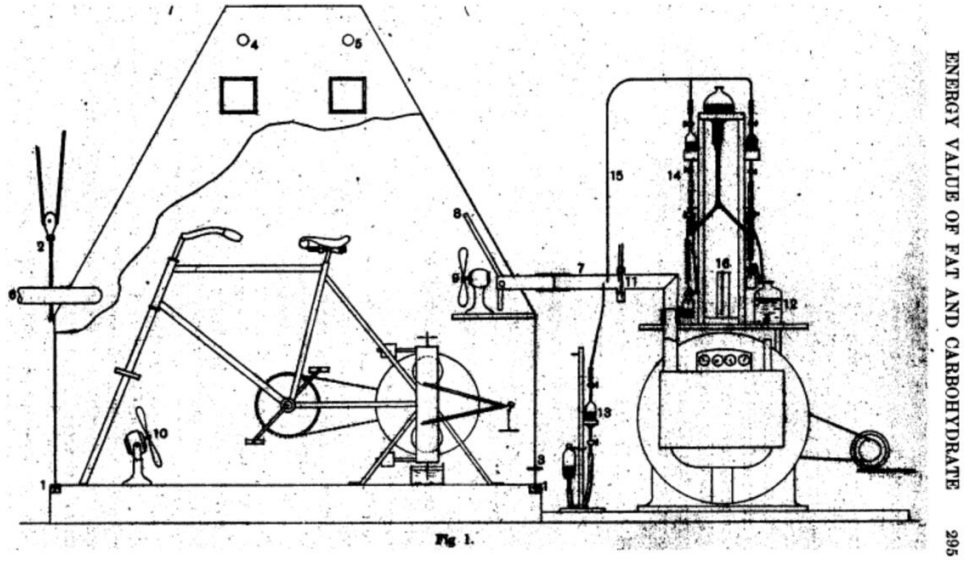
In South America, stimulants like mate tea, coffee and coca were used to increase performance. It has been reported that the Incas chewed coca leaves to cover the distance between Cuzco and Quito, in Ecuador (>1600km). (Saltin & Jeukendrup, 2010, p. 10).

1.1.2 The first experimental approach

An experimental approach to the field of human muscle energy metabolism had its start in the middle of the 19th century. In 1842 Justus von Liebig stated that the primary fuel for muscular contraction was protein. However, within two decades this was proven wrong by von (von Pettenkofer & Voit, 1866). Subsequent laboratory experiments focused on whether carbohydrates and fat could be used directly by contracting skeletal muscle. After some initial studies by Chaveux, supporting the view that fat had to be converted to carbohydrates before it could be used by muscle, Zuntz (1901) claimed that both carbohydrates and fat were oxidized by skeletal muscle,

not only at rest but also during exercise. This was confirmed in later studies by Krogh and Lindhard (1920). They also demonstrated that both fuels were used at the same time, in most instances, while protein normally did not play a role as a supplier of energy. (Saltin & Jeukendrup, 2010, p. 10).

Figure 1: Gas Analysis Jaquet Apparatus



Source: Krogh and Lindhard, 1920, p. 295.

This is the experimental Krogh and Lindhardt (1920) used to measure carbohydrate and fat utilisation during exercise. Oxygen consumption and carbon dioxide production were measured; and from this, carbohydrate and fat oxidation were calculated.

Carbohydrate can be converted and stored as fat, but fat cannot be converted or stored as carbohydrate (although some of the breakdown product (glycerol) can be used in gluconeogenesis to make glucose).

> Other researchers [in the early 20th century] had a more applied approach. They studied the diet of Arctic explorers crossing ice caps in the world. The Polar expeditions established that with an energy intake of up to 60-70% coming from fat, subjects could still maintain a relatively high daily high exercise output. The sledge dogs could, however, perform their heavy task with a diet containing up to 90% fat. (Saltin & Jeukendrup, 2010, p. 11).

The importance of carbohydrate feeding

> Important observations were also made by Levine and colleagues in the 1920s [Levine, Gordon, & Derick, 1924]. They measured blood glucose concentrations in some of the participants of the 1923 Boston Marathon..

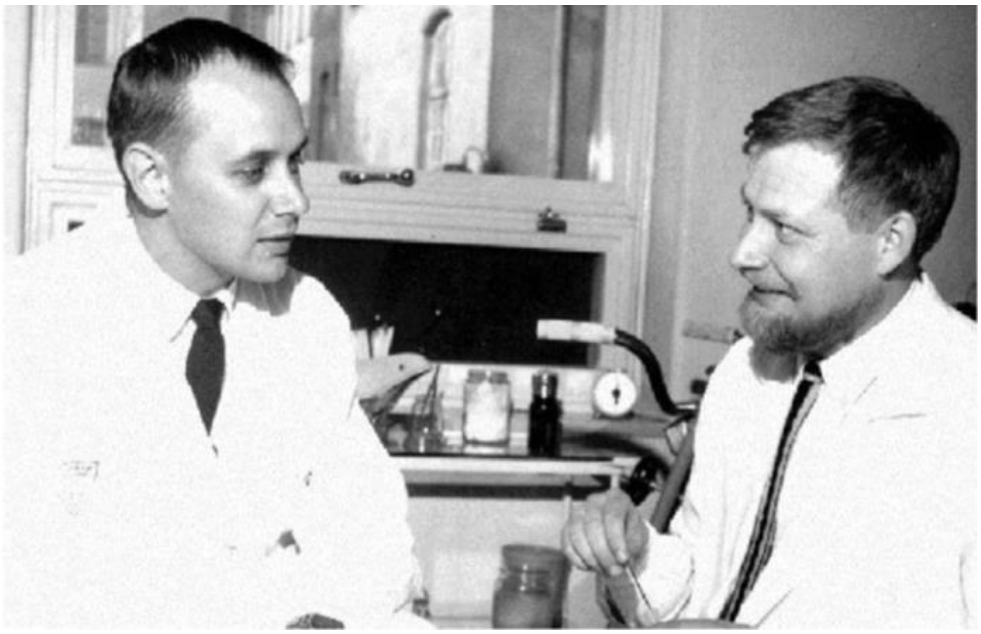
They observed that glucose concentrations markedly declined after the race in most runners. These investigators suggested that low blood glucose levels were a cause of fatigue. To test that hypothesis, they encouraged several participants of the same marathon the following year to consume carbohydrates (candy) during the race. This practice, in combination with a high-carbohydrate diet before the race, seemed to prevent hypoglycemia (low blood glucose) and significantly improved running performance (i.e, time to complete the race).

