- **Free radicals are particles which attack the body's cells, damaging or killing them**
- **Your own metabolism, smoking, sunbathing and strenuous exercise all produce free radicals**
- **Free radical damage is a major cause of ageing. It contributes to the gradual deterioration of organs and to illness such as cancer, arthritis, cataracts and heart disease**
- **The better your defences against free radicals, the longer you tend to live**
- **Anti-oxidants reduce free radical damage**
- **New anti-oxidant drugs are being used to treat stroke, ulcerative colitis, pancreatitis and other diseases**

Chapter 4

Under attack – the battle against free radicals

Ten years ago, hardly anyone outside specialised research areas knew very much about free radicals. Now you'll find them all over the popular press, from health magazines to the covers of *Time* and *Newsweek*.

From all the publicity, you'd think they were the cause of all illness, ageing and disease. That's taking things too far, but it's true that free radicals are involved in many of the diseases which ultimately kill most of us. It's also becoming clear that they are deeply involved in the ageing process.

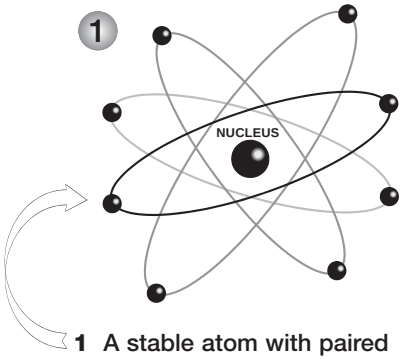
As a result, many scientists now believe that anti-oxidants will make as big an impact on public and individual health as did antibiotics half a century ago.

Chain reactions of destruction

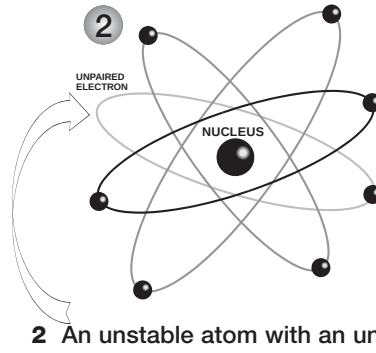
Our bodies are built up from many hundreds of thousands of different types of molecules. These molecules are built, in turn, out of rather less than a hundred different kinds of atom.

All atoms consist of a nucleus at the centre surrounded by a shell of electrons spinning round the nucleus, like planets round a sun. Generally the electrons in the outer shell are paired, which is

a stable arrangement; but certain processes such as radiation or oxidation may knock an electron out of the shell, leaving an unpaired electron. Atoms with unpaired electrons, and the molecules of which they form a part, are free radicals. Stable radicals are safe; but unstable free radicals behave very aggressively towards biological tissues, ransacking them for replacement electrons.



1 A stable atom with paired electrons round it.



2 An unstable atom with an unpaired electron (arrowed). This becomes a free radical and will try to 'grab' an electron from another atom – setting off a damaging 'chain reaction'. Anti-oxidants work by neutralising these free radicals, thus stopping the chain reaction.

Burning wood in a fire produces useful heat, but also potentially dangerous sparks and smoke. Burning petrol in an engine produces useful energy also, but dangerous exhaust fumes are given off. When you 'burn' glucose in your body cells, free radicals are the potentially dangerous by-products of the energy producing process.

Cells are attacked by unstable free radicals many thousands of times every day. Unstable radicals will grab an electron from wherever they can; thus creating more free radicals. Chain reactions occur where thousands of free radicals can be generated in seconds, unless the body's defences catch them in time.

If a chain reaction takes off it can kill the cell. At lower levels, it may damage the cell membrane, making the cell less able to

Free Radical poisoning

In the face of sustained attack by free radicals, unprotected biological tissues turn rancid and die.

Free radicals can be thought of as a subtle poison which is constantly weakening us, and contributing to our eventual demise in a slow death of a thousand million cuts.

handle nutrients, less reponsive and less efficient. If free radicals attack the cell's genetic material (DNA) this can, if not repaired in time, lead to cancer. If free radicals attack the mitochondria (the cell's power generators), they can impair the cell's energy balance to such an extent that the cell eventually commits 'suicide'.

