Orthopaedic implications of physeal arrest following meningococcal septicaemia.

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Declaration

I, Dr. Jean-Pierre du Plessis, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, or is to be submitted for another degree in this or any other university.

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To Professor EB Hoffman thanks for the inspiration and guidance during this study and for your tireless commitment to teaching.

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Literature review

Introduction

Thirteen patients seen at Red Cross Children's and Maitland Cottage hospitals have under gone complex treatment for the significant deformities caused by meningococcal septicaemia. These patients underwent 62 surgical procedures between them. These procedures were directed at the treatment of sequelae of growth arrest alone and excluded amputations, contracture releases, skin grafts and flaps. The extent of the surgical problems caused by this disease brought about the realisation that a thorough review of the literature and follow up of these patients was required. This would hopefully be of use in assessing the outcomes of various surgical treatment options employed and in developing guidelines for the future management of physeal arrest in these patients.

The aims of the literature review were:

> To assess the extent of the problem as reported by orthopaedic units in other parts of the world, in particular to ascertain the incidence of physeal injury following meningococcaemia.
>
> To evaluate the nature and distribution of the growth arrest reported in the literature so that it could be compared later with findings in this study.
>
> To determine international trends and results in the surgical management of physeal arrest following meningococcal septicaemia.

To this effect a literature review was carried out using the internet search engine Pubmed and the reference lists from relevant articles. The focus of the review was specifically physeal arrest caused by meningococcal septicaemia. This was expanded to include literature on the pathophysiology and medical management of the disease in order to gain more introductory background knowledge on the subject. Papers dedicated to the management of soft tissue complications both acute and delayed were only included if

reference was made to growth plate injuries as part of the research. They were otherwise excluded.

History

The first description of meningococcal disease, as noted by De Souza et al.[1] was by Vieusseux in 1805 during the epidemic of cerebrospinal fever in Geneva. The understanding of the disease at this stage was however flawed as the transmission was attributed to 'bad air' rather than person to person contact.

Since then there have been numerous advances in the understanding, diagnosis and treatment of this devastating illness. The discovery of a meningococcal antiserum in 1906 by Flexner[2] reduced mortality rates from 75-80% down to 30%.[3] The world wars had a profound effect on the spread of the disease in the close living quarters of army recruits and the introduction of sulphonamides during this time reduced the mortality rate further to around 15%.[3]

Herrick stated in 1919 that "the meningeal picture resulting from meningococcus infection has so fixed the attention of clinicians and pathologists that possibilities of extrameningeal infections by the organism have had scant notice".[4] He further noted that this had resulted in the failure to recognise the true nature of the disease as a meningococcal septicaemia which had implications on the management of the disease.[4] These observations highlighted the complex nature of this illness and its' treatment difficulties which persist today.

Today, with improvement in the diagnosis and management of the acute illness there is an increase in the survival rates of patients with meningococcal septicaemia. With improved survival rates there is an increase in the number of long term orthopaedic complications reported in the literature.

Epidemiology, pathophysiology, histology

Neisseria meningitidis can be isolated from the nasal cavities of up to 10% of healthy individuals.[5] They are transmitted by direct inoculation of mucous membranes or inhalation

of aerosolised droplets[1] and outbreaks typically occur in closed populations with close living conditions such as military recruits.

The colonisation and subsequent invasion of the nasopharyngeal mucosa is the initial step in the pathogenesis of meningococcal disease.[1,6] The virulence of the strain, susceptibility of the individual and certain undefined environmental variables are the main factors that influence transmission and the presentation of disease.[1,6]

Most individuals develop protective IgA antibodies during the carrier state. These individuals are not necessarily carriers of the pathogenic *Neisseria*. Antibodies produced to the polysaccharides of other *Neisseria* are cross reactive.[6] For some patients carrying the pathogenic strains of *Neisseria* the spread of the bacteria to the bloodstream occurs too rapidly for the antibodies to develop and provide protective immunity. In these cases bacteraemia may result in meningitis, endotoxaemia and septicaemia.[6,7] The foetus receives transplacental antibodies which persist up to the third month of life and are generally not detectable by eight months.[7] Studies have shown that there is then a slow increase in the amount of antibodies as the child ages[7]. This results in the highest incidence of life threatening infections occurring between the ages of 6 months and 2 years.[6,8]

Meningococci appear histologicaly as gram negative diplococci and are non-motile, non-sporulating and non-acid fast.[6,7] *N. meningitidis* is distinguished from *N. gonorrhoea* by the presence of a polysaccharide capsule external to the cell wall.[6] The cell wall of the meningococci contain a short chain lipopolysaccharide referred to as lipooligosaccharide (LOS).[6,8] This LOS is the bioactive substance released by the meningococcus and is an endotoxin.[8,9] It has been shown to activate the immune response via the Toll-like receptors (TLR), specifically TLR-4.[10] The TLR activation results in gene transcription and inflammatory mediator production via the nuclear factor kB. This initiates a powerful inflammatory cascade in the intravascular space and central nervous system[9] and results in a vasculitis and disseminated intravascular coagulation.[7,11] The prothrombotic state presents as ischaemia and is clinically manifested as pupura fulminans.[1] Bradykinin is also produced via the kallikrein-kinin pathway causing increased capillary permeability and increased nitric oxide production in the endothelial cells.[9] Nitric oxide influences vascular tone and its' levels are related to the severity of the disease.[12] Myocardial depression may

complicate the disease and contribute to poor tissue perfusion.[13] In the acute disease the end point of critically impaired tissue perfusion caused by these factors is shock and multiorgan failure with a mortality rate ranging from 7-15%.[14,15]

Orthopaedic manifestations

By definition multiorgan failure involves all systems and the musculoskeletal system is not spared. The combination of hypoperfusion and DIC result in skin necrosis, gangrene and compartment syndrome requiring fasciotomies and amputations and leading to soft tissue contractures. Physeal growth plate injury manifests later as growth abnormalities which present as shortening or angular deformity of the limbs.

The management of the initial limb ischemia, with or without fasciotomy, and the treatment of skin necrosis and soft tissue contractures is well described in the orthopaedic literature.[14,16,17] The problems associated with amputations (especially below knee), such as stump overgrowth and contractures, often necessitating through knee amputations, is also well documented.[11,14,16]

This literature review deals primarily with the physeal injury which occurs as a result of ischaemia secondary to the vasculitis and to a lesser extent as a result of osteomyelitis.[11] These changes have been demonstrated on histological specimens taken at the time of amputation from patients with the acute illness.[11,18] Although the osteomyelitic involvement of bone (epiphysis, metaphysis and diaphysis) usually recovers without sequelae, damage to the physis leads to permanent physeal arrest.[11,18]

Physeal arrest: the literature

The first reported cases of bony deformities following meningococcal septicaemia were by Fernandez et al. in 1981.[19] Previous bony abnormalities following meningococcaemia were reported in 1977 but these resembled sickle cell dactylitis and resolved without sequelae.[20] A patient with residual ankle valgus was also described in 1973 but no mention was made of underlying bone abnormalities.[21] Fernandez et al. however reported on three cases which presented between 4 and 18 months after an episode of meningococcal septicaemia. The presentation was that of epiphysiometaphyseal irregularities in all three

patients, varus tibiae with “slanting of the tibiotalar joint” in two and necrosis of the talar dome and navicular in one. The upper limbs were reportedly unaffected apart from the surgical amputation of a number of phalanges. No mention is made of the link between the deformities and physeal growth plate damage. The authors theorised that the changes in the bony architecture were secondary to bone infarcts that occurred at the time of the acute illness. They also suspected that the localisation of the abnormalities to the lower limbs was as a result of the increased stress secondary to ambulation. Importantly they suggested that all patients who had suffered from meningococcal septicaemia with intravascular coagulation should be followed up closely and suggested delaying ambulation if bony deformities were encountered.[19]

Later that year Patriquin et al.[22] presented 4 cases of bony deformity following meningococcaemia and described the classic ball-and-socket configuration seen as the epiphysis “invaginated into the metaphysis”.[22] They compared this radiological appearance to that seen after frostbite, burns and infantile scurvy and examined the literature regarding the blood supply to femoral head.[23,24] The conclusion was that disruption to the blood supply of the epiphysis damaged the most vulnerable area of the growth plate, the central germinal layer, causing the ball-and-socket picture.

Robinow et al.[25] described the deformities in more detail in 1983. They also theorised that physeal damage was secondary to vascular occlusion in the acute setting. The authors reported on one case but had the benefit of reviewing the cases of two other authors[19,22]. They described two types of deformities. The first was that of asymmetric epiphyseal destruction with adjacent metaphyseal growth disturbance and the second was symmetrical epiphyseal-metaphyseal lesions of the lower extremities. The already described ball-and-socket appearance of the epiphysis[22] was highlighted and Robinow et al. predicted that with improved survival rates seen with meningococcal septicaemia the bony deformities would be encountered more frequently.[25]

Another theory for the cause of the growth disturbances seen in these post meningococcal septicaemia patients was also proposed in 1983 by Watson and Ashworth.[26] They reported on 2 cases in which patients developed angular deformities (one with a varus knee and the other cavovarus of the foot) which occurred under areas of significant skin scarring. They postulated that the damage to the overlying soft tissues at the time of the

septicaemia had in effect caused an injury to the growth plate analogous to a type 6 physeal injury resulting in tethering under the scar tissue. They treated one patient with completion of the epiphysiodesis of the damaged physis, complete epiphysiodesis on the contralateral side and corrective osteotomy at a later stage. This was the first patient followed to skeletal maturity with successful treatment of deformity.[26]

In describing the complications surrounding amputations in these purpuric patients Jacobsen and Crawford (1984) also mentioned 2 cases of limb length discrepancy and angular deformity.[27] One of these patients required treatment (dome osteotomy) 10 years after the index infection. They summarised quite succinctly what other authors would later complicate by describing physeal growth disturbance as being either peripheral (causing angular deformity) or central (causing metaphyseal cupping and shortening).[27]

In 1985 Barre et al.[28] produced another case report and review of the previous papers and 8 cases already reported.[19,22,25] The patient presented in their paper developed similar bony changes despite having no evidence of bone involvement during the acute illness. Metaphyseal and epiphyseal defects were seen in the medial aspect of the left femoral condyle with resultant genu varum, there were similar less severe changes on the right and evidence of right proximal tibial physeal closure with fibula overgrowth. Arthrograms done by this group showed that the 'defect' seen in the distal femoral condyle was intact and was "apparently composed of cartilage".[28]

The literature to this point is composed largely of case reports in which the morphology of the osteoarticular lesions are described and theories are proposed as to the pathophysiological cause and prognosis of the osteoarticular changes. Incidence has not been established and treatment outcomes are scantily reported.[26] The problem has however now been identified and more substantial articles follow.

