Chapter 6

Attention deficit hyperactivity disorder (ADHD)

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Introduction

Attention Deficit Hyperactivity Disorder (ADHD) — characterised by attention-deficit, impulsivity and hyperactivity — is one of the most common neurobehavioral disorders affecting children and adolescents today. The incidence of ADHD is rising with the annual prevalence in Australia in 2001 being estimated at 11% (diagnosed by DSM-IV criteria), equating to a 7.5% prevalence in people aged 6–17 years.

There has been a concomitant rise in the use of stimulant medications, namely phenylmethidate and dexamphetamine, despite a lack of studies regarding long-term social and psychological effects, and cardiovascular and neurophysiological clinical effects. Although stimulants are very helpful in 60–70% of patients, many families seek alternatives because of adverse reactions, lack of compliance and the fact that stimulants cannot be given late in the day, limiting the benefits largely to school hours.

The use of complementary and alternative medicines (CAM) for ADHD has increased, both by parents and health care providers. Parents are especially drawn to CAM interventions in order to avoid or decrease the use of psychotropic medications. Because of the wide-ranging disruptive impact on the lives of both patients and their families, an integrative approach to management simply reflects the multifactorial aetiology and nature of this disorder.

A recent Australian survey demonstrated that the most common CAM therapies used include dietary modification, nutritional supplementation, aromatherapy and chiropractic. It has been advised that doctors should always inquire about the use of CAM and use available resources to help guide families in their therapeutic choices.

The exact aetiology of ADHD is unknown and, indeed, may differ from individual to individual. Genetics and genetic polymorphisms certainly play a role, however, major aetiological contributors may also include adverse responses to food additives, intolerances of foods, differing biochemical pathways and nutritional deficiencies, sensitivities to environmental chemicals and exposure to neurodevelopmental toxins such as heavy metals and tobacco smoke.

ADHD is a complicated condition that requires multidimensional treatment strategies. It is imperative to understand that the aetiology and hence the management of ADHD may be different for each individual. One must attempt to elucidate all possible contributory factors and eliminate or treat each respectively.

Neuropsychological and imaging studies indicate that ADHD is associated with alterations in the prefrontal cortex (PFC) and its links to the striatum and cerebellum.

The PFC, especially the right hemisphere, is crucial to the regulation of behaviour and attention. It is extremely sensitive to its neurochemical environment, with either too much or too little catecholamine release weakening the individual’s cognitive control of both behaviour and attention.

Individuals with ADHD are known to have depleted levels of dopamine and noradrenaline most likely as a result of dysfunctional transporter systems. The role of other neurotransmitters such as histamine, acetylcholine, glutamine and serotonin in modulating catecholamine pathophysiology in ADHD is yet to be elucidated.

Lifestyle

Most of the lifestyle factors associated with ADHD are covered under the appropriate headings below.
Mind–body medicine

Neurobiofeedback

Electroencephalogram (EEG) biofeedback is a promising alternative treatment for patients with ADHD.20 It is a form of behavioural training aimed at developing skills for the self-regulation of brain activity.21 Most individuals with ADHD, as compared to matched peers, show abnormal functioning of their anterior cingulate cortex with excess slow-wave (theta) activity and reduced fast-wave (beta) activity during tasks of selection attention.22,23

In particular, it is well documented that hyperactive behaviour in many children with ADHD is due to abnormally enhanced 4–8Hz Theta activity in both frontal and central cortical areas of the brain.24 In the last decade there has been a multitude of clinical trials and literature reviews that demonstrate the positive effects of biofeedback on these children with clinical improvement being primarily directly related to declining theta/beta ratios and/or amplitudes over the frontal/central cortex.25–42 These have largely been good quality studies that have tended to overcome the methodological shortcomings of earlier studies.21

Research findings published to date indicate a positive clinical response (reduced hyperactivity and impulsivity, improved attention, IQ, processing speed and music performance) in approximately 75% of patients treated in controlled group studies. The Association for Applied Psychophysiology and Biofeedback and the International Society for Neuronal Regulation deem EEG biofeedback to be ‘probably efficacious’ for the treatment of ADHD, particularly for those patients who do not respond to medications.30,36,38

During biofeedback, individuals are taught to increase their beta activity and suppress their theta activity over a period of usually 30 or more sessions.29,30,32,33 This enables the child to become an active agent of their own coping strategies and thus increase their internal locus of control.43 EEG biofeedback therapy works by rewarding scalp EEG frequencies that are associated with relaxed attention and suppressing those frequencies associated with under or over-arousal.20 It provides immediate feedback to the individual about his/her brain-wave activity in the form of a video/computer game, the action of which is influenced by the individual meeting predetermined threshold of brain activity.25

Obviously, the child must be at an age where they are able to play such games — most studies include children aged 6 years and above.28,29,30,33

There are many different forms of biofeedback available. The regulation of cortical excitation thresholds are also considered to be impaired in children with ADHD and the training of slow cortical potentials addresses the regulation of cortical excitability. It has been suggested that the regulation of frontal–central negative slow cortical potentials affects the cholinergic-dopaminergic balance, allowing children to adapt to task requirements with more flexibility.21,25,30

Recently published studies using quantitative EEG (QEEG) techniques indicate that power spectral analysis and event-related cortical potentials may be useful in differentiating ADHD from other disorders, such that QEEGs may be used clinically in the assessment, diagnosis and treatment of ADHD.25,35 In particular, a deficit in low frequency wave (approximately 1 Hz) activity associated with levels of hyperactivity and impulsivity has been demonstrated in both children and adolescents with ADHD. This marker is evident across a range of tasks and may, indeed, be specific to ADHD.25

Several recent neuro-feedback trials have demonstrated comparable results with Methylphenidate (Ritalin) in terms of increased attention span and reduced problem behaviour (impulsivity and hyperactivity) in children with ADHD without the side-effects often associated with medication.20,22,31,37,39,44

It is also important to note that in those studies of children using both biofeedback and methylphenidate, only those children who had received biofeedback sustained these gains when reassessed without Ritalin. Furthermore, Quantitative Electroencephalographic Scanning Process (QESP) studies show a significant reduction in persistent cortical slowing only in those patients who underwent EEG biofeedback.39,45 This is confirmed by parent and teacher evaluations who report significant behavioural and cognitive improvements for at least 6 months after the cessation of treatment.29

Psychosocial and/or cognitive behaviour therapy (CBT)

Although pharmacological treatments have traditionally been considered the first-line therapy for ADHD, many individuals continue to experience major functional impairment or choose not to use such medications. Behavioural school interventions and parent training have been supported by empirical evidence.1,46 It is important to note, however, that the children respond to such behavioural interventions only when they are appropriately implemented both at home and in the classroom setting.47
Psychosocial therapies, especially behavioural modification techniques, should be considered for children with ADHD and oppositional behaviours whilst cognitive behaviour therapy (CBT) may be useful for adolescents and adults.48, 49 When behavioural therapies have been combined with medication, improvements in function have been demonstrated and the amount of stimulant reduced.50

