

Killing

Us

Softly

Dr Mark Donohoe

With special thanks and gratitude, I dedicate this book to my friend and intellectual playmate, William Vayda, who died in early 1997. William was a man ignored by medical practitioners and science, much to medicine's shame. He remains the most effective healer I have ever met, a man capable of integrating the most diverse and apparently unconnected information for the benefit of his patients. I miss his companionship and his challenges greatly

This is a book commenced, but never completed, in 1995 and 1996. It was “completed” of sorts around mid 1998. I have made only minor changes since then, and so I now pass it out to the community as a summary of the views and opinions I formed from the many years of wonderful education provided to me by my chemically injured patients.

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Introduction

In 1995 and 1996, I was invited by the Australian Chemical trauma Alliance to address their annual conference. The pay is lousy, the conditions sparse, and the travelling to distant “chemical free zones” is always exhausting. I would not miss one for the world.

Why?

Because of two things - the debt I owe to those who suffer from environmental illnesses and who have spent patient hours educating me; and the wonderful opportunity to catch up with people like Gunnar Heuser, Archie Kalokorinos, Larry Budd and the other caring, brilliant and innovative physicians who have put their reputation on the line by daring to deal with these unpopular low level adverse chemical effects on health.

It is to these acquaintances, as well as Bill Rea and his colleagues in the American Academy of Environmental Medicine, that I owe a great deal, and without their support, guidance, inspiration and advice, I feel I would have bowed to the pressure years ago, and returned to a simple and profitable medical practice centred on painful orifices and runny noses!

After the 1996 conference, Dr Heuser had a chat with me about spreading the ideas in my presentation further. This led to some months of gathering my thoughts and feelings on this challenging and complex issue, and moving towards a coherent view of the problem.

I could not do it.

As I wrote, whole streams of ideas, stories, insights, theories and memories emerged and have simply been set to paper. Many may find my style distracting and annoying, as I move in and out of vaguely related issues on the way through a subject. My guess, however, is that my mind, when put to the task of such a subject, has adopted some of the loosened associations so common to those who suffer the illness. If so, this book may make more sense to those with multiple chemical sensitivities than to those without it. I can only suggest that the reader simply flow with the stories, and see if, at the end, I have provided a worthwhile understanding of the condition, its social context, and the people who suffer it.

My aim here is to stimulate thought on the subject, to touch on some of the significant issues as I see them as a medical practitioner and researcher specialised in this field, and to tell some of the stories which define for me the principles of multiple chemical sensitivities. It is not designed to be a scientific treatise, nor is it intended to be too dogmatic. I have little time for psychiatry, toxicology, law, agrochemical manufacturers and plastic surgery. Although I feel the world would be the better if these fields were all to evaporate without a trace, I am prepared to live with them – their flaws provide fodder for contemplation.

These are among my only real gripes in life, though. I feel thoroughly energised by a magical and wonderful world, and I am inclined to do some work to make sure it survives and thrives, and continues to enthral my three daughters, and their future children as well. I suspect that, should we fail to pay attention to those with multiple chemical sensitivities, we may be missing the early warning signs not of sick people, but of a dying planet.

I thank those people who have sought my help over the past decade for their health problems related to adverse effects of low dose chemicals on their health. The education provided to me by those brave, ignored, persistent, infuriating and inspiring people and their carers over thousands of hours has been a privilege. I have provided the time and the ears, while they have enlightened me with the stories which, taken together, have given me and my colleagues a unique insight into medicine, our society, and the resourcefulness of those people who suffer most in the name of progress. To those people I owe my deepest gratitude.

The story of multiple chemical sensitivities is a difficult one to set in a social context at present. The understanding is emerging, and the data which seemed to be lacking in the past are now flooding in. I will be satisfied if, after reading my contribution, a reader has his or her faith in regulatory bodies, manufacturers and medicine shaken.

Growing up is often a painful experience in which blind faith must be discarded, and in which we seek the truth for ourselves. The truth, for me, is the people who see me and relate their all too similar stories day after day. It is not theory, experts, authorities or newspaper stories. I urge and invite you all to lose your faith, and grow your own knowledge and understanding. Believe nothing I or others say without testing it against your experience. Then, do not doubt the truth you find, no matter what the "experts" say.

Dr Mark Donohoe

2004

Chapter 1

The day the church burned down

*Smells detonate softly in our memory like poignant land mines,
hidden under the weedy mass of many years and experience.*

Dianne Ackerman - A Natural History of the Senses

There are smells that I shall not forget as long as I live.

As a seven year old in a small catholic country primary school, there was one day a most unusual smell in the classroom. Different than the day to day smells of the classroom, I recall the eerie quietness in the classroom as we all sniffed the air, seeking a match from memory, from past experience. With none forthcoming, not even from Sister Celestine, we were bewildered. Apprehensive. Silent.

Someone burst through the door and the future meaning of that aroma was set forever in all of us, crystallised by the adrenaline rush of the emergency. The local church, only thirty yards from the classroom, was ablaze. We ran outside, and our young senses were assailed by a most dramatic experience. Flames soared heavenwards from the top of the old wooden building, the heat blasted our face, sirens and fire bells progressively drowned out the screams of panic, and the thick smoke left an oily taste in our mouths.

These were dramatic moments in our young lives, and the most vivid details were the sights and sounds. As the years have passed, though, the one persistent memory - the one which evokes the *feeling* of that day 33 years ago - is the smell.

It has happened only half a dozen times in all those years, but each time I have smelled it, this aroma has transported me across time - a vulnerable, scared and confused child, the feelings as immediate and real as the day the church burned down in Katoomba.

Chapter 2

Another World - Smell and the brain

*The face on you, the smell of you,
Will always be with me*
Sinead O'Connor - Three Babies

The first and most intimate sense

What is this strange sense, so tied with emotions and memories? Why, with the shrinking of our olfactory receptors to vestigial remnants of their prior evolutionary glory, does the sense of smell still have this powerful effect upon us?

First, we need to know what we mean when we use the term "smell". For vertebrates, this is relatively simple, as it can be defined as the stimulation of the first cranial (olfactory) nerve. For other life forms, those without cranial nerves or even noses, a different definition is needed.

For insects, one could say that "smell" occurs when the stimulating molecules are airborne, but we need a more generic definition.

All life forms on earth are bathed in a fluid of some type, be it a gas or a liquid (usually air or water). This fluid is their immediate environment, and their shared link with other matter. The sense of smell could then be defined as the information generated (or sensation elicited) by small molecules carried by this fluid on interaction with a living organism.

We know little of the origins of life on earth, but the best guess is that it emerged from some type of primordial "soup", with some form of self-replicating molecule. To do this, each molecule needed to find its match in the soup. In a real sense, therefore, the molecular match which comprises smell and taste developed at the same moment as life itself!

Finding familiar molecules, while avoiding toxic ones, has been the main preoccupation of life since it first began. Success in finding mates and food, while avoiding predators and poisons, has been what separates the life which we now see around us from those evolutionary forms that did not make it.

For some of the lineages from the soup, the link has become more tenuous over time. Most birds, for example, find olfaction of little value, and the visual sense now dominates behaviour. Except-

tions such as vultures, with single minded obsession for the smell of carrion, do exist, but they are avian oddities. Nature provides the peacock with absurdly extravagant plumage, and sweaty male triathletes with androsterone. The owners of these sexual advertisements clearly have common goals, and the future of their respective species depend upon their success!

For most mammals, with nose and genitals at around the same altitude, the sense of smell is at its peak. The air near the ground is heavier, moister, and more redolent with the scents of life. The behaviour predicated by the sense of smell is sometimes more compelling, more urgent than life itself.

As we moved from four to two legs, we traded smell for vision. In extending our visual horizons, our dependence on olfaction shrank away to nothing. Or so we would have it.

Why does the sense of smell challenge us so greatly? Why do we feel more comfortable with our other senses? We deodorise, sanitise, disinfect, wash continuously, and consume soap by the ton. We cannot stand the smell of ourselves. Why is this?

My feeling is that we of the "first world" have become "external" creatures, divorced from our inner selves. We find our smells too intimate, too revealing, too embarrassing, too close to a forgotten self. Like dreams half-remembered on waking, they are hard to get hold of, impossible to carry over to our rational side.

Our other senses have more direct links, or so we would think. In fact, we are comfortable with them *precisely* because they are less direct. We can match the others with our thoughts, our minds, and our memories, and the match seems comfortably direct. Our other senses are far more vivid and obvious than smell. We *notice* the other senses far more, but none are so deeply linked to those places in ourselves which define who we are.

That is it, I think. We are comfortable with senses two through five. Our first sense, however, slips past consciousness, strips the facade of culture, and links us to our ancestors. We are reminded of our heritage. No wonder we feel uncomfortable.

Smell is our most intimate sense. The olfactory pathway is the direct link between the brain and the outside world. It is the bond between mother and child, helps us find mates with genes usefully different from our own, and draws us together around the meal table.

Yet we find it hard to describe smells, to layer language over the sensation so that someone else can share in our personal experience. When we do describe smell, we describe it obliquely, using analogy and metaphor, or we describe the emotion or sensation evoked. We call aromas "disgusting", "light", "floral", "fruity" and "mysterious" even though none of these convey anything about the nature of the sensation.

Some have suggested that there is only one useful dimension to the sense of smell, and that is along a line from pleasant to unpleasant. The point is that this would be in keeping with the function of olfaction, namely attraction and avoidance. The Oxford Companion to the Mind goes so far as to suggest that this may be the *only* way for organisms to classify odours.

I think this is patent rubbish! Nature is frugal with her molecules and receptors. If one dimension of input is all that is required, one dimensional receptors are created, such as pressure receptors

in the skin. It is a patent waste to invest extra energy in the morphogenesis of an unnecessarily complex organ or system.

Smell has no currency, no language of its own. It is tucked safely away, so that we hardly even notice it. In fact, we may be unable to "notice" it at all.

Recently, it seems, the vomeronasal organ (VNO) has been discovered in humans. It is situated low down on the nasal septum, and is regularly obliterated by ENT surgeons doing septoplasty and other fairly gross adjustments to the nose. While its significance is being widely discussed and disputed, I have no doubt that we will find some profound, though subtle, functions as time passes. It reminds me most of those subtle, small speakers of fine stereo systems, set far from the main speakers and sound, which give a depth, a richness, a life to the sound itself.

I rather hope surgeons will make an effort to leave the VNO alone, but this is probably a forlorn hope. More likely they will identify it as a pathological organ, causing irrationality and pheromonally mediated abnormal behaviour syndrome (P-MAB - I could propose it for the DSM-V psychiatric inventory/manual), and plastic surgeons will charge \$10,000 for its removal from the noses of fortune 500 executives. Especially in women, where everyone knows that there must be some hidden cause for irrationality and synchronous menstruation.

Smell is the subliminal advertising of most animals. The fact that we may not notice smells tells us nothing of the magnitude or power of their effects. In fact, the ability of the sense of smell to bypass the thalamus and neocortex, to go straight to the rhinencephalon, then on to the limbic system and hypothalamus in the brain, is what makes it so powerful.

And so dangerous.

Olfaction and immunity

The olfactory nerve, the first cranial nerve, is not a nerve at all. At least not in the usual sense of a nerve. It is, in my opinion, the strangest organ one could imagine. It is mysterious, primitive, courageous and an absurdity all at once.

In each other link between the inner world and the outer world, the messages are received through specialised receptors, converted to electrical impulses of varying frequencies, and the message is passed from neuron to neuron all the way to that part of the brain designed to interpret and respond to the message. Along the way, certainly, there are reflex arcs, collateral branches to eponymous nuclei, and a good deal of eavesdropping by other neurons. But the basic path is from external stimulus to internal perception - the outer world to the inner world.

The path is far from direct, however, and there is plenty of room for magnification, suppression, and misinterpretation along the way. The reason is that peripheral nerves, including the cranial nerves, converse only with the brain through synapses. These are the gaps between nerves, and the message changes from electrical to chemical transmission momentarily as this gap is crossed. The chemical transmitters, known as neurotransmitters, include acetylcholine, serotonin, dopamine, histamine, and dozens of others. As the chemical is ejected from the axon of one nerve to the dendrite of another, the private message of the nerve becomes, as it were, more public.

Nearby nerves eavesdrop on the message, picking up a fragment here and there, and spread the gossip to nearby nerves. The nerves seem to then indulge in a crude form of democracy, collecting opinions to decide the fate of the message proffered from below.

This indecipherable rabble of activity then organises itself, contributes its opinion, sometimes strengthening, sometimes suppressing, sometimes re-routing the message. More often than not, the message does not make it to the cortex, where the brain's owner may become aware of it. It is lost along the way, extinguished entirely or passed on to parts of the brain responsible for these types of messages. Even when the messages reach the cortex, the likelihood of perception is low unless the stimulus is novel, alarming, or at least a little unexpected.

The point is that all nerves face the 'sensorship' of synapses.

All except one.

The olfactory nerve is less a nerve than it is a misplaced piece of the brain, dangling almost unprotected in the outside world. Like tubes of pork through a mincing machine, the brain cells spread through a finely fenestrated bony plate behind and slightly above the level of the eyes. Within deep clefts high in the roof of the nose, a square inch of deep yellow tissue on either side is home to around thirty million olfactory cells. Every last one of them, a card-carrying member of the central nervous system.

Even more astounding is the fact that these brain cells are "used up", with a monthly cycle of regeneration of new cells to replace the old. Somehow, the "learned" response of those which degenerate is passed backwards to those which are to follow, preserving the learned olfactory responses and the receptor patterns.

It seems, to top it all off, that olfaction has an uncanny resemblance to another remarkable organ system - the immune system. And the resemblance is more profound than mere analogy.

Both immunity and olfaction are designed to detect molecules - those that belong to us, and those that most definitely do not.

The immune response manages admirably with large molecules, typically water soluble peptides, starches, nucleic acids and glycoproteins. These are typically swallowed, inhaled, or enter through breaches in our outer coverings. They become internal threats, and their presence is announced to the body through antigen presenting cells. These "consume" the foreign molecules, digest and splinter them, then sort through the debris to present just a few critical fragments on their surfaces. Not just any fragments, mind you. Only those sufficiently available and obvious, and those sufficiently different from our own molecules to ensure the future attack leaves healthy tissue of the host alone.

These often overlooked macrophages really are the brightest of the body's cells, combining the skills of a computer, a librarian, and an entire judicial system in a single cell. Many may say (and I am not one of them, mind you) that this last added quality adds nothing to the total of its wonders.

A novel virus appears, say, on the nasopharynx, along with many of its friends. This is surely a splendid place to take up residence, they think among themselves. All facilities laid on - moisture, darkness, sugars, mucus - heaven on a stick in virus terms. Before long, however, in the normal

course of business, a scene reminiscent of a third rate 1960s Japanese movie emerges. A monstrous, formless blob, the size of a whole building, flows into an outstretched tentacle of its own making, and consumes dozens of the viruses sitting smugly in the soggy warmth of their new-found home.

Within minutes, the verdict is in. "Guilty - Not welcome", and the message along with a molecular snapshot of the offender is hoisted on wanted notices all over the surface of the macrophage.

The jig is up. The vacation for the intruder is about to come to an end, and the story is finished apart from the mopping up operation. Within minutes this is carried out by lymphocytes blaring their own chemical sirens. These sidle up alongside the macrophage, take a photocopy of the offender's image, and then clone themselves, each with an image of the intruder in mind. The virus has little chance at this point, and must surely consider the whole deal a little like a seaside holiday in a hurricane. The only escape is into the cells surrounding them, where the whole process starts again.

The olfactory receptors, on the other hand, are well designed to detect smaller molecules, almost exclusively fat soluble. The greasy surface of the of the receptor area is almost impervious to water soluble molecules, and the design of the roof of the nose is such that proteins and dust are rarely encountered. They are just too heavy, too sticky and too big for this. They become trapped in the mucous and hairs of the nasal cavity, and are most often swept back out in that act of almost orgasmic delight and relief, the sneeze.

Each of us has around three hundred or so distinct odours, and the unique combination goes to make up our own "smell signature". Just as with the immune system, which learns the "immune signature" of its owner in the thymus gland in infancy, we are "blind" to our own signatures most of the time. Were it not so, we would be attacking our own tissue unmercifully (as is the case in autoimmune disease), or drown in our own redolent aromas, losing all possibility of distinguishing the faint scents upon which we depend.

The structure of our noses is less amenable to showering of the receptors than it is for many of our mammalian relatives. Sheep dogs and Alsatians not only have around forty times more olfactory receptors, they have an air pathway through the nose which guarantees molecular intermingling with the deep reddish-brown mucosal surfaces. We humans need to flare our nostrils, squint our noses, and draw breath in a most unusual fashion to really get those aromatic molecules into the folds of our upper noses.

We usually need to "sniff" to really get a grip on these ephemeral messengers. A single molecule is sufficient to cause a response in a single nerve, but this will still be lost in the noise of the other, more abundant molecules trapped in the sniff. We seem to need about forty or so nerves firing before the cascade of magnification in the "smell brain" occurs. One can imagine that the increase in "olfactory noise" which has occurred as a result of our chemicalised century would be making this process more difficult and tenuous all the time. It is my own opinion that we really do smell less these days than when I was a child, and there is some evidence for this. That, however, is a different story.

What happens between reception and recognition is something of a divine mystery, one we are only beginning to unravel using tools from chaos theory, functional brain imaging, and animal studies.

There is no easy way to understand what occurs in the olfactory bulb, and how that message is disseminated for use from that point. Those familiar with the concept of chaos and "attractors" have a better chance than most, but it is still a wonderfully mysterious process, deserving of our urgent attention.

As the molecules in question bind to the nerves with the matching molecular "receptors", the nerve not only gives an electrical "quiver", it seems that the molecule itself is transported into the cell itself, in an event reminiscent of the poor viruses and the macrophage.

Why would we want these molecules inside our cells? More specifically, why would we want them in our brain? In medicine, we learned of a mythical creature known as the "blood-brain barrier", the purpose of which was to prevent foreign molecules from entering the territory of thought and consciousness. So why would there be such a shoddy back door to such an elaborate system of protection.

To understand the purpose, we may need to understand the brain.

What is a brain?

What is a brain?

The answer seems obvious. It is a thinking machine, an exquisite and infinitely complex computer. Some may even say that the brain is the seat of consciousness, the thing that makes us who we are.

Closer inspection is less than supportive of this cerebro-centric view of the human brain. In fact, when you really get down to the basics, this view seems more and more like the view of the ancients, that the earth is the centre of the universe, and all revolves around it.

The brain is a gland. Or rather, it is a part of a glandular complex called the endocrine system. Most of the brain conducts boring, slow hormonal business, gaining input from its distant receptors throughout the body, and sending molecules forth to ensure that the internal environment remains a fit place to live. This miracle, known as homeostasis, allows past sea dwellers to live on the dry and inhospitable atmosphere.

We carry our private seas within, and our hormones are bottled messages, adrift on the waves and tides which bathe our every cell. They drift in their billions. Some, like thyroid stimulating hormone, usually carry fairly simple messages; "Doing fine, maintain course"; "Temperature dropping, step it up a little", and the like. Some, such as adrenaline, fire off more complex and urgent missives, such as "Predator chasing - breathe faster, open airways, open vascular flood-gates to muscles, pump stronger, cease digestion, and run for your life."

They are certainly amazing molecules, hormones. They are the language within, the phonemes, utterances and gossip of the body. Each has their own factory and chain of command, each has

a shape which seems to actively seek out receptors on the cells designed to receive their message, each has specific and powerful effects at astonishingly low concentrations, and each participates in a most extraordinary and exquisite feedback system.

The hormones have ghosts, you see. The molecule is made in the gland, the receptor is made in the cells which listen for, even yearn for the message. One would think that that was that. Message sent. Message received. Over and out.

The truth is far from that. Firstly, hormones need a feedback mechanism, a way of asking for more and communicating

their satisfaction. This is where the brain comes in handy. It is a good organiser and is able to sort through conflicting and complex messages as if designed for the task. The foot hits the appropriate accelerator or brake, and the stimulus is reset.

There are a couple of levels to this. Usually, the organs which produce hormones - the pancreas, gonads, adrenals, thyroid and many more - are dotted around the body for no particularly good reason. Far flung outposts, they seem on the end of a tenuous and indirect communications system. When compared to the nervous system, these remind me of smoke signals compared to telephones.

It may be the reason that doctors have long overlooked the importance of the endocrine system - it is too old, indirect and messy to have too much relevance for "modern man". It is not "sexy" to be an endocrinologist. Compared to brash, self assured immunologists, trendily neurotic psychiatrists, and flashy aesthetic surgeons, this is an occupation for introverts, those who like a special challenge. I can imagine them constructing intricate boats within bottles to wind down after a busy week.

There is no excuse if this is so, for these people converse daily with the molecules of lust and love, fear and fecundity, attraction and aggression. They should be boisterous and invincible, the guardians of the inner secret world. We should be lining up to see these people, not because we are sick, but because we want to live life as it was meant to be lived. Raw, direct, immediate, sexy, fertile.... On second thought, maybe it is as well that they remain a little bashful, and that we know little of their powers and secrets.

What is the value of such an indirect system? It seems that the answer lies in the almost effortless ability of the system to sort itself out, to manage the amazingly complex task of running all the trillions of cells in the body, all without a pilot.

That is it. The endocrine system is our body's autopilot, good enough to manage most day to day tasks which would otherwise require our entire focus and attention.

The brain invests in an automated solution. We are on autopilot, yet like a kid in the cockpit, we are given a wheel to let us pretend that we are driving. Then, like the child, we turn the wheel whichever way the jet goes, feigning control.

Thoughts on perfumes and divorce

Finding the perfect mate is so unlikely that we would do best to forget it. We should search for snowdrifts in the Sahara instead. Finding a good mate, however, is dead simple. Or it was dead simple until recently.

Two items have recently been noted, and it would be best if we paid attention to them.

The first comes from reproductive immunology, in its research on women who miscarry over and over with one partner, even though previous partners caused no such problems. It seems that one of the reasons is that the male is genetically too similar to the female in the liaison. The failure of the fertilised ovum to develop a sufficient variety of genetic markers (technically, histocompatibility antigens) on the surface of the cell marks it somehow as if it were not fertilised, and it is swept away soon after the period was due. Researchers are experimenting with vaccinations made from the man's tissue, given to the women in an attempt to make her immune system recognise his dissimilarity.

Rats and other mammals accurately and optimally mix up their genes by using smell to select partners. Remember that we are "blind" to our own smell. The closer someone else's smell is to our own unique pattern, the lower the pheromonal recognition, and the lower the likelihood of mating.

The second is this. The oral contraceptive pill diminishes a female's ability to select an appropriate partner, with optimal genetic variety, by smell. Off the pill, smell will reliably maximise sexual attraction to enhance genetic diversity. Women select males as far from blood relatives as possible. Once pregnant, so the story goes, women seek the comfort of close genetic stock, namely family, so that security and safety for the offspring is enhanced.

The contraceptive pill mimics the state of pregnancy, yet is used for the purpose of allowing sex without pregnancy. It is a very popular item for fertile young women in search of a mate, yet almost guarantees selection of the "wrong" type of male! All is fine until the pill is stopped, then suddenly the boy seems somehow, well, not as sexy as he used to be. Other men start to look (and smell) quite attractive. The relationship breaks up soon after the commitment to baby making, and mostly it is the woman who leaves, gets bored, finds a lover. Biology at work, unfortunately for the jilted male.

Perfumes mask and enshroud the natural smells of the body, intentionally fooling the nose of potential sexual partners.

I find it more than amusing that our penchant for artificial smells and simple, reliable contraception may have more to do with inappropriate mate selection and subsequent soaring divorce rates than all of our perceived change in social structure and the rest of the psychological bull shit.

