



Paget's Disease of Bone

A booklet presenting comprehensive
information on Paget's disease



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How did Paget's disease get its name?

Sir James Paget was born in 1814 in Great Yarmouth, England. His early training as a botanist made him a disciplined investigator, which enabled him to describe several diseases during his medical career, including this one which bears his name.

What is Paget's disease?

Paget's disease, or osteitis deformans (Latin for deforming inflammation of bone), is a chronic (long-term) disorder of the bones of the skeleton. Although Sir James Paget first described it in 1877, it had been recognised by European Physicians earlier and was, in fact, a disease of antiquity. It had been found in several well documented ancient skeletons, including an early Saxon skeleton and one from an Egyptian tomb.

Paget's disease can vary from a painful or deforming affliction of the skeleton to a symptomless disorder that is only recognised during routine biochemical tests or x-rays. Symptoms such as pain, bone deformities, fractures or arthritis in joints close to affected bone may cause people with Paget's disease to seek medical help.

Bone is a living tissue and, just like other parts of the body, it is constantly being renewed. This process is called bone remodelling. Paget's disease occurs when something goes wrong with the normal process of bone remodelling, resulting in excessive bone breakdown followed by the formation of dense abnormally structured bone. This bone can be painful, enlarged, misshapen and can press on neighbouring nerves. It breaks more easily than normal bone.

Paget's disease occurs most frequently in the skull, pelvis, lower spine and longbones of the leg. One (monostotic) or more (polyostotic) sites may be involved, but any bone can be involved and any number of sites can be affected at the same time. It starts from a single focus in each bone and is thought to advance about 1cm per year. For example, a 30cm stretch of Paget's disease in a leg bone probably started 30 years ago. It does not jump across joints to affect neighbouring bones. It is usually a very slowly progressive disorder and it is rare for someone to die from Paget's disease.

The sites involved in Paget's disease in a series of 100 patients seen in the Paget's Clinic at Concord Hospital in Sydney are illustrated in Figure 1.



FIGURE 1: LOCALISATION & INCIDENCE OF PAGET'S DISEASE

POLYOSTOTIC

(more than 1 site)

(75% of Patients)

1. Skull	56%
2. Clavicle/ Collarbone	6%
3. Scapula	19%
4. Sternum	6%
5. Ribs	10%
6. Humerus/upper arms	30%
7. Spine	78%
8. Pelvis	91%
9. Ulna/radius lower arm	1%
10. Hand	1%
11. Femur/upper leg	46%
12. Patella	7%
13. Tibia/lower leg	32%
14. Foot	25%

MONOSTOTIC

(1 site only)

(25% of Patients)

1. Skull	41%
6. Humerus/upper arm	4%
8. Pelvis	41%
11. Femur/upper leg	9%
12. Tibia/lower leg	23%



How common is Paget's disease?

Paget's disease rarely affects young people and is rarely diagnosed in people under 40. Its frequency increases with advancing age. Approximately 3-5% of Australians over the age of 55 have Paget's disease. Men and women are affected equally.

If one person in a family has Paget's disease, other family members are more likely to develop the disease. The incidence of 'familial' Paget's disease may be as high as 40%.

What causes Paget's disease?

Sir James Paget called the disease 'osteitis deformans' as he concluded that it was a chronic bone infection because of its 'wandering' distribution, affecting only a portion of the bone.

Although the cause is not yet fully understood, it appears to be the result of both a genetic predisposition and a factor from the environment, possibly a virus.

Some researchers consider that this virus may be related to a group of viruses that includes measles and a viral infection of dogs (canine distemper virus) but this has not yet been proven. The virus is thought to lay dormant for many years before symptoms begin to appear (a slow virus disease).

This is not to say that anyone can catch Paget's disease like a cold or 'flu-like' illness. There is also a genetic component which results in some people becoming more susceptible to the changes caused by the virus and later developing Paget's disease.

Paget's disease may occur in more than one family member. Recently a genetic variation on chromosome 18 has been found in affected members in some but not all families with 'familial' Paget's disease. We know that the disease is commonest in Western Europeans (including those people who have migrated to the U.S., Australia or New Zealand) while it is rare in Scandinavian, Black African, Asian, Australian Aboriginal and Polynesian peoples. The incidence, however, is increased in North American Blacks and Europeans of Asian origin, which indicates that both environmental factors (e.g. viruses) and genetic factors play a part in developing Paget's disease.



What Is bone remodelling?