A recent Cochrane review has confirmed that both behavioural and CBT interventions are highly effective, however, access to these treatments is limited due to length of consultations and expense, with significant behavioural improvements taking up to 2 hours of therapist time.51

It has been hypothesised that family therapy without medication may help to develop family structure and may help to manage children’s behaviour. A 2005 Cochrane review has deemed that further research is necessary to determine whether family therapy is an effective intervention for children with ADHD.52

Available data supports the use of group and individual structured, skills-based psychosocial interventions for adults with ADHD.53, 54

**Meditation and relaxation training**

Mindfulness meditation may also improve behavioural and neurocognitive impairments in adolescents and adults with ADHD. One recent study has demonstrated improved attention and cognition with reduced anxiety and depression after an 8 week mindfulness training program.55

A range of studies have suggested that relaxation training can help children with ADHD to learn to relax, thereby decreasing their autonomic activity.7, 56 Reductions in problem behaviour, increased attention span and greater internal locus of control are other potential benefits of relaxation therapy. It should be noted, however, that these skills need to be practised regularly for continued effect.57–60

In the mainstream literature there have been no published studies on the potential application of meditation for ADHD, however, the Royal Hospital for Women, Sydney, has devised a pilot clinic aimed at developing meditative strategies, using Sahaja Yoga Meditation, to help these children (www.sesiah.health.nsw.gov.au/rhw/). The clinic exclusively accepted children with a formal diagnosis of ADHD and whose usual supervising health professional had permitted their involvement. Both the child and at least 1 parent were required to attend classes and practice daily meditation.

The results were very promising. Of the 16 children who completed the program, 6 were able to decrease and 3 were able to stop their medication whilst maintaining completely normal behavioural traits. All parents reported feeling generally better, less stressed and more relaxed and most felt the program had benefited their children.

About half the parents said their child was less restless with improved sleep and that they were experiencing a better relationship with them. Whilst this is not a randomised controlled study, it is at the moment the best available evidence for meditation’s potential role in ADHD and clearly suggests that Sahaja Yoga meditation may be particularly beneficial for this condition. More rigorously designed studies are planned in order to achieve a more conclusive understanding of this radically different approach.3

**Sound therapy**

Recent studies have demonstrated that children with ADHD, upon performing visual discrimination tasks, were less attentive than controls when exposed to distracting novel sounds. Event-related brain potentials corresponding displayed significant differences over the fronto-central left hemisphere and the left parietal scalp region, revealing low control of involuntary attention that may further underlie their abnormal distractibility.61

Systems such as the ‘Tomatis Method’, ‘Integrated Listening System’ (ILS) and Dr Guy Berard’s (ENT physician) Auditory Integration Training (www.integratedlistening.com) have been designed around the brain’s ability to form new neural connections throughout life, changing the way the brain processes auditory information. ILS stimulates both cerebellar activity, in order to strengthen these neural connections, and the vestibular system, in order to improve balance, posture and hand/eye coordination. Such therapies are used by many patients who experience auditory processing difficulties and hypersensitivity to specific auditory frequencies. There are currently no well-designed studies in the literature regarding such therapies, however, anecdotal reports are very promising.

The Moderate Brain Arousal model suggests that dopamine levels modulate how much noise is required for optimal cognitive performance. Studies have shown that individuals with low dopamine levels (ADHD) need more background noise than controls for optimal cognitive performance. This positive effect of noise may be explained by the phenomenon
of Stochastic Resonance (SR), whereby external noise is relayed as internal noise into the neural network subsequently affecting neurotransmitter levels. This method aims to teach children with ADHD to focus and intently listen to specific sounds, subsequently helping with behaviour modification, cognitive development and concentration.

Normally, high dopamine down-regulates stimuli-evoked phasic dopamine responses through autoreceptors, however, abnormally low extracellular dopamine in ADHD up-regulates these receptors so that stimuli-evoked phasic dopamine is boosted. It is postulated that these boosted phasic responses create hypersensitivity to environmental stimuli in ADHD. Empirical data supports the concept that more noise is required for SR to occur in dopamine-deprived neural systems in ADHD.

There is also some evidence to show that music therapy may contribute to a reduction in a range of ADHD symptoms in the classroom.

Sleep and behaviour
It is important to note that, even in children that do not suffer with ADHD, sleep problems during school transitions are common, and are associated with poor outcomes. Future RCTs could determine if sleep interventions can reduce the prevalence and impact of such detrimental sleep problems.

Sleep restoration/melatonin
There is a clear correlation between ADHD and sleep difficulties with substantial evidence that ADHD psychopathology and sleep/wake regulation share common neurobiological mechanisms. Furthermore, there may even be an overlap between ADHD and sleep disorders such as obstructive sleep apnoea and restless leg syndrome (RLS). Anecdotal evidence strongly suggests that magnesium assists in the treatment of RLS.

Approximately 25% of children suffering with ADHD also experience some form of sleep disorder. Unfortunately, in contrast with adults, these often go undetected. Diagnosis of these patients is critical. Therefore, all children with ADHD should be fully assessed for sleep disturbances because adequate treatment is often associated with improvement of symptoms and a decreased requirement for stimulant medications.

The circadian rhythm of melatonin secretion from the pineal gland is reflective of mechanisms that are in control of the sleep/wake cycle. In those individuals with primary insomnia, nocturnal plasma melatonin levels tend to be lower than in healthy controls. Melatonin has been used successfully to treat insomnia in children with ADHD. Several randomised double-blind placebo-controlled trials using 3–6mg melatonin for 1 month demonstrated enhanced total time asleep in children with ADHD and chronic sleep onset insomnia. Melatonin is shown to be a safe and effective treatment for sleep disorders, however this had no observable effect on other ADHD symptoms.

Environment

Outdoor play
Research on children with ADHD demonstrates significant improvement in symptoms such as inattention and impulsivity after exposure to natural views or settings. Four hundred and fifty-two parents or guardians from across the US with ADHD or Attention Deficit Disorder (ADD) children aged 5–18 years enrolled in a study to assess the benefits of playing outdoors in a natural setting. Compared with baseline results, outdoor activities conducted in natural environments significantly improved ADHD symptoms (difficulty in remaining focused, completing tasks, listening and following directions, and in resisting distractions) compared to activities conducted indoors or those in built outdoor settings, such as parking lots.

While the results of this study need to be verified using a more rigorous study design, these findings are promising as spending more time outdoors in natural environments is an inexpensive accessible treatment that is free of side-effects.

