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Bone transplantation and tissue engineering, part III: allografts, bone grafting and bone banking in the twentieth century

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Abstract During the 20th century, allograft implantation waned in popularity as a clinical activity. Reports appeared in the literature describing several small series of patients in whom bone was obtained from amputation specimens or recently deceased individuals. The concept of bone banking became a reality during and after World War II when the National Naval Tissue Bank was established in Bethesda and a number of small banks sprang up in hospitals throughout the world. Small fragments, either of cortical or medullary bone, from these banks were used heterotopically to augment spinal fusions, to implant into cyst cavities, or to serve as a scaffolding for repair of non- or delayed union of fractures of the long bones.

Keywords Allograft history · Bone allograft · Bone bank · Graft technique · Bone bank history · Orthopaedic history

After the prehistoric age of human tissue grafting [26, 27], modern grafting and banking began around the turn of the 20th century. It was characterized by the "direct method," which required physicians and surgeons to redistribute tissue among patients or to solicit grafting material from a patient's family and friends and sometimes from strangers. The direct method is responsible for the creation of a new category of person called a donor; it forged novel relations among both doctors and patients. Early experimental grafts mostly involved tissue taken from living people known to the doctor. Bone was obtained from amputees during the first period of the 20th century. Tissue was seldom recovered from a corpse, and then only by a bold surgeon confronted by a desperate situation. Doctors were acutely aware of the speed at which bacteria proliferate in the corpse and were understandably fearful of the medical consequences of grafting cadaver material into a living patient. Another reason people were reluctant to recover tissue from the cadaver is that it necessitates intervening in powerful and carefully orchestrated rituals staged around death. These rituals, which are observed in some form or other everywhere, also manage the liminal period between death and disposal, a period during which the corpse suffers from categorical ambiguity, a dangerous condition marked by competing claims of custodianship. The competition is widely understood as a battle between death and living people reluctant to relinquish their ties with the person embodied in the corpse. Tissue banking is responsible for introducing a radical and dehumanizing claim: it seeks custodianship of the corpse in order to dismantle it into exchangeable and transplantable parts.

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Developments in the use of bone allograft at the beginning of the 20th century

In 1908, Erich Lexer [40–42] described the first massive allograft, in which tissue harvested from amputees were used to restore motion to joints following osteomyelitis and to reconstruct defects following resection of bone tumours. Erich Lexer (Fig. 1) was born in Freiburg and was the son of a professor of German. During his adolescence, the family moved to Würzburg, where Lexer attended the university, graduating from the medical school in 1890. Following a short period of postgraduate study of anatomy in Göttingen, Lexer began his surgical training in 1892 in the famous clinic of Ernst von Bergmann in Berlin. He remained there for 12 years. During this period he established himself as an investigator and a surgeon. Lexer was appointed Professor of Surgery in Königsberg in 1905. He moved to Jena in 1910, Freiburg in 1919, and finally to Munich in 1928, where he was the

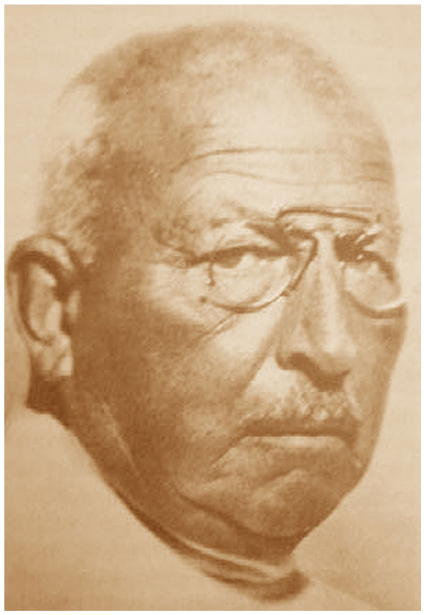

Fig. 1 Portrait of Erich Lexer

Fig. 2 Portrait of Henri Judet (1874–1942)

successor to Sauerbruch. His pioneer work on the transplantation of tissues such as fat, fascia, tendons, nerves, and bone continues to influence orthopaedic and plastic surgery procedures today. His use of whole joints from cadavers as transplants into patients was just a small part of this work. Following his classic work on massive bone allograft transplantation in 1908, Lexer described in 1925 [42] the results of using fresh cadaveric tissue on 11 half joints and 23 whole joints and reported a reasonable success rate. Unfortunately, an acute coronary occlusion brought an abrupt end to his life in 1937, just prior to retirement.

A year later in 1909 in France, Henri Judet (1874–1942), father of the well known Judet brothers, reported a whole-joint transplantation—femur, tibia and patella—in the knee joint of man [37–39]. He was born in the North of the Creuse in 1874 at Lavaufranche, with the old commanderie of the hospital workers having in his chapel the grave of the commander Jehan Grimaux. Henri Judet (Fig. 2) studied medicine in Paris and performed his surgery internship in 1898 to Lariboisière with Delens and Reynier [61]. In 1899, he was with Bouilly at the hospital Cochin, with Edouard Quénu at the hospital Cochin in 1900 and in 1901 at the hospital Boucicaut with Gérard Marchant. Introduced by Gérard Marchant and Dujarier, Henri Judet's career is one of a young surgeon directed towards knowledge and treatment of the osseous pathology. A century ago, in 1908, Henri Judet, at the Intern's Hospitals of Paris, as Doctor of Sciences, specialized in orthopaedic surgery and justified (Fig. 3) his research to preserve an articular mobility facing ankyloses, which were the usual fate of the articular diseases during that period.