The importance of carbohydrate for improving exercise capacity was further demonstrated by Dill, Edwards, and Talbott (1932). These investigators let their dogs, Joe and Sally, run without feeding them carbohydrates. The dogs became hypoglycemic and fatigued after 4 to 6 hours. When the test was repeated, with the only difference that the dogs were fed carbohydrates during exercise, the dogs ran for 17 to 23 hours. (Saltin & Jeukendrup, 2010, p.12)

1.1.3 Scandinavian studies

In the 1950-60s, methodologies improved and new techniques such as the use of isotopes were introduced; also, the biopsy needle was re-introduced to take muscle biopsies and measure muscle glycogen (by Jonas Bergström and Eric Hultman, 1967**)**

Figure 2: Jonas Bergström and Eric Hultman who performed muscle biopsies on each other and started ground breaking work on the role of muscle glycogen



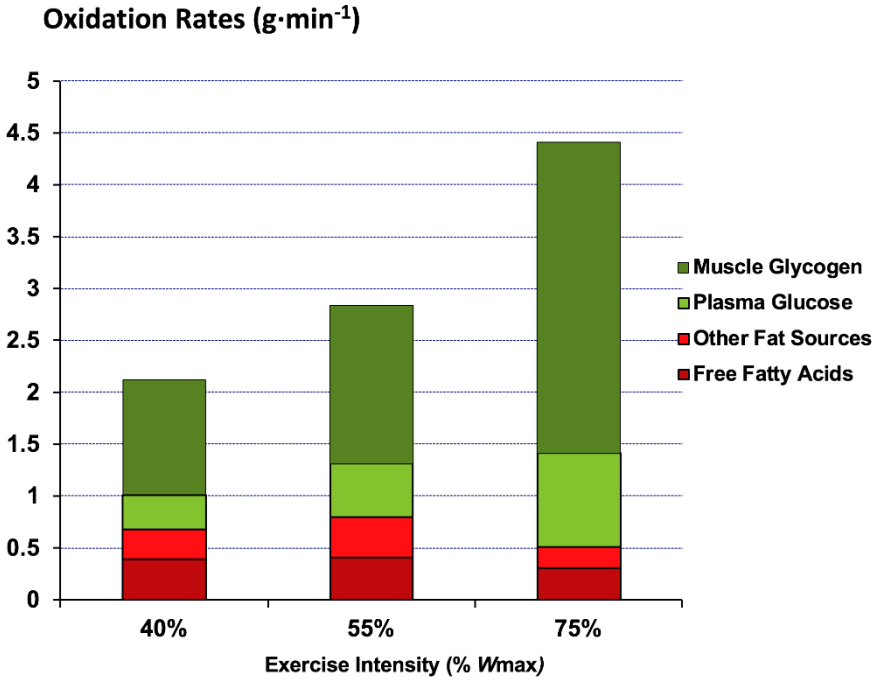
Source: Hawley, Maughan and Hargreaves, 2015, p.14.

This provided new tools that allowed more detailed investigation of substrates used and metabolites produced by the muscle (Bergström, Hermansen, Hultman, & Saltin, 1967; Bergstrom & Hultman, 1967; Hultman & Bergstrom, 1967).

The storage and use of muscle glycogen (Bergström et al., 1967; Bergstrom & Hultman, 1967; Hultman & Bergstrom, 1967) was extensively investigated. But also fat as a fuel received some attention. Fatty acids (FA) became recognized as key players in exercise metabolism (Havel, Pernow, & Jones, 1967).

Since then, many exercise studies have investigated the role of fat and carbohydrate during exercise and their relative contributions to energy expenditure. Many discoveries were made with regards to the factors that limit the use of these substrates and the mechanisms that regulate the use of these substrates. It is clear that carbohydrates are needed for high intensity exercise and that during exercise of 80%VO_2max or more fat oxidation is significantly reduced or even negligible (Randell et al., 2017; van Loon, Greenhaff, Constantin-Teodosiu, Saris, & Wagenmakers, 2001; Venables, Achten, & Jeukendrup, 2005). Fat oxidation is increased significantly after several weeks (usually 10-12 weeks) of endurance training (Holloszy & Coyle, 1984).

Figure 3: Substrate use as a function of exercise intensity



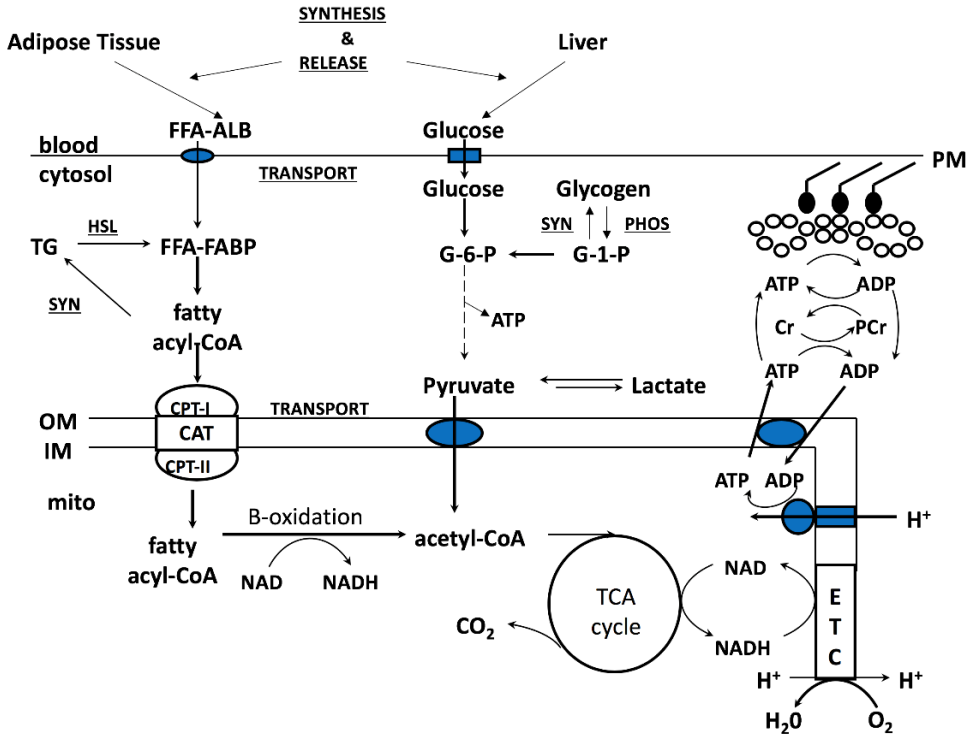
Source: adapted from Romijn, Coyle, Sidossis, Gastaldelli, Horowitz, Endert and Wolfe 1993, p. 385.

Figure 3. Fat oxidation is in red. It can be seen that fat oxidation increases from low to moderate intensity but decreases at higher intensities. This is true for both fat substrates (plasma derived and muscle derived). Carbohydrate oxidation on the other hand increases

with increasing exercise intensity mostly as a result of muscle glycogen use. It is clear that at high intensities (>75%VO_2max) carbohydrate is the dominant fuel.

The roles of plasma and muscle triglycerides (TG) are less clear and continue to be intensely debated. There is also much discussion about the reasons why fat oxidation is limited during high intensity exercise. During high intensity exercise there is an increased demand for energy, yet it is not possible to use fat, even though it is available in abundance. It has been suggested that the transport of FA into the muscle is the rate-limiting step, but there is also strong evidence of an important role for the mitochondrial respiratory capacity. Another theory evolved around the regulation of the FA uptake into the mitochondria.