Heavy metals and chemicals

Lead
Lead is a common environmental contaminant such that in the year 2000, nearly 1 million preschool-aged children in the US alone were shown to have elevated blood levels (>10ug/dL). In 1991, the US Centres for Disease Control and Prevention (CDC) established 10ug/dL as the lowest concern for children's blood lead levels. However, in recent years, there has been a wealth of evidence-based clinical trials demonstrating that levels below 10ug/dL may impair neurological development. In fact, there is now sufficient and compelling scientific evidence to call for the CDC to lower the blood lead action level in children to a level as low as 2ug/dL.
Indeed, no level of lead exposure appears to be safe with multiple studies now demonstrating reduced IQ and academic deficits in otherwise ‘healthy’ children. There appears to be an inverse relationship between lead levels and IQ levels, particularly at levels <10μg/dL. At lower levels of toxicity, a child may have no specific individual symptoms but may certainly be affected sub-clinically. For this reason, health care practitioners should obtain a thorough environmental history on all children they examine.

Having adjusted for covariates, children with 5–10μg/dL have been shown to have 5 points lower IQ scores compared to children with blood lead levels of 1–2μg/dL. Verbal IQ appears to be more negatively associated than performance IQ, as does reading and maths composite scores. Working memory and attention were also shown to be lowered with increasing lead levels.

In particular, there have been several studies associating ADHD with elevated lead levels. Individuals with ADHD are more likely to have been exposed to lead during childhood, such that ADHD may now be deemed an additional deleterious outcome of lead exposure, even when levels are <10μg/dL. Its effects may be mediated by less effective cognitive control, consistent with a route of influence via striatal-frontal neural circuits.

Chelation therapy is advised for children with blood level concentrations of >44μg/dL, however, there are no evidence-based clinical trials for other gentler chelation treatment options for children with levels less than this. Because lead absorption is partially related to nutritional status, micronutrient supplements may be a possible solution for combating low-level chronic lead exposure. Zinc, in particular, is 1 supplement that has shown some results in effectively reducing oppositional, hyperactive, cognitive problems and other ADHD symptoms in most individuals.

Mercury

Numerous studies report positive correlations between the number of dental amalgams and urinary mercury concentrations in non-occupationally exposed individuals. Experimental evidence consistently demonstrates that mercury is released from dental amalgams and is absorbed by the human body. However, there is much controversy regarding the effects of mercury (from dental amalgams and vaccinations) on neurodevelopment, renal and immune function.

One of the latest randomised controlled studies has confirmed that treatment of children with amalgam restorations leads to increased, albeit low level, exposure to mercury. Amalgam exposure resulted in small, transient immune deficits 5–7 days post treatment, however, it did not cause overt immune defects. The authors concluded that these changes ‘most likely did not need to be of concern to practitioners considering the use of this restorative dental material’. It is important to note, however, the history of what initially constituted toxic lead levels and how this has changed in recent years with accumulated evidence-based studies.

In a similar manner, mean urinary mercury concentrations have been found to be greater in children with amalgams rather than composite dental restorations. Children treated with mercury amalgams did not ‘on average’ have statistically significant differences with respect to neuropsychological function. ‘Although it is possible that very small IQ effects cannot be ruled out’, thus far evidence-based trials largely demonstrate that dental amalgam is not associated with an increase in children’s risk of experiencing neuropsychological dysfunction.

These results support the concept that some healthy children may, indeed, be out of the bell-curve, being more predisposed to toxic effects of mercury at lower levels than others. This is further highlighted by a recent trial specifically concerning children suffering with ADHD. In this study of Chinese children, a significant difference in blood mercury levels was noted between children with ADHD compared with controls, after adjustments for age, gender and parental occupations. The geometric mean blood mercury level was also significantly higher in children with inattentive and combined subtypes of ADHD. In fact, children with a blood mercury level >29nmol/L were found to have 9.69 times higher risk of having ADHD after adjustment for confounding variables. The researchers concluded that high blood mercury levels were associated with ADHD.

Manganese/aluminium

Manganese (Mn) is an essential trace element, however, it has also been shown to be toxic at high doses. Animal studies have recently shown that intra-nasally administered Mn actually circumvents the Blood-Brain-Barrier and passes directly into the brain via olfactory pathways. Long-term exposure to inhaled Mn from shower water as a significant risk for central nervous system (CNS) neurotoxicity is currently being investigated. Similarly, existing Mn drinking water standards may also need to be revised.
A recent study of Canadian children found that those who were exposed to drinking water that was naturally high in Mn had greater scores of hyperactivity and oppositional behaviour (Revised Connor's Rating Scale) than controls. All children with T scores >65 had hair Mn higher than 3.0ug/g.

It is postulated that both aluminium and Mn toxicity may potentiate oxidative and inflammatory stress, subsequently leading to impaired neurological function.

**Industrial chemicals**

It is now accepted that antenatal and early childhood exposures to industrial chemicals in the environment can damage the developing brain and can lead to neurodevelopmental disorders, subclinical brain dysfunction and other conditions including ADHD.

Available data up to 2007 show that at least 202 widely-used industrial chemicals, (including lead, methylmercury, polychlorinated biphenyls, arsenic and toluene) can damage the human brain, the researchers concluding that chemical pollution may have harmed the brains of millions of children worldwide. The specific role these chemicals may play in the development of ADHD is not certain, but a detailed environmental history should be taken in all of those with neurodevelopmental disorders.

**Tobacco smoke, air pollution, pesticides**

Environmental tobacco smoke, air pollution and pesticides have also been shown to have adverse effects on fetal growth and child neurodevelopment.

**Tobacco smoke**

A recent systematic review has demonstrated that both prenatal and possibly postnatal tobacco smoke exposure are significantly associated with increased rates of behaviour problems and ADHD. If causally linked, it is estimated that prenatal tobacco exposure may account for at least 270 000 excess cases of ADHD in American children today.

Like stimulant medication, nicotine has been shown to lower the availability of the dopamine transporter, a significant factor in dopamine metabolism.

**Physical activity**

**Exercise**

Exercise is considered an important part of the management of the child with ADHD as it not only increases coordination skills (that many children with ADHD lack) but it provides opportunities for social interaction. A recent study determining the effects of exercise on children with ADHD suggests that vigorous exercise may provide a dopaminergic adjuvant in the management of behavioural features of ADHD.

It has also been demonstrated that adolescents with ADHD have frontal lobe deficits, particularly on the right sides of their brain. Animal studies were subsequently designed which showed that 'rough-and-tumble' play therapy was able to reduce hyperactivity and excessive playfulness, concluding that this may be a useful new treatment for ADHD.

Another pilot study on Therapeutic Eurythmy — a holistic movement developed by Rudolph Steiner — has also reported shifts in the concentration and motor skills of children with ADHD.

**Yoga**

Randomised controlled trials (RCTs) on the effectiveness of body-oriented therapies such as yoga for children with ADHD are lacking. The effects of yoga were recently compared to the effects of conventional motor exercises in children with ADHD. It was found that yoga was an effective complementary or concomitant treatment for children with ADHD. It should be noted that the training was especially effective for children also taking medications.

Another study of boys with ADHD practicing yoga confirmed this finding, where yoga was particularly effective in the evening when the effects of medication were absent.