"The ideal operation would be the one which, without touching muscles, organs of the mobility, or in ligaments, organs of the solidity of the joint could, with an ultra-economic resection create between both bones a simple crack as a physiological articular cavity. This articular restoration design should return in the anatomical state previous to the disease. An essential element disappeared in the complete ankyloses: the articular cartilages were invaded by the process of ossification which welded both bones. It would thus be necessary to redo articular cartilages. These considerations brought to us the idea of trying to reconstitute by transplantation the articular cartilages destroyed by the inflammation. In the space created by the ultra-economic resection, we wondered what would be the fate of a blade of cartilage applied (Fig. 4) to each of both osseous extremities and pulled in their movement of mutual sliding."

Axhausen [5] entered the debate with his thorough and scientifically rooted studies on osteogenesis and bone transplantation. He showed that the survival and osteogenic property of the periosteum varied between different types of graft: they were highest in autografts, significantly less so in allografts and null in xenografts. He also believed that most of the periosteum would survive and lead to osteogenesis while the transplanted bone would die. Georg Axhausen (Fig. 5) graduated from the Military Medical Academy of Berlin, remained in the German army for some years and started his academic work in Kiel in 1904–1906. After several more years with the army, he returned to Berlin as instructor in the surgical division of the Zahnärztlichen Institute. He was one of the pioneers in studies of bone graft and necrosis. He was the first to use the word aseptic necrosis, or at least the first to have it appear in the mainstream of medical publications. Phemister's work [56] on the same subject followed and recognized Axhausen's contribution, and Phemister's famous phrase "creeping replacement" is well described in Axhausen's work.

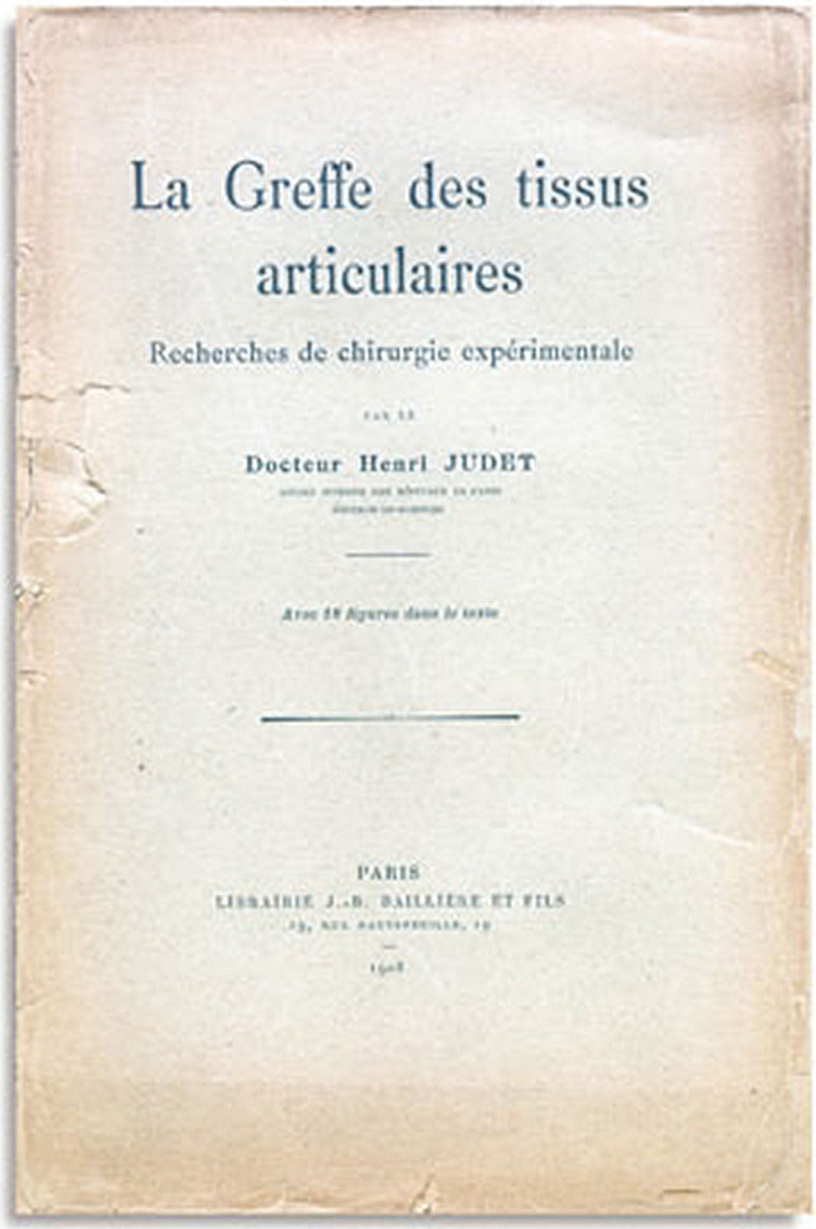

Fig. 3 Book of Henri Judet on osteoarticular graft

Bone grafting becomes popular with Albee

Dr. Frederick Houdlette Albee (April 13, 1876 – February 15, 1945) was born in 1876, the eldest of seven children, on a farm in Alna, Maine. The Albees were of Anglo–Norman ancestry; the Houdlettes, his mother's family, were of a long line of French Huguenots. His maternal grandfather, for whom he had the greatest love and respect, taught him much about tree grafting. Albee learned how to do tree grafting from his uncle, Charles Houdlette. He later applied the principles of grafting, and guarding a tree from outside disruptions, to his bone grafting operations. This grandparent was also a carpenter, a cabinet maker and a master worker with precision tools. What grandfather Houdlette taught young Fred about the principles of the grafting of fruit trees he learned well and applied later in the grafting of bone.

Though he was a hard worker on the farm, he was fascinated by medicine. When he was 16 years old, Albee was sent to the Lincoln Academy in Newcastle, Maine, and furthered his education. He worked his way through Bowdoin College, where he was a member of the Kappa Sigma Fraternity, and got a job as a laboratory assistant to Bowdoin's professor of bacteriology. He also worked hard to get one of the two scholarships offered by the Harvard University School of Medicine. At Harvard, Albee (Fig. 6) assisted Dr. Richard Cabot in the study of the measurement of blood pressure, and in his fourth year, Albee was one of the few medical students chosen to be a prosector, which gave him the privilege of assisting Dr.

