YOUTH MENTAL HEALTH AND LIFESTYLE INTERVENTIONS:

THE ROLE OF INFLAMMATION, THE MICROBIOME, AND NUTRITION

clearthinking

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BACKGROUND BRIEFING

Good nutrition can be decisive in determining growth, brain development, and lifespan. Its impact on the brain affects all aspects of our well-being, including learning, thinking, motivation, stress tolerance, and emotion. Today's challenges require the energy and commitment of all young people: take care of yourself and those around you. Every person has an essential role to play.

Nutrition is the chemistry (biochemistry) and functions (physiology) of how living cells and beings (organisms) use food to maintain structural integrity, utilise energy, grow, and die. **Metabolism** is the sum of all chemical processes within cells (intracellular) and systemically in the body as a whole. It includes anabolic process (biosynthesis or building complex molecules from simpler ones) and catabolic processes (breaking down complex molecules into simpler ones for the purpose of releasing stored energy).

Nutrition includes the processes of:

Food ingestion, involving the disintegration of whole food in the digestive system or gastrointestinal tract or GIT, which includes the mouth, stomach, small intestine, large bowel, and accessory organs such as the salivary glands, pancreas, and the gall bladder.

Following the mechanical breakdown of food, enzymes and acids are released into the intestines to dissolve food particles and facilitate absorption of nutrients (substances ingested and used by an organism to maintain life).

Food absorption, involving the transport of nutrients across the stomach and intestinal lining (mucosa) and into the blood stream.

Nutrient assimilation, involving chemical alteration of nutrient molecules in the blood stream by the liver so that they can be taken up by cells throughout the body (e.g. combining lipids with proteins to make the more soluble, or converting pro-drugs into active drugs).

Anabolism, involving synthesis or building large polymeric molecules from small monomeric molecules (e.g. converting glucose to glycogen, called glycogenesis, in the liver, or converting fatty acids and glycerol into triglycerides, called lipogenesis).

Catabolism, involving enzymatic breakdown for the release of energy (e.g. conversion of glucose into pyruvate, called glycolysis, or converting pyruvate/oxaloacetate ultimately into carbon dioxide, or CO2 and energy in the form of adenosine triphosphate, or ATP, the cellular unit of energy.

Excretion, involving excretion of waste material from the bowel as faeces, or as urine (fluid containing waste water, salts, and breakdown products such as urea, resulting from the catabolism of proteins).

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AN INTRODUCTION TO NUTRITION

Food is what we eat and drink and is essential for survival. Food science studies the biological and physical properties of food, with emphasis on manufacturing, processing and storage of food products. Diets are the composition or pattern of food that a person habitually eats, and can often take a particular form and name, such as: Mediterranean (high carb, whole foods, avoidance of saturated fats), Vegetarian (plant based plus dairy and eggs), Vegan (plant based, excluding dairy and eggs), Ketogenic (high fat, very low carbs), or gluten-free. **Nutrients** are the components of food that are needed or used by our cells and body to stay alive and grow. **Nutrition science** studies the nutrients in food, how the body uses these nutrients, and the relationship between the quality of nutrition, health and disease.

The human body requires six classes of nutrients: **water; carbohydrates; proteins; fats and fatty acids; vitamins and minerals**. Those food we eat in relatively large quantities (carbohydrates, proteins and fats) are called macronutrients and those nutrients we eat in very small quantities (vitamins and minerals) are called micronutrients.

Carbohydrates include **sugars** (e.g. table sugar = sucrose, a 2-sugar disaccharide compound consisting of monosaccharides glucose and fructose linked together); **starches**, polysaccharides composed of many glucose molecules linked together, sometimes called complex carbohydrates (e.g. potatoes, flour-based products, rice, barley, corn, and legumes such as beans, peas and lentils); and **fibre**, complex carbohydrates that the body cannot digest, but which is important for maintaining a healthy intestinal microbiota. Dietary carbohydrates are not essential, in the sense that the body can make glucose from proteins and fats. Your body would function normally if you did not eat any carbohydrates.

