

1. What is bone and what is the bone structure?

The skeletal system includes the bones of the skeleton and the cartilages, ligaments, and other connective tissue that stabilize or connect the bones. In addition to supporting the weight of the body, bones work together with muscles to maintain body position and to produce controlled, precise movements.

Bones grow from their ends (extremities).

Under normal circumstances bones stop growing when the owner reaches his/.her late teens or early twenties.

Bone marrow produces stem cells, such as erythrocytes (red blood cells) and leucocytes (white blood cells).

2. How does the bone development and growth happen in the body?

The growth of the skeleton determines the size and proportions of the body. Bones begin to form in a mother's womb about six weeks after fertilization, and portions of the skeleton do not stop growing until about the age of 25.

Most bones originate as hyaline cartilage. The cartilage is gradually converted to bone through a process called ossification. Bone growth begins at the centre of the cartilage. As bones enlarge, bone growth activity shifts to the ends of the bones (an area commonly called the growth plate), which results in an increase in bone length.

3. What are the functions of bone in the body?

There are 206 bones in the adult body. The bones of the body perform five main functions.

Provide support for the body — The skeletal system provides structural support for the entire body. Individual bones or groups of bones provide a framework for the attachment of soft tissues and organs.

Store minerals and lipids — Calcium is the most abundant mineral in the body. (Ninety-nine percent of the body's calcium is found in the skeleton.) The calcium salts of bone are a valuable mineral reserve that maintains normal concentrations of calcium and phosphate ions in body fluids. The bones of the skeleton also store energy reserves as lipids in areas filled with yellow marrow.

Produce blood cells — Red blood cells, white blood cells, and other blood elements are produced in the red marrow, which fills the internal cavities of many bones.

Protect body organs — Many soft tissues and organs are surrounded by skeletal elements. For example, the rib cage protects the heart and lungs, the skull protects the brain, the vertebrae protect the spinal cord, and the pelvis protects the delicate reproductive organs.

Provide leverage and movement — Many bones function as levers that can change the magnitude and direction of the forces generated by muscles.

4. Explain Bone healing?

When bone breaks, within a couple hours a blood clot forms around the break. Inside the blood clot special cells called phagocytes begin cleaning bone fragments and killing any germs which might have gotten in around the break. Phagocytes are part of the immune system. The word phagocyte means 'cells that eat' and these cells surround and destroy unwanted bacteria and material.

Next, a soft structure mostly of collagen is created around the fracture by another special group of cells called chondroblasts.

A hard structure forms next as osteoblast cells create new bone, adding minerals to make it hard.

Lastly, the bone is remodelled. Special cells called osteoclasts break down extra bone around the fracture until it's completely healed and returned to its original shape. Bone remodelling is a very slow process which can take anywhere from 3 to 9 years to complete!

5. **What is AVN (avascular necrosis of hip, osteonecrosis)?**

The bones and bone marrow of the human body are made up of living cells that need a steady blood supply to stay healthy. If blood flow to these cells greatly decreases, the cells may die. Avascular Necrosis (AVN) is a cellular death of bone component, which occurs when the blood supply to the bones is temporarily or permanently blocked. In the absence of blood, bone tissues die and bone collapses. If this condition isn't treated, it leads to severe pain, resulting in Arthritis. Avascular Necrosis is also called Osteonecrosis or Aseptic Necrosis. . Different stages of osteonecrosis can be distinguished of which stages I & II represent the stages before fracture and stages III & IV the stages after fracture. This condition leads to arthritis and joint gets damaged.

6. **What are causes of AVN?**

Avascular necrosis occurs when blood flow to a bone is interrupted or reduced. Reduced blood supply can be caused by:

Joint or bone trauma. An injury, such as a dislocated joint, might damage nearby blood vessels. Cancer treatments involving radiation also can weaken bone and harm blood vessels.

Fatty deposits in blood vessels. The fat (lipids) can block small blood vessels, reducing the blood flow that feeds bones.

Certain diseases. Medical conditions, such as sickle cell anemia and Gaucher's disease, also can cause diminished blood flow to bone.

7. **What are the common areas affected by AVN?**

AVN is most common in the hip and the shoulder, but can affect other large joints as well, such as knee, elbow, wrist and ankle. More than 20,000 people each year enter hospitals for treatment of Osteonecrosis of the hip. In many cases, both hips are affected by the disease.

8. **What are the early symptoms of AVN?**

Unfortunately many patients with AVN have the disease for quite some time before the symptoms appear. 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.