Figure 4: Schematic overview of energy production in skeletal muscle.



Source: adapted from Spriet 2002, p.1478.

Figure 4. Glucose and fat entering the cell and taken up as pyruvate or fatty acyl-CoA into the mitochondria where they are both converted to acetyl CoA before being used for ATP production through the TCA cycle. When pyruvate cannot be taken up and used by the TCA cycle fast enough by the mitochondria, lactate will be formed.

Early studies also focused on lactate metabolism. This intermediate product of carbohydrate metabolism is produced especially during high intensity exercise. In the 1970s, the theory developed that lactic acid was strongly related to fatigue. In sports, lactate became the most measured blood parameter and it was (and still is) often used to

monitor training intensity. It was thought that lactate was formed as a result of insufficient oxygen supply to the working muscle. However, now we know that lactate is not the cause of fatigue, it is a great fuel for the muscle and it is also formed in the presence of oxygen. Lactate is simply a product of carbohydrate metabolism that is formed when the rate of glycolysis exceeds the capacity of tricarboxylic (TCA or Krebs) cycle activity. Glycolysis is stimulated during high intensity exercise and allows the adenosine tri phosphate (ATP) production required to sustain that intensity. If the TCA cycle activity cannot keep up with the high rates of glycolysis, pyruvate will accumulate and this could shut down glycolysis (through feedback inhibition). Of course this means that the intensity cannot be maintained. So to prevent pyruvate from accumulating, it is converted to lactate. This is a good thing and the fact that we can form lactate means that: 1. Rates of glycolysis can be high and we can continue to generate energy; 2. Pyruvate accumulation is prevented. So whereas lactate, (especially in football) is still thought of as something that needs to be prevented, it is simply a byproduct of carbohydrate metabolism. It would be more of a problem if players could not produce lactate. Diet also affects lactate production. For example, if glycogen concentrations are low, lactate production will be low, but exercise capacity will be lower as well. So, although for many years lactate was thought of as a "bad thing" we now think of lactate as a "good thing" and a good fuel for the working muscle (Brooks, 1991, 2018).

> Although many questions are still unanswered, despite many years of intensive research, it is clear dietary carbohydrates are essential for optimal performance. Equally clear is that a high capacity for lipid oxidation in the active muscles of an endurance athlete is a requirement for optimal endurance performance. (Saltin & Jeukendrup, 2010, p. 12).

Hydration

> In the 80s, there were a number of studies showing that dehydration could reduce performance and extreme dehydration could result in heat stroke and adverse health effects. These studies were soon followed up by work to optimize fluid delivery during exercise. Sports drinks appeared on the shelves of sports shops and supermarkets and were marketed toward a growing number of long distance runners and other athletes.
>
> There was clearly a trend towards drinking more and more during endurance events as evidenced by the IAAF (International Association of Athletics Federation) drinking guidelines and regulations for feed stations during marathon races. In 1953, the IAAF handbook for race organizers indicated that feed stations had to be provided only for marathon aces and only at 15 and 30 km. The 2009 guidelines indicate that water should be available at the start and finish of all events, for events up to 10km drinking

should be provided every 2-3 km and for longer events refreshment stations have to be provided every 5km. In addition, water should be supplied midway between these refreshment stations. Effectively the total number of drinking opportunities during a marathon may be 17! [versus just 2 in 1953!] Over the years the drinking messages got a bit clouded and some runners interpreted the guidelines as a directive to drink as much as possible. However, [the guidelines never actually stated this,] it is clear that drinking too much water can result in hyponatremia [Hew-Butler et al., 2008], and more recently the drinking advice has stressed that overdrinking can be dangerous [American College of Sports et al., 2007; Baker & Jeukendrup, 2014; McDermott et al., 2017]. (Saltin & Jeukendrup, 2010, p. 13).

Micronutrients

Micronutrients have received some attention too. Since their discovery, vitamins have been more or less synonymous with good health because it was clear that a lack of these essential nutrients resulted in illness. Since the 40s and 50s it became common practice for sports people to supplement with vitamins in order to perform better. [Research was mostly focused on the general populations and guidelines aimed to prevent deficiencies]. However, research also consistently indicated that as long as there were no deficiencies, vitamin intakes over and above the daily recommended amounts did not enhance performance. Nevertheless, the use of vitamins and minerals, and antioxidants in particular, is still very popular. More recently, however, studies pointed out that large amounts of antioxidants could actually prevent (or at least reduce) normal training adaptations. It has also become clear that large doses of certain vitamins and minerals can have detrimental health effects. (Saltin & Jeukendrup, 2010, p. 13).

So, although vitamins and minerals are needed, more is not always better and sometimes more is worse.

1.1.4 Football studies

Science arrived relatively late in football and Tom Reilly (Liverpool John Moores University) was certainly one of the pioneers. Some of the earliest studies in football were performed by him and his team. In 1976, they reported that English First division players had about 100 changes in playing activities during a match with each activity having a mean duration of 5-6s. Reilly and Thomas also estimated that on average the intensity of match play was around 75%VO_2max (Reilly & Thomas, 1979).

In the 1960s, it was demonstrated that muscle glycogen concentration was related to fatigue. A higher carbohydrate intake resulted in increased muscle glycogen and increased endurance capacity. It was shown that during a football match muscle glycogen concentration declined to very low levels at the end of the match. On average, muscle glycogen concentrations were 96 mmol/kg ww, 32 mmol/kg ww at halftime and 9 mmol/kg ww at the end. It was also observed that in some players muscle glycogen was already very low after 45 min. The players who started the match with low muscle glycogen (45 mmol/kg ww) had almost depleted stores by half-time. Another important observation was that muscle glycogen concentration was correlated with parameters of running performance. For example, the players with lower muscle glycogen concentrations covered less distance. More importantly, they spent less time completing high-intensity runs (15% versus 27% of total time). (Bangsbo 2014)

In 1982, Ira Jacobs and colleagues took muscle biopsies in 15 Malmo players (Jacobs, Westlin, Karlsson, Rasmusson, & Houghton, 1982). They measured muscle glycogen and found that these concentrations dropped to very low levels after a real match. 24 hours later and 48 hours later muscle biopsies were collected and muscle glycogen was measured again. The main conclusion was that even 48 hours later muscle glycogen concentrations were not back to normal. This happened despite a relatively high carbohydrate intake. It could be speculated that even 72 hours after a match, glycogen would not be back to normal concentrations, which is when players would have to be ready to play again on a 2 matches per week schedule.