**Dietary modifications**

**Food elimination regimes**

There has been much discussion over the last 30 years regarding the possible links between diet and behaviour of the individual with ADHD. In 1975, Benjamin Feingold, an allergist, hypothesised that an intake of salicylates in artificial flavours, colours and preservatives and/or natural salicylates may induce hyperactive behaviour and learning disabilities in children. Although Feingold demonstrated that 50% of children with ADHD improved after eliminating these substances from their diet, this has not been successfully repeated until recent years.

The use of food elimination diets in the management of individuals with ADHD is now well documented. In fact, a strictly supervised elimination diet is considered to be
a valuable instrument in determining whether dietary factors are contributing to ADHD symptoms. In a recent RCT, the number of criteria on the ADHD rating scale showed a scale reduction of 69.4%. Furthermore, comorbid symptoms of oppositional defiant disorder (ODD) also showed a significantly greater decrease in the intervention than the control group.\textsuperscript{113}

There is an accumulating body of evidence that many children with behavioural problems, including ADHD, are sensitive to 1 or more food components that can negatively impact upon their behaviour.\textsuperscript{114} In 1 study, 19 of 26 children with ADHD improved dramatically after eliminating artificial colours, corn, wheat, milk, soy and oranges from their diet. It is interesting that most of the children who responded to such dietary changes had atopic histories implying that atopic children are more likely to benefit from a restricted diet.\textsuperscript{112} Other risk factors associated with a beneficial dietary response were a family history of migraine and young age.\textsuperscript{109} Another study also demonstrated a significant improvement in behaviour in 62% of 40 children with ADHD after a 2-week diet based solely on rice, turkey, pear and lettuce.\textsuperscript{115} This diet is clearly too restrictive for any child but it does demonstrate that nutrition can influence behaviour.

For children showing behaviour problems such as hyperactivity, the use of dietary manipulation tends to be a more acceptable approach to treatment than the use of drugs.\textsuperscript{116} If parents strongly suspect a specific dietary item, a trial of elimination is warranted.\textsuperscript{117} However, there are various regimes; usually this would consist of avoiding the item for 3 weeks then reintroducing it in a step-wise fashion — a little the first day, then challenging the body with a higher dose during the second day if no obvious reaction has already occurred. Depending upon the age of the child, multiple foods may be eliminated simultaneously and reintroduced separately in a similar manner under strict supervision. In conducting such dietary modifications, it is mandatory that all practitioners be aware of the dangers potentially associated with unsupervised restriction diets with children.\textsuperscript{116, 118} It is imperative that a food elimination diet be only short-term and the rechallenge process, well structured and clearly documented by the patient/family at the time. A maintenance diet may then be designed by a nutritional practitioner according to the results of the rechallenge process and with optimal levels of both nutritional health and behaviour modification of the child in mind.

In general, dietary modification plays a major role in the management of ADHD and should be routinely considered as part of the treatment protocol.\textsuperscript{114} Many children with ADHD have associated digestion problems — including diarrhoea, constipation, abdominal bloating, excess burping and/or flatulence, reflux/indigestion or abdominal pain/discomfort. These are generally symptoms of deficient beneficial gut flora (probiotics) and/or food intolerances which may serve as triggers for abnormal behaviour.

A plethora of studies have now shown that food additives have also been shown to increase hyperactivity symptoms in children.\textsuperscript{119, 120} This includes a recent systematic review, which concluded that an additive-free elimination diet was considered Level II evidence with respect to its current level of evidence.\textsuperscript{121}

Although the use of single food additives at their regulated concentrations are believed to be relatively safe in terms of their neuronal development, their combined effects remain unclear. Four common food additives, brilliant blue, L-glutamic acid, Quinolone yellow and aspartame were observed in combination. Neurotoxicity (measured as inhibition of neurite outgrowth) was found at concentrations of additives theoretically achievable in plasma by the ingestion of a typical snack and drink.\textsuperscript{122}

Symptoms that are due to, or exacerbated by, specific food additives usually involve non-IgE mediated mechanisms that are usually less severe than those induced by food allergy.\textsuperscript{123} A recent RCT demonstrated that artificial colours and/or a sodium benzoate preservative in the diet results in increased activity in children aged 3 or 8–9 years old.\textsuperscript{124} This confirmed an earlier study where the adverse behaviour of 3-year olds from the same additives was detectable by parents but not by a simple clinical assessment.\textsuperscript{125}

Despite a plethora of anecdotal reports that sugar increases hyperactivity and disruptive behaviour in the child with ADHD, there are as yet no consistent clinical trials to support this allegation.\textsuperscript{126}

Like most neuropsychiatric disorders, there is evidence that ADHD is associated with increased oxidative stress and therefore increased lipid peroxidation. For this reason, it is postulated that individuals with ADHD may benefit from a whole-food, plant-based diet that is high in antioxidants and devoid of refined carbohydrate products.\textsuperscript{127}

Several recent studies have also reported a possible association of coeliac disease with ADHD. In fact, ADHD-like symptomatology is markedly over represented amongst individuals with untreated coeliac disease. A gluten-free diet can result in a significant improvement of such
Nutritional supplementation

Nutritional supplementation is widely used to help ameliorate the symptoms of ADHD. Many nutrients, (vitamins, minerals, essential amino acids, essential fatty acids) have direct effects on the structure and function of the human brain. Indeed, the role of nutrition in the prevention and management of ADHD is vital, cost-effective and extremely safe.

Magnesium/vitamin B6

Magnesium deficiency has long been known to cause hyperexcitability with seizures in animal studies, effects that have been successfully reversed by treatment with magnesium. Significantly decreased plasma and red blood cell magnesium with concomitant decreases in Mg(2+) ATPase activity have been identified in children with ADHD. Magnesium is required for more than 350 different biochemical metabolism pathways in the human body, including oxidation/reduction and ionic regulation.

Vitamin B6 is essential to the synthesis of many neurotransmitters, particularly dopamine, noradrenaline, GABA, etc (see Figure 6.1).

Several European trials have demonstrated an improvement in the symptoms of ADHD with a combination of magnesium and vitamin B6. Children prescribed a magnesium/B6 regimen (6mg/kg/day Mg, 0.6mg/kg/day B6) for at least 8 weeks displayed a significant reduction in their symptoms of hyperactivity and aggressiveness whilst their attention at school was improved. When the supplementation was ceased, clinical symptoms of the disease reappeared within a few weeks, as did their original lower red blood cell Mg concentrations.

After 1 month of supplementation of magnesium and B6, magnesium homeostasis was again normalised and there were noticeable improvements in behaviour and attention whilst levels of anxiety and aggression were reduced. Thus, it has been postulated that the determination of plasma and red blood cell Mg can be used to detect deficits and monitor the efficiency of treatment.

An earlier study found that even though 32 out of 50 children with ADHD demonstrated low red blood cell Mg levels, all patients showed an improvement in symptoms (hyperexcitability, physical aggressiveness, instability, attention, hypertony, spasm, myoclony) after 1–6 months of treatment with magnesium. Similarly, children with ADHD receiving 200mg/day magnesium showed a significant decrease in hyperactivity compared to a non-supplemented control group.