9. **Who is at risk?**

If a person is completely healthy, the risk of getting Osteonecrosis is quite less. Another way to understand this is that most of the people who get AVN 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 AVN either by a fracture of the hip or more rarely in association with disease of the major blood vessels to the lower leg.

10. What are the treatment options available?

Core Decompression- This is a surgical procedure that involves taking a plug of bone out of the involved area. It's 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. 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 AVN, it does not 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 (Autograft) or from the bone bank (Allograft). The success of this approach depends upon the quantity of bone that has died. Disadvantages of Autograft include limited quantities of bone for harvest and donor-site morbidity. Disadvantages of Allograft include delayed vascular penetration, slow bone formation, accelerated bone resorption, transmission of infection and lack of histocompatibility.

Osteotomy - In Osteotomy, 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 AVN can become the new weight-bearing area. These operations are not very common anymore, but may apply to special cases with smaller defects.

Autologous Bone Implantation (ABI-Ossron) - Bone regeneration by Autologous Cell Implantation is one of the most promising treatment concepts currently being developed. ABI is a patient specific, tailor made regenerative medical treatment and consists of 'cutting-edge' technology. If cultured autologous cells are successfully used for this treatment, some problems related to bone graft techniques might be overcome, such as donor site morbidity in Autografts and immunological problems in Allografts. As the amount of aspiration volume at one site is limited and the number of bone forming cells is small, it's assumed that the culturing of cells and their subsequent implantation is the most feasible method to overcome such a problem.

11. What is the procedure of ABI-Ossron?

Autologous Bone Implantation (ABI) procedure involves the following :-

A biopsy is performed to collect the patient's bone marrow which forms the source of osteoblasts that are to be cultured. It's a minimally invasive procedure where needle is inserted in iliac crest/ hip bone and 4 ml marrow is aspirated. This procedure takes just 10 minutes.

Biopsy is then sent to laboratory where it is cultured and multiplied upto 48 million osteoblasts under highly stringent conditions for approximately 4 weeks. Once the cells reach desired number, date of implantation (stage 2) is decided.

Cultured cells are mixed with a gel that acts as a scaffold, and this cell-gel mixture is implanted at defect site in a minimally invasive surgery. After surgery patient has to undergo proper rehabilitation therapy for regeneration of damaged bone. The patient is required to be in the hospital for 2—3 days post implantation.

12. Who would be a suitable candidate for bone implantation treatment ?

Candidate having hip joint pains, non-union fractures due to accident, bone weakness, immobility and restricted movement in joint etc.

13. Who is a not a candidate for autologous bone implantation ?

Generally people who have previously undergone hip joint arthroplasty, bone marrow transplantation, osteoarthritis, are on osteoporosis drugs and corticosteroids etc.

14. Am I a candidate for bone implantation even if I've undergone other treatments for my problem ?

If you are experiencing pain and swelling in your problem area, and you are limiting your daily activities, you may be a candidate for this therapy.

15. What is bone marrow ? How does the doctor collect my bone marrow cells/ how is biopsy done for this procedure ?

Bone marrow is the soft, spongy substance that fills the inner cavities of bones. It is where blood is produced with red and white blood cells.

When you are taken into the operating room, you will be placed on your stomach. A special needle is placed through the skin into the marrow cavity of the hipbone, where stem cells and blood are aspirated .

About 4 ml of bone marrow are collected during the harvest procedure. Collection generally takes about an hour, but each individual donation varies.

It is a simple day care procedure in the hospital where discharge is given the same day after the procedure has been completed.

16. How long does it take to grow the cells?

After your biopsy is taken, it is sent to Regrow's FDA-licensed and regulated cell therapy manufacturing facility in Lonavala, Maharashtra for processing.

After your biopsy arrives at the facility, it is processed and then cryopreserved awaiting the scheduling of your implantation procedure. You and your surgeon will determine when the time is right for your implantation procedure.

Once your implantation procedure is scheduled, your biopsy is removed from cryopreservation. The bone marrow cells (osteoblasts) undergo the final culturing (multiplying) phase which is timed to be completed a few days prior to your implantation procedure.

In total, it takes about 3 to 5 weeks for the cells from your biopsy to increase to approximately 48 million cells (1-4 vials).

17. Where is Ossron processed?

Processing of ABI-Ossron is done in state-of-the-art facility centre under highly controlled conditions. Laboratory facility is certified with:

- a) Good Manufacturing Practices (GMP)
- b) Good Laboratory Practices (GLP)
- c) Good Clinical Practices (GCP)
- d) Quality Management System (ISO 13485:2013)
- e) Ministry of Science & Technology

In addition to these accreditations, certificate of analysis (COA) is provided by the laboratory to the patient for every Ossron product that passes all specifications given by regulatory norms.