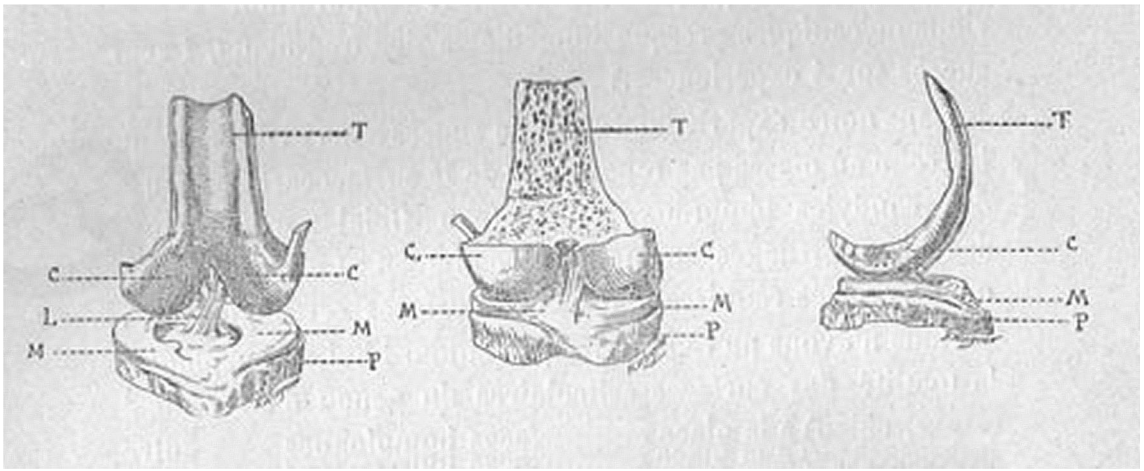

Fig. 4 Drawing of Henri Judet on the whole knee allograft transplantation

Maurice Richardson, the professor of surgery, during operations. Upon obtaining his M.D., Dr. Albee interned at Massachusetts General Hospital. Dr. Albee graduated from Bowdoin College, Maine, in 1899, and from the School of Medicine at Harvard in 1903. His first hospital appointment was at the Massachusetts General Hospital in Boston.

It was in Waterbury, CT, where he first practiced, that his interest in orthopaedic surgery was aroused. This was due largely to association with Dr. Charles Ogilvy, of New York City, who came to Waterbury for orthopaedic clinics. In 1906, he moved to New York at the Hospital for Ruptured and Crippled at 42nd Street and Lexington Avenue. At this hospital he came under the teaching of Dr. Virgil P. Gibney and Dr. Royal Whitman, the two most noted orthopaedic surgeons in New York of that period. After a brief general practice, he became an assistant orthopaedic surgeon at the New York Postgraduate Medical School Clinic. When Dr. Charles Ogilvy retired, Dr. Albee became the chief surgeon. In 1906 he performed an arthrodesis (Fig. 7) of an osteoarthritic hip at the Postgraduate Hospital, a procedure that never before had been attempted. The operation was highly successful and resulted in his being invited in 1909 to give a report of the case before a meeting of the American Orthopedic Association. Later that same year he was asked to talk on the operative fusion of the hip joint before the International Association of Medicine and Surgery in Budapest—quite an honour for a young man only six years out of medical school.

One has said that his outstanding contribution was in creating solid principles of osteoplastic surgery and adhering to these principles. He spotlighted bone-graft surgery in a way that never had been done before. He lived in an era in which there was a gradual transformation of orthopaedics from a specialty of conservative measures with few operations to one of many operations, with orthopaedic surgeons seeing

Fig. 5 Portrait of Georg Axhausen

Fig. 6 Portrait of Frederick Houdlette Albee

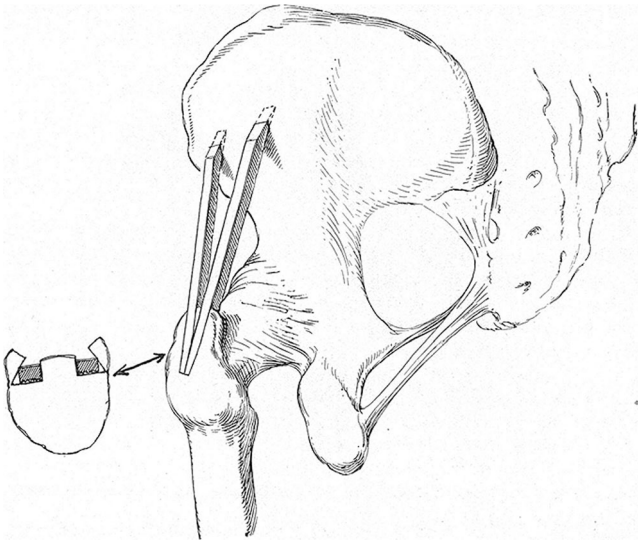

Fig. 7 Albee performed his first extraarticular arthrodesis of the hip with the use of two rigid cortical grafts

surgery as a means of treatment. He was an expert carpenter and mechanic of great ingenuity. In 1909 he developed an electric saw (Fig. 8) with special attachments for cutting bone. This was an adaptation of the Kenyon–Hartly saw. Albee

