



Paget's Disease - The Facts

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WHAT IS PAGET'S DISEASE?

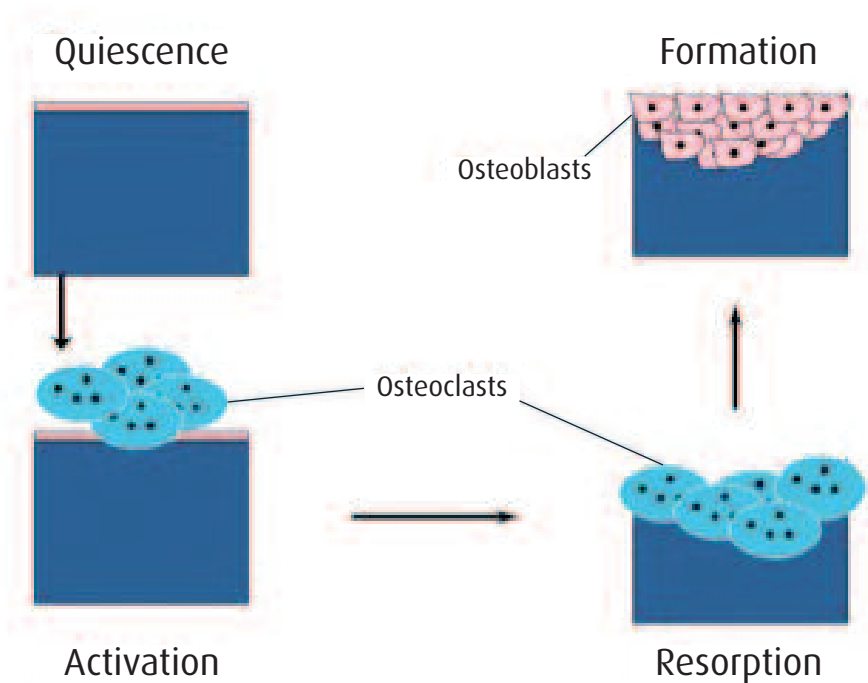
First described by Sir James Paget in 1876, Paget's disease is a common, chronic bone disorder occurring in up to 2% of mainly white adults older than 55 years, with approximately 8% of men and 5% of women over the age of 80 years being affected. The UK has the highest prevalence of Paget's disease in the world but it is also common in western and southern Europe, USA and Australia and New Zealand. Over the past 25 years both the prevalence and severity of disease has reduced in this country. Many people with Paget's disease have no symptoms and are unaware that they have the condition.



HOW DOES PAGET'S DISEASE AFFECT BONE?

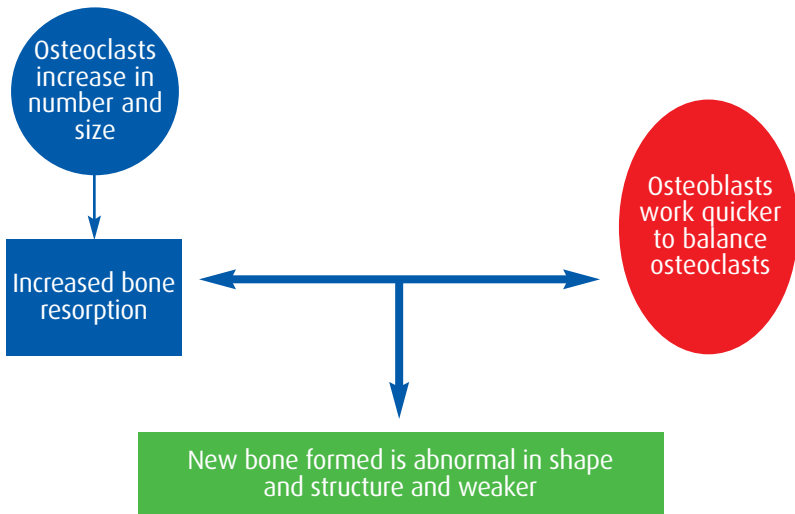
Bone is an active living tissue that is constantly being renewed through a process known as remodelling. Cells called osteoclasts breakdown old damaged bone to make way for new bone that is laid down by cells called osteoblasts (Figure 1). Over time this bone is mineralised, leading to a hard and strong skeleton. Ideally the amount of bone removed is balanced by the amount of bone laid down.

