1. INTRODUCTION

2. OVERVIEW OF LEVELS OF EVIDENCE

3. OVERVIEW OF SICKLE DISEASE

3.1. Pathophysiology

4. SPECIFIC MUSCULOSKELETAL CONDITIONS

4.1. Avascular Necrosis of Bone- The Hip

4.1.1. Classification

4.1.2. Epidemiology and Natural History

4.1.3. Prognosis

4.1.4. Treatment of Early Stage Avascular Necrosis of Hip

4.1.4.1. Physiotherapy/Activity Restriction

4.1.4.2. Core Decompression

4.1.4.2.1. Core Decompression and Bone Graft

4.1.4.2.2. Core Decompression and Tantalum Rod Insertion

4.1.4.3. Injection of acrylic into the crescent line

4.1.4.4. Bone Marrow Injection

4.1.4.5. Extracorporeal Shock Wave Treatment

4.1.4.6. Should we treat early stages?

4.1.5. Treatment of Late Stage Avascular Necrosis of the Hip

4.1.5.1. Excision (Girdlestone arthroplasty)

4.1.5.2. Arthrodesis

4.1.5.3. Considerations Regarding Excision and Arthrodesis in the African Setting

4.1.5.4. Pelvic Support Osteotomy
1. INTRODUCTION

Sickle cell anemia is widely prevalent in Africa and with better survival there are an increasing number of patients suffering from the musculoskeletal manifestations, most notably avascular necrosis of the femoral head, which leads to disabling arthritis in early adulthood. Although the molecular biological understanding of sickle cell anemia dates back more than half a century, this has not led to effective treatments for patients suffering the skeletal manifestations of the disease. For the surgeon, understanding the clinical evidence, will allow for rational decisions, while we await better surgical and biological solutions.

2. OVERVIEW OF LEVELS OF EVIDENCE

Classifying articles by level of evidence can be very useful in making clinical decisions. **Level one evidence** comes from well performed randomized controlled trials, or systematic reviews of such trials. Level one evidence results from true scientific experiments performed in the clinical setting. Physicians are accustomed much level one evidence regarding the effectiveness of medical therapies, particularly new ones, because randomized controlled trials need to be performed before new drugs can be marketed. No such requirement exists in surgery. Furthermore, considerations of expense, lower disease prevalence, and the reluctance of surgeons and patients to randomize operative treatment makes randomized trials rare in surgery and means that we rely on lower levels of evidence to support many of the clinical decisions we make.

**Level two evidence** comes from prospectively performed comparative studies. These studies follow patients forward in time after different treatments which were not assigned randomly (and usually were assigned on the basis of surgeon and/or patient preference). In order to be sure that differences in outcome are related to the treatment, it is very important to consider whether the patient groups were similar to each other prior to treatment.

**Level three evidence** comes from retrospectively performed comparative studies. These can be either retrospective cohort or case – control studies. A retrospective cohort study groups patients according to treatment received and compares the clinical outcomes. A
case – control study groups patients according to the outcomes they had and looks backwards in time for predictors or risk factors. In both cases, comparisons can be made which distinguish one treatment from another.

**Level four evidence** comes from case series. This is still a very common design in surgical clinical studies but it provides poor evidence. There is almost no way to compare the results of one treatment to another by comparing two case series, because differences in the patient population, referral patterns, year of treatment, and methods of identifying patients and assessing outcomes will be different for each series. These factors combined are often far more important than the treatment performed in determining the outcome. Case series are very rarely of genuine clinical value, eg. in the circumstance where outcomes are ‘all or nothing’, such as 100% survival from a previously fatal disease.

**Level five evidence** is expert opinion. Many articles support a particular treatment but contain no actual information about clinical outcomes. These are of very limited value in making clinical decisions.

In this review we will comment where possible on the level of clinical evidence supporting a particular statement. The table below provides a quick guide to the level of evidence associated with each clinical study design. Although the level of evidence schema has been extended and refined to include studies about prognosis, diagnosis, and health economics (see [www.CEBM.net](http://www.CEBM.net)), here we will restrict the discussion to levels of evidence regarding choices of therapy as summarized in the table.

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Type of Study</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Randomized Controlled Trial</td>
</tr>
<tr>
<td>II</td>
<td>Prospective Comparative Study (cohort)</td>
</tr>
<tr>
<td>III</td>
<td>Retrospective Comparative Study (cohort or case – control study)</td>
</tr>
<tr>
<td>IV</td>
<td>Case Series</td>
</tr>
<tr>
<td>V</td>
<td>Expert Opinion</td>
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</table>

3. OVERVIEW OF SICKLE DISEASE

Sickle cell disease is common in Africa and is both biologically fascinating and clinically challenging. It was one of the first diseases for which the molecular genetic basis was understood. Edington reported from Africa in 1955 on electrophoresis to identify the abnormal haemoglobin protein HbS. (1) Despite early biological understanding of the condition there is no curative medical therapy and musculoskeletal manifestations continue to occur, and perhaps increase as improved general care allows prolonged survival.