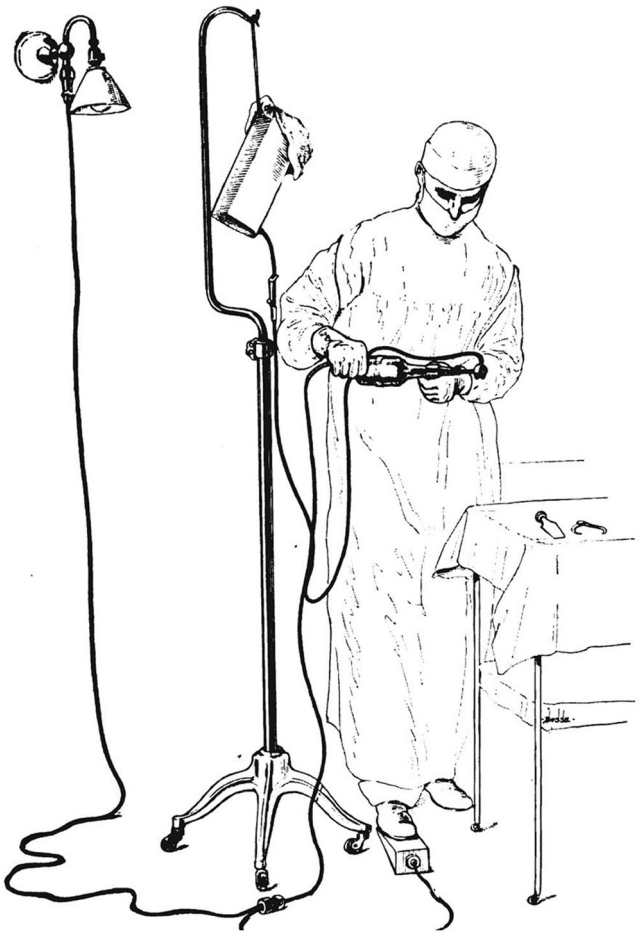

Fig. 8 Electric saw of Albee with special attachments for cutting bone

showed how the power-driven machine tools of the mechanics' trade could be used in bone surgery as precision instruments, thus increasing tremendously the scope of orthopaedics. With this system a new era of surgery commenced. With his electric saw he inaugurated a new era. Some called him the "world's greatest bone carpenter." His directness in his surgical approach and the dispatch with which he worked were always outstanding: 9 minutes for a spinal graft and 14 minutes for a tibial graft in the easy cases when everything went right in the operating room.

In 1909 he did his original bone-graft operation for fusion of a tuberculous spine. This was reported at a meeting of the American Orthopedic Association on May 15, 1911 but was not published until September 9, 1911 [1]. Just 13 days later, on May 28, Dr. Russell A. Hibbs, of the New York Orthopedic Hospital, published a description of another type of spinal fusion that has since borne his name [31]. For years afterward, there was heated controversy over the priority of spine fusion.

During 1912, Albee did many bone-graft experiments on dogs at Cornell University School of Medicine. He demonstrated to his own satisfaction that rigid cortical bone was much better for transplantation than cancellous bone. Today many think differently. He also showed that of all the types of transplants, the autogenous graft had the greatest measure of success. He perfected his techniques including the classification of bone types and, in 1912, invented the "Albee Bone Mill", a power-driven machine that reduced the time needed for a bone graft to as little as ten minutes.

In 1912, he published his first work on bone grafting in ununited fractures. It was in this type of surgery that his tools were most useful and his exactness superb; he would obtain fits and create self-sustaining grafts, almost unheard of before this time. During his career he devised bone-graft procedures for nearly every part of the human skeleton. In 1913, in London, at the International Congress of Medicine at the Royal National Orthopedic Hospital, he demonstrated his bone-grafting techniques with his motor-driven saw. In 1914, four months prior to the start of World War I, he demonstrated again his bone-mill and bone-grafting techniques at the opening of the German Orthopaedic Congress in Berlin.

In 1913, Albee designed a special fracture table that became a most useful addition to the armamentarium of the orthopaedic surgeon. In 1936, the table was modified by the use of a central hydraulic hoist and became known as the Albee–Comper table. In 1913, Albee performed his first extra-articular arthrodesis of the hip with the use of two rigid cortical grafts. Also in 1913, he first performed a bone-peg operation for ununited fracture of the hip. Later he reported 90% good results. This operation, it is said, was a great stimulus to hip surgery.

Dr. Albee's pioneering discoveries in medicine came just before the First World War. Prior to the development of Dr. Albee's methods, the primary treatment for a soldier's

seriously fractured limb had been amputation because of the need to prevent the spread of infection. The German Orthopaedic Surgical Congress had invited Albee to present his techniques in April 1914, and Dr. Albee worked in Allied military hospitals close to the Front, so his work prevented countless amputated limbs on both sides of the war. Dr. Albee's 1915 textbook, "Bone Graft Surgery", came out as the War ended its second year. Albee adopted a carpenter's technique, fitting a cortical graft from the tibia as a snug inlay in a cancellous bed, exactly adapted to its new site—periosteum to periosteum, cortex to cortex, medulla to medulla. He used an electric saw (Fig. 9), at first with one blade and then with two, and rapidly employed this for spinal fusion in Pott's disease. He wrote a monograph on grafting in 1915 [3] and eight years later was able to report his results in 3000 operations. This was at exactly the same time that Hibbs was also fusing the spine with cancellous flaps turned up and down from local structures. The spinous and transverse processes and spinal articulations of Albee's method suddenly made bone-grafting popular and successful after decades of rather sterile debate, conducted mostly in laboratories. Why was this? It must have been because of the ease of removing a tibial graft with a power-driven saw, because of the attraction of tight carpentering techniques for the 'handy' orthopaedic surgeon, the practical man averse to theorizing—orthopaedics is not one of the more intellectual disciplines—and because it manifestly worked. Grafting in the limbs was initially for non-union, fibrous or pseudoarthrotic; later it was extended to delayed union and even to fresh fractures known to be likely to present problems. Albee cut a slot for an exactly fitting inlay graft, without screws or pegs; this might come from a normal tibia or be a sliding graft from the fractured bone itself.

