1. Introduction

Due to the growing of HIV pandemic in the world and especially in Africa during the last two decades, it has become more and more frequent to find HIV infected patients with an absolute indication of arthroplasty. In fact, the indication of arthroplasty in these patients may be a very challenging issue. Even though all of these patients are not immune depressed, due to the known natural history of HIV carriage, the risk of future immune depression remain and logically the risk of immediate, early, or late infection of arthroplastic implants and subsequent loosening or worse, generalized infection. The literature on this question remains very scarce; the first section of this chapter will present a classification of HIV carriers elected to Arthroplasty, describe protective measures for each class of patients, and present immediate, short and mid term expected results, based on a systematic analysis, and Authors own experience. The second section will be focused on arthroplasty in sickle cell disease (SCD) carriers, as these types of patients usually demand arthroplasty at the end stage of secondary vascular necrosis, the most frequent adult joint complication of their genetic condition. Lastly, as Very few, if any, is known in case where both conditions (HIV & SCD) are combined in the same patient demanding arthroplasty, a short section will be proposed.

Section A: Arthroplasty in HIV carriers

- Introduction
- Pathogenesis of HIV infection
- Work up and classification of HIV carriers elected for arthroplasty
- General principles & practices of antiretroviral therapy
- Antiretroviral therapy in HIV carriers demanding arthroplasty
- Prophylactic antibiotic therapy in HIV carriers undergoing arthroplasty
- Section A Summary

Due to the spreading of HIV worldwide during the latest decades, it had become more and more frequent in the orthopaedic practice, to indicate an arthroplasty, especially of the hip, in patients living with HIV. This virus has been incriminated by many authors as a possible causal agent in the case of bone’s aseptic necrosis. The profiles of the HIV infected patients are variable: some are previous known carriers, other are discovered at the time of the preoperative workup. The duration of the preoperative antiretroviral treatment vary also from one patient to another. Anyhow, the main question for the orthopedic surgeon is to find out what is the level of the immune system of a person living with HIV and who is a candidate for an arthroplasty? In another words, what is the infection risk of the implant,
whether immediately, in the short, the mid and even the long term? These questions may be better understood through a review of the pathogenesis of HIV infection.

1.1 Pathogenesis of HIV Infection
HIV infection is due to the introduction of the related virus in the body mainly through unprotected sexual intercourses, secondly through blood transfusion, and more rarely through other ways. Sometimes the patient may present a minor inflammatory syndrome lasting for few days with a complete recovery and no detectable virus for a long period. In some people, the virus will spread into the body fluids and organs and will slowly, but surely, destroy a specific type of lymphocytes, named CD4; the problem is that, CD4 are the hardware of the body immune system and thus, the protector against numerous common infectious agents. With time, and after many years, no matter the apparent normal clinical state, the CD4 lymphocytes count which is normally above 500 Cells/Ml, will decrease progressively with a proportional depression of the HIV carrier immunity. If nothing is done, the general status of the patient will decompensate with severe weight loss, anemia and fatigue. He will develop opportunistic infections or tumors which are exceptional in an immune competent person. The most common opportunistic diseases are from the skull to the foot: brain toxoplasmosis, mouth and esophageal candidiasis, lung tuberculosis and pneumocystoses, intestinal cryptosporidiosis, leg and generalized Kaposi angiosarcomas, and various lymphomas. At this stage, the majority of patients are killed by a combination of these diseases and their complications. It is obvious that clinical pictures of HIV carriers are numerous, depending on the level of the immune depression; a classification is therefore necessary. The WHO-AIDS has proposed such a classification based both on the clinical picture and biological markers. However, as far as arthroplasty is concerned, the extreme majority of demanders of this surgery look clinically well; therefore, except in case where they declare themselves, if a systematic sample of HIV serology is not done, the surgeon may be taking the risk of a major surgical procedure in an advanced immune depressed patient. In our practice where the HIV carriage is up to 10% into the general population, HIV screening is mandatory before any elective arthroplasty. No matter the result, the benefice is defendable. In fact, in one hand, negative patients may at least undergo an auto transfusion program while, in the other hand, virus carriers will be classified and appropriately managed before or during arthroplasty. Such classification is mainly based on immunological work up, since, as it had been said above, quite all patients look healthy.

