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Quality Control in Hospital Bone Banking

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1. Introduction

The use of allogenic bone transplantation is nowadays a standard orthopaedic procedure. It is widely used for reconstruction of bone defects that arise from trauma (Friedlaender 1987), infection, resection of bone tumours (Mankin et al. 1996) or it is used in spinal fusion (Raizman et al. 2009) and as impaction grafting in revision of total joint arthroplasty (Slooff et al. 1996). Although autologous bone is generally preferred because of its osteoconductive and osteoinductive activity, autologous bone is often not sufficiently available and comes with donor site morbidity (Summers & Eisenstein 1989). Therefore allogenic bone grafts are often used in orthopaedic procedures. These bone allografts are provided by an orthopaedic bone bank. It might be financially attractive for a hospital to manage its own local hospital bone bank, especially if they perform many procedures in which bone allograft is used. The main advantage of managing a hospital bone bank however, is the easy accessibility to and availability of bone allograft. The bone allografts in a hospital bone bank are femoral heads obtained from suitable patients who underwent total hip replacement surgery. Management of an orthopaedic bone bank is a complex process. The bone bank procedure has to meet the requirements of the national law and European guidelines 2004/23/EC and 2006/86/EC. This law states the technical requirements for coding, processing, preserving, storing, and distributing of human tissue and cells. Human tissue should be traceable and serious side effects and incidents with human tissue and cells should be reported. The bone bank procedure should be carefully described in an extensive protocol. Neither in the Netherlands, nor in any other European country, there are official guidelines for the organization and management of an orthopaedic bone bank. Our bone banking procedure protocol is based on guidelines of The American Association of Tissue Banks (AATB 1993), the criteria of the Council for Blood Transfusion of the Netherlands Red Cross (Richtlijn Bloedtransfusie 2004), the recently merged Netherlands Bone Bank Foundation (NBF) and Bio Implant Services (BIS); (NBF-BIS Foundation 2010) and the guidelines of the European Association of Musculoskeletal Transplantation (EAMST). The latter has been discontinued because of diverging European legislation. This bone bank protocol extensively describes the procedure, which includes a thorough questionnaire for donor selection, extensive serological, bacteriological and histopathological examination, as well as standard procedures for registration, processing, preservation, storage and distribution of bone allografts (Zwitser et al. 2010). In this chapter we describe our local hospital bone banking

procedure and protocol. This constantly updated protocol is of the utmost importance in order to prevent the transmission of infectious diseases. Because of the potential risk of transmission of diseases from donor to recipient we performed routine histological examination in the screening protocol. We found a relatively high percentage of pathological conditions in retrieved femoral heads (Zwitser et al. 2009; Sugihara et al. 1999). Therefore, we recommend the routine histopathological evaluation of all femoral heads removed during elective total hip arthroplasty as a tool for quality control. The cost-performance ratio of routine histopathological evaluation is discussed in literature (Kocher et al. 2000; Meding et al. 2000; Lawrence et al. 1999; Campbell et al. 1997). Therefore we performed an intern evaluation of the bone banking process. We compared the costs made to harvest, store and implant one bone allograft of our bone bank and the costs of one allograft obtained from the central bone bank. Furthermore this evaluation brought valuable information of improvements to be made. We describe these conclusions and have suggestions how to further improve the quality and cost effectiveness of the bone banking process in the near future.

2. History of bone transplantation

The history of bone transplantation can be traced back to the seventeenth century. In 1668 Job van Meekeren, a Dutch surgeon was the first to perform bone transplantation (Schweiberer et al. 1990). He repaired a skull defect in a soldier with part of a skull from a dog. As soon as the soldier was informed about the transplant, he requested immediate removal of the dog's skull. This was not possible because the xenograft was already fully incorporated in the man's skull. The first human allograft ever reported describes a case of a bone transplant in a young male who suffered an osteomyelitis of the entire humeral shaft (MacEwen 1881). In 1881, the treatment for osteomyelitis was surgical debridement or resection of the affected bone. After this surgical procedure, it took several years for the infection to extinguish, where after the surgeon could replace the bony defect with fresh allografts from diaphysis of tibial shaft. In the following seven years these allografts slowly but successfully incorporated in the recipient humeral shaft (MacEwen 1909). In the following decades the technique of transplantation of large allografts in septic arthritis and osteomyelitis was further developed and popularised by a German surgeon. He used fresh long bones of amputated limbs and used them as osteoarticular allografts with a reported success rate of 50% (Lexer 1908, 1925). Later, in 1929 Alexander Fleming discovered the antibacterial properties of penicillium and treatment modalities of osteomyelitis changed (Fleming 1929). In the subsequent years antibiotics were further developed and introduced for clinical medical use in the 1950's. From now on, the treatment of choice for osteomyelitis consisted of appliance of antibiotics in stead of surgery.