I chuckle when I think that our reproductive future, as well as our social structures just may be a function of our fear of smell, and our desire to replace it with something less challenging, more sanitised, less redolent and fecund.

It is a delicious irony. One to be savoured with one's lover over truffles and French champagne.

Chapter 3

Doing Medicine

Paradoxical patients - the start of a medical journey

I began in my own primary care practice on that day in October 1983 when John Bertrand beat Denis Connor for the America's Cup. Maybe I was infected with bravado and heroics on that day, the sense that anything was possible for those with the courage to believe in their destiny and follow a voice within. It was a simple yacht race in the playground of the rich on one level. At a deeper level, it was a parable of facing the odds with courage and conviction, and a fairy tale.

In the early days of my practice, I had plenty of time to talk with those who sought my care, and took the opportunity gladly. My first daughter, Misha, had been born earlier in the year, and I had experienced a miracle. Life was never going to be the same after, and I was keen to understand people more.

The more I talked, the more people came to talk. Not just from my local area, but from around the state, then from around the country. Like Forest Gump, I just kept talking, learning, teaching, and reflecting the combined experience of those thousands of people.

I saw many patients there who complained of finding certain smells intolerable, sickening and mood altering. They suffered confusion, disorientation, a complete loss of recent memory, headaches and vicious mood swings after what were clearly minor exposures to common chemicals - mainly common solvents.

What was going on here? Sure, anyone could smell the same smells if they tried hard enough, but it had little effect upon them. These were people whose lives were turned upside down by a world to which the rest of us had adapted admirably. They seemed the proverbial canaries of society, yet as a doctor, I did not really understand their problem. It was unlikely that they were crazy, as the unusual symptoms were repeated in the histories of patient after patient. It was clearly very real, but what was it? I needed some advice to make sense of it.

Bill, Max and the SEAC

I first met Bill Rea in Melbourne in 1986, when he was keynote speaker for the Australian Society of Environmental Medicine annual scientific conference. This strange Texan surgeon, with a penchant for fancy leather boots and justice for his suffering patients, was an inspiration for me. A few years later in the AAEM meeting at Incline Village at Lake Tahoe, we met again, and he gave some wonderful insights into the reasons for the high pesticide levels in Australians. In 1996, I

had the chance to invite him back to present to a few hundred health professionals, for him to inspire them to a greater understanding of the problems of their patients suffering multiple chemical sensitivities.

Bill has guts and determination, and a pigheadedness that only a surgeon's mother could love. He is fiercely devoted to one thing - the care of those who seek his care and protection. He is not a person to stand in the way of, especially if you are threatening his nest.

We visited Bill's Environmental Control Unit (ECU) in Dallas while we were over for the Incline Village conference, and decided on the spot that we needed this facility in Australia. Joachim Fluhrer and I were joined by a third doctor, Peter Dobie, and convinced a fourth doctor, Tom Wenkart, to modify a ward in his private hospital for our purposes and to our specifications. The Special Environment Allergy Clinic was opened in Sydney in late 1989.

We were fortunate in the location of the clinic. Not because of the beach and the climate at Manly, one of Australia's most famous beach suburbs, and certainly not because of our proximity to the North Head sewerage treatment plant, which had been spewing out heavy metals, dioxins and organochlorines for decades. We were fortunate because Manly was home to a "nose" named Dr Max Lake.

Max was a hand surgeon turned winemaker, and his vineyards produced arguably Australia's finest red wines - Lakes Folly. He had written a number of books about the sense of smell, and family health problems had led him to consider the place of this sense in health and illness. I rang him to ask him along to one of our evening dinners, a piece of civilised data exchange if ever there was one. To my delight and surprise, he accepted without a moment's hesitation.

The meal was a sheer delight. The food was passable, the champagne and wine (provided by Max) divine, and Max enthralled us with tales of wine, women, and perfume. Half way through the meal, my soon to be wife walked in, taking the one empty seat beside Max. Max glanced her way, and with a gesture soon to be made famous by Anthony Hopkins in *Silence of the Lambs*, inhaled a scent invisible to the rest of us.

"You are ovulating, young lady", he declared, "and your perfume is delightful. I am not familiar with it."

Now, I have heard some conversation stoppers, but at a table with six males and a single female, this one beat them all. Everyone stared nervously and intently at their plates, not daring to raise their eyes. All except two. Fiona stared at this strange man, somewhat past middle age, and Max regarded Fiona above the rim of a glass of glorious red wine.

"How do you do, Fiona. I am Max Lake."

"Hello Max. I'm fertile."

Observations from an MCS watcher

Dr Fluhrer, Dr Dobie and I opened the Special Environment Allergy Clinic in part to observe and record the health consequences of low level chronic exposure to toxic agents, and in part to see how we could help those people recover. It was a decision which would change my mind, my practice, and my professional life forever.

In the clinic, we noted many things. Some were small things, like the tendency for our clinic patients to have a temperature about half a degree lower than those in the rest of the hospital. Some were big things, like major disorders of respiration during sleep, and mild brain damage. Some fascinated us, such as the tendency of toxic and chemically sensitive patients to develop evidence of liver damage after two days of a fast (we called this our "liver stress test", though it was never popular for either patients or doctors. The problem was eliminated by supplementing non-allergenic amino acid supplements during the fast).

Above all, though, I recall two remarkable properties which bound the multiple chemical sensitivities patients in my mind.

The first was the utter consistency of symptoms, the most important of which appeared to be neurological in origin.

The second was that while their pathology and other tests were consistently abnormal, there was a remarkable inconsistency from patient to patient when we looked at the types, magnitude and direction of pathological alterations.

Symptoms and signs

To my mind, there are a number of important and interesting factors which distinguish multiple chemical sensitivities clinically from anything I had seen before in my training.

Firstly, there is a massive crossover between multiple chemical sensitivities and chronic fatigue syndrome in terms of symptoms and disability. I personally believe that they are different aspects of a single group of illnesses. My rule of thumb was simply that, if the person's primary complaint was apparently triggered by chemical exposure, and heightened sensitivity to the effects of chemicals was a major, early onset and obvious component, the best description was multiple chemical sensitivities. Otherwise, chronic fatigue syndrome was the common diagnosis.

The symptoms and history of a person with multiple chemical sensitivities is difficult to miss, but there are, I believe, a few subtleties.

The single, defining symptom of multiple chemical sensitivities, and one which in some way separates it from chronic fatigue syndrome, is the symptom commonly now termed "pathosmia". This is a combination of a heightened sense of smell generally [hyperosmia] along with a sensation of disgust or aversion to the smell of volatile chemical agents, at a level of exposure which the majority of the population would find innocuous. More recently, it has been proposed that the term

be changed to "dysosmia", reflecting the difference between this sensation and that of the normal population.

Most commonly, a person has had recurrent exposure to certain, potentially harmful chemicals over a period of time without major problems. There are two different stories from this point.

The best known one is that the person receives a clearly excessive accidental exposure to a new chemical (pesticide, paint, incinerator fumes, etc.), and develops severe acute neurological symptoms, including headache, extreme confusion, dizziness, muscular weakness and sometimes collapse.

The other is that the person leaves the place of their recurrent exposure (say, a farm or factory) for a period of months or even years, and are in good health during this time. On return to the site of original exposure, the first "hit" of the chemical, at a dose which previously did not bother her, suddenly sets off an unexpected reaction including many of those described above.

In both cases, a switch seems to be thrown, and their deterioration from that time is somewhat relentless.

If they were previously alcohol drinkers, loss of tolerance to alcohol is an almost universal feature. Some may still drink occasionally, but they note that the effects of a single drink are now excessive, and a reduction of over 75% in alcohol intake is most frequent.

Surprisingly, smokers are rarely able to cease smoking, as the withdrawal effects become greatly pronounced at this time. This can lead to real problems, as doctors and family will say, "How can you be chemically sensitive. You damn well smoke even more than before, and they are full of chemicals." Smoking habits change, usually to smaller hits (half or quarter of a cigarette) and taken more frequently. The person knows and understands that they would be better if they gave it up, but each time they try, they are dramatically sickened.

From the time of original exposure, the sickening effect of the chemical causing the damage is usually enough to force the person to alter her lifestyle considerably, and this usually involves withdrawal from the offending chemical. I am not certain if this accelerates the stage of "spreading" of the adverse reaction to other, unrelated chemical agents or not. I suspect not.

The "spreading" phenomenon is quite a specific and immensely disabling aspect of the illness. There is no proven theory as to exactly how it happens (although it may be a variation of a conditional reflex, or a kindling mechanism of some type), but the increasingly obvious adverse effects of structurally distinct chemicals drives the person further and further from "normality", and more into a sophisticated hermit's existence.

She suffers from problems with short term memory and concentration, and moods swing between anxiety and depression for no reason (in men, it is more commonly between anger/violence and depression). Headaches of an unusual nature, strength, location and frequency begin, and she becomes profoundly and disablingly fatigued. She may be sleeping an extra two to four hours a day now, but the sleep is often broken and unrefreshing. Sometimes when she stands, she feels dizzy or faint, and notices that she is clumsier than before she became sick.

It is usually about this time that family and friends become frustrated and withdraw support, believing that if the person "pulled themselves together" they would soon recover. The injury has no

wound, the person looks well but complains incessantly about chemicals causing symptoms that no one else feels. Worse still, the three doctors to date can find no cause for her problems on examination or pathology testing.

She is given a referral to a psychiatrist.

With those close to her doubting the reality of her symptoms and suffering, and her own doctor referring her to a "shrink", she becomes more labile in her moods, and starts to believe that she is going crazy. She becomes isolated, believing that she is the only person in the world to feel the way she does. Her suffering has no name, no credibility, and no place in society. She is like a termite separated from the nest - dying slowly of loneliness.

This isolation from her friends, her family and her life sets the stage for a psychiatric diagnosis, and more often than not a form of psychoactive medication. When this does not work (most drugs given to multiple chemical sensitivities patients are given at full adult dose, and react either paradoxically or too strongly), the dose is increased or the drug is changed for a new one. The cycle is thus established which eventually sees a previously healthy person in a permanently medicated and chemically affected state.

In passing, I would say that multiple chemical sensitivities patients, while they may derive some benefit from the use of benzodiazepines (such as Valium), have an extraordinarily difficult time ceasing the drug. This may provide a clue as to one place of pathology, namely the GABA receptors, and especially their balance with the NMDA receptors.

We noted from the clinic some interesting signs and details as well.

Firstly, the temperature of multiple chemical sensitivities patients, like chronic fatigue syndrome patients, was nearly one degree Fahrenheit lower than for other patients in the hospital. Most were around 98.6 degrees, ours were around 97.5 degrees. And this despite the fact that many of them complained of what seemed like recurrent viral infections! The staff were trained nurses who worked on other wards, and all noted the difference.

Blood pressure was unusually low overall, with a typical morning BP of around 110/60. As well, the pulse was weak and thready for most.

The patients seemed to have lost some control of the autonomic (automatic) nervous system, the autopilot which most of us rely on for normal health and adequate response to life's little (and big) stresses. In fact, this poor response to any form of stress (physical, infective, psychological, toxicological, etc.) is almost the hallmark of the disease. What for a healthy person is a trivial or easily managed stress is, for multiple chemical sensitivities patients, a major risk factor in deteriorating their health. They are, in the chaos terminology of Prigogine, near a bifurcation point, and are clearly unstable in their adaptive responses. They are highly sensitive to small changes in their environment, and this is typical of systems "far from equilibrium". In plain terms, they are hanging on by a thread, against all odds, and the merest whiff is able to push them over the edge.

This is noted in the emerging field of chaos theory known (inelegantly) as "self-organised criticality", whereby a single grain of sand added to a sand castle can cause quite a significant landslide. It has also been noted in toxic exposure, where a tiny dose can cause quite significant symptoms, if delivered soon after a high dose that did not cause any apparent symptoms.

All functions controlled by the autonomic nervous system are subject to this kind of alteration. Blood pressure, gastrointestinal motility, pupillary response, sweating, diversion of blood supply to and from muscle and bowel - these are all functions which appear to be inappropriate in people with multiple chemical sensitivities. They do not use this part of the nervous system as most of the rest of us do, to stabilise against stress and co-ordinate basic functions. The responses are chaotic, unpredictable, and often paradoxical.

Weight seemed to be increased in the early stages of the illness, along with decreased exercise tolerance. As time went on, however, nutritional defects and malabsorption began to lead to weight loss, and this was a poor sign as far as prognosis went.

When we put multiple chemical sensitivities sufferers into the SEAC in the first few months, we fasted them on water only for four days. To our surprise, nearly half developed mild liver damage, with disturbance of the liver enzymes. This was completely fixed by the addition of an amino acid supplement to provide the necessary cysteine for glutathione protection in the liver and other organs.

We called this our "liver stress test", because the normal person can normally fast for nearly two weeks before these changes should be seen! Unlike cardiologists, we gave ours away!

One final item worth mentioning may sound strange, but gives a real insight into the illness.

On discharge from the hospital, the patient would go down to the office in the "unclean" area of the hospital to finalise payments of their bills. They had gone through 3 to 4 days of "re-acclimatisation" to the outside environment (there were some very funny stories there), and the instructions were to get back to their "safe" home as soon as possible.

One day, sometime in the second year, we had a hospital staff party, and I was talking with the administration staff. "Wow," one said, "are those chemically sensitive patients strange."

"Yes," I replied, "I know. They probably can't add up simple bills".

"That's not it", she said, "they come down and stand in the office, and look at the bill blankly for minutes. Then suddenly, they focus on one item, a telephone call, a pill, something. And they stand there arguing and fighting over a one dollar item for half an hour in a room with a photocopier, perfume, flowers and three smokers, getting worse and worse before our eyes, but completely unable to give up on this minor detail. The other five thousand dollars doesn't register. Just the one dollar phone call!"

It is an interesting fact that the brain injury of multiple chemical sensitivities places the person at risk of continuing exposure and further damage with the loss of judgement, insight and perspective. The feedback loop is set up, and deterioration is almost guaranteed.

The sight impaired have guide dogs. Maybe the chemically challenged need full time chaperons!

Test results

As I said earlier, while tests were consistently abnormal for each individual, the range and direction of abnormalities across the multiple chemical sensitivities population was quite remarkable.

Some had endocrine (hormonal) abnormalities, some had immune system abnormalities, and others primarily had brain problems. Some had only one type, many had two of the three, while most showed changes in all three. Some had endocrine function up-regulated, some down-regulated. For some it was thyroid, for others it was adrenal, while for others, sex hormones were grossly disturbed.

Some showed clear evidence of autoimmunity (in which the body's immune cells and antibodies attack the owner's own tissue), while for others immune function was clearly depressed, with opportunistic infections.

• *Immunology*

The lymphocyte numbers were generally low, between 0.8 and $1.5 \times 10^9/L$. For the majority of patients, all subsets were on the low side, but the HLA-DR subset (antigen specific, or 'committed' T-lymphocytes) were consistently abnormally low.

The ratio between helper and suppressor T-lymphocytes varied considerably, sometimes well below 1, often above 5 (the "normal range" is between about 1.2 to 3.5, with an average in a healthy person of around 2 helpers for each suppressor). The distribution was also clearly "bimodal", meaning that it seemed like there were two populations rather than one (see Fig 2).

Despite these observations, I believe it is fair to say that multiple chemical sensitivities is not primarily an immunological disease. These abnormalities are probably either an epiphenomenon, one of many toxic effects following chemical exposure.

• *Breathing differences*

We were told by staff in the hospital that our chemically sensitive patients "breathed differently" at night. Occasionally, I was around the ward, and while the variations in breathing were quite impressive, varying from hyperventilation to long apnoeic periods. They were not snorers, nor were most of them overweight to the extent that I would have suspected sleep apnoea.

There seemed to be a problem, but I was unable to get Sydney's sleep clinic interested in the problem. They were too busy making a fortune from obstructive sleep apnoea, selling C-PAP machines, and convincing wives that the real health risk to their family was the overweight, alcohol quaffing, unfit executive husband. This clinic was so rich, they were conducting an expansion program within the public (taxpayer owned) hospital, despite opposition from the more sensible parts of the profession. In any event, they were not about to take on multiple chemical sensitivities or chronic fatigue syndrome patients, who are generally in the poor (most have not been able to work for years, making a mockery of the "yuppie 'flu" tag that they were continually labelled with.

Then one day we were approached, out of blue sky, to assess a new type of sleep apnoea monitor. Why we were approached, we could not figure out, except that its inventors had had a good deal of trouble breaking into the growing market for assessment of children at risk of sudden infant death syndrome (SIDS). If the obstructive sleep apnoea was a bit of a scam, the whole SIDS industry in Australia is an absolute rot, an embarrassment to any thinking person. Fortunately for those who manage it and are forced to publish occasionally, most do not think.

After many years of "Red Nose Days" (in which small plastic red "clowns noses" are purchased by almost the whole of the Australian population at outrageous prices, knowing that the money will go to research into the cause and management of SIDS), millions of dollars have been appallingly misdirected to a small coterie of researchers and clinics, and the result has been predictably poor. These people stand like the emperor, without clothes. The research has led nowhere, the approaches defy logic and science, and the outcome is pathetic. Do not lie children face down in their cots. Do not lie children on their sides, or they may maliciously flip themselves onto their fronts and suicide.

Doctors should be forced to study evolutionary biology. In any hypothesis relating to health, disease and especially death, a critical question must be, "If this hypothesis were correct, would humans with this trait have successfully survived to the present?", If the answer is, "No, this trait would tend to reduce the chances of survival for any human that possessed it", then the hypothesis had a problem.

The strongest hypotheses on disease and death are those which show how there could in the past have been a distinct evolutionary advantage to a particular trait, and that this prior "advantage" has turned to work against those who possess the trait as a result of some definable change of diet, environment or alteration of lifestyle away from our evolutionary roots. To suggest "faulty" children, putting their life at risk because they do what over half of all children do (i.e. lie on their sides or fronts) is intellectually untenable. Yet we all find it hard to call the bluff of experts, especially in such frightening, senseless and tragic illnesses.

Still, as my father used to say so eloquently, time wounds all heels. The lack of accountability and progress for the money contributed by the community will, one day, be called to account.

We placed the respiratory monitors under the adults mattresses at night, for this was the forte of the new sleep monitor. It was not worn, nor did it disturb in any way the sleep of the person. In addition, it possessed a computerised automatic gain, which allowed for data to be collected from a person whose weight was as low as one kilogram, all the way up to one hundred and thirty kilograms.

We had six cases, and six age and sex matched healthy controls selected from staff and relatives of staff. The data were collected blind, and the units returned to the supplier.

Vera rang us a day after, with the words, "It is chalk and cheese. We can tell you who the cases and controls were right now. We will just do the statistics, but your cases look just like 'at risk' babies. Long gaps between breaths. They would have set the alarms off all night if we had enabled the buzzer."

We waited for the graphing of the data, certain we were on to something big. When we sat around the table, and looked at the graphic output of the results, it was far from “chalk and cheese”. It was “mouse and elephant”.

I recall attending a wonderful lecture by Jaques Benveniste in Nevada in 1988. During this inspiring talk, he told us in a delightfully tortured French accent, “there are some things which are totally obvious. You do not need a double blind, prospective crossover clinical trial to determine which is taller, a man or the Eiffel Tower. You use your eyes and common sense. I call it the ‘bloody obvious test’.”

What is obvious is not always true, so we went through the process of graphing out the differences. It was not only that there were longer gaps between the breaths measured for the multiple chemical sensitivities patients, there was a whole different phenomenon occurring during sleep (*Fig 1*). Because the monitors discarded data on gaps between breaths of less than six seconds, we were left wondering about the extent of the compensatory hyperventilation (which we could determine was happening simply by looking at sleeping patients). The apnoeic periods, however, were undeniable.

Reworking the figures, we learned that in an average night’s sleep of eight hours, nearly two hours was spent in apnoea, presumably with a compensatory hyperventilation after each apnoeic episode. No wonder people woke feeling unrefreshed in the mornings!

In addition, we realised that this was evidence of brain injury at a fairly profound level, interfering with the normal neurological mechanisms controlling respiration during sleep.

We have yet to really follow this aspect of the illness up, but I believe that it may yet provide some critical insights into the illness. I will be prepared to bet that the sleep clinics will grab this finding, and make it really pay, especially as the adult sleep apnoea falls out of fashion.

• **Central evoked response testing**

Another test of neurological function, the Auditory Evoked Response Potential test, proved bimodal in a way similar to that of the immunology. This is a simple, cost effective test of neurological function, often used to determine the degree of neurotoxic damage from solvents in the workplace. The critical single figure was the P3 latency, a measure of the time taken for the “peak” of the recognition wave to occur. The average for the population is a value of around 308 milliseconds, or just under a third of a second following the sound. The spread of the healthy population is a normal distribution, sometimes known as the “Bell Curve” (*Fig 2*).

The average for our multiple chemical sensitivities sufferers was 328 milliseconds, but there were two distinct groups (*Fig 3*). One group showed a delay in the P3 wave, averaging over 340 milliseconds. The other, smaller group, showed a speeding of the P3 wave, averaging around 275 milliseconds. There were very few of our multiple chemical sensitivities patients where the peak would be expected, around the 308 millisecond mark.

There are a few points to make here about the Auditory Evoked Response Potential test, and all of them, I believe, lead to some insights into the disease process.

The first is that although there were two distinct groups, individuals did not move from one group to the other. Their AERP responses were, in fact, quite stable and were among the best descriptors/predictors of the degree of disability. That is, the more abnormal the AERP was, the more neurologically disabled the person tended to be (there are some subtleties to this, for not everyone is neurologically damaged in multiple chemical sensitivities, but this will do for now).

As well, recovery of the AERP was the single best predictor of good outcomes in multiple chemical sensitivities. Those with stable, abnormal AERPs tended to recover poorly, while those with improving (even slowly improving) AERPs tended to do well. There is a strange aspect to this recovery, however, and if it is not understood, it can lead to all sorts of problems in management.

Severely abnormal AERPs are associated with severe neurological impairment, but not always with many complaints from the sufferer. It is more the family and friends who notice the problems. Why? My own guess is that at this level of damage, the brain becomes an unreliable auditor of its own function and disability. We see this in Alzheimer's disease, and alcoholic brain degeneration, where everyone but the sufferer is acutely aware of the disability and damage. To a lesser extent, anyone who has been drunk can appreciate that one's own opinion of one's neurological loss is often at odds with reality. People continue to jump into cars, believing themselves to be capable of driving without problems, when any of their sober friends can see that they are seriously incapacitated.

Alzheimer's disease does not recover, while multiple chemical sensitivities can certainly improve, even if they do not "recover" in the usual sense of the word. The paradox is that, during the recovery phase, the sufferer will often complain increasingly bitterly about their problems, and tell their doctor that things are worsening rather than improving. The doctor may notice that they are clinically improving (they could not complain at all coherently previously!), yet assume that something is really making them worse, as they say, and institute a fruitless search for this "confounding factor".

The AERP provides a useful "window" on this situation, and is a very good tool for feedback on progression or improvement of the illness. The other useful tool is the sufferer's chaperon (spouse, child, parent, etc.).

As the person improves in neurological function, the AERP and the close family both are sensitive "indicators" of objective improvement. If the sufferer is complaining more vehemently about things he cannot do or remember, but the chaperon and the AERP both suggest improvement, then things are improving as expected and the person can be reassured that their complaints will soon improve. It is only when the P3 is getting close to 308 milliseconds (say, between 290 and 330 milliseconds) that the person will start to notice the improvement and "normalising" of their previous problems.