Clinical treatment of musculoskeletal conditions is challenging because the treatments are not perfect, particularly for entities such as avascular necrosis of the femoral head which causes considerable disability in young patients. Although there is some randomized trial
evidence available to guide treatment of early disease, the level of evidence regarding
treatment of late stage disease is poor and there are legitimate questions about whether
reported results of total hip replacements from Western countries can be applied to
clinical decision-making in Africa. The authors will attempt to support a pragmatic
approach to care by balancing a discussion of levels of evidence in the published
literature with clinical experience in West Africa.

3.1. Pathophysiology

All humans have two genes for the beta-globin subunit of the hemoglobin molecule. A
single amino acid substitution mutation results in the production of abnormal hemoglobin
HbS which polymerizes under conditions of low oxygen saturation and causes red cells to
stiffen into a sickle shape. Heterozygotes (HbSA) produce roughly half abnormal HbS
and half normal HbA and clinically have sickle cell trait, but have very few
manifestations of disease. Homozygotes (HbSS) produce nearly all HbS and clinically
have sickle cell anemia. Heterozygotes lacking the normal HbA gene (HbSC) have an
intermediate form of the disease. Persistence of fetal hemoglobin (HbF) provides
relative protection against sickling in early infancy, but following this the clinical
manifestations begin to occur. (2)

Among homozygotes, sickling and red cell adhesion to endothelium on the venous side of
the microcirculation, is common in many organs. As the circulation slows the
surrounding blood becomes deoxygenated, leading to further sickling and further vessel
occlusion. My pathology professor described this as a vicious viscous sickle cycle.
Stuart has written a review article, which gives tremendous insight into the current
understanding of the biological details. (2) Clinical manifestations include infarcts of
bone marrow, bone, lung, kidneys, spleen, and brain. This Surgery in Africa review
concentrates only on the musculoskeletal manifestations.

4. SPECIFIC MEDICAL CONDITIONS
4.1. Avascular Necrosis of Bone - the Hip
4.1.1. Classification

Two popular classification systems for avascular necrosis (AVN) of the hip are
summarized in the Table 1. These classifications are used for avascular necrosis from
other causes (trauma, steroids, alcoholism) as well as for avascular necrosis from sickle
disease. It is worth paying close attention to the etiology of avascular necrosis as well as
the stage of disease because sickle cell AVN has a very poor prognosis compared with
other causes, as further detailed below. In addition to the stage of collapse, the Steinberg
classification also includes quantification of the area of the femoral head involved by
careful measurement of the plain x-rays.

The Ficat classification was described in a paper published in 1985 which is among the
classics in defining the pathoanatomy and pathophysiology of avascular necrosis. (3) In
this paper Ficat argued that avascular necrosis was analogous to a compartment syndrome
of bone and could be treated in an analogous way by core decompression. The
classification relies on functional testing of the bone with measurement of intraosseous pressure, venography, and core biopsy all of which are painful and invasive procedures no longer in widespread use. It is the clinical and plain x-ray aspects of the classification which have stood the test of time. Most textbooks, and therefore most trainees, discuss the Ficat system, but there are advantages to using the classification proposed by Steinberg.

Steinberg’s classification is quite similar to that of Ficat for stages 0, 1 and 2 (early stage disease) with the main difference being that disease, not apparent on radiographs, is detected by either bone scan or MRI instead of functional testing of bone. (4) While Ficat considered a crescent line to be ‘between stages 2 and 3’ (difficult!), Steinberg has divided late disease into finer stages with 3 being the crescent line and 4 through 6 progressive degenerative changes as outlined in the table. Importantly, for use in Africa, the Steinberg system relies only on careful evaluation of plain radiographs for all distinctions except that between stage 0 and stage 1.

Table 1

<table>
<thead>
<tr>
<th>Stage</th>
<th>Ficat 1985</th>
<th>Steinberg 1995</th>
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<tbody>
<tr>
<td>0</td>
<td>Suspected disease (usually because opposite hip involved)</td>
<td>Normal X-ray, normal MRI and / or bone scan</td>
</tr>
<tr>
<td>I</td>
<td>Normal X-ray, groin pain, abnormal intraosseous pressures, venography, or biopsy</td>
<td>Normal X-ray, abnormal MRI and / or bone scan</td>
</tr>
<tr>
<td>II</td>
<td>Cystic or sclerotic changes on X-ray, no crescent line</td>
<td>Cystic or sclerotic changes on X-ray, no crescent line</td>
</tr>
<tr>
<td>III</td>
<td>Sequestrum of femoral head with or without collapse of sequestrum</td>
<td>Crescent sign, &lt;=1mm flattening of femoral head</td>
</tr>
<tr>
<td>IV</td>
<td>Joint space narrowing and osteophytes</td>
<td>Collapse of femoral head &gt;1mm, no joint space narrowing</td>
</tr>
<tr>
<td>V</td>
<td></td>
<td>Collapse plus joint space narrowing</td>
</tr>
<tr>
<td>VI</td>
<td></td>
<td>Advanced degenerative changes</td>
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</table>

