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Advanced CLINICAL NATUROPATHIC MEDICINE

Leah Hechtman

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ADVANCED CLINICAL NATUROPATHIC MEDICINE

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Acknowledgments

It is with much gratitude that we birth *Advanced Clinical Naturopathic Medicine* (ACNM). ACNM was developed from a yearning to contribute more deeply to the naturopathic body of work, to support the development of the evolving profession and to guide clinicians and students through complicated areas of expertise and specialisation. ACNM brings together a team of true experts to achieve this vision.

As with CNM, a book of this depth requires the commitment and dedication of a number of individuals, and I am again deeply grateful to and humbled by those I have been privileged to work with to achieve this collaborative goal.

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Additionally, my heartfelt thanks to Dr Sue Evans for writing the Foreword of this text. For this volume, I was intent on ensuring a balance of the sexes and ideally wanted someone Australian who I perceive as a wise elder, firmly rooted in the history and tradition of our treatments and philosophies and connected to and practising our evolving practice. Sue, you embody all of these admirable attributes and your humble wisdom shines through as always. Thank you.

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To my colleagues at UNSW, it is from my connections with you all that I am able to critically assess and contribute meaningfully in an academic context. You have supported me to seek and find answers to my enquiries which consistently provide foundational platforms with which to expand as a clinician and educator. Learning, growth and contribution are some of my core values, and my gratitude for these opportunities that you bestow on me are heartfelt and celebrated. Thank you.

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Finally, my gratitude to my patients – past, present and future. It is the relationships I share with my patients, their stories, journeys and experiences that drive me to seek out answers to understand and to provide help and support. Without these heartfelt experiences, I would not be as moved or determined to push, to search, to seek and to find how I can help. When your heart is touched and a connection felt, it is the humility of the experience that opens up the universe to you to find answers. I am deeply grateful for each person I am privileged to treat.

Preface

The release of *Advanced Clinical Naturopathic Medicine* (ACNM) is a hallmark achievement supporting the evolving practice of the profession. No longer limited to merely general practice, clinicians have broadened and expanded into specialty practices. This shift in our treatment has seen more specific courses and sub-practices develop, with clinicians narrowing their focus to key areas of expertise.

That the contributors in ACNM are experts in their fields is evident. All have completed advanced training and have years of clinical experience and a deep love of their specialty areas. The chapters showcase the many diverse pathways within the profession and highlight both the opportunities for aspiring clinicians as well as the depth of practice required to truly excel in these specialty areas of expertise.

Each contributor elevates their knowledge. All aspects of their careers aptly highlight the commitment and dedication required to perfect and hone their craft.

ACNM offers both new and experienced clinicians, educators and researchers an opportunity to dive into the hearts and minds of these leaders. It showcases how truly transformative and effective naturopathy is and offers insight into the depth of our practice.

As with *Clinical Naturopathic Medicine*, the publishing of this text is an opportunity for the profession to reclaim and celebrate our vital role in the healthcare system. Our system of healing is unique and relevant; our treatments efficacious and therapeutic; our methodology and outcomes logical and supportive.

I hope this text provides assurance for clinicians and gives them confidence to take on more responsibility and be more active in the welfare of their patients' wellbeing; certainty to be more forthright and transparent with treatment strategies, methodologies and approaches; and determination to consistently strive for excellence and have the patient's best interests at heart.

Naturopathic core principles guide our intentions, with patient-centred care as the primary principle. Our elders always focused on the importance of the inter-relationship between clinician, patient and nature.

My hope is that ACNM provides the platform with which to seek answers and formulate the best care possible.

Leah Hechtman
March 2020

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Leah is an experienced and respected clinician and has been in private practice for over 20 years. She specialises in fertility, pregnancy and reproductive healthcare for men and women and holds fellowships and memberships with a number of International organisations.

She has completed extensive advanced training and is currently completing her PhD through the School of Women's and Children's Health (Faculty of Medicine [UNSW]).

Leah is the Director of The Natural Health and Fertility Centre in Sydney, Australia, where she maintains her clinical practice.

She is a keynote speaker at conferences locally and internationally to both the functional and the complementary medicine communities as well as the wider fertility and gynaecological areas of medicine. She is the author of multiple seminal naturopathic textbooks and is a contributor to journals and other texts within the naturopathic and functional medicine areas, as well as general gynaecology, fertility and infertility.

Most importantly, she is a mother to two gorgeous boys who keep her grounded, humbled and consciously aware. They have helped and continue to help her be a better version of herself and provide insight and direction for her spiritual practice.

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2 Environmental medicine

Nicole Bijlsma

Environmental medicine is the evaluation, management and study of detectable human disease or adverse health outcomes arising from exposure to external physical, chemical and biological factors in the general environment.[1,2] Environmental medicine is a speciality field that has been adopted by occupational and environmental doctors, but largely ignored in patient-centred general practice despite the fact that toxicants alone have been implicated in many chronic diseases typically seen in routine medical practice.[3] There are several reasons why this may be so:

- Most chronic diseases arise from a complex interaction between genes and the environment and, until recently, this relationship has been hampered by limited knowledge of the human genome and the inclination of scientists to study disease using models that consider exposure to single agents at high doses[4]
- Very little of the vast amount of literature on environmental exposure is published in general medical journals[5]
- It takes years to translate scientific discovery to clinical practice[6]
- Clinicians do not undertake house and workplace visits to identify obvious triggers
- There is competition from other disciplines in crowded medical curricula
- There are limitations in adopting a reductionist approach to compartmentalise the body into separate systems
- The need to provide evidence-based medicine that is conclusive and leaves no room for doubt has delayed action on environmental toxicants.

Widespread exposure to toxicants occurs in the human population from the womb to the tomb at levels known to cause adverse health effects.[7–10] This is largely because the burden of proof is not on industry to prove that its products or technologies are safe, and the inadequacies of chemical risk assessment fail to consider multiple routes of exposure, mixture effects, transgenerational epigenetic effects, the impact of endocrine-disrupting chemicals (EDCs) during critical windows of human development and individual susceptibility,[5] although some countries are attempting to address this (for example, the REACH directive in Europe and the Toxic Substance Control Act in the US). Consequently the history of medicine is littered with numerous examples of missed opportunities, wasted resources and counterproductive policies due to an inability to act on available evidence.[11] In 1857, the father of epidemiology, Dr John Snow, was able to demonstrate that 'contagions' in water were responsible for a cholera epidemic[12]; in 1950 Dr Richard Doll published his findings correlating smoking with lung cancer[14]; and in 1956 Dr Alice Stewart was able to prove that one fetal x-ray doubled the incidence of childhood leukaemia.[13] These clinicians were ostracised from their peers and the medical establishment at the time of their findings and it took decades for their work to be validated. There are many environmental hazards that have had devastating consequences on human health, such as lead, mercury, asbestos, benzene, organochlorine pesticides and polychlorinated biphenyls (PCBs).[15] The question we as clinicians need to ask ourselves is, 'When is there sufficient evidence to act?'[5]

Despite calls from numerous organisations[16–19] to provide clinicians with more training and awareness in environmental health, there are multiple barriers to the clinical assessment of toxic environmental exposure. Clinicians are limited in their capacity to test for environmental exposure as many of the tests available have not been validated (e.g. provocation testing, lymphocyte sensitivity tests, DNA-adduct and mitochondrial testing, visual contrast sensitivity tests), are inconsistent or controversial (hair mineral analysis, detoxification profiles), only assess short-term exposure (blood, stool and urine), may not be predictive of adverse health outcomes (genomic profiling), are costly or are not available. In addition, there may be no reliable biomarkers, such as those involved with electromagnetic field exposure. While emerging technologies in the field of metabolomics are predicted to have a profound impact on medical practice in years to come,[20] in the interim clinicians can do many things to address environmental exposure. This starts with taking a thorough history of the patient's health symptoms and environmental exposure, establishing the patient's inherent susceptibility to environmental toxicants and educating the patient on how they can reduce their exposure to toxicants: these topics are the focus of this chapter.

HISTORY-TAKING

According to Bijlsma and Cohen,[5] history-taking should encompass the following:

- A detailed symptom history that includes a timeline from the prenatal period

- A family history that includes previous generations
- An obstetric, paediatric, dietary, environmental and occupational exposure history (links to questionnaires developed for chemical, electromagnetic field and mould exposure are provided in this chapter)
- A history of pharmaceutical and recreational drug use
- A detailed place history that includes places of residence, school and work across the lifespan including primary modes of transportation, with a focus on proximity to toxicants (mining, industry, traffic and other sources of air and water pollution), allergens and electromagnetic fields
- Use of external data sources, geographical information systems and apps to assess exposure to electromagnetic fields (real time) and exposure maps (mining, radon, traffic, pollen), as well as government or non-government environmental pollution reporting regarding ambient air monitoring and drinking water quality
- A physical examination to look for physical signs of metabolic, neurological, reproductive or other disease and comorbidities
- Assessing current toxic load by performing various biomonitoring tests including assessment of biomarkers in various body tissues to evaluate long-term accumulation of toxicants
- Networking with other professionals who can assess the patient's home and/or workplace to establish sources of exposure.

WHO IS SUSCEPTIBLE?

Why is it that a person may work in a department store spraying perfumes day by day, year by year, and be completely unaffected by the environment while a person walking past the same area develops a headache that makes them unwell for the rest of the day? Why do people react differently to pharmaceutical drugs? Why can one person smoke heavily all of their life with no apparent symptoms, while another dies from smoking-related disease in middle age? Establishing a patient's inherent susceptibility to environmental toxicants requires an assessment of their genetic predisposition, age and timing of exposure, gender, gut microbiome, nutrition, drug use and disease states.

Genetic predisposition

Genetics loads the gun, but the environment pulls the trigger. Professor Judith Stern

Environmental exposure and individual susceptibility go hand-in-hand. Simply put, you cannot address one without the other. Until recently, clinicians were limited in their scope to assess individual susceptibility to eliciting the patient's race/ethnicity status and taking a thorough family and personal history, as alterations in highly penetrant genes (mutations) explain only a small fraction of complex diseases. Completion of the human genome in 2003, however, shifted attention to explore the impact of gene variants or SNPs (single-nucleotide polymorphisms) in the aetiology of chronic disease as the direction and magnitude of the exposure-response effect can vary with different genetic polymorphisms.[4,21,22] For example, there is a higher incidence of asbestos-induced respiratory disease in carpenters with a homozygous deletion of the *glutathione-S-transferase Mu 1* (*GSTM-1*) gene, which plays an important role in phase II liver detoxification.[23] Human variability in phase I and II detoxification can vary more than ten-fold depending on genetic polymorphisms in metabolic enzymes.[24,25]

Studies that explore polymorphisms in the aetiology of chronic disease are frequently inconsistent, inconclusive and contradictory. They often fail to demonstrate cause and effect because multiple genes are involved, polymorphisms in some genes may be compensated by other genes and few studies consider these SNPs within the context of the patient's lifestyle and/or environment. Taking breast cancer as an example, although well-established risk factors have been identified for breast cancer (including age, menarche/parity/menopause, family history, being overweight, drug use, smoking, high penetrance gene mutations [*BRCA1*, *BRCA2*, *TP53* and *PTEN*] and gene variants in detoxification and DNA repair pathways), individually they confer only a small or negligible risk.[3,26] When polymorphisms are combined or considered within the context of relevant environmental and lifestyle exposure, such as being overweight, smoking, using alcohol or drugs, or following toxicant exposure, especially during the prenatal and pubertal periods, the statistical power becomes significant in some[27–31] but not all studies,[32,33] depending on which polymorphisms and environmental factors are investigated. This gene–environment interaction may explain why US-born Asian women have an almost two-fold higher incidence of invasive breast cancer than native Asian women.[34] Like most complex chronic diseases, determining the aetiology and pathogenesis of breast cancer requires big data resources[32] involving large-scale multicentre studies that include detailed individual data, environmental background and gene–gene and gene–environment interactions.[35] The synergistic relationship between genes and the environment in the aetiology of chronic diseases like autoimmune diseases, metabolic disorders, neurodevelopmental disorders such as autism, neurodegenerative disorders such as Parkinson's disease and various cancers has been confirmed by numerous studies.[26,36–39]

While the cost of gene testing has become more affordable, few clinicians implement it because of the time involved, a lack of training, ethical considerations and the fact that very few of the one million-plus SNPs have clear functional implications and actionable outcomes that are relevant to mechanisms of disease.[3,40] Furthermore, current attempts to predict a person's reaction to drugs and toxicants based on their genetic predisposition alone have not met the anticipated success.[41] In addition, the implications for clinical practice have been limited[42] because other compounding factors such as age, gender, gut microbiome, nutrition and lifestyle factors have been

shown to influence the way in which toxicants are metabolised in the body.