If that cell is in the kidney, kidney function will gradually be impaired. If the affected cell is in the skin, it will mean a slower turnover of skin cells, less collagen deposition, and a gradual loss of skin tone and texture.

This all sounds pretty grim – but just because we've only recently found this out doesn't mean free radicals are something new. They are as old as life itself, and all living species have evolved defences against these destructive agents. In fact, the rule of thumb in nature is that the better your defences against free radicals, the longer you live: humans and elephants, for instance, have much better anti-radical defences than shorter-lived species such as mice.

Free radical damage:

- **Exacerbates inflammation in the joints (rheumatoid and osteo arthritis)**
- **Oxidises the cholesterol in our blood (leading to heart disease)**
- **Damages our eyes (leading to cataracts and blindness)**
- **Degrades the DNA in our body cells, which can either kill them or turn them cancerous**
- **Is deeply involved in most major non-infectious diseases and inflammation**
- **Plays a major role in gingivitis, asthma, Alzheimer's, pancreatitis and ulcerative colitis**

An unprotected cell being attacked by free radicals.

A cell protected with an anti-oxidant shield.

There are some rare human genetic conditions where the anti-radical defences are damaged, and in these cases, accelerated ageing, early illness and death is the outcome. Certain nutritional deficiencies, where one or more of the micro-nutrients used in the body's anti-radical defence shield are missing from the diet, have similar results; the victims are far more prone to age-related diseases, such as heart disease, cancer and blindness.

Smoking – a free radical production line

Smoking loads the body with trillions of free radicals.

Each puff of cigarette smoke produces 10^{14} free radicals – that's 100,000,000,000,000 – which is why half of all smokers die before their time.

It's been calculated that each cigarette reduces the life expectancy of a smoker by 10 minutes, because of the damage caused by all those free radicals.

The link between smoking and premature death was first discovered by statisticians, but it is the free radical theory which explains why cigarettes are linked with heart disease and cancer.

The increased free radical load uses up the body's anti-oxidants, such as Vitamin C. Smokers (even passive smokers) typically have subnormal Vitamin C levels in their blood[1] – many of them could be said to be suffering from borderline scurvy. Low levels of anti-oxidants cause damage to the lining of the arteries.

At the same time, the free radicals cause lipids (fats) in the blood to oxidise and turn rancid. These rancid lipids attack the damaged artery walls and start building atheromatous plaque (furring of the arteries). This helps to explain why smokers are so prone to heart attacks.

Free radicals also damage the DNA in a smoker's body cells, leading to mutations which may eventually give rise to cancer.

So what about the few smokers who defy the odds and live out a reasonably normal life span? It is almost certainly because they have better anti-oxidant defences.

There may be a genetic factor: some individuals may be better at making anti-oxidant enzymes. Long-life smokers may eat a better diet, containing higher levels of anti-oxidant nutrients.

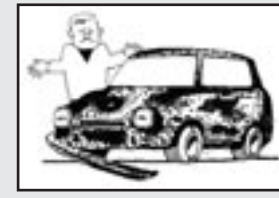
This suggests that if you cannot (yet) give up smoking, you should at least try to minimise the damage by supplementing with a well-designed mix of the key anti-oxidants.

A threshold of 100mg of Vitamin C reduces the amount of DNA damage[11] and should reduce the risk of cancer. Vitamin E, Co-enzyme Q10, anti-oxidant minerals and the flavonoids are equally important.

EVERYDAY FREE RADICAL DAMAGE

Take the milk out of your fridge in the morning, put it somewhere warm, and by the evening it's sour. Cut an apple in half, and watch it turn brown. Leave butter exposed to air (oxygen) and the fat turns rancid. Leave a scratch on your car untreated, and you'll soon see the exposed metal corroding.

These are all very similar chemical processes. In each case free radicals do the damage – it's called 'oxidative stress' and it's basically rusting.