Santos and Boavida et al. retrospectively reviewed 22 patients who had been hospitalised with meningococcal septicaemia and invited these patients back for clinical and radiological follow up.[29] They found a 21% incidence of radiological osteoarticular abnormalities. Along with similar lesions reported by the earlier authors[19,22,25,28], they found all the patients to have dystrophic patella changes. The importance of these changes has not been established. What was important was that this study confirmed a high incidence

of late osteoarticular defects in these patients. This was something that until this point had only been speculation.

The paper in 1989 by Grogan et al. was the most comprehensive to date.[11] Nine patients who had major orthopaedic problems as a result of meningococcaemia were reviewed. They noted clinical findings of limb shortening and angular deformity in the patients and attributed this to the pattern of growth plate arrest. Partial arrest resulted in angular deformity and complete arrest in limb length discrepancy. Physeal arrest was also described as premature with a diffuse appearance. This occurred in physes previously thought to be normal and was thought to be heralded by excessive undulation in that physis. A recurrent pattern of deformity was that of marked tibial recurvatum secondary to anterior physeal closure of the proximal tibial growth plate. Treatment outcomes were discussed for the first time and the unpredictability of physeal bar resection was noted with success in only 4 out of 7 attempts. This was thought to be due to the underlying abnormality of the rest of the radiologicaly normal growth plate. Outcomes of osteotomies were not reported. The authors also made an interesting recommendation with regards follow up; that previously meningococcaemic patients be monitored with bone scans or radiographs on an annual basis with particular vigilance during the adolescent growth spurt.[11] The use of bone scans was not followed up on in any of the subsequent literature.

The importance of the research by Grogan et al. was in the histopathological findings.[11] Amputation specimens taken in the acute phase of the disease were examined as were those taken years after at the time of revision of amputation. These studies showed that histological changes to the diaphysis, metaphysis, epiphysis and physis in the acute phase were a combination of intravascular coagulation and acute inflammation. Vascular involvement was particularly variable within the cartilage canals with some being blocked by extravascular exudate or intravascular thrombosis and others still patent. The germinal zone of the physis was most commonly involved. These findings were confirmed in an as yet unpublished study which was presented at the South African Orthopaedic Association (SAOA) in 2000 in Durban.[18] Here occlusive vasculitis and to a lesser extent osteomyelitis were shown to be present in the amputation specimens taken in the acute phase of the meningococcaemia. Physeal damage was seen in specimens taken 6 to 15 days after the acute illness and presented as disruption of cellular columns.[11] In the chronic specimens there was evidence of bone bridges across the physis and loss of the normal columnar

pattern of cartilage cells. These findings confirmed the conjecture of some of the previous authors regarding the histopathological cause of the bone deformities.

In 1989 the case reports continued with Jay Nogi[30] reporting on 3 cases and O'Sullivan et al.[31] reporting on another 2 cases the following year. Nogi reported on 3 children who had amputations due to purpura fulminans as a result of meningococcal septicaemia. All 3 developed growth arrest in the physes of long bones adjacent the level of the amputation. In all cases there was involvement of the upper limbs.[30] This was in contrast to the preceding studies which found upper limb involvement to be rare.

O'Sullivan et al. described 2 cases of distal tibial growth arrest resulting in varus deformity of the ankle.[31] The deformities occurred at 12 months and 6 years following the index infection (which occurred at 18 and 30 months respectively) illustrating the unpredictability of the skeletal deformity progression. They related the delicate epiphyseal blood supply at the ankle to the occurrence of the deformity at this site. The epiphyseal blood supply supplies the germinal layer of the physis and because it is an end arterial system with no anastamosis it is easily affected by hypotension and thrombosis which occur during purpura fulminans. The resultant physeal damage can cause angular deformities at the ankle which may be varus[22,31], or less commonly valgus.[21]

An orthopaedic condition is nothing without a classification system to hang it on. It was however not until 2002 when Appel and Pauleto et al.[32] from Brazil attempted to fill this void. They examined the radiographs of 11 patients and reviewed the literature to devise a descriptive radiographic classification of the types of bone injury seen following meningococcaemia. They divided the types of injury into either bone injury or chondral injury patterns. The patterns of bone injury were then subdivided into: lytic lesions, periosteal reactions and cortical destruction (in order of decreasing frequency seen). The chondral patterns were subdivided into: peripheral asymmetric physis destruction (PAPD), epiphyseal nucleus destruction (END), destruction of central physis (DCP) and complete physis destruction (CPD). The bone patterns had a more benign course with less long term sequelae and the chondral injury patterns resulted in more severe chronic deformity and disability which was confirmed by earlier literature.[11,27] Appel et al.[32] found in contrast to other authors[11,27] that the bone injury patterns occurred more frequently than the chondral patterns. The classification system was purely descriptive. There was no

correlation with any particular pattern of clinical deformity and it did not direct management. Although there seems to be some prognostic value in separating the bone from the chondral patterns this has not been confirmed with sufficient numbers and the sub classifications are not prognostic. It does however have the potential to provide a description of bone changes seen on radiographs which could be used to standardise literature on the subject. The inter- and intra-observer variability of the classification have not been tested and use of this classification in subsequent literature is not seen.

Wheeler, Anderson and De Chalain (2003) reported on 21 patients requiring 117 surgical procedures for purpura fulminans as a result of meningococcal septicaemia.[14] These cases were gathered over a time period of 13 years. Most surgical procedures performed were amputations, skin grafts and flaps and soft tissue releases. Although these were the most severe cases only one case was noted to have growth abnormalities requiring treatment. This was a patient with bilateral genu valgum who underwent corrective osteotomies with poor success and was then lost to follow up. It was interesting that while the incidence of osteoarticular lesions has been quoted as 13-21%[15,29] this group had a particularly low incidence.

In 2005 Belthur et al.[16] published an extensive retrospective review spanning 11 years. Twenty four patients with late orthopaedic sequelae after meningococcal septicaemia were investigated. Twenty three of these had evidence of growth arrest with 49 physes involved. This study was note-worthy in that it reported on the treatment of the largest group of patients to date. Although only 2 of these patients were followed up beyond 14 years of age important insight into the treatment of this condition was gained. Similar patterns of deformity were noted to those found in the earlier literature with lower limbs more involved than upper and varus deformity predominating over valgus. The pattern of varus and recurvatum of the proximal tibia was again prominent. The authors noted that there was a statistically significant difference in the incidence of recurrence of angular deformity after corrective osteotomy done for knee deformity (when completion of epiphysiodesis of the affected growth plate was not done) when compared to that done for angular deformity of the distal tibia (when completion of epiphysiodesis was done routinely). The unpredictable growth of the remaining growth plate may have accounted for this. They also found resection of physeal bars to be unsuccessful in these patients after 3 attempts. The

important treatment recommendation from this study was that an epiphysiodesis of the affected physis should be completed at the time of the angular correction.[16]

Another retrospective review “orthopaedic sequelae of meningococcal septicaemia” was published from Melbourne in 2006. Bache et al.[15] followed up 143 patients with meningococcal septicaemia who presented over 17 years. There were 21 deaths. Forty of these patients required surgical intervention for vascular, cutaneous or skeletal complications of the disease. Sixteen of these developed growth arrest giving an incidence of 13%. They found a high incidence of growth arrest adjacent to amputation sites and underlying areas of skin necrosis and scarring and concurred with previous authors[26,30] that these events should heighten suspicions of associated growth arrest and should be closely followed up. Interestingly a high proportion of their patients who presented with growth arrest were diagnosed after radiological investigation prior to clinical deformity indicating high levels of suspicion and a good screening program. The authors felt that significant scarring over the anterior tibia was highly predictive of underlying growth abnormalities. They found physeal arrest in 10 of 11 patients with scarring in this region and postulated that this area was susceptible to damage because the anterior compartment of the lower leg is supplied by only one angiosome.[33] A weakness of this study was that 11 of the 28 patients who required soft tissue surgery and were thus flagged as being high risk for growth arrest were lost to follow up. Despite the promising title of the paper the majority of procedures reviewed were soft tissue procedures and amputations. Five limb lengthenings, 4 fibula epiphysiodeses and 4 osteotomies were done. The aim of this study was to “assess results of surgical intervention”[15], there was however no mention of length of follow up after skeletal surgery or outcomes of these procedures. No mention either was made of whether an epiphysiodesis of the affected growth plate was done concurrently with angular correction as recommended by previous authors.[16]

The most recent paper published on this subject was by Buysse et al.[34] in 2009. They aimed to identify predictive factors in the development of skin scarring and orthopaedic sequelae after meningococcal septicaemia. They found a 6 % incidence (7 out of 120) of growth arrest with resultant angular deformity or limb length discrepancy. All but one of these patients was already under the care of an orthopaedic surgeon at the time they were called back for follow up. This again suggests vigilant follow up protocols. The one

undiagnosed patient presented with the common pattern of ankle varus due to distal tibial growth arrest. Six of the 7 patients underwent corrective surgery in the form of either epiphysiodesis or realignment osteotomy and although mention was made that they all remained under orthopaedic care at the time of the study no mention was made of the outcome of the procedures or for how long they had been followed up. The importance of this study was that it found an association between the development of skin scaring, amputations and growth arrest and certain parameters measured at the time of the index infection. Age of the patient on admission to the paediatric ICU was an important determinant of development of late soft tissue and skeletal manifestations with younger patients being statistically more likely to develop orthopaedic sequelae presumably due to the increased susceptibility of immature tissues to ischaemia.[34] Disease severity scoring systems were also predictive of the development of orthopaedic problems. The disseminated intravascular coagulation score (DIC score) and the paediatric risk of mortality score (PRISM score) were both predictive. Although these predictors may guide the intensity of future follow up they do not exclude any survivors of meningococcal septicaemia from vigilant long term monitoring. One of the weaknesses of this study was that although 170 patients were eligible only 120 (71%) were available for follow up. This left a significant portion of the population excluded from the follow up and raised a question mark as to the validity of the results.