Age and timing of exposure

Age is an important risk factor for susceptibility, as exposure to toxicants during critical windows of development (prenatal, childhood and prepubescent) has been correlated with a range of adverse health effects. The first association of transgenerational inheritance of disease was documented in the Dutch famine of 1944–1945, when nutritional deprivation in utero was associated with increased risk of obesity later in life.[43] Since then, poor nutrition and chemical exposure in utero have been widely reported.[44–47] However, it wasn't until a series of events beginning in the 1960s – diethylstilboestrol and adverse reproductive outcomes, thalidomide-induced limb defects, tobacco smoke and low birth weight, Minamata disease and mercury, and fetal alcohol syndrome – that our understanding of the placenta as a protective barrier was deemed unfounded.[48]

Early life exposure to toxicants in air, water, food, soil and consumer products can increase the risk of cognitive, behavioural or social impairment, as well as specific neurodevelopmental disorders such as autism and attention deficit hyperactivity disorder.[49] There is convincing evidence that industrial chemicals such as lead, mercury, arsenic, pesticides, fluoride, flame retardants, plastic derivatives, combustion-related air pollutants, PCBs and various solvents like toluene are contributing to a global pandemic of neurodevelopmental disorders.[49–51] Toxicants that persist in the fat and bones of the mother over a life time may expose the fetus to heavy metals such as lead[52] and persistent organic pollutants such as organochlorine pesticides. The fetal and infant brain are vulnerable to lipophilic toxicants as the central nervous system is the dominant repository of fetal fat.[3] Furthermore, concerns about the impact of early life exposure to EDCs have grown following the publication of Rachel Carson's book *Silent Spring* in 1962,[53] Theo Colburn and Pete Myer's text *Our Stolen Future* in 1996,[54] the World Health Organization's report in 2013,[55] the International Federation of Gynecology and Obstetrics' statement in 2015[56] and the TENDR consensus statement in 2016.[49] Since then, there has been a flood of research correlating in utero and early childhood exposure to EDCs with the rising incidence of testicular dysgenesis syndrome, cancers, infertility, metabolic diseases and neurobehavioural disorders.[55] The fetal origins of health and disease proposed by Barker[57] have subsequently morphed into the developmental origins of health and disease (DoHAD), which focuses on the role of early life exposure in chronic disease aetiology.[58]

Breast-fed infants accumulate higher toxicant burden being at the top of the food chain.[59] Compared with adults, neonates are more vulnerable to toxicants because they have fewer binding proteins in the blood,[60] and infants have a higher hand-to-mouth ratio and therefore ingest up to eight times more dirt than adults. Infants also consume more food and drink per unit of body weight to meet their growth and developmental needs, extract more nutrients and toxicants from ingested food, breathe twice as much air, have a breathing zone closer to the ground where most toxicants are found (in household dust), are more susceptible to EDCs, have a longer life expectancy, do not recognise danger, have an undeveloped blood–brain barrier and underdeveloped and immature body systems (e.g. immune, respiratory, renal).[60–62] Apart from immature detoxification pathways, the biodiversity and abundance of a child's gut microbiome (in particular, those that metabolise xenobiotics) is significantly less when compared to an adult's.[63] Consequently the health impact of chemical exposure is most evident in paediatric medicine, where chronic disease has overtaken infectious disease as the major burden of paediatric illness.[64] A well-known example of child–adult differences in metabolic processing is caffeine. Caffeine's half-life in newborns is 14-fold higher than in adults, which is probably the result of the immaturity of the enzyme CYP1A2.[65,66]

Children are also uniquely susceptible to the radiofrequency electromagnetic energy (RF EME) used in wireless technologies because, unlike adults, their skulls are thinner,[67] they absorb twice as much microwave radiation,[68] they are physically smaller in size, they have a longer lifetime exposure and their cells undergo rapid cell division. This is likely to have serious implications for the developing brain, where neurons are being formed at a rate of 250 000 per minute on average in an unborn child over the course of a pregnancy[69] and the proliferation of radial glia and neurons continues to develop until almost 3 years of age.[70]

Gender

Gender differences in toxicant exposure are well documented. For example, women have higher peak blood alcohol levels than men when given the same dose because they metabolise alcohol more slowly than men,[71] have a smaller volume of distribution for alcohol and a higher percentage of body fat.[72] Similarly, multiple chemical sensitivity is significantly higher in women than in men,[73,74] which is suspected to be due to women's higher body fat-to-muscle ratio resulting in a higher body burden of toxicants and because women are often the primary consumers of personal care and cleaning products that contain solvents and EDCs.[7,75] In contrast, autism is four to five times more common in males than in females[76] and has been correlated with exposure to EDCs such as pesticides, phthalates, PCBs, solvents, toxic waste sites, air pollutants and heavy metals.[38] Most of these toxicants are anti-androgens and xeno-oestrogens, which have been shown in animal models to affect both brain and genital development in male progeny[77] and coincides with the sharp rise in the number of male reproductive abnormalities over the past 50 years.[78]

Gut microbiome

The metabolic activity of the gut microbiome is comparable to that of the liver,[79] with 850 bacterial genera involved in the metabolism of xenobiotics[63] and drugs.[79] A study conducted by the Pfizer pharmaceutical group discovered 'accidentally' individual variances in drug metabolism arising from the patient's gut microbiome.[80]

The metabolic profile of a patient's urine was tested before and after ingestion of paracetamol and it was found that the presence of *p*-cresol sulfate (a metabolite from *Clostridium difficile* bacteria found in the gut) significantly altered the ratio of paracetamol-sulfate and paracetamol-glucuronide metabolites in the urine. It was deduced that in patients with a gut microbiome excreting large amounts of *p*-cresol, the *p*-cresol competes for the same enzyme-binding sites and takes up a large part of the rate-limiting phase II sulfation pathway, such that paracetamol is forced to undergo phase II glucuronidation instead of sulfation.[80] In these patients, paracetamol-induced hepatotoxicity is increased, because depletion of glutathione levels causes the reactive metabolites to bind to macromolecules in hepatocytes.[81] Competitive inhibition (between toxicants and metabolites originating from the gut microbiome), resulting in higher blood levels of each chemical, is a phenomenon observed with increasing mixture complexity.[82]

This may explain why many mould-affected patients with associated gut dysbiosis appear to become chemically sensitive. *Why is this significant?* Many drugs, environmental toxicants and their metabolites, catecholamine neurotransmitters such as dopamine, adrenaline and noradrenaline, and hormones undergo phase II sulfation, so this has wide-reaching ramifications for human health. Interestingly, autistic children have been shown to have higher levels of *Clostridia*[83] and low sulfation capacity, which could cause a cerebral increase of catecholamines and subsequent changes in behaviour, especially when they eat foods high in phenolic amines (chocolate, wheat, corn sugar, apples and bananas).[84] Furthermore, *Clostridia* are present in higher numbers in many chronic illnesses such as Alzheimer's, Parkinson's disease and type 2 diabetes,[85] which coincidentally are also diseases commonly associated with various toxicant exposure to pesticides and heavy metals – both of which have been shown to alter gut flora. Depletion of glutathione stores may result in increased oxidative stress levels, especially in neurons and glial cells,[86] as well as many other downstream effects because of glutathione's involvement in iron metabolism, phase II glutathione conjugation, DNA synthesis and repair, protein synthesis, prostaglandin synthesis, amino acid transport and enzyme activation.

The gut microbiome is a major player in the pathogenesis of chronic metabolic and central nervous system diseases.[85,87] Gut microbes can influence the fate of neurons in various regions of the brain,[88] as well as the development and maturation of the microglia; produce neurotransmitters like GABA,[89,90] nitric oxide,[91] serotonin, noradrenaline and dopamine[92]; and influence anxiety and depression,[93] autism spectrum disorder,[88,94] Parkinson's disease[95] and psychiatric disorders in patients with intestinal dysbiosis.[96] Gut microbes produce short-chain fatty acids (SCFAs) from non-digestible carbohydrates, which have many biological actions including: being an important energy source for colonic epithelial cells[97]; regulating gene expression by binding to G-protein-coupled receptors found in a wide variety of tissues and cells (adipocytes, immune and endocrine cells)[98,99]; modulating intestinal gluconeogenesis and appetite[100]; regulating inflammation by acting on T regulatory cells[101,102]; and regulating the production of leptin.[103–105] This host–microbial relationship is bidirectional and is the end product of a billion years of permanent interaction with our environment.[106] Gut microbial diversity and composition are profoundly influenced by host diet, lifestyle, drugs, disease, the presence of pathogens, genetic background and environmental factors.[100,107–109]

Nutrition

Nutrition plays an important role in both the onset and the prevention of many chronic diseases associated with toxicant exposure. Complex interactions of multiple polymorphisms play a key role in how individuals respond to dietary interventions (*nutrigenetics*) and how some nutrients may affect gene expression (*nutrigenomics*),[110] which may inadvertently affect the way individuals deal with environmental toxicants. About 25 tonnes of food passes through a person's gut in their lifetime, making food the primary source of exposure to microbes and toxicants. The past 20 years have shown that diet and nutrients not only contribute to shaping the gut microbiota composition, but they also affect many genes related to inflammation and oxidative stress and provide key nutrients for a large number of biological processes vital for detoxification, the immune response (including gene expression), protein synthesis, modification and degradation, metabolism, signal transduction, and cellular proliferation and survival.[111,112] Numerous constituents in nutraceuticals (foods that provide health benefits) have been identified, including antioxidant flavonoids, proanthocyanidins, carotenoids, dietary fibre, phyto-oestrogens, glucosinolates, catechins, saponins and lignans,[113] which may explain the effectiveness of health-promoting diets like the traditional Mediterranean diet in lowering the risk of chronic diseases.[114,115]

Recent longitudinal studies investigating dietary intake in human centenarians have shown that micronutrients (zinc, copper, selenium) and polyphenolic antioxidants in fruits and vegetables play a pivotal role in maintaining and reinforcing the performance of the immune and antioxidant systems, as well as in affecting the complex network of genes.[112,116] Similarly, many foods have been implicated in the development of disease. A high-fat diet has been shown to disrupt Gram-negative intestinal populations of animals, liberating lipopolysaccharide and resulting in low-grade chronic inflammation.[79] Alcohol induces CYP2E1 enzyme (which is involved in phase I detoxification, activates various carcinogens and is responsible for metabolising many volatile organic compounds) and simultaneously depletes glutathione levels in the liver, thereby reducing the ability to detoxify other chemicals.[82] It is well established that a Western diet produces chronic inflammation due to excessive levels of omega-6 oils, saturated fat, sugars and starches, as well as a deficiency in micronutrients and antioxidants.[117,118]

Ethnicity

Ethnicity is an important marker for susceptibility to environmental toxicants and is the outcome of the

interaction between genetics, diet and geography, as family members who share a family history of heart disease are also more likely to share other risk factors such as diet, activity and place history.[119] Polymorphisms in key detoxification pathways and gut microbiota with distinct xenobiotic metabolising capacities also vary with ethnicity.[63]

ENVIRONMENTAL TRIGGERS OF DISEASE

Chronic non-communicable diseases share a common cluster of environmental and genetic risk factors that ultimately affect the individual's resilience and capacity to cope within their environment. The exposome of the individual, which is the totality of all human environmental exposure from conception to death, will vary depending on the dose, timing, duration, frequency and route of exposure to toxicants, as well as the individual's susceptibility. The increase in allostatic load brought on by environmental exposure results in an increase in the steady-state reactive oxygen species (ROS) known as oxidative stress at the cellular level, and low-grade systemic inflammation, which paradoxically are also the hallmarks of ageing and chronic disease.[86] While nutrition and xenobiotic metabolising enzymes derived from the gut and within the body (detoxification) can modify the risk of exposure to toxicants, in the absence of exposure, the presence or absence of gene polymorphisms becomes irrelevant. Consequently, the focus of clinical practice should be on educating the patient on how to reduce their exposure to harmful toxicants (see Fig. 2.1).[120]

TOXICANTS

The chemicals humans are exposed to, through their diet, home, workplace or environment, can have a profound effect on their health[121]: 27% of global chronic disease mortality is attributed to exposure to radon, ozone, lead, workplace chemicals, cigarette smoke, wood smoke (from cooking fires) and air pollution.[122] There are more than 124 million chemicals registered for use on the world's largest database, the Chemical Abstract Service,[123] and most of the artificial portions of these chemicals have never been tested for their impact on human health. Large population biomonitoring studies have revealed widespread exposure to toxicants at levels in humans known to cause adverse health effects.[7–10] While chemical exposure is ubiquitous in the general population, environmental hazards are inequitably distributed according to class, race, location and lifestyle factors.

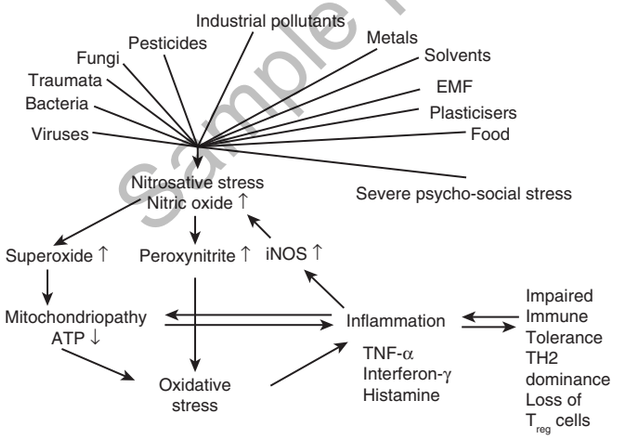

FIGURE 2.1 Pathogenesis of inflammation, mitochondriopathy and nitrosative stress as a result of exposure to environmental triggers.

Von Baehr V. Rationelle labordiagnostik bei chronisch entzündlichen systemerkrankungen. Umwelt Medizin Gesellschaft 2012;25(4):244–247.

