

The body is constantly renewing itself. To do this it needs amino sugars – the basic building blocks of soft tissues

Infection and certain inflammatory diseases break down tissue faster than the body can regenerate it

The rate of regeneration slows with ageing

Taking amino sugar supplements helps the body speed its natural healing

Amino sugars could provide kinder treatments for arthritis and irritable bowel disease, and help protect the skin from the impact of ageing

Chapter 10

Amino Sugars – the regeneration game

Amoebas and flatworms can regenerate almost their entire bodies. Octopi and salamanders can re-grow missing limbs. Many lizards can, if needed, shed their tail and grow another later on.

How do humans rate on the regenerative scale? We can't re-grow missing limbs, but our powers of self-healing are still quite impressive.

Even if 90 per cent of the liver is lost or damaged, the remaining 10 per cent will grow and expand until it replaces the original. If a kidney is lost, the other kidney grows to compensate. Blood vessels, bones, ligaments, even nerves can all mend. After surgery or injury, cut or torn muscle, gut and skin will, if all goes well, repair themselves.

The capacity for self-repair is strongest in the young. If a foetus in the womb is operated on, it heals quickly and without scarring. But after that, it's downhill all the way.

As youth gives way to middle and then old age, our ability to heal and mend slows down from a sprint to a walk, and finally a crawl. Most people assume that this slow-down is an unavoidable part of the ageing process, but they're largely wrong.

Just as with the immune system (where the run-down that comes with age can be reversed with well-designed supplements), recent work shows that healing rates can be accelerated, often dramatically, by improved nutrition.

Healing benefits

In the last few years, spurred on by the need to cut medical costs, hospital groups have found that post-operative healing is improved, complications reduced, and recuperation speeded by general nutritional programmes^(1, 70-72).

But this is just the beginning, because these nutritional programmes are far from optimal. They are merely multi-vitamin and mineral preparations, similar to the commercial products stocked in health food stores. Supplements designed specifically to support the healing process would give better results.

In medicine, improved tissue healing means shortened recovery times after surgery, and a new approach to chronic health problems such as Irritable Bowel Disease, arthritis and psoriasis.

In the world of sports and athletics, faster healing after injury promises to save or extend careers, and minimise expensive down-time. And in the world of nutritional cosmetics, improved tissue protection and regeneration holds the promise of extended youthfulness (see Chapter 6, Flavonoids & isoflavones).

A nutritional approach to cutting healthcare costs

Faster healing cuts medical costs, aids chronic diseases, helps sports professionals recover from injury, and keeps skin looking younger, longer.

Cut and paste

The exciting new science of tissue regeneration emerged in the late '60s, when experimenters looked for ways to speed wound healing.

Working initially with rats, but then with humans, scientists achieved positive results with a paste made of ground cartilage and later shrimp shell. When this was applied to open surgical wounds, tissue regeneration was significantly improved; healing was faster and the scar was stronger⁽²⁾.

Cartilage and shrimp shell both contain large molecules called GAGs, which consist of long chains of a smaller molecule, the amino sugar glucosamine.

Shrimp shell turned out to be even better at tissue regeneration than cartilage – and so did pure glucosamine obtained from fungi⁽³⁾. At this point the scientists realised that the tissue regenerator was glucosamine itself, and the rest of the puzzle fell into place.

GAGs and PGs

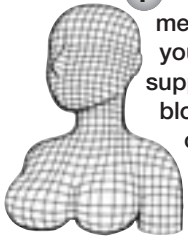
GAG =
Glycosaminoglycan

PG = Proteoglycan

These macro-molecules have important structural properties and form part of the extra cellular matrix.

WHAT AMINO SUGARS DO

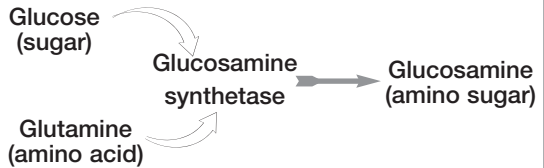
1 The extra-cellular matrix is a mesh of micro-fibres that gives your skin firmness and supports muscles, ligaments, blood vessels and inner organs. Although it is constantly being broken down, it is also constantly being repaired.



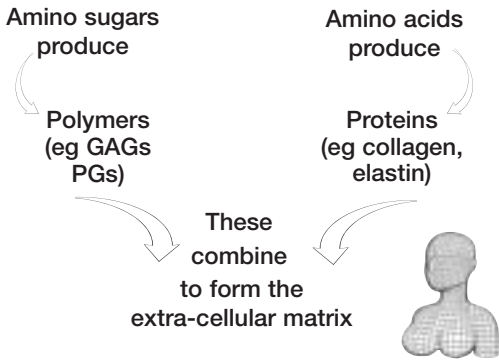
A problem arises if the rate of breakdown exceeds the rate of repair. Then skin (and other connective tissues such as cartilage) lose their structure. This shows up as ageing skin, or thinning cartilage – as in osteoarthritis.