1.2 Work up and classification of HIV carriers elected for arthroplasty
After the diagnosis is done and an indication of arthroplasty is made, especially into the areas of high HIV carriage in the general population, the Orthopedic Surgeon should obtain an inform consent from his patient about this uncomfortable matter. In twelve years practice in our community, we have not had any of our patients for hip arthroplasty resisting to the above arguments, but as with all medical information, discretion is the rule. If the patient is a known HIV carrier already on antiretroviral treatment, we will look up for his latest CD4 count and viral load. In the other cases, the screening is mandatory; if the patient is seronegative, he is managed conventionally with the advantage of auto transfusion program, provided hepatitis B and C serology are negative. In HIV positive screened patients, the next step is the confirmation western-Blot test; if the latest is negative; the patient is qualified as non HIV carrier and managed as usual. In case of confirmed HIV
carriage by western-Blot test, the next step is the CD4 lymphocytes count and the viral load measurement by up to date procedures. The CD4 lymphocyte count is the key point for HIV carriers classification. Patients with less than 500 CD4 lymphocytes / ML are considered immune depressed and named class A arthroplasty demanders. Depending on whether this count is above 300, less than 300 with no opportunistic disease, or less than 300 with an opportunistic disease, Class A patients are further sub divided A1, A2 or A3. Non immune depressed HIV seropositive Patients with low infection risk are classified B; if they were known before and under treatment, they are sub-divided B1, if they have more than 500 CD4/ML with no treatment, they are sub-divided B2. This makes a total of 5 classes of arthroplasty demanders living with the virus (B1, B2, A1, A2, A3) and thus, who need specific protective measures and especially, antiretroviral therapy (ARVT).

1.3 General principles of antiretroviral therapy
Antiretroviral therapy (ARVT) was introduced in the early nineties with the aim to act against the multiplication of the HIV and therefore, to stop the destruction of the CD4 lymphocytes and subsequent immune depression. The drugs are numerous, but have been considered based on their action into 3 main classes which are: antiproteasis, nucleoside inhibitor of reverse transcriptases and non nucleoside inhibitor of reverse transcriptase. Into the middle of the decade, it clearly appeared that none of these classes could solely stop the viral replication and that, in the contrary, the triple combination was efficient. Shortly after, the common presentation became a triple antiretroviral fixed combination drugs commonly named TRITHERAPY.

There are two most common combinations that are: Efavirenz, Zidovudine and Lamivudine into one hand, and on the other hand, Niverapine, Stadivudine and Lamivudine. In case of drug resistance, a second line combination of Indinavir, Zidovudine and Lamivudine is proposed. The first line treatment, which is commonly used, has shown that besides few sides effects seen at the beginning of the treatment, that combination is usually well tolerated thereafter and it is efficient. In a large majority of patients the CD4 level will rise above 500/ML after weeks to months and the virus will be undetectable in the peripheral blood, making them significantly less contagious to their sexual partners. Many institutions in our country give drugs only to severely immune depressed carriers defined as AIDS patients. Moderately immune depressed and non immune depressed carriers are not treated. Therefore, it remained a question weather this policy does not favor the spreading of the disease through the world? Anyway, whenever an arhtroplasty is demanded by a HIV carrier, a different protocol of ARVT should be associated.

1.4 Antiretroviral therapy in HIV carriers demanding arthroplasty
Finally, 5 types of HIV carriers have been considered among arthroplasty demanders; they may need a similar number of protocols regarding ARVT.
1. B1 Arthroplasty demanders are already known as HIV carriers and under ARVT; they should never stop their treatment even the day before and after surgery. There is nothing to do more, compare to non carriers patients. Exceptionally, if their CD4 count is low, they are referred to their physician to find out if this low count is due to drug resistance or to a non compliant attitude. The surgery should be delayed, and the issue corrected by a second line protocol ARVT.
2. Type B2 arthroplasty demanders (HIV carriers with >500 CD4 lymphocytes/ML): they are not immune depressed no matter their viral load; they should be managed
according to the protocol of their physicians. Into our own practice, they will be operated with no ARVT and will be placed on treatment only if the CD4 count fall below 500/ML during the follow-up. After they have started with ARVT, they will continue it forever.