Diseases associated with toxicant exposure

The list of diseases that have been implicated with toxicant exposure is extensive and growing and includes allergies,[124–127] diabetes,[128,129] infertility,[130–132] testicular dysgenesis syndrome[78,133] (which encompasses hypospadias,[134,135] cryptorchidism,[136,137] testicular cancer[138] and poor semen quality[139–141]), ovarian dysgenesis syndrome,[142] neurodegenerative diseases such as Alzheimer's[143] and Parkinson's disease,[144–146] respiratory disorders such as asthma[147] and chronic obstructive pulmonary disease,[148] autoimmune diseases,[149] obesity,[150–152] cardiovascular disease[153–157] and neurodevelopmental disorders.[50,158]

The environment is likely to play the principal role in most types of cancers as genetic factors have been shown to contribute only a minor role.[159] There is a growing body of evidence associating toxicants with various cancers, including air pollutants such as asbestos, radon, hexavalent chromium, tobacco smoke and benzo(a)pyrene with lung cancer[160–163]; EDCs such as pesticides, dioxins, furans and PCBs with an increased risk of breast cancer,[164] endometrial cancer, testicular cancer and prostate cancer[55,165–167]; arsenic and disinfection by-products with bladder cancer[168,169]; vinyl chloride with liver cancer[170]; benzene with leukaemia[171]; and pesticides with childhood leukaemia.[171–174]

Toxicants have also been linked to the rise in idiopathic environmental intolerance characterised by a chronic, complex multisystem disease that frequently and dramatically limits the activities of sufferers. These sensitivity-related illnesses (SRIs) have no clear aetiology or pathogenesis and attract various diagnoses from multiple chemical sensitivity to chronic fatigue syndrome, myalgic encephalomyelitis, biotoxin illness, sick building syndrome, Gulf War syndrome, fibromyalgia, electromagnetic hypersensitivity and systemic exertion intolerance disease. Clinical similarities and frequent comorbidities between these unexplained multisystem conditions of environmental origin have induced many authors to hypothesise that they may share common genetic and/or metabolic molecular determinants connected with polymorphisms in oxidative stress,[175] antioxidant and detoxification genes[176–178] with subsequent impaired capability to detoxify xenobiotics,[179] and mitochondrial dysfunction,[175,176] along with low-grade systemic inflammation in multiple organ systems.[176,180–182]

Sources of toxicant exposure

Taking an exposure history is essential to detect, treat and prevent toxicant exposure – see the ATSDR case studies.[183] Excluding occupational exposure to toxicants and pharmaceutical drugs, the primary sources of environmental toxicants are air, food and water. Rather than describing the numerous classes of chemicals (pesticides, heavy metals, flame retardants, food additives, preservatives, solvents etc.), this section focuses on the source of exposure.

AIR

Sources of air pollutants

- Natural sources: bushfires, storms, seaspray and volcanic activity
- Industrial emissions: living near industrial areas, mining areas, coal seam gas exploration, shipping ports, airports, military bases, municipal or waste sites and other 'sacrifice zones'
- Vehicle emissions: living, working or exercising in built-up areas close to heavy traffic, bus/truck/taxi depots, flight paths, mining areas, military bases; use of lawn mowers, boat motors
- Agricultural chemicals: living or working in close proximity to farming communities, timber plantations, market gardens, schools, parks, golf courses, bowling clubs and so on; applying pesticides and herbicides for pest management, veterinary and/or gardening purposes
- Volatile organic compounds: environmental tobacco smoke, new clothes, bedding, air fresheners, incense, perfumes, moth balls, dry-cleaning solvents, personal care and cleaning products, new building materials and furnishings, paints, thinners, solvents (spot removers, dry cleaning products)
- Particulates: asbestos and lead dust, as well as particulates generated from vehicle exhaust, mining and industry
- Radon gas: from the radioactive decay of uranium in soil, rock and water – levels in a home depend on the local geology and soil type (it is more commonly found in phosphate and granite deposits), house type, construction, materials and ventilation
- Noxious gases arising from unflued gas appliances, the incomplete combustion of solid fuels (wood/coal/dung/crop waste) for cooking or heating (open fireplace), ground-level ozone and photochemical smog in built-up areas.

Tips to reduce exposure to air pollutants

- Homes, workplaces and schools should be located away from known sources of air pollutants such as industrial zones, shipping ports, mining areas, flight paths, military bases, sewage sites, municipal tips and waste sites, bus/truck/taxi depots, carparks and heavy traffic
- New buildings and renovations should consider the microclimate and topography of the site to maximise the use of natural light, promote passive ventilation and good drainage, and reduce the need for artificial heating and cooling. They should also use natural, unadulterated, sustainable and hygroscopic building materials that are low in volatile organic compounds, are not radioactive and do not adversely impact the electroclimate of the space or the health of the occupants
- Homes located near known sources of air pollutants should be sealed and retrofitted with a whole house filtration system that includes HEPA and carbon filters
- Homes built prior to the 1980s should be tested for lead paint and asbestos by a licensed professional prior to conducting any renovations
- Air-conditioning and heating systems and natural gas appliances should be well maintained and serviced in accordance with the manufacturer's guidelines. The air intake for an air-conditioning system should not be located near food outlets or vehicle exhaust (i.e. garage, carpark)
- Heating and cooking sources that use wood, coal or dung as a fuel source (e.g. open fireplace, wood combustion stove) should be avoided
- Cars should not be left to idle in enclosed garages
- Exhaust fans in the kitchen, bathroom and laundry should be regularly cleaned and vented to the outside
- Environmental tobacco smoke, air fresheners, scented candles, incense, and perfume and fragrances in cleaning and personal care products should be avoided
- Furnishings should be made from natural fibres and materials (timber, glass, metal, bamboo, wool, organic cotton) that have been sourced and made locally
- An integrated pest management plan that avoids the use of chemical pesticides should be implemented
- Occupational exposure should implement the *hierarchy of control* in accordance with legislative requirements.

Lifestyle tips to reduce exposure to air pollutants

- Air the house on dry sunny days
- Avoid exercising in industrial and high-traffic areas
- Remove shoes before entering the home, as most pollutants are tracked into the house
- Expose new furnishings, pillows and mattresses to full sun (outside) to allow volatile organic compounds to outgas
- Wash new clothes, soft toys and bedding before use and air-dry them in the sun
- Limit use of personal care products and cosmetics and use products derived from certified organic plant-based ingredients, or still in their natural state, such as cold-pressed seed, nut or vegetable oils (jojoba oil, camellia nut oil, macadamia nut oil, rosehip oil, argan oil, moringa oil, sweet almond oil, coconut oil, tamanu oil, monoi oil)
- Cover up (hat, sunglasses, UV-resistant clothes) to reduce exposure to midday sun and reduce the need for chemical-based sunscreens
- Use slightly damp microfibre cloths to dust and clean the home and use cleaning products made from food-grade (not industrial-grade) ingredients that are fragrance-free
- Use a vacuum cleaner fitted with HEPA and carbon filters to reduce exposure to airborne pollutants.

FOOD

Sources of toxicants in food

- Pesticides, fungicides and herbicides used on fruits, vegetables, legumes, grains and nuts
- Food additives in processed foods such as food colouring, flavours, preservatives, acidity regulators, antioxidants, emulsifiers, stabilisers, thickeners, anticaking agents and sweeteners
- Eating top predators (fish) that are likely to contain heavy metals and persistent organic pollutants
- Antibiotics, agrochemicals and antiparasitic drugs used in livestock
- Radioactive nuclides occurring naturally in soil and water or arising from nuclear accidents
- Heavy metals in plants and animals (arising from artificial and natural sources)
- Food packaging made from plastic (phthalates, bisphenol-A) and tins (BPA lining, lead solder)
- Cooking utensils: copper or aluminium pots and pans, eroding non-stick cookware, plastic bakeware
- Plastic wraps and containers (numbers 1, 3, 6 and 7), lead- or cadmium-containing glazed ceramics or containers with leaded crystal or radioactive glazes
- Freezing or heating food in plastic.

Tips to reduce exposure to toxicants in food

- Eat food that is:
  ***S**easonal* (has adapted to the microclimate of the region)
  ***L**ocal* (low in embodied energy)
  ***O**rganic* (free from pesticides)
  ***W**hole* (still in its natural state)
- Consume less processed (packaged) food and make meals from scratch using ingredients based on the SLOW principles
- Follow a plant-based diet, which is low on the food chain and less likely to accumulate persistent organic pollutants commonly found in top predators
- Store, freeze and cook food in oven/freezer-proof glass, stainless steel, cast iron, ceramics or Corning Ware
- While non-stick cookware should be avoided, ceramic-lined non-stick cookware is available that does not use perfluorinated chemicals.

WATER

Sources of drinking water pollutants

- Contamination of ground and surface water arising from natural sources: bushfires, storms, seaspray, volcanic activity, high mineral content in rocks (arsenic); and from human sources: industrial emissions, vehicle exhaust, fertilisers, pesticides, mining, effluent (animals and humans), municipal tips and proximity to 'sacrifice zones'
- Disinfectant by-products (fluoride, chlorine, alum) used to purify water
- Radioactive nuclides such as radon gas
- Contaminants arising from the mains distribution and domestic pipes such as asbestos, heavy metals (copper, lead, silver), biofilm and phthalates in plastics
- Contaminants arising from the catchment areas used for tank water such as PVC downpipes, asbestos, lead flashing, microbes, solvents, pesticide drift and sealants on roof and solar panels, animal droppings
- Storage vessels made from plastic (polyvinyl chlorine, polystyrene, polycarbonate), acrylonitrile butadiene styrene (ABS), lead-glazed or radioactive ceramics and heavy metals in older pigments.

Tips to reduce exposure to water pollutants

- Use storage vessels made of glass, food-grade stainless steel, unglazed ceramics or Corning Ware
- While there is no ideal water filter system, the type of water filter used depends on the source of drinking water (tap, tank, bore/well or bottled water), which contaminants you want to remove, water pressure, bench space and how much you are prepared to spend to buy and maintain the unit
- Pre-sediment filters filter out larger particles such as sediment and prolong the life of carbon filters
- Carbon filters filter out chlorine and its by-products, pesticides, petrochemicals and other organic contaminants but not heavy metals or fluoride
- Deioniser filters remove fluoride and heavy metals but not organic contaminants such as pesticides and may leave resin fragments in the water
- Ceramic filters reduce bacteria, chlorine, sediment and rust, but are not effective in removing heavy metals or pesticides, and require weekly maintenance to remove the biofilm
- Ozone oxidises organic contaminants such as pesticides and microorganisms, but is an irritant gas that can be lethal at high doses, which is why it shouldn't be used for domestic water filtration. UV filters are used to kill bacteria, algae and parasites and reduce cysts, but they are ineffective in hard or turbid water and their efficiency dramatically declines when dirt accumulates on the lamp. Reverse osmosis removes most contaminants including fluoride (providing the flow rate is not too high), but it is costly, needs to be plumbed in to remove waste water, needs a lot of space (bench or under the sink) for the storage tank and is slow to filter. Consequently, combination filters are often used for domestic purposes. Water filters should be certified with the National Sanitation Foundation (NSF) to confirm the effectiveness of the filter.

ELECTROMAGNETIC FIELDS

Life on earth has evolved within an exquisite and dynamic array of natural electromagnetic energy sources arising from the earth's magnetic field (geomagnetic field), radioactivity (cosmic and x-rays from the galaxy and radioactivity within the earth's crust), the sun, gravity and the Schumann resonances. The geomagnetic field influences both the magnetic alignment and the migration and homing of various animal species from bees, ants, termites and fruit flies to birds, fish, cows and deer.[184] In the human body, terrestrial radiation provides remarkably

low-intensity yet critical frequencies that play an important role in our circadian rhythms, sleep and wake cycles, brainwave activity, neural synchrony, immune function, behaviour and onset of puberty, as well as gene expression, cell communication and metabolism.[185]

In the past 20 years, we have progressively added an enormous amount of artificial frequencies to the planet's natural electromagnetic background to the extent that there is practically nowhere remaining that is not being influenced by it in some way. The rapid uptake of mobile phones (more than 6 billion users worldwide) and deployment of wireless technologies in our homes, schools and workplaces reflects our voracious appetite for technology and has given rise to a plethora of new terms like Google, Facebook, Twitter, Snapchat and digital dementia.[186]

There are four electromagnetic fields that impact the built environment: AC electric fields (voltage), AC magnetic fields (current), radiofrequencies used in wireless technologies, and dirty power (high-frequency spikes and harmonics on electrical wiring). The frequencies that consistently appear in the scientific literature and for which health concerns have been raised are AC magnetic fields and radiofrequencies, and these are the focus of this section.