Bone remodelling is essential for initial growth and later for maintenance of the normal skeleton. Normal bone remodelling involves two types of bone cells called osteoclasts, which break down old bone (resorption) to make way for new bone, and osteoblasts, which lay down new bone tissue (bone formation). Through the addition of calcium (mineralisation), the new bone becomes hard and strong. (Refer to Figure 2)

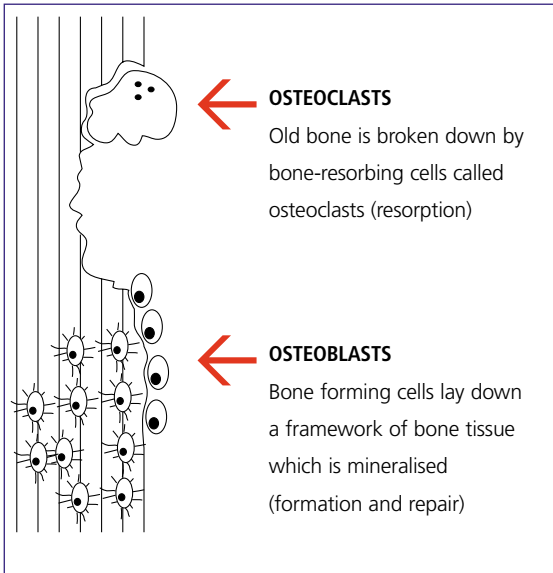
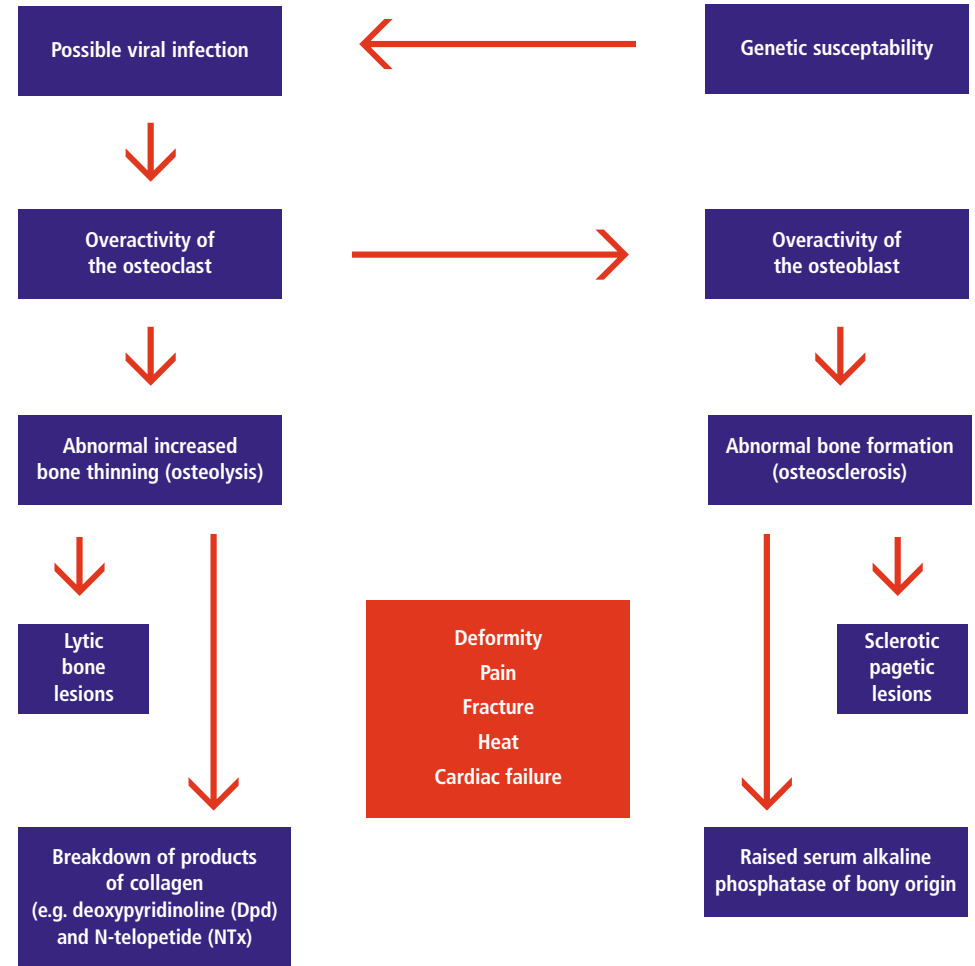


FIGURE 2: BONE REMODELLING

How does Paget's disease develop?

In people with Paget's disease, something goes wrong with the normal process of bone remodelling. The osteoclasts in some bones are overactive, causing the bone to break down more quickly than usual. The osteoblasts then try to work faster to replace the lost bone. The new bone that is formed may be thicker but structurally weaker than normal. (Refer to Figure 3)

FIGURE 3: THE DEVELOPMENT OF PAGET'S DISEASE





What are the symptoms?

In mild cases of Paget's disease, people may have few or no symptoms and frequently these may be vague and difficult to distinguish from other conditions. Many people do not know they have the disease and attribute their symptoms to arthritis or other conditions. In some cases the diagnosis is only made after complications occur.