3. Type A1 patients, (HIV carriers with 300 to 499 CD4 lymphocytes/ML), as they are moderately immune depressed, should be placed on ARVT shortly after the CD4 count results and they should undergo surgery without delay. Although it is not recommend by the official policy, we believe that they do need treatment before they undergo major surgery to give them a protection which may be needed anyway in the future.

4. Type A2 arthroplasty demanders (HIV carriers with less than 300 CD4 lymphocytes/ML, but with no opportunistic disease), who are by definition asymptomatic, but severely immune depressed, are placed on ARVT and their surgery postponed for a few weeks till the CD4 lymphocytes/ML above 300 is obtained. Exceptionally in the emergency setting, the arthroplasty should not be postponed but the patient must be protected by a prolonged antibioprophylaxis which is actually an antibiotherapy.

5. Type A3 arthroplasty demanders (HIV carriers with less than 300 CD4 lymphocytes/ML, but with an opportunistic disease) are first treated for their opportunistic disease, various prophylaxes, ARVT and the surgery postponed as above. In all the cases, prophylactic antibiotic therapy should also be considered.

1.5 Prophylactic antibiotic therapy in HIV carriers undergoing arthroplasty

The aim of classical prophylactic antibiotic therapy (PATB) is to keep the surgical site under antibiotic protection during the short period of decrease immune response around the perioperative period. This period, which is less than 72 hours in a normal individual, may be prolonged in cases of immune depressed HIV carriers. Our previous study has shown that there is no significant difference in rates of post-operative infections between immune depressed and non immune depressed patients when we extend PATB to 10 ten days, what we call prolonged prophylactic antibiotherapy, (PPATB) as one would expect. Although there were only few cases of arthroplasty in this serie. Finally, as far as arthroplasty demanders are concerned, two different regiments of prophylactic antibiotic therapy are to be considered, that is:

1. The classical regiment of PATB with intravenous cefuroxime (or any other second generation cephalosporin); 1.5g at the anesthesia induction, followed by 750 mg every 12h within not more than 72 hours. This is indicated for class B arthroplasty demanders.
2. The extended regiment of PPATB into which the above regiment is maintained during 10 days. This is indicated for all class A arthroplasty demanders.

1.6 Section A summary

Finally, combined protective measures of HIV carriers demanding arthroplasty may be summarized as follow (table I), depending of their classification:

1. B2 patients should continue their previous ARVT and, get normal PABT during the arthroplasty which should not be delayed.
2. B1 may wait to start ARVT when the CD4 count will cross the 500 line; they should undergo normal PABT and their arthroplasty with no delay.
3. A1 patients should start an ARVT and get their arthroplasty not delayed but under protective PPABT.
4. A2 patients should start the ARVT and the arthroplasty delayed when they cross the 300 line in their CD4 count; the surgery should be protected by a PPABT.
5. A3 patient should first be treated for their opportunist disease and later on managed as A2.

With these measures, we think that the results of arthroplasty in HIV carriers should be comparable to HIV seronegative counterparts.

<table>
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<tr>
<td>B2</td>
<td>HIV+, CD4&gt;500</td>
<td>NO</td>
<td>YES</td>
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</tr>
<tr>
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<td>HIV+, 300&lt;CD4&lt;500</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>A2</td>
<td>HIV+, CD4&lt;300 no opportunist infection-</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>A3</td>
<td>HIV+,CD4&lt;300 &amp; some opportunist infection-</td>
<td>YES</td>
<td>NO</td>
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Table 1. Summarizing the use of ARVT, PABT, & PPABT in the five type HIV carriers demanders of arthroplasty

2. Section B: Arthroplasty in SCD carriers

- Definition & history of SCD
- Physiopathology of SCD & related secondary avascular necrosis
- Diagnosis and classification of SCD
- Work-up and management of SCD systemic acute complications
- Section B summary

2.1 Definition & history of SCD

SCD is a chronic hemolytic hemoglobinopathy that is genetically transmitted. During a crisis, red blood cells become sickle-shaped increasing blood viscosity, slowing blood flow, and consequently plugging small blood vessels creating widespread thromboembolic tissue infarction.