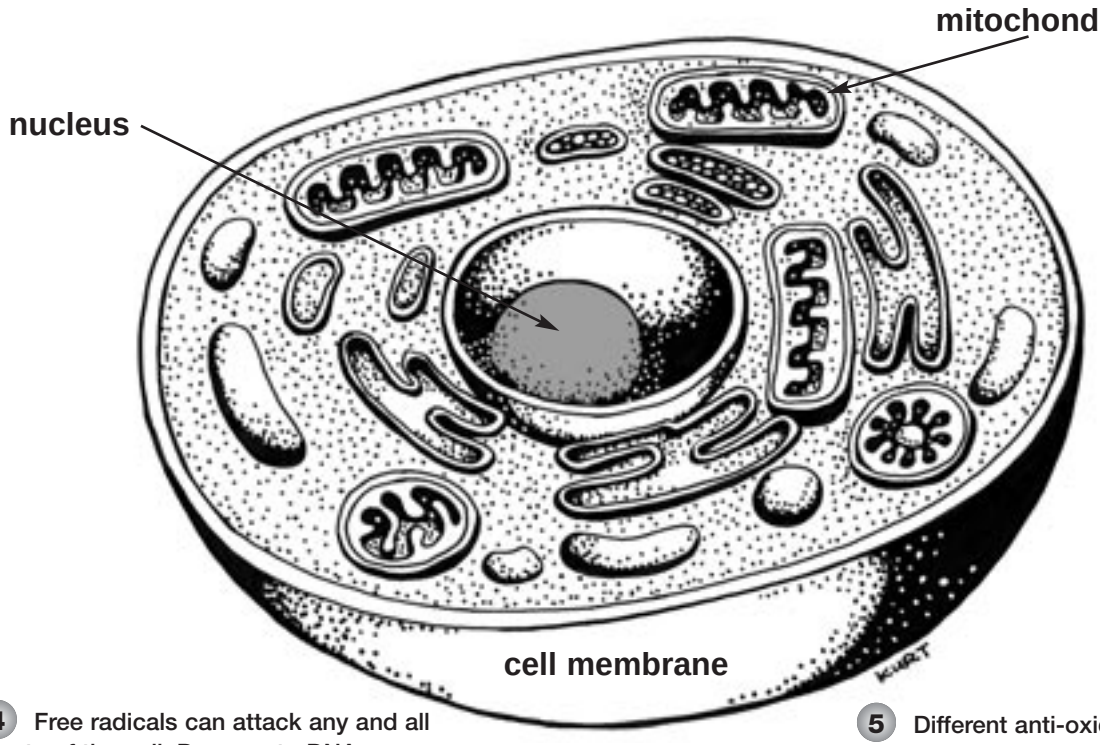


How anti-oxidants protect your cells

1 This is a cross section of the inside of a body cell magnified approx. 10,000 times.

2 Inside the cell is the nucleus which contains most of the cell's DNA. DNA itself contains the genetic codes that make you a unique human being – determining your hair colour, size, shape, features etc.

3 Also inside the cell are mitochondria. They are the energy factories of the body – where the energy in food is converted into energy for you to use.



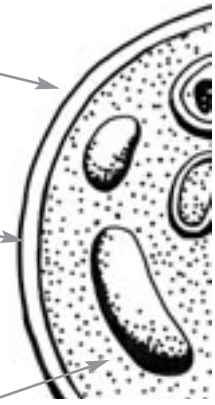
4 Free radicals can attack any and all parts of the cell. Damage to DNA can lead to cancer. Damage to mitochondria can lead to premature ageing.

5 Different anti-oxidants protect different parts of the cell. They are like specialist defence troops.

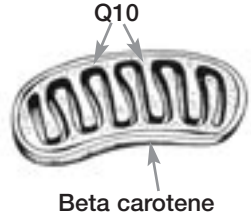
6 Vitamin C is water-soluble, and protects against free radicals in the blood and the watery fluids that bathe our cells.

7 Vitamin E and other fat-soluble anti-oxidants such as the carotenoids and Co-enzyme Q10, protect fatty structures such as cholesterol particles in the blood and cell membranes.

Glutathione is an important anti-oxidant inside the cell.

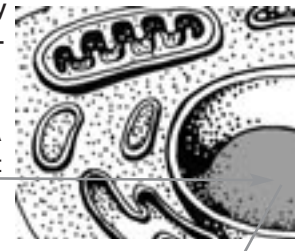


8 Large amounts of free radicals are produced in the mitochondria. Q10 acts inside the mitochondria, and beta carotene protects the mitochondrial walls.