4.1.2. Epidemiology and Natural History

In some parts of Africa between 20% and 40% of the adult population have been found to carry sickle cell trait (heterozygous condition). (1) Epidemiological studies of African Americans show 1 in 14 with sickle cell trait, and 1 in 700 with sickle cell disease. (5) The heterozygous sickle cell trait confers relative protection against falciparum malaria
which accounts for the persistence of the mutation. There are some very rare heterozygous conditions (HbSC or HbS-beta thalassemia) where patients produce half HbS but also produce another abnormal hemoglobin (HbC or beta – thalassemia), these individuals have variable clinical manifestations corresponding to a milder form of sickle cell anemia.

Not everybody with sickle disease will suffer musculoskeletal complications. The most common symptom in sickle disease is painful bony crisis but the vast majority of these have no permanent sequelae. Avascular necrosis of bone, particularly of the femoral head, is challenging for patients and surgeons because it can produce significant pain and functional disability with no clearly proven ways of preventing progression of early stage disease.

Powars followed a cohort of 1056 HbSS homozygous patients for 4 decades beginning in 1959 at an American hematology clinic. This is not a true natural history study because the patients were treated, and also the treatment evolved and improved over time, so it may be considered in some ways a best case scenario. A quarter of the patients died during the follow-up period, and among patients still alive half of them had irreversible organ damage by the fifth decade of life. Avascular necrosis of bone was the second most common organ damage, occurring in 21% of patients and presenting at a median age of 31 years. Iwegbu reported a cross – sectional study of 899 patients aged 6 to 28 years seen at a sickle cell clinic in Nigeria between 1982 and 1983. Twenty nine of these patients (three percent of the total) presented with symptoms of avascular necrosis of the hip, including 28 haemoglobin SS patients and one haemoglobin SC patient.

These days many sickle patients in Western countries are treated with hydroxyurea, a myelotoxic drug. The net effect of the marrow toxicity is to mildly suppress hematopoeisis and stimulate increased production of fetal hemoglobin (Hb-F), which counteracts the tendency to sickle and reduces the manifestations and progression of the disease. This treatment is supported by randomized controlled trial evidence (Level 1) from a US multicentre study led from Baltimore. The potential for benefit to African patients is large if this treatment can be made widely available, but an African based study would also be required to ensure that infectious complications are not a problem in Africa where the spectrum of infectious diseases is different.

Among 84 adult patients with sickle disease (HbSS) referred to an orthopaedic clinic in Yaounde for known or suspected musculoskeletal involvement, the most common diagnoses were avascular necrosis (41%), malleolar ulcer (23%), osteomyelitis (18%) and septic arthritis (7%).

Mijiyawa reported on the common conditions presenting to a paediatric rheumatology clinic in Togo. Most patients (43%) had bone or joint infections, but about 1/3 of the children with infections had sickle cell disease as well. A further 7% of patients presented for painful vaso-occlusive crisis and 1% for avascular necrosis related to sickle disease.
4.1.3. Prognosis

Symptomatic avascular necrosis of the femoral head in adults has a very high probability of progression. Hernigou reported on 92 symptomatic hips among 64 adult patients with sickle disease in a single centre prospective consecutive cohort study. (12) Seventy five hips had no radiographic collapse at presentation and all but ten of them had progressed to collapse within five years, with an average time to collapse of 42 months for stage 1 disease and 30 months for stage 2 disease. After 17 years of follow-up, 88 of the 92 hips had undergone some sort of operative procedure to treat intractable pain. In addition, the contralateral hip (if normal) showed plain X-ray changes of avascular necrosis among 20% of patients, and bilateral disease could be diagnosed in 23% of patients if symptoms or MRI findings were considered also.

This prompted a study of the fate of the asymptomatic hip in patients with sickle disease. The same author published a 2006 paper following 121 initially asymptomatic contralateral hips in patients with sickle cell disease who were being seen for hip pain on the opposite side. (13) Among these asymptomatic hips, 56 had normal plain x-rays and MRIs on presentation, 42 had abnormal MRI findings but normal plain films, and 23 had abnormal cystic or sclerotic appearance of the femoral head on plain films. The vast majority of asymptomatic hips became painful. Among those with abnormal plain x-rays at presentation 80% were painful by 2 years, among those with normal plain x-rays but abnormal MRIs 80% were painful by 3 years, and among those with normal plain x-rays and normal MRIs 80% were painful by 16 years. Progression to collapse of the femoral head was seen in 100% of stage II hips within 5 years, 80% of stage I hips within 8 years, and 50% of otherwise apparently normal hips within 15 years – a dismal prognosis for an asymptomatic and apparently normal hip to say the least!