BONE REMODELLING (Figure 1)



However in Paget's disease the osteoclasts are bigger than usual and break down bone more rapidly. In response to this the osteoblasts deposit new bone at an increased rate and as a consequence the bone may increase in size, though its structure is abnormal (Figure 2). Although any bone can be affected, Paget's disease is most commonly found in the spine, thigh (femur), skull, pelvis and sternum (Figure 3). The disease may be present in only one bone (1:3 cases) or may affect several different ones. Whilst the disease can slowly spread in an affected bone it does not spread throughout the skeleton.

ABNORMALITIES IN PAGET'S DISEASE (Figure 2)

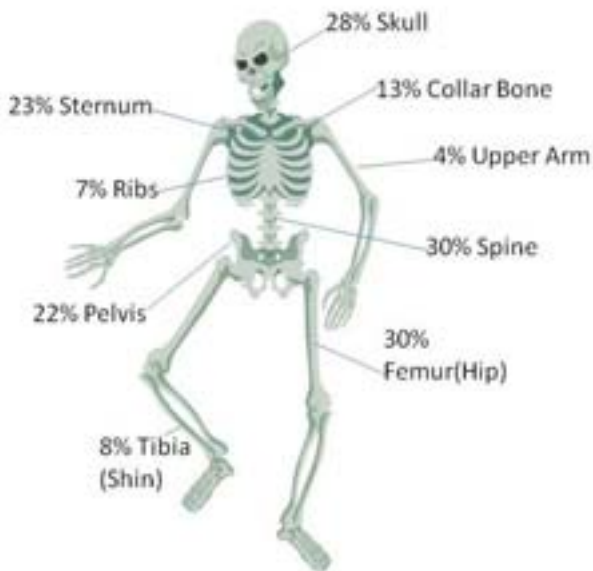


WHY DOES THIS HAPPEN?

The causes of Paget's disease are incompletely understood, but it is agreed that genetic factors play an important role since about 15% of people have a positive family history. A number of genes have been identified which predispose to Paget's disease, one important one being

Sequestosome 1, (SQSTM1) with abnormalities in this gene accounting for 20-50% of cases of familial disease. A study of 300,000 genetic variants has highlighted abnormalities in three genes, called RANK, M-CSF and "Optineurin". These are all involved in regulating the rate of bone repair and they appear to contribute to 70% of the risk of developing Paget's disease. It is possible that environmental factors, including exposure to certain viruses may also influence the development of Paget's disease. It has therefore been suggested that the disease is probably the result of exposure to an environmental trigger in an individual who is genetically predisposed to develop the condition. It is unclear why only certain bones are affected but this may be related to mechanical stresses that are placed on the skeleton at specific sites or differences in the blood supply to particular bones.

BONES COMMONLY AFFECTED (Figure 3)



WHAT ARE THE SYMPTOMS AND POSSIBLE COMPLICATIONS?

In many cases there may be no symptoms and individuals are unaware that they have the disease. It may also be discovered by chance on x-ray or if a blood test is performed for another reason. Of those who are symptomatic, pain is the most common presenting feature.

A bowing deformity of weight bearing bones may also be apparent. Complications include a predisposition to fracture in affected bones, particularly the long bones in the arm or leg. Since Paget's disease starts at the end of long bones it may accelerate the development of osteoarthritis at adjacent joints. Bone enlargement may lead to pressure on nerves in the back causing pain and leg weakness and if the skull is affected this can cause deafness.

An unusual and very rare complication is a type of bone cancer, called sarcoma but this occurs in less than 1:1,000 people with the disease.