I believe that this failure to understand the nature of chemically induced brain damage and the process of recovery lies at the heart of so many failed interventions in multiple chemical sensitivities. Many doctors believe that the job is to make the person complain less, and for a brain injured person, this can certainly be done with strong psychoactive medications. There, a good shot of a major tranquilliser, or a sedative, or an antidepressant and - wow, the person is complaining no more! Miracle cure!

Wrong! Try again!

The person is not complaining as much, true. However, they would complain even less if one simply anaesthetised them! No brain, no pain. The treatment further disturbs the already altered neurological balance, and the person develops new adaptive responses to manage the new insult.

I would go so far as to say that it is not, in theory or practice, possible to normalise the brain chemistry and balance with strong, brain active molecules! My experience is that these well intentioned attempts to “adjust brain balance” are misguided, and themselves are the result of a superficial understanding of this profound illness.

Conclusions from these tests

These tests, in total, suggested two things to me. Well, three things really.

Firstly, we were not dealing with an homogenous, single disease entity. More likely, these people represented a group of disorders with common symptomatology, much as we had found in the closely related chronic fatigue syndrome.

Secondly, if one were not careful to divide this group up into appropriate sub-groups with common defining characteristics, the statistical assessment of the group would tend to average out the variations from the mean, and would fail to find real differences between these people and the “normal” population.

Thirdly, and for me most importantly, it suggested that we were finding stable states of health (or ill health) which were not subject to homeostasis, or a return to “normal” function, any longer. I say this because the peculiarly individual “abnormalities” remained surprisingly constant over months or years, and had all the hallmarks of a stable adapted response. Whatever the original injury and damage, the expected recovery did not happen. Instead, the body’s response altered other parameters of function to “re-stabilise”. So, for example, an autoimmune pattern of antibody responses led to an increase in suppressor lymphocytes to minimise the aggressive response of the immune system, and a drop in thyroid function. The temperature lowered into a state of mild hibernation, minimising physical demands of a system under stress. The person was not well, but was not as ill as they may otherwise have been. More importantly, they were not about to “re-cover” if recovery increased damage and shortened life.

It dawned upon us slowly exactly what this suggested. The problem may have been an adaptive response to an environmental stress of some type. We were not looking at an organism sick and out of balance at all. We were looking at one which had arrived at some type of crude balance with an environment no longer compatible with good health.

This interested me, for as a doctor, I was used to the concept of fixing broken people. What if, in this case, the people were not broken, but their environment was. What was I now treating? What would “recovery” or “cure” look like?

I believe now that I am misguided in attempting to make some people fit into an unhealthy environment. They withdraw, and seem to be healthier (apart from their multiple chemical sensitivities!) than their counterparts. It is hard to know who is sicker, them or the planet.

Ponds Hand Cream

The Special Environment Allergy Clinic (SEAC) was one of life's most exceptional learning experiences for me. It was a zoo of neurological abnormalities, all unnamed and unacknowledged. The neurologist used to say, "There is clearly a neurological problem, but I have not a clue what it is." Nor did anyone else, at that time back in 1990.

One day the three of us entered a patient's private room, at one extreme end of the corridor in the SEAC. The door was firmly closed, and on entering, we saw the patient (who had been doing very well) huddled in one corner and crying. What had happened? "It is Ponds Hand Cream," she answered, "someone is wearing Ponds hand cream in the ward".

We all knew not to wear perfumed creams into the SEAC, and had a strict "visitor sniffing" policy. At its strongest, Ponds hand cream would be difficult to smell, with almost no perfume to it. We all sniffed our hands and the air for any hint of an unusual smell. All was as it normally was, and no other patients were complaining. We tried to reassure our patient, then walked out to continue our rounds. She called from the doorway of her room, "Down there. That's where it is", pointing to the other end of the corridor.

We discussed her olfactory hallucination, and arrived at the opinion that there must have been some deeply rooted psychological problem related to her mother, who we guessed had used the hand cream when our patient was a child. We called over the psychologist, Mirella, who was just finishing a relaxation session with another of the patients, and asked her to see our patient about her "problem". She asked us what the patient felt she was reacting to. "Ponds Hand Cream!", I replied.

Mirella went pale before us, then flushed in embarrassment. Just this once, just today, Mirella had used Ponds Hand Cream before she came to the unit. She had wiped it off carefully, but had not washed. We leaned down to smell, and yes, there was the faintest of aromas. A pleasant, light smell that fell away by the time our noses were a foot away from her hands. Our patient was over twenty yards away.

I learned that day that explanations based on indefinable (and essentially unprovable) psychological explanations are frequently our first answer, but are rarely our best.

Chapter 4

Politics and medicine

The problems with specialising

It seems to me that the more specialised and academic a medical practitioner becomes, the more useless they become. It is such a common and obvious observation, that it begs for an eponymous tag, like "Mark's Maxim". Certainly, if you happen to have the good fortune to be referred to an appropriate specialist, one whose specialised knowledge exactly covers your problems, then you may benefit. The art in this case is with the *referrer*, not the specialist.

In most cases, specialists seem more concerned with real estate investments, stock markets prices or academic advancement than they do with the care of the suffering person before them. They have a certain "detachment", a separation from the needs of those before them. Ultimately, they can send difficult patients back to the referring doctor, not dissimilar to the return of damaged goods, with a note to the doctor.

These are dangerous people, best avoided except for minor technical jobs and specific information. I know there are exceptions - people of great wisdom and humility - but these are rare beings, and usually ones who have grown far beyond the limited bounds of their speciality.

That the rest are reimbursed so highly for contributing so little is a travesty. Specialists and academics have become the medical aristocracy, little concerned with the day to day hubbub of life, the simple catastrophes, the worries of the people they serve. They pontificate without the experience required at the coal-face. On the whole, they are parasites, supported by the community, providing too little in return to consider them symbiotic.

That, I think, is my beef with specialists - they are too clean, too soft of hand, and too sure that they are right. Mostly, they are not.

We need to assign them to community duty in primary care, the "front desk" of medicine, for, say, one year in five. It works for McDonalds, though I am not at all sure that this should be considered a recommendation! Demanding that the gods descend will cause a stink, but will improve the care of those we serve.

Specialists spend much of their time either squeezing hexagonal pegs into round holes, or finding no problems where clearly problems exist.

Both these approaches cause immense problems for those with novel, challenging or emerging illnesses. In the "hexagonal peg" scenario, the problem is reduced to one which fits with the specialist's training or interest. Failing to see the bloody obvious is less dangerous, unless the specialist is to give a report to a lawyer or insurer!

Each approach can lead to gross errors, occasionally flirting with scientific fraud.

In Australia, for example, we have a public hospital unit which persists in labelling people who suffer multiple chemical sensitivities and chronic fatigue syndrome as “food chemical sensitivity”. The director dismisses the multiple chemical sensitivities complaints as “over-smelling” and “chemophobia”.

He clearly has not spent sufficient time with the people, or has not had time to listen. He is actually on far too many important committees to do the day to day work anyway. A very important person, as he will tell anyone prepared to listen. The “unpublished perennial expert”, as many call him.

In this doctor’s view, naturally occurring food chemicals such as salicylates, amines, and nitrites are the real culprits, rather than environmental or food contaminants. The doctor and his clinic have as yet not published this information in reviewed journals (he is too busy chairing important regulatory committees), so assessing their views has proven problematic. The challenges are not appropriately blinded, and are given to people to take home and consume while filling in a diary.

The results of this approach are worse than meaningless. They are misleading. Patients often want to have reactions, if only to prove they are really sick. Many break open the capsules to taste them, attempting to distinguish placebos from “active” compounds.

We used the same challenge capsules in our Special Environment Allergy Clinic, properly controlled and blinded (neither the administering staff nor the patients knew which was which, and all capsules were consumed whole while being watched by the nursing staff). There was little difference between placebo and the food chemical capsules.

The Special Environment Allergy Clinic was visited by this doctor, and he had an inordinate interest in our outcomes. We told him that we could not find a response any greater than placebo, and asked him for his publications and protocols so that we could understand the differences. No such documents existed, and he wrote a rather scathing report of the clinic, and provided it to the government of that day. The logic was that if the SEAC could not replicate the results of his own clinic, that this was, *a priori*, evidence of either anti-science or fraud.

One could dismiss this as a peculiar aberration of a second rate hospital in a single city in a far away country. It is not. It is the recurrent story of those who use their standing and academic position to dictate right and wrong, good and bad, science and anti-science. No data are needed, no logic or reasoning applied, and most dangerously, not for one moment do such people believe they could be wrong. In such a climate, it is no wonder that science and integrity are so often early casualties of “paradigm wars”.

Crazy people, crazy doctors

Changes happen. Being humans, we search for reasons, possibly even more than we search for meaning. Where causes are not easily found, we invent causes. The brief is simple - invented causes need to be unprovable and undisprovable. They need to give the impression of science. They need to make the majority of us comfortable that the causes do not apply to us. We need, in

short, a type of rubbish bin for medicine, where we dump the conditions and people who we either do not understand, or who make us uncomfortable. Psychology and psychiatry will do for now.

These are pernicious bastard children of medicine. Ever ready with an explanation which fits the needs of the medical model, there is no escape for the people trapped in their prejudices.

I have this week been dealing with the destructive potential of this nonsense. In a family who sought my help, the mother and the eldest child, a ten year old, are very chemically sensitive. The family is well off, however, and has been moving from area to area in an attempt to find a place to live where life can be close to normal. The child is slow in learning, as can be expected when a young brain takes a battering from neurotoxic chemicals. The parents are pushing for him to have as normal a life as possible, and have enrolled him in schools wherever they live.

Still, the child can attend school only some of the time, sickened by the textures, glues, paints, perfumes, and other smells which cause only asthma in others. When he is sick, he spends time at home recovering. When he is affected, his behaviour becomes impossible to control.

This situation is untenable for both the school and the community. The other children in the school do not have such problems, and the products used are commercial products, proven to be safe. The school is not to blame. Both school and the community look at the situation, and need another explanation. It must be the parents. They are making the child neurotic, with their obsession with chemicals. They simply cannot discipline the child. A neighbour soon becomes so sure of this that she calls the police with the allegation of psychological abuse on the part of the parents.

The police visit, scaring the wits out of the parents. Their fear triggers a call to the Department of Community Services, who seek a friendly "visit" with the family to help them out. The parents agree, and feel relieved that some help may be at hand. The visit is anything but friendly or helpful, as they find that the "concern of the Department" can lead to the forced separation of their child from the family, "for his own good". They will be keeping an eye on school attendance, and problems here in the future could mean the worst.

Become those parents for just a moment. Feel what it is to be told this. Feel what utter powerlessness is like. What do you feel? What would you be prepared to do? How would you respond?

I am a parent. I have felt the fear engendered by this Department's threats. Tears fill my eyes each time I recall this. I would rather die than lose my child. I would be prepared to kill to prevent someone taking my child from me. They are my responses, as a male with a somewhat abbreviated emotional vocabulary. Others would choose other responses.

While children die of abuse and neglect across the whole country without a passing glance from these social engineers, they meddle and threaten the families they are meant to protect. As the Department of Defence is a department itching for war, so the Department of Community Services is a department desperate for community disruption. They need their shadows to justify their existence. They, like medicine, have become self-serving.

The Department called in a psychologist, an expert two years out of college. On the basis of this person's undisclosed report, they have demanded the parents to attend court with the child, so that a magistrate can decide on custody. The psychologist and the Department cannot believe that

the condition exists, so an alternative, acceptable explanation is constructed. It requires no proof, cannot be disproved, has no need to fit the facts, and is based entirely on opinion. Doctors are brought in as expert witnesses, attesting to the impossibility of the described sensitivity, having never met the family, nor seen such problems before.

The stage was set for a very interesting showdown. The problem is that no one can believe for a moment that they may be wrong. Absence of knowledge is mistaken for knowledge of absence of the condition.

The story has progressed in an unusual and tragic way. The pressure from the Department took a huge toll on the family, culminating in the mother threatening to kill the father for not supporting her with either her own multiple chemical sensitivities, or that of her child. The husband called the police and had his wife committed forcibly to a mental institution in a public hospital. She called me at my surgery with the police on the doorstep, and a psychiatrist there to pronounce her insane. The children were banished to another room with the father, so that they would "not know what was happening". I talked with her, and then to the psychiatric nurse. I told her that medications should be avoided or minimised, and she should be kept from exposure to perfumes, cleaners, and other strong smells. There was a stunned silence on the other end of the phone. "We thought she was deluded in this crazy belief. We can't just change the whole routine for her", she said. "Yes you can, and you will", I replied.

Although the mother was about as stressed as is possible for a human to be, knowing that she was about to be forcibly separated from her children and admitted to a mental ward, she was entirely able to describe what led to this position. She explained that it was an empty, though dramatic, threat to her husband because his work had kept him away from home for weeks, leaving her overloaded with sworn depositions for the case which would decide if the government department gained custody of her children. She was not irrational, though she was hyperventilating!

The good news, if such a story can be said to have good news, was that the young psychiatric registrar at the hospital decided not to medicate her, and listened to her story. He then called me and said he had heard of this condition, but assumed it was rubbish in the past. He asked for medical references, and information on how she should be best managed, and noted that there was no evidence of psychiatric illness, but that there were clear neuropsychiatric changes such as would be expected in solvent induced brain injury.

She was lucky to strike such a doctor, a trainee in psychiatry, rather than a busy specialist, who would not have talked to her or followed up. She could have ended up medicated and unresponsive (because of the excessive effects of "normal" doses of psychotropic medications in multiple chemical sensitivities people), and this would indeed have "proven" her inability to care for her children.

On the other hand, she was unlucky that, in protecting her child with multiple chemical sensitivities, she ran headlong into the stresses which pushed her beyond her own limits.

My point is that for multiple chemical sensitivities people, it is currently safer to keep out of the "system" than to stay in it. Our society finds misfits intolerable, and finds ways to either exclude

them or return them to what we think of as normal. The job, as I see it, is to understand the reasons for the illness, and the causative factors, and either fix the causes or accept the disability.

If you had been the mother in this case, what would you do? Powerless, unbelieving, and stressed by the child's illness and the threat to the family unit, what would or could you have done?

If I were the magistrate, I know what I would do! I would outlaw evidence from psychologists and psychiatrists, or at least rank that evidence the rough equal of fairy tales.

I would also ban medical students from sniffing formaldehyde while doing anatomy at Med School. The brain damage it appears to have caused is an intolerable waste. The intolerance it appears to breed is also intolerable. Psychosclerosis is at present epidemic in the medical profession, and one would have to guess that a preservative like formaldehyde has contributed to this terminal hardening of the attitudes.

The price doctors pay

Today, I received a letter from the Minister for Health and his cur, the Health Insurance Commission. It is a demand for repayment of nearly \$A6,500 of government money paid out for consultations and pathology investigations of people with chronic fatigue syndrome and multiple chemical sensitivities. A further \$A6,500 "administration fee" was required as well. Let's see, maybe I can pull it out of petty cash, or maybe my three year old's piggy bank.

In 1993, I spent a year before an "expert" committee, painstakingly explaining each test in each patient whose medical records they had seized and copied. None of the four doctors had ever seen a person with multiple chemical sensitivities, and they generally did not believe that either multiple chemical sensitivities or chronic fatigue syndrome actually existed as clinical entities. Not surprisingly, they found that appropriate care for these people was unnecessary, and should have been given to a psychiatrist. I spent too long with each patient, and requested tests of immune and hormonal function. Strangely, the fact that most of the testing showed gross abnormalities could not be taken into consideration. The issue was not a question of me being correct, but practising in a way which would be expected of "an average primary care practitioner".

It was found that the average doctor would not have performed these tests, however necessary they may have been, and therefore I should not have done so either! This was the classic, government appointed kangaroo court. No rules of evidence. No natural justice. Decisions made secretly with no requirement to state the logic or argument for any decision. And four doctors who, had they been competent, would have had better things to do with their lives. And absolutely no consideration given to the fact that abnormalities were identified and corrected, and these chronically and severely sick people recovered.

1993 was a shameful year for medicine in Australia. It was a shameful year for the bureaucratic bullies who decided to sacrifice a few of the best doctors careers because of their fear that an unusual new illness would cause a budget blow-out.

I was "requested" to repay only \$A13,000. Two other doctors who were doing exactly the same work and investigations were hit with \$A85,000 and \$A108,000 fines. Same patients. Same pathology testing. Different "judges".

The HIC has driven one doctor out of practice, financially destroyed him, and have now destroyed his health. He is forty, with three young children, over a thousand desperate patients, and he was one of the most resourceful, caring and committed doctors I have ever met. It is a tragedy that he has been wasted in the purge.

I know him well, as I know all of the doctors who were demeaned before these committees. I believe it is important to tell the story, as it is very much a part of the problem of all people who suffers multiple chemical sensitivities or any adverse chemical effects on their health.

It all happened at once, to four doctors in three states. Almost all the seized notes were those of people with multiple chemical sensitivities and chronic fatigue syndrome. Many patients suffered both conditions. The clinical notes were copied and are currently stored at the Health Insurance Commission (HIC) in Canberra. Those health authorities have refused to destroy the copies of those notes following the committees of inquiry.

The doctors are all high quality, thoughtful and caring doctors. I speak of the other three, because, although I believe myself to have these qualities, I am in no position to judge. These doctors spent time with their patients. They took seriously the complaints of people who, to the rest of the profession, simply did not exist. They looked for causes of the suffering and illness. They refused to pass them on to psychiatrists. They guided all their patients to an understanding of their illness, and helped many of them to recover. They did this despite the hours of unpaid work and the threat of retribution by the faceless economic rationalists in the HIC. Their only mistakes were to believe that this was enough to protect them. It was not.

I am proud that I was among them, and that none of us buckled under the demands to "repent". I am ashamed when I hear of doctors who will no longer see people with chronic fatigue syndrome or multiple chemical sensitivities, simply because the HIC has threatened them with the same unwinnable ordeal. And I am deeply ashamed of my profession, when I watch us cower under bureaucratic threat, neglecting our obligations to those who seek our help.

Sometimes, when I consider what has happened, I look forward to the day when we may have an historical perspective on this medieval approach. When I begin to feel anger and bitterness over my own ordeal, I understand how powerless and frustrated those who suffer these illnesses must feel. Each caring doctor we drive from medicine is one more nail in the coffin of a dying profession. As the healing, care, laughter, crying, love and wisdom is driven from this would-be science, people turn away.

For me, life's greatest privilege has been to heal and be healed. It is a mystery and a miracle. From life's starting to life's departing, the joy is to learn of her secrets and reflect them back to those who entrust their care to us. We hold the right to that sacred space in the lives of others'. I do believe that as a profession, we have lost the right to claim that privilege.

It saddens me that doctors are now peripheral to health, reduced to the role of biotechnicians by the insidious demands of government and pharmaceutical multinationals. It saddens me more to see my colleagues believing that they are more than this. We hide behind a pseudo-science, terri-

fied of death, unable any longer to feel the suffering and joy surrounding us, insulated by icons of twentieth century medicine. We all believe we are more, but we are not. We have lost our way, and have become superficial. We can provide no meaning, no soul. Only pills, disease names and prognoses.

No matter. Life survives, even if individuals, communities, even species lose their way. The science of medicine is wonderful in wise and healing hands. Otherwise, as a substitute for care and healing, it is simply another threat to health.

Maybe doctors can relearn the art from their patients such as those with multiple chemical sensitivities. With some humility and enough time to listen and feel with every person who seeks our care, we can yet reclaim the knowledge and wisdom which is the hallmark of the healer.

The politics of testing in multiple chemical sensitivities

I have little time, personally, for the argument that simply making the diagnosis of multiple chemical sensitivities on clinical grounds is enough. In Australia, we are told, testing of these people with expensive pathology and imaging is insupportable and unjustifiable. What benefit can a particular pathology result provide for the patient's best care?

I listened to a cardiac surgeon on television last night. He is a leader in his field, from one of our best known hospitals (it's "real life story" is on TV now, competing with ER! Very strange.), and was talking glowingly of the great age of medicine we find ourselves in, if only we are prepared to pay for it. He looked to the camera and said, "We can take a frail 85 year old woman, do a cardiac bypass with unbelievable safety, and restore her to a normal life again. Who would have believed this possible?"

Who would have believed it possible indeed!

I find it obscene and offensive that no one will stand up to the surgeon and prevent him from misallocating vital funds. I find it obscene that the cost of this one operation, which is borne by the taxpayer, is greater than the entire research budget into multiple chemical sensitivities in Australia. I find it obscene that doctors who spend a thousand dollars or less in the assessment of a young person at risk of becoming permanently disabled and sick are hauled through committees and are professionally humiliated, when the young surgeon drives home in his Ferrari, having earned ten thousand dollars or more for his hard day's work, secure in the knowledge that his profession will protect him from criticism or audit.

The tests used in defining multiple chemical sensitivities are imperfect. All medical tests are. Yet they do provide those vital clues as to where to look for the causative and contributing factors. The doctor's use of the tests become as integral to his assessment as his hands and eyes, and are often idiosyncratically collected over time.

It is a hard thing to explain to economic rationalists (who, by the way, I consider a greater threat to survival than even psychiatrists and toxicologists), and it is hard to explain to disinterested doctors, but I will try here

I was asked once before such a committee, "Doctor, what do you think it would cost the country if every doctor took your approach to assessing and diagnosing these people with these tests?"

I replied, "Much less than it does at present."

Eyebrows were raised, and a patronising snort followed by a chuckle emanated from the chairperson, as he asked, "And just how could that be, doctor?"

"Well, for one, this committee would not have been convened at a cost of over a hundred thousand dollars. Secondly, people would be diagnosed early on in their illness, saving hundreds of unnecessary and costly trips to doctors. And finally, these people would be working instead of sick, and would be earning the country some money." If I had thought more quickly, I could have gone on about medication costs, psychiatric costs, compensation court costs, and the useless payments made to lawyers who take on the fights after the injury is so severe and so permanent that the person has no other recourse.

A two billion dollar error of judgement

"A billion here, a billion there. Pretty soon you are talking real money."

Attributed to J P Getty

There are some mistakes that cost more than others.

I once had a patient with multiple chemical sensitivities who sat down and began with the line, "Doc, I'm losing it at work. I can't focus or concentrate, and we're losing a lot of money because of me."

"You are losing your boss money, and that's why you are here?" I queried.

"Yep. Lost one hundred and forty million last week. I just can't afford to keep doing that."

I regarded this casually dressed, distressed man in his early thirties. I had misheard, surely. "Excuse me", I coughed.

"A hundred and forty million. Eighty million the week before. I work for the Reserve Bank in the foreign exchange department. One bad day, and a billion could go."

Suddenly, the consultation seemed more piquant than most, and I felt a sense of responsibility to the country that I had not previously experienced.

I also thought about this afterwards, and continue to do so years after. How much, I wondered, have we managed to lose through this invisible disease? How much intellectual capacity and function have we managed to destroy, gone before we had the benefit of the asset?

I still do not know the answer, but I do know where two billion went!

We had been running the Special Environment Allergy Clinic for a year or so when I first spoke with Dr Richard Teo, of a state government agency known as WorkCover Authority (WCA). WCA

is an agency designed to set and enforce workplace standards of safety in New South Wales, and has similar parallel organisations in the other states.

WorkCover collected the money from the compulsory “workers compensation employers contribution”, and put it in the bank. That was about it, really. In 1991, it had a healthy account surplus of two billion dollars, largely from the gross overcharging of employers due to actuarial miscalculations stretching back decades. It was a “comfortable” institution, not prone to rocking the boat and disturbing a good thing.

I could reliably get an answer that there was no problem with pretty well any workplace, if I was an employer and was so inclined to ask. Healthy notices were provided to employers of “random inspections”, and many was the occasion that a patient, who had clearly been poisoned in their workplace, was dismissed after WCA gave the premises a “clean bill of health”.