2 To prevent this deterioration you must increase the rate at which the matrix is repaired. And that largely depends on the rate at which your body can produce the amino sugar glucosamine.

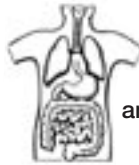
Glucosamine is formed when glucose (blood sugar) and the amino acid glutamine are combined by the enzyme glucosamine synthetase.



3 Glucosamine molecules link up to form polymers such as GAGs and PGs. These together with two protein micro-fibres, collagen and elastin, make up the extra-cellular matrix.



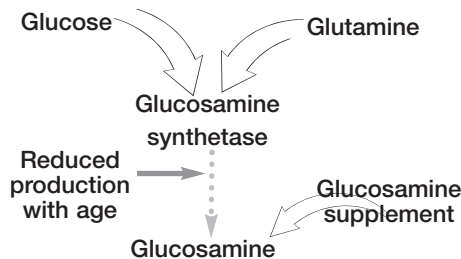
4 The production of amino sugars is important because they also form part of the glycocalyx, a thin layer of tissue which lines and protects the digestive, respiratory and genito-urinary tracts.



Amino sugars also produce GAGs which make up the lubricating fluids that cushion our joints, fill the eyeball and plump the skin.



5 The problem is that, with age, the enzyme glucosamine synthetase becomes less effective, which slows the rate of matrix repair. This is why healing is slower in the elderly.



The solution is to bypass the bottleneck with glucosamine supplements, and thus accelerate matrix repair and tissue healing in skin, cartilage and other connective tissues.

The body's building blocks

Amino sugars are among the most important building blocks in the body.

Dr Frances Burton, an expert in amino sugars at the University of British Columbia, expresses it beautifully: "Amino sugars make up the structure of all tissues, on the surface of cells and in the spaces in between them; forming the substance which binds cells together, the membranes which envelop them and the protective layers which cover them."

Macro-molecules built up from amino sugars, called GAGs and PGs, together with the proteins called collagen and elastin, make up the framework for all our tissues. Combined in different proportions, they make tissues soft, slippery, squashy, stretchy or strong. They give our bodies shape, organisation, definition and function⁽⁴⁻⁷⁾.

GAGs and collagen make up tendons, ligaments, heart valves, skin and finger-nails. Combined with another protein, elastin, they make cartilage in joints and the discs in the spine.

All of these macro-molecules are constantly being broken down and replaced as part of the body's on-going general maintenance programme.

How fast this happens is crucial in maintaining the strength and elasticity of every tissue in the body. However, there is one major problem.

The foundation stone

All the GAG and PG macro-molecules are built up from a single amino sugar – the glucosamine which is the basis of shrimp shell and cartilage. The rate at which glucosamine itself is made is controlled by a single enzyme. So right here is a potential bottleneck and limit to growth, and to tissue regeneration and repair⁽⁸⁾. If you don't produce enough glucosamine your extra-cellular matrix will start to break down.

The older we get, the slower the rate of tissue repair. One of the reasons for this is because, with age, levels of the vital enzyme that controls glucosamine production fall. Older people

A New You

The entire human skeleton is renewed every 10 years or so. This means we all need good tissue regeneration rates to keep us healthy.

Glucosamine speeds regeneration. As long as your rate of repair keeps up with the rate of tissue loss, your bones and tissues stay healthy.

Glucosamine

Glucosamine is made by combining one molecule of glucose (blood sugar), with one of glutamine (an amino acid).

This reaction is catalysed by the enzyme glucosamine synthetase⁽⁸⁾.

THE DEFENCE BOOSTERS : Amino sugars

De-stressing

Nutrition is important, but it's not everything. Psychological stress is another factor that slows down wound healing⁽⁶³⁾.

A de-stressing technique should be considered by anyone wishing to accelerate the healing process.



LOOK FOR

...

a glucosamine supplement of 500mg a day for prevention;

1-2g a day

for treatment.

Combine with

100mcg Vitamin K

10mg manganese

500mg betaine and

500mg curcumin

(the active ingredient in turmeric)

for best results.

Vitamin K is essential for the synthesis of matrix GLA protein and is vital for cartilage and bone production⁽¹¹⁾.