Figure 5: Muscle Glycogen % in a two matches per Week Schedule

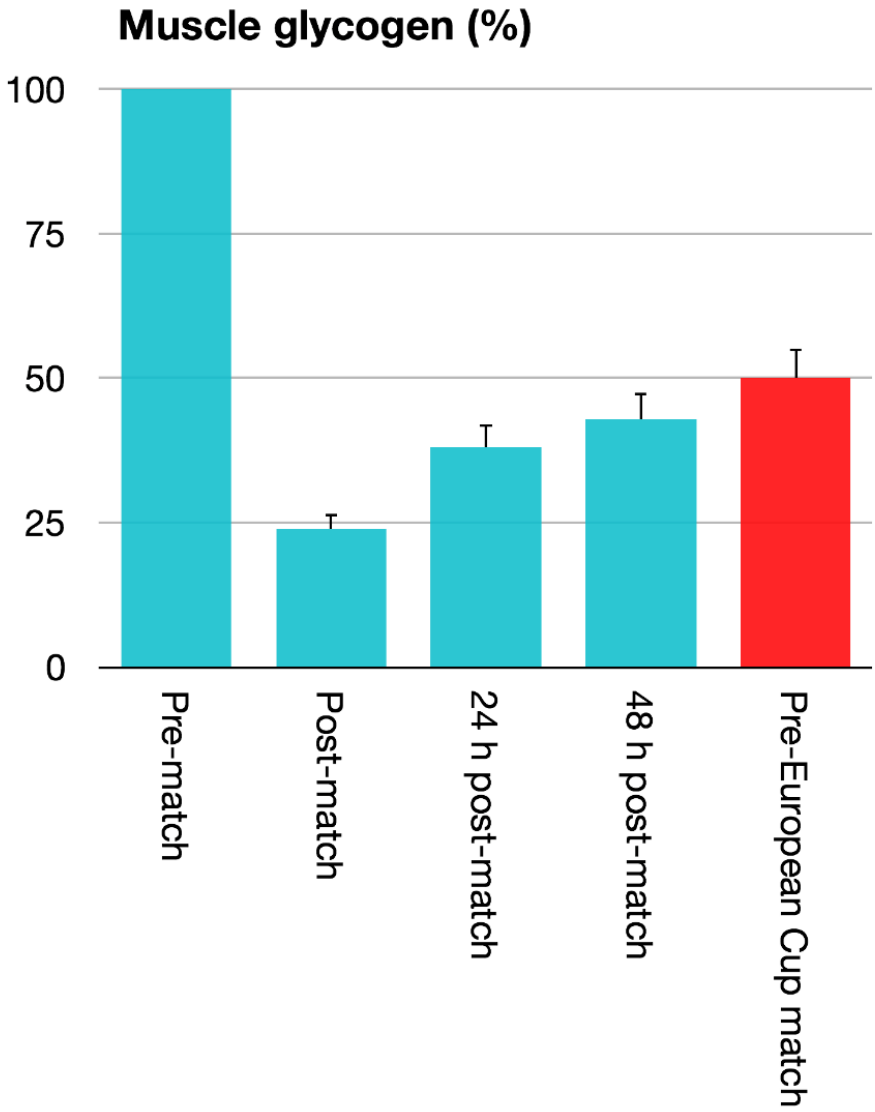


Figure 5. In blue, the muscle glycogen measurements performed in a Swedish football team. The players consumed their normal diet and this was not sufficient to restore muscle glycogen to pre-match levels. In red, the fictive muscle glycogen concentration on a European Cup match 4 days after the first match. It is clear that it is unlikely that muscle glycogen can be completely restored on that day. Source: based on Jacobs et al., 1982.

In the 1980s, studies started to appear demonstrating the benefits of carbohydrate ingestion during endurance exercise. Consistently greater endurance capacity was reported in these studies, especially when the exercise duration was greater than about 2 hours.

Studies in football soon followed. The effects of carbohydrate ingestion and player performance during "live" matches were investigated. For example, in a study (by Kirkendall, Foster, Dean, Grogan, & Thompson, 1988) 10 players were captured on video

on two separate occasions, separated by one day. For each match, players drank either a carbohydrate solution or sweetened placebo before the game and at halftime. Players who drank the carbohydrate solution ran approximately 40% greater distance during the second half of the game, in comparison to when the placebo beverage was consumed. Interestingly, a similar study in which players consumed 0.5 L of a 7% glucose solution 10 min before a practice match and the same volume again at halftime, reported a 39% reduction in muscle glycogen use compared to players drinking a sweetened placebo (Leatt & Jacobs, 1989).

As a returning theme in this course, it is important to note that it is not easy to measure performance in football. There are many aspects to performance and most of these are difficult to measure. This, in turn, results in greater variation which means that it becomes harder to detect small differences. Such differences, however small, could be important for a player's future performance and the team's performance. Therefore, we encourage researchers to report the reliability of their measurements so that interpretation of the data becomes more meaningful. Many studies are using exercise protocols that are inadequate, have poor reliability or have no resemblance to actual football performance. It is essential that we are able to critically read research papers so we can judge them better and interpret the data with more caution when needed.

Unit 1.2 The future

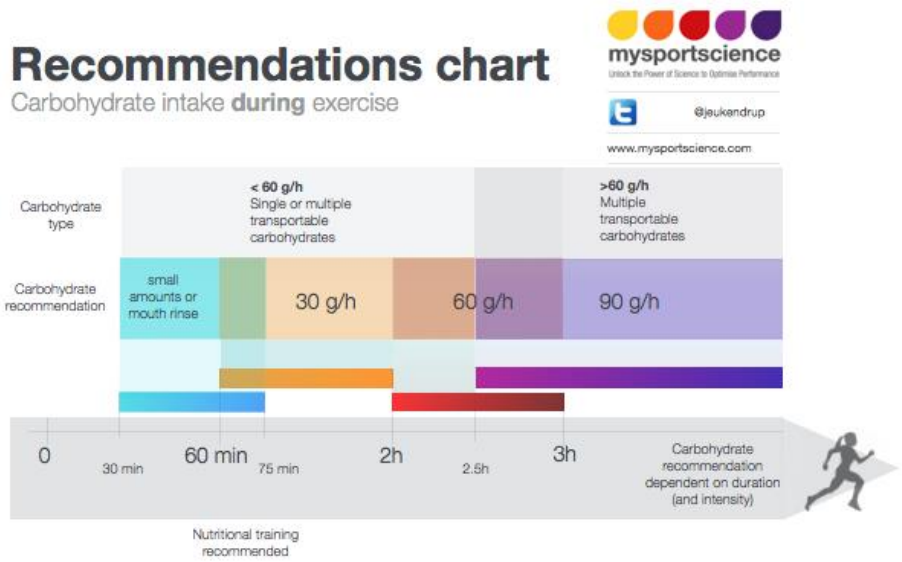
1.2.1 The future of sports nutrition

What the future of sports nutrition looks like may be in the eye of the beholder. If we ask someone working in the sports nutrition industry, their focus will be on customer demand and profit opportunities. Protein will be very high on that list as well as supplements. When a journalist of an average popular magazine is asked a question, it will be about the next "superfood" (a term that is 100% marketing and not evidence based or scientific at all); it will be about the next diet fad or the next supplement with magical effects; it will be about extremes and controversies because this will create the best headlines. When asked as a scientist, the future of sports nutrition may develop in several areas. The first one is personalised nutrition rather than blanket advice for all situations and all athletes, i.e., the advice will become tailored. Secondly, nutritional advice will be periodised as well (we will discuss in more detail what this means on the next section) and will become more integrated with training. Because of this, advice will be specific not only to the athlete (type of athlete, the sport, player position) but also to the goals, the season, and the type of training performed. Thus, nutrition advice will automatically become more personalised because many factors that go into sound nutrition advice are specific to the individual. Personalised nutrition and periodised nutrition will go hand in hand, but cannot be implemented meaningfully without a very close working relationship with the trainer/coach. The biggest challenge is not to figure out what the advice should be, but how to implement this in a real-life situation, the logistics of successful execution, and to manage workload and communication amongst support staff.