Transplantation of large allografts was applied as a limb-saving treatment in high grade malignant bone tumours of the lower extremity (Parrish 1973, Mankin et al. 1976). In a series of 19 allograft replacements for osseous malignancies satisfactory results were reported in 75% of patients. In the largest series of two hundred lower extremity osteoarticular allografts performed between 1976 and 1997 for malignant bone tumours, results were diminished by radiation and chemotherapy (Hazan et al. 2001).

In the first century of bone transplantation the greatest impediment to the use of allografts was availability of fresh bone grafts, because there were no means for preservation.

Only fresh amputated limbs could be used as a donor allograft. For this reason, autografts were used much more frequently than allografts. In the 1940's storage methods were developed for preservation longer than a few days or hours by refrigeration or freezing.

In 1949 in Bethesda, Maryland the first United States Navy Tissue Bank was established, because of a military need for bone allografts (Hyatt 1950). In that Tissue Bank allografts were obtained from the nearby National Naval Medical Centre. In addition, they developed a method for freeze-drying of allografts by lyophilisation, which made it possible to store and preserve allografts for several years without the need for refrigeration or freezing (Kreuz et al. 1951). In the first century of bone transplantation disease transmission was not of great concern. In addition, serological tests for transmittable diseases other than syphilis were not available. The first case ever of the transmission of viral disease by frozen bone was reported by Shutkin in 1954. The donor had undergone an above the knee amputation. The allograft bone was cut into portions under aseptic conditions, placed in double sterile containers and frozen at a temperature of -10 to -20 °C. Five months later, the bone was implanted into a medical student and transmitted hepatitis B. In the early 1980's the first publications concerning a new disease AIDS were published (Centers for Disease Control [CDC] 1981, 1982). Only a few years later in 1984 the first transmission of disease by bone allograft was reported (CDC 1988). A serological test was not yet available at the time of transmission. Even with the first serological tests used for screening purposes another transmission occurred in 1985, due to a very recent donor infection in the so-called "window period" of testing, with a less accurate test. Therefore, in an expert conference guidelines and recommendations were developed (CDC 1988). The most important conclusion drawn was that the disease was transmitted by blood and bone marrow containing allografts. Recommendations concerned donor screening, testing and re-testing of living donors after 6 months. The constant update for screening of donors for infectious diseases proved to be important in the subsequent years with two reports on transmission of hepatitis C virus by bone allografts (Eggen & Nordbø 1992; Conrad et al 1995). In the following years tissue banks developed better techniques for processing and preparation of bone allografts and more reliable blood tests came to market (Busch 1991, 1994; Alter et al. 1990). However, donor screening methods are constantly updated and revised with the introduction of new infectious diseases, like SARS (Lam et al. 2004). The safety of allograft bone transplants can never be taken for granted, but recent safety records for bone allografts are excellent.

As more complex orthopaedic surgical procedures are performed nowadays the need for (safe) bone allografts has increased (Nielsen et al. 2001).

3. Indications for the use of bone allograft

Massive bone defects can arise from trauma, infection, osteolysis after arthroplasty or resection of bone tumours and are a challenging problem in orthopaedic practice. These bone defects can be filled with either autograft or allograft bone transplants. Ideally, autograft is preferred because of its osteoconductive and osteoinductive activity. However, autografts are available in limited number and size and therefore not sufficiently available. In addition harvesting is associated with extended surgical time and involves donor site morbidity (Aro&Aho 1993; Summers and Eisenstein 1989). Therefore allografts supplied by a bone bank are commonly used instead. Allogenic bone exclusively has osteoconductive activity; it serves as an acellular mineralized frame against which newly formed bone gets deposited (Elves and Pratt 1975; Urist 1953). Indications for the use of allografts are wide