Common symptoms may include:

- Pain, either in affected bones or in joints close to affected bone where osteoarthritis is common. Bone pain often has an aching toothache-like quality and occurs particularly at rest or at night. It is often relieved by movement and activity – for example getting out of bed. Joint pain is aggravated by movement and relieved by resting.
- A sensation of heat over the affected bone, which is caused by an increase in blood flow through the abnormal bone.
- Headache when the bone of the skull is involved.
- Deformity of the bone, which may include an increase in head size, enlargement of bones and bowing of a limb, especially weight bearing limbs. Affected bones tend to buckle under the weight of the body.
- With enlargement of the skull, compression of various nerves may cause

impairment of sight, smell, hearing (deafness, ringing in the ears), loss of balance, impairment of facial muscles or pain in facial nerves.

- Pressure on nerves or nerve roots by enlargement of abnormal bone in the spine or the spinal cord may cause muscle weakness, sensory disturbances or loss of balance.
- Fractures most commonly stress fractures (refer to Figure 4) on the surface of weight bearing bones in the upper or lower leg. These may occasionally result in a complete fracture with little trauma. Treatment reduces the risk of fracture.

FIGURE 4: STRESS FRACTURE, TIBIA AND FIBULA. FEMALE AGE 57.



Paget's disease involves the upper half of the left tibia. The bone is sclerotic, thickened and deformed. On the outer cortex of the upper tibia, a partial fissure fracture is present. The patient complained of pain over the site of the fissure fracture which later went on to a complete fracture with trivial trauma.

Fractures

Fractures commonly follow trivial injury. In about half the patients with longbone fracture, no history of significant trauma is given. In the case of femoral fractures in particular, they may be preceded by pain and represent the extension of fissure fractures. The distribution of femoral fracture is quite different from that in elderly patients without Paget's disease. In Paget's disease, subtrochanteric fractures and fractures of the shaft are the most common, and femoral neck fractures are comparatively rare. In contrast, fractures of the femoral neck are the most common in the elderly without Paget's disease. Unlike fractures of normal longbones, complete fractures through pagetic longbones are generally transverse rather than spiral ('chalk-stick' or 'banana' fracture).

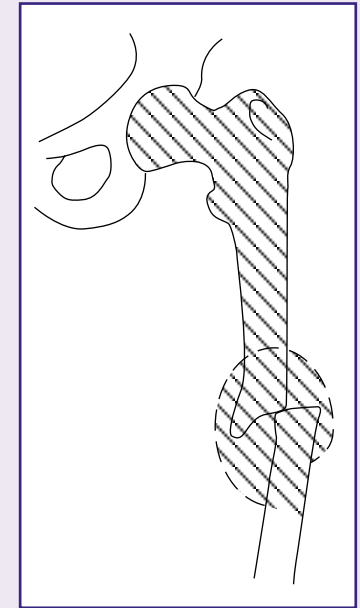


FIGURE 5: FRACTURE THROUGH THE MID SHAFT



FIGURE 6: STRESS FRACTURE



FIGURE 7: TRANSVERSE SUBTROCHANTERIC FRACTURE

Fractures in Paget's disease occur most frequently in the longbones of the lower limb and in the spine. Compression fractures of the vertebral bodies may result in spinal cord compression. Figures 5, 6 & 7 show the characteristic features of fractures in Paget's disease in the femur (longbone in the thigh). In figure 7 there has been a transverse subtrochanteric fracture and in figure 5 a transverse fracture through the mid-shaft. Figure 6 shows a stress fracture through Pagetic bone that may lead to a complete fracture.



Other less common problems

- Congestive heart failure, occasionally in patients with extensive Paget's disease, caused by the heart being overworked in pumping more blood through affected bones. This complication is more likely to occur if other factors that can cause heart disease are also present.
- A form of bone cancer, osteogenic sarcoma, is a rare complication occurring in less than 1 in 100 people with Paget's disease. The risk of developing this complication, although small, is 30 times more likely in people over fifty years of age who have Paget's disease than in people who do not have the disease. These bone tumours in patients with Paget's disease are distributed differently from the normal population. They are especially found in the longbones of the upper and lower limbs, skull and pelvis. Effective treatment may reduce the risk of cancer. Reappearance of pain, a change in the character of pain or a bony swelling are the most frequent symptoms of a developing bone cancer in people with Paget's disease. If detected and treated aggressively, the outcome is improved, but still may be very poor.

How is Paget's disease diagnosed?

The diagnosis is usually made on the results of blood or urine tests, x-rays or bone scans. A bone biopsy is sometimes required. Some of these tests are explained below:

Laboratory tests of blood or urine

Alkaline phosphatase (Total alkaline phosphatase, bone specific alkaline phosphatase): A high level in the blood of this substance indicates that boneforming cells (osteoblasts) are more active than normal. The total alkaline phosphatase is usually measured which includes alkaline phosphatase from organs other than bone. Bone specific alkaline phosphatase can now be measured.

Breakdown Products of Collagen:

High levels of these substances in the blood or urine indicate a high level of activity of cells that break down bone (osteoclasts). Deoxypyridinoline (Dpd) and N-Telopeptide excretion (NTx) are the most widely used tests today. Hydroxyproline is a test that was used in the past.