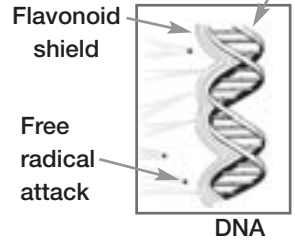
9 Anti-oxidant enzymes neutralise free radicals in almost all areas. They depend on trace elements (see right-hand column).

10 When free radicals damage DNA in the cell nucleus that cell may start to grow out of control, and become a cancer.



11 Some flavonoids may bind to DNA, and could provide a local anti-oxidant line of defence.

Other flavonoids can protect other parts of the cell.



THE SECRET IS A COMBINATION OF ANTI-OXIDANTS

These diagrams show why it's so important to use a supplement that contains a broad range of anti-oxidants in the right amounts and in the right form.

No single anti-oxidant can provide comprehensive protection, as different vitamins and minerals provide different defences in different places.

For example, anti-oxidants that locate in the mitochondria help protect against mitochondrial ageing. And anti-oxidants that protect lipids (fats) slow the process that leads to strokes and heart attacks.

In addition, certain anti-oxidants only function properly in combination with other anti-oxidants. Vitamin E and carotenoids protect fats in your body from oxidation – but only if sufficient Vitamin C is present.

The body can't make vitamins or minerals, but it does make its own anti-oxidant enzymes. Production of these enzymes depends upon there being enough trace elements like selenium, copper, zinc, manganese and iron present in your diet.

What's the damage?

Your body's cells are involved in a running battle of oxidative damage and repair. When the rate of free radical formation is increased, or when the anti-oxidant defences are impaired because of a poor diet, the result is uncontrolled free radical damage – 'oxidative stress'.

If the degree of oxidative stress is relatively mild, it can stimulate the cell into boosting its own anti-oxidant defences. This happens after moderate exercise. Severe oxidative stress, however, kills the cell fast. Oxidative stress somewhere in the middle can damage the cell enough to make it self-destruct – a slightly slower process.

Oxidative stress damages a cell in a number of ways:

- If a free radical attacks a DNA base, the cell's DNA repair enzymes try to cut out the damaged part and replace it with a new one. The damaged, oxidised DNA base is excreted in the urine, so the rate of DNA damage can be estimated by measuring oxidised DNA base levels in the urine. Non-smokers experience roughly 1,000 DNA base 'hits' a day; smokers between three and ten times as many
- When a protein is oxidised it becomes less efficient, or completely dysfunctional. The body is constantly breaking down and replacing its proteins, so damaged proteins are eventually replaced by newly made protein molecules. The oxidised proteins form compounds which can also be measured in blood or urine.
- When the fatty acids (lipids) in a cell are oxidised by free radicals, they form toxic Lipid Oxidation Products (LOPs), and lipofucsin. Lipofucsin accumulates in the tissues at such a constant rate that it has been suggested that lipofucsin levels are an accurate measure of biological ageing[12,13,70].

Thymol

The anti-oxidant drug Centrophenoxine concentrates in lipids, slows lipid oxidation, and allows the body to clear away deposits of the lipid oxidation end-product lipofucsin (otherwise known as the 'ageing pigment') [12, 13].

Age spots in elderly skin disappear and the mental function of elderly rats and humans improves[14, 15].

The highly potent lipid-soluble anti-oxidants such as thymol, extracted from the herb thyme, are reported to have similar effects[16, 17].

The effects of the build-up of lipofucsin depend on which tissues are affected. In skin, lipofucsin forms so-called liver spots, which are merely unsightly. Inside nerve cells, however, the accumulation of lipofucsin contributes to a steady decline in nerve function, and eventually to cell death. In fact, lipofucsin accumulation is one of the factors which contributes to the steady loss of brain cells which occur as we age.

In certain conditions the rate of lipofucsin build-up is accelerated. Severe deficiency of the anti-oxidant Vitamin E, for example, leads to a rapid build-up of lipofucsin and symptoms of nerve damage such as unsteadiness and slurred speech[18-20]. Vitamin E therapy improves these symptoms, suggesting that lipofucsin can be removed by the body's normal clearance mechanisms[18].