18. How long will it take to regenerate new bone after ABI-Ossron?

Following the implantation, patients can immediately return to their daily routine and do not require hospitalization. Naturally, every case is different. In injury cases, the goal is to achieve full range of motion within 12 weeks. As a general guide, 4-5 months are required after the implantation for the osteoblasts to successfully attach and alleviate the symptoms. Most people can safely return to the physical activities they enjoyed before their injury, including all types of sports. However, for all patients, rehabilitation is vital to a successful outcome with Ossron

19. Are there any complications of autologous bone implantation?

There is no fear of implant rejection as osteoblasts are harvested from patients' own body. However, rarely surgical procedure-linked complications may surface unless it is done by experts.

20. Will I need physical therapy following this surgery?

Yes, you will need to follow a rehabilitation program; your doctor and physical therapist will design a program for you based on the size, location, and severity of your bone injury.

Of course, rehabilitation requires dedication, but once you get through it, you should be able to enjoy a long-lasting, positive clinical outcome

21. What is a typical recovery post discharge?

- Patients are instructed not to strain the hip joint with heavy lifting, squatting, jogging, running or other unusual activities.
- Home exercise programs to strengthen the muscles around the buttock and thigh will be given to each patient as follows:

Day of Implant - 4 weeks: Complete Bed Rest

4th week – 6th week: Passive Lower Limb Exercises:

- Do each exercise 10 times or move to the point of resistance and hold for 30 seconds.
- Begin exercises slowly, doing each exercise a few times only and gradually build up to more.

- Try to achieve full range of motion by moving until you feel a slight stretch, but don't force a movement.
- Move only to the point of resistance. Do not force the movement.
- Keep limbs supported throughout motion.

7th Week – 10th Week: Non Weight Bearing (Mobilization with Walker / Crutches):

- Stand comfortably and erect with your weight evenly balanced on your walker.
- Move your walker forward a short distance.
- Then move forward, lifting your operated leg so that the heel of your foot will touch the floor first.
- As you move, your knee and ankle will bend and your entire foot will rest evenly on the floor.
- As you complete the step allow your toe to lift off the floor.
- Move the walker again and your knee and hip will again reach forward for your next step.
- Remember, touch your heel first, then flatten your foot, then lift your toes off the floor.
- Try to walk as smoothly as you can. Don't hurry. As your muscle strength and endurance improve, you may spend more time walking. Gradually, you will put more and more weight on your leg.

Note :- You can return to work at this point of time with limited mobility and care taken

11th Week – 14th Week: Partial Weight Bearing:

- Check the body weight.
- Stand with two crutches
- Bear just 10% of body weight equally on both the foot initially.

After 15th Week: Full Weight Bearing:

- Walking with Cane or Crutch

A walker is often used for the first several weeks to help your balance and to avoid falls. A cane or a crutch is then used for several more weeks until your full strength and balance skills have returned.

Use the cane or crutch in the hand opposite the operated hip.

You are ready to use a cane or single crutch when you can stand and balance without your walker, when your weight is placed fully on both feet, and when you are no longer leaning on your hands while using your walker.

16th Week onwards: Climbing Stairs

- Stair Climbing and Descending

The ability to go up and down stairs requires both flexibility and strength. At first, you will need a handrail for support and you will only be able to go one step at a time.

Always lead up the stairs with your good leg and down the stairs with your operated leg. Remember "up with the good" and "down with the bad." You may want to have someone help you until you have regained most of your strength and mobility. Do not try to climb

steps higher than those of the standard height of seven inches and always use the handrail for balance.

22. What is my activity level after bone Repair? When can I start playing sports again?

Depending on the location and degree of bone damage formation of new bone during rehabilitation ,you and your doctor will decide when you are ready to return to an active lifestyle based on your body's speedy recovery.

23. How is my activity level measured after the implantation?

To assess the efficacy of the OSSRON implantation in AVN patients, Oxford Hip score (OHS) and Harris Hip score (HHS) is used to assess the quality of life, Visual analogue score to see the improvement in pain and bone regeneration based on X-ray/CT-scan/MRI are considered appropriate parameters.