One size fits all

Guidelines are often generalized to all athletes and all situations. Rarely is it made clear exactly who the guidelines are for and in which situations they should be used. This oversimplification makes it very difficult to use the advice in different settings or it is misused or misinterpreted. One example is the advice for carbohydrate intake during exercise. The 2009 *ACSM's Guidelines* (American College of Sports Medicine, as cited in Rodriguez et al., 2009) stated that carbohydrate intake during exercise should be 30-60g per hour. However, this recommendation came without clear explanation regarding who this guideline was for. The recreational athlete? The professional athlete? The marathon runner? The football player? Someone who goes to the gym once a week? Someone who wants to gain muscle mass? Someone who wants to lose weight? Someone who wants to win a race? Or someone who is just doing their weekly training? Clearly the advice would not be exactly the same for all these different scenarios! Therefore, these guidelines were slightly improved by taking into account the duration of exercise and to some degree the level of the athlete (Jeukendrup, 2011, 2013, 2014).

Figure 6: Recommendations for carbohydrate intake during exercise



Source: Jeukendrup, September 15, 2015, https://goo.gl/k92zxC

Figure 6. Recommendations for carbohydrate intake during exercise as discussed in Jeukendrup (2013, 2014). With increasing exercise duration carbohydrate intake requirements increase from no carbohydrate in events under 30 min to 90g/h in events over 2.5h. For football training and matches a carbohydrate intake around 30-60g/h is usually recommended.

> If the exercise is less than 30 min there is no need to take in any carbohydrate. There is little or no evidence that carbohydrate intake or a mouth rinse does anything. It may not harm, but there does not seem to be a need. When the exercise is a little longer, say 45-75 min and it is "all-out" for that duration, performance will benefit from either carbohydrate intake or a carbohydrate mouth rinse. What is best depends on the practicalities of ingesting carbohydrate. Sometimes it is easier to simply rinse or swallow the carbohydrate solution. The type of carbohydrate does not seem to matter much here. For exercise lasting 1-2 hours, some carbohydrate has been shown to improve performance and 30 grams per hour is probably sufficient. (Jeukendrup, September 15, 2017, https://goo.gl/eP6AQr).

With increasing duration, it is recommended to increase the intake up to 60 g/h and beyond 2.5h even up to 90 g/h. For football, which would fall in the 30-60 g/h category, studies seem to suggest that there are benefits of being at the higher end of that range. This will be discussed in more detail when we focus on match day preparation.

1.2.2 The current problem that will get worse in the future

Many people have an opinion about nutrition which is often expressed through the media. Many people, including athletes, are influenced by those opinions. When celebrities with millions of fans make such statements, they can be powerful. Many of the opinions and views, however, are not based on scientific evidence. They are often based on personal experiences, beliefs, hear-say, or they are simply made up. The media will add to this, by jumping on the topics that will hit headlines. Extreme messages will get more attention than anything that is balanced or in moderation. Industry will further cloud the messages through aggressive advertising and false claims. Please note that not all celebrities' views are nonsense, not all journalists are looking just for headlines and not all industry messages are biased and deceitful, but many of them are. It becomes difficult, especially for the average person or athlete to distinguish the evidence-based information from the nonsense.

Because this confusion and vast amount of misinformation out there are real and will not go away (and will probably increase in the future), we must arm ourselves and our athletes with the tools to figure out what is good information and what is not. This will be the goal of the next sections.

Some of the essential skills of a successful evidence based practitioner include:

- Finding good information.
- Reading and interpreting the information (critical reading).
- Recognising pseudoscience.
- Understanding how science works and how evidence is (should be) obtained.
- Understanding the strength of evidence.

1.2.3 Genetic testing

People often expect the future of nutrition to be in gene-specific advice. With decreasing costs of analyses several companies now target the consumer directly with the promise to give them "invaluable insights" into their nutritional needs. Some of these companies target athletes specifically and include advice that is performance-related based on the analysis of the genome. Just a simple saliva swap posted back to the company will result in a report that promises a lot of answers. This picture may sound too good to be true and in fact it is too good to be true.

Much of the existing work on nutrigenetics has focused on the association between genetic markers and various diseases or markers of those diseases (cancer, cardiovascular disease, and metabolic diseases such as obesity and diabetes). Typically,

single nucleotide polymorphism (SNP) is measured. SNPs are the most common type of DNA variations consisting of two different single nucleotide alleles. These SNPs play a key role in determining each individual's anatomy, physiology and disease status. Several gene polymorphisms exist that can be used as screening tools for certain diseases, such as the E4 allele in the APOE gene for Alzheimer's and cholesterol homeostasis, but it is rare that a single SNP holds the key for any given phenotype. There are 2 examples where a single SNP seems almost entirely responsible for the resulting phenotype. These examples are phenylketonuria (PKU) and galactosemia. Both conditions are now easy to identify and can be treated with dietary changes (Kussmann, Raymond, & Affolter, 2006). Characterised by lacking the enzyme to metabolise the essential amino acid phenylalanine, PKU is an example of a monogenic disease which can be successfully managed through diet. Furthermore, the polygenic ceoliac disease, caused by impaired tolerance to dietary gluten, provides an illustration of how personalised nutrition can work. It is extremely rare that one single gene can explain a large part of the phenotypic outcome. The variability in blood pressure response with dietary fibre intake could partly be explained by genetic differences associated with protein polymorphisms of the angiotensinogen gene (Hegele et al., 1997). Another example is selenium supplementation and reduced risk of cancer. In this case, alleles of the antioxidant enzyme glutathione peroxidiase were identified as the potential link. In these cases the SNP explained large part of the variation in phenotype but not everything. But these studies suggest that we may be able to use some polymorphism information and advise individuals on the need to increase or decrease dietary intake of certain nutrients.

However, most of the conditions we are interested in are complex traits where a single SNP can only explain a small part of the variation. Most chronic diseases are a result of complex interactions between multiple genes and the environment (multifactorial genetic disorders) and conclusive genetic markers for disease are rare at best. This means that we require a shift from candidate genes (single SNPs) to genome-wide sequencing. We also need a better understanding of dietary practices and measurement, and a better controlled of cross-over experimental trials (rather than observational, cross-sectional studies). Observational studies provide indirect evidence of the differences in response to certain nutrients within a given cohort, but causal relationships cannot be determined. It will take many years, maybe decennia of research, before we are able to draw more meaningful conclusions from genome-wide sequencing.