This genetic disease which is the most frequent genetic disease in black people, is also the most common cause of femoral head necrosis in them. In fact, SCD touches up to 0.74% of the births in sub-Saharan Africa, while this number is 10-20 times less in Europe and North America. In Nigeria, an estimated 45,000 to 90,000 babies are born each year with SCD. The African blacks are the main victims but the disease is also distributed in the south of Italy, Greece, Turkey, the Arabian Gulf, especially Saudi Arabia, and the Indian subcontinent. In the United States SCD occurs in approximately 1 out of every 500 African American births. People in the USA with sickle-cell disease number 90,000 of which 80,000 are black and 10,000 are Hispanic. The state with the highest sickle-cell population was New York with 8000, followed by Florida with 7500, and Texas with 6700 people with SCD. FLOUZAT-LACHANIEETTE et al. report a series of SCD patients developing secondary avascular...
necrosis that originated from Africa, the United States of America, the Indian subcontinent, the Persian Gulf and from Mediterranean countries. Multifocal secondary vascular necrosis was found to occur in at least 64 percent of patients.

2.2 Physiopathology of SCD & related secondary avascular necrosis
Herrick first described the characteristic sickle-shaped erythrocytes in 1910 and Pauling and colleagues identified the abnormal hemoglobin (HbS) and coined the term “molecular disease” in 1949. Hemoglobin A is normally found in the adult and is composed of four globular protein subunits the α and β globins. A fetal form or hemoglobin F is also found, normally, in small proportion in the adult. In SCD, an inappropriate substitution of valine for glutamine at the sixth position of the β globin chain produces hemoglobin S that polymerizes at low oxygen tensions. This causes the red cell to sickle which increases viscosity in the microvasculature and leads recurrent episodes of vaso-occlusion. These recurring episodes of widespread infarcts in patients homozygous for the sickle cell gene (HbSS) cause life-threatening conditions such as renal failure, acute chest syndrome, autosplenectomy, immune deficiency and infection all leading to an early death. As far as heavy surgery and especially arthroplasty is concerned in SCD patients; the key points and the difference with non SCD patients will therefore be focused into the prevention, the monitoring, and if needed, the management of the above cited acute systemic complications.

But SCD complications are not just acute; these repeated cycles of hypoxia and inflammation due to sickling cause chronic musculo-skeletal pain and finally secondary avascular necrosis of bone ends, especially, femoral and humeral heads, and less frequently, femoral condyles. This secondary avascular necrosis, at the end stages, causes severe chronic joints pain and functional impairment, for which very few solutions except of arthroplasties are currently available. In deed, secondary avascular necrosis is the leading indication of arthroplasty in SCD carriers. Secondary avascular necrosis doesn’t occur only in homozygous HbSS patients; it is also common in heterozygous SCD clinically asymptomatic carriers with AS hemoglobin. In to the other hand, other types of abnormal hemoglobin such as HbC (Substitution of a lysine for glutamine at the 6th position of the β-globin chain) are also found in some patients with similar effects. Finally, secondary avascular necrosis due to SCD is therefore not exclusively observed in homozygous SS patients (HbSS); it should also be suspected in various other heterozygous forms; especially, HbAS and HbSC carriers.

2.3 Diagnosis and classification of SCD and related secondary avascular necrosis
To specifically diagnose SCD, cheap and widely available techniques such as hemoglobin electrophoresis or chromatography accurately determine the levels of HbA, HbF, HbS and HbC.

For secondary avascular necrosis and bony lesions due to SCD, standard X-ray, C-T Scan, Isotope Scan, and MRI are indicated in various stages for diagnosis and staging. However, the FICAT-ARLET classification is the must commonly used world wide. It is divided in four stages as below.

FICAT-ARLET classification of AVN (17):
Stage I: MRI changes
Stage II: Sclerotic and cystic changes
Stage III: Collapse
Stage IV: Osteoarthritis on both sides