Summary

Incidence

The incidence of osteochondral lesions following meningococcal septicaemia in the literature reviewed varies from 6-21%.[15,29,34] Many of the earlier case reports are directed at descriptions of the osseous abnormalities and do not draw conclusions regarding the incidence of arrests noting only that they occur rarely.[19,25,28] Wheeler et al.[14] reported only one case of physeal arrest in their review of 21 patients and did not comment on incidence in particular. The population size in their study is small compared to some of the later ones[15,34] and the low prevalence encountered may be due to this or as a result of low levels of vigilance, the study being directed largely at soft tissue surgery. The incidence also varies depending on what is being described. Santos et al.[29] in quoting an incidence of 21% include all osteoarticular lesions seen, this includes patella dystrophy (which is of

questionable clinical significance). It seems then that the true incidence of physeal arrest following meningococcal septicaemia may be closer to 6-13%.

The other point of interest regarding the incidence is that it seems to remain unchanged over time as noted by Buysse et al.[34] They showed no increasing trend between 1988 and 2001. The first literature reports are however as recent as 1981[19] and with a delay in presentation of up to 14 years it may be that not enough time has passed for the improved management regimens to manifest clinically. It seems that although an increase in survival rates of these patients has increased the frequency of physeal arrest over the last 30 years, there has been no subsequent trend.

Morphology of osteoarticular lesions

The radiological appearance and distribution of osteochondral lesions secondary to meningococcal septicaemia are varied. Physeal injuries range from a single affected growth plate[11,16,19] to symmetrical involvement of all lower limb physes to the point where multiple epiphyseal dysplasia has been considered in the differential diagnosis.[22] There are however some consistencies. Lower limbs are more affected than upper limbs in all but one paper.[30] Common patterns of deformity reported are ankle varus with fibula over growth, knee varus and particularly knee varus with marked recurvatum where the arrest occurs under areas of cutaneous scarring. The central portion of the physis is often affected particularly at the distal femur. This results in frequently reported ball-and-socket epiphysis.[22,25,28] The pattern of growth arrest can be focal, complete or develop as a delayed premature arrest with a diffuse pattern in a physis previously thought to be normal.[11,18,25,32] Focal arrests result in angular deformity and complete arrests in leg length discrepancy. Diffuse premature arrests can cause either angular deformity or leg length discrepancy depending on the extent of the physis involved.[18,27]

The radiological classification system of Appel et al.[32] while providing a thorough description of potential skeletal abnormalities has not been validated to direct treatment or predict outcomes. Some authors[11] agree with the findings of Appel et al.[32] when they reported that bone lesions had a much more benign course than the physeal injuries. Necrosis of the epiphyseal ossification centre is reported as one of the bony changes seen but follow up of these cases is infrequently recorded. Femoral head[19,22,25], distal femur[28]

and talar dome[19] necrosis have been documented. Barre et al.[28] reported that the apparent defects were composed of cartilage but little else has been reported on the outcome of epiphyseal necrosis.

Treatment outcomes

Reported outcomes of surgical procedures directed at physeal arrest are scanty.[11,14,16,26] Results of physeal bar resection are reported in 2 studies[11,16] both of which note them to be at best unpredictable[11] and at worst completely unsuccessful.[16] No mention is made of the size of the bars excised. Current recommendations for the excision of bars as a result of other causes is to attempt them only when the bars are less than 30% the size of the growth plate and more than 5 years of growth remains.[35] The unpredictability of the bar resections is related to the underlying abnormality of the remaining growth plate.[11]

Osteotomies to correct angular deformities were reported on by Belthur[16] who made the important observation that the results seemed to be dependent on the successful epiphysiodesis of the adjacent affected growth plate at the time of osteotomy. Previous authors had poor results.[14] Few of these patients are followed up to skeletal maturity and no parameters are identified by which “good” or “poor” results are defined.

Future avenues of research

There is no literature that explores the influence of different aspects of early medical management on physeal injury. A recent article by Numanoglu and Rode et al.[36] tried to identify different factors in early medical care which influenced tissue loss. The severity of the acute illness has been shown to be predictive of acute and delayed orthopaedic complications of this disease.[34] These factors which improve survival of extremities and decrease amputations may also prevent late orthopaedic sequelae of meningococcaemia but this requires further investigation.

The predictive value of different imaging modalities in the acute setting is unknown. Earlier literature suggested the use of bone scans to assess physeal involvement during the acute stage of meningococcal sepsis[11] but no follow up work has been done to substantiate this

suggestion. The use of MRI scanning in the acute stage or shortly thereafter could also be investigated.

There is little data regarding treatment outcomes in general and almost none with follow up to maturity.

Difficulties in conducting research into this disorder are obvious when one examines the small numbers of patients presented in the literature and the time delay from the acute illness to the development of radiological or clinical deformity (4 months[19] to 14 years[26]). Increased vigilance after meningococcal septicaemia and the development of screening protocols would decrease the delay to presentation and so allow earlier identification and management of physeal arrest and increase the possibility of meaningful research.

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Research Paper

Orthopaedic implications of physeal arrest following meningococcal septicaemia

Abstract

Background

Physeal arrest following meningococcal septicaemia is the result of ischemia secondary to vasculitis. Only three cases have been reported with a long term follow-up to maturity.

Methods

A retrospective study was carried out involving 13 patients treated over 17 years (1991-2007) to assess the orthopaedic manifestations, treatment and long term outcome of the physeal arrest. All patients were followed up clinically and radiologicaly; 8 to skeletal maturity.

Results

The average age at which the acute infection of meningococcal septicaemia occurred was 12 months, and the patients presented with physeal arrest at an average of 5.6 years. Thirty nine physes were involved: 29 focal, 6 complete and 4 had a premature arrest. Sixty two surgical procedures (average 4.6, range 1-11 per patient) were required to prevent or correct angular deformity and/or leg length discrepancy. Seven physeal bars were resected (4 successfully), 26 epiphysiodeses, 20 angular corrections (all at the knee or ankle) and 9 limb lengthenings were done.

Conclusions

These patients may require multiple orthopaedic procedures and should be followed up until skeletal maturity. Once growth is balanced with physeal bar resection or epiphysiodesis, angular correction and limb lengthening have a good outcome.

Introduction

Since the earliest report of bony deformities and growth abnormalities following meningococcal septicaemia in the 1981[1], there has been a steady increase in these complications reported in the literature. There have however, been few reports on the surgical management of physeal arrest following meningococcaemia and even less on the late outcome of this surgery.[2,3,4]

Meningococcal septicaemia is caused by Neisseria meningitidis, a gram-negative diplococcus with a lipopolysaccharide in its cell wall.[5,6] This acts as an endotoxin to elicit an acute inflammatory response via a complex cascade of events ending in vasculitis, disseminated intravascular coagulopathy (DIC), shock and multi-organ failure with a mortality rate ranging from 7 to 15%.[7,8] The DIC and vasculitis affect all organ systems and the musculoskeletal system is not spared. Clinically this may present as skin necrosis, compartment syndrome and gangrene, resulting in amputations and soft tissue contractures.

Physeal injury occurs in 6 to13% of patients[3,9] as a result of ischaemia secondary to the vasculitis and to a lesser extent as a result of osteomyelitis. This has been shown on histological specimens taken at the time of amputation from patients with the acute illness.[6,10] Although the osteomyelitic involvement of bone (epiphysis, metaphysis and diaphysis) usually recovers without sequelae, damage to the physis leads to permanent physeal arrest.[6,10] This manifests in three different patterns[6,10-12]: focal (central or asymmetrical), complete or premature arrest.

As the manifestations of physeal damage are growth dependant they may only present years after the index infection.[1-3,6,7,10-14] Surgical correction of these deformities is difficult and complicated by a high incidence of failure of physeal bar resection and recurrence of the deformities after correction.[2,6]

The management of the initial limb ischemia, with or without fasciotomy, and the treatment of skin necrosis and soft tissue contractures have been well described in the orthopaedic

literature.[2,8,15] The problems associated with amputations (especially below knee), such as stump overgrowth and contractures, often necessitating through knee amputations, are also well documented.[2,6,8]

A multicenter study by Belthur, Bradish and Gibbons et al.(2005)[2], described the late orthopaedic sequelae due to growth plate arrest in 23 patients, but only two were followed up to skeletal maturity. Watson and Ashworth (1983)[4] followed one case to skeletal maturity.

The purpose of this retrospective study was to describe the orthopaedic manifestations and treatment of growth plate arrest and the long term outcome in 13 patients (8 to maturity) following meningococcal septicaemia.

Methods

The orthopaedic manifestations, treatment and outcome of growth plate arrest following meningococcal septicaemia were retrospectively studied in 13 patients treated over 17 years (1991 – 2007). Their clinical and operative notes, radiographs and MRI scans were reviewed. The degree and type of physeal involvement were assessed on A-P and lateral radiographs. If this was not clear, or if growth plate resection was contemplated, biplanar tomography (initially) and/or MRI (now the gold standard to assess physeal arrest) was done.

All patients were followed up annually clinically and radiologicaly; eight of the 13 patients until skeletal maturity. An outcome was regarded as good if LLD was less than 2cms and mechanical axis malalignment did not exceed 5º.

The Wilcoxon rank sum test was used to test the significance of increased incidence of physeal arrest in children who had septicaemia before 10 months of age.

The study was aimed at the management of physeal arrest and therefore problems related to soft tissue contractures, scarring or amputations were not reviewed.

Results

The patients presented to the orthopaedic department at an average age of 5.6 years (range 3 – 12 years). They presented with leg length discrepancy and/or angular deformities of the limbs.

The average age of the children presenting with meningococcal septicaemia was 12 months (range 3 – 24 months). Seven of the children were over 10 months of age when they had the acute illness and had an average of 1.7 physes involved per child (range 1 – 3). Six of the children were under the age of 10 months and had an average of 4 physes involved per child (range 2 – 5). This is statistically significant ($p<0.05$).

Classification and distribution of physeal arrest

The 13 patients had a total of 39 physes involved; an average of 3 per patient (range 1-5). Twenty nine physeal arrests were of the focal type, 6 were complete and 4 were premature physeal arrests (Table I).