Compared with the poor prognosis for either symptomatic or asymptomatic contralateral hips in adults with sickle disease, children seem to fare a little better after osteonecrosis in sickle disease. Perhaps this is related to the remodeling potential of the growing skeleton. Again the study was reported by Hernigou, this time on 52 children with sickle related avascular necrosis from a mean age of onset of 12 years and with 19 years of follow-up. (14) Only 1/3 of them had progressed to symptomatic osteoarthritis (stage IV disease or higher) and progression was more common among children with greater degrees of femoral head deformity from childhood, although some children with a completely round, nondeformed femoral head had progressed to osteoarthritis, strongly suggesting that biological factors play a significant role – for example there may be persistence of inflammatory pannus which eventually destroys even a mechanically perfect joint. Among the 31 patients, 2 had a second episode of avascular necrosis of the same hip during adulthood.

In summary, over 20% of adult sickle cell patients will develop avascular necrosis of the femoral head. Among those who do, progression to end stage hip disease is very common if they are followed for long enough. In addition, even an asymptomatic and radiographically normal contralateral hip has a high risk of progression to end stage arthritis as well.
4.1.4. Treatment of Early Stage Avascular Necrosis of Hip

Treatment of avascular necrosis in sickle-cell disease follows the same principles used for other causes of non-traumatic osteonecrosis. The results for sickle-cell disease are however poorer because of the underlying pathophysiology.

The Cochrane database of systematic reviews is an excellent starting point for finding clinically useful summaries of the medical literature. A Cochrane review identifies studies which meet pre-specified methodological criteria (usually restricted to randomized controlled trials) and summarizes the evidence to guide clinical practice. There is a Cochrane systematic review on treatment of avascular necrosis in people with sickle disease (15). The review identifies only one study which meets its methodological criteria (the randomized trial of Neumayr discussed below) and concludes that there is inadequate evidence regarding sickle disease to guide practice. We will go into more detail on some of the lower levels of evidence, recognizing the limitations.

There has been no consensus on what should be considered early. However, generally the pre-collapse stages of Ficat and Steinberg are considered early.

For the purpose of clarity, early will be Ficat and Steinberg 0, I, II and III. These early stages are usually picked up more in the advanced countries because patients will go to a hospital as their first port of call. In the poor countries, most patients are diagnosed when the pathology has progressed past the collapse stage. Akinyoola et al, 2007 in a retrospective study (level IV) of 416 patients found that, 60.6% presented with stage IV disease (Ficat) while 21.2% had stage III and 18.2% had stage II. (16) No patient was diagnosed in stage I or 0. It is worthy of note that most patients do not have access to MRI and CT scans, and therefore, plain x-rays will continue to be the only and main stay of radiological evaluation for a very long time.

4.1.4.1. Physiotherapy / Activity Restriction

In a multicenter randomized control level II study comparing physiotherapy alone to physiotherapy and core decompression after 3 years follow-up, (17) Neumayr showed that the results of physical therapy alone were as good as the results of physical therapy plus core decompression in improving hip function and deferring the need for additional surgery. Femoral head preservation at 3 years was 86% with physical therapy alone in Neumayr’s report, and the Harris hip score had improved by 15.7 points out of 100. By comparison, with core decompression operation the femoral head survival at three years was 82%, and the Harris hip score had improved by 18.1 points. In the poor regions, this is valuable information. The mean follow-up was only three years, and given the documented natural history of the condition one would expect the results to deteriorate with time. Although the study was a randomized prospective study, it is classed as level II evidence because the sample size was small and there was more than 20% loss of follow-up. There are also questions about the generalizability of this trial, since only 46 patients were enrolled of 176 who were potentially eligible - a common problem with surgical randomized trials.
Physiotherapy is best used for Ficat and Steinberg Stages 0, I, and II. When used for stage III in either classification, there is a 100% likelihood of radiological and clinical progression, but there is postponement of the time when surgical intervention becomes necessary.

4.1.4.2. Core Decompression

Large studies on core decompression have included avascular necrosis of all etiologies, not simply restricted to sickle disease.

Ficat promoted core decompression of the femoral head based on his theory that avascular necrosis was analogous to a compartment syndrome of bone, and that decompression would therefore promote revascularization and healing. (3) He reported the results of core decompression in 121 patients without specifying the follow-up period or using any validated method to assess the outcome. Although Ficat concluded that core decompression was a good idea, the patient material in his original article could not be considered even level IV (case series) evidence by current standards, and there was certainly no comparison made.

Stulberg published a 1991 report of a ‘randomized protocol’ that compared the results of core decompression to the results of nonoperative management in avascular necrosis of the femoral head. Success of treatment was based on lack of progression to total hip replacement. The results of core decompression were reported as better for Stage I and II hips.