There is concern that the dietary guidelines which recommend the most calories come from carbohydrates, whilst animal fats should be excluded, have contributed to the world-wide increasing prevalence of obesity. Ingestion of sugar, which has increased several folds in recent decades, whilst animal fat ingestion has decreased, has attracted concern as contributors to the obesity epidemic. Of particular research interest is the role dietary fructose may play in the development of metabolic disorder, especially fatty liver (non-alcoholic fatty liver disease, or NAFLD). Soft drinks, fruit juices, cakes, sweet confectioneries all contain large amounts of fructose, and one of the correlates of obesity prevalence is the level of fructose intake. Carbohydrates are not essential nutrients in the sense that the body itself can make all sugar and starches it needs in the absence of any dietary carbohydrate. Additional downside risk to eating a lot of sugar is tooth decay.

Fibre is a group of complex non-starch carbohydrates that cannot be used as nutrients within the human body because our digestive enzymes cannot break the energy containing bonds that hold fibre's sugar monomers together. That is, fibre adds no calories to your diet. This may sound like fibre is unimportant to your health, but this impression is far from being true (see later sub-section headed Gut Microbiome).

There are 2 types of fibre, **insoluble** and **soluble**, depending on whether it dissolves in water. Insoluble dietary fibre includes cellulose (a polysaccharide polymer of glucose), and some types of hemicellulose (e.g. arabinoxylan, composed of xylose and arabinose sugar monomers) and lignins (cross-linked phenolic polymers). Insoluble fibre: helps you feel full after eating; speeds up transit time of food in the gut, whilst slowing the rate that glucose is absorbed into the blood stream; and provides bulk to stools, making them softer and easier to defecate. Soluble dietary fibre includes pectins (found in most fruit), beta-glucans (found in oats and barley), and gums such as guar, fenugreek, and locust bean gums derived from seeds. There is evidence that soluble fibre is heart-protective. The main dietary sources of fibre are plant foods – fruits, green leafy vegetables, and whole grains (i.e. they are not found in refined flour). Although humans cannot use fibre as nutrients, the bacteria in the gut (called the microbiome), especially those in the large bowel, can. There is evidence of a link between brain function and mood, and bacterial diversity in the gut, diversity that is increased by providing fibre, a nutrient for the microbiome.

Proteins come from both animal and plant sources. **Animal sources** include red meats, pork, chicken, fish, eggs and dairy products, in particular yoghurt. **Plant sources** include e.g. legumes, nuts, seeds, and soybean-based foods such as tofu. Proteins are broken down in the body into protein building blocks called amino acids (which are linked together by peptide bonds to form proteins). Of the 20 natural amino acids, nine are essential in the sense that the body cannot make these, and must be included in your diet, and another six amino acids cannot be made when you are metabolically stressed or seriously ill. If you eat too much protein, the excess amino acids are turned into glucose, the primary energy source in the body.

The amount of protein ingested by Australians has decreased slightly over recent decades, and there are concerns that some disadvantaged groups may be protein deficient, especially the elderly.

Fats are mainly composed of fatty acids (up to 70% by weight), bound together in long chains. In nature, fatty acids cannot exist in a free state and are usually combined as triplets with glycerol (an alcohol) to form **triglycerides** e.g. in butter, milk, cheese, plant-based and animal-based oils, and meat. Fats are essential in the sense that the body cannot make them from other sources (e.g. the **omega-6 fatty acid** linoleic acid [LA], and the **omega-3 fatty acid** alpha-linolenic acid [ALA]). **Triglycerides** are called fats and are a subgroup of the broader category called lipids, which are hydrocarbon molecules that are not easily dissolved in water. Fats are essential for storing energy, cellular signalling (acting as messengers for receptor – based communication), for acting as structural components of cell membranes, and for producing steroid hormones, based on the cholesterol molecule.

Fatty acids (FAs) consist of a straight chain of even numbered carbon atoms joined together by hydrogen atoms, which provide carbon-to-carbon covalent bonds. Covalent bonds are formed between two atoms in which electron pairs are shared between them. Covalent bonds can be single, double, or triple where 2, 4 or 6 electrons are shared respectively. Single covalent bonds hold considerable energy and do not often break spontaneously. Double covalent bonds (represented as two dashes (=) contain more energy but they are less stable than single bonds (-). Covalent bonds are not soluble in water. At one end of a fatty acid is a carboxyl group (-COOH) that makes the molecule acidic (carboxylic acid). Fatty acids form esters (an acid combining with an alcohol), usually to form **triglycerides** (glycerol esterified with three fatty acids) or phospholipids (also called phosphatides), which contain a hydrophilic phosphate "head" and two hydrophobic "tails" derived from fatty acids, each joined with a glycerol molecule (see Figure 2, page 5). Phospholipids are a key component of all cellular membranes.