and include treatment of bone defects as a result from trauma, tumour surgery and infection (Friedlaender 1987; Mankin et al. 1976, 1996; Finkemeier 2002; Jupiter et al. 1987). In addition it is used in spinal fusion (Raizman et al. 2009; Takaso et al. 2011). However the most applied indication is the use of morselized allograft femoral heads as impaction grafting in revision or primary total joint arthroplasty. Aseptic loosening of the acetabular or femoral component of a total hip prosthesis is becoming an increasingly significant problem in orthopaedic surgery (Slooff et al. 1996). The migration of implants during loosening and procedures to remove the prosthesis and cement during revision induce significant bone destruction, resulting in enlargement of the acetabulum and widening of the femoral medullary cavity. Because of the magnitude of the loss of bone, allograft bone is often needed, at revision, to provide stability for the new socket or stem. Using a technique for revision of the acetabular component with impacted morselized cancellous bone grafting and a cemented or uncemented acetabular component, excellent long term results were described, with a survival of the revised hip prostheses of 87% at 20 years. (Schreurs et al. 2009; Garcia-Cimbrelo 2010; Paxton 2011). In different subgroups of patients this technique was applied with good results: patients under the age of 50, with rheumatoid arthritis, with acetabular fracture and dysplastic hips. In addition femoral revision with use of an impaction bone-grafting technique and a cemented polished stem resulted in an excellent prosthetic survival rate at eight to thirteen years postoperatively. However several studies report on high complication rates on this procedure, mostly femoral fractures and authors refined their indications (Leopold et al. 1999; Meding et al. 1997; Toms et al. 2004; Sierra et al. 2008). Because of the use of femoral head allograft bone in revision hip surgery, which is a common orthopaedic operation, the need for these allografts is increased. The retrieval of these femoral heads in daily orthopaedic practice is simple: the procedure for implantation of a total hip always requires removal of the femoral head. However the bone banking procedure for safe donor selection, retrieval, documentation and storage is a complex process. Therefore in many countries central bone banks were founded, containing bone- and tendon allografts of various sizes and origin, obtained from living and deceased donor patients. These central bone banks also provide femoral head allografts to other hospitals, which can be ordered at a cost price in advance of a planned operation.

Hospitals that perform a high quantity of orthopaedic procedures that require the use of bone allografts (total hip revisions, spine surgery and tumour surgery) might consider foundation of a hospital owned bone bank. In the Netherlands these hospital bone banks contain only allografts of femoral heads of living donors removed at the time of hip replacement surgery. Main advantages for the hospital and orthopaedic surgeons consist of easy accessibility to - and availability of allografts. In addition there might be a financial advantage, depending on the quantity of allografts needed per year. However the break-even point is not clear and dependant on local costs which differ between hospitals, countries and bone banking protocols. In the next paragraph a bone banking protocol is described which meets the requirements of Dutch national law and European guidelines 2004/23/EC and 2006/86/EC and is based on several guidelines: The American Association of Tissue Banks (AATB 1993), the criteria of the Council for Blood Transfusion of the Netherlands Red Cross (Richtlijn Bloedtransfusie 2004), the central bone bank in the Netherlands NBF-BIS (NBF-BIS Foundation 2010) and the guidelines of the European Association of Musculoskeletal Transplantation (EAMST), which has been discontinued because of diverging European legislation.

4. Hospital bone bank protocol

A bone bank procedure should be extensively described in a protocol concerning the five components: organization, donor selection, documentation, storage and processing, and implementation. The Head of Department (HOD), of the Department of Orthopaedics and the bone bank administrator compose this protocol.

4.1 Organization

In an organization chart we describe the responsibilities of different stakeholders. One of the orthopaedic departmental members, preferably the HOD of Orthopaedic surgery, has general responsibility for the bone bank. The HOD should have appropriate technical support by a bone bank administrator, who is responsible for the daily management of the bank. This bone bank administrator can be a paramedic with appropriate training for the required tasks. The bone bank administrators' responsibilities include administration as well as storage and allocation of donor bone. Additionally, the administrator takes care of the maintenance and cleaning of the storage facilities (freezers, etc.), and verifies the registration forms of femoral heads meeting the requirements for storage in the bone bank. Furthermore the team consists of a theatre nurse, a medical microbiologist, an anatomic pathologist, a clinical chemical analyst, a haematological laboratory technician, and a trainer. The knowledge and skills concerning surgical techniques and clinical hygiene are guaranteed by the orthopaedic surgeon and theatre nurse. The bone bank administrator and the trainer are responsible for training of bone bank employees. Apart from an orientation module for new employees, the training program consists of regular refresher courses for all members of the staff, in order to keep the knowledge of the procedures updated.