Iron

Iron is necessary to ensure oxygenation, produce energy in the cerebral parenchyma (via cytochrome oxidase) and for the synthesis of both neurotransmitters and myelin. Iron concentrations in the umbilical artery are critical for the development of the fetus and are specific to the IQ/cognition of the child, playing a major role in both brain structure and function.

Iron deficiency causes abnormal dopaminergic neurotransmission with many studies supporting its contribution to the pathophysiology of ADHD. Serum ferritin levels have consistently been found to be low in children with ADHD compared with controls.

Furthermore, the lower the serum ferritin levels, the more severe the general ADHD (hyperactivity) symptoms. Available data is conflicting as to the relationship of low serum ferritin specifically to cognitive deficits.

As stated previously, there is a documented significant comorbidity between ADHD and RLS. Iron is a cofactor in dopamine production and patients with restless legs have lower levels of dopamine in their substantia nigra. Thus iron deficiency may, indeed, be one of the underlying common pathophysiological mechanisms in individuals with both ADHD and RLS. Thus, it is suggested that physicians assess children with ADHD for RLS, a family history of RLS and iron deficiency.

A recent trial of iron supplementation (ferrous sulfate 170mg/day) resulted in an improvement of ADHD symptoms in those children with low serum ferritin levels. Iron therapy was well tolerated with effectiveness comparable to stimulant medication. However, an earlier Cochrane study has demonstrated that there is no clear evidence that iron treatment in children less than 3 years of age with iron deficiency anaemia will improve psychomotor development after 5–11 days of treatment. There is a need for future investigations with larger controlled trials.
Zinc

Zinc is an important co-factor that is needed for the metabolism of free fatty acids, neurotransmitters, prostaglandins and melatonin. It plays a role in both the structure and function of the brain and indirectly affects the metabolism of dopamine (by inhibiting the dopamine transporter), known to be intricately involved in ADHD.\textsuperscript{18, 132, 145} Furthermore, plasma zinc levels have recently been found to have a direct effect on information processing in children with ADHD through event related potentials. In particular, the latencies of ‘N2’ waves in both the frontal and parietal regions of children with zinc deficiency and ADHD are significantly longer. N2 wave changes may reflect a different inhibition process and further studies are deemed warranted to investigate the effects of zinc on the inhibitory process in children with low zinc and non-low zinc ADHD.\textsuperscript{146} It is also important to note that zinc has a direct effect on the synthesis of GABA, one of our major inhibitory neurotransmitters that contributes to feelings of calm and relaxation.

Numerous controlled studies report cross-sectional evidence that mean plasma and tissue zinc levels have been found to be significantly lower in children with ADHD than controls suggesting that zinc deficiency may play a substantial role in the aetiopathogenesis of ADHD.\textsuperscript{146, 147, 148} Previous reports regarding this have come mainly from countries with differing diets and socioeconomic status, however, recent studies also show that zinc deficiency is common, for example, in middle-class Americans. Although there are mixed results, these studies suggest that inattentive symptoms are more prominent with lower zinc levels.\textsuperscript{149}

A statistically significant correlation has been found between zinc and serum free fatty acids.
acids (FFA) in children with ADHD. A study involving 48 children with ADHD demonstrated a mean serum FFA level of 0.176±0.102 μEq/L compared with 0.562±0.225 μEq/L in the control group and a mean serum zinc level of 60.6 ±/−9.9 microg/dL compared with 105.8 ±/−13.2 microg/dL in the control group. These findings indicate that zinc deficiency may be a significant factor in the aetiology of ADHD. It is yet to be determined whether FFA deficiency is one of the primary causal factors of ADHD or if this is actually secondary to zinc deficiency.

Several recent trials have demonstrated that zinc supplementation is effective in reducing symptoms of hyperactivity, impulsivity and impaired socialisation in patients with ADHD. In a double-blind randomised placebo-controlled study, 150mg/day zinc sulfate was administered to children with ADHD. It was determined that the reduction of the above symptoms were more significant in patients of older age, higher BMI score with low zinc and low free fatty acid levels. Zinc sulfate was well tolerated with a low rate of side-effects.

Several trials have documented a synergistic effect when zinc is used in combination with drug therapy methylphenidate. In a recent 6-week placebo-controlled double-blind RCT children with ADHD were given either medication Methylphenidate plus Zinc sulfate 55mg/day (15mg elemental zinc) or placebo. The parent and teacher rating scale scores improved significantly in the group receiving zinc. There was no difference in side-effects.

A recent double-blind placebo-controlled study determined the relationships between zinc, essential fatty acids and d-amphetamine found that responses to d-amphetamine improved in a linear fashion with zinc levels.

**Essential fatty acids (EFAs)**

There have been numerous studies of late demonstrating a definitive link between essential fatty acids (EFAs) and neurodevelopment. It has been shown that many children suffering from ADHD have significantly lower concentrations of plasma and red blood cell omega-3 and omega-6 EFAs. Both omega-3 and omega-6 long chain polyunsaturated fatty acids (LCPUFAs) are critical for brain development and function. They function exclusively via cell membranes, in which they are anchored by phospholipids.

Docosahexaenoic acid (DHA, an omega-3 EFA) is a major structural component of neuronal membranes and is essential to pre-and postnatal brain development whereas eicosapentaenoic acid (EPA, an omega-3 EFA) appears more influential on behaviour and mood. Both generate metabolites that are neuroprotective. Increasing evidence also indicates that LCPUFA imbalance or deficiencies may be associated with ADHD through involvement in the dopaminergic cortico-striatal metabolism.

The fatty acid composition of neuronal cell membrane phospholipids directly reflects dietary intake. Changes in the fatty acid composition of neuronal membranes subsequently leads to functional changes in the activity of receptors and other proteins embedded in the phospholipid membrane. The ratio of omega-3 to omega-6 fatty acids also influences various aspects of serotoninergic and catecholaminergic neurotransmission and prostaglandin formation processes that are essential in the maintenance of normal brain function. This, again, can be modulated by dietary intake.

There is a direct association between EFA deficiency or imbalance with a variety of behavioural disorders including ADHD. Indeed, it has been demonstrated that children with lower concentrations of omega-3 fatty acids display significantly more maladaptive behaviours, hyperactivity, temper tantrums, learning, health and sleep difficulties than those with higher concentrations of omega-3 EFAs.

It is not known exactly why these children have lower concentrations of EFAs, however, several theories have been postulated, including low dietary intake, decreased conversion of EFAs to LCPUFAs and increased metabolism of EFAs. It has also been suggested that deficiencies of DHA may be responsible for abnormal signal transduction associated with learning disabilities and cognitive deficits. Such abnormalities in this signal transduction process have been shown to be partially corrected by supplementation with DHA.