Where it is difficult to draw conclusions about nutrition and disease where we have hundreds of studies, drawing conclusions about genes, nutrition and sports performance is even more difficult because we have far less studies and the available ones are generally too small to generalize the results. So whether genomics is the future of sports nutrition, it certainly won't be confirmed in the near future. There is a lot of work that needs to be done before such measurements become meaningful.

A practical question is whether different companies currently provide such services. Questions that should be asked are:

1. Will I get the same answers if I send my samples to different companies? The answer is highly unlikely. A quick search on the internet will reveal the stories of customers who sent their samples to 2-5 companies and not surprisingly the interpretations of the results and the advice were all different.
2. Is the advice I will get practically relevant? For example, if the test will tell my athlete he or she is predisposed to become a sprinter, is there any benefit for this simple measuring sprint performance over 50 meters with a stopwatch?

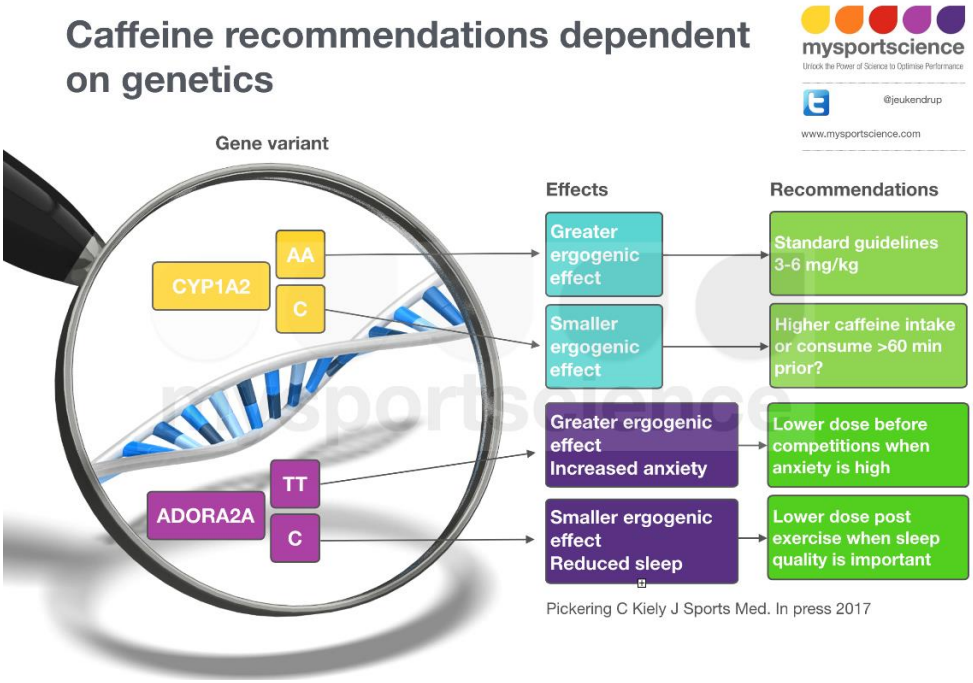
The example below could have some small relevance in sports practice, but this may be the best example we currently have.

Caffeine

It is clear that the effects of caffeine in people is different. Some people will be up all night if they drink coffee before going to bed, whereas others will fall asleep straight away. There is large inter-individual variability in caffeine half-life in humans. Half-life values of 2.5-12h have been reported. These differences are explained by the variability in metabolism and elimination rather than absorption.

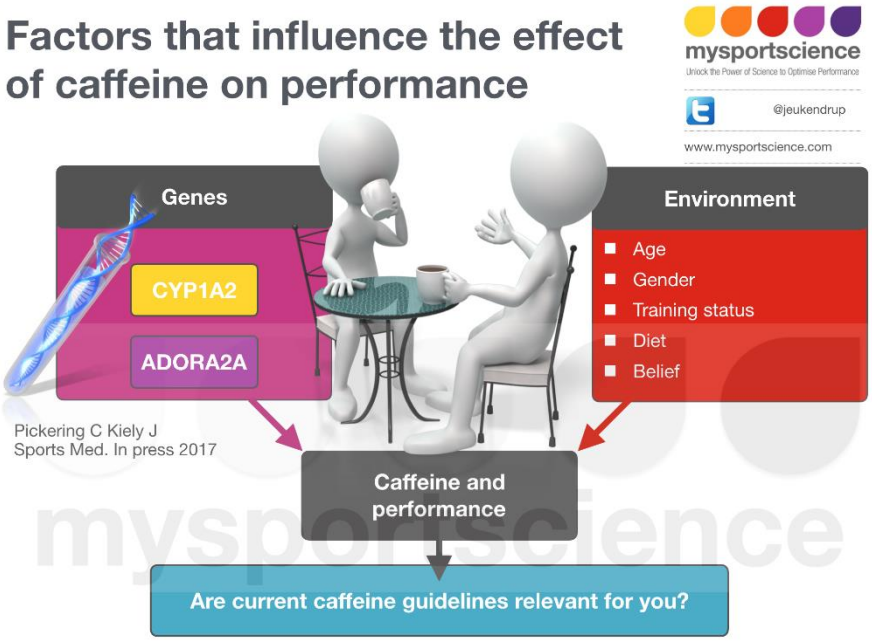
> At present, variation in two genes, called CYP1A2 and ADORA2A has been shown to impact the performance enhancing effects of caffeine, although these early results have not been well replicated. These genes cause these effects through slightly different mechanisms. CYP1A2 creates an enzyme (called cytochrome P450) which is responsible for how our bodies break down caffeine, and a small change in this gene can predispose people to be "fast" or "slow" caffeine metabolisers...
>
> A study from 2012 found that fast metabolisers saw a greater performance enhancing effect of 6mg/kg caffeine than slow metabolisers on a 40km cycle time-trial [Womack et al., 2012]. Whilst these results have been replicated, other studies have shown no effect of this gene on performance enhancement following caffeine, so a definitive answer is not yet possible (Pickering, September 22, 2017, https://goo.gl/7ApTU7).

Figure 7: Effects and implications of different gene variants related to caffeine metabolism



Source: Pickering, September 22, 2017, https://goo.gl/7ApTU7

Figure 8: Both genes and environment will affect the effects of caffeine on performance in an individual



Source: Pickering, September 22, 2017, https://goo.gl/7ApTU7

The second gene that may affect how much caffeine improves our performance is ADORA2A. This gene encodes for an adenosine receptor. When adenosine binds to this receptor it makes us feel tired. One of the

> ways in which caffeine improves our performance is by competing with adenosine for the adenosine receptors. In other words, the more caffeine that binds to these receptors, the less adenosine can. As a result, we feel less tired and lethargic. As such, variation in these adenosine receptors may alter have much caffeine improves our performance. A single study, from 2015, has examined this, finding that this gene did impact improvements in performance following caffeine use [Loy, O'Connor, Lindheimer, & Covert, 2015]. Variation in this gene might also contribute to increased anxiety or poor sleep with increased caffeine intake, which could also affect sporting performance. (Pickering, September 22, 2017, https://goo.gl/7ApTU7).