Mechanism of action

Electromagnetic fields are used in medicine for both diagnostic purposes (magnetic resonance imaging, electrocardiograms, electroencephalograms [EEGs]) and in the treatment of a range of disorders from neonatal jaundice to depression, pain-related disorders, osteoporosis, degenerative affections of peripheral joints, wound healing, rheumatoid arthritis and ankylosing spondylitis.[187–191] Epidemiology and EEG studies provide compelling evidence for the existence of non-thermal effects (low-level exposure effects) arising from the regular use of mobile phones, which use radiofrequency electromagnetic energy.[192] When cells are exposed to low-intensity radiofrequency radiation they produce ROS for several minutes or even hours after irradiation, which can increase the cells' expression of antioxidants.[193,194] Similarly, the health-promoting benefits of magnetic fields are attributed to their ability to alter intracellular concentrations of sodium and potassium ions, resulting in vasodilation, angiogenesis, anticoagulation activity, intensification of the processes of repair and regeneration of soft tissues, and anti-oedematic properties, as well as analgesic activity.[187,190,195] These events may contribute to the activation of protective or damaging processes and are suspected to play a key role in the induction of the radioadaptive response.[196–198] Among 100 currently available peer-reviewed studies dealing with oxidative effects of low-intensity radiofrequency radiation (RFR) used in wireless technologies, 93 confirmed that RFR induces oxidative effects in biological systems.[199]

Paradoxically, the mechanism by which electromagnetic fields may induce protective effects is similar to the way in which they may cause harm. The cell membrane is hydrophobic, consisting of ion pumps to prevent the free movement of ions across the cellular membrane. Electromagnetic fields may cause biological effects by activating L-type voltage-gated calcium channels (VGCCs) in the cell membrane, enabling calcium ions to flow into the cell with subsequent multiple downstream effects.[200,201] This mechanism of action has been confirmed by the observation that these downstream effects can be completely negated with the use of calcium channel blocker drugs.[200,201]

The Russian physicist Igor Lednev demonstrated that when the frequency of the alternating magnetic field is equal to the harmonics, subharmonics or cyclotron frequency of ions (like calcium) bonded to proteins, a resonant response of the biosystem to the magnetic field results that may disrupt or enhance cellular function.[202–204] The subsequent increased intracellular calcium activates nitric oxide synthase enzymes, resulting in the production of nitric oxide, which can lead to one of two pathways: nitric oxide signalling (therapeutic effect) or, after reaction with superoxide, the formation of the very reactive peroxynitrite free radical (harmful effect).[205,206] Low levels of these ROS free radicals activate antioxidant enzymes (superoxide dismutase, catalase and various peroxidases), while high levels inactivate them, resulting in an increase in the steady-state ROS known as oxidative stress.[194,201,207,208]

This may result in mitochondrial dysfunction, DNA strand breaks,[194,201,209,210] inhibition of DNA repair in stem cells[211] and apoptosis (cell death) and cause oxidative damage to proteins, membranes and genes.[116] Furthermore, ROS may contribute to the down regulation of tight junctions and therefore induce the matrix metalloproteinases (MMPs), thereby enhancing the permeability of the blood–brain barrier.[212] Disturbance of this redox balance, uncontrolled activation of free radical processes, overproduction of ROS and/or suppression of antioxidant defence in the cell brought on by radiofrequency exposure[213] at non-thermal effects are often the important signals of some hazardous changes in cell metabolism. Other documented effects include an increase in histamine, which is a major cause of systemic inflammation,[214] and suppression of the 'anticancer' hormone melatonin, which is the body's most potent weapon against cellular and DNA damage.[215,216] The 'dose window theory' in non-ionising radiation-induced adaptive responses[217] is suspected to be nonlinear[193,218] and explains why the impact of low-frequency fields on biological systems appears to induce both protective (within a narrow window) and damaging effects, which makes this field of study both highly controversial and contradictory.

Several authorities (International Commission for Non-Ionising Radiation Protection, US National Cancer Institute, World Health Organization, UK Health Protection Agency, Australian Radiation Protection and Nuclear Safety Authority, Health Canada, New Zealand Ministry for the Environment and the Swedish Radiation Protection Authority) adhere to the concept that non-ionising radiation cannot cause cancer because, unlike ionising radiation, it does not have enough energy to dislodge electrons and harmful effects arising from RF EME occur

only due to heating.[219] Applying the ionisation model to non-ionising radiation is inappropriate because peer-reviewed research has shown that RF EME may indirectly induce cancer by generating ROS, which damages DNA and interferes with antioxidant repair mechanisms.[199,219–222] Electromagnetic fields may potentiate the effects of metals and toxicants. In one study, exposure to magnetic resonance imaging and mobile phones significantly accelerated mercury vapour released from dental amalgams.[223]

Health effects attributed to electromagnetic field exposure

Concerns about electromagnetic fields were first brought to light in military personnel on radar bases during World War II and later in electrical workers involved in the telecommunications industry. However, it wasn't until Wertheimer and Leeper published their research on high-voltage power lines and childhood leukaemia in 1979 that concerns about electromagnetic fields on public health came to the fore.[224] While it is recognised that non-ionising electromagnetic fields typically found in the built environment cannot cause gene mutations, cancers that consistently appear in the scientific literature are childhood leukaemia, breast cancer and brain tumours (acoustic neuromas and gliomas). There is a significant body of evidence showing a link between AC magnetic fields in excess of 3 mG and childhood leukaemia,[224–228] with documented exposure zones up to 600 m from high-voltage transmission lines.[229,230] It is estimated that AC magnetic fields above 3 mG are responsible for up to 2% of all cases of childhood leukaemia annually.[227,231] This exposure level can easily be exceeded in a home if individuals spend prolonged periods of time – such as when sleeping, working or relaxing – within 1 m of a smart meter, meter panel, inverter, oven (while it is heating), fridge (while it is cooling) or any other appliance that draws a high level of current. Two pooled analyses on high-voltage transmission lines and childhood leukaemia in the year 2000[225,232] were sufficient to convince the World Health Organization's International Agency for Research on Cancer (IARC) to classify AC magnetic fields as a possible human carcinogen.[233] Using a mobile phone for more than 25 minutes per day reduces production of the body's most potent antioxidant free radical scavenger, melatonin.[234]

The annual incidence of head tumours coincides with the increased rate of mobile phone subscriptions,[235] although there are significant disparities about the rate even among researchers from the same country.[236,237] Part of the problem lies in when the data were collected. Many studies, including the Danish Cancer Registry, analysed data well before mobile phones were adopted by the general public.[238–244] A significant increase in glioma incidence in the Australian population was identified after 2006,[236] which coincides with the time period when mobile phones were widely adopted.[245] However, these findings contradict the Australian government's findings because the cancer registries were not updated. 'Late ascertainment' is common among cancer registries and is associated with a data lag of between 3 and 5 years.[246] Another issue is that the frequency of brain tumour diagnosis on autopsy has declined substantially due to a general decline in the number of autopsies being performed, rendering some cancer registries unreliable for use in epidemiological studies.[247]

There have been several studies[248–252] and numerous reports[253–256] correlating an increased risk of glioma and acoustic neuroma with mobile phone use. The three most influential case-control studies to date are INTERPHONE (European), CERENAT (French) and Hardell's (Swedish) study, which identified an increased risk of gliomas and acoustic neuromas in people who used their phone for at least 30 minutes per day on one side of the head for a minimum of 10 years. The largest study, the INTERPHONE study involving more than 5000 people, identified a 40% increased risk of glioma,[249] while the CERENAT study calculated a 100% increased risk of glioma,[248] and Hardell's research team identified a 170% increased risk of glioma[251] in addition to increases in other brain tumours (acoustic neuromas and meningiomas).[250,251,257,258] Similar results were obtained in a meta-analysis, which showed an increased risk of gliomas and acoustic neuromas with long-term use of over 10 years.[259] Some have argued that the CERENAT and INTERPHONE studies underestimated the risk because they ignored the radiation emitted from DECT phones.[258,260]

In contrast, there have been many studies for which a correlation has not been observed.[237,243,261–264] Several of these studies analysed brain tumour incidence in patients well before mobile phones were widely adopted by the general public. The INTERPHONE study is an interesting case in point: three groups of researchers came up with completely different conclusions analysing the same data.[263,265,266] The CEFALO multicentre case-control study focused on the possible association between mobile phone use and brain tumours among adolescents and showed no correlation.[267] The authors acknowledged several (major) flaws with their own study, including the fact that mobile phone use was based on the memory of the child or their parents to recall their use (i.e. it didn't measure the dose), the latency period was short as the children had used their phone for less than 4 years and most of the children rarely actually used a mobile phone!

It remains unclear whether the correlation between brain tumours and mobile phone use is coincidental or whether use of mobile phones may cause the development, promotion or progression of specific cancers.[268] There are several reasons why there are discrepancies in mobile phone research:

- The tendency to adjust the research to fit the needs of the industry providing the funding[253]
- Differences in study design – frequency, intensity and duration of exposure – which makes it impossible to compare studies
- The long latency period associated with primary brain tumours
- The time period that the data were analysed
- No exposure data because of reliance on self-reported mobile phone use or data obtained from service providers

- The age of first exposure (higher risks are observed in people who began mobile phone use before the age of 15)[250]
- The use of provocation 'feeling' studies popular among psychologists, which do not allow for the 2–3 days acclimatisation or immune washout typically observed in animal studies.[269–271]

Swedish professor Lennart Hardell, a world expert on mobile phone research, has consistently observed a statistically significant higher risk of developing glioma types of brain tumours in people who use mobile phones using digital frequencies, namely the 3G network, before the age of 20.[250,257] As wide-band microwave signals (3G onwards) were only launched in the early 2000s and it wasn't until 2005 when mobile phones became popular among children,[245] the increased incidence of brain tumours (gliomas and acoustic neuromas) with latency periods of up to 25 years would not be expected until the latter half of the 2020s. Despite this, many existing large-scale population-based studies, including the COSMOS study[272] and the MOBI-Kids study,[273] have failed to gather exposure data, even though apps exist to accurately estimate radiofrequency emissions from mobile devices.[274]

Collecting reliable data on complex and rapidly changing patterns of exposure, while minimising recall bias and errors, will be a significant challenge for ongoing large-scale population-based studies in mobile phone research. Despite this, on 31 May 2011 following an analysis of 900 publications by 30 scientists, the IARC classified radiofrequency electromagnetic energy as a possible human carcinogen.[275] On this basis alone, the precautionary principle should be enacted and the public should be informed about current scientific uncertainty and advised to limit their exposure by adopting the inverse square law (distance).

Electromagnetic fields have also been correlated to other chronic diseases. Two recent reviews concluded an increased risk of female breast cancer following AC magnetic field exposure,[276,277] with some quantifying exposure in excess of 12 mG as being significant[278,279]; however, there are many studies for which an association was not found. Similarly, neurodegenerative diseases like Lou Gehrig's disease (motor neurone disease), Parkinson's disease and Alzheimer's have also been reported following exposure to radiofrequency electromagnetic energy, with inconsistent results.[212,255,280–282]

Electromagnetic hypersensitivity (EHS), or idiopathic environmental intolerance to electromagnetic fields (IEI-EMF), is a syndrome arising from exposure to electromagnetic fields with a broad spectrum of nonspecific symptoms involving multiple organ systems. The wide variation in symptoms experienced by sufferers may be attributed to the local effects that electromagnetic fields may have on voltage-gated calcium channels. EHS is estimated to affect 2–6% of the population (primarily women), with the highest incidence of 13% observed in the Taiwanese population.[283] EHS was first acknowledged as a disability in Sweden when it was documented in computer workers in the 1980s and pressure is mounting on the World Health Organization to recognise it as a medical disease. According to Bevington,[284] the European Academy for Environmental Medicine,[285] the Austrian Medical Association[286] and the British Society of Ecological Medicine,[287] symptoms of EHS may include the following:

- General: long-term fatigue, headache, sleep disturbance, flu-like symptoms
- Heart and circulation: chest pain, increased heart rate, blood pressure changes, arrhythmias, shortness of breath, nosebleeds, cold extremities
- Brain: brain fog (anomia, poor short-term memory, difficulty concentrating), dizziness, confusion, dyslexia, difficulty learning, mood swings
- Ears: earache, tinnitus (ringing in the ears), problems with balance
- Eyes: dry and gritty, eyelid ties, irritation, pressure behind eyes
- Skin: itchy, prickling and biting sensation on the skin like 'electric shocks', rash, lumps, brown 'sun spots', a sensation of warmth or burning likened to sunburn
- Muscles: body aches and joint pains, jaw and teeth pain, numbness or tingling sensations, muscle spasms/tremors, weakness, restless legs
- Sensitivities: chemical, light, noise and/or smell.

Sufferers can often pinpoint which building and/or rooms make them unwell: the symptoms significantly improve when they are away from the electromagnetic field and they are relieved with avoidance, bathing and shielding.

Testing for electromagnetic fields

- *Clinical testing.* The lack of available clinical biomarkers to test for EHS has been part of the problem in gaining recognition for the syndrome. The Austrian Medical Association in 2012[288] and the European Academy for Environmental Medicine in 2016[285] developed guidelines for doctors on how to diagnose and treat electromagnetic field-related health problems as a duty of care, including a detailed questionnaire, the scope of which is beyond this chapter
- *Exposure data.* Collecting individual exposure data for radiofrequency electromagnetic field exposure is freely available through apps such as Quanta Monitor by Cellraid
- *Home testing* for AC magnetic fields and radiofrequency electromagnetic energy fields in the patient's home and workplace by a qualified building biologist is recommended to identify and reduce exposure to potential sources. While AC magnetic fields can easily be measured using a three-axis digital gauss meter, radiofrequency electromagnetic energy fields require specialist equipment such as a spectrum analyser or high-frequency meter (with a wide range from 27 MHz to 10 GHz). In addition, it requires a thorough knowledge of the various frequencies used by wireless devices, an understanding of the way in which radiofrequencies are influenced by metal building materials such as sarking, reflective foil insulation and metal roofs, knowledge of exposure standards that encompass the precautionary principle and the

limitations involved in spot and short-term measurements. AC magnetic fields above 3 mG can easily be exceeded if you sleep against a wall adjacent to a meter panel, smart meter, inverter, fridge, electric hot water system or oven (when it is heating) or have a digital clock radio within 20 cm of the bed.