There would have been a flourishing business available for any entrepreneur to hire out the safety and protective equipment to dodgy firms on a handsomely profitable hourly basis on the inspection days. The employers and building owners knew the rules for worker protection, they simply decided that this was only for “queers and poofters” (the exact words said to me by one building owner), and elected to place those workers lives at risk.

When the day of the inspection came (with 2 weeks notice), the workplace was spotless, no work was being done, and safety equipment never previously seen at the site appeared. Air quality was measured. Noise was measured. Heat and humidity was measured.

No problems found.

Complaining employee humiliated and fired. No compensation for injury or disability. Status quo maintained. WorkCover coffers swell ever larger.

By 1991, it was clear to me and to many of my colleagues that organic solvents, pesticides and other toxic chemicals were damaging people severely. It was equally apparent that the importance and prevalence of this low-level toxicity had been grossly underestimated.

We had by this time the Auditory Evoked Response Potential results and abnormal sleep studies from the Special Environment Allergy Clinic. The evidence, I felt, was pretty clear that something big was happening, so I decided to approach WorkCover and address them about a way of assessing and managing these people.

The principle and the message was simple. Identify those at risk or in the early and reversible stages of damage, remove them from harm, and prevent a lot of damage. Obvious. Simple. Doable with a little money.

I made two mistakes.

I overestimated the intelligence of the WorkCover experts and specialists.

I believed that a government regulatory body could act rationally.

I presented our findings from the Special Environment Allergy Clinic, and proposed a joint venture business of an active workers health monitoring system using the Auditory Evoked Response Potential (which, you may recall, WorkCover already used). Thousands (rather than dozens) could be tested each week, catching the damage at the earliest, reversible stage.

A group of us carefully put a warning to a room of thirty or so "experts" in toxicology and occupational medicine, all far more qualified than ourselves. We predicted that, unless a proactive monitoring system was used to protect the nervous system of workers, the subtle, progressive neurological disease and deficit would be the next major issue in toxicology.

We said, bluntly, that unless WorkCover was prepared to dip into its \$A2 billion surplus, and work with us to develop an early warning, active monitoring system, that they would be considered negligent in their duty of worker protection. We predicted a flood of claims for neurological damage unless such predictive technologies were put in place. We told them that the investment of a million dollars at that time could prevent a pay-out of hundred million dollars within five years.

We were politely questioned, the issue was politely discussed, and the proposal was politely killed over tea and cream biscuits in the corridors of WorkCover. There was no problem, or surely all these experts would have known about it. They were, after all, the specialists in this field.

We were, in fact, wrong in our predictions. By a factor of twenty.

By late 1995, WorkCover was broke. Two billion dollars had been lost in compensation claims in five years. Mysteriously, thousands of claims had emerged for "stress related disorders". They were lumped into "psychological stress" and payments flowed like the waters of the Hudson River.

Guess what. Most had nothing to do with psychological stress.

The people we tested had neurological damage, very distinct from anxiety and depressive disorders, and they came from industries like painting, cleaning, agriculture, and from indoor office environments. Their problems were confusion, emotional lability, loss of short term memory, delayed reaction times and learning difficulties.

A smarter choice in 1991 could have made an impact, and could have prevented at least a billion dollars in pay outs. That money could have been channelled back into early identification and prevention.

Now, however, there is no money for such preventive programs, workers compensation payments by employers have soared, and the State Government has moved to cut out all compensation for "stress disorders". Now, there really is stress for those suffering brain damage, because the law says they cannot be compensated.

One looks back on some days and wonders just how things might have been different, if only.... That day at WorkCover is one of those days for me.

Chapter 5

Problems in Toxicology

Risky benefit

What creates discrepancies between the results of scientific experiments, and the world in which we apply the results of those experiments? Why is it that experimental results, meticulously gathered and truthfully reported by honest scientists have almost no currency in the world around us?

I believe the problem in translation lies at the heart of analytical science itself. I find it difficult to distinguish if this failing is inherent in the scientific process, or simply a consequence of the clumsy and ignorant way in which we currently practice science. My feeling is that the real problem is the former, magnified by the latter.

Look at toxicology.

We are inventing and releasing thousands of novel molecules every year in the pursuit of commercial gain. Each molecule has potential uses (benefits), and potential consequences (risks). How are we to weigh one against the other?

Neo-Darwinism may give us a model for considering the problem. This theory holds that the majority of genetic variations, or mutations, are not beneficial for the individual who develops them. Most are harmful, many are even fatal. Only the tiniest minority of mutations confer an evolutionary advantage, and even then, only in exceptional circumstances such as radical environmental changes. I must admit that I do not personally subscribe to this view, but it is the dominant, almost exclusive, paradigm in biology today.

By analogy, therefore, one may hold an *a priori* suspicion that the majority of “mutated” chemicals would carry with them a likelihood of increased risk, rather than benefit. It is true, however, that the humans who have “mutated” these chemicals have done so in the hope of increasing benefit while decreasing risk. The question is, “Have they been successful?”

The fact is that we have so little understanding of the dimensions and types of risk, that no coherent framework exists for its accurate assessment. We are in no position to know whether we have increased or decreased risk with a new molecule, even when we are certain that we have increased benefit. This is a strange situation, where one side of the equation is known while the other is deeply mysterious. How could this be?

Risk is inherently more complex than benefit. Benefit is targeted, measurable in the single dimension suggested by the proposed application of the molecule. Does it dissolve grease, kill insects, enhance growth or reduce cholesterol better than the previous molecule or not? Because of this, benefit is seen quickly, and is relatively straightforward to determine. The potential for profitable exploitation of the improved product is often vast.

Now the sticky questions about risk arise. There are only a few ways in which things can go right with a novel synthetic chemical, but an almost infinite number of ways in which things can go wrong. Risk analysis in this area is a mess, and I predict that it is a major future opportunity in both science and business which has yet to be exploited in any way.

As an aside, I feel it is worth dealing here with related and oft quoted argument championed by Bruce Ames. It is, in a nutshell, that we should not be concerned with the synthetic molecules we have created, as they are much safer and at much lower levels than natural plant toxins, found every day in our diet.

I have met Bruce, and even discussed this briefly with him. I have enormous respect for his work, and his advancement in the toxicology of carcinogenesis. Yet his viewpoint could only arise from pure scientific reductionism, and a misunderstanding of the interrelationship of life in our evolutionary history.

The life you see around you is the success story of the planet. Surviving nature's poisons has been what separates the life which we now see around us from those evolutionary forms that did not make it. In fact, we are now seeing that many plant poisons act in humans to reduce cancer rates, and extend life. This is why we eat our broccoli and brussel sprouts.

One should also remember that the most pervasive and destructive toxin ever created was made by blue-green algae around a billion years ago. Yet what would we be today without energy-giving oxygen? Toxin, yes. But our co-evolution with it has ensured that those that found it too toxic are now long gone, or in oxygen free niches.

Back to the story of risk assessment.

Risk, unlike benefit, has many dimensions, many time frames, many subtleties and many interdependencies. It would cost too much to even catalogue the potential risks of new chemicals, let alone assess those risks. Risks can be short term or long term. They can be risks to the individual, or to the community. They can be direct or indirect. Organ specific or general. Long term or short term. Obvious or subtle. Micro-environmental or planetary. The permutations are almost endless.

What is a poor multinational to do in order to make an honest buck?

Risk for profit

The answer is to use the "scientific method". Reduce complexity by limiting the questions posed, and controlling the variables. Since no one will know, or more importantly be able to prove, the subtle, the long term, the indirect and the environmental effects, why not just ignore these for now? After all, it is rationalised, if every business and industry had to cover these bases, there would be no industry, no economy. We would all go and live in the cave home of the hippy critics. Troglodytes would rule, and we would be plunged back into the dark ages of superstition and fear.

What to do! What to do!

Well, killing a large number of rodents has always been a bit of a favourite scientific pastime. Not only does it seem scientific, it supports an experimental animal breeding industry, and allows geneticists to fiddle with mammalian genes without much restraint along the way. The LD50 (the dose of a single chemical which kills half of the test animals) has lasted better than Ol' Blue Eyes, a terrifically popular test to release the pent up aggression of socially misfitted lab workers.

The truth is that looking at high dose, short term poisonings of unrelated species has proven something of a "best seller" in the twentieth century. Staggeringly popular for less than very clear reasons. Or are the reasons that unclear?

When the lethality or carcinogenicity is unacceptably high, one can say, "Well you just can't get this dose as a human. It's impossible. Only affects rats this way. No reason for concern". When deaths occur at high doses, and cancers are not seen in six weeks, reassure everyone of the perfect safety of the product.

I want to side-track here for a moment. I was asked to do some research for a new, very promising natural herbicide a few months back. *Nontox* is a wonderfully simple mixture of very safe products, including molasses and sea solids, which diminishes the plant defences against their natural predators and pathogens. The plant dies of highly accelerated natural causes rather than poisoning. One of the components of the mixture is d-limonene, a solvent derived from citrus. If kept from oxidising, it is apparently exceptionally safe in humans. But for male rats, it spells death from unusual kidney tumours. Why is this? Well, it turns out that the male rat produces a protein known as "alpha 2U-globulin", and the epoxide of the d-limonene binds to this protein, leading to kidney damage and ultimately to cancer. It is rotten luck for the rats, but there is an interesting lesson to be learned from it.

When the toxicity in rats was identified, many labs (including Procter & Gamble) turned their attention to showing why it was so toxic to rats. The cancer was focused upon, the hyaline damage identified and analysed, the protein conjugate isolated, and the alpha 2U-globulin was separated from the limonene. The gene for alpha 2U-globulin was identified, and transferred to other species to demonstrate that dogs and mice, which were formerly not damaged by the limonene, could now be killed more easily, and from a cause similar to that of male rats. The protein alpha 2U-globulin was shown to be slightly different from the closest human equivalents, and *PRESTO* Proof of safety for humans! Cool! Great science. Top quality detective work. No expense or resources spared.

To prove it safe. To make a profit. No investment is too great if it can help make a buck. Hell, when you get the patent, it even lets you charge five bucks a shot to cover the costs.

On the whole, compared to petrochemical solvents and other terpenes, limonene is safe. Good call. But there is a flip side to this, and it is deeply worrying.

What if human males had possessed the protein, and male rats had not? Excellent result, I hear some women scream. No matter. What if humans had the protein, and rats didn't.

What is the real worry is that such differences exist between species, and we spend our money and time proving the safety of things that appear unsafe in animals. We spend much less time and money proving the unsafety of things that prove safe in animals. Orders of magnitude less

money. Yet, when it gets down to it, which species the toxicity load falls upon is, in the American vernacular, a crap shoot. Guesswork. A Homer.

This is the problem - we have made the world safer for rats and other test species than we have for humans. This error of interpretation is critical. Every day in my practice I see people who, had they been rats, would not be sick. They had the dreadful misfortune to be humans in a rats world. They exposed themselves to chemicals at doses rats would be fine with, and develop asthma, brain damage, immune disorders, cancers, infertility, damage to the chromosomes, and more. Many, tragically, die.

Who knows what proteins humans harbour that rats do not. Sometimes it is the particular bend or fold in a protein that makes the difference. Imperceptibly small differences make the difference between good health and death.

Most tragically, suffering, illness and disease surround us today in a way we would not have imagined a half century ago. We have banished some diseases only to have them replaced by a grumbling yet profound toxicity which is stripping our children of their rightful future. Our experts tell us that chemicals cannot cause asthma or damage our children's delicate nervous system. Why? Because it takes a million times more to kill a rat! Go figure.

I propose that every chemical manufacturer be forced, from this day forth, to place two dollars into research to prove the unsafety of their products for every dollar they invest to prove the safety of their products. The research money will be distributed by the High Council of Molecular Management (see later) to independent researchers who have demonstrated their ability to track down and identify adverse human and environmental consequences of the use of a chemical, including its complex interactions. Manufacturers will tith a tax deductible 10% (if you will pardon the tautology) to support this ongoing "post-marketing surveillance", half of which will go to consumer groups who care for the victims of adverse responses to chemicals, and who provide environmental protection or surveillance. At the end of one hundred years, an audit will be done to look at the life history of the chemical in question, and the damage it caused. The funds which were not used for a particular chemical, because of its high safety and lack of long term problems, will be returned (with interest) to the company. This dividend will be tax free!

If we could talk to the animals

Back to the main story. We were figuring out just how the Honest John multinational can prove chemicals safe. Remember?

Why are mice and rats such a good choice? They can't talk.

How embarrassing would it be if they could somehow let us know about the headaches, nausea, blurred vision, pains, sleep problems, the burning, the extraordinary fatigue, the light-headedness, and the inability to be able to follow the plot of a John Wayne movie? (My late father used to love John Wayne movie festivals. He could fall asleep at any point in any movie, and on waking could immediately pick up the story, even in a different movie)

Mute species ensure that observable problems occur at higher doses. This makes a bit of a farce of the No Observable Effect Level (NOEL) and No Observable Adverse Effect Level (NOAEL), as no one has really worked out what an "observed effect" or an "observed adverse effect" is in a rodent.

Funnily enough, no observation is really required to define a NOEL anyway! No data on actual acceptable intakes are required for an Acceptable Daily Intake (ADI) either. These figures are mathematically derived from the LD50s and LD1s (LD1 is the dose at which one percent of the test species dies - like the LD50, it is rarely accurately defined), and the logic of the extrapolation is not only far from clear, it is often absurd!

A practical example may help to understand just how absurd these arbitrary estimates can be, and how we and our children test the waters for toxicologists.

I have recently been involved in a very messy incident with a progressive private school in Australia. I was consulted by a family whose child was suffering recurrent vomiting and a range of neurological (nervous system) symptoms. The child was very bright, and in the course of the consultation, it emerged that the problem had arisen after he moved into a classroom in a new section of the school. As well, other children in the same small classroom had illness ranging from leukaemia and Crohns disease to attention deficit/hyperactivity disorder (ADHD). Morbidity in this room at least was unusually high, especially for children of intelligent, upper middle class parents in the private education system. We approached the school for permission to investigate a possible environmental cause.

The school board was less than enthusiastic about such investigation, but finally acquiesced as long as a board member was present during the assessment. Healthy Home Doctors went to the school to conduct a survey of environmental factors such as moulds, dust mite, solvents, cleaning agents and pesticides. As a consultant for Healthy Home Doctors, I had suggested to the testers that I could see little value in testing for organochlorine pesticides, as the classroom was only recently built, and the school had not used these pesticides in the construction for philosophical reasons. (Many Americans may be shocked to know that Australia was still using these toxic and persistent chemicals as recently as 1995 for termite home treatment. The US was dumping these on us as they do poor third world countries. We simply paid more, making us a rich third world US waste site. I have yet to see a single breast milk sample from an Australian mother in which organochlorines would satisfy our own water quality standards!)

The school was tested, and my advice was ignored, thankfully. The four tests for airborne organochlorines showed positive for dieldrin at between 0.15 and 1.0 micrograms per cubic metre (mcg/m³), three were positive for aldrin, and two for heptachlor. The methods and the lab results were checked, and there had been no mistakes.

Now, the question is "What does a level of half a microgram of dieldrin per cubic metre *mean*?" This is not an easy question to answer in isolation, despite the fact that almost every parent and board member became an immediate expert in the field before the day was out. One claimed that she and her husband were "scientists". No more needed to be said!

I am part of a research team at the University of Newcastle which in 1995 published research in the Medical Journal of Australia establishing a link between chronic fatigue syndrome and low

level organochlorine contamination. I know how great a distance there is between accepted standards of safety and actual safe levels of exposure. Our paper was criticised by Dr Loblay in the editorial because it showed an effect two orders of magnitude below that of the known toxicology of the chemicals. Yet, there was the association before our eyes. Peer reviewed and published in a quality journal.

I turned to the medical literature, and to the summarised data of the NIH in the US. There were no data on inhalation toxicity in animals or humans (I sometimes chuckle at that phrase - animals or humans. It reminds me of the phrase "doctors or people"). Nil. Nothing. Nothing on neurological effects. Nothing on immune effects. Nothing on children. Nothing at all. BLANK.

The next question was, "Is this level unusual?" Here, the data were much stronger. The background levels measured in the US in the years in which dieldrin was used averaged just under 1 nanogram per cubic metre. There are a thousand nanograms in a microgram, so the air level in this classroom was five hundred times higher than levels measured at a time the poison was still used! The school room levels were also higher than the peak levels reached in homes on the day after dieldrin application. Ten times higher than a week after spraying, and a hundred times higher than a month after that. There had to be a source, a hot spot, for this to have occurred.

The question a lot of other people asked was, "What do authorities tell us are safe levels?" Given the answer to the first question, this is a meaningless question. It currently has no answer. Why? Because any such estimate is not based on available information, it is based on something else! (That "something else" may be left to your own imaginations, but I am inclined to believe that it is based on the practical requirements to allow a profit on the sale of the products, while minimising liability.)

How do I know this? Well, two ways, really.

Firstly, and most importantly, I had seen and examined the child affected, had a complete medical history gained over many hours, and had tests showing immune and nervous system damage. This is sometimes dismissed as "anecdotal evidence". I call it accurate observation and documentation of an exposed case. No one else has done this to date, apart from the doctors of a few of the children in this classroom. Those I have talked to report observations similar to mine.

Secondly, the acceptable air levels for workplace exposure, the Threshold Limit Value (TLV) was 250 micrograms per cubic metre, or five hundred times higher than the measured level. This is the level in the workplace that should cause no significant health problems for an adult working with the product. 250 mcg/m³. Sounds reasonable, even if it is not for kids not working with the stuff. Not a problem, one may think.

One small sticking point for me is that the saturated vapour pressure for dieldrin is 64 mcg/m³. That is as high as air levels can ever go, even if you are sitting above a pool of pure dieldrin in a closed vat!

So, the safe levels are four times higher than the highest possible level. Yet we have confirmed reports of deaths of people exposed to the vapour! It is thus perfectly safe to be exposed air levels four times higher than the levels which can kill you.

This does not seem sane, until you look at the insanity which produces the result of 250 mcg/m³. The *oral* LD50 for rats is determined in milligrams per kilogram. They eat this. They do not breathe it.

These are quick deaths, not slow deaths. Not brain damage. Not infertility. Not nausea. Not headaches and slow learning. Quick deaths.

Take that figure and multiply it by 70. This is the weight of a healthy young adult.

Not.

This gives the lethal dose for a human, any human.

Not.

Now, divide this arbitrarily by a big number, say one thousand. This is a factor of ten for inter-species difference, ten for intraspecies difference, and ten to get it well away from the lethal area. This gives the safe dose.

Not.

Now figure how much a person breathes a year - say seven thousand cubic metres, and divide this into the safe dose. This is now safe to breathe.

Not.

How far out can this figure 250 mcg/m³ really be? Well, at least 400%, just because of the physics of vapour pressure.

Maximum safe level is now 64 mcg/m³, and falling.

Say a factor of four for the difference between oral and inhaled doses (see below).

Maximum safe level is now 16 mcg/m³, and falling.

A factor of ten needs to be added because we inappropriately use dose per body weight, when we should be measuring dose related to surface area ("On the basis of dose per unit of body surface, toxic effects in humans are usually in the same range as those in experimental animals. On a body weight basis, humans are generally more vulnerable than experimental animals, probably by a factor of about ten." Casarett & Doull's Toxicology)

Maximum safe level is now 1.6 mcg/m³, and falling.

Say the person actually eats and drinks through the course of a year, rather than simply breathing. Reduce the safe level by four.

Maximum safe level is now 0.4 mcg/m³, and falling.

The effects of other chemicals, such as solvents, cleaners and other pesticides, may increase the toxicity by a factor of between ten and one thousand. Let us be kind, and say four.

Maximum safe level is now 0.1 mcg/m³, and falling.

Say the variability between the average and the most susceptible child due to nutrition, genetics, enzyme induction, saturated enzyme responses, concurrent illness and other variables is a factor of one hundred (in fact it is over 1,000, but this is simply a conservative guesstimate).

Maximum safe level for susceptible children is now 0.001 mcg/m³ (1 nanogram per cubic metre), and falling.

Let us stop here. There are other factors, but you may get my drift. We have not even dealt with childhood susceptibility to chemical toxins, which is significantly greater than for adults. Nor the fact that if rats could talk and complain, we may have picked up on migraines, depression, anxiety, fatigue, weakness and more at doses much tinier than the LD1.

The fact is that those who would make pronouncements on toxicity in children in a classroom based on the death of rats are making not only an incredible leap of toxicological faith, they are putting young lives at risk. To put theory before reality is an "independent risk factors" for children. Children rely on adults for their care and safety. When we deny their symptoms on the basis of TLVs, we increase their risk unnecessarily because we keep them exposed when common sense would usually stimulate their withdrawal.

The school in question is the classic example of this increased risk effect. With the first draft of my report on the significance of the dieldrin, and my offer to meet with the board to approach the problem rationally, the school's lawyers threatened me with legal action if I communicated my view to the parents of any children in the school. The school board refused to meet me, and found an industrial environmental toxicologist to repeat the testing. They gained opinions from everyone from the school librarian to the EPA to say the levels were safe. They attempted to discredit me, despite the fact that I was the only published researcher in the field of low dose exposure risk. They held closed meetings, and attacked me publicly, knowing that I could not respond because of their lawyer's threat. Drama and misinformation was everywhere, as the school divided into "pro" and "anti" Mark Donohoe. The latter was the clear majority. Parents who felt there was a possible risk, and that I should put this case to the parents, were themselves threatened with legal action if they promulgated such a view. Information flow became controlled by the school, with the distribution of telephone numbers of "acceptable" authorities which the parents should telephone for reassurance. None of the experts had seen a single sick child from the school.

Somewhere along the line, they forgot the children. They forgot what the consequences were if they were wrong.

John Stewart Mill pointed out over a century ago that it is strange that we promote debate and discussion when we are uncertain of something, but suppress it mercilessly when we are certain. Certain truth should weather unwarranted attack better than anything. There should be no fear of information or opinion. Unless...

Maybe the school board knew all along that there was some problem, or had suspected it for some time. Maybe, when confronted with evidence of the reality of the problem, it was too threatening and painful to deal with. The board, like a person facing bad news, swept through emotional responses of denial, anger, resentment, bargaining, self righteousness, and bitterness in the space of a few months. It confused the problem with the person, and took the approach that if the person could be banished, the problem would too.

This kind of self-preserving behaviour on the part of committees is not acceptable. We cannot afford the luxury of making such mistakes when we are protecting the health of our children.

Acronymphomania

Again, I digress. The school story was included only to demonstrate the practical problems facing toxicology. Back to the story.

Let us see where we stand with setting of NOELs, NOAELs, TLVs, ADIs and other impressive sounding, legislatively backed acronyms.

What we *measure* is the ability of high dose, single chemicals to rapidly cause death or cancer in animals unrelated to humans.

What we *conclude* is that a grossly different exposure level is safe for humans.

Now, I have just a few, minor problems with this way of thinking, and with the conclusions reached. Nothing major. Details, really. Still, it may be worth mentioning just a few. They come down to:

- Inappropriate species to model the toxicity;
- Inappropriate dosage extrapolation;
- Failure to test mixtures or adjust for synergistic effects of combinations of chemicals;
- The high dosages used in testing, and acute effects observed;
- The route of exposure.

First of all, the choice of species is a bother. There are big differences between test animals and humans in biochemistry, physiology, and genetics. Let us take one example.

Most mammals, when challenged with toxic chemicals, proceed through a series of chemical reactions in their livers, resulting in the production of ascorbate, better known to us as vitamin C. Guess which species have lost the vital last step in this protective process. Yes, humans. That is why ascorbate is an essential nutrient, a vitamin, to all of us, but not to most other mammals.