An older randomized study had compared the results of core decompression alone versus nonoperative management (with no mention of the explicit physiotherapy protocol). Within two years, collapse had occurred in 78% of the core-decompressed hips and 79% of the conservatively treated hips, leading the authors to conclude that the core decompression operation alone was of no value in preventing collapse of the femoral head. (18)

We found a single study restricted to core decompression for sickle disease (as opposed to other causes of AVN), this was a small case series of 10 patients with early (stage I or II) disease, none of whom had progressed to further surgery at 3.7 years average followup. (19) Of note, in this population operative complications were high, with one infection, one acute chest syndrome, and one severe transfusion reaction. Although the core decompression may be a small operation, in the sickle cell population the complications of the surgery and anaesthesia itself must be weighed against the unproven benefits of the intervention.

The study of Neumayr et al (17) is also restricted to sickle disease and reported hip survival after core decompression of 82% at 3 years for up to stage III was no greater than that for physical therapy alone. At present, therefore, the core decompression operation alone cannot be recommended for sickle cell patients with early AVN.
4.1.4.2.1. Core Decompression and Bone Graft

After a core decompression, there is an inherent weakness in the femoral neck. Insertion of the bone graft provides mechanical support during the healing stages. This bone graft may be vascularized, in which case there is a theoretical advantage of an additional source of blood supply.

A 1991 case series (level IV evidence) reported no collapse at two years in 18 of 19 AVN patients treated with core decompression supplemented by structural bone grafting using tibia, fibula, or allograft fibula for the graft. (20) A much larger case series was reported in 2001, (21) describing the results of 406 hips in 285 patients, with follow-up from 2 to 14 years. While the authors supported the treatment, the failure rates are substantial (40% to 60%) and therefore the case series evidence is not conclusive.

Using a vascularized fibular graft adds considerably to the complexity of the procedure and to the donor site morbidity because a muscle pedicle must be taken with the graft and a small vessel anastomosis performed. A large case series of 187 patients (of whom 9 had sickle disease) reported 54% of hips remaining stable postoperatively, and 44% progressing clinically or to total hip arthroplasty, at an average of 4.7 years. (22) Similar results were reported by Judet, with 18 year follow-up of 60 patients. (23) In both series, the absence of a comparison group makes it impossible to conclude whether this complicated procedure improves the natural history of the condition.

The core decompression and bone grafting series all include patients without sickle disease, and all constitute level IV evidence (case series) with many failures of treatment over the long run. This operation therefore cannot be currently recommended for patients with early stage AVN from sickle disease.

4.1.4.2.2. Core Decompression and Tantalum Rod insertion

This is also in trial stages for non sickle-cell osteonecrosis. It has the advantage of eliminating donor site morbidity and providing a shorter operative time compared with the vascularized or nonvascularized bone grafting options described. (24) 68% femoral head survival at 48 months follow-up was reported, and patients with chronic conditions (including sickle disease) fared worse than this suggesting that this option may be no better than natural history also.

4.1.4.3. Injection of acrylic into the crescent line

Hernigou reported five year results of ten patients (16 hips) all with sickle cell disease who had an open arthrotomy and injection of acrylic cement beneath the subchondral fracture. Two hips failed and required arthroplasty, eight others showed progression of radiographic degenerative changes, but the clinical results in terms of pain relief and improvement in Harris hip scores were reported as favorable. Again, a small case series
(level IV evidence) with mixed outcomes is insufficient to recommend this procedure for general use.

4.1.4.4. Bone Marrow Injection

A pilot study prospectively compared 10 patients with avascular necrosis treated with injection of autologous bone marrow cells to 8 patients receiving core decompression alone. At two years the rate of collapse was 10% in the bone marrow group, and 60% in the control group. If long term results validate this assertion, it will be very beneficial to poor countries.

4.1.4.5. Extracorporeal Shock Wave Treatment

A single randomized trial (Level I evidence) was published in 2005 comparing treatment of stage I, II, and III disease with extracorporeal shock waves (similar to lithotripsy for kidney stones) with vascularized free fibular grafting. Harris hip scores and pain ratings were better at two years in the shock wave group. This follow-up period is too short to know whether the treatment is influencing the clinical course of the disease. The cause of the avascular necrosis was not specified and may not have included any patients with sickle disease (the study was performed in Taiwan). Although this was a well performed clinical study, the main message to take away for the African setting is that the results of core decompression with vascularized grafting were inferior to the results of a noninvasive technique in a randomized trial. This adds to the evidence suggesting that core decompression with or without vascularized fibular grafting cannot be supported as a routine standard of care.