The level of any or all of these substances (alkaline phosphatase and breakdown products of collagen) may be increased in Paget's disease, reflecting both the amount of bone involved and how active the disease is. Early in the course of the disease, especially if few bones are involved, these tests may be normal.

The levels of these substances are also used to check the response to treatment.

Calcium:

The levels of calcium in blood and urine may be raised, especially in people who are not able to move around for a prolonged period (*i.e. bed rest in hospital*).

X-rays

X-rays allow the doctor to confirm that there is Paget's disease in a particular bone, to assess how much bone is involved and to look for complications. It is usual for the doctor to request x-rays when the disease is first diagnosed and during the course of treatment, as the disease may change and respond to therapy (*e.g. healing of lytic areas, refer to Figures 8 & 9*).



FIGURE 8: LATERAL X-RAY (RADIOGRAPH) OF THE SKULL SHOWING THINNING (LYSIS) OF BONE (OSTEOPOROSIS CIRCUMSCRIPTA) AN EARLY STAGE OF SKULL INVOLVEMENT



Bone Scan

A bone scan is performed by injecting a small amount of a special substance called a radioisotope, which is taken up by abnormal bone (called pagetic bone). The radiation dose is very small. The bone scan is always done when the condition is first diagnosed, to see which parts of the body are affected. The bone scan is more sensitive in detecting the extent of Paget's disease than x-rays (*Refer to Figure 10 & 11*).

Biopsy

Rarely, usually when other tests are not conclusive, it may be necessary to obtain a small sample of bone tissue for examination. This is taken by means of a needle and the procedure is known as a bone biopsy.



FIGURE 9: LATERAL X-RAY OF THE TIBIA SHOWING A TYPICAL WEDGE-SHAPED LYTIC LESION OF ADVANCING PAGET'S DISEASE



Bone scans

Radionuclide scan appearance in patient with polyostotic Paget's disease (Figure 10) and monostotic Paget's disease involving the left tibia (Figure 11). Note the bowing of the tibia & the arthritic changes in the ankle joint. Bone scanning agents such as ^{99m}Tc-labelled polyphosphates or bisphosphonates reveal areas of increase

vascularity & turnover and usually show a characteristic appearance and markedly increased uptake of tracer which is evenly distributed. The appearance, however, may not be diagnostic but is the most sensitive method of detecting early disease and is of particular value in assessing the extent of disease and bones involved.

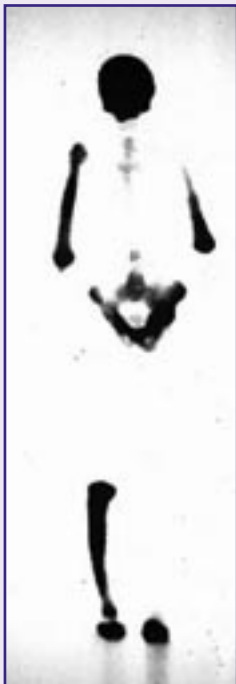


FIGURE 10: POLYOSTOTIC BONE SCAN APPEARANCE WITH EXTENSIVE UPTAKE IN SKULL, BOTH HUMERI, PELVIS AND RIGHT TIBIA



FIGURE 11: MONOSTOTIC BONE SCAN APPEARANCE WITH INVOLVEMENT OF ONLY THE LEFT TIBIA

How should people with a family history of Paget's disease be followed up?

If a member of the immediate family has Paget's disease (e.g. a parent, a child, a brother or sister), a reasonable screening test for other asymptomatic family members would be to have a total serum alkaline phosphatase (blood) test every two or three years. However, this test may be normal in early or mild cases of Paget's disease and a bone scan is more specific. A normal bone scan virtually excludes the presence of Paget's disease. If there is any uncertainty, a referral can be arranged to a specialist physician who is an Endocrinologist or Rheumatologist interested in Paget's disease.

Who should be treated?

The aim of treatment of Paget's disease is to relieve pain, to prevent or reduce future complications (deformity, fractures and nerve compression by pagetic bone) and to maintain mobility.

Some people with Paget's disease do not have symptoms and may not need treatment. For those who do, pain is the most common symptom. If pain is mild, aspirin or other simple pain medicines may be sufficient. Many people with Paget's disease also have 'wear and tear' osteoarthritis of joints next to areas of pagetic bone and, in these circumstances, nonsteroidal antiinflammatory drugs

(NSAID's) are often used. If the pain does not respond to these measures or if the disease affects bones that are important for mobility, then specific 'anti-pagetic' treatment of the disease may be necessary.