LOPs (lipid oxidation products), the other main products of lipid oxidation, are also bad for your health. LOPs in the bloodstream are a potent cause of coronary artery disease[21] (See Chapter 14, Heart disease). In other tissues LOPs are thought to trigger inflammation, contributing to conditions such as asthma and arthritis.

Anti-oxidants such as Vitamin E which can get into the lipids in the cells, protect them from oxidation and reduce the rate of LOPs formation.

Of all the different lipids in the body, poly-unsaturated fatty acids (known as PUFAs) are the most vulnerable to oxidation, and can only be replaced from the diet.

In nature, foods rich in PUFAs like nuts and grains always contain high levels of fat-soluble anti-oxidants. With modern processed foods, however, these anti-oxidants are often stripped away.

If we eat too many foods containing refined PUFAs (ie vegetable oils and the poly-unsaturate-rich margarines), without protecting ourselves with anti-oxidant supplements, we put ourselves at risk of producing more lipofucsin and more LOPs[22] (see Chapter 8, Essential fatty acids).

Balance your fish oil supplement

Because PUFAs are so prone to oxidation, PUFA supplements such as fish oil or evening primrose oil should always be combined with lipid-soluble (ie fat-soluble) anti-oxidants.

These include Vitamins A and E, Co-enzyme Q10, Vitamin K, beta carotene, lutein and lycopene.

These, in turn, must be supported by Vitamin C; and further by selenium and anti-oxidant herbs such as thyme, rosemary and others.

Mice and men

Anti-oxidant supplements are good for elderly humans too. Research groups have showed that long-term anti-oxidant supplements given to old folk improve their mental and physical well-being[72, 73] and reduce the risk of Alzheimer's by up to 66%[77].

Not all bad

We can't avoid free radicals altogether, nor would we want to. Some free radicals are good for our health.

Significant numbers of radicals are generated by immune cells as an essential part of the body's defences against invading micro-organisms.

It is when free radicals are produced *in excess* that they spill over from these physiological functions, and cause tissue damage, illness and accelerated ageing.

REJUVENATED RODENTS

Bruce Ames, the distinguished biochemist at the University of California, has shown that the DNA in each cell of a rat is hit by about 100,000 free radicals a day.

Damaged DNA can either kill a cell, or turn it cancerous, which is why all life forms have DNA repair kits. The rat's DNA repair enzymes work constantly to remove the damage, but they can't keep up.

A young rat has about one million sites of damaged DNA in each cell; old rats have about two million. The DNA repair processes slow down with age because they too accumulate oxidative damage. As a result, older rats have a high cancer rate.

The cancer rate is much lower in humans because, as Richard Cutler at the USA National Institute of Ageing has shown, we have better anti-radical defences – one reason we live so much longer than rats.

In 1993 John Carney at the University of Kentucky Medical Center found that, as expected, levels of oxidised proteins in the brain and other tissues of gerbils increased with age. He gave his elderly, oxidised gerbils an anti-oxidant called phenlybutylnitrone (PBN). This had two important effects – it reduced the oxidative damage in the brain to youthful levels, and it improved the gerbils' short-term memory (see Chapter 17, A Healthy Brain).

Elderly gerbils lose their memory just like many elderly folk do. On PBN their ability to navigate through a maze shot up until they were doing as well as gerbils half their age – indicating considerable restoration of brain cell function.

Free radicals and ageing

The theory that ageing is caused by free radical damage is backed up by a great deal of evidence. For example, Drs Sohal and Rose at the University of California recently succeeded in breeding a mutant super-fly, known as the Methuselah fly, which lives twice as long as its normal brothers and sisters.

When they examined the super-fly, it was different from normal flies in one respect: it was producing extra SOD (super-oxide dismutase) and catalase[3-7] – two key anti-oxidant enzymes whose function is to mop up free radicals.

At more or less the same time, Thomas Johnson at the University of Colorado discovered a super-worm, with a life span 70 per cent longer than normal. This long-lived mutant, like the

super-fly, was producing larger than normal amounts of the same two anti-oxidant enzymes: SOD and catalase. So here was a common link – two mutants, two very different species, both with a significantly extended life span and both with better than normal free radical defences.