4.2 Donor selection

Preceding the hip replacement procedure, the attending orthopaedic surgeon requests the patient for his permission to store any removed tissue for donation. It concerns patients whose femoral head grafts will be retrieved in order to be replaced by a total hip prosthesis. The quantity of corticospongiuous bone removed during knee or shoulder arthroplasty is not sufficient for donor purposes; therefore patients undergoing such procedures cannot be taken into consideration for donation of bone tissue.

The attending orthopaedic surgeon informs the patient both orally and written. In case the patient grants permission he or she signs the consent forms, and fills out a standard survey (see Table 1). The orthopedic surgeon now decides whether the patient is suitable for being a donor; he uses general and specific exclusion criteria (see Tables 2, 3).

All criteria must be met; if not, exclusion necessarily follows. The orthopedic surgeon examines the patient thoroughly: blood samples are collected to determine blood type, Rhesus-factor and Erythrocyte Sedimentation Rate (ESR). (Tables 4, 5).

During surgery, bacterial culture swab samples from the hip capsule are collected and a biopsy of 1 cm³ corticospongiuous bone is sent for histopathological analysis. Serological screening for infectious diseases is performed six months after surgery. Once all requirements are met (Tables 1, 2, 3, 4, 5), a femoral head can be released for donation:

- approval donor
- signed consent forms of donor
- completed survey; all questions should yield a negative answer
- preoperative ESR rates within criteria
- no abnormal bacteriological values in derived tissue

- no abnormal histopathological structures in derived tissue
- no abnormal serological values six months after surgery

4.3 Documentation

Accurate documentation and coding are of the utmost importance for a well functioning bone bank. A unique registration code is allocated to each femoral head. Only the bone bank administrator is able to trace the donor based on this code. Of every registered femoral head, a file, containing the consent forms and results of ESR, bacteriological and histopathological examination, is kept updated. Other relevant data, such as the size of the femoral head and the allocation date are also documented and stored in this file. When the file is completed (which takes at least 6 months due to the serological examination), and no abnormalities are recorded, both bone bank administrator and the responsible orthopedic surgeon sign the forms. The femoral head is now available for transplantation. In case a file cannot be completed in full, or any abnormal values are recorded, the femoral head will be destroyed according to hospitals' protocol.

In the past 3 months, did you suffer any infection? If so, what infection?
In the past 3 months, did you have any vaccination or inoculation, or have you been injected with narcotic drugs?
In the past 6 months, did you have a malaria attack or did you use anti-malarial medication?
Have you ever been infected with a sexually transmitted disease?
Have you ever been diagnosed with jaundice or liver illness?
In the past 6 months, have you been in contact with patients diagnosed with jaundice/hepatitis?
In the past 6 months, have you been in contact with patients diagnosed with AIDS, or individuals at risk to AIDS? If yes, how and when?
Have you ever been tested for HIV/AIDS?
Have you had homosexual intercourse after 1977? (Males only).
Have you emigrated after 1977? If so, to what country?
Are you diagnosed with hemophilia? If yes, are you using anticoagulants?
Are you a sexual partner of an individual for which any of the abovementioned questions can be answered with 'yes'?
Have you been actively involved in prostitution after 1977, or have you been a sexual partner of a person involved in prostitution in the past 6 months?
Have you ever been diagnosed with a hematological disease or any malignant disorder?
Have you ever been treated for diabetes mellitus?
Have you ever been treated for chronic brain- or neurological diseases?
Have you ever received radiation therapy?
Have you ever been diagnosed with rheumatoid arthritis?
Have you ever been diagnosed with tuberculosis?
Have you ever been diagnosed with any disease, other than the abovementioned?
Have you ever received hormonal treatment?
Do you use any prescribed medication?
Have you ever used any narcotic drugs?
Have you recently been exposed to hazardous or toxic materials? If yes, please specify.
What is your alcohol consumption per week?
Have you recently been in surgery? If so, when? Did you receive blood from a blood transfusion?
In the past 14 days, have you been traveling through or staying in a region exposed to a SARS epidemic, or have you been in contact with patients infected with SARS?
In the past 6 months, have you tattooed yourself or did you get a piercing?