A genetic test could probably give a good indication whether someone is a a fast or a slow metabolizer of caffeine. The question remains whether there is added value to the existing knowledge on how these people respond to caffeine. If someone cannot sleep after drinking coffee, they will have already learned to avoid coffee before going to bed.

1.2.4 Food allergies and Intolerances

Another trend that we can see is related to intolerances and allergies. The number of athletes with intolerances has sky-rocketed in the last few years and there may be several reasons for this:

1. Our modern society is changing and various factors such as pollution, stress, food availability etc. could influence allergies and intolerances, making them more prevalent than before.
2. People have become more aware nowadays; whereas in the past these symptoms were ignored, people now visit a doctor who diagnoses and recognizes the symptoms as the result of intolerances and allergies.
3. People hear about allergies and intolerances and use these to explain some of the symptoms they have and essentially self diagnose. There is no clinical diagnosis in such cases.

Although 1 and 2 cannot be excluded the most likely and common tendency is probably number 3. People self diagnose, often without really understanding what an allergy or intolerance really is.

> When the term *allergy* was first introduced in 1906, it referred to an adverse reaction to a food or other substance not typically regarded as harmful or bothersome... Doctors [however] use the word rather differently, and this can be misleading and confusing. Doctors use the word allergy to mean an adverse reaction of the immune system to a substance not recognized as harmful by most people's immune systems. True allergies (e.g., to pollens,

dust mites, fish, shellfish, nuts) are typically associated with the formation of antibodies. Some people... have an inherited tendency to this type of allergy and they tend also to be prone to asthma, eczema and hay fever; this condition is known as atopy. In certain circumstances, and especially during the first few years of life, atopic people may develop IgE [immunoglobulin E] antibodies when exposed to an allergy-inducing protein in a process called sensitization. When sensitization has occurred, the allergy-inducing protein is referred to as an allergen and the resulting antibody (also a protein) as allergen-specific IgE. Although doctors use the term allergy when referring to an adverse reaction that involves the immune system, the term *intolerance* is preferred when an adverse reaction shows no evidence of immune system involvement. The scientific term for an intolerance is *non-allergic hypersensitivity.* (Jeukendrup & Gleeson, 2018)

Allergy

"Adverse reaction of the immune system to a substance not recognized as harmful by most people's immune systems" (Jeukendrup & Gleeson, 2018).

Intolerance

"Adverse reaction [with] no evidence of immune system involvement" (Jeukendrup & Gleeson, 2018).

Food Intolerance

Food intolerance can occur when the body fails to produce a sufficient amount of a particular enzyme needed to digest a food component before it can be absorbed (Jeukendrup & Gleeson, 2018). For example, if a person suffers abdominal discomfort with flatulence and bloating or diarrhea every time they consume milk or milk-derived products (e.g. cream, yoghurt, cheese) they may be suffering from lactose intolerance, a condition caused by lack of lactase, the enzyme that digests the main sugar in milk, a disaccharide called lactose. This is caused by the lactose not being absorbed but instead being fermented by the microbes in the intestine. Food intolerances are normally dose related, meaning the more you eat the worse the reaction is likely to be. There may also be a threshold amount required to be consumed before experiencing any symptoms which can make it difficult to determine the specific cause.

If a person suffers nervous system symptoms because of an amount of caffeine in a mug of strong coffee that would be tolerated by most people, this person would be suffering from a drug-like or pharmacological food intolerance. This can occur either because of an intolerance to chemicals naturally present in foods (such as theobromine in chocolate or

tyramine in aged cheeses), or an intolerance to food additives such as sulphites or benzoates (Jeukendrup & Gleeson, 2018).

Whilst enzymatic and pharmacological food intolerance reactions only affect some people, toxic food reactions affect everyone if an excessive amount of a particular food constituent is ingested. A good example is the false food allergy type of reaction that can occur when sufficient amounts of the substance called histamine accumulates in the flesh of spoilt (decayed) tuna (known as the Scombroid reaction). As histamine is also the natural agent in the human body involved in allergic reactions, Scombroid food poisoning often gets misidentified as a food allergy. This condition is named after the Scombridae family of fish, which includes mackerels, tunas and bonitos, because early descriptions of the illness noted an association with those species; however, other nonscombroid fish including mahi-mahi and amberjack are also known to cause this problem. Cooking the fish does not prevent the illness because histamine is not destroyed at normal cooking temperatures. None of the above examples of food intolerance involve the immune system and, for this reason, none can result in life-threatening allergy or anaphylaxis, but they can result in severe abdominal discomfort (Jeukendrup & Gleeson, 2018).

A person with gluten sensitivity (also known as gluten intolerance) may also have symptoms such as bloating, abdominal pain or diarrhea, but because the immune or autoimmune symptoms are not involved it is not considered as a serious condition as celiac disease or gluten allergy. As many as 6% of people in the USA have gluten sensitivity (This number is far less than the number of self diagnosed gluten intolerances out there).

With the exception of lactose intolerance, for which a conventional test exists, no reliable forms of testing exist for the types of food intolerance described above... Studies that have used food exclusion followed by blinded and placebo-controlled food challenge, have suggested that this kind of mechanism may apply in some cases of migraine, arthritis and irritable bowel syndrome. However, with the exception of dietitian supervised food exclusion and food challenge, no validated test for this type of food allergy has so far emerged. Many companies now provide a service that is based on IgG testing. This test is easy to perform and cheap, and thus it is an attractive business model: the athlete gets tested, gets a report relatively quickly, and this report tells him or her which foods to avoid. There is no evidence to back this up and in fact the presence of IgG is likely to be a normal response of the immune system to exposure to food. Actually, higher levels of IgG in foods may be associated with tolerance to those foods. The general scientific consensus is that the data obtained from IgG blood tests is not scientifically robust and most allergy specialists consider such tests to be unhelpful.

There is another good reason to avoid these tests as they could cause more harm than good. If all the changes that are often suggested are based on such tests, athletes will exclude several important foods from their diet. This means that recovery could be

impaired (for example by removing milk and eggs) or deficiencies could develop (if a larger range of foods is removed). Nevertheless, many of these companies will aggressively promote their business and contact players directly.

Food Allergy

> A true gluten allergy—not to be confused with gluten sensitivity or celiac disease—is caused by gliadin, a glycoprotein that, along with another protein called glutenin, helps to form the gluten protein. Gluten is found in wheat and other similar cereal grains such as barley, oats, and rye. The symptoms of gluten allergy are similar to those of gluten intolerance but can be more severe. Gliadin is also one of the major allergens associated with wheat allergies and a known trigger for celiac disease, a serious autoimmune disorder of the small intestine. (Jeukendrup & Gleeson, 2018).