Secondly, laboratories are a problem. They are far too clean, artificially clean. They are not contaminated by other messy chemical mixtures which we all face out in the real world. This is intentional, so that variables are controlled and results are statistically meaningful. They are just not comparable to messy, multiple chemical exposure in our real environment.

The dosage for testing is a bother to me, but not as much as it is for half of the rodents! Why do we persist in killing millions of small animals in the name of profit and progress? Never in the history of human scientific endeavour have so many given so much for so little. What has it achieved?

"It makes it safe for humans", I hear someone say.

In what precise way do rodents remains, the victims of unnecessary chemicals at intakes thousands of times higher than humans will ever consume, make it safer for humans? It is a long bow to draw, and is becoming less credible by the year.

The way we poison rodents gives me pause. It is not the same way we poison each other with the majority of our toxins. We feed the rodents the toxins, mixed carefully into their food at highly

regulated doses according to body weight. In our world, we breathe the same chemicals at highly unregulated doses.

I have a problem with this because of differences based on anatomy and evolutionary biology. In millennia past, the majority of potentially dangerous toxins were plant toxins. Throughout history, vertebrates have made a habit of eating, rather than inhaling their food. The result was that those vertebrates who could efficiently detoxify food toxins were likelier to survive and thrive than those who could not. Vertebrates developed a vascular and detoxication system designed to keep food toxins from reaching vital organs. All blood from the bowel is directed to the liver, which performs a "first pass" clean up of any toxins. It is an organ very well suited to the task, and can take enormous chemical stresses without failing. As the toxins percolate through the tubules of the liver, they are chemically attacked and bound to "neutralising" chemicals, such as glutathione.

Inhalation, on the other hand, is a whole different kettle of fish. Since the time lungs first became popular, around 300 million years ago, the atmosphere has remained pretty much what we see today give or take a few percentage points. We (and our dimly known ancestors) have been breathing pretty clean air for a few million years, even if the plants were keen to stop us eating them.

So what happens when we dirty the air?

With each breath, we inhale trillions of molecules which simply did not exist in our grandparents days. These are not preferentially directed to the liver, but enter the general circulation and are distributed according to the blood flow to those organs. There is no "first pass" clearance through an efficient and regenerative filter.

Not only do these novel molecules enter through the lungs as we breathe. They have surprisingly direct access to a vital organ before they even make it to the lungs. Most mammals draw air through the nose, which humidifies and warms the air, preventing the membranes of the respiratory tract from drying out. One only has to think of how dry and sore the throat can become when the nose is blocked to realise just how effective this process is.

But there is more to nose breathing than meets the lung! Both the olfactory epithelium, high up in the deep recesses of the nose behind the eyes, and the vomeronasal organ (VNO), low down on the back of the nasal septum, sample the inhaled air for vital information as it passes. This information is in the form of fat soluble molecules (more on that in a moment), and the receptors pass both the molecules and a rough interpretation of their meaning along to the appropriate part of the brain.

Now, you would probably imagine that giving strange molecules direct access to the brain would be rather a stupid thing to do. All kinds of problems could occur if the wrong types were to get in. The brain could suffer permanent damage. So why would vertebrates with this outlandish defect survive over the thousands of millennia?

The simple answer is that the benefits have outweighed the risks, and that the "defect" has, on balance, improved rather than impaired survival and procreation for those blessed with the problem.

There is a silent language of the air, with phrases and words which are designed to lead to lead to particular outcomes with a very high degree of certainty. Poisons are avoided. Sexually receptive females are found. Fertile, genetically dissimilar males are chosen. Food is pursued and consumed. Predators are avoided. Offspring are protected. These are not items which nature leaves open to too much interpretation, and conscious perception of the message may be more of a disadvantage than an advantage.

The perception of fragrances and pheromones lies in the "old brain", and the connections to the thalamus and the "new brain" (neocortex) are sparse indeed. In this way, olfaction through the first cranial nerve is very different from all other sensory input. The parts of smell which are perceived gain access through the glossopharyngeal and trigeminal nerves, and through a non-specific transfer from the olfactory bulb when the stimulus is very high. It serves mainly to ensure a conditional response between smell and events, so that new "smell learning" can occur as time goes by.

The language of smell is so direct that the actual molecules which are inspired are drawn into the nerve and are to be found inside the nerve, and even in the olfactory bulb, the gateway to the smell-brain. The message cannot cease when the aroma fades, and the animal flares the nostrils and inhales deeply to track more of them, and determine the direction through a concentration gradient. For certain moths, a single molecule of bombykol is enough to set them flying around until they find a second, then a third. Pretty soon, they are tracking along a path which, over a mile away, will see them stumble serendipitously over the receptive female. As Lewis Thomas wrote, it must seem like unbelievable good fortune to the moth, who was, after all, only out on a bracing morning to stretch the wings a little.

The molecules of smell are, in a very real sense, the message. Even more, the message is the action. There are no critics, philosophers, or nay sayers along the way. Perception and action are intimately and irrevocably linked, and the smart part of the brain is not asked for permission.

Although there are aromas that we (and presumably other animals) do bring to consciousness, these are almost irrelevant exceptions. We may think that our action is based on this conscious appreciation of smell, but this is very much a post hoc rationalisation. The real action in the old brain has already set the response, and started the reaction, even though we are unaware of it.

So what happens when the "noise" increases? Hundreds of thousands of new molecules, all with no evolutionary history and no appropriate response, bombard the olfactory epithelia and the VNO with every breath. What happens? It is hard to say, as truly novel molecules were a rather rare occurrence until this century. Nature usually edited old and successful molecules, and recycled the general structure of the important ones.

If one had to guess, it is likely that the "default" response to a new molecule would be to interpret it as bad news, a threat or a poison. Why? Because to do otherwise would lead to abbreviated lives for those animals that considered real threats any other way. If a predator or a food shows off a fancy new molecule, the survivors will be the timid ones overall. Running from false threats and not eating new plants will, on the balance, increase survival odds compared to the gung-ho early adopters.

Now, there is a protective mechanism to prevent the total loss of important smells in the background, and it is called variously olfactory attenuation or adaptation. The smell brain “turns down” the effect of constant stimuli (which is why, on the whole, we do not smell ourselves), possibly by matching trapped molecules with inhaled molecules, possibly by simple “exhaustion” of the olfactory receptor nerve. This is fine if the “noise” is constant, such as our own smell, or living near a rubbish tip.

But what if the stimulus varies over time and with location? These smells will generate spurious and unpredictable responses in the smell brain. What kind of responses? This is the trillion dollar question, and remains surprisingly unknown, given its potential impact on our future survival. We can, however, make a few educated guesses based on the links and influences of the smell brain, and then test their validity later.

There are dark areas in the brain, areas about which little is known, and where function is only determined by identifying the effect of damage. Areas with strange names, like the venterolateral pre-optic area (VLPO). Uncharted waters. Most lie within the old brain, and many are microscopic collections of between a few dozen and a few thousand nerves. We have focused on the higher centres of the brain, mainly because of strokes and because effects are easily determined and simple to map out.

The old brain remains our dark ocean, pregnant with the primitive links which remind us of irrational origins. Like a graveyard on a dark night, it is not a popular region for neuroscientists to wander. The experiments are difficult, the results exquisitely difficult and equivocal, and the outcomes are often ones we would prefer not to know too much about. Powerful, deep emotions run through these depths. Sleep, addiction, fertility, temperature, thirst, hunger and sex linger here like evanescent ghosts, not able to be tracked and described, yet so real in their effect on us all.

The landmarks we do know are few, but important. The limbic system (a “catch all” phrase for a collection of these annoying areas) and the hypothalamus are here. The amygdala, hippocampus, and olfactory bulb are here. The VLPO and dozens of other “nuclei” (collections of nerves with a possible common function) are here. What do they do?

We may “broad brush” the functions of the better known locations, but even this is a somewhat fuzzy and inexact process, given the interdependencies and apparent duplication of many functions there.

The hypothalamus is as more gland than brain, and is the interface between the nervous system, the immune system and the endocrine (hormonal) system. It has a subordinate, the pituitary, which responds to the demands of the hypothalamus. Between them, they order the endocrine glands to increase or decrease hormonal production in response to complex feedback from the body as to needs and excesses. They set metabolic rate, responses to threat, fluid balance, thirst, hunger, temperature, sleep, sperm production and ovulation, kidney function, and even help fiddle with digestion and weight. Not insignificant jobs, any of them. We would be worn out and stressed greatly if we had to carry these out through conscious tweaking of the organs around our body, so the hormones act as yet another wonderful autopilot system.

The limbic system is deeper and stranger than anything I know of in humans. It swings off the smell brain, and concocts complex emotions apparently from nowhere. It is a creative and defi-

nitely an “experiential” region of the brain. It is of the old brain, yet it deals with the highest and lowest expressions of humanness. We think of emotions as if they are our own special domain, our own dirty secret. They are not. These emotions are embedded at the very roots of life, although we can say little of how another species experiences these emotions. Fear, anger, joy, hatred, love, despair, hopelessness, dominance, helplessness and more - all spring unpredictably from this dark well of our evolutionary past, percolate through the brain and body, and become as much who we are as what we do. Again, hardly insignificant functions, driving responses and action from indeterminable memories and instincts.

They seem, well, embarrassing. These are quintessential beasts within, challenging our pristine views of ourselves as rational scientific creatures. They assure me that, although we lay a veneer of conscious control above them, we are glorious and wild beasts at heart. They assure me that we have a deep and binding link to the primeval sludge within, and the planet without. Some will be outraged that I should suggest this, dragging humans down to the levels of base and conscienceless animals. I am not. I am simply comforted that our deep links with life are sufficiently strong to compete with our fault ridden rationality. If I had to put a buck on which aspect of us had the best chance of seeing us still here in one hundred thousand years, I would back the beast. It has the steering wheel, and the track record. Sludge to human in three billion years is an excellent effort, and one worth supporting!

These regions are powerful, yet control from the nose has its problems. The potential for mischief of rogue molecules is clearly very high, in part because of the smell brain’s ability to amplify molecular messages. A few stray molecules of pheromones can lead, with a couple of intermediary steps, to a child, the presidency, or a lifetime in jail! It is all a matter of timing and opportunity, via a good dose of chaos.

Here is a question now to ponder. How does counting dead rodents relate to complex alteration of brain function? What is the dose relationship between the two? If you have followed the story so far, you may well have picked up on the absurdity of a few of toxicology’s assumptions.

Death and cancer are most often statistically predictable responses to many milligrams per kilogram of body weight. Sometimes many grams are needed. Pheromonal action can occur with as little as a single molecule in some species, although it seems as though a few dozen molecules are required in humans. Death may require more than 10^{20} (ten to the power of twenty, or one hundred million trillion) molecules, whereas alteration of behaviour or hormonal function may require as few as twenty molecules. Let us say 10^2 (one hundred) molecules, just for the maths. This makes it possible to observe a definite effect at a dose one million trillionth of the lethal dose, possibly even less.

I can hear the criticism now. “On the one hand we have death. This guy is just talking about mood change. That isn’t an effect.” Maybe. Maybe not. If the type of amplified effect is the increasing popular “brain chemistry imbalance” hypothesis which usually accompanies a script for Prozac, then the issues are clearly comparable. Each can lead to death, on the one hand from toxicity, on the other from homicide or suicide. The point by the US National Academy of Sciences that we simply do not know how much of the depression, suicide, chronic fatigue, infertility and immune alterations are due to these low level chemical effects.

The low dose effects are in no way related to the high dose effects because the mechanism is so totally different and unexpected. We (and other animals) are designed to respond to molecules which are similar to those now synthetically produced. We have relied on this low level response throughout evolutionary history. It is physiological, intentional, and important for survival. Unfortunately, it is now increasingly subject to uncontrolled environmental exposures, and from my own clinical perspective, the outcome is an unforeseen disaster in the making.

One is entitled also to ask, "Surely we could not have been so far wrong in our assessments of toxicity. Wouldn't we have seen the effects? Wouldn't it be obvious?"

This question crystallises for me the difficulty the difficulty that rational, logical people have in accepting the reality of low level chronic toxicity. We may not accept that the impressively acronymed ADIs and NOELs and TLVs are absolutely correct, but we estimate that they must be "in the ballpark". Maybe out by a factor of two or so. Possibly five. At the absolute maximum, by a factor of ten.

We are out by a factor of ten before we even start. Astonishingly, we persist in the use of the "dose per body weight", usually expressed as milligrams per kilogram (mg/kg). It was a basic tenet of toxicology for fifty years or more that a dose of, say 10 mg/kg as the LD50 in rats would mean that the same 10 mg/kg in humans would do the same. Almost all of toxicology used to be expressed in terms of mg/kg.

It still is, despite the knowledge over the past few decades that this is inappropriate for poisons, and despite the fact that it underestimates risk for humans greatly. Way back in 1986, in the classic toxicology textbook known as *Casarett & Doull's Toxicology: The basic science of poisons*, the flaw was pointed out as follows:

One might also view dosage on the basis of body weight as being less appropriate than other bases, such as surface area, which is approximately proportional to (body weight)^{2/3}. ...

... while the weight of a human is 3,500 times greater than that of a mouse, the surface area of humans is only about 390 times greater than that of a mouse. Chemicals are usually administered in toxicologic studies as mg/kg. The same dosage given to humans on a weight basis (mg/kg) would be approximately ten times greater in humans than mice if that dosage were expressed per surface area (mg/cm²). Cancer chemotherapeutic agents are usually administered on a surface area basis.

Why did we not change to a more accurate system, given this knowledge. Inertia, comfort, expediency, business needs, slow regulation, and much more reside at this level, maintaining an insupportable status quo.

It affronts sensible people when the suggestion is made that such basic mistakes have been made, and the numbers are out by tens, hundreds or thousands. Not for any good reason, however. It just seems as though a body of research which looks so impressive could not have got the whole issue so damned wrong.

I think it has to do with an irrational faith in written down figures, especially when linked to acronyms and authority figures. Our parents wouldn't mislead us and place our health at risk. Neither would the FDA, scientists or politicians.

Until around eight years ago, when we opened the Special Environment Allergy Clinic (see that section) I believed the same thing. It was during our few years in this hospital unit that we noted important yet inconsistent in the function of the endocrine system, the nervous system, and the immune system that appeared to be out of all proportion to the dose of the exposure. This set me to reading about what was known and what was not known in toxicology. Now, after eight years of reading, I am more and more amazed by our utter ignorance of anything other than death rates and cancer rates in species other than our own.

Toxicology sits today as an inverted pyramid, balanced precariously upon dead rodents. An entire, self-consistent body of knowledge has grown from this fallacious origin, with no one seriously questioning the axioms and assumptions of the field. It draws heavily on epidemiology for its raw material, which is also a bother. Both fields are mutually supportive, with neither sensitive enough to identify the real but non-lethal problems common to the community.

Toxicologists I have not known

Before finishing, I wish to make an observation on toxicologists. It is probably clear that I am, on the whole, not fond of them as a specialty. This is not a personal issue. It is a view gained from the observation of many hundreds of patients who have sought their opinion and care. Toxicologists are clearly a good deal smarter and more useful than, say, plastic surgeons, psychiatrists, politicians and hospital financial controllers. But then, so are their rodents.

One may expect that, if there were subtle problems related to environmental exposure, toxicologists would be the first people to know, and would be the ones most expert in identifying the problem. I would suggest, from experience, that the opposite is true, and that toxicologists will most likely to be the last to know of such problems. Once they do know, however, they will have the training and experience to identify mechanisms and propose management and preventive measures. The reasons are reasonably obvious why this paradoxical situation exists.

Firstly, toxicologists are generally still trained in classic, high dose toxicology, which is itself firmly rooted in definable and obvious endpoints in animals. These are primarily death and cancer, and are usually related to either occupational or accidental high dose exposure. They identify obvious, short term and life threatening effects. While these are clearly important, in first world countries it is now almost insignificant when compared to the potential harm of long term, low dose exposure in the entire population.

Secondly, and this may apply more in Australia than in America, people are referred to toxicologists and occupational physicians by primary care practitioners. If people with low level exposure are referred, and the toxicologists deny the possible link between exposure and symptoms, then the referring doctor will quickly learn not to refer such patients in the future, no matter how frequently they may be seen at the primary care level. It is very much a case of "I'll see it when I believe it".

The majority of low dose exposure patients are, in fact, inappropriately referred to psychiatrists. This is regrettable, but it is the preferred method of management for any complaints which fails to

fit a known diagnosis. Chemically sensitive people suffer from unusual combinations of neurological symptoms and signs, as well as other systems which are difficult to reconcile with a single diagnosis.

Once referred to a psychiatrist, they may be lucky or unlucky, depending on the day, the psychiatrist's own psychopathology, and recent stock-market activity. Psychiatry is far from an exact science. No, psychiatry is far from a science. It remains, even today, the rubbish bin of medicine, the pit into which people are tossed when they refuse to conform to their doctor's opinion, diagnosis or expectations.

If one is lucky, one is labelled neurotic, and sent home. If unlucky, one is diagnosed with depression or a psychosis, and medicated with powerful psychoactive drugs until behaviour and complaints are less bizarre. Often the drugs do the opposite, worsening the problem.

I still cannot get used to the fact that almost all multiple chemical sensitivities patients go through a cycle of being taken seriously at first by their doctor, showing no abnormalities on standard pathology testing, being referred to a psychiatrist, being medicated (usually with poor result), and eventually being told by their doctor that there is nothing wrong with them. Those admitted to our Special Environment Allergy Clinic inpatient unit had seen, on average, eight previous medical practitioners, including around two psychiatrists, all without improvement or understanding of their condition. They consulted a doctor once a fortnight for years, worsening all the time.

Avoiding harm from specialists

What is of concern is the huge number of well-certified people, regulatory bodies and institutions who hold, against all evidence to the contrary, that chemicals are safe until proven otherwise. These fossils have a few characteristics in common, and I would propose the following checklist as a means of avoiding them. More than two items from the checklist should make one seriously consider seeking another opinion:

the person is employed by government. In Australia at least, this usually ensures the minimum in originality of thought, continuing education, and contact with the public.

the person is male

the person has no children, or was not the primary care giver when he or she did have children

the person is trained in occupational medicine

the person's workload would be minimised by holding that toxicity problems do not occur

the person has never worked as a primary care practitioner

the person is a psychiatrist

The question which could be asked (though it may be difficult to know if the answer is honest) is, "Would you willingly expose your own children to this environment, no matter what the consequences?" The problem, of course, is that the majority of people in the positions of authority are male, and are from a generation where strong emotional bonds between fathers and children

was a rarity. Most have children who have grown up, and were working so hard to climb the totem of scientific authority that they did not really have much to do with the care of their own children. Maybe one could seek references from their spouse!

Many may be thinking that this is anti-scientific bunkum, asking about children when the question is a technical one of chemical toxicity. This is my whole point. The question of greatest importance today is NOT the abstract, meaningless intellectual game of deriving magical figures from the remains of dead rodents.

The question of greatest importance today is, "What are we doing to ourselves, our future and our planet by our actions?" This is not a question in any way answerable by theory. It is, in my opinion, answered by using our in-built understanding of our relationship with our world, by watching and observing, by listening to our own children as they struggle for breath, and by noticing the early warning signs as our own families struggle to maintain health. It is answered by talking to the elders of cultures who have maintained their link with the planet. It is answered from within, when we settle in a quiet place without our prejudices, and face what we are doing honestly.

It is answered, in short, by using the qualities which helped us make it through the first half million years or so of human life on this planet, not the qualities which have brought us to the brink of non-existence in a single century.

My feeling is that we need our confidence back if we are to deal with this question. Some may say that only experts should deal with this question. I would agree, and say that the experts are mothers, indigenous people, poets, philosophers, artists, children, the elderly, the sick.

Having seen a rainbow, science can provide an understanding of how it occurs. Science could not predict the rainbow. It has nothing to tell us of beauty and inspiration, of the effect upon us of poetry and paintings inspired by rainbows.

Science is descriptive, analytical, reductionist and void of emotion. Those are simultaneously its great qualities and its most significant shortcomings. Some have said it is inhuman. I disagree. It is a fine human achievement, gathering our intellectual nature in a formidable and powerful way never seen before on this planet. It is however, not balanced by those other aspects of humans which has never gathered and focused in the same way - spirituality, intuition, emotion, compassion, expression and creativity, to name a few. Life is so much more than science, however much our science attempts to circumscribe and contain life. It is the imbalance which creates the problem, not the expansion of the mind of humanity.

We are clever, but we are not yet wise. I hope we can achieve the wisdom before our unbridled cleverness gets us into too much trouble.

The International Council for Molecular Management

Let us propose a solution. Blue sky. What would we do that may undo a half century of negligence and chemoproliferation.

I would propose a council of elders, and give it power and an important title. The International Council for Molecular Management weighs sufficiently for the purposes I have in mind.

One of our biggest problems is that we have added chemicals at will, while we subtract outdated and dangerous far more rarely. Also, for every new and useful molecule invented, there are a dozen knock-offs, me-toos and generic molecules which add no benefit.

The rules of the council are simple, and should appeal to the American psyche. Survival of the fittest and strongest. Winner take all.

The line is drawn now - 1997. From March 14, 1997, the number of types of synthetic molecules will decrease. There will be no additions without subtractions.

A new molecule is made for, say, killing cockroaches. Call it "spider". Spider is the predator molecule, and its manufacturers must identify its prey. One or more competing products are listed, their manufacturer notified, and the site and date for the battle is drawn. It is televised in America. Prime time for the big slug outs.

Comes the day, and the predator must destroy its prey, or die itself. The rules are complex but clear, and it is a simple scoring system not unlike American Football. Spider is given the floor, and the offensive team of lawyers (are there other types?) have four plays with their biggest hits. The following may be an example of the plays:

- Spider has the lowest risk to benefit ratio
- Spider is biodegradable
- Spider has least impact on non target invertebrates and bacteria, and
- Spider has been fully tested for immunotoxicity and neurotoxicity, and is safer than all others

The support papers (which have been before the committee for weeks) are thrown arrogantly onto the desk before the judge-cam (replayed from 3 different angles), and the lawyer is greeted with high fives and frenetic cheerleaders, the offence delirious in their daring attack.

The defenders, feeling the game slipping away, make their own play, and viciously attack the integrity of the labs performing the tests, and exploit the inexperience of the rookie chemical. It is a gouge, and very illegal, but the public expect a good fight over a three billion dollar market, and the old warhorse ain't goin' t' give up that easy.

Still, it's critical yards for spider, as the game is played on a sudden death "first to score" basis.

The referee, an Inuit, flicks his mike on, faces the camera, and says (holding hand over heart), "Illegal personal integrity attack by defence. Five yard penalty. First Down."

The game rocks from one end to the other over hours, as each struggles for that benefit or little bit of dirt to help their triumph. Lawyers are carried out with tongue cramps and psychic damage as the struggle moves to cinematographic dimensions.

Finally, thirty metres out, a desperate defence lawyer lets fly with a long speculator. It is all or nothing, with a minute on the clock. The question sails through the court, seeking an admission of inappropriate toxicity extrapolation for non-target species. Just as the expert witness goes to pluck in the question and score, the almost exhausted spider lawyers make their move. They object on the basis that the expert witness has in fact been offered exclusive ownership of the state of Utah as a success fee, if the defence wins. They swoop on the question and charge the length of the field to score in the final seconds.

The elders consult, yet everyone knows that this is spider's day. The vanquished molecules, emblazoned on the jackets of the defence teams, are in their death throes. They have a year to fade, while spider has a year to assume the crown, and a further year to wear this crown without challenge. A new roachicide is queen, and all must bow to it. There will be no lesser molecules hanging around, dirtying the environment and adding unpredictably to toxins while this wise council of elders prevails!