Table 1. Questionnaire patient for orthopaedic bone donation

4.4 Storage and processing

Retrieval of the femoral head is performed at the time of routine orthopaedic total hip replacement under aseptic conditions. The removed femoral head is inspected and capsule and synovial tissue are cultured on aerobic and anaerobic bacteria. In order to exclude malignancies, auto-immune processes, or infections, a biopsy of 1 cm³ corticospongius bone and capsule is collected for histopathological examination. After determining its size, the femoral head is wrapped in three layers of sterile packing material, labeled and stored in the freezer within 30 min. The freezer has a temperature of -80°C, and has a continuous temperature registration device installed. Should the temperature fall outside the acceptable range of -90 and -70°C, an alarm system gives off a warning signal to the Technical Service, guaranteeing a 24- hours security against temperature-induced damage to the tissue. A nitrogen tank is fitted onto the freezer, as a backup cooling mechanism in case of mechanical breakdown of the freezer. In deep frozen condition, the allogenic bone tissue can be preserved for a maximum of 5 years. The temperature data is stored and managed by the bone bank administrator for a period of at least 5 years.

No permission from patient
 Under aged donor (<18 years).
 Active or recent systemic infection/sepsis
 Active infection of transplantation tissue (especially coxitis/osteomyelitis).
 Previously infected with tuberculosis
 Active "slow-virus" infection or anamnesis in the past
 Anamnesis of previous infection with hepatitis B or C, AIDS or AIDS related complex, or tested positive for HIV
 Active or past syphilis infection
 Recent (<4 weeks). vaccination with live vaccine (measles, yellow fever, mumps, polio, oral typhoid, rubella).
 Rheumatoid arthritis
 Diffuse connective tissue disorders/autoimmune diseases
 Metabolic disorders
 Existing insulin dependent diabetes mellitus
 Treatment with growth hormones
 Chronic medication (especially corticosteroids).
 Recent exposure to toxic substances
 Malignancies
 Donor location has been exposed to radiation
 Chronic neurological disorders
 Dementia
 Language barrier or when patient does not understand the information for any reason (e.g. psychiatric patients).

Table 2. General exclusion criteria

4.5 Allocation and implementation

If during surgery an orthopaedic surgeon decides to use a femoral head as an allograft, a femoral head from the freezer together with its documents are handed over to the orthopedic surgeon and surgery team. The orthopedic surgeon and theatre nurse verify the file and expiration date of the femoral head. The femoral head is thawed in physiological saline; after being defrosted the theatre nurse takes a bacterial culture swab.

The hospital or care institution warrants fulfillment of the traceability requirements, which implies storing the file of the femoral head and records of the receiving patient for 30 years post implantation.

A clinically proven HIV infection
 Men having homosexual intercourse after 1977
 Intravenous medication/ narcotics use, currently or in the past
 Immigrants (after 1977). from countries of which it is known that heterosexual intercourse is an important factor for HIV transmission
 Hemophilic patients administered with clotting factors concentrate
 Sexual partners from abovementioned individuals
 Men and women active in prostitution since 1977, and individuals being their partner in the past 6 months
 Individuals who recently (past 6 months). placed a tattoo or piercing
 Individuals who have had a blood transfusion before 1980
 Individuals who have had a blood transfusion outside Europe or North America
 Individuals who stayed in a SARS epidemic area or individuals who had face-to-face contact with a SARS patient

Table 3. Specific exclusion criteria

Blood type and Rhesus factor
 Erythrocyte sedimentation rate (ESR), age and sex dependant
 Normal values
 Male
 <50 years: 0-15
 >50 years: 0-20
 Female
 <50 years: 0-20
 >50 years: 0-30

Table 4. Hematological examination before surgery

Viral (hepatitis).
 Hepatitis B antigen
 Hepatitis B antibody
 Hepatitis C antibody
 Viral nucleic acid
 Viral (additional).
 HIV
 HTLV
 Bacterial syphilis
 TPHA (Treponema Pallidum, Lues).

Table 5. Serological examination 6 months postoperative

5. Quality control in hospital bone banking

The bone bank protocol contains several procedures to secure the retrieval, storage and implementation of predictable, safe femoral head allografts. To prevent transmission of infectious diseases and malignancies not only thorough donor screening, but also histopathological screening, culture swabs and serological screening are performed as a tool for quality control. In literature these complementary screening methods are discussed.