Fig. 9 Electric saw of Albee with different blades

In April 1917, the United States entered World War I, and in July 1918, Albee, now a Colonel in the US Army, organized and became the surgeon-in-chief and director of an orthopaedic hospital at Colonia, NJ. It was a model of its kind and the first reconstruction rehabilitation hospital that country had ever had. At the end of the war, Dr. Albee found that he personally had done approximately one half of all the bone-graft operations performed in the Army Medical Services, most of them at this hospital. It was here that he became more firmly convinced than ever before that in many ways it was more important to restore a patient to normal mental and spiritual health than to physical health, and that in so doing the patient must also be restored to his place in the economic structure of society. From this experience came Albee's deep and lasting interest in rehabilitation as we know it today.

At least 70 % of war wounds in World War I were orthopaedic injuries. Upon his return to the United States in 1917, Dr. Albee emphasized the need for immediate preparation for a medical emergency. With the cooperation of the War Department and the United States Surgeon General, William C. Gorgas, Dr. Albee was given free reign to open "United States Hospital Number 3", at Colonia, New Jersey, as the first purely orthopaedic hospital [4]. Dr. Albee would note later, "I was privileged to perform approximately half of all the bone-graft operations done in the First World War."

The concept of a bone bank was created in Cuba by Inclan

In 1904, Dr. Enrique M. Porto founded the first orthopaedic service in Cuba separated from paediatrics, with four beds in Dispensario Tamayo in Havana city, and in 1910 he founded another service with 12 beds in Reina Mercedes Hospital in Havana city. Prof. Alberto Inclan consolidated the speciality, and founded a new service in the Emergencia Hospital in Havana in 1916. In 1924, the Orthopaedics and Traumatology School was recognised. Prof Inclan (Fig. 10) was nominated Titular Professor, and the school was transferred to the Reina Mercedes Hospital. From that moment on, orthopaedics was spread all over the country and Inclan began to use bone grafts.

Before advancements in refrigeration techniques, fresh bones were used for most allografts. In 1915, Trout reported the successful bone transplantation between father and child to treat spina bifida, with the use of fresh bone allograft [59]. The trend of using fresh bone allografts continued through the 1930s and 1940s, mainly in cases of bone transplants from parent to child to treat pseudarthrosis, cysts and tumours. In 1910, Bauer demonstrated the successful transplantation of bones stored by refrigeration for as long as three weeks [7, 8]. A year later, Tuffier described the use of thin bone slices refrigerated for as long as five days in the treatment of patients

Fig. 10 Portrait of Alberto Inclan

[60]. Then in 1912, Albee recommended that all tissues (bones included) be stored at 4–5 °C [2].

The use of bone as graft material raised a host of questions, some almost theological in their intensity. Obviously, autogenous bone was the ideal, yet exogenous grafts were often necesssary; a child could not supply enough bone for grafting a scoliosis, where bank bone was better because it reduced operating time and blood loss. If the former (homografts, allografts), there were various possible sources: the ribs of thoracotomized patients in the era of thoracoplasty for phthisis (but this carried a real risk of infecting the recipient with tuberculosis); amputated limbs and excised femoral heads; parents; cadavers. Methods of preservation have been legion [6, 9, 10, 49, 50]. Some have used merthiolated bone [57], with a failure rate of around 30 %, others boiled [43] or autoclaved cadaveric bone, e.g. Gallie [23] had used boiled bone as far back as 1918. If such grafts were not used immediately, they would have to be stored.

In 1942, Inclan [36] reported the successful storing of autologous bones by refrigeration. Inclan obtained his bone in the course of various operations and stored it in blood or saline at just above 0 °C. Hence the concept of the bone bank, which is usually associated with the name of Inclan, in Cuba, whose seminal paper on the use of preserved bone graft in orthopaedic surgery appeared in 1942. The concept was not original. Albee had stored bone, chilled, as far back as 1912 [2], and so had Groves [25] in England. Most orthopaedic surgeons have to remove healthy bone from their patients from time to time and have wished to preserve it, and the early bone banks of the 1940s consisted essentially of the bone removed in clinical practice preserved by refrigeration.

Following the report, the idea of bone banking received much mention in various publications. Influenced by the success of Inclan, Bush [14] and Wilson [65, 66] independently described the preservation of bone grafts at −20 °C and the building of a bone bank for small fragments. After Wilson's report, many orthopaedic surgeons across the United States followed suit. They stored femoral heads collected from their patients in freezers in their own hospitals, and used these small bones on an individual basis much like the practice of a cottage industry.

The US Navy Tissue Bank founded in 1949 established the standard of modern tissue banks

The United States Naval tissue banking efforts started with the parent facility which is located at the National Naval Medical Center, Bethesda, Maryland. This parent facility has been in existence since the time of the Korean conflict. Many of the war casualties were brought to large Naval Hospitals needing complicated reconstructive procedures, the majority of which were orthopaedic. At that time there was a pauclty of desirable materials to perform desperately needed bone grafts and other orthopaedic procedures. It was in the setting that the very beginnings of the Naval Bank originated. On September 1, 1949, the Orthopedic Service of the Naval Hospital, Bethesda, obtained a four cubic foot freezer and began collecting, freezing and storing surplus bone from clean orthopaedic cases until needed for grafting in other patients. Spurred by the needs of the wounded following World War II and encouraged by the climate of interest surrounding bone banking, George Hyatt, an orthopaedic surgeon, founded the US Navy Tissue Bank in Bethesda, Maryland in 1949. Hyatt developed a system for procuring tissue, with a focus on bones, from cadavers in operating theatres, and employed freeze drying to store bones. These helped to increase the availability of allogenic bones [33, 34].

