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The National Osteonecrosis Foundation
and
The Center for Osteonecrosis Research and Education

OSTEONECROSIS

INTRODUCTION

Osteonecrosis (ON) affects approximately 20,000 new patients per year in the United States. Although any age group may develop ON, most patients are between 20 and 50 years old, with the average age in the late 30's. The diagnosis of ON does not affect life expectancy, and for this reason several hundred thousand patients are living with this disease in the U.S. alone.

What is osteonecrosis? First, you should understand that bone is a living tissue with living cells and a blood supply. Osteonecrosis means death of bone which can occur from the loss of the blood supply or by some other means (see 'What Causes Osteonecrosis?'). It has been known by a number of other names including ischemic necrosis of bone, aseptic necrosis or avascular necrosis (AVN). AVN has been quite popular in its use because it is shorter to say and write. More recently the term ON (osteonecrosis) has been adopted.

In the following sections, a review of the factors that play a role in your individual treatment and results of those treatments are discussed. It is important to understand that each patient is unique. Differences in the amount of bone involvement, other diseases that you may have, your level of activity, and other factors are extremely important in determining the appropriate treatment for each individual patient. None of the information presented here is intended to take the place of the individual patient-physician encounter. Rather, this brochure is designed to help you understand more about the disease and will assist you in discussing specific treatment options with your physician.

Who's at Risk?

If a person is completely healthy, the risk of getting osteonecrosis is quite small, probably less than one in 100,000. Another way to understand this is that most of the people who get ON probably have an underlying health problem. Most patients are between 20 and 50 years old with an average age of 38. Patients over the age of 50 are likely to have developed ON either by a fracture of the hip or more rarely in association with disease of the major blood vessels to the lower leg.

Legg-Calve-Perthes Disease

Children, ranging in age from 2 to early teenage years, get a form of osteonecrosis called Legg-Calve-Perthes disease (Perthes for short) after the three doctors who first described it. Treatment for Perthes is completely different than for adult ON. A pamphlet describing this disease is available from the National Osteonecrosis Foundation.

What Causes Osteonecrosis?

There are two major forms of ON, post-traumatic and non-traumatic. Examples of post-traumatic ON, a common cause of ON, include displaced fractures or dislocations. Minor trauma is not believed to cause ON. Even major injury does not often result in ON. Certain kinds of fracture, where the blood vessels to part of the bone have been physically damaged, may result in ON.

Non-traumatic ON occurs when their is no history of trauma. Scientists have identified a number of risk factors that may be associated with non-traumatic ON. We do not know how these risk factors may lead to the development of the disease. There are many different ideas (also called hypotheses). But these ideas have not been proven. There are some cases of osteonecrosis that occur in patients that are otherwise completely healthy with no detectable risk factors. This catagory is called "idiopathic", a word meaning "of unknown cause".

What are the Risk Factors?

One of the most common causes of osteonecrosis of the hip and of other joints is a displaced fracture or a dislocation. However, this brochure focuses on non-traumatic osteonecrosis. The risk factors for osteonecrosis can be separated into two catagories: definite and probable. The most common risk factor is a history of high dose steroid treatment for some medical condition (e.g., Lupus). Low dose steroids (cortisone, prednisone, etc.) commonly used for bee stings, poison ivy and acute allergies are not

thought to cause osteonecrosis. The next most common associated condition is a history of high alcohol use. The greater the alcohol consumption, the higher the risk of osteonecrosis.

CAUSES OF OSTEONECROSIS		
DEFINITE	**PROBABLE**	
• Major Trauma Fractures	• Corticosteroids, High Dosages	• Blood Clotting Disorders
• Dislocations	• Alcohol	• Pancreatitis
• Caisson Disease (Deep Sea Divers)	• Lipid Disturbances	• Kidney Disease
• Sickle Cell Disease	• Connective Tissue Disease	• Liver Disease
• Postirradiation		• Lupus
• Chemotherapy		• Smoking
• Arterial Disease		
• Gaucher's Disease		

First Symptoms

Unfortunately many patients with ON have had the disease for quite some time before symptoms are present. The initial symptoms are usually felt during activity and include pain or aching in the affected joint. Symptoms usually begin slowly and may initially be sporadic. Sometimes, the pain may begin quite suddenly. As the disease progresses, the pain increases and is associated with stiffness and loss of motion of the involved joint. Limping becomes common. The hip is the most common joint affected, and the pain is usually felt in the groin.