If you have Paget's disease here:	You may have some of these symptoms and complications
Pelvis	Pain. Arthritis in the hip joint
Skull	Enlarged head, wide forehead, hearing loss, ringing in ears, headaches
Spine	Curvature, pain, pressure on nerve endings causing tingling, weakness and numbness down legs. Affected vertebrae may fracture
Hip	Pain, related arthritis in hip joint, fissure (partial) fractures in bone that may lead to complete fracture
Shin	Pain, affected bone may feel warm, bowed leg, arthritis in knee joint, fissure fractures in bone, complete fracture

IS PAGET'S DISEASE ASSOCIATED WITH OTHER MEDICAL CONDITIONS?

OSTEOARTHRITIS

If a bone becomes deformed this can place pressure on nearby joints, for example if the bone in the lower leg is bowed this could affect either the knee or ankle joint. It is also possible that the pagetic bone can enlarge leading to excess wear and tear on a joint, for example if Paget's disease is present in the pelvis this could then increase the chance of osteoarthritis in the hip joint. The presence of osteoarthritis will also lead to increased pain.

OSTEOPOROSIS

People with Paget's disease occasionally develop osteoporosis but this is likely to be a coincidence as both diseases are common in older people. Some of the drugs used in the management of Paget's disease are also used for osteoporosis though the treatment regimes differ.

HEART DISEASE

Paget's disease does not directly affect the heart but if it is widespread the heart may have to work harder to pump extra blood to involved bones. Whilst this is rarely a problem, it could place an extra burden on the heart, particularly if pre existing heart disease already exists.

HOW IS PAGET'S DISEASE DIAGNOSED?

Paget's disease may be identified by an x-ray, blood test or bone scan. Pagetic bone has a very distinctive appearance on x-ray and may be found by chance when an area of the body is x-rayed for a different reason; this may also arise with MRI or CT scans. Through a blood test it is possible to measure alkaline phosphatase (ALP) which is a chemical

produced by the osteoblasts. If there is overactivity of bone cells caused by Paget's disease this level will usually be raised. Alkaline phosphatase is also produced from the liver and if there is co-existent liver disease this may also increase ALP levels (in this situation it may be necessary to measure bone specific alkaline phosphatase (BSAP) and bone markers in urine to confirm the source of the elevated ALP).

When Paget's disease is suspected a bone scan may be performed; this uses a small amount of a radioactive tracer which is injected into a vein in the arm. If Paget's disease is present this tracer will highlight increased areas of activity in the skeleton.

Very occasionally a biopsy of the bone may be taken if there is a question about the diagnosis.

WHO NEEDS TREATMENT FOR PAGET'S DISEASE?

In many cases Paget's disease is found by chance, does not cause any symptoms and requires no treatment. However treatment may be recommended if there is pain or bone deformity and may also be advised if the site of the disease is such that there is an increased risk of complications. For example untreated Paget's of the skull could lead to compression of the nerve to the ear and deafness. If the disease is limited and results in occasional mild pain this can easily be controlled by pain killing drugs, for example paracetamol.

WHAT ARE THE COMMON TREATMENTS?

A group of drugs, called bisphosphonates are the main treatment options; they work by reducing abnormal bone turnover thus helping to restore the normal structure of bone. In addition, bisphosphonates can help to reduce

pain caused by active disease. As these drugs are deposited in the bone the benefit may last for several months or years and if given in the early stages may prevent further complications. Bisphosphonates are given as tablets or through a drip directly into the bloodstream (intravenous). Risedronate is the most commonly used oral drug with other options being tiludronate and etidronate. Pamidronate and zoledronate are intravenous preparations.