Table I. Types of physeal arrest.

Focal	29	■ Central – LLD or angular deformity ■ Asymmetrical – angular deformity
Complete	6	LLD
Premature arrest	4	LLD or angular deformity
Total	39	

Asymmetrical, peripheral focal arrest resulted in angular deformity (Fig.1). Central focal arrest was either “tented” (Fig. 2A) or had a “cup-and-saucer” appearance (Fig.2B). Central focal arrest presented with either LLD or an angular deformity (Fig.2B).

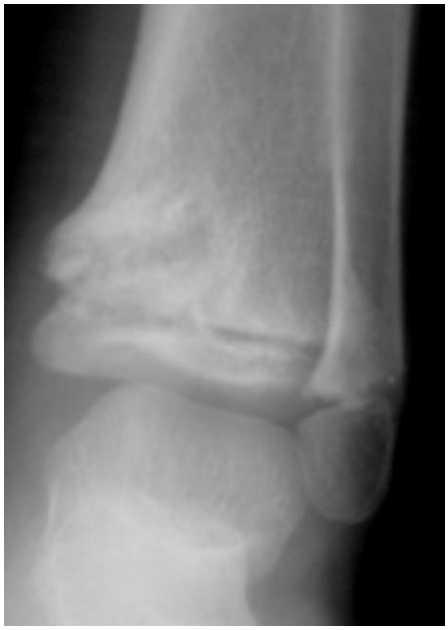


Figure 1. A-P radiograph of the left ankle of a six-year-old girl with a peripheral focal arrest of the distal tibia.

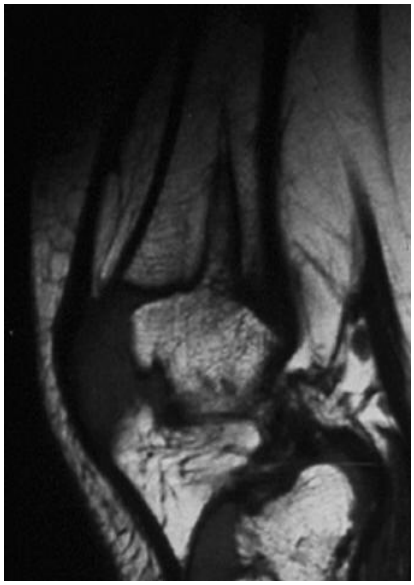


Figure 2A. T1 sagittal MRI of the knee of a five-year-old boy with a central focal arrest with a tented appearance.

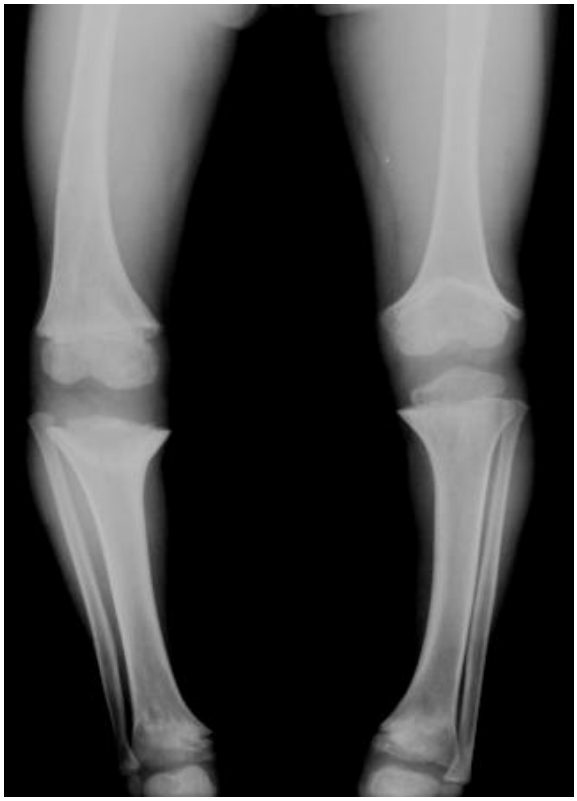


Figure 2B. A-P radiograph of the lower limbs of a four-year-old boy with central focal arrests and “cup-and-saucer” appearance of the right proximal tibia with varus deformity and left distal femur causing LLD.

Complete arrest presented as a LLD (Fig.3). Premature arrest occurred when a documented seemingly normal physis arrested before skeletal maturity. This presented as LLD or an angular deformity, depending whether the arrest was symmetrical or asymmetrical (Fig.4 A and B).

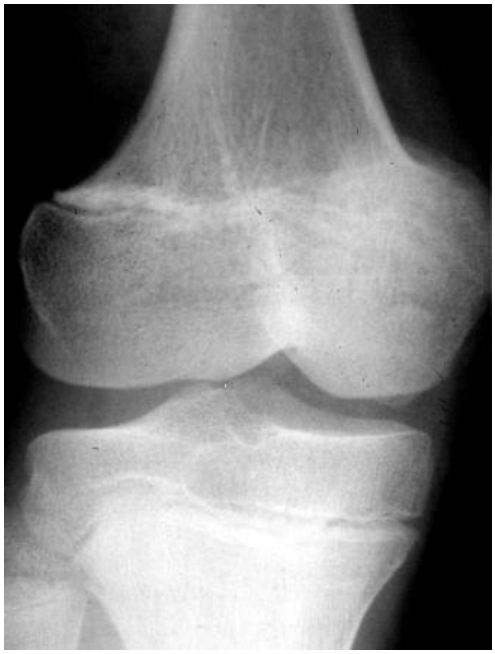
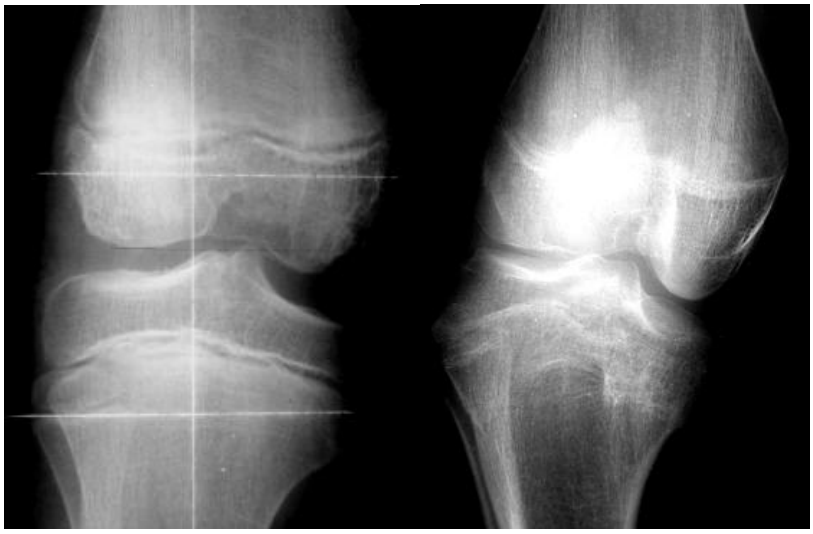


Figure 3. A-P radiograph of the right knee of an eight-year-old girl with complete arrest of the distal femoral growth plate with leg length discrepancy.

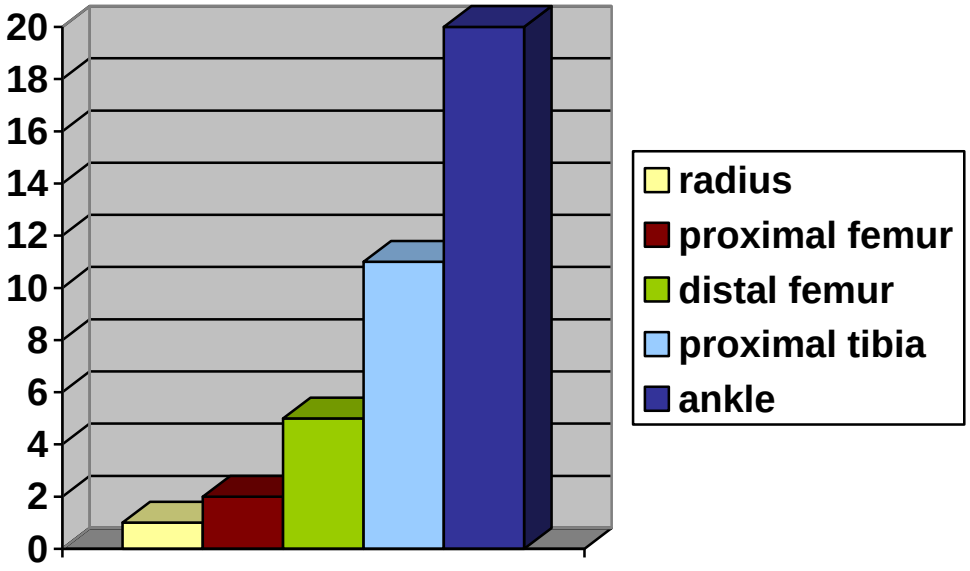


A B

Figure 4A and B. A-P radiographs of the right knee illustrating premature arrest. 4A "Normal" tibial physis at 12 years of age. 4B Medial tibial premature arrest at 15 years.

The anatomical distribution is shown in table II. The vast majority of physeal arrests occurred around the knee and in the ankle with only 3 of the 39 occurring in the proximal femur or upper limb.

Table II. Anatomical distribution of physeal involvement.



Surgical procedures

Sixty two surgical procedures were performed at an average of almost 5 per patient (range 1 – 11). Seven physeal bars were resected, 26 epiphysiodeses were done, 20 osteotomies were performed for angular deformities and 9 limb segments lengthened (Table III).

Table III. Surgical procedures.

Physeal bar resection	7
Limb lengthening	9
Angular correction	20
Epiphysiodeses	26

Epiphysiodesis

Of the 26 epiphysiodeses done, 18 were performed around the ankle (either distal tibia or fibula). In 3 cases the epiphysiodesis was done on the contralateral side to address limb length discrepancy. Twenty five of these procedures successfully arrested growth. The one failure was an epiphysiodesis of the distal tibia in which the growth was not arrested and the angular deformity worsened. Fourteen of the 26 epiphysiodeses were done in the fibula (11 distal and 3 proximal) to address the inequality of growth between tibia and fibula (Fig.5).