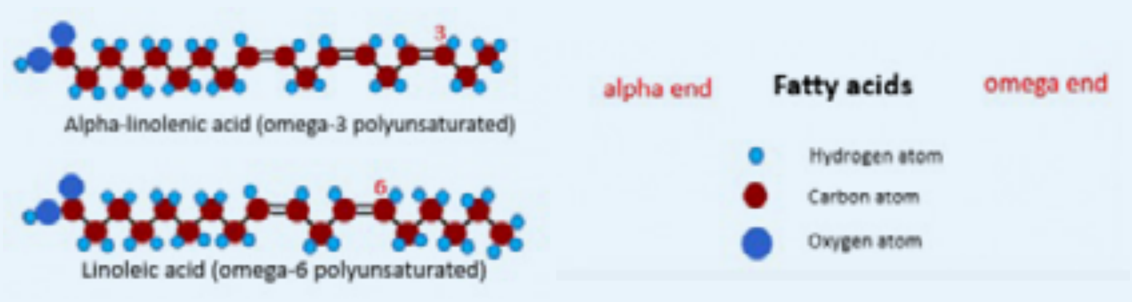
DIETARY FATS

There are two major dietary groups of fatty acids/fats depending on the nature of the C-H-C covalent bonds: saturated and unsaturated fatty acids. Unsaturated fats contain one or more double (=) bonds and therefore can absorb additional hydrogen atoms. In saturated fats, each carbon atom in the chain is bonded to as many hydrogen atoms as possible, and therefore lack linkages between carbon atoms without as many hydrogen atoms as possible (i.e. the linkages are saturated with hydrogen). Saturated fats are less prone to oxidative damage and rancidity: they are solid at room temperature. An unsaturated has at least one double bond between two carbon atoms in its chain, and so cannot be "saturated" with hydrogen. Unsaturated fats (fatty acids) can be further classified as monounsaturated (MUFA) or polyunsaturated fatty acids (PUFA). Monounsaturated fats have only one double bond in their chain, and are relatively resistant to oxidation. Olive oil is an example of a fat with high levels of MUFA, particularly oleic acid. Polyunsaturated fatty acids (PUFA) have more than one double bond in their chain, and they are the least resistant to oxidation of all fats. The body can make MUFA from saturated fatty acids (SFA). Life SFAs, MUFA are relatively stable and can be used in cooking. Olive, almond, pecan, cashew, peanut, and avocado oils are rich in MUFA.

PUFA are liquid at room temperature. The most common dietary PUFA are either omega-3 or omega-6 fats. Omega-3 fatty (written n=3) fatty acids have the first double bond placed three carbon atoms away from the omega end, whilst omega-6 PUFA (written n=6) have the first double bond placed six carbon atoms away from the omega end (see Figure 1, page 5).

Figures 1 and 2 were copied from a fascinating book by Peter Brukner. A Fat Lot of Good. Penguin Random House, 2018.

Figure 1 – Sourced from A Fat lot of Good - Brukner

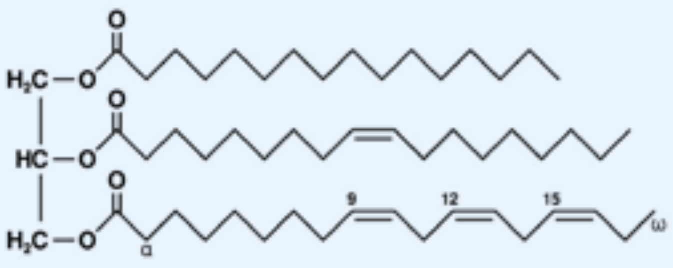


Alpha-linolenic acid – ALA - (n=3)

Linoleic acid – LA – (n=6)

* ω= Greek omega

Figure 2 – Triglyceride (WIFI)



The three most important omega-3 fatty acids are essential (cannot be made by the body from other sources): ALA, DHA (docosahexaenoic acid), and EPA (eicosapentaenoic acid). ALA is found mainly in plant-based food, while DHA and EPA are mainly found in animal foods.