Glucosamine hydrochloride is cheaper and better than glucosamine sulphate, being less likely to cause

simply can't produce amino sugars quickly enough – unless they get round the bottleneck by taking glucosamine supplements.

There is plenty of anecdotal evidence that glucosamine given to older patients can make a huge difference. It reportedly brings their rate of tissue repair and healing back up to the levels of youthful middle age, or better. Glucosamine supplements have been shown in some studies to increase the rate of tissue healing by a staggering 170 per cent^(9, 10).

You might think that if you're not actively growing, or recovering from injury or surgery, the rate of tissue repair doesn't matter. But all the tissues of the body are constantly being repaired and recycled. Some work on a rapid cycle, like skin and blood. Some, like cartilage and bone, regenerate slowly. In fact, the entire body is renewed every ten years or so.

Amino sugar compounds are constantly being broken down, rebuilt and recycled as cells grow, divide, multiply and die, and the rate of re-building is limited by the speed with which the body can manufacture glucosamine. Rapidly renewing tissues like skin or the lining of the gut need supplies of amino sugars constantly. Other tissues need extra amino sugar whenever there is extensive damage and regrowth.

This implies that glucosamine supplements should not only help wound healing after injury or surgery, but also in the treatment of inflammation. Inflammation is a basic element in many diseases where the rate of tissue damage exceeds the rate of tissue regeneration, as in arthritis.

In these cases, a glucosamine supplement can boost the repair process, tipping the balance away from tissue destruction towards reconstruction and health – especially when combined with anti-inflammatory agents such as the flavonoids and Omega 3 oils.

Arthritis

Cartilage, tendon and bone are all living tissues. They grow and regenerate relatively slowly – very slowly in the elderly. But as long as the rate of tissue repair keeps up with the rate of tissue loss, the bones and joints will stay healthy.

In arthritis, however, the rate of tissue breakdown outstrips the rate of repair. As a result there is a progressive loss of cartilage, leading to pain and disability.

The standard medical response is to give pain-killers, and anti-inflammatory drugs. But the problem is that these drugs can **increase** the rate of cartilage loss, and although they may relieve the pain in the short term, in the long run they may make matters worse^(44-46, 73-75).

There is evidence that it may be more effective, kinder, and more rational to increase the rate of tissue repair in the affected tissue^(20-22, 50, 51, 59-61).

This is where glucosamine comes in. By giving glucosamine, the cells that build ligaments and joints get the material they need to carry out repairs and maintenance. In this way the body's capacity to heal itself is boosted.

Based on our current understanding of arthritis, a nutritional programme which combines glucosamine with natural anti-inflammatory flavonoids (see Chapter 6, Flavonoids & isoflavones) should greatly reduce the symptoms and the risk of the disease.

This is likely to produce the best results in the elderly, who are more depleted in glucosamine and anti-oxidants, such as flavonoids. It's a combination which has not yet been properly tested, but it seems logical that such a nutritional programme could halt, or even reverse the progress of arthritis.

Combating arthritis

Combine glucosamine with a natural anti-inflammatory such as ginger or turmeric.

This reduces the rate of tissue breakdown **and** increases the rate of fibre repair – a dual approach to cartilage regeneration.

Glucosamine should generally be combined with manganese. This trace element is an essential co-factor when glucosamine is built into joints and other tissues⁽⁶⁸⁾, and many people are depleted in manganese⁽⁶⁹⁾.

Chondroitin is a cheaper alternative to glucosamine, but is less effective.

THE POWER OF AMINO SUGARS

In one double-blind study, subjects with arthritis of the knee were treated either with the amino sugar glucosamine, or a standard anti-inflammatory painkiller. The glucosamine group did significantly better⁽²⁰⁾.

In a second trial of subjects with chronic arthritis, 14 days of treatment with glucosamine sulphate resulted in a 71 per cent improvement in pain, swelling, tenderness and function⁽²¹⁾. Six more trials which were fundamentally similar in design obtained almost identical results^(22, 50, 51, 59, 60, 61). More recently, glucosamine treatment has been shown to lead to a normalisation of joint function in animal models of arthritis⁽⁶²⁾, and in patients⁽⁷⁸⁾.

Bones too

Glucosamine is also essential for the growth of new bone – especially critical in the elderly.

How arthritis develops?

One way of getting osteoarthritis is via repetitive stress injury. Stress on a joint causes compression of that joint. Compression higher than the blood pressure stops blood flow in the capillary beds. This reduces the amount of oxygen reaching the tissues, which triggers free radical formation.

If compression on the joint is severe and frequent, the bursts of free radicals overwhelm local anti-oxidant defences. Oxidative damage follows, with breakdown of hyaluronic acid in the synovial fluid and phospholipids on the articular surfaces.