Sources of AC magnetic fields

- Outside sources: high-voltage transmission lines, transformers, substations, power lines, tram lines, electricity meters (analogue, digital and smart meters) and inverters (from solar panels)
- Inside sources: all operating appliances that are connected to the building wiring. Higher fields (that draw more current) occur in appliances with a built-in transformer, electronic ballast or motor, including freestanding lamps, halogen desk lamps, energy-saving compact fluorescent lamps and bulbs, older style fluorescent lights, digital clock radios, mobile phone chargers, electronic beds, water beds, fridges, ovens, fish tanks and pool/water feature pumps. High AC magnetic fields also arise when the active and neutral wires are separated, such as in meter panels, switches, some types of electric blankets and electric underfloor heating (hydronic heating is not a high source). Visual display units/monitors are not a high source of AC magnetic fields because they comply with TCO certification (a type of sustainability certification)
- Transient exposure to high AC magnetic fields above 3 mG (such as walking past a meter panel or under powerlines) is unlikely to create a health issue. However, long-term exposure to low levels should be avoided where occupants spend the greatest amount of time, such as in bed, at a desk while studying or working, lying on a favourite sofa or while at the kitchen sink and benchtop where food is prepared. High AC magnetic field readings on the ground floor of older homes may arise if the metal water pipes carry a charge as the earthing system is connected to the power mains neutral conductor.

Tips to reduce exposure to AC magnetic fields

- AC magnetic fields penetrate most materials including concrete, brick and steel and there are few shielding materials (apart from Mu metal) that contain these fields. The most effective method to reduce exposure is distance (inverse square law). Depending on the source of exposure, a distance of at least 1 m from appliances should apply in areas where the occupant spends long periods of time, such as in bed
- When building or rewiring a home, exposure to the AC magnetic field from the wires can be reduced by bundling the cables together and keeping appliances and power boards away from the walls where people spend time, such as walls against a bedhead, sofa or workstation
- Battery-operated and wind-up devices are also recommended.[186]

Sources of RF EME

- Outside sources: mobile phone towers/base stations, radar (military, airport, sea port, traffic and weather control), TETRA (emergency services), digital television and radio towers
- Inside sources: mobile phones, cordless phones, smart meters and wireless devices (routers, computers, laptops, printers, photocopiers, fax machines, iPads, iPods, fitness trackers, Bluetooth, baby monitors, security systems), hearing devices and communication systems such as wireless paging systems used in hospitals and restaurants. Many new appliances coming onto the market will be fitted with ZigBees to enable them to connect wirelessly to a smart meter. This enables the power company to remotely switch off appliances in the home like air conditioners to conserve power. The adverse health effects arising from exposure to these radiofrequencies has not been studied. It is important to avoid using a mobile phone in a car because (apart from causing accidents) the radiofrequency electromagnetic energy will reflect off the metal carriage thereby multiplying the exposure in the same way these frequencies bounce inside a microwave oven.

Tips to reduce exposure to external sources of RF EME

- RF EME reflects off metal and penetrates glass (windows), timber and bricks. As such, metal roofs and foil insulation in the walls will reduce exposure to external sources but will reflect internal sources back into the home. Shielded fabrics, paints and window films can reduce exposure to external sources. Metal blinds that are closed at night also reduce exposure to external sources coming in through a window.[186] The most effective way to reduce exposure to electromagnetic fields is distance. As you double the distance away from an RF source, you will reduce your exposure by 75%.

TIPS WHEN USING CORDLESS AND MOBILE PHONES

- Use a hardwired corded phone whenever possible to make or receive a call
- Keep cordless and mobile phones away from the head by texting or using the loudspeaker function or using an ear piece when making or receiving calls
- Keep calls short
- Do not carry the phone on your body (in your bra or pocket). Carry it in a handbag or place it in a shielded pouch
- If you must use a cordless phone, purchase an analogue model as they emit radiation only when a call is made, and keep the base unit at least two rooms away from bedrooms
- Avoid using a mobile phone in a moving vehicle (tram, train, bus, car) as it emits higher power to maintain a signal with the nearest mobile tower
- Do not charge mobile phones in bedrooms and do not use them as an alarm clock placed under the pillow

- Avoid making calls in areas with poor signal strength: use the phone when the maximum number of bars are on the screen (with fewer bars, the phone emits higher power to maintain the signal)
- Children under the age of 15 should avoid using mobile phones except in an emergency. Texting is preferred as it keeps the phone away from the head. If children play games on a mobile phone, set it to flight mode in order to turn off the wireless connection.[186]

TIPS WHEN USING PORTABLE WIRELESS DEVICES

- Use appliances that use hardwired cable options that don't connect wirelessly
- When in use, place the device on a table or desk away from your body
- Once you have downloaded the information/app from the internet, turn off the wireless connectivity by putting the device in flight mode.[186]

TIPS WHEN USING A ROUTER (MODEM)

- Use a hard-wired cable connection (ADSL) for desktop computers; however, it will restrict internet connectivity to one area of the home. For multiple users, install an ethernet home network which uses a powerline ethernet adapter (such as a TP-Link) plugged into the power socket using the existing electrical wires in your home. This requires a dual modem (with the wi-fi switched off) with an ethernet plug so that it can connect to the TP Link
- Check with the manufacturer to determine how to disable the modem's wireless function. Be mindful that some new modems do not have a cable option
- Keep the router away from areas where people spend time, such as the bedroom, office and living areas. Instead, install it in the garage or a spare room or formal living room that is rarely used
- Power the router down by 95% so that the RF EME fields don't bathe the entire house. For instructions on how to do this, see the manufacturer's website
- Unplug the router when it is not in use, especially at night
- Avoid using extenders (repeaters). Instead, dedicate a specific area of the house to access the internet
- If you live in a multilevel apartment or if your home is attached to another, encourage the neighbours to switch off their wireless devices at night
- In schools, wireless laptops and work stations should be avoided and replaced with standard or fibre-optic cables connected to a rooftop antenna.[186]

ALLERGENS

The interactions between allergens, the immune response, sensitisation and airways disease are highly complex and not yet completely understood.[289] Current thinking suggests a multifactorial model for allergy, in which an initial trigger (viral or environment) stimulates the innate immune response to effect prolonged chronic inflammation, which might – in those with a genetic susceptibility – interact with exposure to an allergen-facilitating allergy.[289] Where pollen sensitisation is strongly associated with the development of allergic rhinitis, indoor allergen sensitisation is associated with asthma.[290] This section focuses on aeroallergens (not allergies arising from exposure to pharmaceutical drugs or food).

In the past two decades, the incidence of allergies such as asthma, atopic eczema, allergic rhinitis and food allergies has steadily increased in Western countries, with strikingly different time courses observed in various locations.[291–295] Australia is leading the allergy epidemic: 25% of the population have been diagnosed with an allergy,[296] 20% of adults have allergic rhinitis, 10% of adults and up to 25% of children have asthma and 10% of children have food allergies and atopic eczema.[297] The increase in respiratory allergic disease since the 1990s has coincided with a 10% increase in food allergies (to cow's milk, egg, nuts, wheat) and a 30% increase in atopic eczema worldwide.[291,298] During this period, hospital admissions for anaphylaxis has more than doubled in the US[299] and increased four-fold in Australia[297] and six-fold in England and Wales,[300] reflecting similar trends in other Western countries.[301,302]

The introduction of allergenic food to infants has been met with much controversy, as delayed introduction has been shown to increase the incidence of developing food allergies.[303] New guidelines recommend breastfeeding for at least 6 months, introducing a variety of solids at around 6 months of age (but not before 4 months of age), and introducing allergenic solid foods including peanut butter, cooked egg, dairy and wheat products in the first year of life.[304] While most childhood food allergies tend to decline with age (except wheat, shrimp and nuts), around 50% of affected children go on to develop inhalant allergies to house dust mites, grass pollens or cat dander (the most prevalent environmental allergens), resulting in allergic rhinitis and asthma later in life. This is known as the 'Atopic (Allergic) March'. With the exception of allergic rhinitis, which appeared in the latter half of the 19th century when changes in farming practices introduced foreign grass pollens following the repeal of the Corn Laws in the UK in 1846,[305] the increase in allergic disease to perennial indoor allergens did not start until post–World War II, when there were significant changes in farming practices, hygiene, housing and lifestyle factors.

The hygiene hypothesis proposes that a lack of infections early in life predisposes children to allergies later in life.[306] The introduction of television in the 1960s and the push to use chemical cleaning products to 'sterilise' the home resulted in children adopting an indoor lifestyle, which significantly reduced their exposure to 'germs'. Furthermore, the move to create airtight and energy-efficient homes that are warmer and more humid, in conjunction with the use of wall-to-wall carpets and an indoor-centric lifestyle, have resulted in an increased exposure to indoor allergens such as house dust mites and mould.[186] It is an interesting coincidence that childhood asthma began to increase from 1960, and by 1990 had increased to epidemic proportions in all countries where children had adopted this lifestyle.[294] Consequently, the immune system (wanting to be busy all the time) turns its attention to otherwise harmless antigens. While the validity of the hygiene hypothesis is still being debated

among experts,[307] it is interesting to note that the progressive shift to a Western lifestyle in the Middle East and Asia has correlated with a rise in the prevalence of allergic respiratory diseases.[295,308]

The microflora hypothesis has recently emerged as another theory to explain the rise of allergies in Western countries. There is a significant body of evidence to suggest that the gut microbiome plays an important role in the prevention of allergic disease because of its capacity to 'program' immune responses early in life. The rapid evolution of gut microbiota occurs early in life, arising initially from exposure to the mother's vaginal flora during birth. Babies delivered by caesarean section (which occurs more commonly in Western countries) harbour gut bacterial communities that resemble those found on the skin, which is significantly less diverse compared with gut bacterial communities of babies delivered vaginally.[309] Apart from the mode of birth, other risk factors have been identified to explain how the Western lifestyle limits microbial exposure. Breastfeeding rates continue to decline in Western countries, despite breastfeeding being shown to provide a protective role because it is high in oligosaccharides (prebiotics), which are essential for infant gut health and inhibit the binding of pathogens and toxins.[310,311] The overuse of antibiotic drugs in Western countries has been shown to have dramatic and devastating consequences on the infant's gut microbiome.[312] Increased financial pressures, birth control and delaying motherhood have all resulted in a significant decline in the birth rate in Western countries, which may increase the risk of allergies because not only are humans an important source of microbial diversity in the built environment, but they also contribute to resuspension of microbes in the air.[313] Each person contributes 14–37 million bacterial genome copies per hour in the air, and it is interesting to observe that the presence of older siblings appears to induce a protective role against the development of allergies.[314,315] The ubiquitous and indiscriminate use of chemicals such as pesticides, antibacterial chemicals, disinfectants, preservatives and solvents in household cleaning and personal care products and fungicides in building materials have reduced the microbial biodiversity in household dust.[186] The combination of bacterial exposure in dust and higher allergen levels in the first year of life has been shown to be protective against the development of atopic asthma.[316]

Numerous epidemiological studies have shown that children who grow up on traditional farms with livestock and fodder are protected from asthma, hay fever and allergic sensitisation,[317] especially if exposure occurs in the womb and the first year of life.[318] A recent and important study compared the immune profiles and microbiomes of indoor dust levels of Amish versus Hutterite farm children whose genetic ancestry and lifestyles are similar, but whose prevalence of asthma and allergies are strikingly dissimilar.[319] They discovered that Amish homes have very high endotoxin levels in their household dust, which provides intense and sustained exposure to microbes, triggering a healthy innate immune response – which may explain why Amish children have very low rates of asthma and allergies compared with Hutterite farm children. The idea that microbial exposure in household dust may influence the composition of an infant's gut microbiome is quite plausible given that an infant's breathing zone is close to the floor and that infants have a very high hand-to-mouth ratio (they can swallow up to eight times more dirt than adults). The primary difference between the Amish and Hutterite communities lies with their farming practices: the Amish use traditional methods, while the Hutterites use industrialised farming practices that include the use of pesticides. It is interesting to note that the 1950s and 1960s experienced significant changes in farming practices with the introduction and ubiquitous use of pesticides in air, food and water – and this period coincides with the time that asthma incidence began to rise. The first 3 years of life are critical in the formation of future allergies,[320] and coincidently this is also the time when the phylogenetic composition of the bacterial communities found within the gut of most children closely mirrors that of the adult.[321] The state of the gut microbiome in the first 3 years of life may therefore provide important clues to the trajectory of allergenic diseases later in life. Children brought up on farms are less likely to develop asthma and allergies.[322,323]

