

QUESTIONS
AND ANSWERS

ABOUT

PAGET'S DISEASE
OF BONE

A PUBLICATION OF

THE PAGET FOUNDATION
FOR PAGET'S DISEASE OF BONE AND
RELATED DISORDERS

General Information about Paget's Disease

1. Q. What is Paget's disease of bone?

- A. Paget's disease of bone is a chronic disease that can be treated. Although there is no cure, several drugs are approved by the U.S. Food and Drug Administration (FDA) to treat the disease.

The disease tends to enlarge and deform bones in one or more parts of the body. In Paget's disease, the two bone cells called the osteoclast (the cell that resorbs or breaks old bone down) and the osteoblast (the cell that forms new bone) do not interact normally. When this happens, too much bone tissue is broken down; new bone that is formed is weak. As a result, people with Paget's disease can have bone pain, arthritis, fractures and body deformities.

2. Q. What causes Paget's disease?

- A. The cause of Paget's disease is still not fully known. It is likely that a virus and genetics may both be involved. Research suggests that Paget's disease may be caused by a "slow virus" infection of bone. This condition could be present for many years before symptoms appear.

However, Paget's disease is also found to run in families. In fact, having a gene that is linked to Paget's disease may cause a person to be at higher risk for developing a virus infection of the bone.

Several genes have been found that may increase a person's risk of developing Paget's disease. The main gene is called the *sequestosome 1* gene. Others are *RANK* and the *VCP* gene.

3. Q. Which groups of people are usually affected by Paget's disease, and how common is the disease?

- A. Paget's disease is rarely found in people under 40 years of age. One and a half (1½) to 8 percent of older adults have Paget's disease depending on the person's age and area of the world where he or she lives. Ten to 40 percent of people with Paget's disease also have one or more family members with the disease. Almost equal numbers of men and women have the disease.

4. Q. How is Paget's disease usually diagnosed?

- A. Paget's disease may be identified by x-rays, blood tests or by bone scans. Because bones affected with Paget's disease have a distinct appearance in x-rays, x-ray is the main means of diagnosing Paget's disease. Once in a while, a bone biopsy is needed.

When Paget's disease is suspected, the doctor may order a blood test to look for an enzyme made by bone cells. This blood test is called the SAP (serum alkaline phosphatase). In Paget's disease, the bone cells produce too much SAP.

Another test which may suggest Paget's disease is a bone scan. A bone scan is done by injecting a safe amount of a radioactive tracer into the blood. The tracer goes to areas where there is Paget's disease. Bone scans can tell how much Paget's disease is present and how active it is. If a bone scan suggests Paget's disease, more x-rays of the affected bones are ordered.

5. Q. Should siblings or children of patients with Paget's disease ask their doctors for any special tests?

- A. Yes. After the age of 40, siblings and children of a patient with Paget's disease should have a SAP blood test every 5 years. Though the levels of SAP vary in different labs, a result greater than 125 may mean the presence of Paget's disease. However, a normal SAP test does not mean that a person does not have any Paget's disease. If Paget's disease affects only a small area of the bones, a person may often have a normal SAP level. Liver disease can also cause an elevated SAP.

6. Q. What are the symptoms?

- A. In many cases, there may be no symptoms. When symptoms do occur, they can include:

Bone Pain. This can occur in any bone affected by Paget's disease. Pain is often felt in joints near the affected bones and may be due to arthritis.

Back Pain. This can occur from bone pain due to Paget's disease, from fractures of the vertebra, from arthritis in the spine or from irritation to nerves.

Leg Pain. Pain down the leg may occur due to irritation of the sciatic nerve. It may also be linked with back pain.

Headaches. These may occur when Paget's disease occurs in the skull.

Hearing Loss. This can result from Paget's disease in the skull.

Bone Deformities. Deformities are caused by bones that get larger and weaker. They occur in advanced cases of Paget's disease. Common deformities are increased head size, bowing of a limb or curvature of the spine.

Fractures. Bones weakened by Paget's disease can break more easily than healthy bones. Most fractures that occur in Paget's disease are in the long bones of the legs.

Osteoarthritis. Arthritis is often found with Paget's disease. It causes pain in joints near the bone or bones affected by Paget's disease.

7. Q. Do all people who have Paget's disease know that they have it?

- A. No. Many patients who have Paget's disease do not know they have it. The disease may be so mild that it is not recognized. Sometimes the patient's symptoms are confused with arthritis or other problems. Other times, it is diagnosed only after complications have developed.