In many randomised placebo-controlled double-blind trials, EPA and DHA combinations have been shown to benefit ADHD, amongst many other neuropsychiatric disorders. For instance, 132 Australian children with ADHD recently participated in a 15-week placebo-controlled double-blind RCT where they received PUFA, PUFA + micronutrients or placebo. Improvements in hyperactivity, impulsivity and inattention were recorded in both PUFA groups, with no additional effects being found with micronutrient supplementation. Different doses have been used in each study up to a maximum of 16.2g EPA/DHA daily. In this study of high-dose EPA/DHA, there was also a significant correlation...
between the reduction in the AA:EPA ratio and global severity of illness scores.\textsuperscript{172}

Supplementation with omega-6 EFAs has demonstrated mixed results regarding effects on the symptoms of ADHD. Correct dosage may be critical for optimal effectiveness and further studies are warranted.\textsuperscript{158, 176, 177}

Given that supplementation with EFAs is safe and well-tolerated compared with existing pharmacological interventions, results from such studies strongly support the case for further investigations.\textsuperscript{178, 179}

**Essential amino acids**

Functional and morphological studies in children with ADHD demonstrate a prefrontal cortex (PFC) dysfunction. This region of the brain is regulated by dopaminergic, noradrenergic, cholinergic, serotonergic, glutamatergic and histaminergic pathways. Currently, there is a wealth of evidence showing that those with ADHD have depleted levels of dopamine and noradrenaline, however, there is still much to be learnt regarding how they interact with each other.\textsuperscript{180–190}

The pharmaceutical Methylphenidate primarily affects the PFC and striatum, increasing dopamine and noradrenaline release through multiple means.\textsuperscript{191, 192, 193}

Recent animal studies are now demonstrating that high-dose intranasal dopamine reduces hyperactivity and intermediate-dose improves attention.\textsuperscript{194} Likewise, further studies have now indicated that there is an inverse relationship between 5-hydroxytryptophan (5HT) and aggression in adolescents with ADHD.\textsuperscript{195, 196, 197}

There is also new evidence implicating the glutamatergic prefrontal-striatal pathway in the pathogenesis of ADHD.\textsuperscript{190, 191}

CNS histamine in the PFC is closely linked with cognition and it has only recently become known that Methylphenidate also enhances cortical histamine in animal studies. The newer non-stimulant drugs primarily work as selective noradrenaline re-uptake inhibitors and by increasing extracellular levels of histamine in the PFC.\textsuperscript{198, 199}

Modulation of the H3 histamine receptor can affect cognition via the release of several other neurotransmitters, including acetylcholine and noradrenaline.\textsuperscript{200, 201, 202}

It is imperative to remember that all neurotransmitters are synthesised from amino acids and all require various vitamins and minerals, primarily zinc and vitamin B6, as cofactors. Deficiencies or imbalances in amino acids, vitamins and minerals can therefore profoundly influence neurotransmitter synthesis and breakdown. Supplements that contain the essential amino acids and nutrients can significantly reduce symptoms by their conversion to specific neurotransmitters.\textsuperscript{203}

To date, there is a paucity of studies regarding specific amino acid supplementation and its effects on the symptoms of ADHD. There is increasing evidence for oxidative stress mechanisms underlying the pathophysiology of ADHD, which offers new treatment targets in oxidation biology systems. Of these, the glutathione system has the most favourable theoretical foundation as it is the most generic of all cellular antioxidants. Several studies have shown the efficacy of N-Acetylcysteine, a glutathione precursor, in the treatment of various psychiatric conditions of oxidative stress, indicating that glutathione itself may be a promising therapeutic target.\textsuperscript{204}

Carnitine is another amino acid that has been shown to exert positive effects on the symptoms of ADHD. Acetyl-L-Carnitine (ALC) is essential for energy metabolism and essential fatty acid anabolism. A 16-week placebo-controlled RCT demonstrated that 500–1500mg bd L-carnitine was superior to placebo in treating inattentive-type symptoms.\textsuperscript{205} This confirms earlier studies which have reported significant benefits in ADHD symptoms. Another study has shown significantly reduced attention problems and aggressive behaviour in boys with ADHD supplemented with carnitine.\textsuperscript{206}

Animal studies have demonstrated that ALC increases noradrenaline and the 5HIAA/5HT ratio in the cingulated cortex, subsequently decreasing behavioural impulsivity.\textsuperscript{207} As ALC is safe with no psychostimulant properties, more studies are warranted, particularly for possible significant benefits in the inattentive type.\textsuperscript{207}

**Homeopathy**

An increasing number of parents are turning to homeopathy to treat their hyperactive child.\textsuperscript{208} There have been several placebo-controlled double-blind RCTs demonstrating mixed results for the efficacy of homeopathy in the treatment of ADHD.\textsuperscript{208–211} A 2007 Cochrane review, however, has deemed that there is currently little evidence to support the use of homeopathy, with the recommendation that optimal treatment protocols be developed prior to further RCT being undertaken.\textsuperscript{212}

It is important to note, however, that homeopathy focuses on the individual characteristics of each patient’s experience and symptoms and uses this information to determine the appropriate prescription for
For this reason, RCTs are very difficult to conduct and the results, difficult to interpret. One study of children with ADHD receiving individualised homeopathic treatment demonstrated a 75% response to treatment, reaching a clinical improvement rating of 73% and an amelioration of the Connors Global Index (CGI) of 55%. In comparison, clinical improvement under Methylphenidate was 65% with a lowering of the CGI to 48%. Both treatments appeared to be similar in efficacy and it was concluded that in cases where treatment is not urgent, homeopathy is a valuable alternative to methylphenidate.  

Herbal medicines  

St John’s wort  
There has been only 1 recent study on the effects of Hypericum perforatum on the symptoms of ADHD. No differences were observed between St John’s wort or placebo.  

Ginkgo biloba + ginseng  
A pilot study has recently been conducted on a herbal product containing American ginseng extract, panax quinquefolium (200mg) and ginkgo biloba extract (50mg). One capsule administered twice daily for only 1 month resulted in significant improvements in behaviour of many children with ADHD, warranting further research in this area.  

Traditional Chinese medicine (TCM)  
There have been several clinical trials conducted in China with promising results in the treatment of ADHD. One RCT involving 100 children compared a combination of Bupleurum chinense, Scutellaria baicalensis, Astragalus membranaceus, Codonopsis pilosula, Ligustrum lucidum, lophatherum gracile and thread of ivory with 5–15mg Ritalin twice daily administered for 1–3 months. In the TCM group, 23 cases were ‘cured’ (measured by clinical symptoms disappearing, an increase of 10 IQ units, a normalised EEG and no recurrence of symptoms 6 months post-treatment). Four cases were improved (symptoms and signs markedly improved, an increase of 4 IQ units and normalising EEG) and 11 cases ineffective. In the group taking Ritalin, 6 cases were ‘cured’, 12 cases improved and 2 cases were ineffective. Although there was no significant difference regarding efficacy between the 2 groups in this study, the side-effects of TCM were considerably less.  