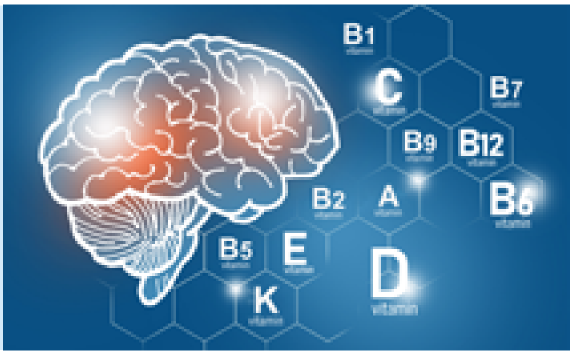
Omega fatty acids are also essential so you need to obtain them from your diet. Omega-6 fats are primarily used for energy. The most common omega-6 fat is linoleic acid (LA), which can be converted to longer omega-6 fats such as arachidonic acid (ARA). To make mono-unsaturated fatty acids (MUFA) and poly-unsaturated fatty acids (PUFA) oils solid at room temperature, hydrogen atoms are added (hydrogenation) industrially to make them less prone to rancidity and increase their shelf life. During manufacture, some double bonds can transform from the cis configuration (H-C-H bonds in the same plane) to the trans configuration (H-C-H bonds that are twisted to be in opposite planes). Strong evidence shows trans fats promote many chronic diseases and should not be eaten. Most countries have regulated trans-fat content in food. You can see from the above that margarines manufactured from hydrogenation of PUFA are basically equivalent to fats (e.g. butter, lard and milk) with high saturated fat content, except the flavour and micronutrients have been removed from hydrogenated PUFA margarines, and potentially harmful by-products may have been added.

All fat containing whole foods contain a mixture of saturated FAs, MUFAs and PUFA fats - it's only the proportions of each that vary. Dairy products are the only foods with more saturated than unsaturated fat. Lard (pig fat) contains more unsaturated fat than saturated fat. A beef steak contains very low levels of both saturated (2%) and unsaturated fats (3%), consisting mainly of water (74%) and protein (21%). Saturated fats are found in animal products such as lamb, pork, poultry, egg yolk and dairy and in plant-based tropical oils such as coconut, palm, and cocoa butter (in chocolate).

In the last 50 years there has been an exponential increase in the PUFA content of the Western diet, whilst the proportion of saturated fat and protein has reduced. The carbohydrate content of Western diet has also increased exponentially, especially in terms of added sugar. The dietary changes have been associated with epidemics of chronic metabolic diseases, especially diabetes. In the past human intake of PUFAs was only about 4% of calories, half as omega-3 and half as omega-6. Now PUFA represents about 30% of the total calories in modern diets. There is evidence that the ideal ration of omega-6 to omega-3 is close to one to one: now it is about 16 to 1 (Simopoulos et al, 2016, Nutrients, 8, 3, 128). The best natural source of omega-3 fats is oily fish, such as salmon, mackerel, herring, sardines and tuna. Vegetable seed oils are the main source of omega-6 fatty acids, with safflower and sunflower being particularly rich in omega-6 fat. Saturated fats have been falsely associated with heart disease, when in fact there is evidence that PUFA, especially omega-6 PUFA, are associated with risk of cardiovascular diseases (see below). Similarly, high fat diets have been related to metabolic disorders including diabetes, when in fact the strongest risk factors may be excess dietary sugar (particularly fructose) and highly processed carbohydrate, and not fats (see below).

MICRONUTRIENTS

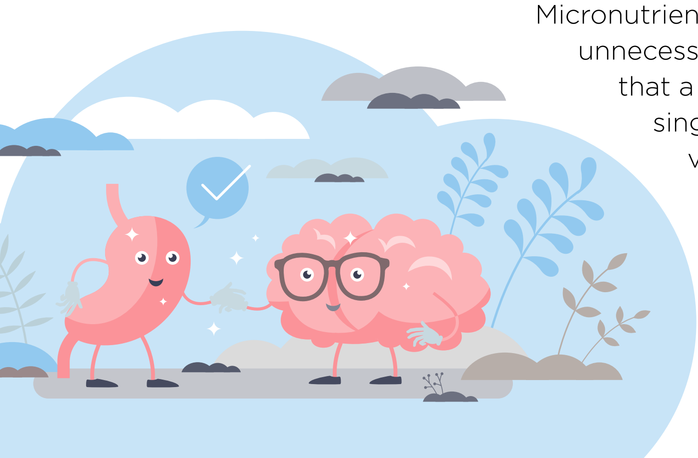
Micronutrients include the essential vitamins and minerals that are needed in our body in tiny ("micro") amounts (less than one gram daily), compared to the macronutrients such as protein which is required in the order of 60 grams per day.