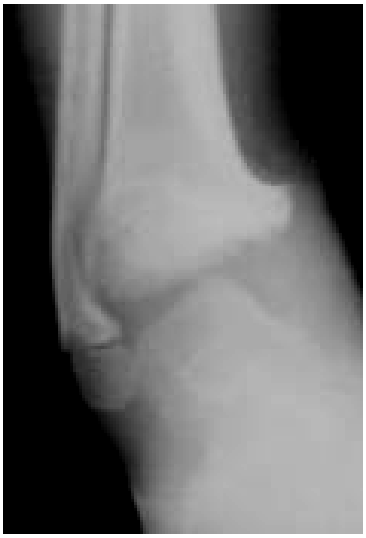
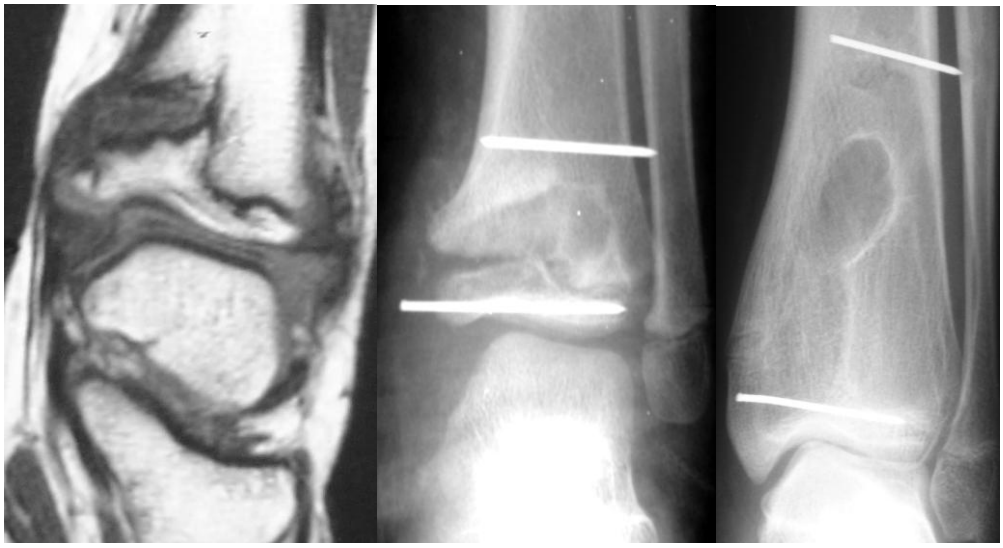


Figure 5. A-P radiograph of the right ankle of a three-year-old girl with varus deformity of the ankle due to distal tibial growth arrest and aggravated by fibular overgrowth.

Physeal bar resection

Seven physeal bars were resected. Resection was considered successful if the growth rate post-operatively resumed to more than or equal to the expected rate for that physis (Fig.6 A,B and C). Four (57%) of the resections were successful. The four physeal bars that were successfully resected were less than 30% of the physeal surface area. The three failures were 40% of the physeal area.



A B C

Figure 6A. T1 coronal MRI of the same patient as in figure 1 with a 20% posteromedial bar of the distal tibial growth plate.
Figure 6B. Radiograph after bar resection.
Figure 6C. At maturity, growth of 42mm over seven years was achieved (150% of expected).

Correction of angular deformity

All of the 29 focal arrests occurred around the knee and ankle. Of these 27 resulted in a varus and only 2 in a valgus deformity. Angular correction was undertaken in 20 cases; the other 9 were corrected with either successful epiphysiodesis (especially distal fibular epiphysiodesis for ankle varus) or physeal bar resection. Successful correction was defined as post-operative correction to less than or equal to 5º of the normal mechanical axis. Nineteen of the 20 angular corrections were successful. A problematic pattern of deformity around the knee was that of severe varus and recurvatum of the proximal tibia. This deformity was particularly difficult to correct and the one failure occurred in this group (Fig.7 A and B).

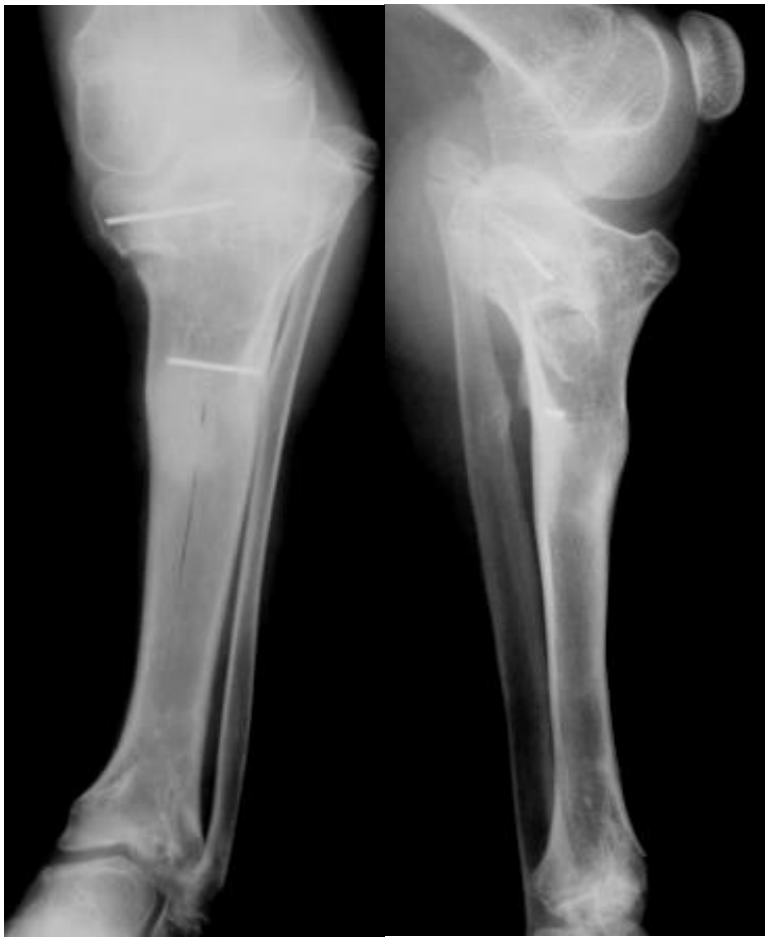


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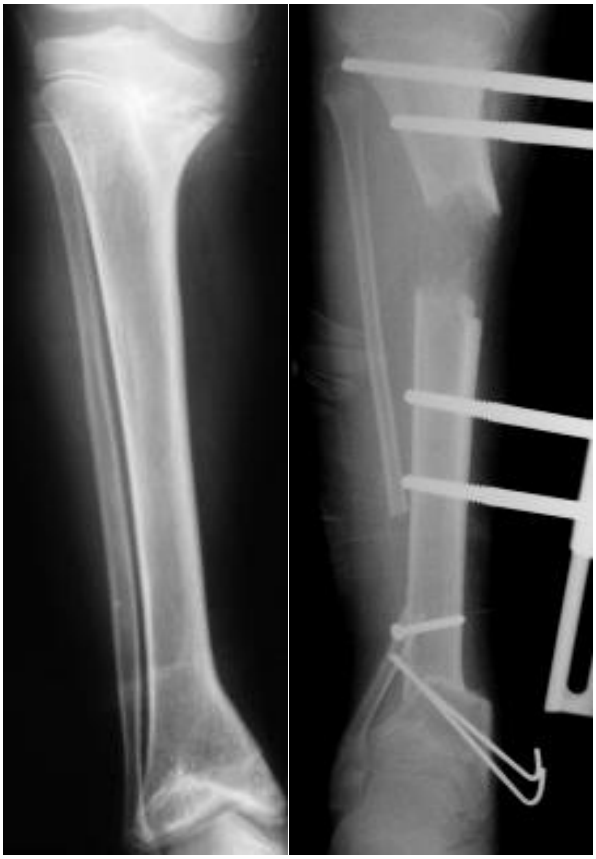
Figure 7A and B. A-P and lateral radiographs of left tibia of ten-year-old girl with previously failed bar resection with severe varus and recurvatum of the proximal tibia.

Different techniques were used with similar results (Table IV). At the distal tibia however, the osteotomy described by Wiltse[16] is now routinely used as it centralizes the talus under the tibia (Fig. 8 A and B). Five limb segments had simultaneous lengthening using either a rail (Orthofix) or circular frame (Taylor spatial frame) (Fig.9 A-E).

Table IV. Methods of angular correction.

Distal Femur	Chevron osteotomy	1
	Corticotomy & rail	2
Proximal Tibia	Barrel vault	3
	Closing wedge	2
	Corticotomy & frame/rail	3
Distal Tibia	Supramalleolar wedge	6
	Wiltse osteotomy	3
Total		20



A B

Figure 8A and B. A-P radiograph of the right tibia of a ten-year-old boy with medial physeal arrest of the proximal and distal tibia. A Wiltse osteotomy of the distal tibia and simultaneous angular correction and lengthening of the proximal tibia were done using a rail. Epiphysiodeses of proximal and distal tibia were completed at the same sitting.