8. Q. Which bones can be affected by Paget's disease?

- A. Any bone can be affected in Paget's disease. It is found most often in the spine, skull, pelvis, thighs and lower legs. Some patients will have the disease in only one bone. Others may have two, three, or more affected bones.

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

- A. The course of Paget's disease varies greatly. It can be completely stable and produce no symptoms or symptoms can develop slowly in affected bones. The disease almost never spreads to nearby normal bones. Overall, the outlook is good, particularly if treatment is given before major problems occur. Treatment can control Paget's disease and its symptoms but is not a cure. When it is not treated, Paget's disease can cause serious problems, depending on which bones are affected and how long the disease is present.

10. Q. Is Paget's disease a fatal disease? Is it related to cancer?

- A. Paget's disease is rarely fatal. A very rare complication of Paget's disease is sarcoma, a form of bone cancer. It is seen in less than one percent of all Paget's disease patients. A patient should call the doctor if he or she has a sudden onset of severe pain or pain that is suddenly much worse than usual. The doctor will first check to see if the new pain is coming from a fracture. If there is no fracture sarcoma should be considered. In most cases, though, sarcoma is not the cause of the increased pain.

11. Q. What is juvenile Paget's disease?

- A. Juvenile Paget's disease (JPD) is a rare bone disease that has some similarity to adult Paget's disease. Most often JPD affects infants and young children. Children can inherit JPD because they do not have enough of a certain protein that controls the breakdown of bone. These children have a high SAP level in their blood. The x-rays of their bones may look like the x-rays of the bones of Paget's disease patients.

JPD affects many parts of the skeleton—not just a few bones as in adult Paget’s disease. Children with JPD have bone pain, fractures and hearing loss very early in life.

The drugs used to treat adult Paget’s disease are also used to treat JPD.

Paget’s Disease and Other Medical Conditions

12. Q. What is the relationship between osteoarthritis and Paget’s disease?

A. Paget’s disease can cause osteoarthritis by changing the structures of the bones around a joint:

(1) Long bones such as the thigh and leg bones may become bowed. They can then distort the way the body is aligned, putting pressure on nearby joints;

(2) Bone that has Paget’s disease may enlarge. This overgrowth can put too much wear and tear on the joint.

Arthritis is a common cause of pain in Paget’s disease, but the disease itself also causes bone pain. In some patients, the pain may be due to both Paget’s disease and arthritis.

13. Q. What is osteoporosis? What is its relationship to Paget’s disease?

A. Osteoporosis is a condition of general loss of bone mass that can lead to fractures. It is often found in the elderly. Some patients may have both Paget’s disease and osteoporosis. The two diseases have different causes and affect the bones in different ways.

The drugs Fosamax[®] and Actonel[®] are used to treat both diseases. However, the doses of these drugs are **different** for these two diseases.

Some doctors might prescribe doses of Fosamax[®] and Actonel[®] that are not the same as recommended doses for treating Paget’s disease. Also, some doctors might prescribe the drug Boniva[®]. This drug is approved for osteoporosis but has not been approved for treating Paget’s disease.

The drug teriparatide (Forteo[®]) is approved for the treatment of osteoporosis. It should not be used for people with Paget’s disease since Paget’s patients have a higher risk for a form of bone cancer called sarcoma. High doses of Forteo[®] have been found to cause this type of bone cancer in animals.

The Paget Foundation recommends the use of those drugs approved specifically for treating Paget’s disease. Suggested doses of these drugs are listed in the chart in Question 23.

14. Q. Is there a relationship between Paget's disease and heart disease?

- A. Yes, some. In patients with widespread Paget's disease, the heart may have to work harder to pump extra blood to affected bones. This does not often cause heart failure except in some people who already have heart disease such as hardening of the arteries of the heart.

15. Q. Is there a relationship between Paget's disease and kidney problems?

- A. No, not directly. Paget's disease is not directly linked to kidney problems. However, kidney stones may be more common in patients with Paget's disease.

16. Q. Do some Paget's disease patients lose their hearing? Can anything be done about this?

- A. Yes. When Paget's disease affects the skull, loss of hearing may occur. It can be a serious loss that grows worse over time. It may involve one or both ears. If the loss of hearing is getting worse and is caused by Paget's disease, treating the disease may slow or stop the hearing loss. Hearing aids often may help improve hearing as well.

17. Q. Can Paget's disease affect vision?

- A. Yes. When the skull is involved, the nerves to the eye may be affected and cause some loss of vision. This happens very rarely.

18. Q. How does Paget's disease affect the teeth?

- A. When Paget's disease is in the facial bones, the teeth may become loose. Chewing can become a problem. Patients may also be at risk of infections after dental work. (Also see questions 24 and 25).