Situations that may require specific anti-pagetic treatment include:

- Progressive skeletal involvement, particularly if deformity of the bones is worsening
- Extensive involvement of weight bearing bones (risk of deformity or fracture) or bones close to joints such as the hip or knee (risk of arthritis)
- Involvement of the vertebrae where there is risk of fracture and spinal cord compression
- Involvement of the base of the skull
- Progressive deafness, if this is shown to be due to Paget's disease
- Nerve compression by pagetic bone, or involvement of bone where there may be a significant risk of nerve compression
- Congestive heart failure associated with extensive Paget's disease
- Prior to surgery involving pagetic bone
- Extensive active disease in the absence of symptoms, especially in young people.

Situations that may not require specific anti-pagetic treatment:

- Limited bony involvement away from joints and in bones with little risk of fracture especially in older patients.





What specific treatments are available?

25 years ago, the late Dr Hugh Barry wrote, "No effective means have been found to make any significant change to the course of Paget's disease." Today, this is no longer true. Modern medicines called 'bisphosphonates' can produce prolonged suppression of disease activity with the expectation that this will prevent complications developing.

Bisphosphonates

Bisphosphonate medicines have become the treatment of choice for Paget's disease. They work by slowing down the abnormal breakdown of bone by osteoclasts. This allows bone remodelling to return to normal and protects the bones from being weakened. In this way, bisphosphonate medicines help to reduce bone pain and to prevent fractures.

Problems of lack of effect and poor tolerance with early bisphosphonate medicines have been overcome by the development of the newer bisphosphonates, which powerfully suppress the overactive osteoclasts without affecting normal bone.

We are still learning how best to use bisphosphonate medicines and, therefore, varying dosage regimens are being used. The recommended dosage regimen may differ from centre to centre, depending on the centre's experience.

The goal of treatment is usually to normalise disease activity, as there is evidence that this prevents complications. Bisphosphonate therapy is usually continued until the biochemistry tests have become normal and lesions seen on x-ray have healed. The disease is then said to be 'in remission.' The length of time that the disease will stay in remission will depend on how much the activity of the abnormal osteoclasts can be suppressed. Treatment is started again when the tests once again become abnormal. With treatment, bone pain can be expected to stop and joint pain next to a pagetic site may also improve.

Case 1

The left humerus is extensively involved with Paget's disease. There is gross deformity and there is loss of the normal bone architecture. The disease extends from the elbow joint to the upper end of the humerus. It is unusual for Paget's not to involve the end of a longbone if other areas are diseased. Effective early treatment with one of the potent new bisphosphonates can be expected to prevent deformity and other complications.

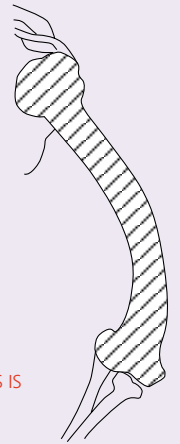


FIGURE 13: ALL OF THE HUMERUS IS INVOLVED BY PAGET'S DISEASE



FIGURE 12: X-RAY OF HUMERUS



FIGURE 14: DEFORMITY OF UPPER ARM



FIGURE 15: BONE SCAN





Intravenously administered bisphosphonates

Most of the early experience with the more potent bisphosphonate medicines has been gained using Pamidronate (Aredia) administered intravenously.

Experience to date with pamidronate has shown that relatively small doses of 60 or 120 mg are very effective in treating mild disease, but higher doses may be required in people affected more severely. In Australia, one regimen is to give 60 mg as a single infusion every 3 months until remission occurs.

Pamidronate is always given as a slow intravenous infusion (drip) into a vein. A 60 mg infusion usually takes about 1 hour. The intravenous administration of bisphosphonates ensures all the medication is delivered to the bones that need the treatment.

Side effects with IV bisphosphonates are uncommon and usually mild and transient. After the first dose, fever and influenza-like symptoms (feeling unwell, chills, fatigue, flushes, headache, aches and pains in bones and joints) may occur within the first 48 hours but are temporary and usually require no treatment. It is unusual for these effects to happen again with later doses. The side effects may be prevented by taking antiinflammatory (NSAID) medication for 2-3 days or simply taking paracetamol as required. While symptoms of a low level of calcium in the blood are rare, people who are at risk of calcium and vitamin D deficiency

may need to take calcium and vitamin D supplements.

Zoledronic acid is a promising, new intravenously administered bisphosphonate which is presently being trialed in Paget's disease as a single 5 mg infusion given over 15 minutes.

Orally administered bisphosphonates

Bisphosphonate medicines are available that can be taken by mouth (e.g. alendronate (FOSAMAX), risedronate (ACTONEL), tiludronate (SKELID). They are poorly absorbed from the stomach and consequently larger doses need to be given. To maximise the absorption of oral medication it must be taken on an empty stomach with a full glass of plain water, waiting at least 1/2 an hour or more before food or beverage. Alendronate and Risedronate are recommended to be taken first thing in the morning after getting out of bed, in an upright position before eating food. This is important to minimise side effects. Nausea, indigestion or heartburn, which may be due to oesophagitis or gastritis (inflammation of the lining of the oesophagus or stomach), may occur and are more likely if the medicine is taken while lying down or if one lies down shortly (within 1/2 hour) after taking the medicine. Tiludronate is less likely to cause gastrointestinal side effects and is usually taken before bed. Oral bisphosphonate medicines are usually recommended to be taken once daily for several months. However, experienced physicians will often recommend different treatment regimens.