At a serious level, the role of the council will be to prevent the proliferation of inferior molecules by eradication and replacement. Occasionally, whole classes of chemicals may be tossed out, judged to be insufficiently useful for the harm they cause. Other times, new niches may be formed for startlingly novel applications. In all cases, it is a winner take all contest, where second and last place are indistinguishable.

This is a job for women, children and traditional people's elders, because most men would get to love the fight, and lose their judgement.

With such far reaching powers, it should be possible to reduce the 65,000 chemicals in common use to just a few dozen. Maybe a few hundred. Most of today's chemicals are either exact copies or near knock-offs of best sellers. The originators deserve their monopoly for a while, and then they deserve to die and fade back to dust in the future if they do not keep at the forefront of their business.

Let us put some thought into the International Council for Molecular Management. If it saves only one planet, it will have been worthwhile!

Chapter 6

Toxicity or Sensitivity

Categorising adverse reactions

Adverse can be broadly classified as either toxic or intolerant responses. A proposed categorisation of adverse responses is set out in Fig 4.

The coat-hanger is useful for “mapping” the type of response we are talking about, and for making what I believe are some critical decisions as to where multiple chemical sensitivities should be situated.

Toxic responses are statistically predictable responses to an insult of some type. These insults are usually chemical, physical (trauma) or biological (infection). The feature of this type of response is the statistical nature of the response for both individuals and for the population. As the dose goes up, a higher percentage of the population is adversely affected, and each individual is increasingly and progressively adversely affected.

Intolerances are idiosyncratic adverse responses, not predictable on a statistical basis (though clearly predictable once a person has had a reaction). They commonly do not follow a “dose-response” curve, but have a threshold for each individual, below which no symptoms occur, and above which all symptoms are evident. This “all or none” response is very different to the more progressive toxic response.

Intolerances need further subdivisions. The main one is that of a hypersensitivity and non-hypersensitivity. Often, the term hypersensitivity and intolerance are incorrectly used interchangeably.

The hallmark of hypersensitivity is that the reaction for the first dose is less than the reaction to subsequent doses. This happens because the first dose is usually required before “sensitisation” can occur. A good example is penicillin allergy, where a person has one course of penicillin without problems, but reacts dreadfully to the 2nd or 3rd course.

In non-hypersensitivity reactions, the first dose is the equal of any other dose. This is typical of enzyme defects, such as lactase deficiency.

Finally, the hypersensitivity responses can be divided into inflammatory and non-inflammatory types. The best known inflammatory response is allergy, which is known as a Type I hypersensitivity. There are others, known as Type II, III, and IV hypersensitivity (aren't immunologists clever and creative?), discussion of which can be left for another time.

It is the non-inflammatory hypersensitivity reaction which is of great interest to us, because this has been the traditional dwelling place of multiple chemical sensitivities. Exposure to a first dose does little, but a subsequent dose has a massive effect. After the “sensitisation”, adverse reactions oc-

cur at exceptionally low doses, and have widespread bodily effects. The process seems analogous to allergy, except that inflammation is less evident.

We need to think this through before accepting it

The dangers of assuming

There is a danger in assuming that multiple chemical sensitivities is a non-inflammatory hypersensitivity.

I have patiently explained to patients over the years that they are not suffering from toxicity (the term that they and their naturopaths, chiropractors, herbalists and astrologers use), but from a hypersensitivity. They were, I explained, different from the majority of the population. They responded at doses too tiny to cause harm, I explained. I reassured them that there was little chance of tissue damage or permanent adverse effects because there was little or no inflammation, and the doses were too low to be toxic.

I in fact lectured around the country on this distinction, which I believed was very important for sufferers to know. The coat-hanger was displayed, allergy was placed in the lower left corner, and multiple chemical sensitivities was placed just to the right of it.

Yet the neatness bothered me, and I wondered why I was not fully convinced. Logically, it all seemed fine, yet something was not right and I could not put my finger on it.

One day, a patient was discussing her asthmatic child, telling me that the child was suffering from "toxicity to the lung". I chipped in, interrupting her to tell her it was an allergic response. She stared at me as if I were a complete idiot and said, "It may be an allergy where you come from, but in our area it is from the toxic air pollution". End of conversation.

Now I know that asthma is primarily an allergic disease, and I know that allergy is a relatively inherited disorder. I know that dust mite and grasses can trigger allergy and asthma, even at tiny doses.

I also know that the asthma rate in Australia has risen from around 13% in 1985 to around 27% in 1995. Some estimates place it as high as a third of our children or more. Something is happening, clearly, and it is a catastrophe in need of urgent attention.

Do the airborne pollutants such as sulphur oxides (SO_x), nitrogen oxides (NO_x), ozone and formaldehyde cause asthma? On the whole, they do not, and allergists keep telling us that we do not have allergic responses to these chemicals.

Do they contribute to, or worsen asthma? Clearly the answer is yes. Two conditions must occur together, namely the hyper-reactive airways (usually due to allergy) and sufficient quantity of an irritant chemical. The allergic component is something of an all or none affair (although there are degrees of severity), while the irritant chemical acts as a toxic response in the susceptible individuals. The irritants had the dose-dependent relationship, and could be shown to cause progressive worsening in an individual with increasing dose. As well, at a community level, as the diver-

sity and levels of irritant pollutants rise, asthma increases in incidence, severity and frequency of attack.

The chemicals were acting in a toxic manner for a susceptible group of the population, yet apparently having little respiratory effect on the rest of us until doses went very high (you and I know this is probably not true, but let us humour the toxicologists for a moment).

This really set me thinking about multiple chemical sensitivities. In asthma, the inflammation of the allergy damages lung tissue over time, making the lungs more prone to toxic chemical injury at progressively lower doses over time. This made the chemical response far more dramatic than in people not suffering asthma, and made the chemical toxicity look somewhat like a sensitivity.

Could it be that multiple chemical sensitivities was in fact a toxic response also, playing its role on top of underlying genetic, biochemical or other individuality?

I looked back over some hundreds of cases in 1993 and 1994. There was nothing in family histories to predict that these people would develop multiple chemical sensitivities, as far as I could tell. There was little in their past history to help predict, except for some particular groups such as breast implant patients, patients with previous adverse reactions to anaesthetics or vaccinations, location (there seem to be clusters of cases from certain 'hot spots', especially cotton growing regions in Australia, and certain areas of increased industrial contamination in the city), and possibly certain occupations such as agricultural workers, hospital work, hairdressing, painting, printing, screen printing, builders, plumbers, photographers, and teachers (these are examples, and the list is not intended to be exhaustive).

The patients often were in apparent good health prior to the triggering event, suffered exposure to an agent, underwent a rapid and severe deterioration of health in a short period of time, and afterwards appeared to become sensitive to the effect of the particular chemical. Initially adverse reactions were only apparent to the chemical which triggered the response, but as time went by, the number and classes of chemicals causing adverse reactions increased in the so-called "spreading phenomenon".

This had to be a hypersensitivity reaction, surely. It seemed like the allergic hypersensitivity in some ways, but something did not seem right.

For a start, no mechanism was known. Allergy and delayed hypersensitivity had mechanisms which, though far from totally understood, could make sense of the process, and allow for predictions to be made. (Just this week, though, a strain of mouse in which the IgE antibodies were missing, yet which still developed allergic sensitivity, was announced. It just proves that every hypothesis, no matter how 'true' is simply waiting for its nemesis).

Many mechanisms had been put forward for multiple chemical sensitivities, many of them revolving around kindling and limbic sensitivity, yet none really made sense of the whole process.

Secondly, the damage of sensitivities such as allergy are due to inflammation. If the sensitivity is non-inflammatory (as is suggested in multiple chemical sensitivities), why was the neurological deficit so profound and so long lasting after the insult? We had assumed that the neurological effect was a symptom of continued low dose exposure, but only because we assumed it was a sensitivity reaction.

I wish to propose something a little challenging, something which will annoy many people, and something about which I am more than prepared to be proven incorrect. It is a strange thing, when I consider it, because I have seen so many patients over such a long time, and have gathered so many statistics. I do not know why it has taken me so long to reach this conclusion, nor why I feel so uncomfortable about writing it.

Multiple chemical sensitivities causes permanent and irreversible brain injury. Possibly other permanent injury as well, but at least brain injury.

I have been seeing multiple chemical sensitivities patients for over a decade now, and I am yet to see a single multiple chemical sensitivities patient recover completely. I have seen around fifteen hundred multiple chemical sensitivities patients in that time, a few hundred in the Special Environment Allergy Clinic, and the rest in clinical practices. Some were so severe they were bed-bound, some so mild that they could still work a full and normal working week.

Maybe this just means I am a poor doctor. I don't believe so, and I would defer to the hundreds of doctors around the world with greater experience.

Before anyone reading says, "Hey, I am clearly better now than when I was really sick", or "Almost all my patients get better", I had better explain.

People with multiple chemical sensitivities do get better. So do stroke victims and people who lose a limb. They get better not by recovery, but by adaptation. This is what I believe happens in multiple chemical sensitivities.

What evidence do I have?

Firstly, the Auditory Evoked Response Potential testing, while it improves over time with appropriate chemical avoidance and management, rarely returns to normal. It plods along over time towards normality, but most often stops well short of acceptable.

Secondly, when I first started to wonder if this were true, I began to ask those patients of mine who had done well whether they were back to normal health. None said yes! Not one.

They had all done well, but they had not returned to that resilient state of good health that they enjoyed before getting sick. They had lost their reserves, and their health was now more fragile, more 'brittle' than before.

As well, although they said they were well, they all had adopted "adaptive" techniques to help them get by. All who were working had changed jobs to ones which were less demanding of either mental function or stamina. All had found ways to minimise disability, varying from siestas, to moving home to less polluted regions, to minimising chemical use and exposure in their own homes, to writing everything on note pads or Apple Newtons (the handwriting computer, which has been almost custom made for this kind of injury - despite the shortcomings, I can thoroughly recommend the newer versions to any multiple chemical sensitivities patient. It is like an external brain which does not vary from day to day. Anyone want to talk to Apple about this?)

I do admit to one confounding factor, though. As a doctor, I see those people who have health problems, not those who have fully recovered (if there are any). There may be plenty of complete

recoveries around, those back to their former state of health without limitation. If so, I would be more than happy that it were so.

So, having got that out, what could be happening if the damage is permanent. The answers are speculative, but could be useful to consider.

Well, it could be that there is an inflammatory process to the sensitivity, and this inflammation actually affects the brain.

It could be that the condition leads to apoptosis (programmed cell death) of certain cells, with them simply disappearing without trace following toxic insult.

It could be that, once sensitised, there is no escape from the background of volatile chemical exposure in the late twentieth century. In some ways, this could mirror the inexorable rise of asthma, in which the allergens and chemicals conspire to turn susceptible people into cases.

It could also be that the process is truly direct neurotoxicity, and that once the brain cells have died, they are simply do not return. This is the hypothesis I tend to prefer at present, at least from the available choices.

Why?

Because it is the most important possibility to deal with, and I am aware of no facts as yet to deny its truth. This is in some ways like the precautionary principle. If I am wrong, it will do no harm to check and prove it wrong. If I am right, and we are missing widespread neurotoxic brain damage in the population, much harm is done by trivialising the problem, and attributing it to a small section of the population.

My hypothesis is that the people we call "multiple chemical sensitivities" are not suffering a hypersensitivity response at all. They are suffering neurotoxic injuries, and are susceptible individuals in the normal population.

To understand the difference, consider the difference between Fig 5 and Fig 6. Fig 5 shows 2 different populations, the sensitive and the normal groups. Fig 6 shows 1 population, with the left edge being the more affected group (in Australia, we have a couple of 'ethical and environmental' political parties, namely the Greens and Democrats. These 'sensitive' politicians are very different to those of the 'tougher' major parties. It's a local joke, but I would bet every country can identify similar political groups).

"So what?", I hear you ask. Well, it means not all that much now. However it means a great deal in the future, and in our attitude to the risks demonstrated by people suffering multiple chemical sensitivities.

If the people now complaining are part of a small, strange subgroup of the world, different from the rest of us in some essential trait, then the problem is less immediate and less 'real' for the rest of us.

If these people are, however, the leading edge of the main curve, then we are all at risk, and the problem is both important and immediate.

The best way of appreciating the difference is to look at Fig 7 and Fig 8. The lines are drawn vertically relating “dose” to a date in the future, say 2020 AD. Let us assume that we keep adding chemicals to the environment, and that a higher total chemical load exists in 2020.

In Fig 7, we see that the increase does not affect the ‘normal’ population by 2020, but has “burned out” most of the chemically sensitive people. This is what many of us want to believe, no matter what the evidence.

In Fig 8, the problem is clearly more urgent. We are at the leading edge of the curve, and moderate increases in dose affect large numbers of the normal population. Failing to pay attention to the multiple chemical sensitivities patients would be at our peril.

We do not know who is likely to fall next in multiple chemical sensitivities. When it can be your own children, siblings or friends, and when it happens without warning or prodrome, then the need to do something to prevent the escalation in chemical use is high.

I personally believe that those with multiple chemical sensitivities tend to have certain personality traits. They are mostly emotionally sensitive, sensitive to the needs of others, and have increased sensitivity to other stimuli such as noise, touch, taste, temperature, and sexuality. These people are more often artistic, expressive, caring and passionate about their family, friends, environment and health. They are actors, writers, painters, mothers, creators. Mainly they have decades of exposure, being in their 20s to 40s.

Recently, though, the population is spreading, and this is a worry because it tends to suggest that the affected people are less “different” from average. They are younger, older, plainer people. People I would not thought would have been damaged this way five years ago. It leads me to believe that my initial views of this “sensitive” subset of the population are not, in fact, so different from us.

There are many reasons we may have mistaken toxicity for sensitivity. One I favour is that we mistook a change in dose-response curves (lets assume such curves are accurate at present) for the “all or none” tendency of allergy.

For a given trait, say short term memory loss, there may initially have been a progressive response (Fig 9) which became far less progressive over time (Fig 10). The effect of this is seen in Fig 11, where one can see that as dose is increased, even a small amount, the effect in the rapid curve is that symptoms go from near zero response to massive responses with an almost insignificant dosage increases. This can happen, for example, when paracetamol is given as a medication. As it approaches saturation point for the available glutathione, the body becomes unprotected. Finally, small doses make a huge difference in response, and we guess that they are sensitivities.

A further possibility includes the complexities of many dose response curves for many different organs within the one person (Fig 12). Each organ interacts with all others, sometimes leading to “positive feedback loop”. An example would be the cytochrome p-450 (stage I) hepatic detoxication enzymes and glutathione (stage II) conjugation systems. If the P-450 increases beyond the capacity of the elimination (stage II) system, than the intermediate metabolites (“half-way” molecules) build up rapidly, and can be rapidly toxic, in one quick step.

It is simpler to pose the hypothesis of toxic responses underlying multiple chemical sensitivities for other reasons as well as these observations. Firstly, the mechanisms and processes are known and understood, and lend themselves to experimental assessment. Secondly, the so-called detoxification programs run by many well respected doctors throughout the US do appear to be effective in improvement of health and symptom reduction. They are certainly effective in depuration (removal) of fat soluble chemicals such as pesticides and heavy metals. The reduction of "total load" (see below) is integral to this approach, and this fits the hypothesis of toxicity well, under known toxicological auspices.

There is an additional reason for assuming a single population, and a progressive toxic response, and it is a very human reason.

As long as a distinguishing factor can be found (or assumed) between the majority and some minority who suffer a problem, we tend to trivialise the problem, and cast the sufferers out. Still, today, we blame the victim for being a part of the affected group. We segregate them, whether they have the plague, HIV, or allergy, and believe the problem to be "theirs", for them to fix. Not our problem.

If ever there was evidence of the stupidity of this recently, it has to be asthma. While we have been busy thinking of them as "allergic", somehow separated from the rest of us, we have failed to deal with the problems of prevention, and environmental change for us all. Now, over a third of our children cannot breathe, and we continue to think of it as a problem of allergic people only.

The problem of multiple chemical sensitivities is, in my opinion, a toxic problem which will, over the next decade, affect almost everyone in some way. If we fail to notice the "silence of the canaries" on our way into the mine, we are doomed eventually to silence as well.

Total Load

If the concept of progressive complex toxic responses is to be understood, then the process of this occurring is probably best described by the term "total load". This is based on conceptual and observational data, rather than on experimental evidence, but the underlying logic is relatively straightforward.

In short, when the total of "stressors" from all sources and of all types are looked at, they may, at a particular time, exceed the body's ability to cope with those stresses, leading to a progressive overload of the person. In this state, the "total load" exceeds the person's capacity to withstand the stress, leading to the adoption of a new (and somewhat stable) state of health lower than previously enjoyed, and with less "reserves" to protect against future illness.

With regards chemical exposure generally, and in multiple chemical sensitivities particularly, the components of the process may be explicitly described as follows:

- Most synthetic chemicals are tested only for toxicity of certain types, most often lethality or carcinogenicity in rodents. Under two percent have been tested for neurotoxicity, immunotoxicity, genotoxicity or reproductive toxicity in animals. Almost none have been so tested in humans.

- So-called “safe levels of exposure” for humans are derived from these data in an arbitrary way (normally by dividing the dose which kills half of the test animals [LD50] by a factor of between 105 and 107), and the agents are released into the environment.
- No data are obtained for potential synergistic effects, nor for additive effects of these chemicals when used in combination with other commercial chemicals. Often chemicals are delivered in a complex commercial mixture, in which the “active” ingredient is among the lowest concentrations in the mixture. The effects of this commercial product on humans are not known, and are only likely to be discovered by effective and vigilant post-marketing surveillance.
- The population as a whole is exposed to many thousands of common chemicals in their day to day lives. Such exposure is usually at levels within the “acceptable range” for each individual chemical agent. This implies nothing about the potential for adverse effects of the environmental exposure.

Suppose that each of 1,000 noxious chemicals were all below the “No observed effect level” (NOEL) at a concentration of 0.1%. It would be possible to construct a gas consisting entirely of such noxious chemicals, and without any of the usual atmospheric gases. Would this gaseous mixture still be considered ‘safe’? Clearly the answer is “No”, as it would be rapidly lethal. Yet the chemicals are all at or below the NOEL!

Now consider medical drug therapy. Four drugs are administered, each at the recommended dosage, yet the patient dies as a result. This is not as unusual an outcome as is often suggested. What happened? Clearly, drug interactions can increase and decrease the effect and toxicity of the drugs dramatically, to the extent that there are large sections of drug handbooks given over to the management of such interactions.

Yet in environmental and occupational medicine, the release of huge numbers of novel agents into the environment and workplace has precluded such studies because of the logistical and financial constraints. Only a few interactions are known, such as asbestos and smoking, and these are usually because of the unusual nature of the disease caused.

Does this mean that such adverse effects do not occur? No. Does it mean that we cannot ever know the effects? No. What it does mean, though, is that the biosphere has become something more akin to an experiment designed to test the limits of acceptable contamination. Except that the experimenters have gone home, and are not watching the outcome. The precautionary principle has been discarded, and the backup system, post-marketing surveillance, is virtually non-existent.

The “acceptable range” of exposure for the mixture is unknown, but is clearly finite. That is, there comes a point where the number, dosage and interactions of the chemicals is no longer compatible with good health of the population, and a further point at which deaths will occur as a result of exposure. Each chemical may be at an “acceptable” level, yet cause the death of an organism through additive and synergistic effects, as was reported in *New Scientist* some years ago.

- In the body of each person, detoxication and elimination is a biochemical process, the effectiveness of which varies according to a normal distribution, with a person to person variation in

the order of 10⁴ (that is, the most effective detoxifiers are able to eliminate up to 10,000 times more efficiently than the least effective).

Thus, in a large population with an increasing number of chemicals, there will come a point at which the least protected (biochemically) will be adversely affected while others are not. As the dosage increases, greater numbers will be affected, in ways no longer defined by the toxicity of the individual chemicals.

For people with a limited biochemical detoxication or elimination response, especially those whose enzymes cannot be induced due to genetic factors or toxic effects, there comes a point at which a small increase in chemical exposure will cause a rapid deterioration in health, further impairing the biochemical response in a positive feedback loop. This is seen for example in paracetamol overdose, at the point at which available glutathione (GSH) is consumed.

For these people early on, and for more as the increasing range and dose of exposure extends over time, the situation is analogous to the classic experiment in chaos theory demonstrating the phenomenon of "self-organising criticality". One grain of sand at a time is added to a pile, producing initially a small bump, then a hill with progressively steeper sides. The occasional small "slide" occurs along the way reasonably frequently. Larger "slides" occur less frequently but can make significant changes in the structure of the pile. Each time, the agent of change is a single, almost insignificant grain of sand, yet when the right moment arises, that one single grain can make for a very large change in the system, as it self-organises, or collapses to a more stable state.

This is also a critical factor in multiple chemical sensitivities. It is a "stable state", not subject to homeostatic readjustment. It would seem to have much to do, potentially, with self-organising criticality.

- The health effects are unpredictable from a knowledge of the toxic agents, and can only be determined by observation and post-marketing surveillance. This is not being done at present, except by primary care health professionals.

It is my contention that unless we act upon multiple chemical sensitivities as if it were a toxic response to an increasing environmental "total load", we run a huge risk - we may lose our ability to survive through progressive damage to immunity, reproduction, and mental and emotional function.

We should be looking at multiple chemical sensitivities as though our very lives, and those of our children, depended upon it.

Chapter 7

Hypotheses for consideration

Conditioned responses (part I)

There are some strong arguments to be made for the process of multiple chemical sensitivities being a conditioned reflex, a reflex celebrated in the tale of Pavlov and his salivating dogs.

Before going into these, however, it is useful to look at the career of Pavlov, just as it is important to make a clear distinction between a conditioned reflex (or conditional reflex, as it was originally termed by Pavlov) and psychological disorders. These are often confused, even among medical practitioners, and the confusion is at the heart of much of the controversy surrounding multiple chemical sensitivities.

Ivan Pavlov was the son of a priest, born in Ryazan, Russia, in 1849. He studied natural science at St Petersburg University from 1870 until 1875, and completed his doctorate at the Military Medical Academy in 1883. It was here that he began his celebrated experiments on digestion, earning him his Nobel prize in 1904, and establishing him as arguably the most famous of Russia's scientists.

Ivan was a rebel.

Not Ivan the terrible, but rather Ivan the wholist!

Ivan stood apart from most of his peers in two main ways.

The first was that he studied the "course of physiological processes in whole and normal organisms". What's worse, he spent a good deal of his time promulgating his view that all other physiologists should do the same. This was close to heresy among an orthodoxy which was increasingly experimenting on isolated organs and tissue samples.

The second was his belief that the mutual interactions between organs within the body, and between an organism and its environment, were of primary importance in understanding function. That is, not only did the whole organism need to be considered for any worthwhile understanding of the mechanisms of life, it needed to be observed and studied in its own usual environment.

This, for physiologists, was almost too much. No sooner had they developed their experimental, analytical methods, with them all having a fine time at the party, than Ivan moseys along and tips a bucket on the whole affair. Only a Russian, they probably thought, could be so impertinent.

The reason I bring this up before looking at Ivan's discoveries is that this was a profound historical moment for biology, a bifurcation, a choice. We have yet to fully recover from the choice we made at that fateful time, almost a hundred years later. It was the choice of every inquisitive child throughout the history of humanity.

We decided to pull things apart.

Admittedly, it was a choice made in all scientific disciplines at different times. It was in all likelihood a most necessary interim step to help move us from primitive superstition and blind religious faith to something more rational, more credible. But it was an interim step which led to such a burst of knowledge and apparent power that we have so far neglected to put things back together again.

It is easy to overestimate just how knowledgeable we really are. What we have learned, we have learned from the universe around us. What we have created, we have created from blueprints given to us. Our brains are constructs of our universe, yet contain universes within. We have pulled many things to pieces, yet have created nothing new, for all it may seem otherwise.