19. Q. Is there a relationship between Paget's disease and an overactive parathyroid gland?

- A. Yes. A few patients who have Paget's disease also have too much parathyroid hormone made by the parathyroid glands. This is known as primary hyperparathyroidism. When a person has this condition, the level of calcium in the blood becomes too high. It also causes the kidneys to excrete too much calcium. The reason why some patients have both diseases is not known.

Diet and Exercise

20. Q. Is there a relationship between diet and Paget's disease? Is calcium and/or vitamin D linked to Paget's disease?

- A. A person's diet does not cause Paget's disease. However, people who do not eat enough calcium and vitamin D may not have healthy bones. Among the elderly, this is quite common. Therefore it is suggested that all elderly people, including those with Paget's disease, have the recommended amount of calcium and vitamin D each day.

The recommended amount of calcium is 1000-1500mg a day.

For vitamin D the recommended amount is 1000 units. The preferred type of vitamin D is D₃ (cholecalciferol.) Recent studies show that vitamin D₃ stays in the blood longer than vitamin D₂ (ergocalciferol). Therefore D₃ is a better choice than D₂ for a vitamin D supplement.

These calcium and vitamin D supplements are most important for patients being treated with the bisphosphonate drugs. (See question 23)

Paget's disease patients with a history of kidney stones should discuss the use of calcium and vitamin D with their doctor.

Patients should discuss their intake of calcium and vitamin D with their doctor.

21. Q. What role does exercise play in managing Paget's disease?

- A. Exercise is very important for a number of reasons. It helps to keep bones healthy and joints mobile. It also helps control weight. However, before starting an exercise program, a Paget's disease patient should discuss the program with his or her doctor. It is important not to put too much stress on bones affected with Paget's disease.

Treatment

22. Q. Which doctors are specialists in Paget's disease?

- A. ● Endocrinologists (doctors who specialize in disorders of the hormones and metabolism) and
● Rheumatologists (doctors who specialize in disorders of the joints and muscles including arthritis)

Other specialists who may be called upon are:

- Orthopedic surgeons (surgeons who operate on bones and joints)
- Neurologists (doctors who treat disorders of the nervous system) and
- Otolaryngologists (ear, nose and throat doctors)

23. Q. What is the goal of treatment? What treatments are available in the U.S?

A. The goal of treatment is to relieve bone pain and keep the disease from getting worse.

In general, the therapies of choice are the four most potent bisphosphonate drugs: Reclast[®], Actonel[®], Fosamax[®] and Aredia[®]. Didronel[®], Skelid[®] or Miacalcin[®] may work well for some patients, but are seldom used.

Below is a description of drugs and their recommended doses for the treatment of Paget's disease. They are approved by the U.S. Food and Drug Administration (FDA). However some doctors who are experts in Paget's disease may sometimes prescribe different doses. None of these drugs should be used by people with severe kidney disease.

Bisphosphonates. Six bisphosphonates are now approved. Four are in tablet form to be taken by mouth and two are for intravenous use. As a rule, the drugs taken by mouth should be taken on an empty stomach. Specific instructions for taking each drug are in the chart below.

Patients who receive Reclast[®] and Aredia[®] should have kidney tests before each treatment as these drugs could harm the kidneys. Patients should drink fluids (such as water) before getting Reclast[®] or Aredia[®].

Calcitonin. Miacalcin[®] is a brand of synthetic salmon calcitonin. It is given by injection. The dose may vary from 50 to 100 units each day (or three times a week) for 6 to 18 months. Repeat courses can be given after brief rest periods. The nasal spray form of this drug is not approved or recommended for Paget's disease.

Drugs approved in the U.S. for the treatment of Paget's disease:

I. Bisphosphonates	Administration and Dosage
Intravenous	
<p>Zoledronic Acid (Injection) Trade Name: Reclast[®] (Novartis) Approved by FDA 2007 Reclast[®] is also marketed for treating Paget's disease with the name Aclasta[®] in more than 50 countries outside the U.S.</p>	<ul style="list-style-type: none"> ● Intravenous ● FDA approved administration is a 5 mg infusion given over 15 minutes ● To reduce the risk of low blood calcium after infusion, patients should receive 1500 mg calcium and 1000 units of vitamin D (preferably D₃) daily for two weeks after taking Reclast[®]. ● Patients with either low blood calcium or vitamin D deficiency should not be treated with Reclast[®] until the low blood calcium or vitamin D deficiency problems are corrected. ● Patients with significantly reduced renal function should not receive Reclast[®]. ● 4 mg zoledronic acid (injection) with the name Zometa[®] is marketed for oncology indications. ● Patients who have been treated with Zometa[®] for cancer-related conditions should not be treated with Reclast[®].
<p>Pamidronate Disodium Trade Name: Aredia[®] (Novartis) Approved by FDA 1994 Several generic forms of pamidronate are available.</p>	<ul style="list-style-type: none"> ● Intravenous ● The FDA approved regimen is a 30 mg intravenous infusion given over 4 hours on 3 consecutive days. <ul style="list-style-type: none"> - A single infusion of 60-90 mg given over 2-4 hours is effective in mild disease. - For more severe disease, 60 mg infusions given over 2-4 hours for 2 or more consecutive or non-consecutive days may be administered. <p>A course of pamidronate may be readministered at intervals as needed.</p> <ul style="list-style-type: none"> ● Serum creatinine (a measure of kidney function) should be tested before each pamidronate treatment. ● Serum calcium should be tested after each treatment. ● To reduce the risk of low blood calcium after infusion, patients should receive 1500 mg calcium and 1000 units of Vitamin D (preferably D₃) daily over two weeks. ● Patients with either low blood calcium or vitamin D deficiency should not be treated with Aredia[®] until the low blood calcium or vitamin D deficiency problems are corrected.

Oral Tablets	
Risedronate Sodium Trade Name: Actonel[®] (Procter & Gamble/ Aventis) Approved by FDA 1998	<ul style="list-style-type: none"> ● 30 mg tablet taken once daily for 2 months ● Must be taken on an empty stomach, with 6-8 oz tap water, in the morning ● Patients should wait at least 30 minutes after taking Actonel[®] before eating any food, drinking anything other than tap water, or taking any medication ● Should not lie down for at least 30 minutes after taking Actonel[®] (Patient may sit)
Alendronate Sodium (Fosamax[®]) Approved by FDA 1995	<ul style="list-style-type: none"> ● 40 mg tablet taken once daily for 6 months ● Must be taken on an empty stomach, with 6-8 oz of tap water, in the morning ● Same instructions as for Actonel[®] <p>Fosamax[®] 40 mg (Alendronate Sodium) tablets are available in generic form at retail pharmacies with the name <u>Alendronate Sodium Tablets</u>. A prescription is required.</p> <p>Fosamax[®] 40 mg brand tablets are no longer available through the Merck Paget Patient Support Program which was discontinued.</p>
Tiludronate Disodium Trade Name: Skelid[®] (Sanofi-Synthelabo) Approved by FDA 1997	<ul style="list-style-type: none"> ● 400 mg (two 200 mg tablets) taken once daily for 3 months ● Must be taken on an empty stomach with 6-8 oz of tap water ● Skelid[®] may be taken any time of day, as long as there is a period of 2 hours before and after eating food, drinking anything other than tap water, or taking any medication
Etidronate Disodium Trade Name: Didronel[®] (Procter & Gamble/ Aventis) Approved by FDA 1977	<ul style="list-style-type: none"> ● 200 to 400 mg taken once daily for 6 months ● Though the approved regimen is 200-400 mg once daily for 6 months, the higher dose (400 mg) is preferred ● Didronel[®] may be taken any time of day, as long as there is a period of 2 hours before and after eating food, drinking anything other than tap water, or taking any medication. ● A course of Didronel[®] should not exceed 6 months ● Repeat courses can be given after rest periods of at least 6 months duration

Fosamax[®], Skelid[®], and Actonel[®] should be used with caution by patients who have disorders affecting the esophagus or the stomach.

II. Calcitonin	Administration and Dosage
Trade Name: Miacalcin[®] (Novartis) Approved by FDA 1990	<ul style="list-style-type: none"> ● Injection ● 50 to 100 units daily or 3 times per week for 6-18 months

The cost of these drugs varies depending on where a patient lives and his or her insurance coverage.

Calcium and Vitamin D

To prevent low blood calcium, it is also important to take calcium and Vitamin D supplements, as prescribed by your doctor—except for patients who have had kidney stones

- calcium (1000-1500 mg daily) in divided doses such as 500 mg three times a day or 750 mg twice a day
- vitamin D (1000 units a day—preferably D₃)

Other Treatments

Pain medicines may help to relieve pain in bone and near joints. Examples of these are aspirin and NSAIDS (non-steroidal anti-inflammatory drugs) such as ibuprofen. The use of walking aids, shoe lifts, canes and physical therapy may be helpful when a patient has trouble walking due to the bowing of one or both legs.