Progression of the Disease

In the earliest stage of the disease, x-rays appear normal and the

diagnosis is made using MRI. Once it can be seen on x-ray, it is not actually the dead bone that can be seen but the healing response of the living bone to the area of necrosis. The advanced stages of ON begin when the dead bone starts to fail mechanically through a process of microfractures of the bone. Eventually, this will result in damage to the other side of the joint, requiring major joint reconstruction.

These x-rays of the hip show the different stages of the disease. At first (stage I), there are no detectable changes on x-ray (fig A). In stage II, there are some changes but the surface is still intact (fig B). As the disease progresses, the surace begins to collapse (fig C) until, finally, the integrity of the joint is destroyed (fig D).

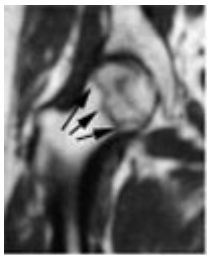
In the more advanced stages of the disease and/or when more of the joint is damaged, it is less likely that the natural joint can be preserved. Fortunately, joint replacement procedures today are highly successful, even in the relatively young patients affected by ON. It is always the physicians desire to preserve the normal joint whenever possible. Unfortunately many patients do not visit the doctor until their joint has an advanced stage of the disease.

Extent of Disease

The femoral head (the ball part of the hip) is the most frequent bone involved and will be used for this discussion. It is rare for the entire weight-bearing surface of the femoral head to be involved. However if more than half of the surface is involved, treatments designed to preserve the femoral head have a much lower chance of success.

MRI's of Femoral Heads
diagnosed with Osteonecrosis

Small Lesion



Large Lesion

How Is Osteonecrosis Diagnosed?

The first, and most important, thing that a physician can do is to perform a thorough physical examination and to ask questions about your medical history. Once there is a suspicion of osteonecrosis, your physician will likely obtain one or more of the following tests:

- X-ray
- Magnetic Resonance Imaging (MRI)
- Bone Scan
- Computed Tomography (CT)
- Biopsy

The principle diagnostic tool is the x-ray. By the time that most patients have significant symptoms, the disease is advanced enough to be seen on standard x-rays. In most cases the x-ray will show the area of bone that is involved. However, the very earliest stages of ON cannot be seen on a regular x-ray. A widely used tool is called an MRI. [This test does not involve x-ray radiation.] These special images are able to detect tissue changes that are not seen on a plain x-ray. Occasionally, your doctor may order a CT scan, which is a special series of x-rays interpreted by the computer to show the three dimensional structure of the bone. Any of these tests will help the doctor to determine how advanced the disease is in your case.

TREATMENT

Introduction

Before entering into a description of some of the treatments available for ON, it is important to understand the concept of risk/benefit ratio. Any surgical procedure has a certain element of risk involved. Even no treatment at all has the risk that the disease will progress, so doing nothing is not risk free. Some procedures may have a lower likelihood of success but have very little risk. Other procedures may have a higher

degree of success, but also have a higher degree of risk. The physician must work with the patient in assessing all the factors that evaluate both risk and benefit for the patient in their particular circumstance. What is right for one patient may be absolutely wrong for another. This is particularly true for ON because each patient presents with a unique set of factors (age, associated disease, specific joint(s) involved, extent and progression of disease). Any treatment needs to be determined between you and your treating physician. Ask questions, get answers!