Double-blind studies comparing the effects of Duodongning (DDN) with Ritalin have also shown similar clinical responses with a marked reduction of side-effects in those taking DDN. These effects have once again been seen with Tiaoshen liquor. Its therapeutic mechanism is thought to be related to improvements in information transmission through cholinergic neuron synapses and enhancement of hypoxia tolerance of cerebral tissues. A further randomised controlled study involving 200 children assessed the effects of Ritalin, YiZhi mixture (YZM) and a combination of both, for a period of 3 months.  

Pycnogenol  
Oxidative stress has been implicated in the pathogenesis of many chronic diseases, including ADHD, with correspondingly new targets for the development of different therapeutic interventions. Pycnogenol, an extract from the bark of the French maritime pine, is a potent polyphenol complex that contains phenolic acids, catechin, taxifolin and procyanidins. It acts as a highly powerful antioxidant and chelating agent that stimulates the activity of other antioxidants such as SOD (superoxide dismutase) and eNOS (endothelial nitric oxide synthase). Concentrations of catecholamines have been found to be higher in the urine of patients with ADHD compared with healthy children. Furthermore, adrenaline and noradrenaline concentrations positively correlate with plasma levels of oxidised glutathione. Several placebo-controlled, double-blind RCTs have shown that pycnogenol reduces symptoms of hyperactivity and improves attention,
visual-motor co-ordination and concentration in children with ADHD. One month of pycnogenol (1mg/kg/day) significantly reduced oxidised glutathione and increased reduced glutathione compared with placebo. Urinary catecholamines (dopamine, adrenaline and noradrenaline) were also decreased. Thus, pycnogenol reduces oxidative damage to DNA, normalising total antioxidant status of ADHD children. At 1 month post-cessation of Pycnogenol, a relapse of ADHD symptoms was noted.

Physical therapies

Massage
Massage intervention is known to benefit childhood mental wellbeing. For instance, a meta-analysis of the literature demonstrated massage intervention can be of benefit in promoting mental and physical wellbeing in any child under the age of 6 months by improving the mother–infant interaction, sleeping and crying, and on hormones influencing stress levels which may impact positively in children’s behaviour in later life.

Massage has been shown to increase serotonin levels which may modulate dopamine levels in children with ADHD. One study demonstrated increased concentration and decreased hyperactivity after children with ADHD received 15 minute massages for 10 consecutive school days. More recently, massage for 20 minutes twice weekly for 1 month benefitted students with ADHD by improving short-term mood state and longer-term classroom behaviour.

Chiropractic
In 1 small study, chiropractic manipulation has been shown to decrease autonomic nervous system activity and improve behaviour in children with ADHD, thus warranting further investigation in this area.

There is currently a placebo-controlled, double-blind RCT underway in Australia investigating the effects of Neuro Emotional Technique (NET), a branch of chiropractic, on children with ADHD. The control group are continuing their existing medical regime whilst the intervention and placebo group have the addition of NET and sham NET protocols added to their regime, respectively. These NET/sham NET protocols are performed twice weekly for the first month and then monthly for the next 6 months. This study should provide good evidence as to the efficacy of NET as an adjunct therapy to conventional medical therapy.

Conclusion
ADHD is a chronic, complex and multifactorial illness that has become one of the most common cognitive and behavioural disorders diagnosed among children of school age today. Current conventional treatment includes the use of stimulant medications which significantly influence catecholamine concentrations. Not all children respond to these medications and the risk of side-effects combined with concerns regarding the safety of the long-term use of such medications makes CAM therapies an attractive option. There is a wealth of evidence for the use of many of these therapies and an holistic approach to the management of our future generations is well warranted. Management of ADHD should include various behavioural and lifestyle changes that include avoidance of chemicals and smoking, sleep restoration, dietary changes, exercise outdoors in a natural setting and relaxation strategies. Table 6.1 summarises the best evidence for CAM therapies for ADHD.
### Table 6.1 Levels of evidence for lifestyle and complementary medicines/therapies in the management of ADHD

<table>
<thead>
<tr>
<th>Modality</th>
<th>Level I</th>
<th>Level II</th>
<th>Level IIIa</th>
<th>Level IIIb</th>
<th>Level IIIc</th>
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<td>Other supplements</td>
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Continued
### Table 6.1 Levels of evidence for lifestyle and complementary medicines/therapies in the management of ADHD—cont’d: TCM herbs)—cont’d

<table>
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<tr>
<th>Modality</th>
<th>Level I</th>
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<tr>
<td>Ginkgo biloba and/or Ginseng</td>
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<tr>
<td>Traditional Chinese medicine mixture:</td>
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<td>[Bupleurum chinense, Scutellaria baicalensis, Astragalus membranaceus, Codonopsis pilosula, Ligustrum lucidum, lophatherum gracile and thread of ivory) Duodongining Yihzi mixture Pycnogenol</td>
<td>x</td>
<td>x</td>
<td>x</td>
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<td>Chiropractic</td>
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</table>

**Level I** — from a systematic review of all relevant randomised controlled trials, meta-analyses.
**Level II** — from at least 1 properly designed randomised controlled clinical trial.
**Level IIIa** — from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
**Level IIIb** — from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a parallel control group.
**Level IIIc** — from comparative studies with historical control, 2 or more single-arm studies or interrupted time series without a parallel control group.
**Level IV** — opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees.
**Level V** — represents minimal evidence that represents testimonials.
Clinical tips handout for patients — attention deficit hyperactivity disorder (ADHD)

1 Lifestyle advice

Sleep
- All children should be fully assessed and treated for underlying sleep disorders.
- Appropriate amount of physical activity during the day can help sleep.
- Herbal teas such as chamomile can be helpful in some cases.
- Magnesium (up to 350mg elemental) can be used to calm the child during the day and assist sleep at night (3 month trial).
- L-Tryptophan (50–100mg in children and 100–200mg adults) may be trialled for 1 month 1 hour before bedtime (not with antidepressant medications).
- Melatonin (3mg for children and 3–6mg for adults) at bedtime may be trialled for 1 month (not with L-Tryptophan or antidepressant medications).

Sunshine
- At least 15 minutes sunshine is needed daily for vitamin D production. More sun exposure may be required in cooler areas, winter and in people with dark skin.
- Sunscreen can block the conversion to vitamin D so this should be avoided during this specified time period.

2 Physical activity/exercise
- Play outdoors in a natural environment such as a natural park or countryside as much as possible. As little as 30 minutes daily can make a significant difference.
- Vigorous exercise and ‘rough-and-tumble’ play can help to reduce levels of hyperactivity and assist sleep.
- Yoga practice is a useful adjunct to ADHD medications.

3 Mind–body medicine
- Neurobiofeedback in the form of video games can be very helpful in reducing symptoms of hyperactivity and impulsivity, and can improve attention, IQ, processing speed and music performance.
- The child should be 6 years of age or older.
- Usually 20–30 sessions of biofeedback are required to achieve results comparable to methylphenidate.
- Significant behavioural and cognitive improvements are reported for at least 6 months after cessation of biofeedback.