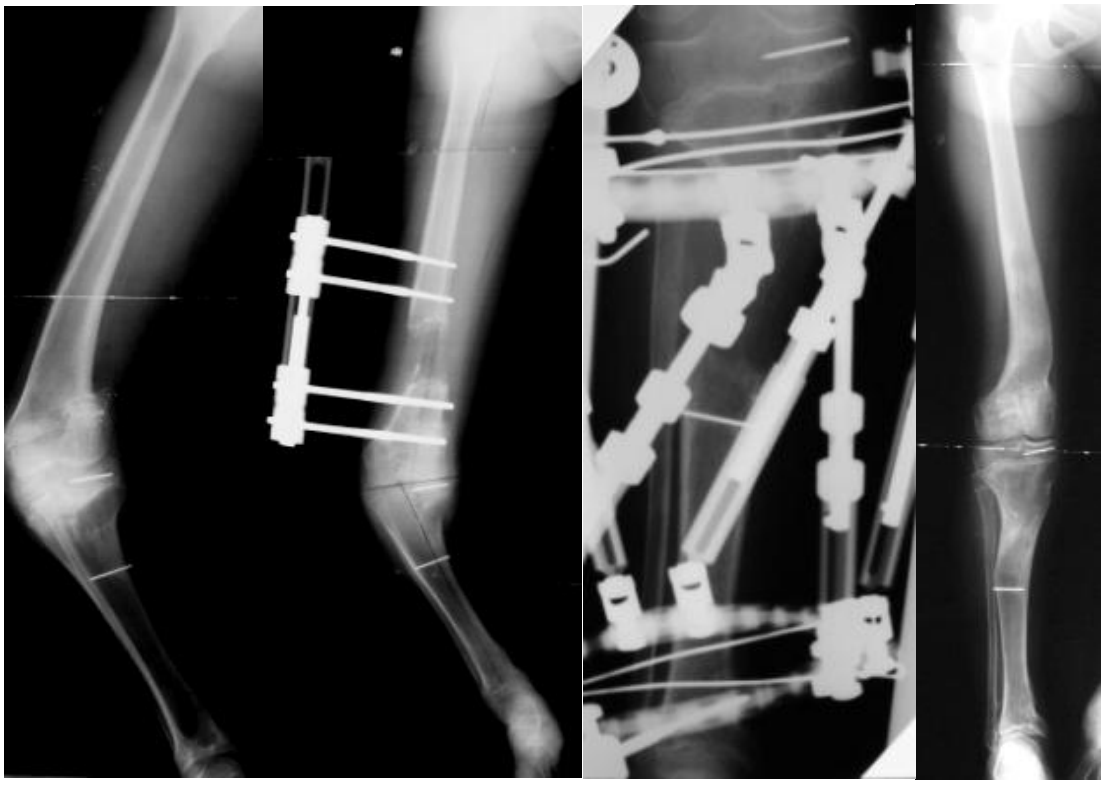


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Figure 9A. A-P radiograph of the right femur and tibia in a ten-year-old girl. Previous bar resection of the proximal tibia maintained growth but did not correct the varus deformity.
Figure 9B. Right femur had simultaneous correction of varus and lengthening of 4 cms using a rail.
Figure 9C. Tibial varus was corrected and lengthened 5 cms using a Taylor spatial frame.
Figure 9D. Good result at 2 year follow-up. Note that all epiphysiodeses were completed at the time of angular correction.

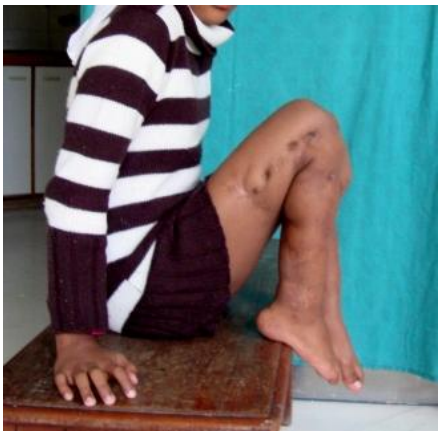
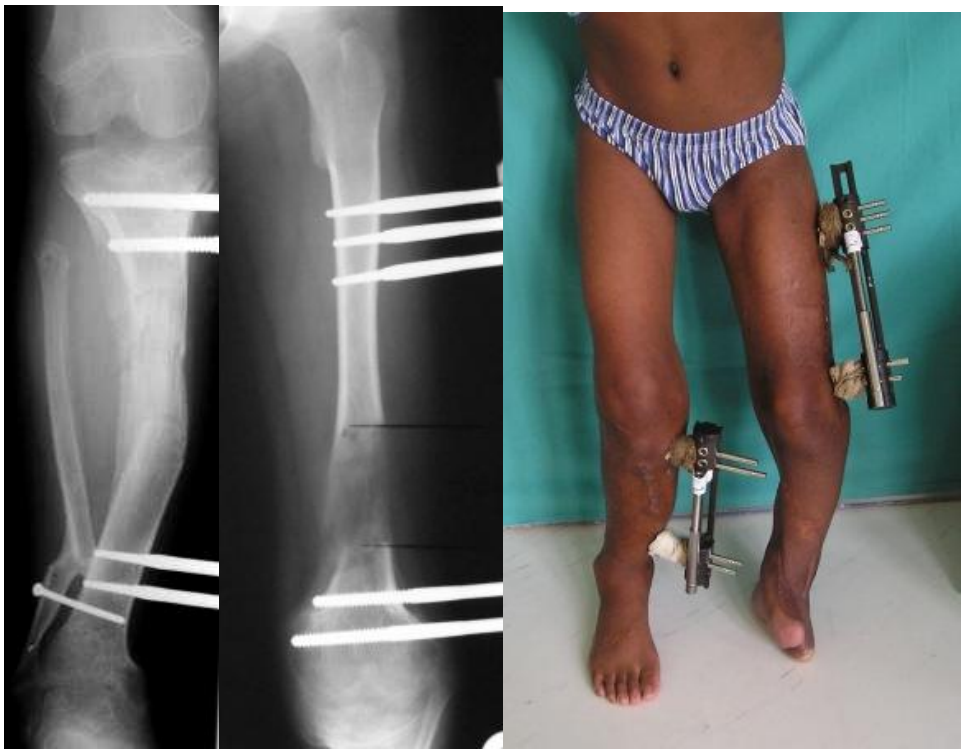


Figure 9E. Post-operative clinical picture showing return to full range of motion of the knee.

Limb lengthening

Nine limb segments were lengthened; 5 tibiae, 3 femurs and 1 radius. Three femurs and 3 tibiae were lengthened with a rail (Orthofix) (Fig.10A-C), 2 tibiae with a Taylor spatial frame and the radius with an Ilizarov circular frame. The average length gained was 5.8 cm with a range of 3.2 – 9.3 cm. A successful lengthening was defined as lengthening to within one centimetre of the pre-operative target.

All three tibiae lengthened with a rail had distal migration of the fibular head (Fig 10A).This did not have any clinical significance.



A B C

Figure 10A and B. A-P radiograph of the right tibia and left femur of the same patient shown in figure 2B. Simultaneous angular correction and 6 cm lengthening of tibia were done. Note distal migration of proximal fibular head. The left femur was lengthened 5cm. Figure 10C. Clinical picture; left tibial varus and shortening still have to be addressed.

Follow-up

Eight of the 13 patients had reached skeletal maturity at the time of this study and 7 were available for follow up; 6 had a good result. One patient had residual bilateral ankle varus but copes well clinically.

Discussion

Incidence

Osteoarticular lesions are seen in 6 to 21% of patients following meningococcal septicaemia.[8,9] Difficulties in accurately defining the incidence arise as a result of the long delay between index infection and the effects of the resultant physeal arrest. This delay makes it difficult to define the population group from which the affected patients are drawn. Studies that have followed up a large group of meningococcal septicaemia survivors provide the most accurate estimates.[7,9] Even in these studies however as many as 21% of patients are lost to follow up.[9] Another difficulty occurs as a result of the variability in what the literature defines as relevant lesions. Some authors report on ossification abnormalities of the patella[8] which have questionable clinical significance. Conclusions regarding the incidence and distribution of arrests are made with inclusion of those in the metacarpals and metatarsals by some authors[17] and exclusion by others.[7] Attempts at standardising description of these lesions through classification systems[11] have not been universally accepted.

No conclusions regarding the incidence of skeletal abnormalities could be made from this study because only the affected patients were followed up. However a significantly higher incidence of growth arrests was found in patients who had meningococcal septicaemia before the age of 10 months. This concurs with the findings of Buysse, Oranje, Zuidema et al. (2009) who suggested that this was probably due to the higher vulnerability of the bony vasculature in younger patients.[9]

The physeal injuries, being growth dependant, present later than the bony changes seen in the acute phase of the illness.[1-3,6,7,10-14] Patients in this study presented at an average of 4.6 years following the acute illness, with a range of 3 – 12 years of age at presentation, the literature reports a range of 4 months[1] to 14 years.[4] This indicates the unpredictability of this pathological process and stresses the need for follow-up to skeletal maturity of all these patients.

Histopathology

Physeal arrest is caused by ischaemic occlusion of the microvasculature supplying the physis, and to a lesser degree the acute inflammatory response as a result of metaphyseal osteomyelitis. The germinal zone of the physis is most markedly affected by the ischaemia as it is supplied primarily by the epiphyseal end artery system which is most vulnerable. Examination of the physis of an acute amputation specimen of a meningococcaemic patient showed areas of disorganization with loss of the normal columnar pattern of the chondrocytes and relative hypocellularity. The adjacent metaphyseal bone showed a prominent inflammatory infiltrate (acute osteomyelitis). Later specimens taken at revision amputation showed complete recovery of the osteomyelitis, but the ischaemia resulted in bony bridge formation across the physis and loss of the normal columnar pattern of the cartilage cells. These findings were initially reported by Grogan, Love, Ogden et al (1989).[6] Other authors reported similar findings.[10]

Classification and anatomical distribution

Complete arrest resulted in limb length discrepancy. **Focal arrest** resulted in angular deformity if asymmetrical and if symmetrically central, resulted in leg length discrepancy. The central arrests either had a tented appearance (Fig.2A) or were shaped like a “cup” or “ball-and-socket” (Fig. 2B) as described by Robinow, Johnson, Nanagas et al. (1983).[12] They suggested two reasons for the development of this appearance. Firstly the centre of the growth plate is more vulnerable than the periphery which receives anastomoses from periosteal vessels. Secondly occlusion of the transphyseal vessel, which exists in infants less than one year of age, damages the physis and metaphysis centrally.

Premature arrests resulted in either leg length discrepancy or angular deformity depending on their site. They occur in a diffuse irregular pattern in physes previously documented to be normal on radiographic examination. Grogan, Love, Ogden et al (1989)[6] suggest that excessive undulation of a growth plate may be a warning sign. This was not the experience in the current study (Fig. 4A and B), but earlier MRI studies did show small areas of physeal arrest not obvious on radiographs.

The deformities seen in the 13 patients in this study occurred with a similar distribution to those reported in the literature.[1-3,6,7,10-14] The majority of arrests (36/39) occurred around the knee and ankle. The biggest reported series in the literature was by Belthur and Bradish et al. (2005)[2] who reported on 24 patients with 49 physeal arrests. Only one patient in the current study group had an upper limb growth arrest (distal radius) which was complete. Nogi (1989)[17] was the only author to report a higher incidence of physeal arrest in the upper limbs but he included arrests in the metacarpals which were not included in this review. The reason for the increased incidence in the lower limbs remains unclear.