Case 2

Severe Paget's disease of the skull with irregular thickening of the vault, and patchy areas of sclerosis and translucency giving rise to a characteristic fluffy appearance. The base of the skull is flattened and the pituitary fossa is indistinct. Moderate basilar invagination is present. Such patients may have headache, deafness and, rarely, the cranial nerves, brain and/or spinal cord may be affected. Early treatment with the new potent bisphosphonates is expected to prevent these changes developing.

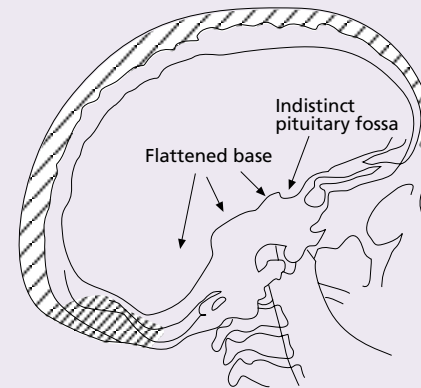


FIGURE 16: SEVERE PAGET'S DISEASE OF THE SKULL



FIGURE 17: ENLARGEMENT AND DEFORMITY OF SKULL

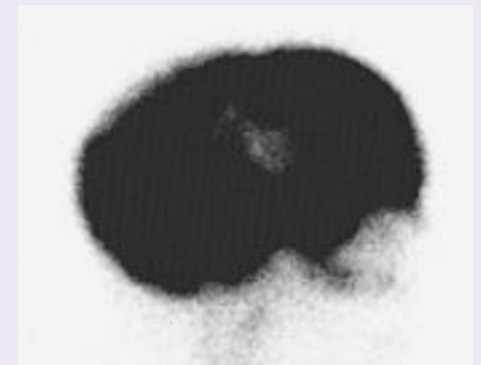


FIGURE 18: SCAN SHOWING EXTENSIVE INVOLVEMENT



FIGURE 19: EXTENSIVE INVOLVEMENT ON X-RAY



Historical treatments

Calcitonin and Mithramycin:

Before bisphosphonates became available, calcitonin was the principal treatment for Paget's disease. It is much less effective than the bisphosphonates and is now rarely used. Calcitonin is a hormone produced by special cells in the thyroid gland in the neck. It slows down the rate of bone breakdown and remodelling. It is usually given daily or three times per week by injection under the skin or into the muscle. Symptoms generally show some improvement after three to six weeks of treatment, but the benefits of treatment may not be fully evident for many months. A disadvantage of calcitonin is that it is usually given by injection. Almost 30% of people will report fleeting feelings of flushing, warmth or mild nausea immediately following the injection. Nevertheless, there do not appear to be any serious side effects. The duration of treatment with calcitonin will vary from person to person. If effective and well tolerated, it will usually be continued for six to twelve months, and in some cases, longer.

Mithramycin is a potent cytotoxic drug that has been used in the past to treat severe cases of Paget's disease. It is administered by intravenous infusion, and its action is to destroy the abnormal osteoclasts, which are actively breaking down bone.

Orthopaedic management

In people with nerve involvement, damage to joints such as the hip or knee, deformity of longbones, fractures or tumours, orthopaedic surgical treatment may be necessary in addition to drug therapy.

Case 3

Right tibia – effect of disease & treatment. The tibia is extensively deformed by Paget's disease which extends throughout the bone. The bone is expanded and bowed. Severe pain was a feature of the disease and the overlying skin was hot and the bone tender to pressure. With bisphosphonate therapy, the patient's pain resolved, the skin temperature returned to normal, the biochemical indices of activity of the disease returned to normal and there was marked improvement on the bone scan.

FIGURE 20: X-RAY



FIGURE 21: CLINICAL PHOTOGRAPH



FIGURE 22: BEFORE



FIGURE 23: AFTER





What is the outlook for people with Paget's disease?

The outlook for people with mild to moderate Paget's disease (and this means most patients) is good. Abnormal bone remodelling may continue in Paget's disease for more than 20 years in the active stage of the condition. After a variable number of years, an inactive stage of the disease may develop.

Paget's disease rarely develops in new bony sites after it has been diagnosed. However, the severity and extent of involvement within each bony site may increase over the years from a situation in which no symptoms are occurring, to one in which the bone may be quite severely affected. If new sites of possible Paget's disease appear, the doctor will take care to exclude other possible causes, such as spread of cancer to bone.

Early recognition and treatment of Paget's disease can be expected to bring about an excellent response in the overwhelming majority of cases. Specific medicines such as bisphosphonates can slow the rate of disease progression and control its activity, and treatment offers the possibility of long-term control, prevention of complications or even 'cure'.