Non-Surgical Treatment

Protected weight bearing Canes, crutches or a walker are useful in alleviating the pain associated with ON. They can also be useful in protecting the joint between the time of diagnosis and scheduling of elective surgery. Limiting weight bearing may also play a role in limiting progression while associated medical conditions are managed. However, protected weight bearing alone is never an adequate treatment for ON nor will it result in cure of the condition, no matter how long it is maintained. Rarely, an associated medical condition may result in a patient not being able to have surgery. In this case, protected weight bearing may be recommended for pain management.

Pharmaceutical Treatment for Osteonecrosis

There are no established pharmaceuticals (drugs) for the prevention or treatment of osteonecrosis. In order to treat the disease, we must first understand how the disease develops. In spite of considerable effort by researchers, we still do not know for sure what causes some forms of osteonecrosis (that is, the forms that are not a result of a fracture or radiation). We've identified several risk factors, but it is not known what effect eliminating or treating the risk factors has on the disease once the disease has begun. However, this is not meant to be a pessimistic outlook for the pharmaceutical treatment of osteonecrosis. There are several studies that are being undertaken to evaluate the potential of pharmaceutical treatment. This article will summarize their findings to date.

There are several levels of evidence that can be used to support a position by the medical community. They range from the treatment of one patient (a case report) to comprehensive studies evaluating large numbers of patients. Most of the studies concerning the pharmaceutical treatment of osteonecrosis fall somewhere in between – with many being a report of a series of patients treated with a medication with no control group receiving a placebo. It is important to understand this so that you can place the significance of these reports in their proper context.

Lipid Lowering Agents

Two hypotheses concerning osteonecrosis relate to lipids (fats). One hypothesis proposes that there is an increase in the number of fat cells (lipocytes) in the bone marrow of the diseased joint. Another hypothesis is that there is an increase in the amount of fat contained within cells that eventually causes the cell to malfunction or die. With this in mind, scientists have investigated whether lipid-clearing agents can be used to prevent the development of osteonecrosis1,2,3. In a clinical study of 284 patients taking high dose corticosteroids – the type of steroid used to treat inflammation, a lower incidence of osteonecrosis (1%) was found than is usually reported for this patient population (3-20%)3. Further studies are needed to confirm or disprove these findings.

Anticoagulants

There is increasing evidence that there are abnormal levels of specific factors involved in the coagulation/blood clotting system in some patients with osteonecrosis4,5. One study evaluated the use of Stanozolol, an anabolic steroid, in 5 patients6. They had variable results with several patients having relief of pain yet progression of the disease as observed by x-rays. In a separate study, twenty-eight patients (35 hips) were treated for 12 weeks with Enoxaparin, a drug used to prevent clotting or prevent existing clots from getting larger (an anticoagulant) 7. After two years, most of the hips had not progressed past the early stage of the disease (Ficat Stage I or II) and most (31/35) did not require surgery. Further studies are needed to confirm or disprove these findings.

Hypertensive Medications

Hypertensive medications are drugs used to treat high blood pressure. Several studies have shown that osteonecrosis is associated with an increase in the pressure within the affected bone. One surgical treatment for this is core decompression. It is believed that a core biopsy or biopsies in the diseased bone relieves the pressure and thereby relieves the pain. Another approach to this would be to treat the patient with blood pressure lowering medications. In one study, seventeen patients with early stage osteonecrosis underwent treatment with ilioprost, a vasodilator – a drug used to reduce high blood pressure8. At one year, function and pain levels improved for these patients. The average clinical assessment scores were significantly improved following treatment. They also found that the amount of bone edema (extra fluid) present in the bone was significantly less. Similar results were found for another drug, Nifedipine9. Further studies are needed to confirm or disprove these findings.

Bisphosphonates

Bisphosphonates are a class of drugs that have been used to treat osteoporosis – a disease that is characterized by a low bone mass. Recently, in an effort to reduce bone loss, one bisphosphonate - alendronate has been evaluated in 60 patients diagnosed with osteonecrosis of the hip10. All patients had symptomatic improvement at one year. Although the follow-up time ranged from three months to five years, only six patients (ten hips) progressed to the point of needing surgery. It is important to note that these patients were also instructed to avoid bearing weight on their affected hip. Recently, concern has been raised relating to a possible association between bisphosphonate therapy and an increased incidence of osteonecrosis of the jaw11,12. Further study is needed to clarify this possible complication.