In a person with a gluten allergy, small amounts of gluten may be tolerated, but a person suffering from with celiac disease cannot tolerate any gluten at all. When a person with celiac disease eats gluten, the immune system initiates an unnecessary inflammatory response, and this eventually damages the lining of the small intestine. Celiac disease restricts absorption of nutrients and may lead to malnutrition and weight loss. Because celiac disease shares symptoms with a number of other disorders, including a gluten allergy, it is important that a test is conducted to confirm the condition. Gluten allergies and celiac disease are a major public health concern. It is estimated that 0.6% of children and 0.9% of adults in the USA have a gluten allergy while another 1% suffer from celiac disease. A less common but dangerous allergy is to proteins in nuts. Each year there are several reported cases of fatalities due to a rapid, severe anaphylactic shock following ingestion of nuts, or more usually, to inadvertently eating foods (e.g. curries, cakes, pastries, cookies) containing nuts or nut extracts in people with nut allergies (Jeukendrup & Gleeson, 2018).

The only way for a person to find out if he or she has a gluten allergy for sure is to be tested. One of the most common tests to determine whether a person has a gluten allergy is to use an elimination diet. In an elimination diet, a person removes all gluten-containing foods, such as wheat or pasta, from his or her diet for a period of time (usually a few weeks) to see if the allergic symptoms resolve (Jeukendrup & Gleeson, 2018). “However, an elimination diet will not rule out [either] celiac disease or gluten sensitivity” (Jeukendrup & Gleeson, 2018).

> The conventional allergy tests used by doctors... depend on the presence of allergen-specific IgE antibodies. The two most used are the skin prick test and the specific IgE blood test (previously called a RAST test). However, it is very important to realize that although allergy is unlikely when allergen-

specific IgE is absent, the presence of allergen-specific IgE only indicates that sensitization has occurred; it does not diagnose the allergy. When completely healthy and symptom-free people are tested for allergies, positive results are often found. These results are called false positives. For this reason, reliable allergy diagnosis is dependent on an allergy-focused history. A good allergy clinician can usually suspect the likely allergen(s) from the history alone, and allergy tests may not be needed. However, because a negative allergy test may point to a different, unrecognized allergy or a different explanation altogether, allergy tests are very useful to confirm the diagnosis. This is especially important in the case of suspected food allergy when an inaccurate diagnosis might commit the patient to lifelong, but unnecessary, food avoidance. Allergy tests are also useful if there is any confusion as to whether symptoms are being caused by true allergy or whether some other condition is involved. This is why allergy tests need to be interpreted by a health-care professional who is qualified in allergy and who will interpret the results in light of an allergy-focused history. This also explains why it is important not to test everybody for every known allergen, which would inevitably lead to erroneous diagnosis.

Occasionally, clinicians may be faced with a situation where the allergy history points strongly in one direction whilst an allergy test points strongly in another. This is when a provocation challenge test may be useful. The test is only undertaken under specialist supervision in a hospital. The patient is exposed to tiny, but gradually increasing, amounts of the suspected allergen source (typically a food such as peanut or cereal) until there is the tiniest hint of a rash, swelling, breathing difficulty or drop in blood pressure (the initial signs of an anaphylactic reaction). This is the gold standard amongst allergy tests. (Jeukendrup & Gleeson, 2018).

Another available allergy test for that area is the skin contact (or 'patch') test that is used as a conventional test by skin specialists in cases of contact dermatitis.

The test diagnoses a delayed, or cell-mediated (as opposed to antibody-mediated) type of allergy that mainly affects the skin. Unconventional allergy tests that are considered to be of no value include skin end-point titration tests (in which increasing amounts of a diluted allergen solution are injected under the skin until a reaction occurs),.applied kinesiology (based on measurements of muscle strength, the idea being that muscle weakness may become evident when the individual is exposed to the suspected allergen), auricular cardiac reflex (based on measurements of the pulse at the wrist), hair analysis (based on a pseudo-scientific concept called bioresonance), blood cytotoxic tests (based on an examination of the

white blood cells when exposed to a suspected allergen) and the Vega test (based on acupuncture theory and electromagnetism).

> Another common test which has become popular among athletes and others is the IgG blood test. In IgG testing, the blood is tested for IgG antibodies instead of being tested for IgE antibodies (i.e., the antibodies typically associated with food allergies). Some practitioners (particularly unconventional ones) claim that the existence of serum IgG antibodies towards specific foods is an effective tool to diagnose food allergy or intolerance. The problem with this is that IgG is a "memory antibody" which means that IgG signifies previous exposure to a food rather than an actual allergy to a food. Because a normally functioning immune system should [indeed] make IgG antibodies to foreign proteins, a positive IgG test to a food is a sign of a properly working immune system. In fact, a positive result can actually indicate tolerance for the food rather than intolerance. Thus, there is no good scientific evidence to support IgG testing for the diagnosis of food allergies. (Jeukendrup & Gleeson, 2018).

Allergies in Athletes

"There are some claims that athletes may actually be more susceptible to symptoms of food sensitivities because the stress of constant training taxes the immune system" (Jeukendrup & Gleeson, 2018). In other words, a stressed body will be less able to handle foods that are causing inflammation, but there is currently no convincing scientific evidence to back this up. Although there is some belief among athletes that gluten intolerance is higher in those who are highly physically active much of this may arise from the recent trend to have food intolerance tests performed using non-validated methods such as the IgG blood test or hair analysis (several websites for this can easily be found) mentioned in the highlight box. However, unrecognized intolerance to foods or supplements consumed during exercise could lead to increased risk of gastrointestinal problems and could be a potential cause of impaired performance in certain sports, particularly endurance events (Jeukendrup & Gleeson, 2018).

It has been established that high level athletes present an increased risk for asthma and allergies affecting the respiratory tract.

> Classical postulated mechanisms behind EIA [exercise-induced asthma or bronchoconstriction] include the osmotic, or airway-drying, hypothesis. Hyperventilation leads to evaporation of water and the airway mucosal surface liquid becomes hyperosmolar, providing a stimulus for water to move by osmosis from any cell nearby, which results in the shrinkage of cells and the consequent release of inflammatory mediators that cause

> airway smooth muscle contraction. But the exercise-induced asthma/bronchoconstriction explanatory model in athletes probably comprises the interaction between environmental training factors, including [increased lung exposure to airborne pollutants and] allergens and ambient conditions such as temperature, humidity and air quality; and athlete's personal risk factors, such as genetic and neuroimmuneendocrine determinants. (Jeukendrup & Gleeson, 2018).

The examples of genetic testing and food allergies and intolerances were used to show that trends in the market often form our ideas of what the future of nutrition will look like. However, a detailed analysis reveals that these are more trends or even fads that have little evidence or little practical relevance. The future of sports nutrition is more likely to be more fundamental: establishing individual goals and needs, and finding the best nutritional strategy. We will discuss personalized nutrition and periodised nutrition in much more detail in this course, because it is likely that this is where the field of sports nutrition will develop.

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