The resulting loss of lubrication and shock absorption in the joint leads to further tissue damage, more free radicals, inflammation, and an increasing rate of tissue destruction which eventually overtakes the body's regenerative capacity.

This is not the whole story. New research suggests that changes in local bone pre-date and contribute to the loss of cartilage. This underlines the importance of a total health approach, which incorporates bone support (see Chapter 15, Bones).

The other main type of arthritis, rheumatoid arthritis, is an auto-immune disease, where the joint is attacked by the body's own immune system.

This probably happens after infection with certain bacteria, such as the bacteria which cause urinary tract infection. These bugs carry molecules on their surface which resemble molecules in the joints. The body generates an immune response to the bacteria, which has the unfortunate side effect of attacking the similar molecules in the joints.

This produces inflammation in the joint, which leads to the release of free radicals – which once again triggers the breakdown of hyaluronic acid and phospholipids, the loss of lubrication, and further tissue destruction.

Whatever the original cause of the condition, pain and stiffness eventually indicate that the joint has been attacked by arthritis.

But does this mean that it's too late to tip the balance towards repair and renewal? Glucosamine combined with high dose anti-inflammatory flavonoids (such as those in turmeric) and fish oil, can improve joint function dramatically within 1-2 months.

I would also recommend betaine, which encourages GAG and PG synthesis⁽⁵³⁻⁵⁷⁾; manganese⁽⁶⁸⁾, Vitamin K⁽¹¹⁾ and the bone health package described in Chapter 15, Bones.

Other applications

Defective amino sugar metabolism has been reported in rheumatoid arthritis and osteoarthritis⁽¹¹⁾; diabetes⁽¹³⁾; nephrotic syndrome⁽¹⁴⁾; inflammatory bowel syndrome^(15, 16, 17); and cystic fibrosis⁽¹⁸⁾.

Glucosamine may be helpful in all these conditions.

Irritable Bowel Syndrome (IBS)

The cells lining the gut have a very high turnover rate. In chronic inflammatory conditions, the rate is even faster.

In these conditions, the rate of cell growth may outstrip the rate of glucosamine and GAG (glycosaminoglycan) production. In fact, the inflammation itself may inhibit the making of GAGs, and increase the rate at which they are broken down⁽²³⁻²⁷⁾.

Patients with active inflammatory bowel disease (including Crohn's Disease and Ulcerative Colitis) have very low levels of GAGs in their intestinal walls⁽¹⁷⁾. A depletion here would be expected to cause local vascular problems, increasing leakage of

fluid into the surrounding tissues, and contribute to several distinct types of local tissue damage that are, in fact, all found in chronic inflammatory bowel disease^(28- 33).

Low levels of amino sugar compounds bring another set of problems. They would eventually affect the thin but vital glycolipid layer which protects the intestinal wall⁽¹⁶⁾. Since the gut, more than any other organ, is constantly challenged by bacteria, viruses, digestive juices and dietary antigens, losing this vital protection could lead to health problems⁽³⁴⁾, including food allergies, which are thought to occur in conditions where the gut wall is abnormally permeable.

All this suggests that a glucosamine supplement might be very helpful in treating IBS and food allergies, and there is a substantial body of anecdotal data that this is indeed the case. However, this is a new area, and much more work needs to be done; including, of course, properly designed clinical trials.

Coronary Artery Disease and Thrombosis

Amino sugar therapy suggests an entirely new approach to the huge health problem of coronary artery disease. This is because GAGs play a key role in determining the risk of blood clots forming inside the blood vessels.

GAGs in the blood vessel walls carry electrically charged sulphate groups which repel platelets and discourage them from sticking to the vessel walls⁽⁷⁾. GAGs also stimulate two important anti-clotting factors^(5, 6). **So if amino sugar levels in the blood vessel walls fall, the risk of clots would increase^(32, 33), and so would the risk of heart attacks and strokes.**

Does this ever happen? Interestingly, there are two conditions where this may be important.

In Irritable Bowel Syndrome, low GAG levels are thought to be the cause of an abnormally high rate of thrombosis, not just in the gut itself but elsewhere in the circulation too^(35, 36). Old age, when the rate of GAG formation slows, is also when the risk of thrombosis and related complications increase.

Glucosamine and skin complaints

Anecdotal reports suggest that amino sugar supplements may help in the treatment of eczema and psoriasis.

These skin conditions are characterised by an increased skin cell turnover and a possible amino sugar deficiency⁽²³⁻²⁵⁾.