ORAL DRUGS

Name of treatment	Mode of treatment
Risedronate (Actonel)	<ul style="list-style-type: none"> • One 30mg tablet taken daily for 2 months • Taken on an empty stomach with a full glass of water, first thing in the morning • Wait at least 30 minutes before taking food, drink and other medication • Do not lie down after taking medication • Further course may be given after 6 months
Tiludronate (Skelid)	<ul style="list-style-type: none"> • Two 200mg tablets taken daily for 3 months • Taken on an empty stomach with a full glass of water • Taken at any time as long as there is a period of 2 hours before and after food, drink and other medication
Etidronate (Didronel)	<ul style="list-style-type: none"> • Two 200mg tablets taken daily for 6 months • Taken in the same way as Tiludronate

Side Effects

Side effects include indigestion and stomach discomfort. Risedronate and tiludronate are occasionally associated with joint and bone pains and can rarely give rise to skin rashes and inflammation of the eyes. Osteonecrosis of the jaw (ONJ) has very rarely been reported with risedronate.*

INTRAVENOUS DRUGS

Name of treatment	Mode of treatment
Zoledronate (Aclasta)	<ul style="list-style-type: none">• Given directly into the bloodstream over 15-30 minutes• One dose appears to be effective for at least 2 years
Pamidronate (Aredia)	<ul style="list-style-type: none">• Given directly into the bloodstream over 2-4 hours• Dosage and frequency will depend on severity of symptoms

Side Effects

Flu like symptoms can occur 24-48 hours after infusion and both treatments can be associated with occasional bone and joint pains. There may be occasional redness and swelling at the site of infusion and rarely inflammation of the eyes. Pamidronate and zoledronate may cause a decrease in calcium levels and as a precaution dietary calcium intake may be assessed and vitamin D level checked (by a blood test) before the infusion. If necessary calcium and vitamin D supplements would be given prior to treatment and continued for at least two weeks after the infusion. Measuring vitamin D levels may be impractical in some centres and in this case calcium and vitamin D supplements will be given routinely. Infusion with zoledronate can occasionally be associated with atrial fibrillation (irregular heart beat) but a causal link for this has not been established. ONJ has been rarely reported *

* For further information see section: When Should Bisphosphonates Be Avoided?

HOW DO I KNOW IF THE TREATMENT IS WORKING?

All bisphosphonates are usually effective at reducing pain in the pagetic bone though the amount of pain relief will vary between individuals. Alkaline Phosphatase which is an indicator of disease activity should be measured prior to starting treatment and repeated 2-3 months after the end of oral or intravenous therapy when it should have decreased. If the level does not fall to within the normal range and symptoms related to active disease are still present, further treatment may be required.

WHEN SHOULD BISPHOSPHONATES BE AVOIDED?

Whilst it is important that treatment is given to control Paget's disease, this decision may be modified if an individual has other serious medical problems that could be aggravated by bisphosphonates.

* On rare occasions bisphosphonates are associated with osteonecrosis of the jaw, a condition which may present after dental surgery when the gum over the affected area is worn away and the exposed bone fails to heal. The risk of this condition is greater if bisphosphonates are given for cancerous conditions and is very rarely seen in those with Paget's disease. However as a precaution it is important to inform your dentist that you are taking bisphosphonate treatment if you have to undergo extensive dental procedures and it is probably wise to complete any extensive dental treatment prior to starting this medication.

Bisphosphonates are excreted by the kidneys and they should be avoided if a person has severe kidney disease.

Although bisphosphonates are rarely used in younger people they should be avoided during pregnancy as their effects on the foetus are unknown.

OTHER TREATMENTS

CALCITONIN

Although this was the standard treatment for Paget's disease in the past it is now used rarely. Given as a daily injection for 6-18 months it may be less effective than bisphosphonate treatment in controlling the condition although it may offer good pain relief. Common side effects include nausea and flushing.

CALCIUM AND VITAMIN D

Many older people may have low vitamin D levels and may therefore require additional supplementation with vitamin D. Additional calcium would also be required if an individual has a low intake of dairy produce.

PAIN KILLERS

Although bisphosphonates and calcitonin can help to reduce bone pain, many people require additional medication for maximum pain relief. This may be required if co-existing arthritis is present in certain joints. Medications commonly used include paracetamol, co-codamol and dihydrocodeine. In addition, anti inflammatory drugs like ibuprofen may occasionally be recommended by a doctor for pain relief.