4.1.4.6. Should we treat early stages?

The natural history study presented by Hernigou suggests that patients with early stage AVN who are symptomatic will progress to femoral head collapse at a median of 42 months for stage I disease and 30 months for stage II disease. This inevitable decline has led to a wide range of proposed treatments, usually a sign that none of the treatments proposed works all that well. The best evidence is that from randomized controlled trials comparing femoral head decompression to non-operative management, and two such trials suggest that surgery confers no advantage. More complicated surgical strategies involving bone grafts, vascularized grafts, or tantalum rods added to the core decompression are only supported by case series (level IV) evidence and are not currently appropriate for most African settings, nor are they of proven value compared with the natural history of the disease. Most articles promoting these therapies have included avascular necrosis of all forms, not just that from sickle disease which is known to have a poorer prognosis. Therefore, at present, we should not treat early stage avascular necrosis of the hip in sickle disease in Africa except by simple non-operative methods such as activity modification, relief of weight-bearing, and physical therapy.
4.1.5. Treatment of Late Stage Avascular Necrosis of Hip

Late stage avascular necrosis of the hip is characterized by femoral head collapse with joint space narrowing causing marked stiffness, pain, and activity restriction. Unfortunately this is an all too common presentation for young adults who face the demands of work and raising a family. There is no ideal treatment and selecting the correct treatment will rely on judgment and making tradeoffs including surgeon, patient, and facility / setting factors.

Reconstructive operations can be divided into biological (excision, arthrodesis, and osteotomy) and artificial (hip replacement arthroplasty). The widespread availability and increasing success of hip replacement arthroplasty has led Western experts to assert (level V evidence) that non-replacement operations should not be considered if they substantially compromise the results of a later hip replacement. (27) This thinking probably does not apply yet in most African settings, and we will consider the biological approaches first.

4.1.5.1. Excision (Girdlestone arthroplasty)

This is used for advanced degenerative disease, Steinberg V and VI and Ficat IV. This involves excision of the head and neck of femur. It creates a floppy limb. It causes at least 4cm shortening. However, it eliminates pain. If there is an infection, this may also be eliminated. Theoretically, it can be converted to a total hip arthroplasty at a later and more suitable date. It can also be used as a salvage procedure when osteotomies and arthroplasties have failed. Sometimes, the tip of the greater trochanter may impinge on the ilium causing pain. Case series reporting results of the girdlestone arthroplasties are not directly applicable to the young African population. An Indian case series reports excellent pain relief but reliance on walking aids following Girdlestone arthroplasty after failed reconstruction for trauma. (28) A Dutch case series describes similar clinical results following Girdlestone arthroplasty for failed total hip joints. (29) Small case series have supported the conversion of Girdlestone arthroplasties to total hip replacements at a later stage. (30)

4.1.5.2. Arthrodesis

This involves fusion of the joint, which may be intra-articular or extra-articular.

It provides a solid painless column for walking. Stover et al report on 18 young patients with hip arthrodesis; 16 returned to work with good relief of pain and restoration of function. (level IV evidence). (31) They also assert that a hip arthrodesis can be later converted to a total joint arthroplasty if there are degenerative problems in the spine or in the knee. They consider the best indication for a hip arthrodesis to be unilateral disease in a young healthy patient with potentially heavy physical demands.
4.1.5.3. Considerations Regarding Excision and Arthrodesis in the African Setting

Sickle disease is highly likely to produce bilateral symptomatic avascular necrosis, with half of completely normal contralateral hips progressing to painful collapse within 15 years. (13) The high likelihood of having to deal with bilateral disease, combined with the practicality of living with a resection arthroplasty or hip fusion, has led to the following pragmatic approach.

Most of the patients are in the reproductive age. For the woman, hip fusion creates problems with coitus since she cannot abduct at the hips. This has the potential of affecting her marriage. She cannot be placed in the lithotomy position during child birth. In effect, she is condemned to caesarian section. In the poor countries where access to health care is not optimum, there is a high risk of birth related complications.

Again, in the poor countries where access to a water closet is not global, people have to take care of business in the wilderness, and this involves squatting. With a hip fusion they may be free of pain, but certainly not grateful. In a man however, he may the better be served by arthrodesis on one side and excision at the other if it is bilateral. This gives him a solid painless column for walking and a flexible, shorter and unstable other for taking care of personal hygiene.

4.1.5.4. Pelvic Support Osteotomy

A pelvic support osteotomy is a femoral osteotomy performed at the level of the ischial tuberosity to place the proximal part in extreme valgus – thus allowing the pelvis to be supported against what was the medial aspect of the femur without relying on the hip joint for a true articulation. This is a biological reconstructive option for end-stage hip disease in a young patient who wants to preserve range of motion. The current approach to this reconstruction includes a distal femoral osteotomy and lengthening using an external fixator and ilizarov principles. The combination of a proximal osteotomy and distal lengthening allows restoration of length and mechanical alignment, restoration of abductor muscle function, maintenance of hip flexion range, and improvement in gait. Accomplishing this without hip replacement arthroplasty makes this a potentially appealing approach to hip reconstruction in some African settings. A report from Egypt on a case series (level IV evidence) of 25 hips showed improvement in gait in 20 of 25 patients, improvement in flexion (90 degrees pre-op to 127 post-op), and improvement in comfort and function measured by an increase in the Harris hip score from 55 pre-op to 82 post-op. Patients in this series had a mixture of initial pathologies, with 5 of the 25 being operated on for avascular necrosis. (32)