There is a significant body of evidence correlating air pollution with allergic diseases such as eczema, asthma and allergic rhinitis.[125–127,324–326] Part of the problem lies with the fact that many air pollutants are associated with allergic sensitisation, damage the nasal mucosa, impair mucociliary clearance and potentiate the allergic immune response.[126,327,328] Furthermore, individuals with allergic diseases are generally more responsive to airborne irritants.[316] Air pollutants that have been shown to increase asthma and indoor allergen potency include environmental tobacco smoke, ground-level ozone, nitrogen dioxide and traffic-related air pollutants such as diesel particulate matter.[329–331] Atopic individuals living within 200 metres of a major road have an increased risk of asthma and allergic outcomes.[126]

House dust mites

House dust mites (HDMs) affect up to 21% of the population, making it one of the most common allergies in the world.[332,333] HDMs are the leading cause of hay fever and allergic asthma worldwide[333,334] and up to 85% of asthmatics are allergic to them.[335] Atopic individuals react to the combination of allergenic proteins (Der p 1 and Der p 2) and microbial by-products in dust mite faeces (frass).[336] House dust mite ratios are significantly higher in a bed (1884 mites/g of dust) as opposed to a carpet (601 mites/g of dust).[337]

SOURCES OF HOUSE DUST MITES

HDMs require moisture, warmth (above 25°C) and food (human and pet dander, cellulose from textile fibres, pollens and microbes). High levels of mites are typically found in bedding, carpets, soft furnishings, fabric window dressings and soft toys. Levels greater than 10 micrograms/g (equivalent to 500 mites/g of dust) are deemed capable of causing acute asthma in sensitised people.[335] HDM allergies peak in spring and late autumn, 2 months after a spike in mite numbers during late summer when humidity is highest

and average monthly temperatures exceed 23°C.[334,338] These conditions occur in beds (where we sweat and shed skin cells), which is why HDMs are most prevalent in bedding. HDM allergens in Australian homes are among the highest recorded worldwide and often well above the 10 micrograms/g (500 mites/g of dust) deemed capable of causing acute asthma in sensitised people.[338, 339]

HEALTH CONCERNS ASSOCIATED WITH HOUSE DUST MITES

Unlike pollens which occur seasonally, HDM allergies occur all year round, so the symptoms are generally always present to some extent, although their intensity varies over time depending on humidity and temperature and the prevalence of mites in the indoor environment. Typical symptoms include itchy and watery eyes; sneezing; an itchy, runny or blocked nose; a dry persistent cough; wheezing; and dermatitis.[289,334,340] Symptoms are worse at night and upon waking and generally improve when sufferers are away from the source. People with an HDM allergy are often diagnosed with asthma, hay fever, perennial sinusitis or eczema. Non-allergic individuals may experience an exacerbation of asthma, and continual exposure to dust mite allergen may be a contributing cause of chronic bronchial hyperreactivity.[341]

TESTING FOR HOUSE DUST MITES

- Allergies can be confirmed by an allergy specialist or clinical immunologist who may perform skin prick tests (used for food and inhaled allergens such as pollen, dander and dust mites) or blood (RAST) tests
- The use of in-home test kits to measure HDMs along with education may beneficially influence behaviours and attitudes towards dust mite reduction strategies and help reduce residential dust mite allergen levels.[342] Safe levels are regarded as less than 2 micrograms of Der p 1/g of dust (100 mites/g of dust).[343]

TIPS FOR REDUCING LEVELS OF HOUSE DUST MITES

As there is no cure for HDM allergy, it is essential to reduce HDM levels as far as is practicable in the home. The best place to start is the bedroom.

- Reduce dust levels in the bedroom: this is important as carpeted floors have been shown to have twice the amount of dust mite allergen.[344] Replace carpets with hard flooring such as timber, linoleum, bamboo or tiles (hot climates) and washable rugs. Avoid using heavy draped curtains, soft furnishings such as decorative pillows and blankets (that aren't used for sleeping), soft toys, books and all forms of clutter (especially under the bed). Use window coverings such as timber or metal blinds that can be wiped with a slightly damp microfibre cloth
- Discard old mattresses, bedding, carpets and soft furnishings. Discard pillows more than 2 years old, and mattresses, wool and feather-filled doonas more than 10 years old. New mattresses and carpets are associated with significantly lower levels of HDM[345]
- Wash bed sheets and pyjamas in hot water on a weekly basis. Washing textiles regularly with a detergent at high temperatures will remove most HDMs.[346] While bed sheets, pillow cases and pyjamas should be washed weekly in hot water (55°C), items such as pillows, soft toys and bedding (blankets, doonas) should be washed at least every 2 months and air-dried in the sun. Only washable toys should be given to a child with HDM allergies. Rugs, blankets, cushions and bedding such as doonas, pillows and mattresses should be aired outside on hot dry days as often as possible. Pull back doonas/blankets daily to allow the mattress to dry
- Use HDM-resistant covers and bedding. HDM-resistant covers are available for mattresses, pillows, doonas and quilts and are an effective way to reduce exposure to dust mites.[347] Breathable covers made from natural fibres such as cotton, silk or eucalyptus are preferred over synthetic materials like nylon, acrylic and polycotton blends with a PVC backing. Dust mite covers should be washed at least every 2 months. Pillow, mattress and doona covers/encasements should be made from natural fibres such as linen, bamboo, organic cotton, hemp or silk. Avoid underlays and blankets made from wool
- Reduce humidity levels. Humidity is a critical factor for mite prevalence, as higher concentrations of mites are found in damp homes[345] and in microclimates where the relative humidity regularly exceeds 60%. A dehumidifier or refrigerated air-conditioning unit (which cools the air by removing water) should be used continuously when the relative humidity exceeds 60%. Optimal relative humidity levels to prevent dust mite and mould growth are between 40% and 55%. Maximise ventilation in wet areas of the home to prevent the build-up of humidity and condensation. Vacuum daily. Vacuum cleaners that are not fitted with a HEPA filter will temporarily increase the amount of HDM allergen in the air (for around 20 minutes)[348] because the mite allergens are attached to large particles.[341] Once you have vacuumed, replace the bag (even though it won't be full) as dust mites thrive in them. Vacuum mattresses daily[349]
- Use space bags: store linen, cushions, blankets and clothes that will not be used for a season or more in a space bag (a bag from which the air has been sucked out) to kill the dust mites.[186] Children who are raised in a house with two or more dogs or cats during the first year of life are less likely to develop allergies.[350]

Pet allergens

Pets that commonly trigger allergic responses include cats, dogs, horses, birds, rabbits, hamsters, guinea pigs, rats and mice. Pets also contribute significant amounts of dust, dander, pesticides and microorganisms into a home. Paradoxically, early life exposure (in the prenatal period and during the first 12 months) to furry pets and their microbial genre appears to be associated with a substantial reduction of allergy and asthma in childhood. This is suspected to be mediated through exposure to a more diverse microbial community in the home,[350] which is in line with the Amish

study discussed previously. Individuals with pet allergies are not born with this condition; rather, it takes about 2 years to develop. Contrary to popular belief, it is not pet fur that is the problem, but skin flakes (dander), saliva and urine, which means that there are no 'low allergy' breeds when it comes to dogs and cats.[351] Even after removing a pet from the home, the dander can remain on dust, carpets and furnishings and may take several months of good housekeeping to remove. While the highest concentrations of cat and dog allergens are generally found in the homes of pet owners, the settled dust and air in schools and the cars of pet owners may also be important sites of exposure.[352] Cat and dog allergens remain airborne for much longer than dust mites and the potential for exposure to these pet allergens outside of the home is markedly greater.[353]

SOURCES OF PET ALLERGENS

- Cats produce a protein called Fel d1 in their sweat glands, which they spread when they lick themselves and which can trigger an allergic response in susceptible individuals and exacerbate asthma.[341,351] The allergen is so pervasive that it can be measured in the homes of non-pet owners, in school classrooms and on the clothing of workers who don't have pets. It is thought to be transferred and deposited indoors when attached on the clothes or hair of cat owners.[353,354] Therefore, sensitisation to cat allergens can occur in individuals who do not keep a cat
- The main source of dog allergen (a protein called Can f 1) is in the saliva, which dogs spread to their hair and skin when they lick themselves. This protein may trigger an allergic response in susceptible individuals and exacerbate asthma[341]
- There is limited evidence of an association between exposure to birds and exacerbation of asthma, which may in fact be triggered by the mites harboured by birds.[341] Bedding that contains feathers may be protective for lung problems because it is generally lower in dust mites levels; however, down pillows are suspected to be a risk for asthma because of their higher dust mite content.[341] There are a variety of diseases that birds can pass on to people as a result of microorganisms in their droppings. Psittacosis is one such disease; it causes flu-like symptoms and can progress to pneumonia and death
- Allergies to horses, mice, rats, rabbits and guinea pigs are not as common as cat and dog allergies.

HEALTH CONCERNS ASSOCIATED WITH PET ALLERGENS

Hay fever and asthma are the most common diagnoses attributed to pet allergies. Symptoms range from sneezing, a runny or stuffy nose, itchy and watery eyes, asthma, cough, eczema and hives to an anaphylactic reaction requiring immediate hospital attention. Up to 50% of people with pet allergies will not experience immediate symptoms.[351]

TIPS FOR REDUCING PET ALLERGIES

Individuals with established pet allergies need to implement avoidance strategies to prevent or reduce their symptoms.

- If possible, do not allow pets inside. Indoor pets should be kept away from bedrooms, carpeted areas, furnishings, slippers and stuffed toys. They should be confined to a dedicated mat, which is shaken outside daily as well as washed and air-dried in the sun at least twice a month
- Remove carpets, especially in the bedroom. Alternative types of flooring are timber, bamboo, cork, natural linoleum, slate, marble and ceramic tiles (although the latter may be too cold in a cool temperate climate). To clean these floors, mop with a damp microfibre cloth. Rugs are a better option than carpets, as they can be beaten outside and exposed to the sun
- Brush and wash the pet weekly to remove loose hair and allergens (a non-allergic person should carry out this task). Alternatively, wrap a damp cloth around a brush and brush the pet down rather than bathing them (do this outdoors)
- Wash hands after touching the pet
- Keep pet birds in an outside aviary
- Use air filters fitted with a HEPA filter, as they have been shown to be effective in reducing airborne concentration of pet allergens[316,355–357]
- Use a vacuum cleaner fitted with a HEPA filter and motorised head at least twice weekly.[186]

Pest allergens

Pest allergens such as cockroaches and rodents are present in higher concentrations in urban housing and have repeatedly been linked to asthma morbidity in sensitised children.[329] Pests are generally found in buildings that have a means of ingress, are warm and provide a source of water, food and shelter.

Sources of, and health concerns associated with, pest allergens

- There are more than 4500 species of cockroach, four of which are pests that can exacerbate asthma, hay fever and eczema in allergic individuals.[341,358] Some 30–40% of children with asthma are sensitised to cockroaches and are more likely to miss more school days.[359] Inner-city children who are exposed to high traffic related air pollutants have an increased likelihood of sensitisation to cockroach allergen.[360] Cockroaches have a lifespan of 1–2 years and prefer warm, moist and enclosed habitats. They have a taste for sugar and fat, although they have been known to consume soap, glue and rubbish,[358] and quickly become cannibalistic when food becomes scarce. Cockroaches that are visible in a home are evidence of an active infestation of live cockroaches, which increases the level of exposure to cockroach allergen (Bla g 1/2). In one study cockroach allergen was detected in almost half of all homes tested, even though the occupants reported no signs of cockroaches in the previous 12 months.[344] Individuals who have asthma, hay fever or eczema, or a strong family history of allergies, should be assessed for cockroach sensitivity
- Rodents (mice and rats) carry various infectious diseases such as Salmonella and can enter a hole as

narrow as a pencil to gain access to a building. Mice can mate when they are 1 month old, so it is important to take action as soon as you see one. Wherever they go they leave a trail of urine which contains a protein that can trigger allergic reactions in susceptible individuals. Rodents are more frequent in inner-city homes and have been linked with an increased risk of asthma, rhinitis and eczema in inner-city children[361–363]

- Insect allergies may arise when an individual is stung by a bee, wasp, mosquito, midge, March fly, bedbug, caterpillar, tick or ant. Whereas some individuals experience a localised itch and swelling that settles within a few days after being stung, others may experience hives or develop a potentially life-threatening anaphylactic reaction. The latter generally occurs after a susceptible individual is stung by a honey bee, wasp or Australian Jack Jumper ant[364]
- Ticks attach to the tips of grass blades and bushes and from there transfer themselves to passing animals and humans. Tick bites may result in local irritation and swelling at the site of the bite that can last for several days. Anaphylaxis may occur when the tick is disturbed, so ticks should be killed first (freeze-dried) before they are removed, otherwise the tick may inject more allergen-containing saliva.[365]

Testing for pest allergies

- Allergies can be confirmed by an allergy specialist or clinical immunologist who may perform skin prick tests or blood (RAST) tests. However, there is no reliable skin or blood allergy test to confirm a diagnosis of tick allergy
- Sticky traps strategically placed around the affected area can be used to identify the severity of a cockroach infestation by determining the number of different stages of development in the captured cockroaches. Household dust samples can be used to quantify the allergen load: cockroach antigen Bla g 1 levels should be below 1 unit/g of dust and Bla g 2 should be below 0.02 micrograms/g of dust. An important question to ask is 'Have you seen cockroaches daily, weekly, monthly or never in the recent past?'[358]

Tips for avoiding pest allergies

Allergen avoidance is considered the first line of treatment for patients with indoor allergen sensitivities. Thus the focus should be on creating an environment that doesn't attract pests.