4 Counselling/psychotherapy
- Both behavioural and cognitive behaviour therapy (CBT) interventions are highly effective for children and adults with ADHD.
- Children respond positively to behavioural interventions only when they are appropriately implemented at school and in the home.
- Mindfulness meditation, Sahaja Yoga meditation and relaxation training can all be effective in improving symptoms of ADHD. (see: www.sesigs.health.nsw.gov.au/rhw/)
- Anecdotal evidence strongly supports the use of soothing music and sound therapy (Tomatis Method, integrated listening system eg. www.integratedlistening.com).

5 Environment
- Playing outdoors in a natural environment such as a natural park or countryside as much as possible to avoid air pollution, traffic, and breathe fresh air.
- Lead, mercury, manganese, aluminium, copper and industrial chemicals (PCBs, arsenic) have all been found to be possible contributing factors to ADHD.
- All children with ADHD should ideally be tested for the presence of heavy metals.
- This can be done by hair mineral analysis or comprehensive urinary element profile through a health practitioner.
- Only with heavy metal toxicity detected: Chelation therapies can range from gentle (Epsom salt/clay baths, coriander, chlorella, chelating foot-pads) to stronger means (zinc supplementation, metallothioneine promoting supplements, DMSA, DMPS chelating agents) where necessary. Discuss this with your doctor.
- Avoidance of chemicals, pesticides and tobacco smoke is important.

6 Dietary changes
- Many children have digestion problems (‘irritable bowel syndrome’) (abdominal bloating/discomfort, diarrhoea, constipation, excess burping/flatulence, reflux) which may adversely affect their behaviour.
- An abdominal X-ray can often reveal hidden constipation.
- Supervised food elimination regimes are extremely important in identifying problem foods that trigger hyperactivity, impulsivity and inattention. There is no point using...
other therapies if the child is eating something every day that continues to trigger certain behaviours.

- The most common problem foods include artificial additives, sugar, wheat (gluten), cow’s milk (casein) and salicylates.
- Foods may be eliminated for a period of 3 weeks, then each food/component reintroduced separately (e.g. wheat/yeast/gluten; lactose-free, ‘A2’ milk).

### Supplementation

#### Probiotics
- **Indication:** to aid digestion and reduce ‘IBS’ symptoms. They should be used in conjunction with dietary modifications.
- **Dosage:** 1–2 capsules before breakfast.
- **Results:** 1 month.
- **Side-effects:** if using wrong probiotic, digestion symptoms may get worse.
- **Contraindications:** true dairy allergies if dairy in preparation.

#### Digestive enzymes
- **Indication:** to aid digestion in the short term and improve quality of life (e.g. at birthday parties) where children are exposed to ‘problem foods’.
- **Dosage:** 1 capsule 10 minutes before ‘problem food’.
- **Results:** immediate.
- **Side-effects:** very mild and rare.
- **Contraindications:** nil known.

#### Gut-healing herbs and nutrients (glutamine, aloe-vera, slippery elm)
- **Indication:** to assist healing of the digestive system whilst avoiding ‘problem foods’.
- **Dosage:** maximum dose as directed.
- **Results:** 1–3 months.
- **Side-effects:** diarrhoea.
- **Contraindications:** hypersensitivity to ingredients.

#### Magnesium
- **Indication:** to reduce hyperactivity, restless legs, teeth grinding, ‘growing pains’, chocolate cravings and to improve sleep.
- **Dosage:** up to 350mg elemental milligrams/day until age 12 or equivalent usual weight: 750mg/day for adults.
- **Results:** 1–3 months.
- **Side-effects:** diarrhoea, gastric irritation; oral magnesium can cause gastrointestinal irritation, nausea, vomiting, and diarrhoea. The dosage varies from person to person. Although rare, toxic levels can cause low blood pressure, thirst, heart arrhythmia, drowsiness and weakness.

- **Contraindications:** Renal failure, kidney disease, heart block.

#### Vitamin B6
- **Indication:** to reduce hyperactivity/ anxiety and increase attention in combination with magnesium.
- **Dosage:** Pyridoxal-5-Phosphate (Activated B6) up to 20mg/day.
- **Results:** 1–3 months. Always need to be combined with B complex in long-term use.
- **Side-effects:** paraesthesia in extremities, bone pain, muscle weakness at high levels. Reversible on cessation of supplement as soon as symptoms develop; may cause long-term problems with long-term use and with very high doses (>50mg/day).
- **Contraindications:** caution with amiodarone, phenobarbitone, phenytoin.

#### Zinc
- **Indication:** to treat zinc deficiency (note white marks on nails, plasma zinc ideally >14). To chelate heavy metals (if evident upon testing). To assist with reducing hyperactivity, impulsivity, impaired socialisation and reducing inattention.
- **Dosage:** needs to be individualised as some children need very high doses depending upon their biochemistry. Minimum dose 10mg elemental zinc.
- **Results:** 1–3 months.
- **Side-effects:** nausea and vomiting (if taken in excess), metallic taste in mouth, reduced copper after long-term use.
- **Contraindications:** sideroblastic anaemia, severe kidney disease, above normal plasma levels of zinc (>18 micromols/litre).

#### Fish oils (EPA/DHA)
- **Indication:** To improve attention, IQ, sleep and reduce hyperactivity, and impulsivity.
- **Dosage:** Ideally DHA>EPA for learning, processing disorders. Doses between 1-9g EPA/DHA daily.
- **Results:** 1–3 months.
- **Side-effects:** Fishy burps, diarrhoea, gastrointestinal discomfort.
- **Contraindications:** Fish allergy. Caution with anticoagulants at very high doses.

#### L-Tyrosine
- **Indication:** to reduce hyperactivity and impulsivity.
- **Dosage:** 500mg up to 3 times daily as required.
- **Results:** 1–3 months. Can be as early as 1 week.
• Side-effects: migraines, gastrointestinal upset, fatigue, reflux, arthralgia, insomnia, nervousness.
• Contraindications: melanoma. Caution with manic conditions, hyperthyroidism, antidepressants (MAOIs, SSRIs TCAs).

Iron
• Indication: to treat iron deficiency, restless legs at night, reduced hyperactivity.
• Dosage: depending on age and serum levels, between 20mg-40mg/day.
• Results: 3–6 months.
• Side-effects: constipation, dark stools, nausea, diarrhoea, reflux.
• Contraindications: haemachromatosis, haemosiderosis, above normal iron levels.

Carnitine
• Indication: inattention, possibly aggressive behaviour.
• Dosage: 500–1500mg twice daily.
• Results: 1–3 months.
• Side-effects: mild gastrointestinal symptoms-nausea, vomiting, diarrhoea, changes in body odour.
• Contraindications: caution with anticoagulants, epileptic, chronic liver disease.

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Integrative and complementary approaches to common clinical problems


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