Optimal health requires at least 12 vitamins: Vitamin A, Vitamin D, Vitamin E, Vitamin K, Vitamin C, and members of the B complex vitamin family (thiamine, B1; riboflavin, B2; pantothenic acid, B5; niacin, B6; biotin, B7; folate, B9; and cyanocobalamin, B12). Recommended Daily Allowances (RDAs) may be as small as several micrograms (one millionth of a gram). Vitamins are classified as fat soluble (Vitamins A, D, E and K) or water soluble (Vitamins C and B-complex, and choline, the last not called a vitamin but it is still essential). The fat-soluble vitamins are stored in adipose tissue (fat cells), and it is possible to overdose on them. As water soluble vitamins are not stored and any excess is quickly excreted in urine, it is almost impossible to overdose on them. Because dietary vitamin sources are diverse, including green vegetables, unrefined grains and nuts, dairy products, eggs and meat, this led to recommendations for a "balanced or mixed whole food" diet, sometimes referred to as the Mediterranean Diet. There are many descriptions of the roles and dietary sources of Vitamins (e.g. CA Rinzler, Nutrition for Dummies 6th Edition, J Wiley & Sons Inc 2016, pp 117-132) so these details will not be presented here.

Minerals are elements and substances that consist of one kind of atom. They are inorganic, meaning they do not contain carbon, hydrogen and oxygen atoms. Minerals are found in the soil in which plants are grown; plants absorb these minerals, and we eat the plants. Minerals are categorised as electrolytes or major minerals (e.g. sodium, potassium and calcium), and others are referred to as essential trace elements, such as iron, zinc, iodine and selenium. The only difference between major minerals and trace elements is the amount stored in the body and the quantity needed to maintain a steady supply.

RDAs for trace elements are in microgram quantities, while RDAs for electrolytes such as sodium and chloride are expressed in milligram amounts. As with the vitamin, sources of minerals are diverse: animal meat and eggs for iron and zinc; seafood for iodine and selenium; copper from nuts, lentils, and prunes; chromium from egg yolk; and, molybdenum from dairy products.



Micronutrient supplements are heavily marketed, but are usually unnecessary with a nutritious diet. There is preliminary evidence that a broad-spectrum approach to micronutrients, in contrast to single-micronutrient supplementation, may offer therapeutic value for certain developmental disorders (e.g. ADHD and autism) and mood disorders (e.g. depression and bipolar disorder). This evidence is summarised by J. Rucklidge and B. Kaplin, The Better Brain, Penguin London, 2021. Broad spectrum micronutrient supplementation is expensive and may only help a minority of people with mental health issues, and a major problem is predicting who might benefit. Rinzler, 2016, pp 133-146 provides additional non-technical information about minerals.

WATER

Without water, you will die in a matter of days, yet its role in nutrition is often overlooked. A healthy body must have the right amount of fluid inside and outside each cell: this is called fluid balance, and it is maintained through the action of electrolytes (e.g. sodium and chloride) which when dissolved in water become electrically charged particles called ions.

Normally, cells contain more potassium (K^+) than sodium Na^{2+}, and fluids outside the cell contain more sodium than potassium. The cell (plasma) membrane is a semi-permeable membrane, which allows selective passage of molecules. To ensure the unequal concentration of Na^{2+}: K^+ across the membrane, it contains the sodium pump, which can actively pump Na^{2+} out of the cell.

For these vital processes to function optimally, and because the body does not store water, water must be drunk every day. Water is lost in urine, with defecation, breathing and perspiration. On average these loses add up to about 2000 ml (about 10 glasses) of water per day.

Most of this water must be ingested, i.e. come from what you eat and drink: recommendations are that women drink about 2.7 litres (8 cups/glasses) per day, and men drink about 3.7 litres (10 cups/glasses) per day. In Australia tap water is clean and strictly regulated for safety. In metropolitan areas, tap water has the advantage of being fluorinated providing major protection against tooth decay in young children, and against osteoporotic fractures in the elderly. The popularity of purchased bottled water has resulted in a plastic waste disposal problem, costs to the household, usually a loss of the benefits of fluoride, and occasionally the risk of added salt (see below). If plain water is considered too plain, a few drops of lemon or lime juice can be added.