Higher up the evolutionary tree, one experimenter claimed that mice fed on the anti-oxidant Co-enzyme Q10 increased their life span by up to 50 per cent (see Chapter 9, Q10 and L-carnitine). The various anti-oxidants work in tandem, and the addition of other anti-oxidants to the mice's diet might have extended their life span still further.

From mice to men is a relatively small step, evolutionarily speaking. Mice are mammals and their metabolism is in many ways similar to our own. It's not identical, but there are more similarities than differences. It follows that much of what is known about free radical damage and ageing in rodents, the most commonly used lab animals, probably has a direct bearing on the human condition.

Check your supplement

The anti-oxidant protection offered by foods is now measured in ORACs (Oxygen Radical Absorbance Capacity).

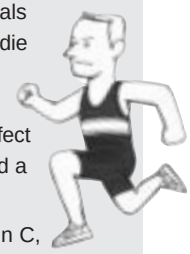
A diet of five servings of fruit and vegetables a day typically provides 1500 ORACs a day: the evidence suggests we need 3-5000 to stay really healthy[69].

But don't rely on the A-Z type supplements to boost your anti-oxidant status much. A typical 'one-a-day' A-Z supplement provides under 100 ORAC units a day. My recommendation for a supplement provides you with a much higher ORAC score – and hence protection (see Chapter 22, Selecting the right supplements).

EXTREME EXERCISE: DON'T OVERDOSE

When you exercise, you breathe faster, use more oxygen and produce more free radicals. Moderate exercise stimulates the production of the body's anti-oxidant enzymes, which slow the ageing process. This explains why moderate exercisers live longer than 'couch potatoes'[23].

Top athletes, however, have shorter lives. They are more frequently ill[24, 25], as their immune systems are depressed [66, 74, 75] both by excess free radicals, and exercise-related falls in the amino acid glutamine – the immune cells' 'fuel'[76]. Their very high level of exercise creates more free radicals than their defences can cope with so, like smokers, they tend to die prematurely with heart disease, cancer, etc. This is why many athletes today supplement with high dose anti-oxidants (called 'tanking'). This is not just an insurance policy: a welcome side effect is reduced muscle damage, pain and stiffness after an event, and a faster recovery time [24-38, 40].



Excessive exercise depresses the immune system.

N.B. Excessive Vitamin E or carotenoids, if taken without Vitamin C, may be counterproductive[39].

The powerhouses run down

A significant part of the ageing process is due to damage caused by free radicals to nuclear DNA and to the lipids in cell membranes. However, some experts believe that the key to free radical ageing occurs elsewhere – in the mitochondria, the power generators which are found in each cell of the body.

DNA in the cell nucleus is protected by DNA repair enzymes and anti-oxidant substances such as the histones. DNA inside the mitochondria, however, is unprotected. This is where the cell's oxidative fires burn most fiercely, and where DNA is most vulnerable. The only safety factor is that each mitochondrion has multiple copies of DNA, so that when one strand of DNA is burned out, another takes over. But there are only a limited number of copies, so eventually the mitochondrion starts to break down.

This is why mitochondria become less efficient with age. This was proven by Gino Cortopassi and Norman Anaheim at the University of Southern California, and Douglas Wallace at the Emory University School of Medicine, who showed that the loss of efficiency in ageing mitochondria is directly related to the steadily increasing number of DNA defects. As the mitochondria run down they produce less energy for the cells, which leads directly to cell and organ decline, systems failure, illness and death.

Co-enzyme Q10 is an anti-oxidant which enters the mitochondria, where it mops up free radicals and slows the rate of oxidative damage. But it has another, equally important role. It is a link in the process whereby energy from the food we eat is transferred to ATP, the energy molecule. By adding Q10, a faltering mitochondrion can produce more energy, thereby giving elderly cells a strong anti-ageing boost. (See Chapter 9, Q10 and L-carnitine).

That mice fed on Q10 lived half as long again as other mice, suggests that something very profound is going on. Q10 is one of the first nutritional interventions that seems capable of slowing down the hands of the biological clock to such an extent. It is unlikely to be the last.