Drug Studies

You do not need to be in a drug study to receive pharmaceutical treatment for osteonecrosis. These medications are not experimental and can be prescribed by a physician. However, whether they will be prescribed for you is dependent on the physicians experience and your individual circumstance (the size of the affect area, how far along the disease has progressed, for example). As we have emphasized, all of these treatments must be evaluated more thoroughly before the medical community will accept them as standard treatment.

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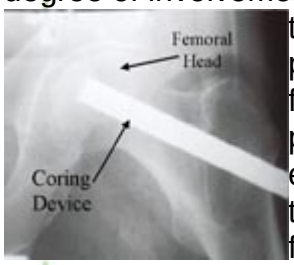
Surgical Treatment

Core Decompression This is a surgical procedure that involves taking a plug of bone out of the involved area. It is applicable for mild to moderate degree of involvement that has not yet progressed to collapse. Because



this involves creating a hole in the bone, six weeks of protected weight bearing is necessary to avoid fracture through the hole. Pain relief from this procedure has been excellent, but it has not been as effective at delaying the progression of the disease in the long term. In centers that do this procedure frequently, most studies have reported good results in the appropriate cases. However, there is some controversy about this procedure with a few studies that have been reported showing generally poor results.

Bone Grafting When a section of the bone has died, as is the case in ON, it doesn't spontaneously heal. One approach to this problem is to surgically remove the dead bone and fill the empty space with bone graft that is either taken from the patient or from the bone bank. The success of this approach depends upon the quantity of bone that has died.

Vascularized Bone Grafting Regular bone graft, whether from the bone bank or from the patient, is itself dead bone. It serves as a scaffold for the body to build new bone around, but the body also has to grow a new blood supply. For this procedure, a bone with its blood vessels is taken from the patient and hooked up to blood vessels near the hip. The dead bone is removed from the femoral head and replaced with the grafted bone that carries with it its own blood supply. The advantage of this approach is that the body doesn't have to rebuild a new blood supply and the bone graft keeps its physical and mechanical properties. This is most appropriate prior to the collapse of the joint, but is sometimes used in cases with early (limited) collapse.

Healing and complete filling of the defect still has to take place, during which time crutches or a walker has to be used. The disadvantage of this procedure is that a substantial piece of bone has to be taken from the lower leg (the fibula, the smaller bone of the lower leg below the knee). Some patients may develop pain in the area from which the bone graft is taken. The operation also takes several hours and requires a team experienced in these techniques. The patient is also required to be on crutches for several months. If both hips are involved, it may be necessary to delay treating one hip for quite some time during which period the femoral head may undergo collapse.

Osteotomy (Cutting the Bone) Usually the location of the ON is in the area of the bone that bears weight. In some cases the bone can be cut

below the area of involvement and rotated or turned so that another portion of the bone, that is not involved in the ON, can become the new weight-bearing area. These operations are not very common anymore, but may apply to special cases with smaller lesions.

Femoral Head Resurfacing [FHR] Initially only the femoral head is involved, not the socket of the hip joint. FHR involves implanting a metal hemisphere over the femoral head, which exactly matches the size of the original femoral head. This is similar to capping a tooth when the root is still good, as opposed to pulling the tooth and putting in a false tooth. It is known that over a period of many years, the metal head will gradually wear out the socket and will need to be converted to a total hip replacement. This procedure is designed to "buy time" for the younger individual whose extent of disease or degree of progression is such that one of the preservative procedures listed above cannot be performed. Most patients with ON are under 50. It is generally believed that total hip replacement (THR) today will not last the 30+ years most of these patients will require. Therefore, it is possible that at least two procedures will be necessary for the treatment of this disease during a patient's lifetime. If the 2 procedures are a femoral head resurfacing followed later by a primary total hip replacement, this is preferable to a primary THR followed by a revision THR. However, although the early results have been favorable, FHR is still a relatively new procedure which is currently being evaluated.