4.1.5.5. Hip Replacement Arthroplasty

Although hip replacement arthroplasty has the potential to provide excellent function and pain relief, the enthusiasm for using this operation in patients with sickle disease has been tempered by the generally unsatisfactory results reported. Clarke showed a 59% failure
Friedman reported a failure rate of 40% in 7.5 years and an infection rate of 20%. A recently published series of 312 consecutive total hip arthroplasties for sickle cell avascular necrosis has reported substantially better results, with only 3% infections, 8% acetabular loosening, 8% femoral loosening, and 13.5% revision rate at 13 years. These results come from a high volume dedicated sickle cell clinic in France and involve extensive precautions against infections including pre-op cholecystectomy (to remove a frequent source of bacteremia) and the use of antibiotic impregnated cement. It is unlikely that these results can be replicated in a lower volume or general orthopaedic unit and the higher complication rates from the older case series may be a more reliable guide to what can be expected.

Most of these patients are very young and active, thus making them poor candidates for selection. The micro-infarction continues and therefore, fixation at the bone-implant interface is suboptimal, thus predisposing them to loosening and infection. Peri-operative morbidity is high. With as high as 60% complication, one must expect frequent trips into the operating room with all potential complications.

Arthroplasty has a place in Africa, but patients must be carefully selected. Patients and their families must be made aware of these complications in advance. Manpower and expertise may not be easily available for subsequent revisions and all the complications associated. Frequent trips to the operating room and anesthesia may be luxuries in developing countries.

4.2. Bone Crisis

The most common clinical presentation of sickle cell disease is a vaso-occlusive crisis producing bone marrow edema and pain. This occurs in 57 times per 100 person years of patient follow-up. Any bone can be affected with tibia and humerus being the most common sites. Fever and mild increases in white cell count accompany local swelling, redness, and tenderness at the involved site. Vaso-occlusive crisis is managed by rest, rehydration, and analgesics and does not generally present to the surgeon unless there is a question of infection (discussed below). A prospective multicentre cohort of sickle patients within the first decade of life recorded 32.4 sickle crises per 100 patient years, and 1.1 deaths per 100 patient years with most deaths being due to sepsis.

4.3. Infection

People with sickle cell anemia are susceptible to osteomyelitis (salmonella, staphylococcus aureus, streptococcus pneumonia) and to sepsis (strep pneumonia) because splenic malfunction does not allow them to mount an appropriate immune response. Strep pneumonia sepsis is the most common cause of death among sickle cell children to age 5. In a landmark randomized clinical trial, prophylaxis with oral penicillin was shown to reduce infections by 84% among children under 5 and dramatically increase survival.
The clinical presentation of osteomyelitis or septic arthritis overlaps substantially with that of vaso-occlusive crisis. Vaso-occlusive crises, which are the most common presentation of sickle cell disease, present with bone pain and tenderness, fever and sometimes an elevated white blood cell count. A ‘left shift’ (higher neutrophil count) is suggestive of infection, as is fever above 38.5 celsius. Aspiration and culture may be required in difficult cases. A retrospective review of osteomyelitis and septic arthritis among children with sickle disease in the United States found cultures were positive in 75% of tissue biopsies, 58% of the blood cultures, and 70% of the bone or joint aspirates. (38)

The distinction between a vaso-occlusive crisis and an infection of bone cannot be reliably made by imaging modalities including radionuclide bone scans, or MRI scans. (39) The combination of a normal bone marrow scan (showing no infarction) and an abnormal bone scan was highly correlated with culture proven osteomyelitis in one American series, but such scans are not widely available in low income countries. (40)

Epps (1991) reported on 15 cases of osteomyelitis in patients with sickle disease, of which 8 were staphylococcus aureus and six were salmonella. A protocol of operative decompression plus six weeks of intravenous antibiotics resulted in resolution of infection in all but one patient. (41)

Treatment of septic arthritis of the hip includes arthroscopy and irrigation to decompress the joint and prevent avascular necrosis and cartilage damage by surgical dogma. Septic arthritis of other joints is more controversial, with physicians favoring treatment by needle aspiration, and surgeons favoring arthroscopy and joint lavage. We found a single randomized trial performed in Africa which demonstrated that for children with septic arthritis of the shoulder, needle aspiration was equivalent to open surgical lavage measuring both clinical and radiographic outcomes at two years. (42) Accordingly the simpler treatment (joint aspiration) can be recommended. This trial considered all children with septic arthritis, most (86%) grew salmonella, only one child had sickle cell anemia.