The bank had been opened in June 1949 in the Naval Hospital, Bethesda, Maryland, the flagship of navy medicine, which treats sailors and their families. The bank was the brainchild of George Hyatt, an orthopaedic surgeon investigating bone preservation. Hyatt had found salvaging bone removed during surgery on "clean" orthopaedic cases a time-consuming method of collection, which also provided scant material for his research. Cadavers were the answer: the bank's motto was Ex Morte Vita—from death comes life (Fig. 11). Dead bodies deteriorate rapidly and the time allowed for tissue recovery is brief. And the moment of death is notoriously unpredictable. Hyatt organized a round-the-clock rotation of four or five trained technicians ready to recover tissue when a suitable patient died in the Naval Hospital. Dismantling a cadaver into up to 125 grafts of all types took 12–14 hours and involved five hampers of linen, 50 gowns, 400 towels, 200 sheets, and a host of miscellaneous material including 500 wrappers. As a mark of respect for the dead person, talking was prohibited and hand signals were used for communication.

Fig. 11 The US Navy Tissue Bank's motto was Ex Morte Vita—from death comes life

Establishment and development of tissue banks

Outside of the military, however, storage of human tissue was not common, tissues for transplantation were scarce, and the lack of professional standards and government control meant that the effectiveness of allografts were uncertain. It soon became evident to Dr. Theodore I. Malinin (Fig. 12), a graduate of the U.S. Naval Medical Center, that there was a need for a civilian tissue bank. Subsequently, in 1970, Dr. Malinin founded the University of Miami Tissue Bank in Miami [46]. Dr. Malinin received training and gained experience in tissue banking under the direction of Dr. George Hyatt, orthopaedic surgeon at the Naval Medical Center in Bethesda, MD.

Fig. 12 Portrait of Theodore I. Malinin

During the same period, the Central Institute of Traumatology and Orthopaedics of the USSR's Ministry of Health established laboratories for the low temperature preservation of organs and tissues in Leningrad in 1952 and in Moscow in 1956. Volkov and Immamaliev [35] reported on joint or half-joint transplantation to the 10th congress of SICOT in Paris in 1966 and Immamaliev discussed the subject in a British publication in 1969 and Volkov [62] in the Journal of Bone and Joint Surgery in 1970. On the whole, the Russians seem to have favoured massive grafts taken from the cadaver in cases of sudden death from injury or heart attack within six hours, to be stored at very low temperatures (−70 °C for 24 hours, then at ~30 °C for up to six months, though this may now have changed). This was considered to diminish antigenicity, especially if storage was for not less than 25 days. Sometimes antibiotic solutions were used for storage; in some cases sterilization was with X-rays. Under the leadership of Janus Komender and Kazimierz Ostrowski, followed by Anna Dziedzic-Goclawska, the tissue bank went on to become the oldest tissue bank in the world to employ radiation technology in the sterilisation of tissue grafts. This method was adopted later in France [28, 29, 45]. Many other banks were also founded in Europe during this period.

Operations using massive bone allograft were far and few between until the 1970s, when Volkov in Russia reported a large series on transplanting whole joints and articular surfaces [62]. At around the same time, Carlos Ottolenghi in Buenos Aires, Argentina, reported his use of deep frozen allografts for mostly bone tumours [52]. Together with his successor, Luis Muscolo, he later presented the results of a series of long-term follow-ups on massive bone allografts transplanted [53]. In Houston, Texas, Frank Parrish [54] performed a series of experiments on the use of frozen massive osteoarticular allografts in reconstructing defects following the removal of tumour. The efforts of these surgeons inspired other groups [19, 20, 24] to look towards bone allograft as an alternative to metallic implants. One of these group, led by Henry Mankin [47, 48] at the Massachusetts General Hospital, reported the largest clinical series on the use of bone allografts in bone tumour surgery and showed success in three quarters of the patients with Tomford [58] and Enneking [19].

Development of the living bone allograft

While the use of massive bone allografts gained impetus in the 1980s, it was during this same period that the problems with allografts were reported. Enneking [20] performed a series of experiments to investigate the fate of large bone allografts and

found that the allografts were often poorly incorporated into the host bone and were vulnerable to infection and fatigue fractures. Solutions were needed to overcome the histoincompatibility of bone allografts and to improve allograft incorporation. One such solution came in the form of a living bone.

The possibility of a living bone was first raised by Curtis in 1893 [17], when he described the ideal "living bone which will exactly fill the gap and will continue to live without absorption". This ideal living bone inched towards reality with the birth of vascular surgery, then with further developments in microsurgery in the 1960s. In 1975, the first free vascularised graft was performed by Ostrup [51]. Following that, the technique of revascularising bone with anastamosis became adopted in transplants for treating bone tumours in the 1980s [63, 67].

Allograft immunogenicity

In the 1960s, Geoffrey Burwell, an orthopaedic surgeon in Leeds, embarked on a series of experiments on bone transplantation [2, 12, 13] which led to his discoveries in allograft immunogenicity. He showed that the bone marrow was responsible for the immune response to fresh allogenic bone and that frozen bones performed better compared to fresh allogenic bones. More significantly, his experiments shed light on the science of bone preservation and led to the development of the protocol for bone preservation we use today [64].

Many other investigators sought to understand the immunology behind allografts and most reached the same conclusion, as summarized by Friedlaender [21, 22], namely, fresh bone allografts were the most immunogenic; freeze-drying dramatically reduced the immune response and frozen bones had an immunogenicity that was between that of the former two.

The issue of disease transmission

The first case of AIDS surfaced in 1981 and the first case of HIV-1 transmission in bones was reported in 1984, followed by a second case in 1985 [11, 15, 18]. The transmission of disease came at a time when proper screening methods were yet to be developed. Two cases of hepatitis C transmission were also reported in the 1990s, the second case occurring despite the existence of a first-generation screening test [16].

The occurrence of disease transmission prompted the development of proper donor-screening and bone preparation and processing methods. When Kenneth Sell became the head of the US Navy Tissue Bank, he started a program in which a group of fellows researched on graft technology. Many prominent investigators, including Andrew Bassett, Gary Friedlaender, Theodore Malinin, William Tomford, and Michael Strong, were recruited. The findings of the programme helped immensely in advancing the knowledge in ensuring the safety of allografts and the prevention of disease transmission in the field of tissue banking [44].