The superoxide radical

The free radical most commonly formed in the body is the superoxide radical, H_2O_2.

It's not particularly destructive but, in the presence of free iron or copper, it produces hydroxyl radicals, which are much more active and dangerous.

Anti-oxidant defences

Anti-oxidant defences can be increased by taking anti-oxidant vitamins; together with the vital mineral co-factors – zinc, copper, selenium and manganese.

Because micro-nutrient depletion is so prevalent [2, 41-68] anti-oxidant supplements improve the body's defences in most cases.

Rancid people!

Some nutritionists and geriatricians have remarked that old people smell differently from younger folk.

This is nothing to do with hygiene. They are talking about a sour smell, which the smell of rancid oil. This is especially common in elderly folk who, either for preference or because they have dental problems, eat a diet low in fruit and vegetables. This means they aren't getting enough anti-oxidants, leaving themselves vulnerable to free radical attack[71].

The smell of rancid oil is simply a symptom of an unhealthy rate of oxidation taking place in the body, which will, sooner or later, culminate in serious illness.

It is fairly widely accepted that these people are at increased risk of many from the major diseases, and some companies have developed diagnostic tests which give a rapid 'rancidity' reading, and tell exactly who needs anti-oxidant help.

These test systems should be widely available in the next few years. In the meantime, a well-designed anti-oxidant supplement should be an essential part of anyone's health and longevity programme. Similar supplements have been shown to reduce 'rancidity' in the elderly[8, 9,].

Sexually adventurous researchers have reported that partners who eat a Mediterranean diet taste sweeter than those who live on junk food – indicating that an anti-oxidant-rich diet reduces rancidity on younger subjects also.

Why older people need supplements

When you reach 50, many micro-nutrients are less well absorbed – especially Vitamins D and B. Also many older people are on prescription drugs which can significantly affect vitamin and mineral levels. Appetite and food intake often fall – reducing micro-nutrient intake further.

Fighting off free radicals

Our defences are reasonably good at keeping free radicals at bay. The body can adapt to a moderately increased free radical load by making more anti-oxidant enzymes[3,4,8]. But when the free radical load gets too heavy, as in smokers or those who live in intensely polluted areas, it overrides the body's defences and leads to illness and premature death, **unless the defences are built up with supplements.**

The next section shows you just what that means.

Iron alert

Be careful with iron supplements!

High iron intake is linked to an increased risk of colo-rectal cancer – and iron supplements increase free radicals in the colon[10, 67].

Make sure your supplement does not contain iron unless you really need it.

BREATH OF LIFE – AND DEATH

A fire can't thrive without oxygen and neither can we. We need oxygen in order to be able to 'burn' the food we eat, releasing its energy and converting it to ATP, the 'energy molecule' which fuels the activities of cells, such as growth, movement and repair.

Around 95 per cent of the oxygen we breathe forms ATP. The remaining five per cent forms free radicals.

By measuring how much oxygen we take in we can calculate that about two kilograms of free radicals are formed in the body every year.

Oxygen, the colourless, odourless gas essential for life, is eventually responsible, via the formation of free radicals, for many of the ills which plague and eventually kill us.

SUMMARY

Free radicals

- Free radicals are atoms or molecules with unpaired electrons that attack other atoms in your body. They can be highly damaging to DNA, which can lead to cancer.
- They damage mitochondria (the power plants in each cell), which can cause premature ageing.
- They oxidise lipids in cell membranes, leading to cellular dysfunction and death.
- They oxidise the cholesterol in the blood which can cause furring up of the arteries and heart disease.
- Anti-oxidants protect against the oxidative damage that free radicals cause.
- Evidence from animal experiments shows that better anti-oxidant defences are associated with a longer life span.
- A comprehensive anti-oxidant strategy needs to involve a combination of anti-oxidant nutrients as each nutrient has its own specialist function, and may protect a different part of the body and its cells.
- We can now measure the anti-oxidant power of foods and supplements. Many A-Z type supplements that contain nutrients at just their RDA levels provide a disappointingly low level of anti-oxidant protection.