Femoral Head Replacement This is basically half a total hip replacement. All comments about femoral head resurfacing apply to femoral head replacement. However, because a femoral head replacement also puts a stem inside the femoral bone (the femoral shaft) it is a little more extensive than the resurfacing procedure. If it needs to be revised, it is a little more difficult to convert to a total hip replacement than the resurfacing procedure. There is also no evidence that a femoral head replacement is more successful than a femoral head resurfacing.

Metal-on-Metal Resurfacing The original concept of replacing the surface of the femoral head with metal and the acetabulum with a plastic liner had a high failure rate due to failure on the acetabular side. The concept has reappeared with a metal liner on the socket side. Experience is limited but the procedure shows promise.

Total Hip Replacement [THR] When the ON is advanced to the point that there is involvement of the socket as well, then the only thing that will be effective is either a hip

fusion (making the hip completely stiff) or a total hip replacement (THR). THR is one of the most successful surgical procedures ever devised. Success rates are usually above 95%! The problem with total hip replacements for patients with ON is that it is not uncommon for the patient to have a life expectancy of more than 40 or even 50 years. With current technology we don't think that it is likely that a THR will last that long. For this reason, many physicians will want to try some procedure to put off THR for a few years even when it is known that that procedure will not in itself be successful forever. If your disease is advanced, and/or extensive, then THR may be the only thing that makes sense. Work is currently in progress to develop and evaluate newer total hip replacements, such as ceramic-on-ceramic devices, which may be much more durable than present components, and which theoretically might last a lifetime even in younger patients with ON.

Osteonecrosis of the knee and shoulder and ankle

Ninety per cent of patients afflicted by osteonecrosis have osteonecrosis at the hip. However osteonecrosis also can attack the knee, shoulder and ankle in that order frequency. Moreover, patients who have osteonecrosis at the hip are more likely to have another joint involved. However, any of these other joints can be involved independently. About 3% of patients with osteonecrosis will have more than two joints involved. The most common combination is hip and knee. It is uncommon for the shoulder or ankle to be involved as an isolated joint. Much of what has been written earlier about osteonecrosis of the hip also applies to these other joints. The classification systems are essentially the same, and the progression of the disease is similar, passing from x-ray negative, to x-ray positive without collapse, too early collapse and finally to extensive joint destruction. These other joints also may experience small or large lesions with the same significance as for the hip. The larger the lesion, the more likely it is to collapse. The further the progression, the less likely that the joint can be preserved. There are some differences with each of the individual joints in both treatment and consequences of osteonecrosis which are based partly on the function of those joints, partly on the anatomy, and partly on the success of joint replacement which is the ultimate treatment for advanced disease. This section will detail each of the joints and their peculiarity.

Osteonecrosis of the knee -- the knee is the second most common joint to be affected by osteonecrosis. Although the numbers are difficult to determine with any degree of accuracy, in our experience we see about one case of osteonecrosis of the knee for every 10 cases of the hip. Although some of these patients will have knee involvement as an isolated joint, most patients with osteonecrosis of the knee will have osteonecrosis

somewhere else. The knee is a very complex joint and can really be divided into three compartments; the medial compartment which is the inside of the knee between the femur bone and the tibia or shinbone, the lateral compartment which is the outside of the day the, and the patellofemoral compartment (kneecap). The most common involvement is the distal femur or the thigh bone portion of the knee. It is not uncommon for the tibia or shinbone also to be involved, but it is unusual for the patella (kneecap) to be involved.

In the hip, if the lesion is large enough, progression to collapse is almost certain. There are some small lesions, usually asymptomatic, that do not collapse. This is not necessarily the case in the knee. The natural history of osteonecrosis of the knee is less certain than it is for the hip. In general we do not treat asymptomatic osteonecrosis of the knee, i.e. osteonecrosis that is picked up by MRI but for which the patient has no symptoms. If the patient has symptoms, and the lesion has not collapsed, we have performed and reported on core decompression with good success. Core decompression usually results in immediate relief of symptoms. However, because the natural history and natural progression of osteonecrosis of the knee is less predictable, it is not certain that the core decompression alters the natural history. We have had patients with osteonecrosis and knee pain who have been treated with core decompression and continued to have pain relief for up to 20 years.