Conclusion

Finally, it is evident that the ultimate breakthrough in the field of bone allogeneic transplant will be the development of a safe and efficacious system of altering either the immune mechanism of the host or the immune composition of the donor part [32]. Such an approach could be part of a general alteration of the host but this has such sufficient disadvantages that it is more likely the ultimate system will be in relation to that donor segment. Such discoveries could ultimately lead to major contributions such as living joint transplants, microvascular anastamosis of host vessels to donor parts and transplants of viable epiphyseal plates to individuals with disturbed growth patterns. Such research is currently in its early phases and clearly has far to go. One solution could be allograft loaded with stem cells [30, 55].

References

1. Albee F (1911) Transplantation of a portion of tibia into the spine for Pott's disease. J Am Med Assoc (JAMA) 57:885–886
2. Albee FH (1912) Discussion of preservation of tissues and application in surgery by Alexis Carrel. J Am Med Assoc (JAMA) 59:527–536
3. Albee F (1915) Bone-graft surgery. Saunders, Philadelphia
4. Albee F (1923) Fundamentals in bone transplantation. Experience in 3000 bone-graft operations. J Am Med Assoc 81:1429
5. Axhausen G (1907) Histologische untersuchungen uber knochentransplantation am menschen. Duetsche Zeitschr F Chir 91:388–428
6. Bassett CAL (1962) Current concepts of bone formation. J Bone Joint Surg 44A:1217–1244
7. Bauer H (1910) Ueber knochentransplantation. Zentralbl Chir 37:20–21
8. Bauer KH (1927) Homoiotransplantation von epidermis bei eineiigen zwillingen. Beitr Klin Chir 141:442–446
9. Berkin CR (1957) Freeze-dried bone grafts. Lancet i:730
10. Brown KLB, Cruess RL (1982) Bone and cartilage transplantation in orthopedic surgery. J Bone Joint Surg 64A:270
11. Buck RE, Malinin TI, Brown MD (1989) Bone transplantation and human immunodeficiency virus. An estimate of risk of acquired immunodeficiency syndrome (AIDS). Clin Orthop 240:129–136
12. Burwell RG (1965) Osteogenesis in cancellous bone grafts considered in terms of cellular changes, basic mechanisms and the perspective of growth-control and its possible aberrations. Clin Orthop 40:35–47
13. Burwell RG, Gowland G (1961) Studies in the transplantation of bone. The changes occurring the lymphoid tissue after homografts