5.1 Histopathological screening

There is no uniform practice concerning histopathological evaluation of femoral heads retrieved from living donors. Some hospitals routinely examine all removed tissue specimens histopathological, suitable for bone banking or not. At some only gross examination is performed and at some neither evaluation is done. The utility and cost-performance ratio of routine histopathological evaluation is discussed in literature. Several studies doubt the cost effectiveness and necessity of routine histopathological examination (Campbell et al. 1997; Kocher et al. 2000; Lawrence et al. 1999; Meding et al. 2000; Raab et al. 1998). Campbell et al. performed a retrospective review of 715 pathologic findings of specimens obtained at total joint arthroplasties (283 hips and 432 knees). Of 715 specimens 3 were suggestive for low grade lympho-proliferative disorder and 3 for rheumatoid arthritis. In none of these cases this resulted in alteration in patient care. Follow up by telephone at 35 months revealed no signs of systemic disease. Therefore they conclude that routine histopathologic evaluation is not cost effective (Campbell et al. 1997). Kocher et al. performed 1234 arthroplasties (471 hips 763 knees) and found discrepant diagnoses in 28 patients, including (pseudo)gout, pigmented villonodular synovitis, osteonecrosis, granulomatous disease, hemochromatosis and rheumatoid arthritis. In two patients they found hypercellular marrow suggestive for lympho- proliferative disease. They performed no formal hematological work-up. They conclude that because of low prevalence of findings that altered patient management, routine pathological examination has limited cost effectiveness (Kocher et al. 1998). Meding et al. drewed similar conclusions. They found 27 discrepancies in pathology in 951 cases, however no neoplasia was noted. Lawrence et al. found malignancies in 11 of 1388 patients, including three cases of lympho- proliferative disease. They stated that the surgeon was able to identify malignancy with a sensitivity of 100 % and a specificity of 99.9%. They conclude that the surgeon preoperatively can exclude the possibility of malignancy and should reserve histopathological analysis for cases where the diagnosis is suspect or in case of unsuspected intra-operative findings (Lawrence et al. 1999). Raab et al. found two malignancies in a group of 168 patients, one of which had findings suggestive for lympho-proliferative disorder, however patient management did not alter. One patient showed osteomyelitis and this had clinical significance for patient treatment. In retrospect this turned out to be a misdiagnosis (Raab et al. 1998). The authors of these studies state that omission of routine pathology would bring about substantial decreases in charges. Campbell et al. estimated that the potential annual cost savings would be between \$43 million to \$61 million if all hip and knee arthroplasties in the USA were considered. Kocher et al. reported on \$122,000 in total costs for them to discover only one unexpected case of granulomatous inflammation. Total reimbursements were only slightly more than \$106,000, leaving them with a \$16,000 loss for the hospital. Clearly, desisting with routine pathology for presumed osteoarthritis in elective total joint cases could substantially decrease expenditures. The earlier described studies make compelling arguments for omission

of routine pathologic examination after elective joint arthroplasty for presumed osteoarthritis. The cost savings they estimate are enormous and patient management did not change because of an unexpected histologic diagnosis.

On the other hand some studies find higher percentages of unexpected pathological diagnoses and therefore advise routine histopathological examination (Billings et al. 2000; Clark et al. 2000; DiCarlo et al. 1994; Lauder et al. 2004; Palmer et al. 1999; Sugihara et al. 1999; Zwitser et al. 2009). DiCarlo et al. documented a 5.4% disagreement between the clinical and pathologic diagnoses of 1794 femoral heads from total joint arthroplasties, with a large-cell lymphoma, myeloma, sarcoma, ochronosis, Gaucher's disease, Paget's disease, and enchondroma. The authors recommended routine pathology for elective arthroplasty to both verify the diagnosis and to serve as a measure of quality control. Billings et al. described the unexpected finding of an occult primary bone sarcoma in two patients with otherwise benign clinical findings and therefore underscore the necessity for routine pathological examination of femoral head specimens from patients who are at risk for the development of a secondary malignant tumor (Billings et al. 2000).