We have treated our world more like a Lego set than anything else. We have pulled it to bits and recombined it in a lot of astonishing ways, but we are yet to create something really new. We can describe and explain pretty well everything we see and do, but when it really gets down to it, we are fiddling with things we know precious little about. We walk a dangerous path with only glimpses of light here and there to guide us. It is remarkable that we have survived the dangerous century just passed.

Science can describe a rainbow, and even tell you how it occurs. Yet science could neither predict a rainbow, nor tell us a single thing about the irrationally exhilarating experience of catching a glimpse of one, glorious against the black rain clouds in the late afternoon sun.

Again, I digress.

Ivan described two distinct entities in his seminal work on "conditional responses", now usually termed conditioned responses and conditioned reflexes.

The first is his best known work, about classic conditioning, but has less to do with multiple chemical sensitivities than his second (which you will now need to wait for).

You have most likely been told the story of the dogs, the bell and the digestive juices. Most simply, the dogs were fed each day, and the food was preceded by the ringing of a bell. The dogs produced gastric juice in their stomachs, which was observed by Ivan and his friends through a surgical 'widow' cut into the dog (they were wholists, but not yet aware of animal rights!).

After a short period of time, the food was no longer needed, and the ringing of the bell was all that was required to elicit the same response as the food would have. This was termed "psychic salivation" by Pavlov, although the term "psychic" carried none of its current connotations at that time. The food and the salivation to food were termed the unconditional stimulus and unconditional reflex, respectively. The bell, and the salivation to the bell alone, were termed the conditional stimulus and the conditional reflex, respectively. A mistranslation of Pavlov's term conditional to conditioned is the reason this process is most commonly known as the conditioned reflex these days.

The strangest thing about this whole response is that the only thing which needs to be perceived by the organism is the conditional stimulus. The unconditional stimulus and the responses may not be perceived at all.

This was shown by some elegant work at the University of Newcastle some years ago, where an immune suppressant drug was given to volunteers along with an artificially sweetened and coloured drink which itself had no effect on a control group of volunteers.

The drug had no taste, and caused a depression of immunity of which the subject was totally unaware. Despite this, once the conditional response was established, the sweet blue drink was able to elicit as marked a degree of immune depression as the drug provided. This is frightening news for drug companies!

There is, in my opinion, an incredible degree of misunderstanding of this response, especially in the medical profession. It is continually being confused with psychological and psychiatric disorders. It is not a disorder or an abnormality. It is a normal response of every organism with a nervous system, vertebrate or invertebrate. Earthworms do it. Crabs do it. Hell, there is a recent suggestion that even psychiatrists do it, though that has yet to be confirmed by independent studies.

One suggestion of the reason for the conditional reflex, and its preservation in so many disparate life forms, is that it provides a crude type of early warning system which allows our slightly slow biological processes to respond to the first hint of a stimulus, rather than waiting for the full, unconditional stimulus. An adrenal response to the crackling sound of paws on sticks or to the first faint whiff of a predator would be far preferable to waiting for the visual stimulus or pain. All of higher life sifts through the memories in search of the ideal stimulus to give it an advantage over others in holding on to life. The more stressful the unconditional response, the quicker the association.

The response is, I repeat, both normal and essential for successful life.

Many people with multiple chemical sensitivities say they are sickened by pesticides, on the basis that it was exposure to pesticides which first caused their health problems. One third of our admissions to the Special Environment Allergy Clinic came from agricultural Australia, principally the cotton growing regions, even though under ten percent of Australia work and live in those regions. It was an unfortunate fact of life that tens of thousands of Australian children were used as low cost spray markers, standing on the edges of the field to signal to the aerial pest sprayer just where to drop the load.

Whatever the cause, it is more than pesticides which perpetuate the problem.

At the time of exposure, the person is exposed to both a highly toxic molecule (the pesticide), and a less toxic, volatile compound. The toxic pesticide molecule has its biological effect (say, depression of lymphocyte proliferation) and is the unconditional stimulus. The short term depression of immunity is the unconditional response. The smell of the volatile and less toxic "carrier" (usually a solvent) is the conditional stimulus.

The affected person then responds to the common environmental solvents in an extreme way, replicating the full effect of the high dose toxic exposure. The conditioning is further reinforced by the fact that the solvents themselves are neurotoxic, and cause literal progressive brain degeneration over time.

Conditioned Responses (part II)

There is a variation on the “conditional response” which I have not so far mentioned, but which I believe may be of particular relevance to MCS, particularly to the mysterious “spreading” effect in which people react to a broader and broader range of molecules over time. This aspect of MCS has always bothered critics, who point out that allergies do not spread to unrelated allergens over time, as if this were a useful rebuttal of the complaint and clinical observations.

It relates to a finding of a researcher named Shenger-Krestovnika, who was investigating with Pavlov the various types of conditional responses in 1921. The response gained what would now appear to be the unfortunate name of “experimental neurosis”.

The researcher developed a conditional response in dogs, based on the shape of a circle rather than a sound. The circle was associated with feeding, while an ellipse was associated with not being fed. The dogs could distinguish even small differences between the shapes very well, at least initially.

As exposure to the similar shapes continued, however, the dogs behaviour took an unexpected turn. Their conditional response became, well, confused. The dogs became unable to distinguish obvious differences in shapes, and the conditioned response was triggered by an increasingly broad range of shapes. The dogs became excited and agitated during the experiments. Even more strangely, this type of conditional reflex varied greatly from one dog to the next, with some types of dog “personality” more susceptible than others

The researchers termed this “experimental neurosis”. It is worth noting that “neurosis” in late nineteenth century Russia held quite a different meaning to the one we commonly give it today. Ivan thought of “neurosis” as an imbalance between the excitatory and inhibitory processes of the nervous system, rather than having any psychological associations. It was considered to be a type of “hardware” problem, intricately linked with the connections within the nervous system.

This model of experimental neurosis, given its apparent similarities with MCS and the associated spreading effect, certainly would seem to deserve a revisiting, and an experimental design. My guess is that homo sapiens sapiens would not be except from their biological heritage. It may be very easy to experimentally create MCS.

It is a different question as to whether this would be a good idea. I may leave this to bioethicists and University ethics committees. They seem to have a handle of animal abuse for the greater good.

Neurotransmitters - please consider

There is a lot of discussion about neurotransmitters these days. So much, that one could be mistaken for guessing that we have the faintest idea of what we are talking about. I have heard so many patients tell me, “Oh, yes, I am on Prozac, but not as a drug. The doctor told me that I have a chemical brain imbalance, and this just restores the normal balance”.

Bullshit! Pure, unadulterated bullshit.

Our knowledge of brain chemistry in 1997 is analogous to our knowledge of atomic theory in the eighteenth century. We could build engines that would do work without any clear knowledge of why they worked, or what exactly was happening.

These days, we can manipulate serotonin, monoamines, acetylcholine, GABA and the myriad of other brain-active chemicals with powerful drugs. We confuse the ability to fiddle with an understanding of the processes involved. Give a child the controls of a jumbo jet, and certainly something will happen! It does not mean that the child knows what is happening, nor does it mean that he is in control.

At least one doctor in the US has "supplemented" all his patients with serotonin altering drugs, apparently believing that he is correcting a stupid oversight in body design. It is so...so...so American. Buy a new car. Beat up the world's baddies. Cure baldness. Banish sadness forever.

There, that is better. It's out, and I am feeling much better for having relieved myself of that heavy anti-American sentiment I have been carrying since I travelled from west to east back in 1982. Now, back to my coffee, and to my musings on neurotransmitters.

There are two issues with neurotransmitters which I believe deserve a showing in the MCS and CFS expo, and about which precious little has so far been said.

Histamine

Histamine is best known for the part it plays in allergy. We all know of antihistamines, and the way some doctors talk, you could be mistaken for thinking that histamine itself was another of those "design flaws" in need of medical attention!

Few people know of the essential function of histamine as a neurotransmitter. It is globally active in primate and human brains, although concentrations in the olfactory and limbic areas make it particularly attractive as a potential player in MCS.

One of the things I had noted clinically in a small group of patients who had developed MCS with CFS was that they described having significant allergies up until the time that they developed their CFS/MCS! I was uncertain what to make of this until a visit one day to Newcastle University in 1990. Because the people I was there to see were lecturing at the time, I was politely "parked" by Hugh Dunstan in a small room with two neurophysiologists. Hugh told me he would be back in an hour, and that he felt I would find their work "interesting". Not!

I stared around the rotten little room with its hand tooled apparatus (if that is the plural of apparatus), the socially incompetent, wide-eyed experimenters, and the smell of glutaraldehyde, and wondered if it was possible to excuse myself for lunch at 10AM.

One of the researchers turned to me and asked, "So, doc, what do you do?". I inhaled, paused, and thought, "OK, you asked!". I let them have it, blabbing on about CFS and MCS and the deep mysteries to be solved in the research program we were planning with Dunstan and the others.

The two of them watched me intently during my (rather animated) soliloquy, clearly somewhat bemused by my response to the glutaraldehyde. When I paused for breath, they turned back to their work without a word. A few moments later, still peering down into the bowels of his tangled equipment, one murmured to the other, "Sounds like a histamine problem to me." The other nodded.

"No", I said to them, "not much to do with allergy, really". I was thinking that I would just put the smart-arses back in their place with the one remark, then break for an early lunch.

"No", the murmurer chirped back, "not allergy. Brain histamine." He reached under his desk, fished around in a box, and pulled out a couple of papers on the distribution and actions of histamine as a neurotransmitter.

I looked blankly at the papers for a moment while he went on. "It sounds like the global effect is similar to the effect of the old, non-selective antihistamines. Sleepiness, fatigue, poor memory and concentration, lowered sex drive, slow reaction times. And the triggering from just the right place - the olfactory region. And all those limbic responses seem like a globally active neurotransmitter. Worth thinking about, wouldn't you agree?"

The researchers, clearly pretty happy with themselves, broke for an early lunch, leaving me open mouthed and staring down at the papers before me. All I could think at the time was, "Why haven't I thought of that before. Why haven't I read that before. How could something be so damned obvious, and be missed."

I looked through these papers over the missed lunch, and wept. Well, not really. That's more a girl thing. If I had been in touch with my emotions, though, I would have wept. Before me was one key in CFS, and one mechanism whereby a chemical olfactory trigger could induce the range of CFS symptoms. In some ways, this was the missing link for me. Why, I had wondered, did the olfactory stimulus in adult MCS so reliably induce CFS symptoms? Why were the conditions, though distinct, so closely linked?

We all know of the H1 and H2 (histamine type 1 and type 2) receptors - the former, when stimulated, leads to allergy symptoms. The latter, when blocked, stops acid production in the stomach. H1 antagonists are widely known as antihistamines and are used to reduce allergic symptoms, while H2 antagonists are used as anti-ulcer medications.

Few of us have heard of the H3 receptors, however. This is an auto-inhibitory receptor, a part of a negative feedback loop, and is probably protective against the damaging and potentially lethal effects of allergy. Alpha-methylhistamine (AMH) is released in the histamine response, and binds to the H3 receptors, which in turn "tones down" the strength of the allergic response. That is the positive, protective side of H3 stimulation.

The downside of this inhibitory response is that it is global, and "turns down" brain histamine activity as well, leading to sleepiness, poor ability to learn and other "CFS-like" symptoms in cats, dogs and primates.

The link with MCS is that the neurological responses of CFS and MCS are often remarkably similar. In fact, for many MCS sufferers, the major problem of the pathosmia is that it effectively trig-

gers relapses of CFS. As well, the highest concentration of H3 receptors in the brain is in the olfactory bulb, at the very site of the action in MCS.

Thus, a normal response designed to enhance survival (the inhibition of an over-aggressive allergic response) has an unintended (or possibly even an intended) effect of turning down the brain function, inducing sleep, and producing pathological fatigue. The change in brain function would tend to match those effects of the old antihistamines. The problems with those match the major symptoms of MCS, with the exception of the pathosmia.

There is a final piece to this, and one open to experimental assessment. The H3 receptors can themselves be blocked by a drug that has been used experimentally for a number of years now to do just that. It has been researched extensively in France, and is now being used in the treatment of narcolepsy. The downside of the drug is that by blocking the H3 receptor, it blocks the inhibition of histamine, potentially increasing allergic sensitivity.

In the animals so far tested, alpha methylhistamine induces what for the animals certainly seems to be a state familiar to CFS and many MCS sufferers. They sleep excessively, cannot concentrate or learn, and are fatigued very easily. The symptoms are rapidly and apparently completely reversed by the administration of the drug, without other apparent effects.

OK. The name of the drug is thioperamide. I am not suggesting for a moment that it is a treatment or cure for either CFS and MCS. I am not suggesting anyone move to Paris or claim to be narcoleptic to get on a treatment program. I am simply saying that we may have a piece of the puzzle before us for a subset of the MCS sufferers where CFS is triggered, and who were previously allergic.

I do suggest, however, that it may be an experimental animal model worth looking at, and it may provide a new perspective on few of our preconceptions.

The Chaos Of The Mind

The whole issue of "excitatory" and "inhibitory" aspects of our nervous system is poorly understood. It is not at all like an accelerator and a brake, with two separate sets of controls and two separate circuits.

Think of a hotel on a Saturday night (my father was a publican, and my work from age 13 until my graduation at age 24 was in hotels). The drug of choice is (currently) alcohol, a neurological "depressant". Watch the experiment as a few hundred primates ingest the drug to their own estimate of an appropriate end-point. What do we see?

One or two drinks in, most of the cohort seems little, if at all, affected. But even here, a few are clearly changing behaviour. Most, at this point, are female, partly because of the missing alcohol dehydrogenase on the surface of their small intestine, an area known as the "brush border". Many are simply becoming quieter, appear internally focused, and are responding less and less to the conversations around them. Others are giggling or accelerating their speech, with smaller pauses between phrases, in a snowballing chatter, with others finding this somewhat amusing.

Move on half an hour, and a few more drinks. Almost everyone is feeling different and is acting differently now. Some of the "hard" drinkers remain unaffected, their enzymes able to keep up with the toxic insult, keeping the alcohol and acetaldehyde levels lower than the others. But the surprising thing is that there is now clearly two groups, very different in their "personalities". Some are active, garrulous, dancing and clearly "twitchy". Others are laid back, apparently calm (some to the point of sleepiness), chatting slowly, with uncomfortably long pauses, and apparently "sedate". One group is "disinhibited", the other "inhibited", or so it seems.

However, if we move in closer, this apparent division of the group is not so clear. Speech is becoming slurred and less comprehensible in both groups. Co-ordination is decreasing (easily measured by total "spillage" at the bar), responses to questions are taking longer. All, in one sense, are suffering depression of nervous system responses, as would be expected with a depressant drug such as alcohol. Yet the behaviour which emanates from such a response is not so easy to predict.

It is now closing time, 2AM. The drinks have stopped, and only about half of the original "study group" have made it to the end of the experiment. The "imbibing rate" has fallen off greatly in the last few hours (some cynics have suggested that this is the only reason Australian pubs ever close!), and most of the subjects have chosen a drinking schedule which does little but maintain their "set point" and forces them regularly to the toilet to either vomit or pee. Usually both. This alcoholic-bulimic effect now dehydrates the subjects, guaranteeing a hangover they will soon forget, only to return to the experiment the next night and the next night

But even at this late stage, there is a massive difference in the activities of different individuals. Most are near sleep, often draped in the arms of people who only hours before were strangers. Some are singing boisterously, still in apparent good humour, though dreadfully out of time and tune. Some are plotting revenge for perceived insults and wrongs. And some are punching or scratching each other, normally over the "turf" of a potential lover each wishes to claim for the night, utterly oblivious to the fact that unconsciousness will precede sexual congress by at least an hour. If sexual congress were at all possible in the first place!

What is this thing called, love?

What is the point of this story, one probably well known to most? Well, there are a few points.

The first is that our biochemical individuality (detoxifying enzyme levels, location of those enzymes, nutritional history, body fat distribution and the like) ensure a massive difference between individuals when exposed to psychotropic agents. Even in a single individual at different times, the combination of these factors can make a massive difference to the outcome

The second is that the nervous system is not homogeneous, changed equally all over in a given individual. Nor is it necessarily changed similarly in different individuals. The effect of the drug may well be universal (e.g. prolongation of nerve conduction with alcohol), but the higher level effects (which we normally ascribe to the frontal lobes of the brain) are reasonably unpredictable from the knowledge of the neurophysiology.

Thirdly, there are layers upon layers in the nervous system of humans, many of them predicated by experience or expectation, and this complexity again makes prediction of intermediate effects

inherently difficult to predict, even though the final outcome, such as vomiting, polyuria and eventually profound sleep or unconsciousness is very easy to predict.

Finally, each neuron (nerve cell) seems to have receptors responsible for "turning down" that nerve's activity, and others which "turn up" that nerve's activity. For example, the GABA receptors and NMDA receptors seem to work on neurons in this way, the former turning down activity, the latter turning it up. So, while the nervous system as a whole is not well described as a simple "up-down", "high-low", or "positive-negative", the components within may well be so described.

The complexity of the nervous system guarantees that with such a "polling" of individual cells, the entire system will behave in a way that is inherently unpredictable, or chaotic. This is not uncontrolled chaos, however, leading to wildly implausible states of consciousness (or unconsciousness) in different people. It is the more "refined" chaos of the "attractor", binding possible responses towards a relatively predictable final outcome.

As a brief illustration of what I mean (and I apologise to those who already understand), think of a bath with a few tiny plastic bubbles floating on the surface. The plug is pulled. Where will the individual bubbles travel? At the end, we know they will go down the plug-hole, but does that help us determine just where each will be, say, ten seconds after the plug is pulled? No, we cannot say much about how they will travel to their final destination, but we can say that it will not be via the living room, or through the North Island of New Zealand (except for baths so situated). Their paths will be constrained within the bath, with a high degree of certainty, and will tend towards the plug-hole (which is in this case the "attractor") over time. But there is little else we can say. Each ball takes its own individual path, varying from quick disappearance straight down the plug-hole to wildly eccentric swings around it to the very edges of the bath. But in the end, the fate of each is the same. Sorry, but the drain will get you in the end.

It is in this chaotic response of the brain to a stimulus that we may find the roots of MCS. There is no longer any doubt that the olfactory message and signal is inherently chaotic. It has been measured for a range of aromas, and it seems that the way the olfactory bulb "homes in" on the smell is via the signature of the resulting attractors. From here, the messages spin out to the limbic system and hypothalamus, triggering similarly chaotic responses, again bound by attractors. They will not turn a female into a male, but they may, for example, tend to synchronise menstrual cycles over time. They may turn down metabolism, inducing a hibernational response to some perceived stressor. They may even lead to mating, and the creation of a new individual, with all the chaos carried in that outcome!

Chaos in the action of GABA and NMDA receptors seem unlikely places to search for the origins of MCS, but it is open to experimental testing as we now have stimulants and inhibitors of each. We know little of the responses in humans yet, but I suspect that the manipulation of these with diet, nutrients, amino acids and, eventually, patented analogues of these will prove fruitful.

At the very least, it should make a night in the pub more interesting.

Biochemical Individuality

While I have touched on this in the story above, there is clearly a bigger picture of biochemical individuality. I have been assessing the detoxication responses of people with MCS for eight years now, and two extraordinary facts have arisen.

The first is that the biochemical responses to chemical challenges are as individual as fingerprints. I have never seen two the same, not even in identical twins.

The second in the consistency of the finding that MCS sufferers are different in their detoxication processes than most of the rest of the population. This may seem strange, given that a distinction has always been made between sensitivity and toxicity, and detoxication responses are intimately involved with toxic responses.

Let me explain.

When challenged with, say, a fat soluble toxin such as an organochlorine pesticide, how does the body manage to clear it out? Remember, this chemical was constructed less than 50 years ago, and never existed in nature prior to its widespread use as a pesticide. Surely, one would think, it would be difficult to clear such unknown chemicals from our bodies.

The answer is both yes and no, depending on the person and a complex combination of biochemical responses. It also depends on how the toxin entered the body.

If we are lucky, we ate the toxin. Why? Because everything we eat hits the gut first, and is absorbed into a special, separate part of the bloodstream known as the portal circulation. All this blood heads back to the normal circulation via the liver, where it percolates through a sophisticated filtration system. This is a survival strategy was a necessity for us to make it through to the present day, as most of the poisons consumed in our evolutionary past were from foods - the defence systems of the plants against predators - insects and herbivores.

If we are less lucky, the toxin enters through the lungs or skin. This is because our past did not adequately prepare us for this type of intoxication - it just was not common enough to invest the energy in. Whatever we may think about our current world, there is no doubt that every breath of every breathing animal contains traces of hundreds, possibly thousands, of chemicals which were not in the air two hundred years ago.

The problem is that chemicals entering through the lungs and skin become distributed throughout the body tissues, and do not go through a "first pass" filtration in the liver. Our more vulnerable organs, our brains, bone marrow, and reproductive organs, are exposed to the source chemical at doses they are not well designed to handle. The results are unpredictable, but logic would suggest that the outcome would be poorer than it would have been with hepatic (liver) protection

The liver is a remarkable organ, not dissimilar in function to an almost endless routine of "tasters" for an unpopular head of state! The world provides a variety of toxins, and the liver responds by being poisoned and finding the right strategy to detoxify the poison, often at the expense of millions of hepatic cells. The response of the animal is either to die (the liver did not manage to head off the threat), be sickened (some of the poison got through, but not enough to kill), or do well (the toxin was detoxified and eliminated without real harm). The first two outcomes lead to avoid-

ance of the source by the individual or others of that individual's group. The latter requires little but biological adaptation over time.

There is a problem with this system, though, and that relates to the differences between individuals in detoxifying capacity. Some individuals may be hundreds of times more susceptible to a particular toxin than others, while handling other toxins with alacrity.

This biochemical individuality is the engine of survival as far as a species goes, but can be a bit of a problem for a given individual. The mixing of genes for, say, cytochrome enzyme function ensures that the natural evolutionary experiment continues, sometimes to the disadvantage of a given individual, ensuring a range of possible responses to any circumstances within a population. The odds are that a few members will have a good (if not always the best) response to the varied challenges of life 'red in tooth and claw', and this will allow them to do as Mr. Spock proposed, 'live long and prosper'.

Or so the Darwinian fairy-tale would have it.

Winners and losers are harder to determine than this in the complex web of conditions and contingencies that we call life. Darwinian evolutionary theory is not 'wrong', any more than Newtonian physics is 'wrong'. It is, in my humble opinion, incomplete. A subset of the interaction between life and its universe, true at one level, but a poor wretched shadow of the whole relationship.

A discussion of this must, sadly, be left for another book!

The detoxication of undesirable or dangerous chemicals is far from a simple business, but for the sake of clarity, I will over-simplify it here. There are broadly two parts to detoxication, termed "biotransformation" and "elimination". These are often termed "stage I" and "stage II" detoxication processes.

Biotransformation is the process of changing the structure or composition of a molecule so that it is able to be removed through one of the body's elimination organs or systems. Many of the current chemicals are highly "lipophilic", meaning that they dissolve very poorly in water, but easily in oil and fat. These are acted upon by liver enzymes to make them more water soluble, which in turn prepares them for stage II, elimination. The enzymes involved are generally known as mixed function oxidases and cytochrome p-450 enzymes, and are found in high levels in the liver and certain other organs necessary for survival, such as the brain stem.

A problem with biotransformation is that, although it prepares the chemicals for elimination, it is as likely to increase the toxicity of the original chemical as it is to decrease it. Many of our most notorious toxins, such as benzopyrenes, are of no great concern to the body until they have been biotransformed, whereupon they become highly toxic and often carcinogenic. In a sense, our detoxication responses can create a greater problem than the one we started with.