In relation to electrolytes, there is a view that there is excessive salt (sodium chloride) in the average diet of Australians (see later).

MANUFACTURE AND PREPARATION OF FOOD

This section will focus on ultra-processed food.

Industrial Food Processing

The average Australian adult obtains 36% of their total daily energy requirements from discretionary ("junk") foods. We now eat less red meat, full-fat dairy, fruit and vegetables, and eat more white meat, reduced-fat dairy, vegetable seed oils and processed foods with added sugars and salt. Ultra-processed foods (UPFs) are products that contain several manufactured ingredients not generally used when cooking at home with whole foods, including natural and artificial flavours or colours, sweeteners, preservatives, and other additives. Examples of ultra-processed foods include mass-produced soft drinks ("sodas" such as Coke, Pepsi and Fanta), sweet or savoury packaged snacks (e.g. Kit Kats, Cherry Ripes, Cheezels, Kettle Potato chips), packaged baked goods (Danish pastry, apple turnovers, meat pies, sausage rolls), cakes and biscuits (Tim Tams, doughnuts, Anzac biscuits, chocolate cake), fish and chicken nuggets, and other processed meats (sausages, frankfurts, salami, bacon), and instant noodles and soups.

UPFs are typically high in added sugar, trans-fat, sodium and refined starch, as well as low in fibre, proteins, vitamins, and minerals. Many of these products are cooked in potentially hazardous seed oils (see later section). A recent study showed that more than half of all calories consumed in the USA come from UPFs, a figure that Australian consumption probably only slightly lags behind. Research has demonstrated a strong association between UPF consumption and obesity especially in young people, cardiovascular disease, and total mortality (e.g. Juul et al. 2021, J Am Coll Cardiol, 30, 77, 12, 1520-1531; Srour et al. 2019, BMJ, 365, 1451; Fiolet et al, 2018. BMJ, 360, K322; Schnabel et al, 2019. JAMA Intern. Med, 179, 4, 490-498).

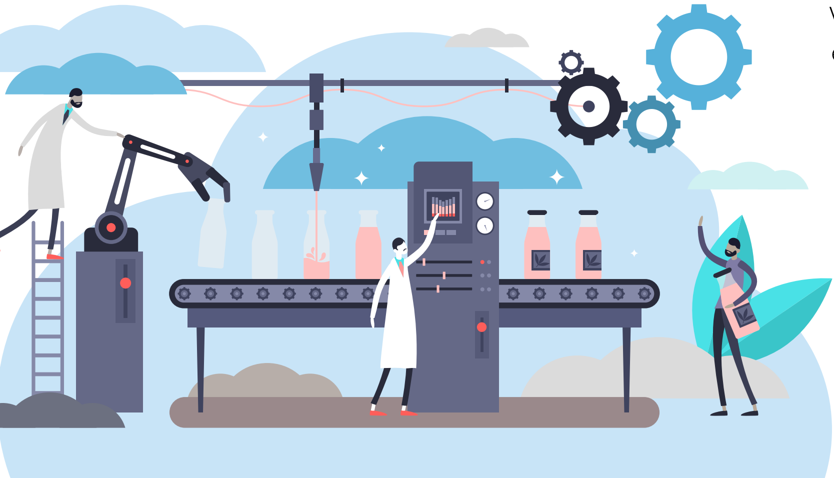
Fast food consumption is driven by market deregulation and density of fast-food outlets in OECD countries (De Vogli et al, 2014, Bull WHO, 92, 99-107A) and associated sales of sugary soft drinks. The sugar (e.g. Coke) and carbohydrate (e.g. French fries) content appears to be causing obesity rather than fat content of food. UPF is only one of many identified factors contributing to what is now referred to as an obesogenic environment, which will require societal rather than individual action to correct.

Take-away / Eat Out Feeding

Another factor driving the obesogenic environment is change in lifestyle resulting in people eating at home less often, and eating outside the home more (Mills et al. 2017, Int J Behav Nutr Phys Activity, 14, 109; Moser A. 2010, Appetite, 55, 99-107; Smith et al. 2013, Nutr J, 12, 45). This trend has caused two potential obesogenic factors to converge with each other - increased consumption of ultra-processed food, and use of cheap vegetable oils in commercial cooking.