Lauder et al. describe a patient with histopathological findings indicative for a low grade B cell lymphoma who developed systemic disease after 8 months. They underscore the fact that without routine pathologic examination, neoplasms could still be missed, even in patients who lack risk factors for malignancy and despite of a thorough preoperative evaluation. Furthermore they discuss the fact that studies in which low grade malignancies were found, suggested that their patients had been free of signs or symptoms for underlying disease, but did not perform a formal hematological evaluation for malignancy (Kocher et al. 2000; Campbell et al. 1997). They ask what the cost-benefit is when one is able to diagnose an unsuspected occult malignancy (Lauder et al. 2004). Clark et al. conclude that the routine histological evaluation of tissue excised from patients with an uncomplicated case of osteoarthritis may not be necessary at all hospitals, but when a patient has suspicion of another disorder than osteoarthritis and when gross examination suggests an unexpected finding, or when the results of such analysis are used for ongoing quality-assurance studies, histological examination is warranted. Other studies performed analysis of histopathological screening of femoral heads for bone banking screening purposes.

Palmer et al. analysed the histological findings in 1146 osteoarthritic femoral heads which would have been considered suitable for bone bank donation to determine presence of pathological lesions and found that 91 femoral heads (8%) showed evidence of disease. The most common benign conditions were chondrocalcinosis (63), avascular necrosis (13), osteomas (6), metabolic bone disease (2) and rheumatoid arthritis (4). Three cases of malignant tumour were described (one case of low-grade chondrosarcoma and two of well-differentiated lymphocytic lymphoma). They conclude that occult pathological conditions are common and recommend that histopathological screening should be included as part of the screening protocol for bone bank collection (Palmer et al. 1999). Sugihara et al. describe similar histological findings in routine bone bank screening of 137 femoral heads and found abnormal histopathological findings in five femoral heads: three were highly suspicious of low-grade B-cell lymphoma, one of monoclonal plasmacytosis and the other of non-specific inflammation of bone marrow (Sugihara et al., 1999). In routine histopathological screening the subsequent years this group found variable numbers of low-grade B-cell lymphoma, even in a group of femoral heads that were eligible for bone transplantation. In a long term follow up of these patients, with serendipitously found low grade B cell lymphoma on routine histologic examination, two developed systemic disease. Therefore we recommend

and perform routine histopathological screening as part of the bone banking protocol (Zwitser et al. 2009).

5.2 Culture swabs

In order to prevent transplantation of infected bone allografts we routinely perform culture swabs of the femoral head and synovium. If these culture swabs are positive for bacterial contamination the femoral head is discarded. Because femoral heads are readily available, any suspicion of contamination is respected, regardless of the source of the organism. At the time of implementation another two culture swabs from the thawed femoral head are performed. A culture of a specimen at the time of use of the femoral head serves two purposes: it is a quality-control check on the banking procedure, without the risk of additional contamination by separate culturing and handling, and it also allows the surgeon to administer an appropriate antibiotic should the culture be positive, especially if an infection occurs postoperatively (Tomford et al. 1986). However literature suggests that routine culture swabs are not always able to detect bacterial contamination.

Veen et al (1994) describe analysis of 75 fibular specimens obtained from cadaver donors under sterile conditions. All specimens were culture swabbed as routinely performed for retrieved allografts. Of these allografts 92 % were contaminated when cultured entirely but swab cultures were positive in only 45%. After swabbing, all specimens were placed in BHI-culture medium. Three different protocols were subsequently followed: 1) culture of the entire bone specimen in BHI-culture medium, 2) culture of the swab incubated on blood agar and chocolate plates, and 3) culture of the swab in BHI-culture medium. A control group included 20 sterilized bone specimens that were cultured entirely according to Protocol 1. The negative predictive value and sensitivity and were found to be 9% and 10% in Protocol 2 and 13% in Protocol 3. Therefore they conclude that swab cultures are inadequate to detect bacterial contamination of bone allografts in all cases. However, because of an acceptable infection rate after transplantation of the allografts that does not exceed those reported in other similar series, there is suggestion of an acceptable bioburden. Vehmeyer et al (2002) analyzed the bacterial contamination of 106 allografts of femoral heads obtained from living donors. From 15 initially swab positive grafts only five grafts were contaminated when cultured entirely. From 10 of 91 initially swab culture negative allografts microorganisms could be isolated when cultured in their entirety. They conclude that the routine swab culture technique seems to be less suitable for assessing the bacterial load of femoral heads obtained from living donors. Therefore they advise to routinely perform antibacterial processing before releasing an allograft for transplantation.