Bache and Torode (2006)[7] reported a propensity for skin necrosis around the anteromedial aspect of the knee and that nearly half of the patients requiring debridement and grafting developed growth arrest. They suggested that the high incidence of proximal tibial physeal arrest could be due to the anterior compartment of the leg having a vascular supply from one angiosome only, making the tissues more susceptible to ischaemia. In this study skin scarring overlying areas of physeal arrest was not routinely documented, it was however a prominent feature in patients with severe proximal tibial involvement (Fig.11).

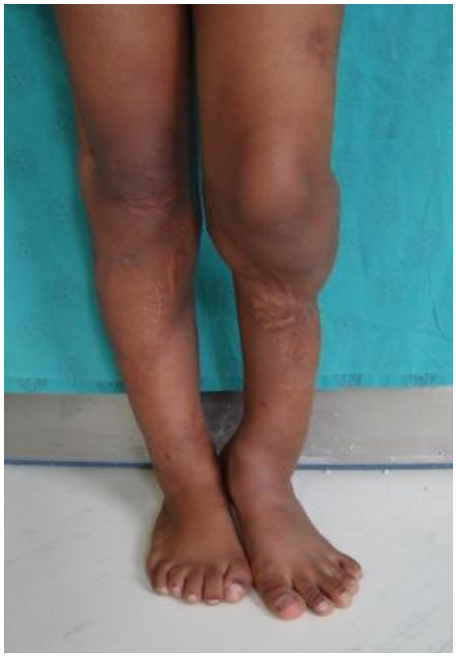


Figure 11. There is prominent antero-medial skin scaring of the left proximal tibia. This overlies an antero-medial growth arrest causing varus and recurvatum of the proximal tibia.

Treatment

These patients may require several orthopaedic procedures. In this study group 62 surgical procedures were performed on 13 patients, an average of nearly 5 per patient and as many as 11 in one. Two of these patients are still awaiting further corrective osteotomies and lengthening procedures. Belthur and Bradish et al. (2005)[2] reported on 52 procedures in 24 patients emphasising the high surgical demand of treating these patients.

Procedures performed were classified into two broad groups. They were either growth balancing procedures (epiphysiodesis or physeal bar resection) or salvage procedures (angular correction or leg lengthening). An important point is that salvage procedures should not be undertaken in the presence of unbalanced growth. Procedures from both groups can be done at the same time, but if growth is not balanced the deformities will recur. This was also noted by Belthur and Bradish et al. (2005)[2] who found that they had a higher recurrence of angular deformities after correction around the knee (when epiphysiodeses were not performed) than at the ankle (when they were). In this study epiphysiodesis or successful bar resection preceded angular correction and/or leg lengthening. There was no recurrence of angular deformity or leg length discrepancy in those patients followed to skeletal maturity.

Epiphysiodesis

The most commonly performed procedure was an epiphysiodesis and this was most commonly performed around the ankle. It was performed for a three reasons: to balance the growth in a limb affected by an asymmetrical focal arrest, on the contralateral limb to address limb length discrepancy, or on the proximal or distal fibula to address fibular overgrowth when the adjacent tibial physis was affected. Early epiphysiodesis to balance growth is preferable to the severe angular deformities which may result if it is delayed.

Physeal bar excision

In this study physeal bar excision was unpredictable. Only four (57%) of 7 excisions were successful. Grogan, Love, Ogden et al (1989)[6] reported similar results, and Belthur and Bradish et al. (2005)[2] attempted three resections without success.

Although a discrete bar is radiologicaly identifiable, one cannot presume that the rest of the growth plate is healthy and there may be a more "diffuse involvement".[2,7] Whether this "diffuse involvement" is detectable as small areas of arrest on MRI is currently being investigated. Similar factors are probably responsible for premature arrest in a previously "normal" growth plate. Because of the inevitable failure of bar resection in this study where more than 30% of the physeal area was involved, the current policy is to attempt bar resection only if the arrest is less than 30%, the rest of the growth plate is normal on MRI, and the patient has more than 5 years of growth remaining.[18]

Correction of angular deformity

A high recurrence rate of angular deformity following corrective osteotomy has been reported in the literature, and is attributed to failure to complete the epiphysiodesis at the same time.[2] This study has shown that if balanced growth is achieved, with completion of the epiphysiodesis or with successful physeal bar excision, alignment is maintained.

All 20 angular corrections were at the knee (11) or ankle (9). The vast majority (18) of deformities were varus.

A problematic pattern of deformity was that of severe proximal tibial recurvatum and varus. This has been shown by Grogan, Love, Ogden et al (1989)[6] to be due to involvement of the anterior part of the epiphysis of the proximal tibia. This was a particularly difficult deformity to correct and the one failure in this study occurred in such a patient due to the development of a peroneal nerve palsy.

Ankle varus

Ankle deformity was varus in 7 of 8 patients. This was due to focal arrest of the distal tibia with resultant fibular overgrowth. Fibular growth arrests were far less common than in the tibia. The growth arrest in the distal tibia was mainly of the “cup-shaped” central type as described by Robinow and Johnson et al. (1983)[12] and should have resulted in leg length discrepancy, but fibular overgrowth caused or contributed to a varus deformity (Fig.5).

Belthur and Bradish et al. (2005)[2] and Bache and Torode (2006)[7] showed that an early fibular epiphysiodesis prevented ankle varus. In late presenters with established varus, a valgus osteotomy should be done at the same time as the fibular epiphysiodesis. In some late presenters, although the talus was tilted in varus, it was centralized on the tibia. As the foot was well aligned a fibular epiphysiodesis only was required. At long term follow-up these patients were coping well with a “ball-and-socket” appearance of the ankle joint (Fig.12).

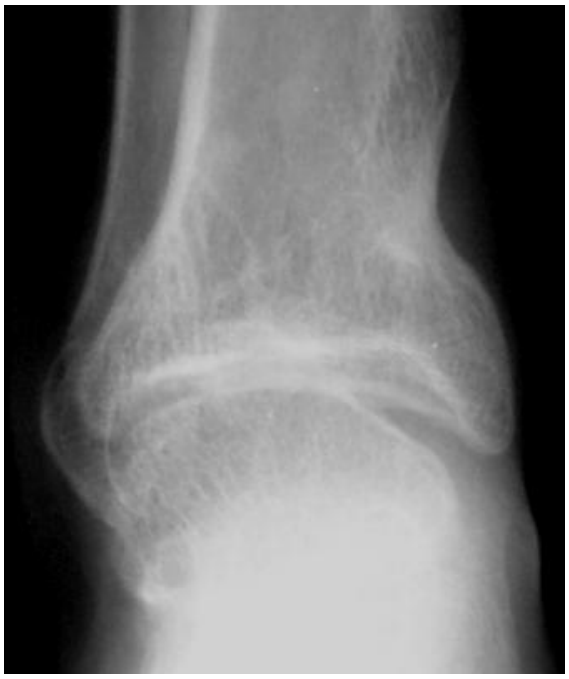


Figure 12. A-P radiograph of the right ankle of a 12-year-old girl who had a fibular epiphysiodesis and completion of her tibial epiphysiodesis at 5 years of age showing a “ball-and-socket” appearance of the ankle joint.

Limb lengthening

Limb lengthening had good results. A complication noted during lengthening of the tibia was that of distal migration of the proximal fibular head (Fig 10A). This occurred as a result of premature union of the distal fibular osteotomy. This had no clinical significance.

Loss of range of motion of adjacent joints was a common complication in lengthening procedures and lengthening was stopped if less than 30º of flexion was achievable at an adjacent joint. Although loss of motion was noted in all patients during lengthening, no lengthenings had to be abandoned and all patients regained full range of motion post-operatively (Fig.9E).

Summary

This is a complex and demanding condition to treat requiring commitment from the patients, parents and doctors involved. Although multiple complex treatment options are available there is little literature documenting their outcomes to assist the orthopaedic surgeon. If however, growth is balanced prior to corrective procedures being performed, then good results can be anticipated at skeletal maturity.

This article is the sole work of the Authors. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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Appendix 1
Literature review

Author	Case	growth plate involved	bone changes	deformity	treatment	outcome
Fernandez	1	bilateral PF, PT, DT		genu varum		
	2	L PF	L femoral head necrosis			
	3	bilateral DT	bilateral talar dome necrosis			
Patariquin	1	bilateral DR, DF, PT, DT		coxa vara, LLD 6cm, bilateral ankle varus	bar resections DT	not recorded
	2	bilateral PF,PT & DF	femoral head delayed ossification	coxa vara	subtrochanteric osteotomies	not recorded
	3	bilateral DF		genu varum		
	4	bilateral DF, DT		LLD 1cm & ankle varus		
Robinow	1	R PF & PH, bilateral DF & PT	hypoplasia R humeral & femoral head	varus R PH, 'bow legs', external rotation R femur		
Watson	1	R DF		varus R knee, LLD 1.5 cm	bilateral DF epiphysiodesis, DF osteotomy	normal alignment, LLD 9mm
	2	L 1st metatarsal		L cavovarus foot		
Jacobsen	1	R DF & PT		varus R knee, LLD		
	2	bilateral DR & DU		R radial head dislocation		
Barre	1	R PT, DT & bilateralDF		R ankle varus (fibula overgrowth), L genu varum 18°	R distal fibula epiphysiodesis, L DF valgus osteotomy	

Nogi	1	R PT, bilateral finger mid-phalanges, L MT				
	2	bilateral DR & DF, R MC				
	3	bilateral DR, DF & MC				

Santos	1	bilateral DF & PT	patella ossification abnormalities	bilateral genu valgum, LLD 3.5 cm	bilateral femoral varus osteotomies	genu valgus persists
	2		patella ossification abnormalities			
	3		patella ossification abnormalities			
	4	L Dfib	patella ossification abnormalities & dislocation R patella	L ankle valgus		