2.4 Work-up and management of SCD systemic acute complications

2.4.1 General
Preoperatively the HbS level should be of less than 30% of the circulating hemoglobin before major surgery such as Arthroplasty; however, VICHINSKY et al., have shown in a randomized controlled trial that, exchange transfusion may not be necessary to avoid complications. In all cases, it is prudent to take the preoperative hemoglobin concentration to 100 g/L and to keep it at this level in the early postoperative phase; this objective may be obtained by ordinary transfusion of normal red blood cells as it may be confirmed by post transfusion electrophoresis or chromatography. This will also reduce the risk of perioperative thromboembolic complications. The above target hemoglobin level may be rich by preoperative oral folic acid of few weeks, in those SCD patients with less than 30% of HbSS during the initial work-up; however, at least postoperatively, blood transfusion will be needed. It should be clear that, to the best of current literature, there is no place for autologous blood transfusion in SCD patients; these patients should always be managed with homologous bank blood products. In the other hand, Reduction of HbS concentrations may be obtained by the chronically use of hydroxycarbamide because this increases the concentration of fetal hemoglobin (HbF) which reduces hemolysis and prevents vaso-occlusion. It is also well known that that hypothermia, acidosis, hypoxemia and dehydration should be avoided pre and postoperatively.

2.4.2 Acute chest syndrome
Acute chest syndrome is a specificity of SCD and affects around 20% of the patients. A combination of thoracic pain, fever and infiltrates on thoracic x-ray characterizes this syndrome. The etiology is multifactorial including pulmonary embolism, microvascular occlusion and infection Severity varies, but 13% of patients require mechanical ventilation and 3% may die. In a post operative period of any arthroplasty procedure in SCD patient, this syndrome should be seriously considered in establishing etiologies of acute chest pain. In fact, it prevention and management include respiratory support, antibiotics, blood transfusions and deep venous thromboses prophylaxis/therapy. At times corticosteroids may be indicated.

2.4.3 Infection
Susceptibility to infection is an issue in SCD. Many of these patients are immunocompromised because of autosplenectomy and osteonecrotic tissues tend to be colonized by Gram negative organisms. Several organisms have been identified as important causes of infection including S pneumoniae, H influenza, and non-typhi Salmonella species and appropriate antibiotic prophylaxis and immunization must be instituted in these patients. Therefore, a systematic preoperative investigation should be undertaken prior to any Arthroplasty procedure in a SCD patient to rule out occult infection; this should a least include urine culture, ENT consultation and dental examination and corrections. If there is a suspicion of infectious foyers a full antibiotic
treatment should be undertaken with normalization of biological markers prior to the joint procedure. After arthroplasty, bone fragments from joint resection and reaming should also be send for bacterial analysis; if positive, a specific antibiotic testing should be undertaken. Subsequently, a long term antibiotic therapy should be undertaken in collaboration with the infectious diseases team, and till the normalization of biological infectious markers.

2.5 Section B summary
Finally, arthroplasties of the Hip, the knee, the shoulder or any other joint may commonly be demanded by SCD patients, mainly due the high frequency secondary avascular necrosis as a chronic complication of their genetic condition. The procedure may be performed with at least acceptable results, provided the following precautions are properly taken:
- Conventional biological work-up and especially, the hemoglobin types/ratios, and comprehensive research of occult infections.
- Preoperative treatment of any occult or evident infection
- Enhancement of the fetal hemoglobin ratio by chronic preoperative administration of hydroxycarbamide.
- Enhancement of the total Hemoglobin level to 100G/ml preoperatively, by chronic oral folic acid, and maintaining it so per and post operatively by homologous red blood cells
- Optimal oxygenation during the early post operative period
- Optimal fluid infusion during the early post-operative period
- Adequate warming during the early post-operative period
- Avoiding any acidosis state by blood gas control and correction during the early post operative period
- Culture of bone resection/reaming products and subsequent long standing and targeted post arthroplasty antibiotic therapy
- Avoiding autologous blood transfusion

3. Section C: Arthroplasty in HIV & SCD carriers
- Introduction
- HIV carriage in SCD patients
- Antiretroviral therapy in SCD patients
- Summary of section C

3.1 Introduction
After sexual intercourse, blood transfusion had been considered as one the possible pathway HIV contamination. Into the other hand, due acute episodes and chronic anemia, SCD patient had been to be more frequently transfused than normal hemoglobin carriers; it therefore appear rational to hypothesize that SCD patients present a higher risk of HIV infection. The literature on this matter is very scars; and the clinical experience does not confirm this theoretical thinking. This may be due to at least a reduction on the transfusion rate in sickles and a better safety of blood banking systems. In the other hand, both HIV &
SCD have been incriminated as high risk factor or secondary aseptic necrosis, mainly of the hip. Provided the standard treatment of aseptic necrosis of the Hip is total hip arthroplasty, it become evident although rare and not reported currently, combination of both condition (SCD& HIV) in patients demanding arthroplasty, may in the next future, become a challenging issue. There is no evidence base on this precise issue; however, since the above both section A and B have been focused respectively on arthroplasty in HIV carriers in one hand, and in another one, Arthroplasty in SCD, knowing about HIV carriage in SCD patients may help to set up our thinking regarding arthroplasty in patients with both conditions.