Once the osteonecrosis has progressed to collapse, the only treatment is total knee replacement. In general, we do not recommend partial knee replacement, because non-replaced areas of bone can progress, leading to the need for revision or conversion of the partial knee replacement to a total knee replacement. We have not yet seen a patient whose osteonecrosis was so advanced or so extensive that a total replacement could not be done.

Shoulder -- osteonecrosis of the shoulder has an even more variable natural history than the knee. The area of the involvement of the humeral head (shoulder) is that area of the head which is in contact with the socket when the elbow is held at about 40° of flexion and 20° away from the body. It is possible to effectively use one's hands with the elbows held at the side, and therefore avoid contact of the humeral head with the socket in the area to involvement with osteonecrosis. Therefore unless the lesion is very large, or collapse is extensive, most patients will benefit from core decompression. Although shoulder replacement is done, the success rate is not as great as for the hip and knee, and the results may not be as long-lasting. Therefore if a conservative procedure like core decompression can grant the patient relief of symptoms and delay the need for shoulder replacement, that conservative procedure is justified. We have had good

results from core decompression even in those patients with early collapse. This is not the case with early collapse of the hip, for which core decompression should not be done except in unusual cases.

Ankle -- the ankle bone (talus) is fortunately not involved with osteonecrosis very often. It represents a real problem for the orthopedic surgeon (and the patient). Historically ankle replacements have not been very successful. Ankle fusion can be performed with extensive bone grafting. However, when the ankle bone is involved with osteonecrosis, because the bone is dead, ankle fusion is also not very successful. We have had some limited success with core decompression and would recommend it as a trial, mostly because nothing else works very well. An exterior ankle brace may be necessary.

Can It Be Prevented?

At present, there is no known prevention. However, it is reasonable to believe that if some of the risk factors are treated or eliminated, you would decrease your risk for getting the disease. For this reason, steroids should only be taken as necessary and alcohol consumption should always be in moderation. Some experimental drug protocols are being evaluated which may have a place in treatment or prevention in the future.

Early Recognition and Intervention

An important message has been learned over the past few years in the treatment of osteonecrosis. Early diagnosis and early intervention provides the best opportunity for alleviating the collapse of the joint surface and delaying the need for hip replacement surgery. The only other treatment option is hip arthrodesis - surgical fusion. Since this condition commonly occurs in both hips, it’s important that both hips be thoroughly assessed at each evaluation. Furthermore, if osteonecrosis is first diagnosed in a joint other than the hip, the hip should also be evaluated.

THE FUTURE

Currently, there are several studies being conducted to evaluate drugs that may lead to the prevention of this disease. The effectiveness of these drugs has not been proven in scientifically controlled studies in large numbers of patients. But they do offer hope for the future.

Other treatments are being evaluated to improve the results of the current surgical treatments. Bone graft substitutes and electrical stimulation are being studied in select centers throughout the country.

The future is dependent on a better understanding of why some people get the disease and some do not even when they have the same underlying conditions (steroids, alcohol, etc.) Because the disease does not affect large numbers and because most physicians do not see a lot of patients with osteonecrosis, it is important that an organization like the **National Osteonecrosis Foundation** brings together patients, their families, and physicians to promote increased awareness of this disease and to support large scale research efforts.

The National Osteonecrosis Foundation

The National Osteonecrosis Foundation is made up of a group of patients, their families, physicians, and other caring individulas who are interested in finding a cure for osteonecrosis. It is the mission of this foundation to provide support for medical research and for the education of patients, physicians, and other health professionals. If you are interested in more information, please contact us:

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Websites:

NONF Website
http://www.osteonecrosis.org

Support Group for Patients with ON
http://osteonecrosisavnsupport.org/index.html

Support Group for Patients with Perthes
http://maxpages.com/lpsupportgroup

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