Bisphosphonates are the treatment of choice in Paget's disease and are capable of inducing suppression of the disease which may persist for years after treatment is stopped. Suppression of disease activity is expected to minimise the development of complications.



Effect of Treatment

Radionucleotide appearances in a patient before treatment (*Figure 24*) with extensive disease affecting the skull, right scapula, right humerus, many vertebra, pelvis, both femora and the right calcaneus and (*Figure 25*) after bisphosphonate treatment, there has been marked improvement in disease activity.

Radionucleotide scan appearance in a patient with polyostotic disease affecting the left clavicle, spine, pelvis, femora and tibia before (*Figure 26*) and after (*Figure 27*) bisphosphonate therapy.



FIGURE 24: BEFORE



FIGURE 25: AFTER



FIGURE 26: BEFORE



FIGURE 27: AFTER



Where can I find more information?

Further information may be obtained from:

The Paget's Clinic

Level 6, C64, Medical Centre
Concord Hospital NSW 2139
Phone: 02 9767 7413
Fax: 02 97677472
Email: langf@email.cs.nsw.gov.au

The Australian and New Zealand Bone and Mineral Society

145 Macquarie Avenue
Sydney NSW 2000
Phone: 02 9256 5405
Fax: 02 92518174
Email: anzbms@racp.edu.au
www.racp.edu.au/anzbms

The Paget's Support Group Arthritis Foundation of NSW

Locked Bag 16
North Parramatta NSW 1750
Phone: 02 9683 1622

The Paget's Support Group, a special interest branch of the Arthritis Foundation of New South Wales, was formed in 1983. Its main aims are to gather and provide information about Paget's disease, to give support to people who have Paget's disease, to increase public awareness of the extent of Paget's disease and encourage research into the cause and treatment of Paget's disease. You can help by joining and giving us your support to carry out these aims. The Foundation is a registered charity (donations over \$2 are tax deductible).

International Paget's Support Groups

UNITED KINGDOM

National Association for the Relief of Paget's Disease – UK
Ms Marylin McCallum Director – NARPD
323 Manchester Road, Walkden, Worsley, Manchester, M28 3HH, UK
www.paget.org.uk

UNITED STATES

The Paget Foundation
Ms Charlene Waldman, Executive Director
120 Wall Street, Suite 1602, New York, NY 10005, USA
www.paget.org

Paget's clinics

The Paget's Clinic

Endocrinology and Metabolism
Level 6 Medical Centre
Concord Hospital
Concord NSW 2139
Phone: 02 9767 7413
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The Department of Endocrinology and Metabolism at Concord Hospital is carrying out research on various bone diseases, including Paget's disease. This research can be supported by making a donation (tax deductible) to the Endocrine Research Fund, Endocrinology and Metabolism, C64, Concord Hospital, Concord, NSW 2139.

This is a revision on behalf of the Medical Affairs Sub-committee of the Australian and New Zealand Bone and Mineral Society of a brochure previously prepared by Clinical Nurse Consultant Fay Lang, and A/Prof Michael Hooper from the Department of Endocrinology and Metabolism, Concord Hospital, Sydney.

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Goodwood SA 5034

SUMMERLAND

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Ballina NSW 2478

SYDNEY

Mr D Greenfield
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Croydon Park NSW 2133

TASMANIA

Sister Judy Lee
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WOLLONGONG

Mr M Butler
103 Little Lane Crescent
Warilla NSW 2520



Glossary

Alkaline phosphatase:	is a chemical (enzyme) produced by bone forming cells (osteoblasts) and is overproduced in Paget's disease
Anti-pagetec Treatment:	treatment that suppresses the activity of Paget's disease and it's progression
Bisphosphonates:	an anti-pagetec drug that inhibits the activity of the cells that initiate the abnormal bone remodelling in Pagets Disease (osteoclasts)
Calcaneus:	heel-bone, large bone that forms the projection of the heel behind the foot
Collagen:	a protein that is found in bone matrix and other tissues such as the skin and ligaments, in fibres that have high tensile strength
Femur:	thigh-bone, a large bone between the hip and knee. The head of the femur articulates with the acetabulum of the pelvis to form the hip joint
Fibula:	outer and thinner bone of the lower leg
Humerus:	a bone in the upper arm, from the shoulder to elbow (fig 1)
Hydroxyproline:	a substance that can be measured in urine which reflects the amount of osteoclastic bone resorption
Monostotic:	one bone involved
Osteoblasts:	cells responsible for bone formation
Osteoclasts:	large multinucleated cells that break down bone
Osteoarthritis:	a disease of joint cartilage with secondary changes of the underlying bone causing pain and impairment of function of the involved joint
Osteosarcoma:	a malignant bone tumour most commonly occurring in children but also in adults especially those with Paget's disease
Patella:	a lens-shaped bone that forms the knee-cap in the front of the knee
Polyostotic:	more than one bone involved
Radius:	the outer and shorter bone of the forearm
Resorption:	thinning or breakdown of bone
Scapula:	shoulder blade, a triangular bone
Symptom:	an indication of a disease or disorder, i.e. pain or deformity, that is noticed by an individual
Sternum:	breastbone, a flat bone extending from the base of the neck to just below the diaphragm in the middle of the front of the chest
Tibia:	the shin-bone, inner and larger bone of the lower leg
Ulna:	inner and longer bone of the forearm
Vertebra:	one of the 33 bones that make up the backbone or spine



Questions and answers

Q. What is Paget's disease?

A. A chronic localised bony disorder characterised by excessive bone breakdown and formation which results in fragile, and/or enlarged and deformed bones in one or more regions of the skeleton.