IS SURGERY NEEDED TO TREAT PAGET'S DISEASE?

There are several situations when surgery may be necessary. It is possible for the affected bone to break and depending on the site of the fracture this may require an operation to stabilise it. Osteoarthritis can be associated with Paget's disease and can lead to marked damage of the joint. If symptoms and disability become severe, joint replacement surgery may be considered. Marked bone deformity, usually seen in the lower leg may require an osteotomy,

this involves the bone being broken then reset in a more normal shape. Paget's disease in the spine can press on the spinal cord causing a narrowing that occasionally needs to be corrected surgically if medical treatment fails.

DOES DIET AND EXERCISE AFFECT PAGET'S DISEASE?

There is currently no evidence that diet influences the risk of developing the disease or its severity. However being excessively overweight can place extra strain on the joints and can exacerbate wear and tear if these are affected by osteoarthritis.

Regular exercise helps to keep the joints more mobile, maintains muscle tone and also helps to control weight. Care must be taken however to avoid excess stress on a pagetic bone and any type of intensive exercise programme should be undertaken with caution.

WHAT CAN THE PAGET'S ASSOCIATION OFFER?

The Association was founded by the late Mrs Ann Stansfield MBE in 1973 due to her personal experience of lack of interest and understanding of this condition in her husband. The original aims of the Association were to:

- Inform and support people with Paget's disease, their families and carers
- Raise awareness about the condition amongst the medical profession and the general public
- Encourage, promote and assist research into the diagnosis, treatment and prevention of Paget's disease

Whilst there have been many improvements and advances since 1973 the work of the Association continues to focus on supporting people with Paget's disease, both those who are newly diagnosed and those with longstanding disease. Information is available through written publications, a quarterly newsletter and via the Association's website. There is also a dedicated helpline managed by an experienced nurse that can be accessed via a letter, telephone call or e mail. Meetings for members are organised throughout the year giving delegates the opportunity to listen to presentations from experts, raise questions and meet with one another. A few areas in the UK operate support groups but if there are insufficient people to establish a group, informal networking is possible through telephone or written contact.

Some health professionals have limited knowledge about Paget's disease and are uncertain about the most effective diagnostic and treatment options. The Association therefore has an important role to play in highlighting the disease to health professionals and providing them with accurate up to date advice if required.

Research informs progress and the Association has been the major funding body for several high quality projects over the past three decades with over £600,000 invested in the past 10 years. These grants have supported projects on scientific, genetic, social and quality of life issues resulting in advances in the understanding and treatment of Paget's disease.

The Paget's Association is proud of its progress over the past thirty seven years. However it is not complacent and aims to continue with its commitment to fund research and offer information and advice to those with Paget's disease and others who contact the organisation. As a registered charity it relies almost entirely on voluntary contributions, gifts, legacies and fundraising activities in order to continue and develop its work.

This booklet has been prepared in conjunction with the Trustees of the Association. Whilst it is intended to offer you information on Paget's disease it is not designed to replace specific guidance you may receive from a health professional with respect to individual care.

WHAT OTHER ORGANISATIONS CAN PROVIDE SUPPORT?

Carers UK

20 Great Dover Street, London SE1 4LX.

www.carersuk.org

Tel: 020 7378 4999,

E-mail: info@carersuk.org

Age UK (formerly Age Concern and Help the Aged)

Free post (SWB 30375) Ashburton, Devon, TQ13 7ZZ.

www.ageconcern.org.uk

Free helpline: 0800 00 99 66

Expert Patients Programme Community Interest Company

www.expertpatients.co.uk

Tel: 08009885550

E-mail: get.info@eppcic.co.uk

Arthritis Research UK

Copeman House, St Mary's Court, St Mary's Gate, Chesterfield, Derbyshire S41 7TD

www.arthritisresearchuk.org

Tel: 01246 55 80 33

Arthritis Care

18 Stephenson Way, London NW1 2HD

www.arthritiscare.org.uk

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