Currently there is a major controversy over the role of vegetable cooking oil (seed oils), especially the omega-6 polyunsaturated (PUFA) oils; high rates of sugar ingestion, especially fructose; and, high salt content of ultra-processing of food, in the causation of the pandemic of obesity, metabolic disease, diabetes, depressive and anxiety disorders, degenerative brain disorders such as Alzheimer's and Parkinson's disease, and cardiovascular disease. The single biggest change in human nutrition in the industrialised world has been the increased use of seed oil in food manufacture and preparation.

For an entertaining prosecution of the argument that seed oils (omega-6 fats) may be harmful, open YouTube and see Chris Knobbe's talk titled Diseases of Civilisation: https://www.youtube.com/watch?v=7kGnfXXIKZM. The basis for this hypothesis is that seed oils have only recently been introduced into the human diet and the massive increase in their use has been associated with correspondingly massive increases in many modern diseases (of course the same argument could be made about sugar). Two driving forces behind widespread use of seed oils (e.g. soybean, corn, canola, cottonseed, grapeseed, sunflower, and safflower oil) have been their cheap industrial production and official dietary guidelines that recommend avoidance of saturated fats, especially animal fats. This recommendation was based on flawed observational studies that seemed to indicate that there was a strong relationship between levels of dietary saturated fats/cholesterol and prevalence of heart disease, studies which are more than 50 years old. Today, there is compelling evidence that eating saturated fats is safe (e.g. Mente et al. 2017, Lancet Diabetes Endocrol, 5, 774-787; Dehghan et al. 2017, Lancet, 390, 2050-2062), unless eaten in extreme amounts. Moreover, there is robust evidence in intervention studies that replacing dietary saturated fats with unsaturated fats or carbohydrates offers no benefit whatsoever (Hooper L et al, Cochrane Database of Systemic Reviews, last updated in 2020). To reinforce the arguments against dietary fat causing heart disease, at a mechanistic level the data concerning the key linking molecule between dietary fat and heart disease, LDL-C (low density lipoprotein cholesterol), has also been called into question (e.g. Ravnskov et al. 2018, Expert Review of Clinical Pharmacology, 11, 10, 959-970), and cardiologists are now calling for review of guidelines that limit intake of dietary saturated fats (e.g. Astrup A et al. 2020, Journal of the American College of Cardiology, 767, 844-857).



With the safety of dietary saturated fats established concerns shifted to the unsaturated omega-6 PUFAs as being potentially harmful, as many suggested. However, evidence concerning omega-6 and omega-3 PUFAs is highly inconsistent. There is evidence, mainly based on animal studies, that omega-6 seed oils are obesogenic, diabetogenic, and might promote inflammation and oxidative stress (e.g. di Nicolantonio & O'Keefe, 2018, Open heart, 5, e000898; Arslan et al. 2019, J. Am Coll. Nutr, 38, 5, 424-432; E Muhlhausler & Ailhand, 2013, Current Opinion Endocrinology, 20, 1, 56-61; Deol et al. 2015, PLOS one, 10, 7, e0132672; Leung et al. 2019, Free Radical Biology & Med, 145, 349-356). The above literature is at variance with a major review of prospective observational studies that did not find increased cardiovascular mortality with dietary omega-6, and indeed, reported a benefit of omega-6 consumption (Marklund et al. 2019, Circulation, 139, 2422-2436). That is, despite highly suggestive evidence of an association between seed oil consumption and metabolic disease, especially with macular degeneration (Knobbe & Stojanoska, 2017, Medical Hypothesis, 109, 184-198) in animal studies and at a population level, at an individual level the case for harm due to seed oils remains an open question.

The literature concerning increased harm from increased sugar consumption, especially fructose, appears to be more consistent in both animal and human studies, at both individual and population level, especially in relation to the development of diabetes (e.g. Stanhope et al, 2009, J. Clin. Invest. 119. 1322-1334; Basu et al, 2013, PLOS one, 8, 2, e57873; Schillinger, 2017, Annals of Internal Medicine, doi.org / 10.7326 / M16-2754), so much so that almost all dietary guidelines recommend reducing dietary sugar intake.