Q. What causes Paget's disease?

A. There is a hereditary (genetic susceptibility) component and probably an environmental factor thought by some to be a 'slow virus'.

Q. If a family member has Paget's disease what should you do?

A. Individuals with a Family history have a greater chance of developing the disease. A possibility is to screen annually with a alkaline phosphatase level after 40 years of age. This test however will be normal early in the course of the disease and its elevation depends on the extent and activity of the disease. If the alkaline phosphatase is elevated your doctor can order a bone scan and then if positive x-rays of involved bones.

Q. Who is affected by Paget's disease?

A. The condition is commonest in Caucasians of Anglo-saxon descent. It's incidence increases with age and about 3% of individuals over 60 are affected. Both men and women are affected.

Q. What are the symptoms?

A. Many affected individuals have no symptoms particularly early in the course of the disease. Bone or joint pain are the commonest symptoms. Headache, enlargement of the skull and hearing loss may occur if the skull is involved. Pressure on nerves in the spine may cause pain. Deformities are common when weight bearing bones are involved. Pagetic bone is more susceptible to fractures.

Q. How is the diagnosis established?

A. The alkaline phosphatase may be elevated or x-rays may show a characteristic appearance. A bone scan should be done to determine the sites of increased activity followed by x-rays of these sites of apparent involvement as an initial investigation.

Q. Which bones are involved?

A. Any bone can be involved but some bones including the skull, spine, pelvis and leg bones are more frequently involved.

Q. What is the 'alkaline phosphatase'?

A. The alkaline phosphatase is a chemical (enzyme) produced by bone forming cells (osteoblasts) and is overproduced in Paget's disease. The total alkaline phosphatase includes sources of alkaline phosphatase from sources other than bone but for most occasions remains the most clinically useful test to assess disease activity and response to treatment. A bone specific alkaline phosphatase test is now available.



Q. What is the prognosis for patients with Paget's disease?

A. The course of the disease varies greatly in different individuals depending on the location of involved bones, the extent and activity of the disease. Early treatment before significant complications have developed can be expected to prevent the development or progression of serious complications. After diagnosis it is unusual for additional sites of involvement to develop in other bones.

Q. Why does arthritis occur in Paget's disease?

A. Arthritis develops when the bone adjacent to joints is involved with enlargement of the bone and destruction of the articular cartilage and because of deformity of longbones causing undue stresses on joints. Weight bearing joints are commonly affected.

Q. Will hearing loss occur?

A. If the bone which surrounds the inner ear (the temporal bone) is involved progressive hearing loss may occur. Treatment may prevent, slow or stop hearing loss but is unlikely to reverse changes that have already occurred. If hearing loss has occurred aids may be beneficial.

Q. Will my sight be affected?

A. Rarely when the skull is involved around the orbit the nerves to the eye may be compressed and vision affected.

Q. Will I loose my teeth?

A. If the bone in the jaw (maxilla and mandible) are affected the teeth may become loose.

Q. Will my heart become affected?

A. This is unlikely but if Paget's disease is very widespread and active the heart has to work harder to pump the blood through the vascular Pagetic bone. If there is underlying heart disease this extra work the heart is required to do may result in heart failure.

Q. Does Paget's disease affect the kidney?

A. No, but kidney stones are more common in active Paget's disease.

Q. Will my Paget's disease cause my death?

A. Paget's disease is rarely fatal. A particular rare type of bone cancer (osteogenic sarcoma) is more common in active Pagetic bone than normal bone but appears to be even rarer after treatment.

Q. Is diet and exercise important in Paget's disease?

A. There is no relationship between diet and the development of Paget's disease. Nevertheless it is still a good idea to ensure adequate calcium and Vitamin D nutrition as deficiency is another risk factor for minimal trauma fracture. Regular exercise is also beneficial in skeletal health but special advice may be required in regard to affected bones.

Q. How is Paget's disease treated?

A. A number of relatively new potent very effective therapies from a class of medicines called bisphosphonates are first line treatment for Paget's disease today and have displaced an earlier bisphosphonate (etidronate) and calcitonin which were used in the past.

Q. When is surgery indicated in Paget's disease?

A. Surgery may be required for fixation of fractures, for severe arthritis and to correct deformity and relieve compression of nerves.



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