The OHS is a patient-centred questionnaire that is designed to assess functional ability and pain from the patient's perspective. In this study limitation to joint function and pain are assessed by using this self-assessment questionnaire from start until and after 6 months post implant. All patients generally show significant improvement in both pain and functional ability within 6 months of follow up period. HHS questionnaire is subject evaluation of domains of pain, function, activity, deformity, and motion. To know more about this, you can consult your doctor .

24. Can any orthopedic treat me with ABI therapy?

Only experienced orthopedists with extensive training in diagnosing and assessing cartilage injuries of the knee that have clinical expertise with Ossron may perform the treatment.

25. What are the advantages of ABI Ossron?

Cultured Autologous Cell Technology has created a new dimension in tissue engineering and regenerative medicine. Few of the advantages are:

Simple, fast, and minimally invasive surgical procedure.

Accelerated and effective bone formation.

Supports natural bone growth.

Shorter recovery and rehabilitation.

Poses virtually no risk of disease transmission to patient since it comes from patients own tissue i.e. Autologous.

Provides optimal solutions against various problems raised by Autografts or Allografts.

26. How many patients have been treated till date?

We have performed almost 158 cases for various defects with Ossron across India. We have also published various research publication including a paper on Ossron in European journal on maxillofacial defects.

27. What is the success rate of ABI-Ossron?

A 98% success rate has been observed in hundreds of cases performed in India and worldwide.

28. Is Ossron a safe and successful procedure?

Autologous bone implantation has been product Ossron is a safe drug approved by Central Licensing authority i.e CDSCO (The Central Drugs Standard Control Organization (CDSCO) is the national regulatory body for Indian pharmaceuticals and medical devices, and serves parallel function to the European Medicines Agency of the European Union, the PMDA of Japan and the Food and Drug Administration of the United States.) and state licensing authority i.e. FDA (Food and Drug Administration and Zonal CDSCO

29. What data has been under observation that leads you to conclude that ABI is successful and safe procedure?

We had 14 randomized patients with Avascular Necrosis (AVN) in our clinical trials who had undergone Autologous Adult Live Cultured Osteoblasts (OSSRON™) implantation procedure as defined in the protocol and were followed subsequently. All 14 randomized patients were followed successfully up to 24 weeks post implant procedures.

In CT-scan/MRI/X-ray studies at visit 7 (24 weeks post implant) compared to baseline recording suggest, there was huge decrease in necrotic tissue at the affected area of AVN in all patients. However, OSSRON implant was effective in showing bony regeneration at area affected with AVN in follow up period of six months.

30. How long will ABI implant be durable?

ABI-Ossron takes cells from patients own body and implant them back at defect site after multiplying to manifold. Thus, ABI-Ossron supports natural healing of damaged bone. Hence, the durability of ABI-Ossron implant is 15-20 years

31. What is the cost of ABI-Ossron?

The cost of the procedure and other details will be provided once you have consulted your orthopaedic doctor at one of the nearest Apollo hospital /clinic

32. How is this procedure superior and more efficient than other procedures currently being offered for bone problems ?

Autologous Osteoblasts Implantation is the first of its kind patient specific autologous cell based therapy and only curative treatment option, where bone marrow (osteoblast/bone cells) are harvested from patient's iliac crest. Collected bone marrow specimen is sent under controlled temperature at 2-8°C to cell processing centre (Laboratory) for culturing about 3-4 weeks, where healthy bone cells (osteoblasts) are minimally manipulated (limited only to expansion) and through small opening the dead bone is removed from necrotic area of the hip joint and patient's own cultured osteoblasts are implanted back onto the necrotic area of the same patient's hip joint. When osteoblasts are implanted into necrotic area of hip joint, osteogenesis is initiated wherein new bone is regenerated and thus joint is preserved.

Temporary pain relief surgical management such as core decompression is currently practiced and same is not recommended for large lesions (extent more than 30% necrosis of the femoral

head) as failure rate is more than 80% which will progress to femoral head collapse and patients would be forced to undergo total hip arthroplasty

In summary, there are two advantages of autologous bone implantation when compared to other methods: (1) regeneration of bone with normal biological properties and (2) better long-term results with increased quality of life. In the studies done, we evaluated the safety and efficacy of Autologous Adult Live Cultured Osteoblasts (OSSRON) in patients with Avascular Necrosis (AVN) with the aim to overcome the limitations of the current methods, and the result is that we could produce bone with similar biomechanical properties that are as identical to normal bone as possible.

33. Will my insurance cover the ABI Procedure?

Yes, this procedure is covered under insurance. For Further enquiries, please consult your doctor and relevant authority for complete information and procedures.