The case for harm from sugar consumption is compellingly reviewed in two interesting books, (J. Yudkin. Pure, White and Deadly, Penguin Group, 1972/1986 and G.Taubes. The Case Against Sugar. Portobello Books, 2017). Although John Yudkin's book is quite old, it is very instructive about how science can be distorted by politics, corporate profits, and the narcissism of scientists with celebrity status. The debate about sugar has spilled over into a debate about the role of carbohydrates (CHOs) in general in the causation of obesity. Despite populations in the US and Australia following dietary guidance to reduce the amount of fat in their diet and increase their carbohydrate intake, the prevalence of obesity and diabetes has relentlessly increased. Concern about the harmful effects of excess CHO was also driven by evidence that ingestion of carbohydrates rather than fat was the strongest predictor of increased cardiovascular mortality (Dehghan et al, 2017, Lancet, 390, 2050-2062). This association was particularly evident with take-away food, sugary soft drinks and French fries, primarily driving obesity and cardiovascular disease, rather than food with higher fat content e.g. hamburgers (Veronese et al, 2017, Am J Clin Nutrition, 106, 162-167; Mozaffarian et al. 2011, N England J Med, 364, 25, 2392-2404; de Vogli. R. 2014, Bull WHO, 92, 99-107; Malik V et al, 2010, Circulation, 121, 1356-1364).

Another concern about ultra-processed food is its salt content. At an individual level, the effect of reducing dietary salt is at best a modest reduction in blood pressure (He FJ. Et al, 2013, BMJ, 346: f1325). However, at a population level this reduction is significant enough to stimulate government campaigns to reduce salt in processed foods. This is why McDonalds French fries now taste bland compared to how they once tasted.

Most of the salt in our diet is sourced from processed food, and the small amount sprinkled on food at home is unlikely to be a risk factor for almost all of us. The more important issue is for each of us to have the GP check our blood pressure, and if high, you might want to explore the benefit of personally reducing your salt intake in terms of a lowered blood pressure. It is also important to note that reducing salt intake alone is not likely to be effective in controlling hypertension. Hence the key message in relation to nutrition and hypertension is that hypertension is more likely to result from the metabolic effects of obesity, metabolic syndrome, and diabetes, than from excess dietary salt, and this might be a more effective therapeutic approach to hypertension than salt reduction.

In summary, ultra-processed food has multiple potential hazards, some of them clearly identified as risk factors for metabolic disorder, and others not so clearly linked. The bottom line message that all dietary guidelines endorse, is to limit consumption of processed foods, especially in children who are most at risk from these food (Reuter et al. 2019, PLOS one, 14, 10, e0224140).

CONCLUSIONS

This review is the first of two to be uploaded to the Clearthinking QLD website. This document is intended to be an introduction to the field of nutrition. The second review will cover mechanisms controlling metabolism and how they can go wrong to cause disease. A key mechanism in translating poor nutrition into disease risk and ultimately to diseases is **inflammation** (see schematic below) and this topic will be covered in detail in the next document.

CHRONIC METABOLIC DISEASES SCHEMATIC

RISK FACTORS		HIGH RISK HEALTH CONDITIONS		DISEASE STATE
• Poor nutrition – – High CHO[1] – Omega-6[2] and excess trans fats – High fructose • Smoking • Stress, especially loneliness • Inactivity • Sleep disorders, especially sleep apnea • Oral disease	**Hyperinsulinemia** **Hyperlipidemia**	• Central obesity [3] • High blood triglycerides • LAFLD[4](e.g. raised GGT & ALT[5]) • Gut microbiota dysbiosis • Low-grade inflammation • Major depression	**Insulin resistance** **Low-grade Inflammation**	• NASH[6] • Cardiovascular disease • Type 2 Diabetes • Auto-immune disease • Neuro psychiatric disease

[1] Carbohydrates
[2] Polyunsaturated (PUFA), vegetable oils, except for olive and coconut oil
[3] Central obesity refers to deposits of fat around the abdominal organs and midriff, causing 'sugar belly' (waist larger than hips)
[4] LAFLD – Non-alcoholic fatty liver disease
[5] GGT (gamma –glutamyl transferase) and ALT (alanine transaminase) liver function tests
[6] Non alcoholic steatohepatitis