- Food and water will attract pests, so good housekeeping is the key. Don't leave food (including pet food) around the home and clean up after every meal. Ensure all foods are properly stored in sealed containers. Waste and compost bins should be emptied daily and kept away from the house. Ensure the stove exhaust fan is clean and working and that the exhaust air is ducted to the exterior and not the roof cavity, to avoid distributing cooking odours to other parts of the home. Promptly repair water leaks, spills and dampness. Place plugs in all drains
- Avoid clutter in, under (crawl space) and immediately around the house including wood piles and rubbish bins as it provides the ideal home for pests. Keep gutters clean and well maintained
- Inspect the perimeter of the home and crawl space (if you have one) and caulk and seal cracks and holes. Install door sweeps and weatherproofing seals on exterior doors. Install fly screens on windows and doors and attic vents. Remove excess vegetation from around the home and prune branches near the building. Mosquito nets around beds are a cheap and effective physical barrier
- To remove frass (faeces, insect parts), clean carpets with a HEPA vacuum cleaner that is fitted with a motorised head to dig into the carpet pile. Discard the bag after each use
- Discard cockroach-infested mattresses and carpets
- To avoid insect allergies and tick bites cover up with light-coloured clothing (no florals) and wear shoes at all times, wear gloves when gardening, avoid perfumes and fragrances, keep grass areas mowed and get a professional to remove insect mounds and nests[364]
- Consider integrated pest management involving the use of sticky traps, baits, gels, boric acid and food-grade diatomaceous earth. Use chemical-based solutions only as a last resort and use a licensed pest controller. For more information on integrated pest management, refer to www.beyondpesticides.org.

Plant allergens

Pollens are a common cause of seasonal allergies. It is the wind-pollinated plants, however, which account for 10% of all flowering plants, that people with allergies such as asthma and hay fever are likely to react to because they are smaller and lighter (reaching the small airways of the lungs) and produced in large quantities that can be carried over long distances from their source (hundreds of kilometres in some cases). Plants with bright showy flowers are generally pollinated by insects and birds, while plants with small inconspicuous flowers are generally wind-pollinated. Grass pollens also rely on the wind to distribute their pollen over long distances.

SOURCES OF PLANT ALLERGENS

Susceptible individuals may be allergic to one or several types of pollen. With regard to allergic rhinitis and asthma, tree, weed, grass and crop pollinating plants are often the culprits. Grass pollens are the most frequent cause of allergic rhinitis: they are generally released in the early morning in summer and descend in the evening. As such, symptoms that occur in the evening may be indicative of allergies to grass pollen. Pollen maps and apps that provide daily pollen counts are available in many countries. Also contact the local asthma authority for a list of grass, weed and tree pollens in your area.

HEALTH CONCERNS ASSOCIATED WITH PLANT ALLERGENS

Pollens may trigger allergic rhinitis (sneezing, congestion, itchy and watery eyes, and runny nose), asthma, sinus

headaches and, less commonly, contact dermatitis, eczema and joint pain, which typically occur seasonally and generally improve after it rains. Symptoms may be immediate upon exposure, or can be delayed by a few days. Thunderstorms and weather changes may trigger asthma attacks in some individuals, as the pollen grains absorb moisture and burst, releasing hundreds of small allergenic particles into the air.[366]

TESTING FOR PLANT ALLERGENS

Allergies can be confirmed by an allergy specialist or clinical immunologist who may perform skin prick tests or blood (RAST) tests.

TIPS FOR AVOIDING PLANT ALLERGENS

- During the allergy season, remain indoors on hot, dry windy days and after thunderstorms when pollen counts are likely to be high
- Use an air conditioner (in the car and/or at home) or air filter that is fitted with a HEPA filter when the outdoor pollen count is high
- To reduce pollens in the home, shower after outdoor activities, damp-brush pets prior to entering the home and avoid hanging clothes on the line on high pollen count days (dry clothes inside instead)
- If allergic to grass pollen, do not mow the lawn or exercise in the early morning in spring and summer. Pollen allergy in tropical climates is more common during the dry season
- Wear glasses that wrap around the eyes during allergy season
- Avoid having flowering plants, including cut flowers, inside the home or office.

Mould

Fungi are nature's greatest decomposers and consequently they are found everywhere on the planet, including in our homes. Approximately 120 fungi are associated with poor indoor air quality and 400 are related to diseases relevant to people, animals or plants. Despite fungi being present for millions of years, their impact on human health has recently gained more attention in the scientific community. Why? The recent push to build airtight and energy-efficient homes with compromised passive ventilation has resulted in an increasing number of new homes experiencing condensation and mould-related complaints. It is estimated that 1 in 4 homes in Nordic countries and New Zealand, 1 in 3 homes in Australia and Canada, and 1 in 2 homes in the US are water-damaged.[367–369] Between one-quarter and one-third of the respiratory health outcomes observed in New Zealand can be explained by indoor dampness[370] attributable to cold, draughty and poorly insulated buildings.[369] The introduction of fungicides into building materials and paints in the 1970s created pathogenic strains of fungi that are more dangerous to human health than those seen previously. The introduction and use of cheap artificial timbers like MDF, plywood, oriented strand board and particle board (chipboard) containing chemicals like formaldehyde have changed the pH, and the type of nutrients (substrate) and therefore the genre of fungi likely to grow in a water-damaged environment. In contrast, solid hard timbers, traditionally used in years gone by, contain resins that are naturally resistant to fungal growth.

SOURCES OF MOULD

Buildings should reflect a Mediterranean type of environment: dry and stable. When we add moisture, we transform a dry stable environment into a living thriving ecosystem where microbes will kill other competing organisms by secreting chemicals to enhance their survival. As mould spores can remain dormant for many years, they will thrive when they are given food and water. As most conventional building materials and furnishings are the ideal 'fast' food for fungi, the key to addressing mould-related problems is to get to the source of the moisture. Within 48 hours of moisture being present, the spores – which are already sitting on all surfaces – will begin to germinate.

Moisture-related problems can occur during building construction, or arise from external or internal sources. Moisture often occurs during building construction with concrete floor slabs, masonry and walls because they contain a large amount of unbound water that needs to cure prior to erecting the frame. Mortar, grout filling and rain can also add moisture to concrete during the construction process. Poor building practices resulting in absent or inadequate water proofing of wet areas (bathrooms, laundry and kitchen) or insufficient drainage in the subfloor or immediately around the home may also cause moisture problems. Timber-framed homes are often exposed to rain or dew during construction, which is why the timbers are commonly contaminated with Trichoderma species. Inadequate insulation and/or single-paned windows commonly result in condensation issues on the walls, around the window frames or behind the curtains.

External sources of moisture that can penetrate the building envelope include: a climate that regularly exceeds 70% relative humidity; natural events such as storms and floods; water damage after a fire; and leaks through the building envelope from blocked and/or damaged gutters, missing or damaged flashing around exits on the roof, cracks in cladding and deteriorating building materials. Buildings that lack eaves or don't have facings around windows are at the mercy of the weather, and enclosed balconies and internal or box gutters are notorious for moisture problems.

Subfloor moisture may occur: due to building on a flood-prone site, swamp or above an aquifer; with blocked, a limited number of or missing subfloor vents; due to landscaping issues where garden beds cover subfloor vents and/or butt up against the house (with no water proofing); from garden sprinklers aimed at the house; with renovations that block off existing subfloor vents; due to the topography of the land (house built on or into a hill), where the surrounding ground level is higher than the ground level under the home; with poor groundwater drainage immediately around the home; from blocked storm water drains or gully traps; or from leaking stormwater, waste or water pipes under the house.

Internal sources of moisture typically occur from: high humidity and condensation generated from bathing, showering, laundering and cooking activities combined with

inadequate passive ventilation; unflued gas appliances; indoor spas, pools and saunas; indoor plants, open fish tanks and indoor water features; humidifiers; accidental floods such as an overflowing bath, kitchen sink or laundry sink; steam cleaning of carpets or furnishings that did not dry within 48 hours; leaking plumbing pipes, dripping taps and leaking appliances; and water-damaged furnishings bought from antique or second-hand stores or brought in from a previous water-damaged home. Heating, ventilation and air conditioning (HVAC) systems can also be a source of mould if they are not regularly serviced and maintained.[186]

HEALTH CONCERNS ASSOCIATED WITH MOULD

It has long been established that exposure to mould and dampness results in lung problems like asthma, bronchitis, cold and flu-like symptoms, hay fever and, less commonly, pneumonia and eczema.[371–373] In New Zealand up to one-third of respiratory diseases (in particular, asthma) are attributable to indoor dampness.[370] Traditionally this was thought to be an IgE-mediated response; however, it is now known that fungal products can activate both innate and adaptive immune responses resulting in chronic inflammation.[374]

Water-damaged buildings contain a 'chemical stew' of: airborne bioaerosols from actinomycetes, lipopolysaccharides, bacteria, fungi and their by-products (endotoxins, mycotoxins); ultrafine particles; microbial volatile organic compounds; cell fragments; and inflammagens such as beta glucans, mannans, haemolysins and proteinases.[375–378] In healthy individuals, these microbes are identified by the body's immune system (pattern recognition receptors), which induces downstream events (phagocytosis, cytokine and chemokine release) that in turn polarise a Th17 adaptive immune response designed to eliminate the pathogen from the host.[379] However, advances in gene screening have identified that 24% of the population do not have the immune response genes (*HLA-DR*) required to form antibodies to biotoxins,[380] which means every time these individuals walk into a water-damaged building, a persistent innate immune inflammatory illness ensues, which can affect virtually any organ system of the body.

Chronic inflammatory response syndrome (CIRS) is a chronic, progressive, multisystem, multisymptom syndrome characterised by HLA genetic predisposition, exposure to biotoxins, altered innate and adaptive immunity, peripheral hypoperfusion at multiple sites and multiple hypothalamic-pituitary-end organ dysregulations.[381] Symptoms include fatigue and headache, brain fog (difficulty with recent memory and concentration, and anomia),[382] vertigo, metallic taste, aches and pain in the joints, numbness and tingling, and sleep disturbances. In addition, around half of sufferers experience excessive urination and thirst and increased electric shocks because of alterations to antidiuretic hormone. Remarkably, most of these symptoms disappear during pregnancy, because the anti-inflammatory neuropeptide (melanocyte-stimulating hormone) in the brain increases during pregnancy.

TESTING FOR MOULD

A symptom-based assessment of risk for CIRS following exposure to a water-damaged building is available in a consensus paper in *Surviving Mold*.[383]

Clinical testing

IgE-mediated allergies to fungi can be confirmed by an allergy specialist or clinical immunologist who may perform skin prick tests or blood (RAST) tests. According to McMahon and colleagues[381] and Shoemaker and colleagues,[382] a diagnosis of CIRS requires:

- Exposure to a water-damaged building
- The presence of a multisystem, multisymptom illness
- Laboratory abnormalities in five of the following eight blood protein biomarkers: vasoactive intestinal polypeptide, alpha-melanocyte stimulating hormone, complement component C4a, metallomatrix proteinase-9 (MMP9), vascular endothelial growth factor (VEGF), transforming growth factor beta-1 (TGF β-1), osmolality/antidiuretic hormone balance and cortisol/ACTH balance.

Other useful tests

- A nasal swab can be used to detect multiple antibiotic resistant coagulase negative staphylococcus (MARCoNS)
- Brain scans have identified gliotic areas on MRI scans[382]; elevated lactate and depressed ratios of glutamate to glutamine in MR spectroscopy; atrophy of the caudate nucleus; and bilateral enlargement of the pallidum, forebrain parenchyma and cortical grey using the MRI volumetric software NeuroQuant® [381,382] suggesting inflammation in the brain
- Genetic susceptibility (HLA DR DQ)
- Visual contrast sensitivity (VCS) is a simple, non-invasive eye test that measures the ability to distinguish between finer and finer increments of light versus dark lines, which can affect visual function even with 20/20 vision.[384] Transient deficits in visual contrast have been observed in patients in water-damaged buildings,[385] while permanent deficits have been documented in patients with neurodegenerative and inflammatory diseases affecting the optic nerve such as multiple sclerosis[386] and Alzheimer's disease,[387] ophthalmological disease (glaucoma, cataracts, diabetic retinopathy and macular degeneration) and occupational exposure to solvents, heavy metals and petroleum products.[385]

House testing

House testing should be instigated following a history of water damage that correlates to the development of the above symptoms or the presence of dampness as determined by visible water damage or stains, visible mould and odour from microbial growth.[373,388] Refer to the recent article by Chew and colleagues.[388] There are several reports that document how to test and remediate water-damaged buildings, but the most detailed is ANSI/IICRC S520-2015 on mould remediation.[389] An inspection should be carried out by a qualified building biologist,

indoor environmental professional or IICRC-accredited mould remediator and should involve an exterior and interior site inspection of the property including the heating, ventilation and air-conditioning (HVAC) system for evidence of visible mould, damp smells and signs of dampness. It should also involve the use of indoor air quality meters (to compare outdoor and indoor relative and specific humidity levels and temperature), thermal imaging cameras to identify temperature variances with any anomalies verified by a moisture meter, borescopes to identify hidden mould and moisture meters to identify the source and extent of moisture intrusion in building materials. In addition, the inspector should conduct air, dust (ERMI or HERTSMI-2) and/or surface sampling to quantify the genre and prevalence of various fungi and their mycotoxins.