Cystitis remedy

If the thin layer of GAGs which lines the bladder is disturbed, a non-infectious cystitis follows. This has recently been successfully treated in human cases with glucosamine, but vets have known about this for years, and routinely treat cats with sterile cystitis in the same way⁽⁷⁹⁻⁸²⁾.

Reduced risk of thrombosis

Glucosamine supplements may help to maintain the integrity of the blood vessels; and thereby reduce the risk of thrombosis.

UV and ageing

To see clearly the ageing effects of UV, compare the texture of middle-aged facial skin to that of underarm skin, which is rarely exposed to UV and ages considerably less rapidly as a result.

Further benefits

Some nutritionists recommend GAG therapy, using such molecules as chondroitin (extracted from cartilage) for coronary artery disease and even certain cancers⁽³⁹⁻⁴¹⁾. Further work is needed.

Cross-links

Glucose-induced cross-linking in the extra-cellular matrix is an important part of the ageing of skin and other tissues (and is accelerated in diabetes). Other cross-links (ie pyridine) are essential for all connective tissues.

Skin Ageing

In the exposed skin of the face and hands, much of the ageing is caused by free radicals liberated by sunlight.

Free radicals damage collagen and elastin fibres in the skin, and the GAGs and PGs. This damage to the extra-cellular matrix leads to a loss of firmness, plumpness and elasticity, and is a large part of skin ageing.

The amino sugar compounds in the skin are constantly being broken down and replaced. As much as one fifth of the glucose in the blood is destined for connective tissue formation. But if the glucosamine-producing enzymes slow down, as they do with age, they cannot keep pace with the deterioration caused by exposure to ultra-violet light (UV), cigarette smoke, pollution and other sources of free radicals.

The connective tissue that gives the skin strength, elasticity and firmness deteriorates, with all-too-obvious results.

To protect the skin, you need amino sugars such as glucosamine, and Vitamin C and zinc for collagen and elastin synthesis. To maintain the extra-cellular matrix requires an anti-oxidant mix containing the procyanidin flavonoids (eg bilberry or grapeseed), which concentrate in the connective micro-fibres and protect them from free radical damage; plus mixed carotenoids, which have a similar effect⁽³⁶⁾.

You also need an anti-glycosylant. Glycosylation (the attachment of sugar molecules) of collagen and elastin increases with ageing. This disrupts the connective tissue in a process known as cross-linking. This has the unfortunate effect of leaving the skin less elastic, less permeable and more prone to wrinkles.

Half a tablet of aspirin helps prevent glycosylation⁽⁴³⁾, as does a tablespoon of turmeric⁽⁷⁷⁾. Vitamin C has a similar effect⁽⁵⁶⁾, and is another essential part of the anti-ageing programme; especially as it is essential for the synthesis of the skin protein collagen⁽⁵²⁾.

A supplement of silicic acid may also be appropriate. High levels of aluminium damage the fibroblasts and other cells responsible for building and repairing the extra-cellular matrix, in

the skin and elsewhere. Silicic acid is the most effective shield against ingested aluminium, and can enhance the regeneration of the extra-cellular matrix^(12, 65-67).

For more information on skin ageing turn to Chapter 18, Skin.

Which silicon?

Silica (eg in horsetail extract) is inert, and ineffective. Silicic acid in colloidal form is recommended – and available in some countries as 'Silicol'.

SUMMARY

Amino sugar guide

- There are several different amino sugar supplements – n-acetyl glucosamine (NAG) and glucosamine (sulphate or hydrochloride).

NAG is more rapidly absorbed than glucosamine^(37, 38), but is more expensive and no more effective⁽⁴⁷⁻⁴⁹⁾.
- I prefer glucosamine hydrochloride. The sulphate products contain large amounts of salt (which can raise blood pressure); and the sulphate itself is linked to colon diseases, see page 112.
- Take amino sugars with anti-oxidants. Amino sugars are very susceptible to oxidation, and anti-oxidants protect them.
- Vitamin C protects amino sugars while they are in circulation, but not necessarily once they have been taken up into the areas where they are required.
- Procyanidins, the flavonoids which target the connective and supportive tissues, protect amino sugars against attack by the destructive MMP enzymes (see Chapter 6, Flavonoids & isoflavones).
- Smoking, heavy drinking and diabetes increase the free radical load and the oxidative damage of the amino sugars, reducing their effectiveness.
- The glucosamine dose needed to help alleviate arthritis symptoms may be 1-2g a day. Combine with ginger or turmeric.
- The glucosamine dose needed to help slow the ageing of the skin may be about 1-2g a day; but can probably be reduced when combined with a supplement that contains Vitamin C, flavonoids and mixed carotenoids (see Chapter 18, Skin).