Antibiotic rinsing of the allograft seems not to be an effective decontamination method in allografts obtained from post-mortem donors (Deijkers et al. 1997).

James et al. (2002; 2004) determined whether the swab culture results had any clinical implication on wound problems or infections in the donor. In performed studies the rate of contamination was 9%, which is consistent with other studies. There was no difference in the complication rate of patients with a positive culture swab compared to those with a negative culture swab and therefore they conclude that positive culture swabs have no clinical implications for the donor.

5.3 Immunogenic screening

A question of interest to all bone banks was raised by a case report of a young Rhesus-negative female patient in whom antibodies to a Rhesus antigen developed after she

received a femoral-head bone allograft that had been stored by freezing. The graft was procured from a Rhesus positive donor, and the recipient had no other sources of sensitization (Johnson 1985). The immunogenic reaction of allografts is well known and extensively described in literature (Stevenson & Horowitz 1992). This immunogenic response is a reaction on the blood and bone marrow in the allograft. Fresh allografts, which have not been frozen, cause a massive vascular reaction, as has been recently proven by a CAM model (Holzmann et al. 2010). However, freezing of the femoral heads to -80°C for only three days caused a significant reduction of early vascularisation. Keeping the allografts frozen for longer than one month minimizes the angiogenic potential. Therefore a transfusion reaction after transplantation is unlikely. However, as shown by that case report, sensitization is possible, particularly to the Rhesus (D) (Rh-positive) antigen, which is highly immunogenic. We currently record blood type of all donors, however we only provide Rhesus-compatible grafts to Rhesus-negative women of child-bearing age, in an attempt to prevent problems with future pregnancies or transfusions.

5.4 Audit of a bone bank; further improvements

As a tool for quality control we performed an intern audit of our hospital bone bank, containing only femoral head allografts from living donors. For this audit we assessed all data from the bone bank registry from November 1994 and March 2010. We also included data from potential allografts which eventually pointed out to be not suitable for transplantation as determined by the aforementioned in-and exclusion bone banking criteria. We retrieved 643 femoral heads as potential allografts from 550 donors. Of 643 harvested femoral heads 242 (38%) were discarded. Based on one or more exclusion criteria 123 grafts were excluded based on the questionnaire or due to incomplete pre-operative donor data or tests. Furthermore, 34 grafts were discarded based on positive microbiological, histopathological or serological examination. In total, 64 grafts were discarded due to missing microbiological, histopathological or serological test after at least 6 months. The rest had to be excluded because of tears in the package, loosening of labels, discovery of malignancies in the donor patient and deceased donors in which serological examination could not take place. We calculated the costs associated with complete testing of one femoral head as potential graft which includes all laboratory, histopathological and bacteriological tests. If all completely tested femoral head allografts would be suitable for donation this bone bank would be financially advantageous, even with routinely performed histopathological assessment. It is never possible that all potential donor allografts are suitable for bone banking. However in our bone bank the major loss of potential allografts is mainly due to managing, administrative and logistic omissions. Therefore currently managing our own hospital bone bank offered no financial benefits. We provide safe and reliable allografts with good accessibility. We calculated that hospital bone banking can be a financially viable strategy, when logistic procedures are more accurate. We made improvements in the logistic procedure of testing and retesting and expect future improvements of our financial bone banking balance.

6. Conclusions

There are no uniform guidelines for management of a bone bank. The bone bank protocol should meet national law. The described bone bank protocol from our hospital provides for safe and easy accessible allografts. We routinely perform histopathological screening, this

practice is extensively discussed on in literature. At this moment we have no financially viable bone bank. This is due to organisational and logistical problems, which have our attention in order to further improve the bone banking process in the near future.

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Quality control is a standard which certainly has become a style of living. With the improvement of technology every day, we meet new and complicated devices and methods in different fields. Quality control explains the directed use of testing to measure the achievement of a specific standard. It is the process, procedures and authority used to accept or reject all components, drug product containers, closures, in-process materials, packaging material, labeling and drug products, and the authority to review production records to assure that no errors have occurred. The quality which is supposed to be achieved is not a concept which can be controlled by easy, numerical or other means, but it is the control over the intrinsic quality of a test facility and its studies. The aim of this book is to share useful and practical knowledge about quality control in several fields with the people who want to improve their knowledge.

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