Solutions for water-damaged buildings

The first phase of therapy includes eliminating offending toxin exposure (see below), short-term use of a bile acid sequestrant such as cholestyramine (CSM), and eradicating nasal MARCoNS if present.[381] The second phase includes the correction of antigliadin antibodies, dysregulated androgens, dysregulated ADH (antidiuretic hormone) and osmolality; elevated MMP-9, VEGF (vascular endothelial growth factor; bimodal dysregulation) and complement components C3a, C4a and TGF β-1.[381]

The key to addressing a water-damaged building is to locate and eliminate the source of moisture. Most of the time this will be obvious, such as clogged gutters, inadequate ventilation, broken roof tiles or a history of flooding. If the source of the moisture cannot be identified, a licensed plumber, drainage specialist, building biologist, indoor environmental professional or IICRC-accredited mould remediator may be required to find the source. If the moisture is simply due to living in a hot, humid climate, having the air conditioner or dehumidifier on continuously will keep humidity levels below 70%. Patients with suspected sensitivities to mould should avoid working with garden compost or mulch or mowing the lawn.

For non-porous surfaces, mould can be removed with a microfibre cloth soaked in a solution of dishwashing liquid and water to remove the biofilm. For porous surfaces such as plaster, insulation, particleboard or soft timbers, an alcoholic solution (70% alcohol to 30% water) is effective. If the mould has infiltrated the material, abrasive methods such as wire brushing, sanding or media blasting may need to be employed by an accredited mould remediator.

Non-porous water-damaged contents (metal, laminate, plastic, glass, sealed timber, ceramic and porcelain) and semi-porous items (plasterboard, concrete, plywood, masonry, unsealed timber, oriented strand board and brick) should be vacuumed using a HEPA vacuum cleaner, then wiped with a slightly damp microfibre cloth and vacuumed again. Porous items such as clothing, soft furnishings, carpet, underlay, plasterboard, ceiling tiles, leather, paper (books), taxidermy, fine art, insulation, particle board and medium-density fibreboard that didn't dry within 48 hours of water damage should be discarded. Clothes that don't have visible mould on them can be washed in a hot cycle and dried in the sun. To save expensive items like fine art and books, specialised laundering companies should be consulted. Note: appropriate personal protective equipment such as a P3 particulate respirator and protective clothing may be warranted during mould remediation.

The HVAC system should be cleaned according to the National Air Duct Cleaners Association 2013 standard and contaminated flex ducting (typically used in residential homes) should be replaced as it is impossible to clean.[186]

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APPENDIX 11.3

hCG interpretation

hCG testing

Human chorionic gonadotrophin (hCG) is a hormone secreted from the placenta into the maternal circulation with a role in the maintenance of a viable pregnancy. The serum concentration of hCG is used to detect and monitor pregnancy and some malignant conditions.

hCG during pregnancy

During the first weeks of pregnancy, hCG serum concentrations rise rapidly, with a doubling time of about 2 days. This rate of rise then slows, and the peak hCG concentration is reached between 8 and 12 weeks of gestation. The concentration then falls to a plateau, which persists over the second and third trimesters. After delivery, hCG falls, with a half-life of 1–2 days.

High levels may be found in patients with twin or multiple pregnancies or with gestational trophoblastic disease. Low levels may be a marker of non-viable pregnancy (e.g. ectopic pregnancy).

A doubling time of less than 2 days should arouse suspicion of either a possible ectopic pregnancy or a non-viable intrauterine pregnancy. Gynaecological opinion should be sought in this instance. hCG is usually detectable in ectopic pregnancies, but this is not a universal finding.

At hCG concentrations >2500 U/L, a normal intrauterine pregnancy should be visible on a transvaginal ultrasound scan. Note that hCG levels should never be used in isolation for diagnosis of any of the above conditions.

TABLE A11.3 Interpretation of quantitative serum hcg results

Reference ranges		Serum hCG (U/L)
Weeks since last menstrual period	Approximate hCG range (U/L)	Comment
Women	Premenopausal	<2.0 U/L
	Postmenopausal	<2.0–10 U/L
Men		<2.0 U/L
PREGNANCY TEST		
	Serum hCG (U/L)	Interpretation
	<2 U/L	Negative (if taken after first missed period)
	2–25 U/L	Borderline result (suggest repeat in 48 hours)
	>25 U/L	Consistent with pregnancy (Note: most laboratories will request a repeat assessment if reading is <100 U/L)
PREGNANCY STAGING		
3–4	0–130	Week prior to first missed period
4–5	75–2600	Week after first missed period
5–6	850–20 800	
6–7	4000–200 000	
7–12	11 500–289 000	
12–16	18 300–37 000	
16–29	1400–3000	Second trimester
29–41	940–60 000	Third trimester

APPENDIX 11.4

General IVF protocol

Step 1: controlled ovarian stimulation

1 Optional: oral contraceptive prescription prior to embarking on stimulating cycle to regulate and control timing.
2 Serum E2, P4 and LH to confirm new cycle.
3 Stimulate the ovaries with injections of FSH.
   (a) A small amount of LH will be included in the preparation for follicle development and proper development of the egg.
   (b) Dose of FSH will be calculated based on the woman's weight to prevent hyperstimulation: dose range 100 U (40 kg) to 450 U (120 kg).
   (c) Objective will be to stimulate a small number of recruits, as only one follicle will be used per cycle (ideally).

APPENDIX 13.1

Tools to assess NVP

Tool	Description
PUQE: Pregnancy-Unique Quantification of Emesis and Nausea	Three questions regarding nausea, vomiting and retching during previous 12 or 24 hours For each component: 0 = no symptoms, 5 = worst possible symptoms Maximum score = 15 Score ≥13 indicates severe symptoms
RINVR: Rhodes Index of Nausea, Vomiting and Retching	Eight questions about duration, amount, frequency and distress caused by symptoms of nausea, vomiting and retching For each component: 0 = no symptoms, 5 = worst possible symptoms Maximum score = 40 Score ≥33 indicates severe symptoms
McGill Nausea Questionnaire	Measures nausea only using a nausea rating index that has nine sets of words that describe sensory, affective, evaluative and miscellaneous afferent feelings related to nausea that women rank An overall nausea index: 0–5, where 0 = no symptoms, 5 = excruciating symptoms Plus a VAS: 0 cm = no nausea, 10 cm = extreme nausea
NVPI: Nausea and Vomiting of Pregnancy Instrument	Three questions relating to nausea, retching and vomiting over the past 7 days For each component: 0 = no symptoms, 5 = worst possible symptoms Maximum score = 15 Score ≥8 indicates severe symptoms
VAS: Visual Analogue Scale	Patients rate their symptoms on a scale of 0–10, where 0 = no symptoms and 10 = extreme symptoms

Source: Adapted from O'Donnell A, McParlin C, Robson SC, Beyer F, Moloney E, Bryant A et al. Treatments for hyperemesis gravidarum and nausea and vomiting in pregnancy: a systematic review and economic assessment. Heal Technol Assess 2016;20(74).

APPENDIX 13.2

Edinburgh Postnatal Depression Scale (EPDS)

Question	Score
1. I have been able to laugh and see the funny side of things	
☐ As much as I always could	0
☐ Not quite so much now	1
☐ Definitely not so much now	2
☐ Not at all	3
2. I have looked forward with enjoyment to things	
☐ As much as I ever did	0
☐ Rather less than I used to	1
☐ Definitely less than I used to	2
☐ Hardly at all	3
3. I have blamed myself unnecessarily when things went wrong	
☐ Yes, most of the time	3
☐ Yes, some of the time	2
☐ Not very often	1
☐ No, never	0
4. I have been anxious or worried for no good reason	
☐ No, not at all	0
☐ Hardly ever	1
☐ Yes, sometimes	2
☐ Yes, very often	3
5. I have felt scared or panicky for no very good reason	
☐ Yes, quite a lot	3
☐ Yes, sometimes	2
☐ No, not much	1
☐ No, not at all	0

Interactions table

HERB/NUTRIENT–DRUG INTERACTIONS TABLES

Compiled by Liesl Blott

Potential herb–drug and nutrient–drug interactions are described in the following tables. These tables have been formulated to include information on interactions between herbal medicines, nutrients/nutritional medicines and drugs. They include a summary of the potential outcome, a graded recommendation and a comments section that explains the nature of each interaction in more detail.

The recommendations are broadly divided into four categories: avoid, caution, monitor and beneficial. Factors that were taken into account when determining these interaction categories include currently available evidence and safety data; potential severity and clinical consequences; the likelihood of an interaction; whether the interaction is based on clinical studies or extrapolated from case studies, laboratory or animal studies; and commonly applied integrative prescribing principles. However, new safety data and evidence are constantly emerging, and best practice regarding some of these interactions may change with time.

The tables do not include information on possible contraindications, for example use in pregnancy, nor do they include herb–herb, herb–nutrient or nutrient–nutrient interactions.

Practitioners are encouraged to use the interactions tables as a guide, but to apply professional judgment on the appropriateness of use of a combination of herb–drug or nutrient–drug for each individual patient. It is imperative that health practitioners investigate whether there are any known safety concerns or interactions when prescribing herbal or nutritional medicines for patients already taking pharmaceutical medicines.

Health practitioners of all disciplines are encouraged to make use of available resources to allow for informed decisions, so as to optimise patient wellbeing without compromising patient safety. When recommending complementary medicines in combination with pharmaceutical medicines, both anticipated benefits and potential risks should be taken into consideration.

ACNM herbal interactions table

Herbal medicine	Drug/drug class	Potential outcome	Recommendations	Comments
Achillea millefolium	Acid-reducing drugs (antacids, H_2 antagonists, proton pump inhibitors)	Theoretical decreased drug effect	Monitor – may not be clinically significant	Yarrow may increase gastric acidity. Use may theoretically antagonise drug action, resulting in decreased drug effect.
	Anticoagulant/ antiplatelet drugs	Theoretical increased risk of bleeding	Caution with use of this combination	Yarrow may have antiplatelet properties. Combined use with anticoagulant and antiplatelet drugs will theoretically increase the risk of bleeding and bruising.
	Barbiturates e.g. phenobarbital	Theoretical increased sedation	Caution with use of this combination	Yarrow may theoretically prolong barbiturate-induced sleep time.
	Lithium	Theoretical increased risk of drug toxicity	Caution with use of this combination	Yarrow may have diuretic properties. Combined use may theoretically precipitate lithium toxicity.

LEGEND
- Combination okay to use
- Use of combination should be monitored
- Use combination with caution
- Avoid combination

Continued

ACNM herbal interactions table—cont'd				
Herbal medicine	**Drug/drug class**	**Potential outcome**	**Recommendations**	**Comments**
Actaea racemosa	Androgen blockade chemotherapies	Theoretical decreased drug adverse effects	May be beneficial – medical supervision recommended	Androgen deprivation in prostate cancer patients can result in hot flushes and decreased libido. Black cohosh may theoretically reduce vasomotor symptoms in patients taking drugs that reduce androgen levels. Benefits are speculative and more data is required.
	Cisplatin	Possible reduced drug effects	Avoid combination	Preliminary evidence suggests that black cohosh may decrease the cytotoxic effects of cisplatin on breast cells. Avoid combination until further data becomes available.
	Chemotherapy drugs	Variable effects possible	Avoid combination	Variable effects have been reported with concomitant use of black cohosh and chemotherapeutic agents. Some studies have shown a decreased effect and others an increased drug action and risk of toxicity, depending on the agent. Concomitant use should be avoided unless under strict medical supervision.
	CYP2D6 substrates	Theoretical increased drug levels	Caution with use of this combination	Limited evidence suggests black cohosh may modestly inhibit CYP2D6. Theoretically, this can result in increased drug levels and risk of toxicity of drugs metabolised by this enzyme.
	Hepatotoxic drugs	Possible increased risk of liver toxicity	Caution with use of this combination	The risk of liver damage may be increased with concomitant use of black cohosh and hepatotoxic drugs.
	HMGCoA reductase inhibitors (statins)	Possible increased risk of liver toxicity	Caution with use of this combination	One case report describes a patient who was taking atorvastatin who developed significantly raised liver enzymes after commencement of black cohosh. It is unclear if this was due to the drug, the herb or the combination.
	Hormone replacement therapy (HRT)	Possible additive effects	Combination may be beneficial	Black cohosh may theoretically provide additive benefits for the reduction of menopause symptoms such as hot flushes and night sweats when used with HRT. Theoretically, concomitant use may allow for lower HRT doses. Direct research investigating the safety and efficacy of combined use is lacking.
	Tamoxifen	Possible reduction of hot flushes	Caution with use of this combination	Some studies suggest that black cohosh may help to treat hot flushes in women with a history of breast cancer and taking tamoxifen. Appropriateness of use is, however, the subject of debate as the oestrogenic effects of black cohosh may also potentially have negative consequences. Medical supervision is recommended.