In children under four years of age, dactylitis is common presenting as multiple acutely swollen and painful fingers and toes, this presentation decreases after the age of four when hematopoetic marrow is no longer present in digital bones. These are infarcts and are typically not infected, they require only supportive and symptomatic treatment. Sequelae of the dactylitis are rare but can include growth arrests producing short fingers. (39)

5. PERIOPERATIVE CONDITIONS
5.1. Transfusion

Patients with sickle cell anemia are, by definition, anemic and therefore preoperative transfusion is widely practiced. A randomized controlled trial published in 1995 established that simple transfusions to achieve a preoperative hemoglobin of 10 grams per deciliter was superior to an aggressive exchange transfusion regimen designed to
bring the hemoglobin-S level down to 30% or lower. (43) The patients with the simple transfusion regimen had substantially fewer transfusion related complications (7% versus 14%), and an equal number of other serious perioperative complications and events (35% versus 31%). Based on this level one evidence the standard of care is to follow a simple transfusion regimen to increase the preoperative hemoglobin to 10 grams per deciliter or more.

5.2. Complications of Surgery

Vichinsky et. al. reported on the peri-operative complication rate for orthopaedic surgery in sickle cell disease, on behalf of the US National Sickle Cell Surgery Study Group. Among 188 patients undergoing 138 surgeries at 26 centres, the overall serious complication rate was 67%. (44) The most common operation was hip replacement (38%), followed by hip coring (16%) and other hip surgery (14%). Excessive intra-operative bleeding (>10% blood volume) was the most common complication, occurring in 44% of patients. Sickle cell events, including acute chest syndrome (16%) and vaso-occlusive episode (13%) occurred in 17% of patients overall. Infections or fevers occurred in 14%, transfusion related complications in 12%, and neurologic complications in 4%. There were 2 deaths related to surgery (1%). Both deaths were related to acute chest syndrome, one in a 43 year old undergoing revision hip arthroplasty, and one in a 16 year old, who had an elbow arthrotomy for joint swelling. Clearly the high complication rate related to sickle disease needs to be taken into account when considering the risk benefit ratio of orthopaedic procedures, and the peri-operative care needs to be optimized.

One randomized trial showed substantial benefit from using incentive spirometry to prevent acute chest syndrome among hospitalized sickle patients with chest pain including those from rib infarcts. Atelectasis and infiltrates developed in 1 of 19 hospitalizations when spirometry was used, and 8 of 19 when it was not. (45) This level one evidence can be used to support a recommendation that post-operative patients, who are also at risk of acute chest syndrome, could be treated prophylactically with incentive spirometry.

5.3. Tourniquet Use

The aim of using a tourniquet is to provide a bloodless field during surgery and also to minimize blood loss. Because a tourniquet causes stasis, deoxygenation, and acidosis the traditional dogma has been that tourniquet use be avoided in patients known to have sickle cell disease. There are two case series supporting the use of the tourniquet in sickle disease, both describe small series of patients operated on using tourniquets and without major complications, specifically without inducing a sickle crisis. (46),(47) By contrast, a retrospective cohort study from Nigeria found seven complications of tourniquet use including three significant (sickle crisis, pain, jaundice) among nineteen sickle patients, and no significant complications of tourniquet use among a matched control group without sickle disease. (48) None of the clinical evidence is definitive, but the best strategy is to avoid tourniquet use for routine cases in sickle cell patients, and to
ensure optimal physiological management for those in whom a tourniquet is considered necessary.

6. SUMMARY

Sickle cell anemia presents difficult decisions for the musculoskeletal surgeon. The highest level clinical evidence does not necessarily answer the most important clinical questions for the surgeon. Randomized trial evidence (Level I) supports the prophylactic treatment of patients under 5 with oral penicillin to prevent infection, supports the use of hydroxyurea to improve the clinical course of the disease, and supports simple transfusions (to 10g per dL) pre-operatively. There is also randomized trial (Level I) evidence supporting a conservative, physical therapy based approach to management of early stage avascular necrosis of the hip. Other operations (core decompression with or without grafting, vascularized grafting, or tantalum rods) have not been shown superior and come with a high complication rate so at present the best evidence supports that the best care is very conservative for early stage disease. For late stage hip disease there are many options, none perfect, and a generally low level of evidence (level IV case series) supporting any of them. Thinking through the options and discussing the pros and cons of each in light of the patient’s circumstance allows us to practice the art of medicine, but we should also be encouraged, collectively, to advance the science for the sake of this large population of patients. Other presentations of sickle disease include infections, which can be difficult to distinguish from aseptic sickle bone crises. The highest level of evidence surrounding these infections is a randomized trial from Malawi demonstrating that simple aspiration is equal to arthrotomy in treating septic arthritis of the shoulder in children. Beyond its clinical utility, this trial shows how a simple, well performed study in Africa can fill fundamental gaps in the clinical science of surgery.

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7. REFERENCES


13. Hernigou P, Habibi A, Bachir D, Galacteros F. The natural history of asymptomatic osteonecrosis of the femoral head in adults with sickle cell disease.[see comment].
http://simplelink.library.utoronto.ca.myaccess.library.utoronto.ca/url.cfm/51910

http://simplelink.library.utoronto.ca.myaccess.library.utoronto.ca/url.cfm/51911


http://simplelink.library.utoronto.ca.myaccess.library.utoronto.ca/url.cfm/51913

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