Grogan	1	L PT, R DF		L knee recurvatum	L knee disarticulation, osteotomy R DF, bar excision R DF	4 of 7 bar excisions successful
	2	PT		knee recurvatum	bar excision R PT, osteotomy R PT	
	3			LLD > 2.5 cm	epiphysiodesis L DF	
	4				L talocalcaneal arthrodesis	
	5	PT		knee recurvatum		
	6			LLD, valgus R knee	bar excision L PT (twice), osteotomy L PT (three times), bilateral DT & Dfib epiphysiodesis	
	7	bilateral DF & PT		valgus R knee, LLD > 2.5 cm	bar excision R DF, osteotomy R DF & L PH, epiphysiodesis L PH	
	8			valgus L knee	bar excision L DF, osteotomy L DF	
	9	PT		LLD > 2.5 cm, varus & recurvatum R knee	bar excision R DT & L DT, osteotomy L DT	

O'Sullivan	1	bilateral DT	varus R ankle		
	2	L DT	varus L ankle		

Wheeler	1	bilateral PT	bilateral genu valgum	osteotomy R PT	poor outcome

Appel		**PAPD**	**DCP**	**CPD**	**END**	**bone lesion**
	1	Y	N	N	N	LL
	2	N	N	N	N	LL
	3	Y	Y	Y	Y	LL,PR,CD
	4	Y	N	Y	N	LL, PR
	5	Y	N	N	N	LL,PR,CD
	6	N	N	N	N	LL
	7	N	N	N	Y	LL
	8	Y	Y	N	Y	LL,CD
	9	Y	N	N	Y	LL, PR
	10	Y	Y	N	N	LL,PR,CD
	11	N	N	Y	N	

		growth arrest site	deformity	treatment	outcome
Belthur	1	bilateral PT, L DF	bilateral knee varus	22 realignment without epiphysiodesis	recurrence in 15 of 22
	2	bilateral DF & PT	bilateral knee varus/recurvatum	8 realignment with epiphysiodesis	recurrence in 1 of 8
	3	DR, DT, bilateral PT	bilateral knee varus	3 physeal bar resections	failure of all 3
	4	DF, bilateral PT & DT	bilateral knee varus		
	5	PT	varus R knee		
	6	DF, PT	varus L knee, LLD		
	7	DF ,PT	varus recurvatum R knee		
	8	DF, PT	varus R knee		
	9	bilateral DF & PT	bilateral knee varus		
	10	DT	varus L ankle, LLD		
	11		equinovarus foot		
	12	PT	varus R knee		
	13	PT	varus R knee		
	14	DF	varus R knee		
	15	DF	varus R knee		
	16	DF, PT	varus/recurvatum R knee, LLD		
	17	DF, PT	varus R knee		
	18	DF, PT, bilateral DR	LLD		
	19	DT	varus L ankle		
	20	DT	varus L ankle, LLD		
	21	DT	varus L ankle		
	22	bilateral DT	bilateral ankle varus		
	23	bilateral DT	bilateral ankle varus		
	24	PT	bilateral knee varus/recurvatum		

Bache	**16 patients, individual cases not reported**		**treatment**	**outcomes**
	no. Arrests	growth arrest sites		
	1	PH	5 limb lengthenings	not mentioned
	2	DH	4 fibula epiphysiodesis	
	1	DR	4 osteotomies	
	6	DF		
	11	PT		
	15	DT		
	4	Dfib		

Buysse		**growth plate involved**	**deformity**	**treatment**
	1	R DR & DF	LLD 3.5cm	osteotomies & epiphysiodeses (no. not mentioned)
	2	R DF, PT, DT, bilateral PF	LLD 13cm, genu varum	
	3	L DF, PT, DT	LLD 3cm, genu varum	
	4	R DF, bilateral PF	LLD 5cm, R genu varum, L genu valgum	
	5	R PT, bilateral PF	LLD 3cm, genu varum	
	6	R PT	LLD, genu varum	
	7	R DT	LLD 3.5cm, L ankle varus	

Key

R	Right
L	Left
PH	proximal humerus
DH	distal humerus
DR	distal radius
DU	distal ulna
PF	proximal femur
DF	distal femur
PT	proximal tibia
DT	distal tibia
Dfib	distal fibula
LLD	leg length discrepancy
MT	metatarsals
MC	metacarpals

PAPD	peripheral asymmetric physis destruction
CPD	complete physis destruction
DCP	destruction central physis
END	epiphyseal nucleus destruction
LL	Lytic lesion
PR	Periosteal reaction
CD	Cortical destruction

Appendix 2
Patient data

Name	Age 1	Age 2	clinical	LLD	fibula overgrowth	bar (&shape)	BE	epiphysiod-esis	osteotomy	lengthening	complications/outcome
HY	2	12m	L.DT varus			DT partial		L.DFib			copes with bilat. residual ankle varus at 10yrs
			R.DT varus			DT partial		R.D.Fib			
RH	9	6m	R.PT varus	R.Tib short		PT M			R.tib valgus		
									R.Fem varus supracondylar		
			R.DT neutral			DT complete					
			L.DT varus			DT partial			L.DT valgus		ankle neutral
								L.DF (contralat.)			leg lengths equal @ 8yr F/U
LW	3	7m	R.DT varus		Y	DT complete/ epiphyseal destruction		R.Dfib	R.supramalleolar valgus		
			L.DT varus		Y	DT complete/ epiphyseal destruction		R.Dfib	R.supramalleolar valgus		
			R.DF	R.Fem 9cm		DF irreg premature				9.3cm	Equal leg lengths
			R.PT	R.Tib 1cm		PT irreg premature					
			R.DRad	R.Rad 3cm		DR complete				3.2cm	
SD	6	11m	L.DT			DT 30%PC	Y				successful excision to maturity

LN	5	24m	R.DF varus			DF 40%PM	Y-failed		R.supracondylar valgus		failed bar excision
			R.PT varus (focal)			PT (focal)			R tib corticotomy, valgus & lengthend	9cm	1cm short at maturity, normal alignment
			L.PT varus (focal)			PT (focal)			L tib barrel vault valgus		
WW	12	24m	L.DT valgus & Fib arrest	Nil	N	DT & complete Dfib			L.supramalleolar varus		coronaly aligned, soft tissue scarring causing equinus
SL	7	20m	L.PT valgus	L.Tib 5cm		PT 40%PL	Y-failed		L.PT closing wedge	waiting	failed bar excision, 5cm short at maturity: lost to follow up
RD	2	10m	L.PF			PF irreg premature			awaiting trochanteric advancement bilat. For trendelenberg gait		AVN femoral heads, coxa magna
			R.PF			PF irreg premature					
LF	5	4m	R DF varus	R.Fem 4cm		DF 20% M		R.DF	R. supracondylar valgus	40mm	
			R.PT varus & recurvatum	R.Tib 5cm		PT 20% AM	Y		R.Tibia & TSF	50mm	gained 3.2cm length in 5 years, corrected recurvatum 24deg to 0deg
			L.PT varus & recurvatum	L. Tib 5cm		PT 40% AM	Y-failed		L.Tibia & TSF	failed	L peroneal nerve palsy, lengthening and correction abandoned,L medial skin slough required SSG
			R.DT varus		Y	DT 50% C		R.DT &Fib			
			L.DT varus		Y	DT 50% C					

DA	3	8m	R.DF varus	R.Fem 1.5cm		DF 25%PM	Y				
			R.PT varus			PT 20%AM	Y				
			R.DT varus		Y	DT 30%C (tented)		R.DT &Fib	R.Wiltse valgus		
			L.DT varus (supramalleolar)	L.Tib 1cm	Y	DT 70%AM		L.DT &Fib (failed)	L.supramalleolar valgus L.Wiltse valgus		recurrence of varus, corrected successfully by Wiltse osteotomy
SJ	5	24m	L.DT varus &L.Fib partial arrest		N	DT 50%C (tented) & Dfib partial					
			R.DT varus &R.Fib partial arrest		N	DT 50%C (tented) & Dfib partial		R.DT & Fib	R.supramalleolar valgus		lateralised ankle, but well aligned
DG	10	3m	R.PT varus	R.Tib 6cm		PT 50%M		R.PT & Fib	R.barrel vault	5cm	Well aligned, continuing follow up
			R.DT varus		Y	DT 70%M		R.DT & Fib	R.Wiltse valgus		
								L.PT & Fib (contralateral)			
KW	4	6m	L.DF normal alignment(LFA 90)	L.Fem 4.5cm		DF 30%C (tented)				5cm	Successful lengthening & realignment L Fem
			L.PT varus	L.Tib 6cm		PT 30%C (tented)			awaiting osteotomy & lengthening		
			L.DT varus		Y	DT 50%C (tented)		L.DT&Fib			
			R.PT varus	R.Tib 6cm		PT 30%C (tented)		R.PT&Fib	barrel vault	6cm	Successful lengthening & realignment R tib
			R.DT varus		Y	DT 30%C (tented)		R.DT&Fib			

av. 13	av. 12.2m		tot. seg. 14	Y 9	Tot. 39	Tot. 7	tot.26	tot 20	av 5.8cm
		DT varus 14	fem 4	N 3	PF 2	success 4	DF 2	Wiltse 3	failed 1
		DT valgus 1	tib 9	Not rec 5	DF 5	failed 3	PT 3	supramalleolar 6	range 3.2-9.3cm
		DT neutral 1	rad 1		PT 11		Pfib 3	supracondylar 3	
		DT not rec 1			DT 17		DT 7	barrel vault 3	n - 9
		17			Dfib 3		Dfib 11	PT closing wedge 2	
		Dfib partial 2			DR 1			PT corticotomy TSF/rail 3	
		Dfib complete 1							
		3			F 29				
		PT varus 7			C 6				
		PT varus & recurvatum 2			IP 4				
		PT valgus 1							
		PT neutral 1							
		9			**focal**				
		DF varus3			Asymmetrical	19			
		DF neutral 2			Central	10	alignment normal	1 DF	
		5					Varus	7 DT	Fibula over growth
		PF irreg prem 2						2 PT	5 Y 2 N (asymmetrical fibula arrest)
		2							
		DR 1							
		1							
		39							

Key			
		R	Right
Age 1	age at presentation	L	Left
Age 2	age of infection	PH	proximal humerus
BE	bar excision	DH	distal humerus
Y	yes	DR	distal radius
N	no	DU	distal ulna
fem	femur	PF	proximal femur
tib	tibia	DF	distal femur
rad	radius	PT	proximal tibia
F	focal	DT	distal tibia
P	partial	Dfib	distal fibula
IP	irregular premature	LLD	leg length discrepancy
av.	average	MT	metatarsals
m	month	MC	metacarpals