1.2 The future

1.2.1 The future of sports nutrition

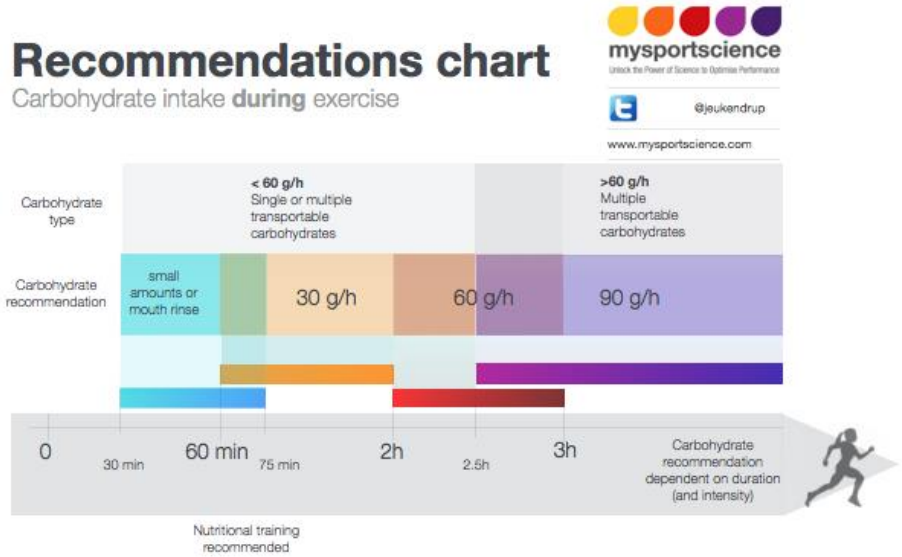
What the future of sports nutrition looks like may be in the eye of the beholder. If we ask someone working in the sports nutrition industry, their focus will be on customer demand and profit opportunities. Protein will be very high on that list as well as supplements. When a journalist of an average 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.

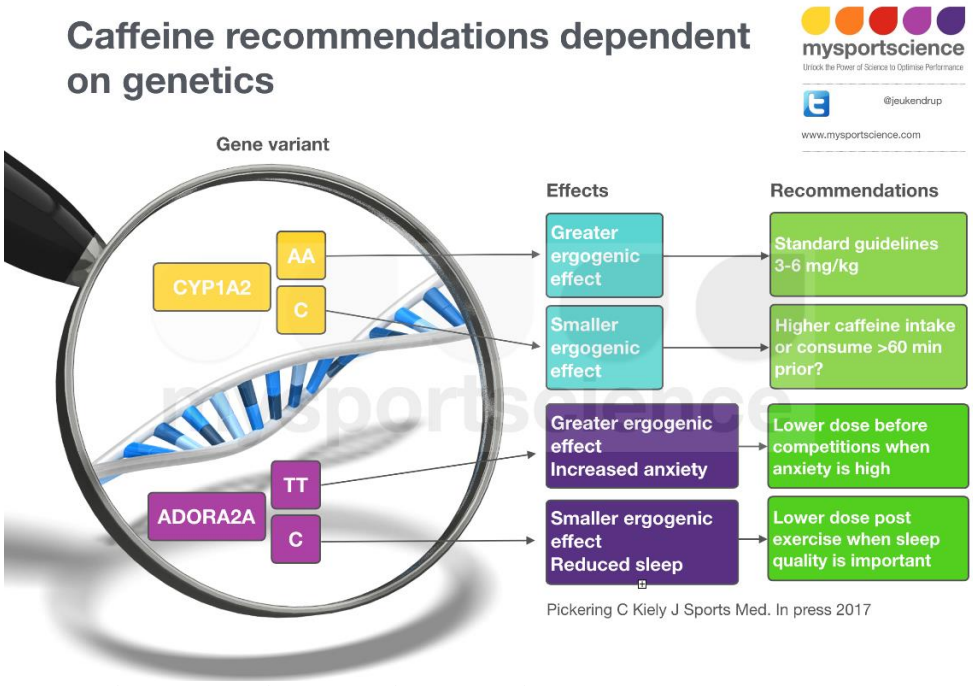
Caffeine

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

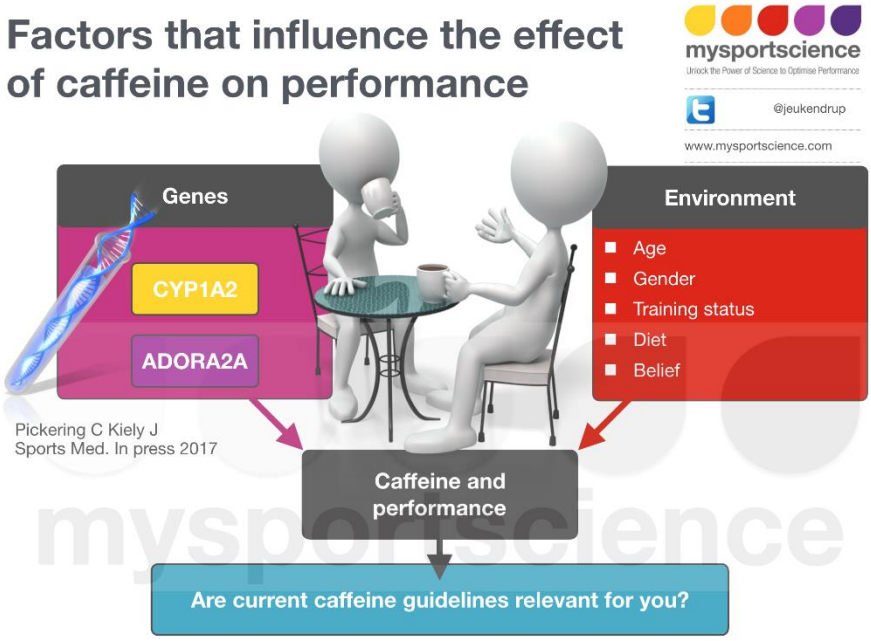
[Womack et al., 2012]. Whilst these results have been replicated, other studies have shown no effect of this gene on performance enhancement following caffeine, so a definitive answer is not yet possible. (Pickering, September 22, 2017, https://goo.gl/7ApTU7).

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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