3.2 HIV carriage in SCD patients
As it has been said above, the literature on HIV carriage in SCD patients is very scars, due to the paucity of patients themselves. In fact, the clinical experience in Central Africa where HIV carriage is higher than 10% in general population, shows that this rate is not significantly higher in homozygous HbSS patients. Further more, as the large majority of HbSS homozygous patients are also sexually active, it make sense to believe that the HIV infection in these specific set, is got through the same pathways with the general population. One of the rare related paper we could found regarding this matter is the one of Bagasra O et al; it suggests that, in patients with both SS and HIV-1 infection, the retroviral disease may be ameliorated by host factors of which absence of splenic function prior to HIV-1 contamination may be one. In another term, this author assume that HbSS carriage makes the body more resistant to HIV process as into his experimental case-control study of ten years follow-up, both the CD4 count and the Viral load were better in HbSS patients with HIV infection compare to HbAA counter part with the same viral infection. This may be explained by the fact that, as the spleen and lymph nodes are major sites of human immunodeficiency virus type 1 replication, mutation, and genetic variation in vivo; and as a major portion of this lymphatic tissue, such as the spleen, is removed or otherwise is unavailable for invasion by the HIV-1 virus, the course of this infection is altered. The clinical consequence is a prolonged symptom-free interval or even increased survival that we experience in daily clinical follow up of homozygous HbSS patients. Into the contrary, as it was reported by Sellier P et al, no significant difference in HIV infection progression is observed between heterozygous SCD carriers with HIV and their normal Hemoglobin counter part with the same virus.

Therefore, as far as HIV carriage is concerned in SCD patients, we should always distinguish homozygous patients in which, the expected course of retroviral process is slow than usual in one side, and in the other side, heterozygous patient in which it does not differ from that of the non SCD-non HIV patients. The same differentiation may be necessary regarding the management of antiretroviral therapy (ARVT) in this field.

3.3 Antiretroviral therapy in SCD patients
If we agree to distinguish Homozygous patients from their heterozygous counterpart regarding the HIV carriage, it makes sense to do the same in the matter of ARVT. Regarding first homozygous HbSS patients, to the best of our knowledge, no evidence exist on the use of ARVT on them. However, on observing a short cohort of 5 patients in our practice at the Central Hospital of Yaoundé in Cameroun in to the last 5 years, our standard
protocol of ARVT has been well tolerated by homozygous HbSS patients, provided all the other measures of SCD control are well conducted. In the contrary, we have more heterozygous SCD patients with HIV carriage under ARVT; as said above; the tolerance and efficiency of ARVT on them does not differ from the general non SCD population.

3.4 Summary of section C
There is very little evidences and experience on how to manage patients demanding arthroplasty, in cases where they are simultaneously HIV and SCD carriers. This little experience shows that those who are heterozygous should be managed as non SCD patients. In those who are homozygous, a simultaneous protocol of SCD care protocol as presented in section B, should be added.

4. References


The purpose of this book was to offer an overview of recent insights into the current state of arthroplasty. The tremendous long term success of Sir Charnley’s total hip arthroplasty has encouraged many researchers to treat pain, improve function and create solutions for higher quality of life. Indeed and as described in a special chapter of this book, arthroplasty is an emerging field in the joints of upper extremity and spine. However, there are inborn complications in any foreign design brought to the human body. First, in the chapter on infections we endeavor to provide a comprehensive, up-to-date analysis and description of the management of this difficult problem. Second, the immune system is faced with a strange material coming in huge amounts of micro-particles from the tribology code. Therefore, great attention to the problem of aseptic loosening has been addressed in special chapters on loosening and on materials currently available for arthroplasty.

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