The whole process of biotransformation is a little like collecting and packing the garbage from around the home into garbage bags, ready for collection.

Stage II, the elimination process, has its own subtleties. The primary strategy is a process known as conjugation, whereby a biotransformed toxin is bound to a "chaperon", a chemical which will bind to it and ferry it to the outside world through the bowel, kidneys, sweat glands, hair and

nails, or lungs. Sulphur is a critical component of adequate elimination, usually in the form of a small tripeptide known as reduced glutathione (GSH). The sulphur of the cysteine (an amino acid component of the glutathione) binds to the biologically active sites of the toxin, ferrying it out of the body with minimal risk of damage.

At its best, the detoxication response matches the stage I and stage II processes. The chemical is prepared for elimination (with its attendant risks), then quickly bound and eliminated. It is the liver which has the highest total capacity for both processes in succession. Imbalances in this two stage process can have significant consequences.

MCS sufferers are most commonly fall into the category known as "pathological detoxifiers". The first stage is raised when compared to the second stage. Whether this happens as a result of exposure to environmental agents or was the prior condition leading to the MCS, I am not in a position to say. This requires a prospective trial of a large number of people, to see if the healthy pathological detoxifiers are more likely than the rest to develop MCS.

It is worth remembering that it is not only the liver that detoxifies. Every metabolically active cell in the body does so as well, with widely variable rates. The brain stem, vital to breathing and survival, has the highest levels of the stage I (biotransforming) enzymes, with other areas of the brain such as the olfactory bulb, mid brain, thalamus and limbic system not too far behind.

If the brain is exposed to lipophilic chemicals, the rapid biotransformation along with low elimination may accelerate brain damage. In fact, the potential for increased toxicity of the intermediate detoxication products may be the reason for the link between pesticide exposure and brain damage, including Parkinson's and Alzheimer's disease.

Testing of the detoxication pathways is not assessed by standard medical "liver function tests". In fact, the standard biochemical tests are more correctly termed "liver damage tests". They are useful for assessing damage to hepatocytes (liver cells) from acute toxicity, hepatitis, and some forms of food poisoning, but are of little use in assessing liver function.

I earlier mentioned one type of crude functional test, namely the "liver stress test", in which we fasted people on entry to our SEAC environmental unit. These people quickly showed biochemical evidence of liver damage after only a few days fasting, something which should have taken nearly two weeks. Once the nutritional supply of sulphur containing amino acids (methionine and cysteine) was ceased, the stage II elimination was reduced to pathological levels. The liver cells were damaged simply by their processing of the toxins stored in the body fat, which was mobilised in response to the food reduction. This problem was reversed by simple amino acid supplementation during the fast.

There is a simpler and safer way to assess the detoxication pathways. The liver is challenged by mildly toxic agents, such as caffeine, acetaminophen (paracetamol in Australia and aspirin, and the breakdown products are measured in sputum and urine. The efficiency of the various stage I and stage II pathways can be inferred, and mismatches identified.

The Liver, The Gut And The Brain

The liver function alterations are not, by any means, totally due to external chemical toxicity. One of the “invisible” forms of liver toxicity arises from abnormal microorganisms in the gastrointestinal tract. This may explain some of the association between MCS and the common symptoms such as irritable bowel syndrome (IBS).

A frequent history provided by MCS sufferers is one of long term antibiotic use some years prior to the onset of the MCS. The most frequent group in Australia are the tetracycline antibiotics, which was commonly used for acne and recurrent respiratory infections in Australia. The majority of those on the antibiotics feel few problems at the time they were used, apart from occasional fungal infections, especially vaginal thrush (*candida albicans*) in women.

About one to three years after ceasing the antibiotics, the person develops increasingly severe irritable bowel syndrome. This is investigated, no cause is found, and the person is told that they must be “psychologically stressed”, and are usually referred to a psychologist or psychiatrist. While this helps the people feel better, it does not cure the condition - it simply convinces them to complain less about it (as I would if confronted with the alternative of rivetingly boring and expensive sessions with these people!)

A year or so after the onset of the IBS, the person begins to suffer from sleep disturbances. This “creeps up” on the person, with prolonged sleep latency (difficulty falling asleep), increased night-time waking (often the person will get up to urinate, but only passes smallish volumes), sleeps very lightly, and wakes feeling unrefreshed the next morning. Not all of these occur in every person, of course, but there is a noticeable change in sleep patterns. Sometimes this is “disguised” if a pregnancy occurs around this time, as pregnancy and babies are other frequent disruptors of sleep.

Next, the person develops chronic fatigue a further year or two later, with increasing olfactory sensitivity. It is around this time that the person fulfils the diagnostic criteria for both CFS and MCS, with certain chemicals and smells “triggering” the full range of symptoms.

What is going on here, and how are these linked?

While I do not pretend to know the whole story, there are more than a few hints to help us through the maze of unusual symptoms.

Firstly, without doubt, long term broad-spectrum antibiotic use can lead to dysbiosis, or altered bacterial balance in the gastrointestinal tract. We have learned much about how bacteria live and thrive in the past decade, and what we have learned is increasingly looking more like an X-files episode than science. We had thought of these simple organisms as free-floating scoundrels, ever ready to turn on their host without warning unless immune vigilance was high. These were little packages of bad news, and could be identified on swabs and cultures when things went wrong.

In fact, microorganisms exist most usually in complex colonies known as biofilms. These biofilms are like ad hoc organisms, with a structure enhancing survival of all the inhabitants. Ghettos abound, with some parts specialised in absorption of nutrients, passing on the “food” to others in the biofilm through microscopic channels. Some parts deal with natural and synthetic antibiotics, detoxifying them, providing physical barriers, or even pumping them out again. Others are good

at toxin elimination, by pumping them into the lumen of the bowel or into the portal blood stream. Either way, these toxins will soon end up in the liver, which will have to put its own detoxication processes to the added load.

It is this added load which is so little considered by doctors, but which is the critical factor in overloading the liver, inducing certain enzymes which will increase the toxicity of other environmental agents.

Clearly, the biofilms are likely to be resistant to the antibiotics which have been most used in the person. Further use of these will only enhance the survival of these biofilms over their competitors, making the person feel sicker after the interminable courses of such antibiotics overprescribed by doctors.

The biofilms are tough, large "superorganisms", taking years to assemble to their final composition (thus the initial delay in symptoms), and incredibly resistant to destruction. They easily resist the natural defences of digestive enzymes, secretory IgA (an antibody on the surface of the mucous membranes, including the gut), and both branches of the immune response (because they are independent organisms within the lumen of the gut, rather than easily accessible to immune cells in the blood). They are far from fleeting, variable, free floating organisms. These biofilms, once established, can remain lifelong, like many other parasites.

They can also disrupt the bowel as well, damaging the digestive process and protective integrity of the bowel. This can lead to malabsorptive problems, especially of the food components which require "active transport" across the bowel wall. The paradox here is that while absorption of the macronutrients (fats, proteins, carbohydrates, sodium and the like) is not a problem until advanced stages of the illness, the absorption of micronutrients, such as vitamins and trace elements, can be quite disturbed, leading to subtle but profound biochemical alterations in the host.

Large molecules, especially partially digested proteins, can enter the bloodstream and lymphatics because of the physical disruption to the surface of the bowel. This can easily lead to food allergic responses in susceptible (usually allergic) people, causing rashes, asthma, sinus problems, headaches and many more symptoms.

Finally, the biofilms can act as miniature "breweries", fermenting free sugars in the diet to alcohol and gas, contributing to some of the IBS symptoms of bloating and wind, as well as the light-headedness and hypoglycaemic responses.

The problems are not simple to diagnose with certainty, beyond the typical clinical symptoms. Recently, though, two tests have proven valuable in assessing damage to the bowel wall (so-called "leaky gut"), and the alterations of gut flora leading to these problems.

The first is the lactulose-mannitol test, in which a mixture of two complex sugars is ingested, and the urinary output is measured. One is transported across the surface cells on the bowel wall, while the other sneaks into the blood stream through the gaps between bowel cells. When the bowel is damaged, the cells on the bowel surface shrink, the gaps between cells open up, resulting in increased leakage into the blood and eventually into the urine. It is now, therefore, possible to diagnose and quantify the "leaky gut" by this test.

The other test, performed by Great Smokies Diagnostic Laboratories, is the comprehensive digestive stool analysis (CDSA). This is a complex test, covering nutritional and metabolic components in the faeces, sensitive parasitology, antigenic identification of many microorganisms, acidity and more. It is a rich test of the function of the bowel and the composition of the faeces. In my own practice, it has made a dramatic difference to the certainty of diagnosis, and has provided a means of assessing change (improvement or worsening) over time.

Abnormal gut organisms cause an additional, and somewhat unexpected, problem. They can seriously alter sleep patterns!

I first met Richard Brown at Newcastle University in 1992, and he was one of the few people who I can honestly say turned my understanding and theories on a medical subject upside down and inside out. The understanding of this world view has been a delightful and profound addition to my understanding of what it is to be human, and how the world is viewed.

In short, it provides a new and very different answer to the question, "Why am I here?", and it starts from a different question, "Why do we sleep?"

Sleep has always been a bit of an enigma. We perceive that we sleep in order to "rest", and the fact that we awake refreshed is adequate proof of this. Do we rest, though? This depends on your definition of rest, but there is no reduction in brain activity, and no reduction of muscle energy use compared to sedentary work. In many ways, sleep is the antithesis of rest. Much hormonal activity increases, some immunological activity increases, brain energy expenditure increases, and tissue repair is more rapid.

So, why do we sleep, if not for rest? And why do we awake refreshed, if we are not resting?

We sleep, it seems, because our bacteria force us to!

During the day, as bacteria go about their business in the bowel, they divide, die, and shed muramyl dipeptides from their cell walls. Only bacteria possess or produce muramyl dipeptides - mammals do not. Yet the muramyl dipeptides accumulate in the fluid surrounding the brain, the cerebrospinal fluid, as the day goes on. This is called "sleep factor 1", and as the concentration rises, the person feels drowsier and feels a greater and greater need for sleep. On falling asleep, an enzyme is liberated in the cerebrospinal fluid which breaks down the muramyl dipeptides, after which they are cleared from the nervous system. When this is done, and the person awakes, there is a feeling of refreshment and recovery, which is really nothing more than the removal of the sleep inducing chemical.

Failure to heed the call of the muramyl dipeptides leads to certain symptoms which may be familiar to MCS sufferers. Sensory perception is enhanced, with diminished inhibitory responses in the brain leading to a somewhat "hyperresponsive" state. This leads to the state familiar to those who have spent entire nights awake, where the sunlight is almost painfully sharp, sounds "invade" the ears, preventing any concentration, certain smells are sickening, and sensation over the body is exquisite, especially on the eyes and mucous membranes.

This amazes me. We sleep because of our gut bacteria, the very bugs we lovingly feed and nurture for our best health. When these go wrong, and abnormal bacteria move in, the whole proc-

ess goes awry. Our sleep processes become disturbed, sensory perception changes, and chronic fatigue sets in.

It raises the question of the nature of humans.

In an anthropocentric view, we are the most successful species on earth, conforming the environment to our requirements, dominating all but the most inhospitable fringes of the planet. We are, to coin a phrase, the pinnacle of evolution.

In a microbiocentric view, long espoused by Lynn Margulis, we humans are merely extraordinarily successful apartment blocks, supplying the microbes with food and shelter, incubating their offspring, removing their waste, and even passing them on to other human apartment blocks. They wake us, put us to sleep, produce the aromas that attract mates, clean our orifices, and protect us against bad-ass pathogens.

Our bacterial masters outnumber our own cells ten to one. They cover every square micron of our bodies. We cannot survive long without them, although they, as the direct descendants of the primordial soup, will survive as long as life itself. We are a passing wonder, a wink in the three billion years that they have been running the planet.

In fact, one could imagine that we had better be very careful with our masters, and hope that they cannot determine the intention of their subjects. We have come to see our masters as our mortal enemies, and have taken steps to eliminate them with the proliferation of antiseptics and antibiotics. We fear microbes more than anything else in the world.

We desperately need to learn to again live in harmony with microbes. Otherwise, we are likely to be demolished, and reconstructed without that fatal phobia and flaw.

Microbes really deserve and demand our respect and admiration. They certainly have mine, and I thank them for my health every morning when I wake.

Fiddling With Hormones

Another largely unexplored area in need of understanding is the tendency of many solvents, pesticides and plastics to mimic hormones. Oestrogen, testosterone, cortisone, thyroid hormones, growth hormones, and dozens more roam the tides of our body fluids, regulated by dozens more controlling hormones, themselves regulated by the hypothalamus, itself regulated by the olfactory bulb and plenty of feedback from the body. It is, to put not too fine a point on it, a complex system which is susceptible to screw-ups.

Enter the xenobiotic chemicals (ones not naturally found in or produced by the human body). We studied them for toxicity for decades at a pretty superficial level, and did not find them to be a problem. The problem is that we looked in the wrong place, because we didn't even know the questions which needed to be asked. We did not ask about immunity. We did not ask about neurotoxicity. We did not check for chromosomal damage. And we did not even think of hormonal interference.

Why?

Because these were novel, synthetic chemicals targeted at plants, insects, moulds and other kingdoms of life. What could these possibly have to do with human hormones?

It is easy to forget one's origins, and it is often an important mistake.

The hormones in mammals, including humans, are primitive molecules. Concerned with mating, eating, drinking, managing stress, regulating all aspects of cell function in all organs throughout the body. These are not "Johnny-come-lately" experiments in molecular design. These are building blocks, basic molecules of life. And life tends not to re-invent molecules if she can recycle them, bend them to a different purpose, set them to manage a familiar but subtly different task.

In short, it should not have been a surprise that novel chemicals designed to have obvious effects on members of another genus or even kingdom should interfere with the primitive, subtle and complex messages of our hormones.

The jury is still out on the extent or the importance of this oversight. At best, it may be the reason for the drop in male fertility in the past few decades, and little else. At worst, it could be affecting every aspect of our health and future, altering energy, growth, fertility, digestion, immunity, sexual attraction, mental function, body composition, response to stress, fluid balance, and menstrual responses.

I believe the issue of chemical hormonal effects will prove to be most interesting in MCS. Not because it causes MCS, but because MCS allows the individual to detect low level chemical exposure, allowing avoidance of chemicals which could otherwise lead to these problems. MCS may be, just possibly, an adaptive mechanism, reducing the likelihood of acquired infertility and possibly other endocrine abnormalities in sufferers.

It would be ironic if, in avoiding the chemicals which could destroy fertility and our future, the resultant fatigue should so diminish sexual desire that the result is much the same!

"Catching" MCS

Let's keep going with another "difficult" concept - that of catching MCS.

This requires a re-think of two things - evolutionary theory and viruses. I will not attempt to explain this in detail here, just flow with this for a few moments.

What would enhance the process of evolution? What process would increase the potential for survival of a species, beyond the concept of "survival of the fittest"?

Suppose for a moment that the environment changes, and only a single member of a species had a particular mutation of a particular gene which enabled the individual to survive. The rest all die.

Does this mutation enhance survival of the species? If the species depends on sexual reproduction, the answer is clearly "no". A second member of the species with the same mutation is needed, and it must be of the opposite sex to the first, and in a physical location compatible with each meeting the other.

There may be another way, one which improves the odds in favour of survival of species.

One member has the mutation required for survival, as described above. What if it were possible to shuttle this gene into the DNA of some other member of his or her species, enhancing their chances as well. One would think that such a trick would be an advantage in the tenuous struggle for survival among all of life's contingencies.

Viruses are enigmatic creatures, to be sure, but they are essential strands in the web of life on our planet. If I were to guess, I would say that something like a virus would be the hallmark of life anywhere in our universe. It is, viewed one way, the very engine of life. A shuttle for genetic material, capable of swapping around good ideas, seems a prerequisite for life construction in the rapidly changing circumstances of a hostile young planet. It continues as a good tool in environments which change too quickly for heritable traits to percolate down through generations.

DNA is in no sense a fixed entity in an individual over time. Even the DNA of one cell is not necessarily the same as the DNA of its neighbour, no matter what the textbooks say.

I am surprised by the number of people who have developed MCS after a viral infection, such as glandular fever, 'flu or the like. If we were to consider, as I have written above, that the avoidance of most chemical exposure would be likely to enhance survival and possibly reproduction, and if this "ability" were encoded in certain genes, wouldn't it be useful to the species to share that "solution" around? Pass on the ability to detect and avoid dangerous chemicals - yep, I'll have a dose, please.

The herpes viruses are interesting in this regard. They contain human genetic material - snippets from elsewhere - wrapped up in a message delivery system without peer. The package of the virus is released from one person to another, sometimes as an infection, and the virus delivers its DNA message to its new host, which dutifully makes thousands of replicas which pass the news on to other cells. The viruses can remain inactivated within the host cells for years, only stirring things up under certain environmental stresses.

I know it is a long shot, and I am not suggesting I know it is true (certainly, not the details). I have no proof of a "gene" for MCS (though there are such genes for cytochrome enzyme systems, which may be critical in MCS), nor mechanism for identifying and transferring "beneficial" genes for transfer.

I simply know that many people develop MCS immediately after a severe viral infection. I also believe that evolution would favour a system which passed on the best available solution in an individual to as many as possible of the same species.

It may be worth checking the material being carried within the viruses, and seeing what they are, and where they turn up. We may find that nature has already perfected genetic engineering, and that this is why we all die with more DNA per cell than when we started. We can choose appropriate genetic responses from an expanding menu over time.

MCS Is Normal - It Is The World That Is Weird

Let us reverse totally the view of MCS.

MCS is neither an illness nor a disease. It is entirely normal.

Not having MCS, however, is a real problem.

What if the environment were incompatible with normal, healthy life? And what if this environment arose over a single generation or so? What would a successful biological response to this threat look like?

Most of the biggest chemical health threats can, in this hypothetical environment, no longer be smelled, as imperceptibly tiny doses are sufficient to damage, and possibly even kill. They are, however, used with chemicals that can be smelled.

The biologically successful response would be one which could identify and minimise such exposure. One which could induce a sufficiently strong aversion response to prevent ongoing risk and damage. MCS.

MCS sufferers may not be "broken" but the environment which induces an MCS response may well be bad for health.

The only evidence I have for this adaptive response is the theoretical value of reducing total chemical exposure, a discussion with Dr Bill Rea in which he talked to me about the flow incidence of other diseases (like schizophrenia, heart disease, strokes and cancer) in MCS sufferers, and my own experience in my decade in this field.

MCS may, in short, be an adaptation to a lousy environment by developing the skills to avoid such environmental exposure.

Those with MCS may, in fact, be the most normal people in the world. One could even suggest they are advanced compared to the rest of us, with a heightened sense able to detect and minimise risk for survival.

Chapter 8

Epilogue

I want to digress, finish my contribution, and tell a tale of amoebae now.

A billion years or so ago, the high energy UV rays were increasingly penetrating the upper atmosphere, as the sun became hotter and the atmospheric composition changed. Amoeba-like organisms floated free near the surface of the ponds, munching away on bacteria and algae. None initially noticed the increasing UV exposure, lacking receptors for a threat which had not previously existed.

Let us imbue the amoebae with some personality, using terms we may find familiar.

Some of the amoebae don't feel so good, yet the reason is not obvious. A few of them sink down below the surface, where most of the food resided, because of reduced energy. The other amoebae laughed, kicked algae in their pseudopodia, and chatted among themselves about the "wimps" that couldn't hack surface life. Despite this, the problem increases.

Expert amoebae are brought in to examine the problem, and to rehabilitate the "sick" amoebae. "Surface Trauma Syndrome" (STS) is diagnosed, being a pathological fear of the surface, most likely due to traumatic cell division in a past life. The alternative diagnosis of "Sunlight Sensitivity Syndrome" is discounted, as sunlight is no different than it has been for generations.

Amoebic Behavioural Modification Therapy is proposed, and the amoebae are dutifully tethered to the surface during daylight hours with algal chains.

Some, of course, elect not to do this, and slip down a centimetre or so below the surface. They lose their friends, their relatives do not understand them, and they face derision and vilification from the amoebic community when they return to the surface in the evening.

Doctors give them a new, experimental drug, one which induces air bubble formation, to make them buoyant, holding them at the surface. It works, although the amoebae feel worse rather than improved by it. Most cease it forthwith, and return to their depths each day.

It is noted by doctors some time later that many previously healthy amoebae are developing strange tissue damage. The pseudopodia are easily damaged, and eating algae causes bloating and wind. Most of the problems are worse following cell division, and more and more siblings are looking decidedly strange. This is all very strange, as no cause, no pollutant can be found. The community is dying - from good health to death in just a few thousand generations.

All except the neurotic "bottom dwellers", as they are called. They seem to be doing fine, dividing successfully without damage, and doing well between divisions.

Within a few thousand more generations, the surface dwellers are gone, part of the mythology of the "bottom dwellers". No one really believes, of course, that surface dwellers ever existed - not with that vicious UV radiation - but the myths persist.

Right now, they have to deal with the crazies who are fleeing to cooler ponds. Against all scientific evidence, they are claiming that the warming of the current pond is making them sick and tired. "Thermophobia" has to be included in the next issue of the Amoebic Psychological Inventory XII. They can then be incarcerated and brought back to their social group.

It may yet be profoundly true that the meek shall inherit the earth.

Just how they will inherit it is a story for another book!

Captions for figures referred to in book

Note that these figures and graphs have been “misplaced” upon the journey. I put in the captions so that one may have a “feel” for the content

Fig 1 (graph entitled “Cotwatch Respiratory Monitor test”)

“Respiratory monitoring shows major differences in multiple chemical sensitivities compared to controls. In MCS, much of the time asleep is spent in apnoea, with gaps of over 20 seconds between breaths common”

Fig 2 (graph showing bell curve, entitled “Evoked response P300 wave latency)

“Distribution of the so-called P3 latency of the Auditory Evoked Response Potential test is distributed normally in the population.

Fig 3 (graph showing 2 bell curves, entitled “Evoked response - MCS and CFS patients)

“In multiple chemical sensitivities, many of the physiological measurements were not normally distributed as a single population. In the AERP, a test of nervous system function, two distinct populations emerged.

Fig 4 (“coathanger”-shaped hierarchical chart)

“Proposed formal categorisation of different types of adverse reactions. One important question is that of where multiple chemical sensitivities should be placed on this structure.

Fig 5 (entitled “Sensitive and Normal separate” - two bell curves)

“In the usual interpretation of multiple chemical sensitivities, sufferers are considered a separate population to the majority.

Fig 6 (entitled “Sensitive People Part of Normal population” - one bell curve)

“Multiple chemical sensitivities may represent one end of the population, typified by the characteristics of certain known groups!

Fig 7 (entitled “Sensitive and Normal separate - No worries” - two bell curves)

“The potential harm for the majority of the population by, say, 2020 may not be great if the sensitive population really is different from the majority...”

Fig 8 (entitled “One population - start worrying now” - one bell curve)

“If we are part of a single population, small changes in exposure may see a rapid increase in the proportion of the population affected.

Fig 9 (single line graph, entitled “Progressive dose-response curve”)

“Standard dose-response curve with low slope and near linear relationship over most of the range.

Fig 10 (single line graph, entitled “Rapid escalation dose-response curve”)

“A dose-response curve with a rapid rise, giving appearance of an “all or none” response.

Fig 11 (two line graph, entitled “Rapid escalation dose-response curve”)

“Comparing the curves, the rapid escalation curves give almost zero response at the first vertical line, and virtually a full response by the third.

Fig 12 (entitled “Many different dose-response curves”)

“Dose-response curves may be complex, organ specific, and interdependent, making the concept of a predictable response to a dose of a particular chemical or other environmental toxin inherently unpredictable