24. Q. What is osteonecrosis of the jaw (ONJ)?

- A. Osteonecrosis of the jaw (ONJ) is a rare dental condition. It is an area of exposed jaw bone (top jaw bone or bottom jaw bone) that shows no sign of healing for 8 weeks. On those rare occasions when ONJ does occur, an invasive dental procedure, like a tooth extraction, implant surgery or other procedure has been performed. The gum over the affected area is worn away and the underlying bone is exposed. There may be pain in that part of the mouth. Antibiotics will heal the area for some patients.

Over the last few years, cases of ONJ have been reported mainly in cancer patients who have been treated with the intravenous bisphosphonate drugs. The dose used for treating cancer patients is as much as 10 times the dose used in the treatment of Paget's disease. There is concern - but not proof - that bisphosphonate drugs might cause ONJ. Many of the cancer patients were also treated with chemotherapy and steroid hormones. These treatments could also be risk factors for the development of ONJ.

Two known causes of ONJ are radiation therapy to the face (with exposure to the jaw bones) and severe mouth infections, particularly in individuals whose immune system is compromised.

25. Q. Should Paget's disease patients be concerned about taking bisphosphonate drugs because of the risk of developing ONJ?

- A. Probably not. Bisphosphonate drugs are used to treat osteoporosis as well as Paget's disease. Millions of osteoporosis patients have taken these drugs. Only an exceedingly small number of these osteoporosis patients have ever developed ONJ. There have literally been only a handful of patients with Paget's disease who have been reported to have developed ONJ.

All patients who are going to be treated with bisphosphonates for Paget's disease should have a routine dental exam and be in a regular program of oral health. This program does not have to be any different from what is recommended under normal circumstances for patients who are not being treated with bisphosphonates.

If a patient needs to have extensive dental work or oral surgery, it is best if the bisphosphonate treatment be delayed until the dental work is done. The dentist should be told if a patient is taking bisphosphonates if dental or oral surgery is needed. He or she can then choose the least invasive procedure.

It does not seem to matter if bisphosphonate drugs are being taken at the time of the dental work because these drugs stay in the bones for a very long time. So even if the bisphosphonate treatment is stopped, the drug is still in the bone.

26. Q. When should the patient follow up with his or her doctor after treatment with the bisphosphonate drugs?

- A. Patients who are taking the oral drugs should have an SAP blood test at the end of the treatment and again in three months. Then the SAP will be checked every six months to one year, depending on whether it was normal after the treatment.

Patients who are taking the intravenous drug should have an SAP blood test after the last treatment and then every three to six months.

27. Q. How does the doctor know if the drug treatment is working?

- A. The best way is the SAP blood test. If a patient's SAP was higher than normal when treatment was started and is in the normal range after the treatment, this means that the treatment has been successful. In some cases urine tests are also used to see how well the treatment is working.

28. Q. When is surgery recommended for Paget's disease?

- A. There are generally three problems due to Paget's disease which may lead to surgery. The first is fractures in bone affected with Paget's disease. If surgery is used to repair these fractures it may help the fractures heal in a better position. If needed, metal rods may be put in to stabilize the bone.

The second is arthritis where the joint is severely damaged. If drugs and physical therapy are no longer helpful and if disability is severe, the hip or knee joint may need to be replaced.

The third involves bone deformity, especially of the tibia—shin bone. Surgery can help to realign the bone with Paget's disease. This in turn may reduce the pain in the joints, especially the knees.

If it is possible, a patient having surgery on a bone with Paget's disease should be treated with Reclast[®], Aredia[®], Actonel[®], Fosamax[®] or calcitonin several months before surgery. This helps decrease bleeding and may prevent other complications. The patient having surgery should discuss pre-treatment with his or her doctor.

Surgery on the head and spine (neurosurgery) can be helpful for:

- enlargement of the skull that causes the back of the skull to deform and injure the nervous system or bone; and
- overgrowth of the spine that presses on the spinal cord and spinal nerves.

However, if medical treatment corrects the symptoms surgery may not be needed.

The Paget Foundation for Paget's Disease of Bone and Related Disorders provides information and programs for consumers and health professionals on several bone disorders including Paget's disease of bone, primary hyperparathyroidism, fibrous dysplasia, osteopetrosis, and the complications of certain cancers on the skeleton.

Foundation programs and services include:
Patient Education and Assistance, Professional Education, Public Education,
Research & Advocacy

A copy of the Foundation's annual report is available by writing to the Foundation office or the Office of the Attorney General, Charities Bureau, 120 Broadway, New York, NY 10271.



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