and autografts of fresh cancellous bone. J Bone Joint Surg 43B:820–843
14. Bush LF (1947) The use of homogenous bone grafts. J Bone Joint Surg 29:620–628
15. Centers for Disease Control (1988) Transmission of HIV through bone transplantation: case report and public health recommendations. Morb Mortal Wkly Rep 37:597–599
16. Conrad EU, Gretch DR, Obermeyei KR (1995) Transmission of the hepatitis C virus by tissue transplantation. J Bone Joint Surg 77A: 214–224
17. Curtis BF (1893) Cases of bone implantation and transplantation for cyst of tibia, osteomyelitis cavities and ununited fractures. Am J Med Sci 106:30–43
18. Eggen BM, Nordbo SA (1992) Transmission of HCV by organ transplantation (letter). N Engl J Med 326:411
19. Enneking WF (2005) Transplanting allografts. J Am Coll Surg 201(1):5–6
20. Enneking WF, Burchardt H, Puhl JL, Piotrowski G (1975) Physical and biological aspects of repair in dog cortical-bone transplants. J Bone Joint Surg 57A:237–246
21. Friedlaender GE (1976) The antigenicity of preserved allografts. Transplant Proc 8(suppl 1):195–200
22. Friedlaender GE, Mankin HJ, Langer F (1983) Immunology of osteochondral allografts: background and considerations. In: Friedlaender GE, Mankin HJ, Sell KW (eds) Osteochondral Allografts. Biology, Banking, and Clinical Applications, Little, Brown & Co, Boston, pp 133–140
23. Gallie WE (1931) The transplantation of bone. Br Med J 2:840
24. Gross AE, McKee N, Farine I, Czitrom A, Langer F (1984) Reconstruction of skeletal defects following en bloc excision of bone tumours. In: Uhthoff HK, Stahl E (eds) Current Concepts of Diagnosis and Treatment of Bone and Soft Tissue Tumours. Springer-Verlag, Berlin, pp 163–174
25. Groves EWH (1917) Methods and results of transplantation of bone in the repair of defects caused by injury or disease. Br J Surg 5:185–242
26. Hernigou P (2014) Bone transplantation and tissue engineering, part I. Mythology, miracles and fantasy: from Chimera to the Miracle of the Black Leg of Saints Cosmas and Damian and the cock of John Hunter. Int Orthop 38(12):2631–2638. doi:10.1007/s00264-014-2511-y
27. Hernigou P (2014) Bone transplantation and tissue engineering. Part II: bone graft and osteogenesis in the seventeenth, eighteenth and nineteenth centuries (Duhamel, Haller, Ollier and MacEwen). Int Orthop. doi:10.1007/s00264-014-2578-5
28. Hernigou P, Delepine G, Goutallier D, Julieron A (1993) Massive allografts sterilised by irradiation (clinical results). J Bone Joint Surg (Br) 75B(6):904–913
29. Hernigou P, Delepine G, Goutallier D (1989) Control of sterility in bone banking with irradiation. In: Aebi M, Regazzoni P (eds) Bone banking. Springer Verlag, Berlin, pp 174–175
30. Hernigou P, Pariat J, Queinnec S, Homma Y, Flouzat Lachaniette CH, Chevallier N, Rouard H (2014) Supercharging irradiated allografts with mesenchymal stem cells improves acetabular bone grafting in revision arthroplasty. Int Orthop 38(9):1913–1921. doi:10.1007/s00264-014-2285-2
31. Hibbs RA (1911) An operation for progressive spinal deformities. NY Med J 93:1013
32. Hinsenkamp M, Muylle L, Eastlund T, Fehily D, Noël L, Strong DM (2012) Adverse reactions and events related to musculoskeletal allografts: reviewed by the World Health Organisation Project NOTIFY. Int Orthop 36(3):633–641
33. Hyatt GW (1950) Fundamentals in the use and preservation of homogenous bone. US Armed Forces Med J 1:841–852
34. Hyatt GW, Turner TC, Bassett CAL, Pate JW, Sawyer PN (1952) New methods for preserving bone, skin and blood vessels. Postgrad Med 12:239–254
35. Immamaliev AS (1969) The preparation, preservation and transplantation of articular bone ends. In: Apley AG (ed) Recent Advances in Orthopaedics. London, Churchill, p 209
36. Inclan A (1942) The use of preserved bone graft in orthopaedic surgery. J Bone Joint Surg 24:81–96
37. Judet H (1908) Essai sur la greffe des tissus articulaires. CR Acad Clermont-Ferrand, 146, 193 and 600
38. Judet H (1909) La greffe des articulations. Rev de chirurg, Paris 40: 1.J
39. Judet H (2008) Rencontre dans « Maîtrises orthopédiques » (175):1–4
40. Lexer E (1908) Ueber glenktransplantation. Med Klin 4:817
41. Lexer E (1908) Die verwendung der freien knochenplastik nebst versuchen uber gelenkversteifung und gelenktransplantation. Arch Klin Chir 86:939–954
42. Lexer (1925) Joint transplantations and arthroplasty. Surg Gynecol Obstet 40:782–809
43. Lloyd-Roberts GE (1952) Experience with boiled cadaveric bone. J Bone Joint Surg (Br) 34:428
44. Lord CF, Gebhardt MC, Tomford WW, Mankin HJ (1988) The incidence, nature and treatment of allograft infections. J Bone Joint Surg 70A:369–376
45. Loty B, Courpied JP, Tomeno B, Postel M, Forest M, Abelanet R (1990) Bone allografts sterilised by irradiation. Biological properties, procurement and results of 150 massive allografts. Int Orthop 14(3): 237–242
46. Malinin TI (1976) University of Miami Tissue Bank: collection of postmortem tissues for clinical use and laboratory investigation. Transplant Proc 8(2 Suppl 1):53–58
47. Mankin HJ, Hornicel FJ, Gebhardt MC, Tomford WW (2005) Bone allograft transplantation: theory and practice. In: Lieberman R, Friedlander GE (eds) Evolution of allograft transplantation, p 25
48. Mankin HJ, Vogelson FS, Thrasher AZ (1976) Massive resection and allograft replacement in the treatment of malignant bone tumors. N Engl J Med 294:1247–1255
49. Orell S (1931) Experimental chirurgische Studie tiber Knochentransplantate and ihre Anwendung in der praktische Chirurgie. Dtsch Z Chir 232:701
50. Orell S (1937) Surgical bone grafting with ‘os purum’, ‘os novum’ and ‘boiled bone’. J Bone Joint Surg 19:873
51. Ostrup LT, Frederickson JM (1974) Distant transfer of a free living bone graft by microvascular anastomoses: an experimental study. Plast Reconstr Surg 54:274–285
52. Ottolenghi CE (1966) Massive osteoarticular bone grafts. J Bone Joint Surg 48B:646–659
53. Ottolenghi CE, Muscolo DL, Maenza R (1982) Bone defect reconstruction by massive allograft: technique and results of 51 cases followed for 5 to 32 years. In: Straub LR, Wilson PD (eds) Clinical Trends in Orthopaedics. Thieme-Stratton, New York, pp 171–182
54. Parrish FF (1973) Allograft replacement of all or part of the end of a long bone following excision of a tumor. J Bone Joint Surg 55A:1–22
55. Pećina M, Vukičević S (2014) Tissue engineering and regenerative orthopaedics (TERO). Int Orthop 38(9):1757–1760
56. Phemister DB (1914) The fate of transplanted bone and regenerative power of its various constituents. Surg Gynecol Obstet 19:303–333
57. Reynolds FE, Oliver DR, Ramsey R (1951) Clinical evaluation of the merthiolate bone bank and homogeneous bone grafts. J Bone Joint Surg 33A:373

58. Tomford WW, Thongphasuk J, Mankin HJ, Ferraro MJ (1990) Musculoskeletal allografts. A study of the clinical incidence and causes of infection associated with their use. J Bone Joint Surg 72A:1137–1143
59. Trout HH (1915) Spina bifida, tibial transplant, father to child. Surg Gynecol Obstet 22:523
60. Tuffier T (1911) Des greffes de cartilage et d'os humain dans les resections articulaires. Bull Mem Soc Chir Paris 37:278
61. Vayre P (1898) Judet's tree, genealogy of an orthopedic family. www.bium.univ-paris5.fr/acad-chirurgie. Accessed 11 January 2015
62. Volkov M (1970) Allotransplantation of joints. J Bone Joint Surg 52B:49–53
63. Weiland AJ, Moore JR, Daniel RK (1983) Vascularized bone autografts: experience with 41 cases. Clin Orthop 174:87–95
64. Williams LB, Irvine LW (1954) Preparation of the inorganic matrix of bone. Science 119:771
65. Wilson PD (1947) Experience with a bone bank. Ann Surg 126:932
66. Wilson PD (1951) Follow-up study of the use of refrigerated homogeneous bone transplants in orthopaedic surgery. J Bone Joint Surg 33A:307
67. Wood MB, Cooney WP, Irons GB (1985) Skeletal reconstruction by vascularized bone transfer: indications and results. Mayo Clin Proc 60:729–734